ULTIBRO® BREEZHALER®: AN EVIDENCE-BASED SOLUTION FOR PATIENTS WITH COPD WITH1,2 OR WITHOUT3 A HISTORY OF EXACERBATIONS

ULTIBRO® BREEZHALER® is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD) .

*Patients had at least one moderate or severe exacerbation in the previous 12 months.

85 micrograms/43 micrograms inhalation powder, hard capsules (indacaterol/glycopyrronium) BID, twice daily; COPD, chronic obstructive pulmonary disease.

ULTIBRO® BREEZHALER® is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). Precautions:

- Patients had at least one moderate or severe exacerbation in the previous 12 months.

- Patien.tes had at least one moderate or severe exacerbation in the previous 12 months.

- Salmeterol/fluticasone 50/500 µg BID.

Turn the page in the management of COPD: For improved lung function,2,3 less breathlessness3 and superior exacerbation control* compared with Seretide® Accuhaler® – prescribe ULTIBRO® BREEZHALER® as a steroid-free alternative for patients with COPD

ULTIBRO® BREEZHALER® * PRESCRIBING INFORMATION

85 micrograms/43 micrograms inhalation powder, hard capsules (indacaterol/glycopyrronium) Refer to Ultibro® Breezhaler® Summary of Product Characteristics (SmPC) before prescribing.

- Patients had at least one moderate or severe exacerbation in the previous 12 months.

- Salmeterol/fluticasone 50/500 µg BID.

- ULTIBRO® BREEZHALER® is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). Precautions:

- Patients had at least one moderate or severe exacerbation in the previous 12 months.

- Patien.tes had at least one moderate or severe exacerbation in the previous 12 months.

- Salmeterol/fluticasone 50/500 µg BID.

Indications: Ultibro Breezhaler is indicated as a maintenance bronchodilator treatment to relieve symptoms in adult patients with chronic obstructive pulmonary disease (COPD). Presentation: Hard capsules for inhalation containing 110 micrograms indacaterol and 50 micrograms glycopyrronium, with the delivered dose equivalent to 85 micrograms of indacaterol and 43 micrograms of glycopyrronium. Dose and administration: The recommended dose is the inhalation of the content of one capsule once a day using the Ultibro Breezhaler inhaler. Ultibro Breezhaler should be administered at the same time of day each day. No dose adjustment is required for elderly patients or patients with mild to moderate renal impairment or patients with mild to moderate hepatic impairment. There is no relevant use of Ultibro Breezhaler in patients under 18 years. Ultibro Breezhaler capsules are for inhalation use only and must not be swallowed. Contraindications: Hypersensitivity to the active substance, lactose monohydrate or magnesium stearate. Precautions: Ultibro Breezhaler should not be used for the treatment of asthma. Ultibro Breezhaler is not indicated for the treatment of acute episodes of bronchospasm, i.e. as a rescue therapy. In clinical studies with Ultibro Breezhaler, paradoxical bronchospasm was not observed. However, paradoxical bronchospasm has been observed with other inhalation therapy and can be life-threatening. If this occurs, Ultibro Breezhaler should be discontinued immediately. Immediate hypersensitivity reactions have been reported after administration of Ultibro Breezhaler components. If signs supporting allergic reactions occur, in particular, angioedema, urticaria or skin rash, Ultibro Breezhaler should be discontinued immediately and alternative therapy instituted. Ultibro Breezhaler should be used with caution in patients with narrow-angle glaucoma or urinary retention. Patients should be informed about the signs and symptoms of acute narrow-angle glaucoma and should be informed to stop using Ultibro Breezhaler and contact their doctor immediately should this event occur. In patients with severe renal impairment, including those with end-stage renal disease requiring dialysis, Ultibro Breezhaler should be used only if the expected benefit outweighs the potential risk and those patients should be monitored closely for potential adverse reactions. Ultibro Breezhaler should be used with caution in patients with a history of cardiovascular disorders such as coronary artery disease, acute myocardial infarction, cardiac arrhythmias and hyperparathyroidism. Beta2-adrenergic agonists may produce a clinically significant cardiovascular effect in some patients; if such effects occur, treatment may need to be discontinued. Patients with unstable ischaemic heart disease, left ventricular failure, history of myocardial infarction, arrhythmias (excluding chronic stable atrial fibrillation), a history of long QT syndrome or whose QTc was prolonged were excluded from the clinical trials, and as there is no experience in these patient groups, Ultibro Breezhaler should be used with caution. Upon initiation of treatment plasma glucose should be monitored more closely in diabetic patients. Use with caution in patients with convulsive disorders or thyrotoxicosis. Patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine. Drug interactions: Concomitant administration of orally inhaled indacaterol and glycopyrronium, under steady-state conditions of both components, did not affect the pharmacokinetics of either component. No specific interaction studies were conducted for Ultibro Breezhaler. Information on the potential for interactions is based on the potential for each individual component. The concomitant use of Ultibro Breezhaler with beta-adrenergic blockers, anticholinergics or sympathomimetic agents is not recommended. Caution is required with the concomitant use of hypokalaemic treatment. Pregnancy and lactation: There are no data from the use of Ultibro Breezhaler in pregnant women. Indacaterol may inhibit labour due to a relaxant effect on uterine smooth muscle and therefore Ultibro Breezhaler should only be used during pregnancy if the expected benefit to the woman justifies the potential risk to the foetus. The use of Ultibro Breezhaler by breastfeeding women should only be considered if the expected benefit to the woman is greater than any possible risk to the infant. Effects on ability to drive and use machines: This medicinal product has no or negligible influence on the ability to drive and use machines. However, the occurrence of dizziness may influence the ability to drive and use machines. Undesirable effects: Very common (≥1/10); upper respiratory tract infection. Common (≥1/100 < 1/10): nasopharyngitis, urinary tract infection, sinusitis, rhinitis, dizziness, headache, cough (usually of mild intensity), oropharyngeal pain. Uncommon (≥1/1000 < 1/100): nausea, diarrhoea, skin reactions, contusions, infections, pyrexia, chest pain, upper respiratory tract infection. Rare (≥1/10000 < 1/1000): severe skin reactions (including bullous eruption), dyspepsia, dizziness, hyperglycaemia. Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis on 01276 698370.

References


Date of preparation: May 2016. UK/ULT/16-0309v.

BID, twice daily; COPD, chronic obstructive pulmonary disease.
British Thoracic Society
Winter Meeting 2016

QEI Centre
Broad Sanctuary
Westminster
London SW1P 3EE

7 to 9 December 2016
Programme and Abstracts

Approved by the Federation of the
Royal Colleges of Physicians of the UK
for 18 category 1 (external) credits
(6 credits per day).
Code: 107602
PowerPoint preview facilities will be available throughout the three days of the Meeting on the ground floor of the Centre. All presenters and chairs should report to the Speakers’ section of the Registration Desks on arrival.
The Queen Elizabeth II Centre – Ground and First Floors

Full café facilities will be open in the Pickwick on the 1st floor from 8.00am to 4.00pm on Wednesday 7 and Thursday 8 December and from 8.00am to 2.30pm on Friday 9 December. A snack bar, serving hot and cold drinks, sandwiches and confectionery only, will be open at the same times in the Whittle & Fleming on the 3rd floor.
Full café facilities will be open in the Pickwick on the 1st floor from 8.00am to 4.00pm on Wednesday 7 and Thursday 8 December and from 8.00am to 2.30pm on Friday 9 December. A snack bar, serving hot and cold drinks, sandwiches and confectionery only, will be open at the same times in the Whittle & Fleming on the 3rd floor.
Full café facilities will be open in the Pickwick on the 1st floor from 8.00am to 4.00pm on Wednesday 7 and Thursday 8 December and from 8.00am to 2.30pm on Friday 9 December. A snack bar, serving hot and cold drinks, sandwiches and confectionery only, will be open at the same times in the Whittle & Fleming on the 3rd floor.
### DAILY PROGRAMME

**WEDNESDAY 7 DECEMBER 2016**

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.00am – 9.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming/3rd</td>
</tr>
<tr>
<td>8.45am – 4.00pm</td>
<td>Poster viewing</td>
<td>P1-P15 Pleural disease assessment and outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P16-P23 Lung cancer investigations</td>
</tr>
<tr>
<td>Authors present</td>
<td></td>
<td>P24-P36 Clinical aspects of pulmonary vascular disease</td>
</tr>
<tr>
<td>10.00am – 11.00am</td>
<td></td>
<td>P37-P50 Imaginative imaging in lung disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P51-P63 Clinical studies in COPD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P64-P77 Sleep apnoea and NIV</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P78-P88 How can we improve lung cancer pathways?</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P89-P100 Cystic fibrosis</td>
</tr>
<tr>
<td>8.45am – 4.00pm</td>
<td>Moderated poster viewing</td>
<td>M1-M9 Attitudes and barriers to healthcare</td>
</tr>
<tr>
<td>8.00am – 8.30am</td>
<td>BTS Journal Club</td>
<td>Emphysema Albert/2nd</td>
</tr>
<tr>
<td>8.30am – 10.00am</td>
<td>Symposium</td>
<td>Sarcoiosis: conquering the enigma? Churchill/Ground</td>
</tr>
<tr>
<td>8.30am – 10.30am</td>
<td>Symposium</td>
<td>Evolving treatments for sleep apnoea Mountbatten/6th</td>
</tr>
<tr>
<td>8.30am – 10.30am</td>
<td>Joint BTS/BALR symposium (part 1)</td>
<td>Developing tomorrow’s respiratory medicines today Westminster/4th</td>
</tr>
<tr>
<td>8.45am – 10.15am</td>
<td>Spoken session</td>
<td>S1-S5 The difficult asthma patient Windsor/5th</td>
</tr>
<tr>
<td>8.45am – 10.15am</td>
<td>Spoken session</td>
<td>S6-S10 Lung cancer biology and mechanisms Abbey/4th</td>
</tr>
<tr>
<td>8.45am – 10.30am</td>
<td>Spoken session</td>
<td>S11-S16 Progress in the ITU St James/4th</td>
</tr>
<tr>
<td>10.00am – 11.00am</td>
<td>COFFEE/TEA</td>
<td>Understanding the clinical course of IPF Moore/4th</td>
</tr>
<tr>
<td>10.30am – 12.00pm</td>
<td>Spoken session</td>
<td>New answers to old questions: advancements in COPD Churchill/Ground</td>
</tr>
<tr>
<td>10.45am – 12.15pm</td>
<td>Symposium</td>
<td>The “big picture” – the role of national policy in achieving better lung health for future generations Mountbatten/6th</td>
</tr>
<tr>
<td>10.45am – 12.15pm</td>
<td>Spoken session</td>
<td>S22-S26 Sleep apnoea: the big sleep St James/4th</td>
</tr>
<tr>
<td>10.45am – 12.45pm</td>
<td>Symposium</td>
<td>Malignant pleural disease: genetic advances and results of RCTs in fluid management Windsor/5th</td>
</tr>
<tr>
<td>11.00am – 12.00pm</td>
<td>SAG Open meeting</td>
<td>Tuberculosis Rutherford/4th</td>
</tr>
<tr>
<td>11.00am – 1.00pm</td>
<td>Joint BTS/BALR symposium (part 2)</td>
<td>Developing tomorrow’s respiratory medicines today Westminster/4th</td>
</tr>
<tr>
<td>12.00pm – 2.00pm</td>
<td>LUNCH Cash catering only</td>
<td>Pickwick/1st and Whittle &amp; Fleming/3rd</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>SAG Open meeting</td>
<td>COPD Churchill/2nd</td>
</tr>
<tr>
<td>12.45pm – 1.30pm</td>
<td>The Snell Memorial Lecture</td>
<td>What will it take to End TB? Churchill/Ground</td>
</tr>
<tr>
<td>12.45pm – 2.15pm</td>
<td>Spoken session</td>
<td>S27-S31 Cough sensation St James/4th</td>
</tr>
<tr>
<td>12.45pm – 2.35pm</td>
<td>Poster discussion</td>
<td>P1-P15 Pleural disease assessment and outcomes Moore/4th</td>
</tr>
<tr>
<td>1.15pm – 2.15pm</td>
<td>Poster discussion</td>
<td>P16-P23 Lung cancer investigations Abbey/4th</td>
</tr>
<tr>
<td>1.15pm – 2.15pm</td>
<td>SAG Open meeting</td>
<td>Sleep Apnoea Rutherford/4th</td>
</tr>
</tbody>
</table>

**Please see page Axii for a complete list of the days and times of BTS Specialist Advisory Group Open Meetings.**

Coffee and tea is complimentary ONLY during the coffee/tea break times shown above. Outside these times, drinks may be purchased from the café in the Pickwick (1st floor), or the snack bar in the Whittle & Fleming (3rd floor).
### DAILY PROGRAMME (cont.)

**WEDNESDAY 7 DECEMBER 2016**

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
</table>
| **1.45pm – 3.15pm** | Joint BTS/BPRS symposium  
Building bridges and networks: the powers of communication and remote monitoring | Mountbatten/6<sup>th</sup> |
| **2.00pm – 3.30pm** | Moderated poster discussion  
MI-M9  
Attitudes and barriers to healthcare | Cambridge/5<sup>th</sup> |
| **2.00pm – 3.30pm** | Symposium  
T1-T6  
BTS/BALR/BLF Early Career Investigators Awards | Westminster/4<sup>th</sup> |
| **2.00pm – 3.35pm** | Poster discussion  
P24-P36  
Clinical aspects of pulmonary vascular disease | Albert/2<sup>nd</sup> |
| **2.00pm – 3.45pm** | Spoken session  
S32-S37  
Beyond FEV<sub>1</sub> in COPD | Rutherford/4<sup>th</sup> |
| **2.00pm – 3.45pm** | Poster discussion  
P37-P50  
Imaginative imaging in lung disease | Windsor/5<sup>th</sup> |
| **2.00pm – 4.00pm** | Symposium  
T1-T6  
What’s new in mycobacterial disease! | Churchill/Ground |
| **2.30pm – 4.05pm** | Poster discussion  
P51-P63  
Clinical studies in COPD | Abbey/4<sup>th</sup> |
| **2.30pm – 4.15pm** | Poster discussion  
P64-P77  
Sleep apnoea and NIV | St James/4<sup>th</sup> |
| **2.45pm – 3.45pm** | SAG Open meeting  
P78-P88  
How can we improve lung cancer pathways? | Moore/4<sup>th</sup> |
| **2.45pm – 4.10pm** | COFFEE/TEA  
Whittle & Fleming and Britten/3<sup>rd</sup> and Cambridge/5<sup>th</sup> (3.15pm – 3.30pm only) |  |
| **3.00pm – 5.00pm** | Poster discussion  
P89-P100  
Cystic fibrosis | Mountbatten/6<sup>th</sup> |
| **4.15pm – 4.40pm** | Award Presentations  
Churchill/Ground |  |
| **4.40pm – 5.30pm** | The BTS President’s Address  
“Research: why bother?” | Churchill/Ground |
| **5.30pm – 6.00pm** | BTS AGM  
BTS Annual General Meeting (BTS members only) | Churchill/Ground |

*Please see page Axii for a complete list of the days and times of BTS Specialist Advisory Group Open Meetings.*  
Coffee and tea is complimentary ONLY during the coffee/tea break times shown above. Outside these times, drinks may be purchased from the café in the Pickwick (1<sup>st</sup> floor), or the snack bar in the Whittle & Fleming (3<sup>rd</sup> floor).
### DAILY PROGRAMME

**THURSDAY 8 DECEMBER 2016**

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.00am – 9.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming/3rd</td>
</tr>
<tr>
<td>8.45am – 4.00pm</td>
<td>Poster viewing</td>
<td></td>
</tr>
<tr>
<td>Authors present</td>
<td>P101-P108 Improving lung cancer care and outcomes</td>
<td>Whittle &amp; Fleming/3rd</td>
</tr>
<tr>
<td>10.00am – 11.00am</td>
<td>P109-P119 TB: clinical aspects</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P120-P134 Clinical studies of asthma</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P135-P147 Disease progression and burden in obstructive lung disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P148-P160 Asthma treatments and what matters to patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P161-P175 Treating idiopathic pulmonary fibrosis</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P176-P186 Paediatric respiratory disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>P187-P197 From oxygen to the ITU</td>
<td></td>
</tr>
<tr>
<td>8.00am – 8.30am</td>
<td>BTS Journal Club Cough</td>
<td>Albert/2nd</td>
</tr>
<tr>
<td>8.30am – 10.00am</td>
<td>Joint BTS/BTOG symposium</td>
<td>Churchill/Ground</td>
</tr>
<tr>
<td>8.30am – 10.00am</td>
<td>Joint BTS/BPAS symposium</td>
<td>Mountbatten/6th</td>
</tr>
<tr>
<td>8.30am – 10.00am</td>
<td>Spoken session S38-S42</td>
<td>St James/4th</td>
</tr>
<tr>
<td>8.30am – 10.15am</td>
<td>Spoken session S43-S48</td>
<td>Abbey/4th</td>
</tr>
<tr>
<td>8.30am – 10.30am</td>
<td>Symposium</td>
<td>Windsor/5th</td>
</tr>
<tr>
<td>8.45am – 10.15am</td>
<td>Spoken session S49-S53</td>
<td>Moore/4th</td>
</tr>
<tr>
<td>8.45am – 10.30am</td>
<td>Spoken session SS4-SS59</td>
<td>Westminster/4th</td>
</tr>
<tr>
<td>9.00am – 10.00am</td>
<td>SAG Open meeting Interventions</td>
<td>Victoria/2nd</td>
</tr>
<tr>
<td>9.00am – 10.00am</td>
<td>SAG Open meeting Tobacco</td>
<td>Rutherford/4th</td>
</tr>
<tr>
<td>10.00am – 11.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming and Britten/3rd</td>
</tr>
<tr>
<td>10.30am – 12.00pm</td>
<td>Symposium</td>
<td>Mountbatten/6th</td>
</tr>
<tr>
<td>10.30am – 12.15pm</td>
<td>Symposium</td>
<td>Churchill/Ground</td>
</tr>
<tr>
<td>10.30am – 12.15pm</td>
<td>Spoken session S60-S65</td>
<td>St James/4th</td>
</tr>
<tr>
<td>11.00am – 12.00pm</td>
<td>Open meeting</td>
<td>Gielgud/2nd</td>
</tr>
<tr>
<td>12.00pm – 1.00pm</td>
<td>SAG Open meeting</td>
<td>Pulmonary Vascular</td>
</tr>
<tr>
<td>12.00pm – 2.00pm</td>
<td>LUNCH Cash catering only</td>
<td>Pickwick/1st and Whittle &amp; Fleming/3rd</td>
</tr>
<tr>
<td>12.15pm – 1.45pm</td>
<td>Open session</td>
<td>The UKRRC Respiratory Research Road Map Project</td>
</tr>
<tr>
<td>12.30pm – 1.15pm</td>
<td>The BTS Lecture</td>
<td>Churchill/Ground</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>SAG Open meeting</td>
<td>Nurse Advisory Group</td>
</tr>
</tbody>
</table>

Please see page Axi for a complete list of the days and times of BTS Specialist Advisory Group Open Meetings.

Coffee and tea is complimentary ONLY during the coffee/tea break times shown above. Outside these times, drinks may be purchased from the café in the Pickwick (1st floor), or the snack bar in the Whittle & Fleming (3rd floor).
### Thorax

**2016; XX (Suppl X):Ai–Alxxxiv**

Please see page Axii for a complete list of the days and times of BTS Specialist Advisory Group Open Meetings.

Coffee and tea is complimentary ONLY during the coffee/tea break times shown above. Outside these times, drinks may be purchased from the café in the Pickwick (1st floor), or the snack bar in the Whittle & Fleming (3rd floor).

---

**DAILY PROGRAMME** *(cont.)*

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.30pm – 1.30pm</td>
<td>SAG Open meeting</td>
<td>Cystic Fibrosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Albert/2nd</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>SAG Open meeting</td>
<td>Occupational and Environmental Lung Disease</td>
</tr>
<tr>
<td>1.00pm – 1.45pm</td>
<td>SAG Open meeting</td>
<td>Lung Cancer and Mesothelioma</td>
</tr>
<tr>
<td>1.45pm – 3.00pm</td>
<td>Spoken session</td>
<td>Improving outcomes during COPD hospitalisations</td>
</tr>
<tr>
<td>1.45pm – 3.15pm</td>
<td>Symposium</td>
<td>BTS Clinical Audit and Quality Improvement</td>
</tr>
<tr>
<td>1.45pm – 3.15pm</td>
<td>Symposium</td>
<td>Novel science, innovative imaging and a clinical update in pulmonary hypertension</td>
</tr>
<tr>
<td>1.45pm – 3.30pm</td>
<td>Spoken session</td>
<td>Infections and the impact on childhood respiratory disease</td>
</tr>
<tr>
<td>1.45pm – 3.30pm</td>
<td>Spoken session</td>
<td>Acute lung injury and ILD</td>
</tr>
<tr>
<td>2.00pm – 3.00pm</td>
<td>Poster discussion</td>
<td>Improving lung cancer care and outcomes</td>
</tr>
<tr>
<td>2.00pm – 3.00pm</td>
<td>Open session</td>
<td>BLF: research highlights</td>
</tr>
<tr>
<td>2.00pm – 3.25pm</td>
<td>Poster discussion</td>
<td>TB: clinical aspects</td>
</tr>
<tr>
<td>2.00pm – 3.30pm</td>
<td>Symposium</td>
<td>Highlights from Thorax</td>
</tr>
<tr>
<td>2.00pm – 3.50pm</td>
<td>Poster discussion</td>
<td>Clinical studies of asthma</td>
</tr>
<tr>
<td>3.00pm – 4.00pm</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming and Britten/3rd</td>
</tr>
<tr>
<td>3.15pm – 4.15pm</td>
<td>SAG Open meeting</td>
<td>Specialty Trainee Advisory Group</td>
</tr>
<tr>
<td>3.15pm – 4.15pm</td>
<td>Open session</td>
<td>Quality improvement and the RCP: examples from the National COPD Audit Programme and the Future Hospital’s development sites</td>
</tr>
<tr>
<td>3.30pm – 5.05pm</td>
<td>Poster discussion</td>
<td>Disease progression and burden in obstructive lung disease</td>
</tr>
<tr>
<td>3.30pm – 5.05pm</td>
<td>Poster discussion</td>
<td>Asthma treatments and what matters to patients</td>
</tr>
<tr>
<td>3.30pm – 5.20pm</td>
<td>Poster discussion</td>
<td>Treating idiopathic pulmonary fibrosis</td>
</tr>
<tr>
<td>3.30pm – 5.30pm</td>
<td>Symposium</td>
<td>New treatments for smoking cessation</td>
</tr>
<tr>
<td>3.45pm – 5.10pm</td>
<td>Poster discussion</td>
<td>Paediatric respiratory disease</td>
</tr>
<tr>
<td>3.45pm – 5.30pm</td>
<td>Spoken session</td>
<td>Pulmonary vascular disease</td>
</tr>
<tr>
<td>4.00pm – 5.00pm</td>
<td>SAG Open meeting</td>
<td>Pulmonary Rehabilitation Quality Improvement Advisory Group</td>
</tr>
<tr>
<td>4.00pm – 5.15pm</td>
<td>Spoken session</td>
<td>TB: from screening to side effects</td>
</tr>
<tr>
<td>4.00pm – 5.25pm</td>
<td>Poster discussion</td>
<td>From oxygen to the ITU</td>
</tr>
<tr>
<td>5.30pm – 7.00pm</td>
<td>The President’s Reception – All welcome!</td>
<td>Britten/3rd</td>
</tr>
</tbody>
</table>

---

_BTS Specialist Advisory Group Open Meetings_
## DAILY PROGRAMME
**FRIDAY 9 DECEMBER 2016**

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.00am – 9.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming/3rd</td>
</tr>
<tr>
<td>8.45am – 2.00pm</td>
<td>Poster viewing</td>
<td></td>
</tr>
<tr>
<td>Authors present</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10.00am – 11.00am</td>
<td>Authors present</td>
<td></td>
</tr>
<tr>
<td>8.45am – 2.30pm</td>
<td>Moderated poster viewing</td>
<td>Cambridge/5th</td>
</tr>
<tr>
<td>8.00am – 8.30am</td>
<td>BTS Journal Club</td>
<td>Albert/2nd</td>
</tr>
<tr>
<td>8.30am – 10.00am</td>
<td>Symposium</td>
<td>Mountbatten/6th</td>
</tr>
<tr>
<td>8.30am – 10.00am</td>
<td>Spoken session</td>
<td>St James/4th</td>
</tr>
<tr>
<td>8.30am – 10.00am</td>
<td>Spoken session</td>
<td>Abbey/4th</td>
</tr>
<tr>
<td>8.30am – 10.15am</td>
<td>Symposium</td>
<td>Churchill/Ground</td>
</tr>
<tr>
<td>8.30am – 10.30am</td>
<td>Symposium</td>
<td>Windsor/5th</td>
</tr>
<tr>
<td>8.45am – 10.15am</td>
<td>Spoken session</td>
<td>Moore/4th</td>
</tr>
<tr>
<td>10.00am – 11.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming and Britten/3rd</td>
</tr>
<tr>
<td>10.30am – 11.30am</td>
<td>SAG Open meeting</td>
<td>Albert/2nd</td>
</tr>
<tr>
<td>10.30am – 12.00pm</td>
<td>Spoken session</td>
<td>St James/4th</td>
</tr>
<tr>
<td>10.30am – 12.00pm</td>
<td>Spoken session</td>
<td>Westminster/4th</td>
</tr>
<tr>
<td>10.30am – 12.00pm</td>
<td>Spoken session</td>
<td>Abbey/4th</td>
</tr>
<tr>
<td>10.45am – 11.45am</td>
<td>SAG Open meeting</td>
<td>Victoria/2nd</td>
</tr>
<tr>
<td>10.45am – 12.15pm</td>
<td>Symposium</td>
<td>Churchill/Ground</td>
</tr>
<tr>
<td>10.45am – 12.20pm</td>
<td>Symposium</td>
<td>Mountbatten/6th</td>
</tr>
<tr>
<td>12.00pm – 2.00pm</td>
<td>LUNCH Cash catering only</td>
<td>Pickwick/1st and Whittle &amp; Fleming/3rd</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>SAG Open meeting</td>
<td>Victoria/2nd</td>
</tr>
<tr>
<td>12.45pm – 1.30pm</td>
<td>The Morríston Davies Lecture</td>
<td>Churchill/Ground</td>
</tr>
<tr>
<td>1.00pm – 2.00pm</td>
<td>SAG Open meeting</td>
<td>Albert/2nd</td>
</tr>
<tr>
<td>1.15pm – 3.00pm</td>
<td>Spoken session</td>
<td>Abbey/4th</td>
</tr>
</tbody>
</table>

Please see page Axii for a complete list of the days and times of BTS Specialist Advisory Group Open Meetings.

Coffee and tea is complimentary ONLY during the coffee/tea break times shown above. Outside these times, drinks may be purchased from the café in the Pickwick (1st floor), or the snack bar in the Whittle & Fleming (3rd floor).
Please see page Axii for a complete list of the days and times of BTS Specialist Advisory Group Open Meetings.

Coffee and tea is complimentary ONLY during the coffee/tea break times shown above. Outside these times, drinks may be purchased from the café in the Pickwick (1st floor), or the snack bar in the Whittle & Fleming (3rd floor).
ADDITIONAL SESSIONS

The programme will also include open meetings of the BTS Specialist Advisory Groups (SAGs). Further details may be found online in the Virtual Conference Bag.

WEDNESDAY 7 DECEMBER

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>11.00am – 12.00pm</td>
<td>Tuberculosis</td>
<td>Rutherford/4th floor</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>COPD</td>
<td>Victoria/2nd floor</td>
</tr>
<tr>
<td>1.15pm – 2.15pm</td>
<td>Sleep Apnoea</td>
<td>Rutherford/4th floor</td>
</tr>
<tr>
<td>2.45pm – 3.45pm</td>
<td>Pleural Disease</td>
<td>Victoria/2nd floor</td>
</tr>
</tbody>
</table>

THURSDAY 8 DECEMBER

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.00am – 10.00am</td>
<td>Interventional Procedures</td>
<td>Victoria/2nd floor</td>
</tr>
<tr>
<td>9.00am – 10.00am</td>
<td>Tobacco</td>
<td>Rutherford/4th floor</td>
</tr>
<tr>
<td>12.00pm – 1.00pm</td>
<td>Pulmonary Vascular</td>
<td>Rutherford/4th floor</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>Cystic Fibrosis</td>
<td>Albert/2nd floor</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>Occupational and Environmental Lung Disease</td>
<td>Victoria/2nd floor</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>Nurse Advisory Group</td>
<td>Abbey/2nd floor</td>
</tr>
<tr>
<td>1.00pm – 1.45pm</td>
<td>Lung Cancer and Mesothelioma</td>
<td>Windsor/5th floor</td>
</tr>
<tr>
<td>1.00pm – 1.45pm</td>
<td>Specialty Trainee Advisory Group</td>
<td>Victoria/2nd floor</td>
</tr>
<tr>
<td>3.15pm – 4.15pm</td>
<td>Pulmonary Rehabilitation QI Advisory Group</td>
<td>Albert/2nd floor</td>
</tr>
</tbody>
</table>

FRIDAY 9 DECEMBER

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>10.30am – 11.30am</td>
<td>Critical Care</td>
<td>Albert/2nd floor</td>
</tr>
<tr>
<td>10.45am – 11.45am</td>
<td>Asthma</td>
<td>Victoria/2nd floor</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>Lung Infection</td>
<td>Victoria/2nd floor</td>
</tr>
<tr>
<td>1.00pm – 2.00pm</td>
<td>Interstitial and Rare Lung Disease</td>
<td>Albert/2nd floor</td>
</tr>
</tbody>
</table>

BTS MEDAL AND AWARD PRESENTATIONS

Wednesday 7 December 2016 at 4.15pm in the Churchill, Ground floor

The presentations will be made for the annual BTS Medal, the BTS Award for Meritorious Service, the BTS/BALR/BLF Early Career Investigator Awards and the Medical Student Awards just before the BTS President’s Address. Please come along to this session to congratulate the winners.

THE BTS PRESIDENT’S RECEPTION

Thursday 8 December 2016, 5.30pm to 7.00pm in the Britten, 3rd floor

All participants are warmly invited to join us for this social occasion.
Designed to deliver.

- Ready in one flip of the cover
- For asthma and COPD
- Maintenance and Reliever Therapy (MART) licence in asthma

MEDICAL DESIGN EXCELLENCE AWARDS
2013 SILVER WINNER

*DuoResp Spiromax® is licensed for use in adults 18 years of age and older only.
**For 160/4.5mcg strength only.

Please refer to the Summary of Product Characteristics (SmPC) for full details of the Prescribing Information.

**DuoResp Spiromax** (budesonide/formoterol) 160/4.5mcg/4.5mcg inhalation powder is available as DuoResp Spiromax® (budesonide/formoterol) 160/4.5mcg/4.5mcg inhalation powder Additive-Free. **

Presentation: DuoResp® Spiromax® 160/4.5 Each inhalation dose contains 160mcg of budesonide and 4.5mcg of formoterol fumarate dithiane. This is equivalent to a minimum dose of 200mcg budesonide and 5mcg of formoterol fumarate dithiane. DuoResp® Spiromax® 320/9 Each inhalation dose contains 320mcg of budesonide and 9mcg of formoterol fumarate dithiane. This is equivalent to an average dose of 400mcg budesonide and 15mcg of formoterol fumarate dithiane. Inhalation powder: Indications: Asthma, Treatment of asthma, where use of a combination inhaled corticosteroid and long-acting beta2-agonist is appropriate. COPD: Symptomatic treatment of patients with severe COPD (FEV1 < 50% predicted normal) and a history of repeated exacerbations, who have symptomatic symptoms despite regular therapy with long-acting beta2-agonists. Dosage and administration: For use in adults ≥ 18 years. Not for use in children < 18 years of age. Asthma: Not intended for the maintenance management of a patient who requires rescue treatment of attacks of asthma. Treatment of patients with severe asthma that are not controlled by inhaled corticosteroids and inhaled beta2-agonists. Use in severe asthma, inhalation powder: Indications: Asthma, Treatment of asthma, where use of a combination inhaled corticosteroid and long-acting beta2-agonist is appropriate. COPD: Symptomatic treatment of patients with severe COPD (FEV1 < 50% predicted normal) and a history of repeated exacerbations, who have symptomatic symptoms despite regular therapy with long-acting beta2-agonists. Dosage and administration: For use in adults ≥ 18 years. Not for use in children < 18 years of age. Asthma: Not intended for the maintenance management of a patient who requires rescue treatment of attacks of asthma. Treatment of patients with severe asthma that are not controlled by inhaled corticosteroids and inhaled beta2-agonists. Use in severe asthma, inhalation powder:

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Teva UK Limited on 0207 540 7117 or medinfo@tevauk.com


Advert.indd 1
31/10/16 2:34 PM
FLOOR PLAN OF THE EXHIBITION STANDS

Whittle & Fleming, 3rd floor

18 Adherium Ltd
15 Airsonett AB
6 Alere
31 Ambu
36 Aquilant Endoscopy
3 AstraZeneca
1 Boehringer Ingelheim Ltd
20 Boston Scientific Corporation
30 CareFusion
16 & 23–26 Chiesi Limited
28 Pulmonx
33 & 34 Rocket Medical

27 Trudell Medical International
13 Unisoft
29 Vitalograph Ltd

Britten, 3rd floor

45 Aerogen
40 Baywater Healthcare
47 General Medicine Group
44 Novartis Pharmaceuticals UK Ltd
41 Sandoz Ltd
37 Ventmed
48 Vertex
49 Wisepress Medical Bookshop

Charity and non-commercial stands

Britten, 3rd floor

68 Action for Pulmonary Fibrosis
60 Association for Respiratory Technology and Physiology (ARTP)
63 Association of Chartered Physiotherapists in Respiratory Care (ACPRC)
64 Association of Respiratory Nurse Specialists (ARNS)
55 & 56 BMJ Group
59 British Association for Lung Research (BALR)
71 British Lung Foundation
50 & 51 British Thoracic Society
65 Education for Health
58 European Respiratory Society
38 Future Hospitals Programme, led by the RCP
38 Improving Quality in Physiological Services (IQIPS)
67 Life of Breath
66 Mesothelioma UK
39 National COPD Audit Programme, led by the RCP
39 The National Lung Cancer Audit, delivered by the RCP
70 PCD Family Support Group
62 Primary Care Respiratory Society UK
57 Public Health England
52 Respiratory Futures
61 Royal College of Speech and Language Therapists
Wednesday 7 December 2016

8.00am – 9.00am
COFFEE/TEA will be served in the Whittle & Fleming, 3rd floor

8.45am – 4.00pm
Whittle & Fleming, 3rd Floor
POSTER VIEWING
Authors present: 10.00am – 11.00am

P1-P15
Pleurale disease assessment and outcomes
Discussion of abstracts will take place from 12.45pm to 2.35pm in the Moore, 4th floor

P16-P23
Lung cancer investigations
Discussion of abstracts will take place from 1.15pm to 2.15pm in the Abbey, 4th floor

P24-P36
Clinical aspects of pulmonary vascular disease
Discussion of abstracts will take place from 2.00pm to 3.35pm in the Albert, 2nd floor

P37-P50
Imaginative imaging in lung disease
Discussion of abstracts will take place from 2.00pm to 3.45pm in the Windsor, 5th floor

P51-P63
Clinical studies in COPD
Discussion of abstracts will take place from 2.30pm to 4.05pm in the Abbey, 4th floor

P64-P77
Sleep apnoea and NIV
Discussion of abstracts will take place from 2.30pm to 4.15pm in the St James, 4th floor

P78-P88
How can we improve lung cancer pathways?
Discussion of abstracts will take place from 2.45pm to 4.10pm in the Moore, 4th floor

P89-P100
Cystic fibrosis
Discussion of abstracts will take place from 3.30pm to 5.00pm in the Mountbatten, 5th floor

SCIENTIFIC PROGRAMME

8.45am – 4.00pm
Cambridge, 5th Floor
MODERATED POSTER VIEWING
M1-M9
Attitudes and barriers to healthcare
Discussion of abstracts will take place from 1.30pm to 3.10pm in the Cambridge, 5th floor

8.00am – 8.30am
Albert, 2nd Floor
BTS JOURNAL CLUB
EMPHYSEMA
Professor Robert Stockley (Birmingham)

8.30am – 10.00am
Churchill, Ground Floor
SYMPOSIUM
SARCOIDOSIS: CONQUERING THE ENIGMA?
Chaired by: Dr Joanna Porter (London) and Dr Muhunthan Thillai (Cambridge)

8.30am
New concepts in pathogenesis of sarcoidosis
Professor David Moller (Baltimore)

9.00am
Cardiac sarcoidosis – rhythm, muscle and pulmonary vascular tone
Dr Daniel Culver (Cleveland)

9.30am
Steroids, immuno-suppressants and biologics – what, when and why?
Dr Ling-Pei Ho (Oxford)

Learning objectives
1) There have been several recent important publications in this area and this talk will provide an update on what’s “new”.
2) This is a difficult clinical area and an update is timely and warranted.
3) The management of sarcoid appears to be variable across the country. An update on expert views on best practice is, again, timely and warranted.
SCIENTIFIC PROGRAMME

8.30am – 10.30am
Mountbatten, 6th Floor

SYMPOSIUM

EVOLVING TREATMENTS FOR OBSTRUCTIVE SLEEP APNOEA
Chaired by: Dr Alison McMillan (Welwyn Garden City) and Professor John Stradling (Oxford)

8.30am  Modifying cardiovascular risk – what is the role of CPAP?
Professor Doug McEvoy (Adelaide)

9.00am  Electrical stimulation for the treatment of sleep apnoea – how and for who?
Results of the STAR and TESLA trials
Dr Joerg Steier (London)

9.30am  Effects of CPAP therapy withdrawal on exhaled breath mass spectrometry signature in OSA
Professor Malcolm Kohler (Zurich)

10.00am  Treating central sleep apnoea – when and with what? Role of CPAP, NIV, ASV, alternatives
Professor Anita Simonds (London)

Learning objectives

1) To update the audience about latest data for using CPAP for cardiovascular risk modification in people with OSA with minimal symptoms, so that they can make informed evidence based decisions in the sleep clinic.
2) To highlight the research thus far looking at alternative strategies for controlling OSA, namely hypoglossal nerve stimulation, and discuss whether these have a role yet in clinical practice.
3) To discuss the science behind exhaled breath molecular signatures and potential as a diagnostic tool in obstructive sleep apnoea.
4) To discuss central sleep apnoea, which is seen often in the sleep or cardiac clinic, and how this is best managed.

Wednesday 7 December 2016

8.30am  Drugging the cancer genome and the cancer state
Professor Paul Workman (London)

9.10am  Next generation antivirals to target lung infection
Dr Ken Powell (ReViral)

9.50am  Utilising biologics in the treatment of pulmonary fibrosis
Dr Lynne Murray (MedImmune)

Learning objectives

1) The symposium will open with an overview of new approaches to treating chronic lung disease.
2) The session will continue by discussing recent approaches to developing new antiviral drugs with particular emphasis on the development of anti-RSV therapies.
3) Finally to be discussed will be the role biologics can play in the treatment of idiopathic pulmonary fibrosis, a disease that currently has extremely limited treatment options. The presentation will particularly focus on targeting the αvβ6 integrin with a monoclonal antibody (STX-100) which is currently in Phase IIa clinical trials and showing promise as a new treatment for IPF.

8.45am – 10.15am
Windsor, 5th Floor

SPOKEN SESSION: S1 – S5

The difficult asthma patient
Chaired by: Professor Liam Heaney (Belfast) and Dr Andrew Menzies-Gow (London)

8.50am  S1
Biomarkers in adult asthma: a systematic review of 8-isoprostane in exhaled breath condensate
AM Peel, CJ Crossman-Barnes, J Tang, SJ Fowler, GA Davies, AM Wilson, YK Loke

9.05am  S2
Fractional exhaled nitric oxide (FeNO) suppression to identify non-adherence in difficult asthma
KJ Hetherington, RW Costello, LG Heaney

9.20am  S3
The UK’s largest severe asthma multidisciplinary team meeting; experience from the first 18 months
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.35am</td>
<td>S4</td>
<td>Implications of guidance in Scotland on eligibility for treatment with Mepolizumab and Omalizumab – an IDEAL study analysis</td>
<td>CEA Hartmann, C Gait, NB Gunsoy, RA Mehta, FC Albers</td>
</tr>
<tr>
<td>9.50am</td>
<td>S5</td>
<td>Vitamin D for the management of asthma: Cochrane systematic review and meta-analysis</td>
<td>AR Martineau, CJ Cates, M Urashima, M Jensen, AP Griffiths, U Nurmatov, A Sheikh, CJ Griffiths</td>
</tr>
</tbody>
</table>

**8.45am – 10.30am**

St James, 4th Floor

**SPOKEN SESSION: S11 – S16**

**Progress in the ITU**

*Chaired by: Dr Catherine Snelson (Birmingham)*

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.50am</td>
<td>S11</td>
<td>Decreased anti-inflammatory potential of mesenchymal stem cells after prolonged in vitro expansion will impact on their use as a therapy for acute respiratory distress syndrome</td>
<td>M Aslani, RY Mahida, A Scott, DR Thickett</td>
</tr>
<tr>
<td>9.05am</td>
<td>S12*</td>
<td>Plasma syndecan-1 level as a predictive marker of vasoplegia associated with surgery requiring cardiopulmonary bypass and possible involvement of oxidative stress</td>
<td>MG Rasiah, C Michaeloudes, T Svermova, Z Nikolakopoulou, B Creagh-Brown, PK Bhavsar, A Burke-Gaffney</td>
</tr>
<tr>
<td>9.20am</td>
<td>S13*</td>
<td>Pharmacokinetics and pharmacodynamics of antimicrobials in critically ill patients with lower respiratory tract infections. Are 'one size fits all' doses appropriate?</td>
<td></td>
</tr>
</tbody>
</table>
SCIENTIFIC PROGRAMME

IB Oldfield, K Kipper, CI Barker, BJ Philips, M Cecconi, A Rhodes, A Johnston, JF Standing, EH Baker, M Sharland, DO Lonsdale

9.35am S14
Patients’ perceptions of an exercise programme delivered following discharge from hospital after critical illness (the REVIVE trial)
K McDowell, JM Bradley, DF McAuley, B Blackwood, B O’Neill

9.50am S15
Changes in peri-operative ARDS with time: a comparison of two trials
PA Howells, KA Aldridge, RCA Dancer, O Tucker, DR Thickett

10.05am S16
Simvastatin improves neutrophil migration in elderly patients with septic pneumonia and reduces 6-month mortality and re-admissions: results of the SNOOPI Trial
J Patel, H Greenwood, S Lugg, P Howells, F Gao, E Sapey, D Thickett

*S12 and S13 – BTS Medical Student Awards
Highly Commended

10.00am – 11.00am
COFFEE/TEA will be served in the Whittle & Fleming and Britten, 3rd floor

10.30am – 12.00pm
Moore, 4th Floor
SPOKEN SESSION: S17 – S21
Understanding the clinical course of idiopathic pulmonary fibrosis
Chaired by: Dr Vidy Navaratnam (Nottingham) and Dr Helen Parfrey (Cambridge)

10.35am S17
The burden of idiopathic pulmonary fibrosis in the United Kingdom: a retrospective, matched cohort study
M Storm, I Tran, H Strongman, J Fredriksson, T Maher

10.50am S18
A working definition and natural history of ‘minimal’ ILD
R Ross Browne, A Mathur, A Marshal, PA McFarlane, GA Stewart, J Sharkey, G Ritchie, M Jones, JT Murchison, N Hirani

11.05am S19
The impact of clotting abnormalities on the natural history of idiopathic pulmonary fibrosis: an extended follow up of a population based cohort
V Navaratnam, AW Fogarty, T McKeever, N Thompson, G Jenkins, SR Johnson, M Kumaran, K Pointon, RB Hubbard

11.20am S20
KBILD scores have similar power to predict survival as pulmonary physiology in interstitial lung disease
C Sharp, C Baggott, SS Birring, HI Adamali

11.35am S21
Identification of clinical prognostic parameters in patients with idiopathic pulmonary fibrosis
K Rogers, C Hadinnapola, K Sylvester, M Toshner, H Parfrey

10.30am – 12.30pm
Churchill, Ground Floor
SYMPOSIUM
NEW ANSWERS TO OLD QUESTIONS: ADVANCEMENTS IN COPD
Chaired by: Dr Elizabeth Sapey (Birmingham) and Professor Tom Wilkinson (Southampton)

10.30am “But I didn’t smoke that much, doctor”. The influence of genetics on lung function in COPD
Dr Louise Wain (Leicester)

11.00am “Can you grow me some new lungs, doctor?” Lung tissue bio-engineering for COPD
Professor Daniel Weiss (Vermont)

11.30am “Why will exercise help my lung disease?” Training the mitochondria in COPD
Professor Michael Steiner (Leicester)
**Wednesday 7 December 2016**

12.00pm  “Isn’t there anything else you can give me?” New therapeutic strategies in COPD
Professor Wisia Wedzicha (London)

Learning objectives
1) Dr Wain will open the symposium with an overview of the genetic basis of airflow obstruction and smoking behaviour in the pathophysiology of COPD, to provide insights into why some people are more susceptible to lung damage than others.
2) Professor Weiss will present aspects of his innovative research in tissue regeneration that aims to overcome the need for lung transplantation from human donors.
3) Professor Steiner will present new data on the links between skeletal muscle function, symptoms and exercise therapy.
4) Professor Wedzicha will end this session with an assessment of new medical therapies and therapeutic approaches that might help patients with COPD.

10.45am – 12.15pm
Mountbatten, 6th Floor
SYMPOSIUM
THE “BIG PICTURE” – THE ROLE OF NATIONAL POLICY IN ACHIEVING BETTER LUNG HEALTH FOR FUTURE GENERATIONS
Keynote speakers will explore the current NHS national policy agenda and identify the barriers and opportunities for developing future “big picture” policies that could improve the lung health of future generations.

10.45am – 12.15pm
St James, 4th Floor
SPOKEN SESSION: S22 – S26
Sleep apnoea: the big sleep
Chaired by: Dr Sonya Craig (Liverpool) and Dr Sophie West (Newcastle)

10.50am  S22
Severity of sleep disordered breathing independently predicts metabolic dysfunction in a large population of severely obese subjects: the ESADA study
BD Kent, N Gildeh, P Drakatos, L Grote, J Hedner, WT McNicholas

**SCIENTIFIC PROGRAMME**

11.05am  S23
Neural respiratory drive during sleep at high altitude
J Steier, N Cade, B Walker, J Moxham, CJ Jolley

11.20am  S24
A comparison of pulse transit time between subjects with obstructive sleep apnoea syndrome, nocturnal inspiratory flow limitation and the absence of significant sleep disordered breathing
B Chakrabarti, S Emegbo, S Craig, N Duffy, JF O’Reilly

11.35am  S25
Survey of the new Driver and Vehicle Licensing Authority (DVLA) guidance for obstructive sleep apnoea (OSA): UK sleep centres opinion
EL Palmer, S West

11.50am  S26
Feasibility and patient tolerability of transcutaneous electrical stimulation in obstructive sleep apnoea
KI Reed, MF Pengo, S Xiao, C Ratneswaran, N Shah, T Chen, A Douiri, N Hart, Y Luo, GF Rafferty, GP Rossi, A Williams, MI Polkey, J Moxham, J Steier

10.45am – 12.45pm
Windsor, 5th Floor
SYMPOSIUM
MALIGNANT PLEURAL DISEASE: GENETIC ADVANCES AND THE RESULTS OF RCT’S IN PLEURAL FLUID MANAGEMENT
Chaired by: Dr Rahul Bhatnagar (Bristol) and Dr Lesley Bishop (Portsmouth)

10.45am  Basic genomics of pleural malignancy
Dr Peter Campbell (Cambridge)
## SCIENTIFIC PROGRAMME

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 11.00am  | More than just an indwelling pleural catheter – results of SEAL-MPE trial and IPC-Plus trial update  
Professor Nick Maskell (Bristol) |
| 11.35am  | One, two, three – lessons from the TIME trials                                              
Professor Najib Rahman (Oxford) |
| 12.00pm  | An upside down view of the future of pleural medicine and results from recent Australian pleural RCT’s  
Professor Gary Lee (Perth) |

**Learning objectives**

1) The audience will learn about the latest advances in the genetics and genomics of pleural malignancy, which might identify future novel treatment targets.
2 & 3) The results of several multi-centre RCT’s of optimal fluid management strategies in MPE will be presented. These results will inform the audience of the current guidelines and suggest possible future patient pathways.
4) Anticipated future advances in pleural medicine will be discussed.

**Target audience**

1) This symposium will be of interest to all health care professionals involved in the management and support of patients with malignant pleural disease.
2) It will also be of interest to consultants, SpR’s and specialist nurses and research nurses involved in the running of pleural services.

### Wednesday 7 December 2016

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 11.40am  | Targeting respiratory disease with novel anti-microbials                                   
Dr Rebecca Ingram (Belfast) |
| 12.20pm  | Targeting Ras mutations in lung cancer                                                    
Professor Julian Downward (London) |

**Learning objectives**

1) The first presentation will give an extensive outline of identifying and using biomarkers to target novel asthma therapies to specific subsets of severe asthma patients.
2) We will then discuss how bacterial infections may be targeted and also how novel models of bacterial infection can be utilised to increase success in the development of novel antimicrobial therapies.
3) Finally, we will discuss research investigating the functional consequences of Ras mutations and how this may be translated into the development of new drugs for the treatment of lung cancer.

**LUNCH** will be available to purchase in the café in the Pickwick, 1st floor, and the snack bar in the Whittle & Fleming, 3rd floor.

### COPD

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
</table>
| 11.00am  | Using biomarkers to target novel molecular therapies in asthma                            
Dr Joseph Arron (Genentech) |

---

*Thorax 2016;XX(Suppl X):Ai–Alxxiv* Axix
**Wednesday 7 December 2016**

**12.50pm**  **S27**
The effect of P2X3 antagonism (AF-219) on experimentally evoked cough in healthy volunteers and chronic cough patients  
JA Smith, M Kitt, P Butera, A Ford

**1.05pm**  **S28**
Determinants of cough frequency in adult healthy volunteers  
K Holt, C Gibbard, JA Smith

**1.20pm**  **S29**
A randomised controlled trial of over the counter medicine CS1002 for acute cough  
SS Birring, J Brew, T Kilbourn, AH Morice

**1.35pm**  **S30**
Sensations associated with experimentally evoked cough: a comparison of chronic cough patients with healthy controls  
J Mitchell, B Al-Sheklly, B Issa, T Collier, D Corfield, JA Smith

**1.50pm**  **S31**
Reproducibility of four challenge modalities for chronic cough  
L Douglas, H Fowles, K Arnell, S Thackray-Nocera, A Morice

**12.45pm – 2.35pm**
Moor, 4th Floor

**POSTER DISCUSSION: P1 – P15**

**Pleural disease assessment and outcomes**
*Chairled by: Professor Nick Maskell (Bristol) and Dr David Meek (Cambridge)*

**P1** Pleural effusion size estimation: US, CXR or CT?  
C Brockelsby, M Ahmed, M Gautam

**P2** Incorporation of an in-depth thoracic ultrasound assessment into routine pre-procedural evaluation of patients with pleural effusions  
JP Corcoran, A Talwar, RJ Hallifex, I Psallidas, JM Wrightson, NM Rahman

**SCIENTIFIC PROGRAMME**

**P3** Thoracic ultrasound experiences amongst respiratory trainees – a national survey  
P Sivakumar, M Kamalanathan, A Collett, L Ahmed

**P4** A prospective assessment of the clinical utility of intercostal artery identification in pleural intervention  
A Talwar, JP Corcoran, RJ Hallifex, J Wrightson, I Psallidas, NM Rahman

**P5** Bloody effusions: do the patient’s clotting results or antithrombotic medications matter?  
L Brockbank, R Pinto, M Gautam

**P6** Significance of minimal pleural effusion in non-small cell lung cancer  
GA Martin, S Tsim, J MacLay, C Stewart, KG Blyth

**P7** Clinicians’ perspectives of health related quality of life and priorities in deciding management for malignant pleural effusion  
P Sivakumar, D Curley, NM Rahman, YCG Lee, D Feller-Kopman, A West, L Ahmed

**P8** Negative pleural biopsies – do we need early follow up and imaging?  
S Leyakathali Khan, B Ganaie, M Haris, M Munavvar

**P9** The utility of p16 FISH in differentiating malignant mesothelioma and benign mesothelial proliferations  
A Chaturvedi, J Holme, R Shah, P Taylor, M Evison

**P10** Light may be used to differentiate mesothelioma from benign pleural disease at the bedside  
NK Oswald, A Robertson, P Rajesh, R Steyn, E Bishay, M Kalkat, B Naidu

**P11** Utility of a novel prognostic tool in unselected patients with malignant pleural mesothelioma  
R Wollerton, J Goodliffe, M Slade

**P12** Exploring the characteristics of patients with mesothelioma who decline chemotherapy: a prospective cohort of 200 patients  
The rationale for setting up a dedicated pleural procedure list: benefits for patients and trusts
C Brockelsby, A Wells, P Deegan, W Kent, C Houghton, M Gautam

Examining the outcomes of a pleural disease clinic
DT Whitehall, JB McCafferty

A pilot study of a dedicated ballooned intercostal drain
S Ross, H Ali, L Allsop, NJ Ali, SV Kemp

Radial EBUS biopsy with guide sheath for peripheral pulmonary lesions
K Srikanthan, C Drouot, B Sukumaran, V Johnson, M Walshaw, K Mohan

A retrospective analysis comparing the use of ProCore with standard fine needle aspiration in endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA)
DJ McCracken, TE McManus, A Shamboul

Do bronchial washings improve diagnostic yield in patients undergoing EBUS-TBNA
K Srikanthan, C Drouot, C Smyth, T Giles, M Walshaw, K Mohan

Central airway obstruction in bronchogenic carcinoma
M Hindle, A Sibly, MG Aldik, A Marchbank, C Daneshvar

Haemoptysis in patients with no evidence of lung malignancy on computed tomography – is flexible bronchoscopy necessary?
T Nisar, R Hastings, P Puthran

Pulmonary nodules: assessing the repeatability of imaging biomarkers of malignancy
A Talwar, JMY Willaime, LC Pickup, M Enescu, D Boukerroui, W Hickes, MJ Gooding, NM Rahman, T Kadir, FV Gleeson

Application of the recent BTS guidelines to a population of nodule patients
AJ Morgan, D Rosewarne, A Bapusamy, K Tanner, J Hancock, D Reid, S Mathews

A review of advice given for follow up of lung nodules detected on CT imaging
H Rostom, R Mogal, S Iyengar

Lung cancer investigations
Chaired by: Dr Sadia Anwar (Nottingham) and Dr Mark Slade (Gloucester)

Radial EBUS biopsy with guide sheath for peripheral pulmonary lesions
K Srikanthan, C Drouot, B Sukumaran, V Johnson, M Walshaw, K Mohan

A retrospective analysis comparing the use of ProCore with standard fine needle aspiration in endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA)
DJ McCracken, TE McManus, A Shamboul

Do bronchial washings improve diagnostic yield in patients undergoing EBUS-TBNA
K Srikanthan, C Drouot, C Smyth, T Giles, M Walshaw, K Mohan

Central airway obstruction in bronchogenic carcinoma
M Hindle, A Sibly, MG Aldik, A Marchbank, C Daneshvar

Haemoptysis in patients with no evidence of lung malignancy on computed tomography – is flexible bronchoscopy necessary?
T Nisar, R Hastings, P Puthran

Pulmonary nodules: assessing the repeatability of imaging biomarkers of malignancy
A Talwar, JMY Willaime, LC Pickup, M Enescu, D Boukerroui, W Hickes, MJ Gooding, NM Rahman, T Kadir, FV Gleeson

Application of the recent BTS guidelines to a population of nodule patients
AJ Morgan, D Rosewarne, A Bapusamy, K Tanner, J Hancock, D Reid, S Mathews

A review of advice given for follow up of lung nodules detected on CT imaging
H Rostom, R Mogal, S Iyengar

Radial EBUS biopsy with guide sheath for peripheral pulmonary lesions
K Srikanthan, C Drouot, B Sukumaran, V Johnson, M Walshaw, K Mohan

A retrospective analysis comparing the use of ProCore with standard fine needle aspiration in endobronchial ultrasound guided transbronchial needle aspiration (EBUS-TBNA)
DJ McCracken, TE McManus, A Shamboul

Do bronchial washings improve diagnostic yield in patients undergoing EBUS-TBNA
K Srikanthan, C Drouot, C Smyth, T Giles, M Walshaw, K Mohan

Central airway obstruction in bronchogenic carcinoma
M Hindle, A Sibly, MG Aldik, A Marchbank, C Daneshvar

Haemoptysis in patients with no evidence of lung malignancy on computed tomography – is flexible bronchoscopy necessary?
T Nisar, R Hastings, P Puthran

Pulmonary nodules: assessing the repeatability of imaging biomarkers of malignancy
A Talwar, JMY Willaime, LC Pickup, M Enescu, D Boukerroui, W Hickes, MJ Gooding, NM Rahman, T Kadir, FV Gleeson

Application of the recent BTS guidelines to a population of nodule patients
AJ Morgan, D Rosewarne, A Bapusamy, K Tanner, J Hancock, D Reid, S Mathews

A review of advice given for follow up of lung nodules detected on CT imaging
H Rostom, R Mogal, S Iyengar
### Wednesday 7 December 2016

<table>
<thead>
<tr>
<th>M1</th>
<th>Development of a ‘stop-go’ screening tool for streamlining assessment of common co-morbidities in COPD patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>SL Kennie, HK Lamplough, EH Baker, S McIvor</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M2</th>
<th>Do patients and informal carers agree on symptom burden in advanced COPD?</th>
</tr>
</thead>
<tbody>
<tr>
<td>EZ Mi, EZ Mi, S Mendonca, AC Gardener, MC Farquhar</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M3</th>
<th>Attitudes and barriers to responsible emergency oxygen prescribing among healthcare professionals</th>
</tr>
</thead>
<tbody>
<tr>
<td>T Sanctuary, M Johnson, V Lord, I Patel</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M4</th>
<th>Late asthmatic response to epoxy resins: a case report</th>
</tr>
</thead>
<tbody>
<tr>
<td>E Solano, B Fitzgerald, J Cannon, P Cullinan, J Feary</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M5</th>
<th>The correlation between satisfaction with information about medicines and clinical outcomes in an ethnically diverse difficult asthma cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>H Dhruve, H Khachi</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M6</th>
<th>Improving follow-up in patients attending and discharged from accident and emergency with asthma exacerbations</th>
</tr>
</thead>
<tbody>
<tr>
<td>WJ Newman, O Lamont</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M7</th>
<th>Designing around placebo inhaler device concerns and improving asthma healthcare professional patient training</th>
</tr>
</thead>
<tbody>
<tr>
<td>MJ Sanders, R Bruin</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M8</th>
<th>Asthma management in an inner-city teaching hospital emergency department: real-life after National Review of Asthma Deaths (NRAD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FR Ali, Z Mangera, A Downes, S Obaray</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M9</th>
<th>A high prevalence of obstructive sleep apnoea (OSA) in the severe/difficult to treat asthma (SDTA) population</th>
</tr>
</thead>
<tbody>
<tr>
<td>SE Davies, N Cachada, A Turner, S Wharton, A Mansur</td>
<td></td>
</tr>
</tbody>
</table>

### SCIENTIFIC PROGRAMME

#### 2.00pm – 3.30pm
Westminster, 4th Floor

#### PRIZE SYMPOSIUM: T1 – T6

**BTS/BALR/BLF EARLY CAREER INVESTIGATOR AWARDS**

*Chairered by: Professor Nicholas Hart (London) and Professor Sam Janes (London)*

*Judged by: Dr James Chalmers (Dundee), Professor Louise Donnelly (London) and Professor Gisli Jenkins (Nottingham)*

<table>
<thead>
<tr>
<th>T1</th>
<th>Calcineurin inhibition impairs the dendritic cell transcriptional response to Aspergillus fumigatus infection in lung transplant recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Adlakha, DAJ Armstrong-James, B Lenhard</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T2</th>
<th>Early-life respiratory tract infection and adult susceptibility to chronic mucus hypersecretion – a prospective 64 year national birth cohort study</th>
</tr>
</thead>
<tbody>
<tr>
<td>JP Allinson, R Hardy, GC Donaldson, SO Shaheen, D Kuh, JA Wedzicha</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T3</th>
<th>Human rhinovirus impairs the innate immune response to bacteria in monocyte derived macrophages from patients with chronic obstructive pulmonary disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>LJ Finney, KBR Belchamber, P Mallia, SL Johnston, LE Donnelly, JA Wedzicha</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T4</th>
<th>Global spread of Mycobacterium abscessus clones amongst cystic fibrosis patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM Grogono, JM Bryant, D Rodriguez-Rincon, I Everall, KP Brown, P Moreno, D Verma, E Hill, J Drijkoningen, CS Haworth, SR Harris, D Ordway, J Parkhill, RA Floto</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>T5</th>
<th>Towards human lung regeneration in end-stage respiratory failure: genetically-modifiable 3D organoid culture of human embryonic lung stem cells enables for the first time the study of human lung development in vitro</th>
</tr>
</thead>
<tbody>
<tr>
<td>MZ Nikolic, JA Johnson, D Sun, O Carigt, U Laresgoiti, J Brady, G Allen, A Giangreco, EL Rawlins</td>
<td></td>
</tr>
</tbody>
</table>
T6 Randomised sham-controlled trial of transcutaneous electrical stimulation in obstructive sleep apnoea
MP Pengo, XS Sichang, CR Ratneswaran, NS Shah, KR Reed, TC Chen, AD Douiri, NH Hart, YL Luo, GR Rafferty, GPR Rossi, AW Williams, MIP Polkey, JM Moxham, JS Steier

2.00pm – 3.35pm
Albert, 2nd Floor
POSTER DISCUSSION: P24 – P36
Clinical aspects of pulmonary vascular disease
Chaired by: Professor David Kiely (Sheffield) and Dr Mark Toshner (Papworth)

P24 Short term outcome of patients with acute pulmonary embolism and high lactate at a district general hospital
JB Adizie, ZD Momoh, B Soliman, A Macduff

P25 Retrospective analysis of patients presenting with acute pulmonary embolism (PE) as the first manifestation of malignancy
A Murchison, A Asher, A Van Manen, H Ellis

P26 CT abdomen and pelvis for unprovoked pulmonary embolism – what is the best practice?
R Wahida, S Ahmad, B Saunders, N How, M Anwar

P27 Evaluation and baseline characteristics of patients with chronic thromboembolic disease in a single referral centre
EM Swietlik, D Taboada, A Ruggiero, E Bales, L Harlow, A Fletcher, JE Cannon, K Sheares, DP Jenkins, J Pepke-Zaba, M Toshner

P28 Chronic thromboembolic pulmonary hypertension: long term outcomes in surgical and non-surgical patients
SR Quadery, RA Condliffe, C Billings, R Thompson, CA Elliot, A Charalampopoulous, J Hurdman, N Hamilton, I Armstrong, P Sephton, I Sabroe, A Swift, J Wild, DG Kiely

P29 Exercise intolerance in chronic thromboembolic disease: evaluation, underlying mechanisms and clinical implications

Wednesday 7 December 2016

EM Swietlik, D Taboada, A Ruggiero, E Bales, L Harlow, A Fletcher, JE Cannon, K Sheares, DP Jenkins, J Pepke-Zaba, T Toshner

P30 An evaluation of the use of quality-of-life (QOL) scores in pulmonary arterial hypertension
SC Woolcock, PA Corris

P31 PHA-UK living with pulmonary hypertension 2016 survey
I Armstrong, CG Billings, C Harries, J Yorke

P32 A new nurse led PE clinic 2015
S Goodman

P33 Patients with pulmonary arteriovenous malformations and hereditary haemorrhagic telangiectasia report forced expiratory manoeuvres during pulmonary function tests provoke nosebleeds and migraines
HC Tighe, H McKernan, JT Springett, LBabawale, J Perks, T Patel, CL Shovlin

P34 Long term outcomes for patients with pulmonary arteriovenous malformations considered for lung transplantation
CL Shovlin, JMB Hughes, M Layton, E Boothe, DJ Allison, JE Jackson

P35 A retrospective observational study designed to characterise individuals with pulmonary arteriovenous malformations (PAVMs) and cerebral abscesses at a single institution
EJ Boothen, S Brownlow, JE Jackson, CL Shovlin

P36 Injections of intravenous contrast for computerized tomography scans precipitate migraines in hereditary haemorrhagic telangiectasia subjects at risk of paradoxical emboli: implications for right-to-left shunt risks
T Patel, AEphick, JE Jackson, CL Shovlin

2.00pm – 3.45pm
Rutherford, 4th Floor
SPOKEN SESSION: S32 – S37
Beyond FEV₁ in COPD
Chaired by: Dr Charlotte Bolton (Nottingham) and Professor Robert Stockley (Birmingham)
### Epidemiology of chronic obstructive pulmonary disease (COPD) in the UK: findings from the British Lung Foundation’s ‘Respiratory Health of the Nation’ project

N Snell, D Strachan, R Hubbard, J Gibson, K Gruffydd-Jones, I Jarrold

### Physical activity intervention versus pulmonary rehabilitation in COPD: the LIVELY COPD Project


### Effect of 8 and 12 weeks’ once-daily tiotropium and olodaterol, alone and combined with exercise training, on exercise endurance during walking in patients with COPD

T Troosters, J Bourbeau, F Maltais, N Leidy, D Erzen, D De Sousa, L Korducki, KL Lavoie, W Janssens, A Hamilton

### Efficacy and safety of the direct switch from various previous treatments to glycopyrronium or indacaterol/glycopyrronium in patients with moderate COPD: the CRYSTAL study

C Vogelmeier, M Aalamian-Mattheis, T Greulich, JM Marin, W Castellani, T Similowski, V Ninane, M Gaga, S Lane, X Nunez, F Patalano, A Clemens, K Kostikas

### Coil treatment for patients with severe emphysema and bilaterally incomplete fissures; effectiveness and complications after one-year follow-up. A single-centre experience

K Kontogianni, V Gerovasili, D Gompelmann, M Schuhmann, CP Heussel, FJF Herth, R Eberhardt

### The persistence of eosinophilic inflammation in COPD over time – AERIS cohort

VL Kim, NP Williams, KK Ostridge, MM Naghibi, NA Coombs, JM Devaster, E Aris, SC Clarke, AC Tuck, SA Wootton, SC Bourne, KJ Staples, TM Wilkinson

### Preliminary normal values for structured light plethysmography tidal breathing parameters and age and gender differences

S Fakhr, L O’Reilly, R Wilson, B Cooper, R Iles

### Repeatability of structured light plethysmography (SLP) for measurement of respiratory rate in normal subjects

R Iles, W De Boer, A Khalid, S Motamedi Fakhr, R Wilson

### CTAS – a CT score to quantify disease activity in pulmonary sarcoidosis

YK Kendrick, E Repapi, E Helm, SL Cole, R Hoyles, R Benamore, LP Ho

### Development of 18F and 68Ga-labelled cyclic peptides for positron emission tomography imaging of αvβ6 in idiopathic pulmonary fibrosis

JA Thompson, J Domarkas, C Cawthorne, SJ Archibald, S Hart

### Increased FDG uptake in areas of ‘normal’ lung in idiopathic pulmonary fibrosis

SA Aliyu, G Avery, AH Morice, SP Hart, MG Crooks
### SCIENTIFIC PROGRAMME

**P43** Hyperpolarised Xenon-129 MRI of lungs in healthy volunteers: a safety and feasibility study  
S Safavi, J Thorpe, B Haywood, M Barlow, IP Hall

**P44** Comparison of structural brain abnormalities and cognitive function in COPD patients after hospitalisation, stable COPD patients and healthy age-matched controls  
MK Bajaj, CA Spilling, JW Dodd, PW Jones, FA Howe, EH Baker, TR Barrick

**P45** Non-invasive methods for the estimation of mPAP in COPD patients using cardiac MRI  
CS Johns, D Capener, C Hammerton, K Shotton, DG Kiely, JM Wild, AJ Swift

**P46** Assessment of aortic stiffness and correlation with lung function in patients with COPD using cardiac magnetic resonance  
E De Garate, G Biglino, A Wilson, E Baker, P Jones, C Bucciarelli-Ducci, J Dodd

**P47** The influence of muscle mass in the assessment of lower limb strength in COPD  
R Trethewey, D Esliger, E Petherick, R Evans, N Greening, B James, A Kingsnorth, M Morgan, M Orme, S Singh, L Sherrar, N Tom, M Steiner

**P48** Research BAL using single use disposable bronchoscope  
SZ Zaidi, AC Collins, KD Davies, AW Wright, AG Ganguli, EM Mitsi, JR Reine, JO Owugha, SG Gordon, DF Ferreira, JR Rylance

**P49** Does Valsalva manoeuvre reduce the risk of complications in CT-guided lung biopsies?  
AE Syed, I Syed, R Ahmed, O Parvu, L Panceone, A Alvi, K Novacic, R Akram

**P50** Changing use of CT pulmonary angiography in a UK tertiary hospital over a 6-year period  
R Ratnakumar, JP Corcoran, A Talwar, RJ Hallifax, I Psallidas, JM Wrightson, FV Gleeson, NM Rahman

---

### Wednesday 7 December 2016

**2.00pm** What is “new” in the new NTM guidelines?  
Dr Charles Haworth (Cambridge)

**2.30pm** What is needed in NTM and what happens next?  
Professor Jakko van Ingen (Nijmegen)

**3.00pm** Novel diagnostics in TB – who, where and when?  
Dr Catharina Boehme (FIND)

**3.30pm** MDR-TB treatment – no longer a neglected question  
Professor Andrew Nunn (London)

**Learning objectives**

1) Review the new changes proposed within the imminent NTM guidelines produced by the BTS.

2) Explore the current challenges in the treatment of NTM and of drug-resistant MDR-TB and emerging strategies to overcome these problems.

3) Discuss novel diagnostic strategies relevant to mycobacterial disease and how they can be applied in current and future practice.

4) Describe the current complex drug regimens and monitoring required to treat MDR and XDR TB.

---

**2.30pm – 4.05pm**

**Abbey, 4th Floor**

**POSTER DISCUSSION: P51 – P63**

**Clinical studies in COPD**

**Chaired by: Dr Gillian Lowrey (Derby) and Professor Dave Singh (Manchester)**

**P51** Clinical effectiveness of procalcitonin based protocols to guide the administration of antibiotics in patients presenting with COPD exacerbations: systematic review and meta-analysis  
AG Mathioudakis, V Chatzimavridou-Grigoriadou, A Corlateanu, J Vestbo

**P52** COPD and periodontitis: co-morbidity yes or no?  
S Hobbins, A Usher, S Parmar, R Stockley

**P53** Predicting poor outcomes in COPD patients deemed ‘low risk’ by DOSE score  
LA Rigge, NA Coombs, M Johnson, D Culliford, L Josephs, N Williams, M Thomas, T Wilkinson

---

**2.00pm – 4.00pm**

**Churchill, Ground Floor**

**SYMPOSIUM**

**WHAT’S NEW IN MYCOBACTERIAL DISEASE?**

**Chaired by: Dr Heinke Kunst (London) and Dr Michael Loebinger (London)**
**Wednesday 7 December 2016**

**P54** Can multi-morbid phenotypes be described in patients with advanced COPD using cluster analysis?
BD James, NJ Greening, N Toms, G Woltmann, RC Free, P Haldar, MC Steiner, RA Evans

**P55** Benefits of tiotropium/olodaterol on symptoms and health-related quality of life in patients with moderate to severe COPD with chronic bronchitis and/or emphysema
GT Ferguson, R Abrahams, L Bjørner, L Grönke, F Voß, D Singh

**P56** Efficacy and safety of long-acting beta agonists + long acting muscarinic antagonists vs. long-acting beta agonists + inhaled corticosteroids in COPD: a meta-analysis
RE Villalobos, A David-Wang, J Magallanes

**P57** The cost-consequence of fluticasone furoate/vilanterol 100/25 mcg in the UK using the results from the COPD Salford Lung Study
MT Driessen, S Barnfather, Pj Mulley, Il Boucôt, T Ignacio, G van de Wetering

**P58** Efficacy of budesonide/formoterol in COPD patients with a post-bronchodilator FEV1 50 to <70% of predicted normal: pooled analysis across four phase III/IV studies
C Jorup, GD James, K Pemberton, G Eckerwall

**P59** Factors influencing step-up to LAMA+LABA/ICS in COPD patients initially on LAMA monotherapy: a THIN database study
JR Hurst, M Dilleen, K Morris, S Hills, B Emir, R Jones

**P60** Effect of indacaterol/glycopyrronium (IND/GLY) on patient-reported outcomes in men and women with COPD: a pooled analysis from the IGNITE programme
K Kostikas, I Tsiligiani, S Fucile, K Mezzi, S Shen, D Banerji, R Fogel

**P61** Community oxygen prescriptions and DNACPR discussions in Stockport: an opportunity to improve end of life care planning?
C Morris, S Parry, P Holmes, V Gupta

**P62** Avoiding inappropriate prescribing of high dose inhaled corticosteroid combination inhalers – is the message getting through?
V Mak, G D’Ancona

---

**SCIENTIFIC PROGRAMME**

**P63** Salvage lung volume reduction surgery after failure or complications of endobronchial treatment with one-way valves for severe emphysema
R Bilancia, I Oey, P Perikleous, S Tenconi, D Waller

2.30pm – 4.15pm
St James, 4th Floor
**POSTER DISCUSSION: P64 – P77**

Sleep apnoea and non-invasive ventilation
*Chaired by: Dr Melissa Hack (Newport) and Dr Ian Smith (Cambridge)*

**P64** Multiple dimensions of excessive daytime sleepiness
SKS Smith, J Steier, Y Serry, A Sekaran

**P65** OSAS and driving – BTS return survey to assess consistency of advice given to patients at diagnosis and after treatment – a repeat of the 2013 survey to evaluate the impact of a BTS statement and new DVLA regulations
A Baluwala, D Ghosh, A Dwarkanath, M Twiddy, P Daxter, SL Jamson, M Elliott

**P66** Falling asleep while driving: is driving safety advice given to patients with excessive daytime sleepiness?
AK Khetarpal, KA Anderson, SW West

**P67** Is there a difference between the sleep physiology of obese and super obese patients?
A Rajhan, L Michael, A Bain, A Thomas, M Allen

**P68** To screen or not to screen for obstructive sleep apnoea (OSA) pre-operatively?
CD Turnbull, D Ball, ML Estevez, H Du Plessis, M Hardinge, A Nickol

**P69** Evaluation of the STOPBANG threshold in the pre-operative screening for obstructive sleep apnoea at Sherwood Forest Hospitals Foundation Trust
A Reynor, AW Molyneux, SD Tilbrook, RB Dean, E Crookes, J Tansley, NJ Ali

**P70** CPAP compliance in bariatric patients with obstructive sleep apnoea
PSP Cho, A Rainey, B Mukherjee, KK Lee

**P71** Can postural OSA be identified from oximetry alone?
A Johar, CD Turnbull, JR Stradling
**P72** Baseline data from the ROSA trial: a randomised controlled trial of the effect of CPAP on diabetic macular oedema in people with concurrent obstructive sleep apnoea
SD West, J Hughes, B Prudon

**P73** Acute non-invasive ventilation (NIV)–related nasal bridge pressure ulceration: effect of a proactive prevention approach
G Stygall, K Morley, L Pickup, A Oakes, P Antoine-Pitterson, B Chakraborty, R Mukherjee

**P74** Non-invasive ventilation delivered on a standard respiratory unit compared to use in Level 2 care setting: is there an ideal service delivery model?
AJ Jayadev, KM Mcvinnie, IM Moonsie

**P75** Patient experience of non-invasive ventilation: a qualitative study
N Goldman, L Richardson, S Blakey, L Staveacre, SAA Bloch

**P76** Initiation of long-term non-invasive ventilation (NIV) in a specialist respiratory failure unit in the UK
SJ Tetlow, PS Marino, PD Murphy, H Pattani, J Steier, N Hart

**P77** Experience of a joint palliative and respiratory clinic on NIV treatment initiation in motor neurone disease
T Burden, C Davis, E Johnstone, J Spence, D Shrikrishna

---

**Wednesday 7 December 2016**

**P79** Single point of access clinic (SPOAC): a new regional lung cancer pathway in New Zealand
P Dawkins, J McWilliams, R Sullivan

**P80** Symptoms, delay to presentation and survival in lung cancer
WY Chan, A Clark, U Dernedde, TRoques, M Burton, J Kotecha, A Wilson, C Martin

**P81** Straight to CT delivers earlier first definitive treatment in lung cancer – effect of a simple intervention
P Malhotra, P Murphy, C Dawson, N Hunt, J Hendry

**P82** Outcomes for patients with negative scans on the ‘Straight to CT’ pathway
H Gundersen, A Hufton, R Trafford, MJ Walshaw, M Ledson

**P83** Introduction of “straight to CT” in a lung cancer unit – two years on
RM Trafford, A Hufton, M Walshaw, C Smyth, M Ledson

**P84** The relationship between unadjusted referral to treatment times, disease stage and survival in lung cancer
SA Hodgson, KG Blyth

**P85** Virtual lung cancer clinic: early experience and feasibility
JF Faccenda, LD Calvert, SO Brij

**P86** Optimising patient flow and use of resources in the two week wait pathway
K Goffe, P Ruparelia, CR Sander, C Butler

**P87** The use of a virtual clinic to speed up and improve the cancer diagnostic pathway – 2 year experience
A McIver, N Maddock, J Dunbar, J Hughes, MJ Ledson, C Smyth, MJ Walshaw

**P88** Follow-up after surgical treatment of lung cancer: the potential impact of international guidelines on current UK practice
J Capps, V Grannon, S Baksi, S Khalid

---

**2.45pm – 3.45pm**
Victoria, 2nd Floor
BTS SPECIALIST ADVISORY GROUP
OPEN MEETING

**Pleur al Disease**

**2.45pm – 4.10pm**
Moore, 4th Floor

**POSTER DISCUSSION: P78 – P88**

**How can we improve lung cancer pathways?**
Chaired by: Dr Rob Buttery (Cambridge) and Dr Ian Woolhouse (Birmingham)

**P78** Tackling emergency lung cancer admissions
RV Reddy, Y Vali, M Naeem

---

**3.00pm – 4.30pm**

COFFEE/TEA will be served in the Whittle & Fleming and Britten, 3rd floor and the Cambridge, 5th floor (3.15pm – 3.30pm only)
**Wednesday 7 December 2016**

3.30pm – 5.00pm
Mountbatten, 6th Floor

**POSTER DISCUSSION: P89 – P100**

**Cystic fibrosis**  
Chair by: Dr Caroline Elston (London) and Dr Donna McShane (Cambridge)

**P89** Modeling nutritional outcomes for infants diagnosed with cystic fibrosis by newborn screening  
KD Patterson, T Kyriacou, M Desai, WD Carroll, FJ Gilchrist

**P90** The North-South divide: regional inequalities in demographic characteristics and clinical outcomes in patients with cystic fibrosis in England – a population based cross-sectional study using UK CF Registry data  
S Nyangoma, V Rajabzadeh-Heshejin, P Cullinan, J Sampion

**P91** Trypsin-like protease activity predicts disease severity and patient mortality in adults with cystic fibrosis  
JA Reihill, KL Moffitt, AM Jones, JS Elborn, SL Martin

**P92** Systemic alkyl quinolones as novel biomarkers for pulmonary exacerbations in cystic fibrosis: a validation study  
H Barr, A Fogarty, N Halliday, A Knox, B Quon, D Forrester, P Williams, D Barrett, M Camara

**P93** In-vitro activity of seven hospital biocides against Mycobacterium abscessus  
S Caskey, JE Moore, JC Rendall

**P94** The management of respiratory tract fungal disease in cystic fibrosis – a UK survey of current practice  
M Boyle, JE Moore, DG Downey

**P95** Exploring the timing of hypertonic saline (HTS) and airways clearance techniques (ACT) in cystic fibrosis (CF): a cross over study  
K O’Neill, F Moran, I Bradbury, DG Downey, J Rendall, MM Tunney, JS Elborn, JM Bradley

**P96** Physiotherapy management of adult patients with cystic fibrosis on intensive care units (ICU) – a survey of UK physiotherapists  
F Cathcart, H Parrott, A Jones, N Simmonds

**P97** Gastro-oesophageal reflux in cystic fibrosis  
RW Lord, JS Pearson, PJ Barry, PJ Whorwell, RB Jones, P McNamara, R Beynon, JA Smith, AM Jones

**P98** An 18 (+/−6) month follow up study of cognitive function in adults with cystic fibrosis related diabetes (CFRD)  
HK Chadwick, A Morton, L Dye, CL Lawton, MW Mansfield, D Peckham

**P99** Cystic fibrosis medications at transfer from paediatric to adult care – what are patients actually taking?  
J Strange, K Cox, A Jones

**P100** Pre-transplant c-reactive protein (CRP) as a marker of post-transplant outcomes in patients with cystic fibrosis (CF)  
A Fazleen, J Parmar

---

4.15pm – 4.40pm
Churchill, Ground Floor

**AWARD PRESENTATIONS**

Presentation of the BTS Medal, BTS Award for Meritorious Service, BTS/BALR/BLF Early Career Investigator of the Year Award and the BTS Medical Student Awards

4.40pm – 5.30pm
Churchill, Ground Floor

**THE BTS PRESIDENT’S ADDRESS**

“Research: why bother?”

Professor Edwin Chilvers (Cambridge)  
Introduced by: Professor Mike Morgan (Leicester)

---

5.30pm – 6.00pm
Churchill, Ground Floor

**BTS ANNUAL GENERAL MEETING**

(BTS members only)
Thursday 8 December 2016

8.00am – 9.00am
COFFEE/TEA will be served in the Whittle & Fleming, 3rd floor

8.45am – 4.00pm
Whittle & Fleming, 3rd Floor
POSTER VIEWING
Authors present: 10.00am – 11.00am

P101-P108
Improving lung cancer care and outcomes
Discussion of abstracts will take place from 2.00pm to 3.00pm in the Windsor, 5th floor

P109-P119
TB: clinical aspects
Discussion of abstracts will take place from 2.00pm to 3.25pm in the Moore, 4th floor

P120-P134
Clinical studies of asthma
Discussion of abstracts will take place from 2.00pm to 3.50pm in the Albert, 2nd floor

P135-P147
Disease progression and burden in obstructive lung disease
Discussion of abstracts will take place from 3.30pm to 5.05pm in the Windsor, 5th floor

P148-P160
Asthma treatments and what matters to patients
Discussion of abstracts will take place from 3.30pm to 5.05pm in the Abbey, 4th floor

P161-P175
Treating idiopathic pulmonary fibrosis
Discussion of abstracts will take place from 3.30pm to 5.20pm in the Westminster, 4th floor

P176-P186
Paediatric respiratory disease
Discussion of abstracts will take place from 3.45pm to 5.10pm in the Rutherford, 4th floor

P187-P197
From oxygen to the ITU
Discussion of abstracts will take place from 4.00pm to 5.25pm in the Mountbatten, 6th floor

Thursday 8 December 2016

8.00am – 8.30am
Albert, 2nd Floor
BTS JOURNAL CLUB
COUGH
Professor Alyn Morice (Hull)

8.30am – 10.00am
Churchill, Ground Floor
JOINT BTS/BTOG SYMPOSIUM
TISSUE IS THE ISSUE BUT WILL IT ALWAYS BE?
Chaired by: Professor Sam Janes (London) and Dr Sanjay Popat (London)

8.30am
Understanding tumour heterogeneity – where will it lead us?
Dr Nicholas McGranahan (London)

9.00am
Will liquid biopsies be the future for diagnosing lung cancer?
Dr Caroline Dive (Manchester)

9.30am
In the age of targeted therapies – what does it mean for the chest physician?
Professor David Baldwin (Nottingham)

Learning objectives:
1) To understand how new insights into the biology of lung cancer may change how we manage lung cancer.
2) What role will liquid biopsies play in diagnosing lung cancer and monitoring disease progression in the future?
3) In the era of targeted therapies what does the chest physician need to know when taking biopsies (and re-biopsies)?

8.30am – 10.00am
Mountbatten, 6th Floor
JOINT BTS/BPRS SYMPOSIUM
PRECISION MEDICINE IN CLINICAL PRACTICE
Chaired by: Professor Jane Davies (London) and Dr Steve Turner (Aberdeen)

8.30am
Asthma pharmacogenomics
Professor Kelan Tantisira (Boston)

9.00am
Mutation-specific therapies for cystic fibrosis
Professor Jane Davies (London)
Thursday 8 December 2016

9.30am  Allergen-specific immunotherapy
Professor Stephen Durham (London)

Learning objectives
1) To present the concept of precision medicine and how it differs from conventional therapeutic approaches.
2) To impart an appreciation of current drug development pipelines in asthma, allergy and CF.
3) To discuss some of the limitations to precision or personalised medicine including cost issues.

8.30am – 10.00am
St James, 4th Floor
SPOKEN SESSION: S38 – S42
Non-tuberculous mycobacteria: passengers or pathogens?
Chaired by: Dr Dorothy Grogono (Cambridge) and Professor Wei Shen Lim (Nottingham)

8.35am  S38
Clinical isolates of mycobacterium avium drive collagenolytic and elastolytic activity in mononuclear cells
SJ McFetridge, R McMullan, CM O’Kane

8.50am  S39
Risk of NTM (non tuberculosis mycobacterium) infection in patients on long term prophylactic macrolide antibiotics
JB Adizie, M Qasim, M Pagaria

9.05am  S40
A retrospective study into the clinical relevance of isolating non-tuberculous mycobacteria in pulmonary samples
H Burgess, S Cowman, A Jones, R Wilson, MR Loebinger

9.20am  S41
Clinical relevance of pulmonary non-tuberculous mycobacteria isolated over 7 years at a single UK centre
HF Schiff, S Philpot, A Achaiah, A Pereira, G Stait, B Green

9.35am  S42
Eradication success of non-tuberculous mycobacterial infections in a paediatric cystic fibrosis population
DA Hughes, A Malfitano, A Davenport, SB Carr

8.30am – 10.15am
Abbey, 4th Floor
SPOKEN SESSION: S43 – S48
Innate immunity in lung disease
Chaired by: Professor Alison Condliffe (Sheffield) and Dr Elizabeth Sapey (Birmingham)

8.35am  S43
Hypoxia upregulates PI3Kinase-dependent neutrophil degranulation and neutrophil-mediated tissue injury
KM Lodge, K Hoenderdos, AJ Robbins, DM Storisteanu, ER Chilvers, W Li, AM Condliffe

8.50am  S44*
Pseudomonas aeruginosa induces neutrophil cell death which is reversed by hypoxia
SP Williams, R Dickinson, SR Walmsley, MKB Whyte

9.05am  S45
Evaluating the sensitivity and specificity of active neutrophil elastase as a biomarker for bacterial infection in subjects with COPD
SJ Thulborn, N Akram, V Mistry, CE Brightling, K Moffitt, D Ribeiro, M Bafadhel

9.20am  S46
Neutrophil vascular endothelial growth factor (VEGF) as a driving force for angiogenesis in bronchiectasis?
CC Cole, SC Carnell, KJ Jiwa, JB Birch, KH Hester, CW Ward, JS Simpson, ADS De Soyza

9.35am  S47
Pneumolysin promotes neutrophil: platelet aggregation in vitro
JG Nel, C Durand, AJ Theron, GR Tintinger, TJ Mitchell, C Feldman, R Anderson

9.50am  S48
Targeting siglecs to reduce protease-mediated destruction in tuberculosis
W Beynon, R McMullan, D McAuley, C O’Kane

*S44 – BTS Medical Student Award Winner
SCIENTIFIC PROGRAMME

8.30am – 10.30am
Windsor, 5th Floor
SYMPOSIUM
BLASTS, PARTICLES, FIBRES: FROM (LUNG) INSULT TO INJURY
Chaired by: Dr Johanna Feary (London) and Professor David Fishwick (Sheffield)

8.30am  Lungs at war: what respiratory consequences should we consider in military personnel?
Lt Col Andy Johnston (Birmingham)

9.00am  Cross town traffic: how bad is diesel for our lungs?
Dr Ian Mudway (London)

9.30am  Screening for lung cancer in asbestos workers: the French experience
Professor Jean-Claude Pairon (Paris)

10.00am  Carbon nano particles and the lung: the new asbestos?
Professor Marion MacFarlane (Leicester)

Learning objectives
1) To understand the range of acute and chronic respiratory conditions that may arise in both military personnel and in civilians living in areas of conflict and how best to manage them.
2) To develop a better awareness of the association between diesel fumes and acute and chronic lung diseases.
3) To gain an appreciation for the advantages and disadvantages of screening for lung cancer and other respiratory health effects in people exposed to asbestos.

8.45am – 10.15am
Moore, 4th Floor
SPOKEN SESSION: S49 – S53
Idiopathic pulmonary fibrosis: mechanisms
Chaired by: Professor Rachel Chambers (London) and Dr Chris Scotton (Exeter)

8.50am  S49
The role of platelet-derived TGFβ in pulmonary fibrosis
DLW Chong, C Rebeyrol, A Khawaja, EJ Forty, N Kanda, CJ Scotton, JC Porter

9.05am  S50
Monocytes from IPF patients show pre-conditioned pro-repair features
E Fraser, K Blirando, V St Noble, R Benamore, R Hoyles, A Benlahrech, LP Ho

9.20am  S51
mTOR regulates TGF-β induced profibrotic gene expression in primary human lung fibroblasts
HV Woodcock, JD Eley, C Nanthakumar, TM Maher, PF Mercer, RC Chambers

9.35am  S52
Suberanilohydroxamic acid (SAHA) inhibits collagen deposition in a transforming growth factor β1-driven precision cut lung slice (PCLS) model of pulmonary fibrosis
OJ Brand, A Pasini, A Habgood, AJ Knox, G Jenkins, L Pang

9.50am  S53
Effect of epigenetic inhibitors on lung fibroblast phenotype change in idiopathic pulmonary fibrosis
A Pasini, OJ Brand, G Jenkins, AJ Knox, L Pang

8.45am – 10.30am
Westminster, 4th Floor
SPOKEN SESSION: S54 – S59
Lungs and inflation
Chaired by: Professor Nicholas Hart (London) and Dr Alison McMillan (London)

8.50am  S54
CPAP reduces exacerbations in tracheobronchomalacia
M Demirbag, G Tavernier, T Morris, K Hince, C Ustabasi, D Jones, S Fowler

9.05am  S55
Using continuous positive airway pressure (CPAP) in excessive dynamic airway collapse (EDAC)
APH Hicks, TB Brown, AC Chauhan, KA Adeniji, MQ Quint, SB Babu
**Thursday 8 December 2016**

**9.20am**  
**S56**  
Neural respiratory drive and cardiac function in patients with obesity-hypoventilation-syndrome following setup of non-invasive ventilation for hypercapnic respiratory failure  
A Onofri, M Patout, G Arbane, M Pengo, P Marino, J Steier

**9.35am**  
**S57**  
Qualitative assessment of the experience of telemonitoring in ventilated patients with motor neurone disease  
H Ashcroft, H Ando, R Halhead, B Chakrabarti, CA Young, R Cousins, RM Angus

**9.50am**  
**S58**  
The use of remote monitoring to assess ventilator adherence and outcomes within a regional home mechanical ventilation service  
YM Gn, R Moses, A Vyas

**10.05am**  
**S59**  
Utility of an auto-titrating protocol for the set up of nocturnal non-invasive ventilation  
C Carlin, G McDowell, C Williams, A Brown, C Canavan, R Tourish

---

**10.00am – 10.00am**  
Victoria, 2nd Floor  
**BTS SPECIALIST ADVISORY GROUP OPEN MEETING**  
Interventional Procedures

---

**10.00am – 11.00am**  
COFFEE/TEA will be served in the Whittle & Fleming and Britten, 3rd floor

---

**SCIENTIFIC PROGRAMME**

**10.30am – 12.00pm**  
Mountbatten, 6th Floor  
**SYMPOSIUM**  
**TARGETED THERAPIES IN CYSTIC FIBROSIS**  
Chaired by: Dr Stephen Bourke (Newcastle upon Tyne) and Dr Donna McShane (Cambridge)

**10.30am**  
Targeting inflammation in cystic fibrosis  
Dr Robert Gray (Edinburgh)

**11.00am**  
Molecular and cellular processing of CFTR  
Professor Margarida Amaral (Lisbon)

**11.30am**  
Current status of CFTR modulator therapies  
Professor Stuart Elborn (Belfast)

**Learning objectives**

1) To address key developments in targeted treatments of basic disease mechanisms in cystic fibrosis. To review inflammation as a key target for treatment.
2) To understand molecular and cellular mechanisms of CFTR dysfunction.
3) To review latest developments in bringing CFTR modulator drugs to clinical practice.

---

**10.30am – 12.15pm**  
Churchill, Ground Floor  
**SYMPOSIUM**  
**PLENARY SCIENTIFIC**  
Chaired by: Professor Louise Donnelly (London) and Professor Gisli Jenkins (Nottingham)

**10.30am**  
Non-coding RNAs and respiratory disease  
Professor Mark Lindsay (Bath) (BALR nomination)

**10.55am**  
Matrix proteases in chronic lung disease: a tangled web of targets and actions  
Professor Simon Johnson (Nottingham)

**11.20am**  
Neutrophils, inflammatory pathways, COPD in ageing  
Dr Elizabeth Sapey (Birmingham)

**11.45am**  
Vitamin D and respiratory infections  
Professor Adrian Martineau (London)
Learning objectives

A highlight of the Winter Scientific Meeting programme, as four of the UK’s top respiratory researchers share highlights of their work and its relevance to patients.

10.30am – 12.15pm
St James, 4th Floor
SPOKEN SESSION: S60 – S65
Advances in thoracic surgery

Chairled by: Professor George Santis (London) and Mr Richard Steyn (Warwick)

10.35am S60
Lung cancer surgical survival and volume in England
D West, P Beckett, A Khakwani, R Hubbard, R Dickinson, I Woolhouse

10.50am S61
Risk factors and short-term outcomes of developing postoperative pulmonary complications after VATS lobectomy
P Agostini, ST Lugg, K Adams, T Smith, M Kalkat, PB Rajesh, RS Steyn, B Naidu, A Rushton, E Bishay

11.05am S62
Adequacy of intra-operative lymph node sampling during surgical resection of NSCLC: influencing factors and its relationship to survival
T Edwards, H Balata, C Tennyson, P Foden, P Bishop, M Jones, P Krysiak, K Rammohan, R Shah, P Crosbie, R Booton, M Evison

11.20am S63
Postoperative pulmonary complications and physiotherapy requirements after open thoracotomy versus VATS lobectomy: a propensity score-matched analysis
P Agostini, ST Lugg, K Adams, N Vartsaba, M Kalkat, PB Rajesh, RS Steyn, B Naidu, A Rushton, E Bishay

11.35am S64
Rates and sites of recurrence following radical treatment of stage I lung cancer
MPT Kennedy, KL Lummis, K Spencer, K Franks, M Sne, MEJ Callister

Thursday 8 December 2016

11.50am S65
Developing a multi-disciplinary thoracic surgery research team improves the recruitment into and quality of clinical trials

11.00am – 12.00pm
Gielgud, 2nd Floor
OPEN SESSION
Raising the quality of diagnostic spirometry

Chairled by: Monica Fletcher OBE (Warwick)

Speakers will include: Professor Mike Morgan (Leicester) and members of the Quality Assured Spirometry Steering Group.

Those involved in performing and interpreting spirometry as part of the diagnosis of respiratory conditions need to be competent to do so.

https://www.pcc-cic.org.uk/article/quality-assured-diagnostic-spirometry

The APPG Report on Inquiry into Respiratory Deaths 2014 called for a system to assess and certify the competence of all healthcare professionals undertaking and interpreting diagnostic spirometry. This document, which is part of a suite of resources relating to quality assured diagnostic spirometry, sets out a framework for taking forward the APPG recommendations.

From March 2021 those involved in the procedure will be required to be on a national register held by the ARTP. Find out more about what this means in practice and how you can be part of the implementation.

12.00pm – 1.00pm
Rutherford, 4th Floor
BTS SPECIALIST ADVISORY GROUP
OPEN MEETING
Pulmonary Vascular

12.00pm – 2.00pm
LUNCH will be available to purchase in the Cafe in the Pickwick, 1st floor, and the Snack Bar in the Whittle & Fleming, 3rd floor
Thursday 8 December 2016

12.15pm – 1.45pm
Gielgud, 2nd Floor
OPEN SESSION

The UKRRC – Respiratory Research Road Map Project
Getting your respiratory research funded; what’s out there and how to access it

12.15pm
The UKRRC Respiratory Research Road Map Project
Professor Ian Hall (Chair, UKRRC) and Dr Shahideh Safavi (Nottingham)

12.45pm
Funding opportunities: short presentations and panel discussion
Chaired by: Professor Moira Whyte (Chair MRC Clinical Fellowship Panel)
Panel:
Dr Clare McVicker (Wellcome Trust)
Dr Anthony De Soyza (National Institute of Health Research)
Dr Samantha Walker (Asthma UK)

This session, organised by the UK Respiratory Research Collaborative (UKRRC), will cover a new initiative launched by the UKRRC to create a research road map for respiratory research, which will be followed by short presentations from major funders of respiratory research in the UK and an interactive Q&A session. Come and hear all about the research road map, funding opportunities on offer, and meet potential collaborators and learn how to maximise chances of success in applying. Lunch will be provided.

12.30pm – 1.15pm
Churchill, Ground Floor

THE BTS LECTURE
Epithelial alarmins and asthma
Professor Paul O’Byrne (Ontario)
Introduced by: Professor Edwin Chilvers (Cambridge)

12.30pm – 1.30pm
Albert, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Cystic Fibrosis

12.30pm – 1.30pm
Victoria, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Occupational and Environmental Lung Disease

12.30pm – 1.30pm
Abbey, 4th Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Nurse Advisory Group

12.30pm – 1.30pm
Victoria, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Occupational and Environmental Lung Disease

1.00pm – 1.45pm
Windsor, 5th Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Lung Cancer and Mesothelioma

1.45pm – 3.00pm
Westminster, 4th Floor
SPOKEN SESSION: S66 – S69
Improving outcomes during COPD hospitalisations
Chaired by: Dr Jennifer Quint (London) and Professor Tom Wilkinson (Southampton)

1.50pm  S66
Levels of salivary C-reactive protein, procalcitonin and neutrophil elastase can predict exacerbations in COPD and determine those patients at high risk of re-exacerbation
N Patel, G Thorpe, P Jones, V Adamson, J Belcher, MA Spiteri

2.05pm  S67
Mortality in COPD patients following community acquired pneumonia: a population database analysis of linked healthcare records
N Williams, NA Coombs, M Johnson, L Josephs, LA Rigge, DM Thomas, TMA Wilkinson

1.50pm  S66
Levels of salivary C-reactive protein, procalcitonin and neutrophil elastase can predict exacerbations in COPD and determine those patients at high risk of re-exacerbation
N Patel, G Thorpe, P Jones, V Adamson, J Belcher, MA Spiteri

2.05pm  S67
Mortality in COPD patients following community acquired pneumonia: a population database analysis of linked healthcare records
N Williams, NA Coombs, M Johnson, L Josephs, LA Rigge, DM Thomas, TMA Wilkinson

This session, organised by the UK Respiratory Research Collaborative (UKRRC), will cover a new initiative launched by the UKRRC to create a research road map for respiratory research, which will be followed by short presentations from major funders of respiratory research in the UK and an interactive Q&A session. Come and hear all about the research road map, funding opportunities on offer, and meet potential collaborators and learn how to maximise chances of success in applying. Lunch will be provided.

12.30pm – 1.15pm
Churchill, Ground Floor

THE BTS LECTURE
Epithelial alarmins and asthma
Professor Paul O’Byrne (Ontario)
Introduced by: Professor Edwin Chilvers (Cambridge)

12.30pm – 1.30pm
Albert, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Cystic Fibrosis

12.30pm – 1.30pm
Victoria, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Occupational and Environmental Lung Disease

12.30pm – 1.30pm
Abbey, 4th Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Nurse Advisory Group

12.30pm – 1.30pm
Victoria, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Occupational and Environmental Lung Disease

1.00pm – 1.45pm
Windsor, 5th Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Lung Cancer and Mesothelioma

1.45pm – 3.00pm
Westminster, 4th Floor
SPOKEN SESSION: S66 – S69
Improving outcomes during COPD hospitalisations
Chaired by: Dr Jennifer Quint (London) and Professor Tom Wilkinson (Southampton)

1.50pm  S66
Levels of salivary C-reactive protein, procalcitonin and neutrophil elastase can predict exacerbations in COPD and determine those patients at high risk of re-exacerbation
N Patel, G Thorpe, P Jones, V Adamson, J Belcher, MA Spiteri

2.05pm  S67
Mortality in COPD patients following community acquired pneumonia: a population database analysis of linked healthcare records
N Williams, NA Coombs, M Johnson, L Josephs, LA Rigge, DM Thomas, TMA Wilkinson

This session, organised by the UK Respiratory Research Collaborative (UKRRC), will cover a new initiative launched by the UKRRC to create a research road map for respiratory research, which will be followed by short presentations from major funders of respiratory research in the UK and an interactive Q&A session. Come and hear all about the research road map, funding opportunities on offer, and meet potential collaborators and learn how to maximise chances of success in applying. Lunch will be provided.

12.30pm – 1.15pm
Churchill, Ground Floor

THE BTS LECTURE
Epithelial alarmins and asthma
Professor Paul O’Byrne (Ontario)
Introduced by: Professor Edwin Chilvers (Cambridge)

12.30pm – 1.30pm
Albert, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Cystic Fibrosis

12.30pm – 1.30pm
Victoria, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Occupational and Environmental Lung Disease

12.30pm – 1.30pm
Abbey, 4th Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Nurse Advisory Group

12.30pm – 1.30pm
Victoria, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Occupational and Environmental Lung Disease

1.00pm – 1.45pm
Windsor, 5th Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Lung Cancer and Mesothelioma

1.45pm – 3.00pm
Westminster, 4th Floor
SPOKEN SESSION: S66 – S69
Improving outcomes during COPD hospitalisations
Chaired by: Dr Jennifer Quint (London) and Professor Tom Wilkinson (Southampton)

1.50pm  S66
Levels of salivary C-reactive protein, procalcitonin and neutrophil elastase can predict exacerbations in COPD and determine those patients at high risk of re-exacerbation
N Patel, G Thorpe, P Jones, V Adamson, J Belcher, MA Spiteri

2.05pm  S67
Mortality in COPD patients following community acquired pneumonia: a population database analysis of linked healthcare records
N Williams, NA Coombs, M Johnson, L Josephs, LA Rigge, DM Thomas, TMA Wilkinson

This session, organised by the UK Respiratory Research Collaborative (UKRRC), will cover a new initiative launched by the UKRRC to create a research road map for respiratory research, which will be followed by short presentations from major funders of respiratory research in the UK and an interactive Q&A session. Come and hear all about the research road map, funding opportunities on offer, and meet potential collaborators and learn how to maximise chances of success in applying. Lunch will be provided.
SCIENTIFIC PROGRAMME

2.20pm  S68
COPD in the ED: eosinophils, treatment and outcomes, data from the Pre-AWARD study
REK Russell, T Doggett, I Pavord, R Pullinger, S Beer, M Bafadhel

2.35pm  S69
Troponin levels and risk of death following a myocardial infarction in people with and without COPD
KJ Rothnie, N Ahmed, JK Quint

1.45pm – 3.15pm
Churchill, Ground Floor
SYMPOSIUM
NOVEL SCIENCE, INNOVATIVE IMAGING AND A CLINICAL UPDATE IN PULMONARY HYPERTENSION
Chairied by: Dr Robin Condliffe (Sheffield) and Dr Elaine Soon (Cambridge)

1.45pm  PAH: translating basic mechanisms into novel therapies
Professor Nick Morrell (Cambridge)

2.15pm  Imaging in pulmonary hypertension: current approach and new developments
Professor David Kiely (Sheffield)

2.45pm  Not all pulmonary hypertension is PAH
Dr John Wort (London)

Learning objectives:
1) To highlight the latest research exploring the molecular mechanisms and genetic abnormalities underlying PAH and how this has led to the identification of new drug targets for PAH.
2) To understand the value of current and emerging imaging techniques in the diagnosis and assessment of pulmonary hypertension.
3) To understand how PH due to left heart disease, lung disease and chronic thromboembolism differs from pulmonary arterial hypertension, and to review the evidence for management of these different conditions.

Thursday 8 December 2016

1.45pm – 3.15pm
Abbey, 4th Floor
SYMPOSIUM
BTS Clinical Audit and Quality Improvement
Chairied by: Dr Jonathan Bennett (Leicester)

1.45pm  Welcome and introduction
Dr Jonathan Bennett (London)

1.50pm  The 2015/16 National Paediatric Asthma Audit
Dr James Paton (Glasgow)

2.10pm  The 2016 National Smoking Cessation Audit
Dr Sanjay Agrawal (Leicester) and Dr Zaheer Mangera (London)

2.30pm  The BTS Lung Disease Registry Programme: IPF and Sarcoidosis
Professor Monica Spiteri (Stoke-on-Trent)

2.50pm  The BTS Audit programme – future plans
Dr James Calvert (Bristol)

3.10pm  Closing comments
Dr Jonathan Bennett (London)

1.45pm – 3.30pm
St James, 4th Floor
SPOKEN SESSION: S70 – S75
Infections and the impact on childhood respiratory disease
Chairied by: Professor Jane Davies (London) and Professor Michael Shields (Belfast)

1.50pm  S70
Neonatal airway epithelial cell IL-8 responses to infection are reduced in those who go on to wheeze
SW Turner, D Miller, G Walsh, U Power, M Shields, G Devereux

2.05pm  S71
Do children with troublesome preschool wheeze have evidence of fungal sensitisation?
KA Holden, KG Staley, EA Gaillard
Thursday 8 December 2016

2.20pm  **S72***
Immunomodulatory effects of carbon particulates on macrophage handling of Streptococcal infections
HL Shaw, JC Wallington, M Christodoulides, DI Phillips, TMA Wilkinson, KJ Staples

2.35pm  **S73**
Viruses associated with community-acquired pneumonia in children – a large prospective study in the post-Prevenar 13 era
AS Wort, M Gale, K Devine, AJ Simpson, AD Sails, DA Spencer, MF Thomas, M Brodlie

2.50pm  **S74**
Increased respiratory syncytial virus burden leads to more rapid cell death in Phe508del bronchial epithelial cells
MS Coates, EWFW Alton, DW Brookes, K Ito, JC Davies

3.05pm  **S75**
The T2R38 bitter taste receptor as a modifier of host response to Pseudomonas aeruginosa in cystic fibrosis: does T2R38 genotype impact on clinical infection?
A Turnbull, H Lund-Palau, R Murphy, A Simbo, A Shoemark, K Wong, A Bush, E Alton, J Davies

*S72 – BTS Medical Student Award Highly Commended*

1.45pm – 3.30pm
Rutherford, 4th Floor
**SPOKEN SESSION: S76 – S81**

**Acute lung injury and interstitial lung disease**
Chair by: Dr Charlotte Summers (Cambridge) and Professor David Thickett (Birmingham)

1.50pm  **S76**
Endoplasmic reticulum stress correlates with fibrosis in interstitial lung disease
H Parfrey, E Moseley, B Beardsley, J Knight, SJ Marciniak, D Rassl

2.05pm  **S77**
Modulatory effects of rheumatoid arthritis IgG on neutrophil activation: a potential role in RA-ILD
AA Khawaja, C Pericleous, VM Ripoll, HL Booth, V Holmes, T Mikolasch, I Giles, JC Porter

2.20pm  **S78**
Lymphopaenia and increased ACE levels stratify sarcoidosis patients to underlying increase in IFN-γ+ lymphocyte and TNF-α+ monocytes respectively
YK Kendrick, SL Cole, R Hoyles, LP Ho

2.35pm  **S79**
Reduced CD200 receptor expression on monocytes in sarcoidosis
SD Fraser, LR Sadofsky, PM Kaye, SP Hart

2.50pm  **S80**
Mesenchymal stromal cells (MSC) modulate human macrophages in acute respiratory distress syndrome (ARDS) via secretion of extracellular vesicles (EV) which enhance oxidative phosphorylation and regulate JAK/STAT signalling
TJ Morrison, MV Jackson, C O’Kane, DF McAuley, A Krasnodembskaya

3.05pm  **S81**
Oncostatin M is a novel mediator of human pulmonary endothelial chemokine and protease activity in the lung in ARDS
M Fitzgerald, DF McAuley, CM O’Kane
Thursday 8 December 2016

2.00pm – 3.00pm
Gielgud, 2nd Floor
OPEN SESSION
British Lung Foundation – BLF Research highlights
Chaired by: Dr Noel Snell (BLF Vice-President)

2.00pm
Respiratory Health of the Nation
Professor David Strachan (London)

2.20pm
Isogenic cell lines for targeted therapy discovery and development in BAP1-deficient mesothelioma
Professor Judy Coulson (Liverpool)

2.40pm
Regulating inflammatory signalling in human macrophages in the context of COPD
Dr Lynne Prince (Sheffield)

2.00pm – 3.25pm
Moore, 4th Floor
POSTER DISCUSSION: P109 – P119
Tuberculosis: clinical aspects
Chaired by: Professor Graham Bothamley (London) and Dr Jessica Potter (London)

P109 The impact of TB NICE guidance on resource capacity and contact screening outcomes: a retrospective, observational study within a central London TB centre
M O’Donoghue, H Jarvis, N Drey, MH Almond, S Seneviratne, A Lalvani, OM Kon

P110 The role of TB chemoprophylaxis in renal transplant recipients
JN Periselneris, S Mahendran, P Chowdhury, H Milburn

P111 Older patients with tuberculosis have less typical changes on chest radiographs
A Abbara, Z Mahomed, SM Collin, OM Kon, V Bushell, K Buell, JAL Sullivan, T Hansel, T Corrah, RN Davidson

P112 Serum inflammatory biomarkers as predictors of treatment outcome in pulmonary tuberculosis
A Ritchie, A Singanayagam, K Manalan, D Connel, J Chalmers, S Sridhar, A Lalvani, M Wickremasinghe, OM Kon
Thursday 8 December 2016

P113 Indeterminate IGRA results prior to anti-TNF therapy: stable state testing may be important for immune-mediated inflammatory disorders
W Ibrahim, Y Abunga, J Mamo, S Beck, SO Brij

P114 Implications of NICE 2016 Tuberculosis Guidance for a TB contact screening service
AM Ray, S Oglesby, C Mullarkey, JP Watson

P115 Screening outcomes of household contacts of multidrug-resistant tuberculosis patients in Peshawar, Pakistan
A Javaid, MA Khan, MA Khan, S Mehreen, A Basit, RA Khan, M Ihtesham, I Ullah, A Khan, U Ullah

P116 Multidrug-resistant tuberculosis (MDR-TB) monitoring in Southeast London using current recommendations; does it prevent complications?
B Bradley, M Kamalanathan, AJ Shah, N Read, J Hall, L Baker

P117 Pharmacy-led latent TB infection service: a success story
YO Abunga, SO Brij

P118 How do foreign-born patients with tuberculosis access healthcare? A cohort analysis of referrals from general practice and the emergency department to a tertiary tuberculosis service
S Conway, A Pitcher, S Dart, D Vaghela, MGK Burman, J Potter, VLC White, S Tiberi, H Kunst

P119 Using adverse events in a tuberculosis trial to describe the tolerability of standard therapy
CD Tweed, G Wills, AM Crook, SK Meredith, AJ Nunn, CM Mendel, SR Murray, TD McHugh, SH Gillespie

2.00pm – 3.30pm
Mountbatten, 6th Floor
SYMPOSIUM
HIGHLIGHTS FROM THORAX
Chaired by: Professor Nicholas Hart, Professor Gisli Jenkins and Professor Alan Smyth (Joint Editors-in-Chief, Thorax)

2.00pm Hypoxia and tissue destruction in pulmonary tuberculosis
Professor Jon Friedland (London)

2.20pm Rheumatoid arthritis-associated auto-antibodies and subclinical interstitial lung disease: the multi-ethnic study of atherosclerosis
Professor David Lederer (New York)

2.40pm Chronic electronic cigarette exposure in mice induces features of COPD in a nicotine-dependent manner
Professor Robert Foronjy (New York)

3.00pm Multidimensional severity assessment in bronchiectasis: an analysis of seven European cohorts
Dr Melissa McDonnell (Newcastle upon Tyne)

2.00pm – 3.50pm
Albert, 2nd Floor
POSTER DISCUSSION: P120 – P134
Clinical studies of asthma
Chaired by: Dr Ruth Green (Leicester) and Professor Douglas Robinson (London)

P120 Challenges in using hierarchical clustering to identify asthma subtypes: choosing the variables and variable transformation
MD Deliu, SY Yavuz, MS Sperrin, DB Belgrave, CS Sackesen, US Sahiner, AC Custovic, OK Kalayci

P121 Urban fine and coarse mode particulate matter differentially alter the maturation of monocyte-derived dendritic cells
TR Ho, N Camina, PE Pfeffer, EH Mann, IS Mudway, CM Hawrylowicz
Local sources rather than interactions with oxidising co-pollutant gases determine the geographical and seasonal variation in particulate matter oxidative potential

What causes occupational asthma in cleaners?

An investigation into co-morbidity accumulation in asthma patients with systemic steroid exposure

A primary care audit on asthma patients with frequent exacerbations and the potential impact of National Review of Asthma Deaths (NRAD) recommendations

Insufficient allergy diagnostics in severe asthmatic patients in Germany

Benefits and side effects of nasal irrigation in severe asthma

Comparison of safety and efficacy of airway clearance techniques, hypertonic saline and bronchoscopy in a severe asthma service

Fungal contamination of valved holding chambers (VHCs): potential to prevent, and effect on drug delivery

Prevalence and clinical outcomes of fungal sensitive asthma in a severe asthma population

Outdoor fungal spore levels, lung function and symptoms in patients with asthma and Aspergillus sensitisation

Factors associated with near-fatal asthma requiring extracorporeal membrane oxygenation

Safety and effectiveness of influenza vaccines in people with asthma: a systematic review and meta-analysis

Methacholine challenge to demonstrate therapeutic equivalence of terbutaline via different Turbuhaler devices in patients with mild to moderate asthma: appraisal of a phase III, four-way crossover design

3.00pm – 4.00pm

COFFEE/TEA will be served in the Whittle & Fleming and Britten, 3rd floor

3.15pm – 4.15pm

Victoria, 2nd Floor

BTS SPECIALIST ADVISORY GROUP OPEN MEETING

Specialty Trainee Advisory Group

3.15pm – 4.15pm

Gielgud, 2nd Floor

OPEN SESSION

Quality Improvement and the RCP: examples from the National COPD Audit Programme and the Future Hospital’s development sites

Presentation and panel discussion from the National COPD Audit Programme and Future Hospital Programme, with the following presenters and panel members:

Professor Mike Roberts, Clinical Lead for the National COPD Audit Programme

Dr Noel Baxter, Clinical Lead for the primary care work stream of the National COPD Audit Programme

Dr Rob Stone, Clinical Lead for the secondary care work stream of the National COPD Audit Programme
Thursday 8 December 2016

Professor Michael Steiner, Clinical Lead for the pulmonary rehabilitation work stream of the National COPD Audit Programme

Professor Frank Joseph, Future Hospital Officer

Dr Binita Kane, Consultant Respiratory Physician at University Hospital of South Manchester and Project Lead for the Future Hospital, Central and South Manchester

Dr Arvind Rajasekaran, Consultant Respiratory Physician for Sandwell and West Birmingham and Project Lead for the Future Hospital, Sandwell and West Birmingham

3.30pm – 5.05pm
Windsor, 5th Floor

POSTER DISCUSSION: P135 – P147
Disease progression and burden in obstructive lung disease
Chaired by: Professor Adam Hill (Edinburgh) and Dr Alice Turner (Birmingham)

P135  Treatment of lung disease in alpha-1 antitrypsin deficiency: a systematic review
RG Edgar, M Patel, S Bayliss, E Sapey, AM Turner

P136  Relationship between progression of lung disease in alpha-1 antitrypsin deficiency and cardiovascular risk
C Hall, S Samanta, N Verma, B Gooptu, JR Hurst

P137  Why is erdosteine recommended as a treatment for acute exacerbations of chronic bronchitis? A systematic review of clinical trials
CL Johnson, DF Rogers

P138  An innovative approach to study design: using electronic medical records to inform the feasibility and design of the NOVELTY study (a NOVEL observational longiTudinal studY on patients with asthma and/or COPD)
HK Reddel, M Gerhardsson de Verdier, A Agustí, R Beasley, EH Bel, C Janson, B Make, RJ Martin, I Pavord, D Postma, D Price, C Keen, A Gardev, S Rennard, A Sveréus, AT Bansal, L Brannman, N Karlsson, J Nuevo, F Nyberg, S Young, J Vestbo

P139  The burden of COPD across the European Union: development of the European COPD Atlas

P140  Co-morbidities of Swedish patients diagnosed with chronic obstructive pulmonary disease (COPD) and/or asthma
G Johansson, C Jansen, M Van Der Tol, R Ariely, G Bergman, M Uhde, P Sobocki, H Benhaddi

P141  2-year follow-up of COPD patients in the non-interventional ‘real-life’ DACCORD study in Germany
HW Worth, RB Buhl, CPC Criée, PK Kardos, CM Mailänder, NL Lossi, CV Vogelmeier

P142  The distribution of blood eosinophil count in a COPD clinical trials database: comparing the UK with the rest of the world
E Hilton, C Compton, D Midwinter, N Barnes

P143  Blood eosinophilia as predictor for patient outcomes in COPD exacerbations: a systematic review and meta-analysis
RE Villalobos, J Magallanes, A David-Wang

P144  Specialist domiciliary pharmacy intervention may reduce exacerbation frequency and hospitalisation in patients with severe chronic obstructive pulmonary disease
V Hunt, D Anderson, R Lowrie

P145  Evaluation and quantification of treatment preferences for patients with asthma or COPD using discrete choice experiment surveys
H Svedsater, E Hilton, D Leather, T Robinson, L Bradshaw, H Doll, B Nafees

P146  Mortality and day of admission for acute exacerbation of COPD
A Duffy, J Steer, SC Bourke, C Echevarria

P147  Effect of cannabis smoking on respiratory symptoms and lung function: a structured literature review
L Ribeiro, P Ind
**SCIENTIFIC PROGRAMME**

3.30pm – 5.05pm

Abbey, 4th Floor

**POSTER DISCUSSION: P148 – P160**

Asthma treatments and what matters to patients

_Chaired by: Dr Liz Gamble (Bristol) and Professor Stephen Scott (Chester)_

**P148**

Making sense of patient-reported currently treated asthma using routinely collected data

MA Al Sallakh, SE Rodgers, RA Lyons, A Sheikh, GA Davies

**P149**

Designing a management plan: a mixed methods approach to exploring patient journeys in children with severe and recurrent wheeze

SB Naidu, R Kerr, M Kecman, R Klaber

**P150**

Perceptions of asthma control in the UK – a cross sectional study comparing patient and HCP perceptions of asthma control with validated ACT scores

A Menzies-Gow, G Chiu

**P151**

Effect of high-intensity exercise on lung function, aerobic performance and airway inflammation in asthma

C Winn, M McNarry, G Stratton, AM Wilson, GA Davies

**P152**

Inhaled corticosteroid (ICS) and long acting beta-adrenoceptor agonist (LABA) therapy adherence reporting and monitoring in clinical trials of severe adult asthma drug treatments: a systematic review

MC Mokoka, MJ McDonnell, B Cushen, S Cormican, I Sulaiman, F Doyle, F Boland, RW Costello

**P153**

Does asthma control, mood disturbance or health status influence daily physical activity levels in patients with severe asthma?

T Pandya, S Majd, S Hewitt, T Harvey-Dunston, PH Bradding, RH Green, SJ Singh, RA Evans

**P154**

Safety of tiotropium in pre-school children with symptomatic persistent asthma

H Bisgaard, M Vandewalker, L Graham, P Moroni-Zentgraf, M Engel, G El Azzi, SD Vulcu, H Finnigan, E JLE Vrijlandt

---

**Thursday 8 December 2016**

**P155**

Safety of tiotropium Respimat add-on therapy in patients aged 6–17 years with symptomatic asthma

C Vogelberg, S J Szefler, E Hamelmann, A Boner, P Moroni-Zentgraf, M Engel, G El Azzi, H Finnigan, M Vandewalker

**P156**

Efficacy, safety and tolerability of once-daily tiotropium Respimat add-on therapy in children with moderate symptomatic asthma

O Schmidt, E Hamelmann, C Vogelberg, I Laki, G El Azzi, M Engel, P Moroni-Zentgraf, H Finnigan, M Vandewalker

**P157**

Seasonal variability of severe asthma exacerbations and clinical benefit from Lebrikizumab

DFC Choy, TLS Staton, JRA Arron, JO Olsson, CTJH Holweg, SG Gray, AC Chai, JGM Matthews

**P158**

Fluticasone furoate(VF)/Vilanterol (VI) once daily improves night-time awakenings in asthma

N Barnes, L Yates, MR Gibbs, R Forth

**P159**

Therapeutic benefit of mepolizumab in the Scottish Medicines Consortium (SMC) restricted sub-population – a post-hoc meta-analysis of phase IIb/III trials

RA Mehta, CEA Hartmann, NB Gunsoy, FC Albers

**P160**

Use of Omalizumab in fungal allergic asthma

HV Patel, B Kane, P Foden, LJ Holmes, GOG Tavernier, TB Morris, DM Ryan, RM Niven

---

**3.30pm – 5.30pm**

Churchill, Ground Floor

**SYMPOSIUM**

**NEW TREATMENTS FOR SMOKING CESSION**

_Chaired by: Dr Sanjay Agrawal (Leicester) and Professor Gisli Jenkins (Nottingham)_

**3.30pm**

Nicotine vaccines

Dr Onno Van Schayck (Maastricht)
Thursday 8 December 2016

4.00pm  The effects of electronic cigarettes on health
Dr Charlotta Pisinger (Copenhagen)

4.30pm  The evidence of electronic cigarettes for smoking cessation
Professor Ann McNeill (London)

5.00pm  Behaviour change – what should be done for the patient in front of us?
Professor Susan Michie (London)

Learning objectives
1) To understand the mechanisms, challenges and potential roles for a nicotine vaccine in future tobacco control.
2) Discuss potential effects of electronic cigarettes on health.
3) Provide the evidence for electronic cigarettes as a tool for smoking cessation and reduction.
4) Provide the evidence for models of behaviour change to maximise smoking cessation for the individual.

3.30pm – 5.20pm
Westminster, 4th Floor
POSTER DISCUSSION: P161 – P175
Treating idiopathic pulmonary fibrosis
Chairied by: Dr Rachel Hoyles (Oxford) and Dr Lisa Spencer (Liverpool)

P161  Unmet needs in the treatment of idiopathic pulmonary fibrosis (IPF) – insights from patient chart review in five European countries

P162  Current interstitial lung disease specialist MDT provision across the UK
TA Mikolasch, H Garthwaite, J Porter

P163  Surgical lung biopsy in the diagnosis of interstitial lung disease – a systematic literature review
TA Mikolasch, A Marshall, A Salam, JC Porter

P164  Changing patterns of the use of lung biopsy in interstitial lung disease
L Brockbank, E Hila, J Holemans, J Greenwood, M Walshaw, K Mohan

P165  Surgical lung biopsy in the diagnosis of interstitial lung disease – where are we now?
L Brockbank, E Hila, L Johns, M Walshaw, K Mohan

P166  The emerging role of airway clearance techniques in the treatment of interstitial lung disease
LSP Skevington-Postles, SA Akers, PG George, GH Housley, JB Beadle, AD Devaraj, FC Chua

P167  Does antifibrotic treatment outcomes differ in usual interstitial pneumonia based on HRCT criteria established by ATS/ERS/JRS/ALAT in 2011?
C Ng, J Hornsby, D Anderson

P168  Safety and tolerability of nintedanib in patients with idiopathic pulmonary fibrosis (IPF): one-year data from post-marketing surveillance in the United States
T Maher, I Noth, A Allinger, M Kaui, CS Conoscenti, D Oelberg

P169  Long-term safety of pirfenidone in patients with idiopathic pulmonary fibrosis: pooled analysis of 4 clinical trials
PW Noble, C Albera, L Lancaster, P Hormel, H Hulter, U Costabel

P170  Single centre experience on idiopathic pulmonary fibrosis patient tolerance of pirfenidone; impact on nurse-led ILD helpline usage
A Rathnapala, C Ruggiero, A Fries, LP Ho, RK Hoyles

P171  Health inequality exists in pirfenidone prescription for idiopathic pulmonary fibrosis in the English Midlands according to patient location
FA Woodhead, S Townsend, D Desai

P172  Demographic factors and temporal patterns affecting treatment success with pirfenidone for patients with idiopathic pulmonary fibrosis – a large retrospective review
AD Redfern, N Turner, AC Murphy, FA Woodhead
Reduction in non-elective respiratory-related hospitalizations in patients treated with pirfenidone: pooled analyses from three phase 3 trials of pirfenidone in idiopathic pulmonary fibrosis
B Ley, JJ Swigris, B Day, J Stauffer, W Chou, K Raimundo, H Collard

Effect of continued treatment with pirfenidone following a ≥10% relative decline in percent predicted forced vital capacity (%FVC) in patients with idiopathic pulmonary fibrosis (IPF)
AU Wells, C Albera, U Costabel, I Glaspole, MK Glassberg, L Lancaster, DJ Lederer, CA Pereira, JJ Swigris, B-M Day, W Chou, SD Nathan

Single centre experience of the real-life impact of pirfenidone on lung function in patients with idiopathic pulmonary fibrosis
A Rathnapala, A Fries, Y West, LP Ho, RK Hoyles

Diagnosing asthma in children using spirometry: evidence from a birth cohort study
CS Murray, P Foden, LA Lowe, H Durrington, A Custovic, A Simpson

High prevalence of unrecognised asthma in children with sickle cell disease
M Akthar, G Ruiz, S Chakravorty, C Bossley, D Rees, A Gupta

Childhood asthma management in primary care: implementation of nitric oxide and spirometry (CHAMPIONS) study. Preliminary findings
DKH Lo, A Wilson, B Gaillard, D Rowland, C Beardsmore, E Gaillard

Antecedents of asthma admissions in children: a whole population linkage study
L Thomas, S Turner

Impact of the London low emission zone on children’s respiratory health: a sequential yearly cross sectional study 2008-2014

Transition arrangements for young adults with asthma: UK national survey
CWJ Lee, BR Patel, T Nagarajan, H James, H Burhan, GH Jones

Current characteristics, coping strategies and outcomes of young people with cystic fibrosis transitioning to adulthood
R Miller, K Askew, J Bamford, N Hudson, J Moratelli, A Anderson, S Doe, SJ Bourke

Burden of Illness in school-aged patients with cystic fibrosis (CF) in the United States
J Rubin, M Bonafede, S Sikirica, B Limone, N Adolph, M Konstan

Calculation of conductive inhomogeneity in children with severe CF lung disease: which method works?
N Verger, M Arigliani, E Raywood, JA Duncan, A Bush, P Aurora

Sleep disordered breathing in children with spina bifida. Time to screen?
J Saunders, N Gibson, P Davies

Incidence and outcome of congenital lung agenesis in the North of England
N Robertson, N Miller, J Rankin, M McKean, M Brodlie, M Thomas

SCIENTIFIC PROGRAMME Thursday 8 December 2016

3.45pm – 5.10pm
Rutherford, 4th Floor
POSTER DISCUSSION: P176 – P186

Paediatric respiratory disease
Chairied by: Dr Siobhan Carr (London) and Professor Alan Smyth (Nottingham)

P176
Diagnosing asthma in children using spirometry: evidence from a birth cohort study
CS Murray, P Foden, LA Lowe, H Durrington, A Custovic, A Simpson

P177
High prevalence of unrecognised asthma in children with sickle cell disease
M Akthar, G Ruiz, S Chakravorty, C Bossley, D Rees, A Gupta

P178
Childhood asthma management in primary care: implementation of nitric oxide and spirometry (CHAMPIONS) study. Preliminary findings
DKH Lo, A Wilson, B Gaillard, D Rowland, C Beardsmore, E Gaillard

3.45pm – 5.30pm
St James, 4th Floor
SPOKEN SESSION: S82 – S87

Pulmonary vascular disease
Chairied by: Professor Nick Morrell (Cambridge) and Dr Roger Thompson (Sheffield)
3.50pm  S82
Bone marrow transplantation reduces susceptibility to pulmonary hypertension in BMPR2 deficient mice
A Crosby, E Soon, M Southwood, BJ Dunmore, M Toshner, NW Morrell

4.05pm  S83
Investigating the role of GCN2 in the pathogenesis of pulmonary hypertension
E Soon, A Crosby, M Southwood, S Moore, D Ron, S Marciniak, NW Morrell

4.20pm  S84
Identification of miR-124a as a major regulator of enhanced endothelial cell glycolysis in pulmonary arterial hypertension
P Caruso, BJ Dunmore, K Schlosser, S Schoors, C Dos Santos, C Perez-Iratxeta, JR Lavoie, L Long, L Hurst, ML Ormiston, A Hata, P Carmeliet, DJ Stewart, NW Morrell

4.35pm  S85
Reduction of CD68 macrophages causes gender specific spontaneous pulmonary arterial hypertension in mice
A Zawia, N Arnold, A Braithwaite, J Pickworth, K Hopkinson, J Iremonger, G Miller, A Lawrie

5.05pm  S87
Deficiency of toll-like receptor 3 (TLR3) exacerbates pulmonary hypertension in mice
AAR Thompson, ND Arnold, AT Braithwaite, HL Casbolt, J Iremonger, JA Pickworth, C Monaco, JE Cole, I Sabroe, A Lawrie

4.00pm – 5.00pm
Albert, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Pulmonary Rehabilitation Quality Improvement Advisory Group

4.00pm – 5.15pm
Moore, 4th Floor
SPOKEN SESSION: S88 – S91
Tuberculosis: from screening to side effects
Chairled by: Dr Marc Lipman (London) and Dr Anna Rich (Nottingham)

4.05pm  S88
Neither UK tuberculosis infection testing guideline appears cost-effective in a contemporary HIV infected population
S Capocci, J Sewell, C Smith, I Cropley, S Bhagani, A Solamalai, S Morris, I Abubakar, MA Johnson, MCI Lipman

4.20pm  S89
The use of tuberculosis chemoprophylaxis in patients of renal replacement therapy
N Ahern, H Jarvis, R Charif, OM Kon

4.35pm  S90
The nature and duration of symptoms and time to starting treatment comparing older with younger pulmonary tuberculosis patients
A Abbara, E Hardman, SM Collin, OM Kon, Z Mahomed, JAL Sullivan, K Buell, T Hansel, T Corrah, RN Davidson

4.50pm  S91
Liver function tests during tuberculosis treatment and the implications on monitoring for hepatotoxicity
CD Tweed, G Wills, AM Crook, SK Meredith, AJ Nunn, CM Mendel, SR Murray, TD McHugh, SH Gillespie
SCIENTIFIC PROGRAMME

4.00pm – 5.25pm
Mountbatten, 6th Floor
POSTER DISCUSSION: P187 – P197
From oxygen to the ITU
Chaired by: Dr Mike Davies (Cambridge) and Dr Dominick Shaw (Nottingham)

P187  Potential impact of non-arterial blood gas sampling on clinical practice
RW Thomas, NP Kelly, RT Abraham, GH Jones

P188  Nasal high flow (NHF) – is it appropriately prescribed? A retrospective case review of 93 adult patients requiring nasal high flow oxygen within a district general hospital
A Leadbetter, K Heron, J Robinson, R Mason

P189  Oxygen use is becoming more conservative on intensive care units in the UK
BR O’Driscoll, P Dark, M Wijesinghe, D McAuley

P190  Characteristics and outcome of patients with active tuberculosis requiring intensive care admission, 2010-2015
NM Shah, S Patel, K Myall, H Milburn, RA Breen

P191  Reducing the carbon footprint in a regional long term ventilation service with the use of remote monitoring
R Moses, C Taylor, S Wood, A Vyas

P192  Improving outcomes for patients with respiratory failure using protocol based care plans for NIV (non-invasive ventilation) and HFNO (high flow nasal oxygen)
AW Werpachowska, RO O’Leary, MK Kimberley, FA Archer, CM Maquire, ID Du Rand

Thursday 8 December 2016

P193  Early non-invasive ventilation versus standard oxygen therapy in immunocompromised patients with respiratory failure: a meta-analysis
RV Villalobos, UK Gopez, K Flores

P194  Early warning scores, too imprecise a tool in patients with respiratory disease?
S Forster, G Housley, J Hatton, D Shaw

P195  CURB-65, REA-ICU or SMART-COP: time to rethink CAP severity scores?
S Zaat, CL Tey, B Prathibha

P196  Predicting escalation to intensive care for patients with pneumonia with a new clinical prediction rule: SNA³P
LE Hodgson, BD Dimitrov, C Stubbs, R Venn, LG Forni

P197  Medium term impacts of ECMO on adult survivors
MM Abdelaziz, J Fowles, A Vulysteke, K Valchanov, K Sulankey, J Parmar

5.30pm – 7.00pm
Britten, 3rd Floor
THE BTS PRESIDENT’S RECEPTION
All welcome!
Friday 9 December 2016

8.00am – 9.00am
COFFEE/TEA will be served in the Whittle & Fleming, 3rd floor

8.45am – 3.30pm
Cambridge, 5th floor
MODERATED POSTER VIEWING
M10-M21
Symptom assessment and investigation of lung disease
Discussion of abstracts will take place from 2.00pm to 3.30pm in the Cambridge, 5th floor

8.00am – 8.30am
Albert, 2nd Floor
BTS JOURNAL CLUB
SOLITARY PULMONARY NODULE
Dr Anand Devaraj (London)

8.30am – 10.00am
Mountbatten, 6th Floor
SYMPOSIUM
ARDS: SEEING THE WOOD AMONGST THE TREES
Chair by: Professor Danny McAuley (Belfast) and Professor David Thickett (Birmingham)

Learning objectives
1) Introduce the component causes of ARDS and the resulting processes in the lung that characterise the syndrome.
2) Demonstrate the hyper-inflammatory patient phenotype that is characterised by a poor prognosis and potentially different treatment modalities.
3) Failure of neutrophil de-priming in ARDS could explain why ARDS patients get multi-organ failure which kills many more patients than respiratory failure. The basic science underlying neutrophil interactions with the lung endothelium is novel and compelling.
4) Why do the lungs in ARDS, in contrast to other fibrotic lung diseases, lay down collagen as part of the repair process and subsequently remodel and recover normal architecture?

SCIENTIFIC PROGRAMME

8.45am – 2.00pm
Whittle & Fleming, 3rd Floor
POSTER VIEWING
Authors present: 10.00am – 11.00am

P198-P210
Service design and delivery
Discussion of abstracts will take place from 1.30pm to 3.05pm in the Moore, 4th floor

P211-P224
Patient experiences in COPD
Discussion of abstracts will take place from 1.30pm to 3.15pm in the St James, 4th floor

P225-P233
Breathlessness
Discussion of abstracts will take place from 2.00pm to 3.10pm in the Rutherford, 4th floor

P234-P246
Understanding airways and blood vessels in the lung
Discussion of abstracts will take place from 2.00pm to 3.15pm in the Westminster, 4th floor

P247-P259
Respiratory physiology
Discussion of abstracts will take place from 2.00pm to 3.35pm in the Albert, 4th floor

P260-P271
Pneumonia and bronchiectasis: why fore and where to
Discussion of abstracts will take place from 3.15pm to 4.45pm in the Moore, 4th floor

P272-P284
Clinical characterisation of idiopathic pulmonary fibrosis
Discussion of abstracts will take place from 3.15pm to 4.50pm in the Windsor, 5th floor

P285-P299
Drugs and devices in COPD
Discussion of abstracts will take place from 3.15pm to 5.05pm in the Abbey, 4th floor
SCIENTIFIC PROGRAMME

8.30am – 10.00am
St James, 4th Floor

SPOKEN SESSION: S92 – S96
Predicting risk in pleural disease
Chairied by: Dr Rahul Bhatnagar (Bristol) and Professor Najib Rahman (Oxford)

8.35am  S92
Non-malignant pleural effusions (NMPE): a prospective study into 355 consecutive unselected patients
S Walker, A Morley, L Stadon, D De Fonseka, A Medford, N Maskell

8.50am  S93
Novel biomarkers in prognostication and treatment monitoring of malignant pleural mesothelioma – a systematic review
DT Arnold, D De Fonseka, FW Hamilton, NA Maskell

9.05am  S94
Biological markers of favourable prognosis and successful pleurodesis for malignant pleural effusion
I Psallidas, N Kanellakis, ML Thezenas, P Charles, JP Corcoran, R Hallifax, A Talwar, CC Pascuall, B Kessler, NM Rahman

9.20am  S95
Ambulatory management of pneumothorax: is there a need for a dedicated pleural team-led service?
A Fawzi, N Maddekar, S Khan, S Bikmalla, W Osman, U Maqsood, M Haris

9.35am  S96
Comparative outcomes of outpatient management of primary and secondary spontaneous pneumothorax
FA Khan, RV Reddy, M Naeem, Y Vali, I Masih, N Siddique

8.30am – 10.15am
Abbey, 4th Floor

SPOKEN SESSION: S97 – S101
Idiopathic pulmonary fibrosis therapy
Chairied by: Dr Toby Maher (London) and Professor Luca Richeldi (Southampton)

8.35am  S97
Annual rate of FVC decline in various patient sub-groups with idiopathic pulmonary fibrosis treated with pirfenidone: pooled analysis from 3 pivotal studies
PW Noble, C Albera, W Chou, U Costabel, B Day, I Glaspole, MK Glassberg, L Lancaster, DJ Lederer, SD Nathan, CA Pereira, J Stauffer, JJ Swigris

8.50am  S98
Antacid therapy and disease progression in patients with idiopathic pulmonary fibrosis (IPF) under pirfenidone treatment
M Kreuter, P Spagnolo, W Wuys, E Renzoni, D Koschel, F Bonella, TM Maher, M Kolb, D Weycker, K Kirchgässler, U Costabel

9.05am  S99
Efficacy of nintedanib on acute exacerbations reported as serious adverse events in the INPULSIS® trials in idiopathic pulmonary fibrosis (IPF)
L Richeldi, H Koegler, M Trampisch, S Geier, M Kreuter

9.20am  S100
Cumulative distribution of patients by change in FVC % predicted in the INPULSIS® trials of nintedanib in patients with idiopathic pulmonary fibrosis
U Costabel, KR Flaherty, KK Brown, W Stansen, R Schlenker-Herceg, G Raghu

9.35am  S101
Single centre experience of switching patients with idiopathic pulmonary fibrosis from pirfenidone to nintedanib
A Rathnapala, A Fries, C Ruggiero, LP Ho, RK Hoyles

8.30am – 10.15am
Churchill, Ground Floor

SYMPOSIUM
ASTHMA – FROM RESEARCH TO CLINICAL REALITY
Chairied by: Dr Ruth Green (Leicester) and Professor Liam Heaney (Belfast)
Friday 9 December 2016

8.30am  Academia to the workplace – investigating difficult asthma  
Professor Liam Heaney (Belfast)

8.45am  Treating non-eosinophilic asthma phenotypes  
Dr Dominick Shaw (Nottingham)

9.15am  The role of the upper airway in severe asthma  
Dr James Hull (London)

9.45am  CLOCK genes and asthma  
Dr Hannah Durrington (Manchester)

Learning objectives
After attending the 2016 asthma symposium, delegates will have a greater understanding of the translation of research into clinical practice in a number of key areas relevant to the care of patients with asthma. After an overview of translational research in severe asthma, the symposium will cover the role of phenotyping in tailoring asthma therapy, particularly in the absence of eosinophilic inflammation. The role of upper airway pathology as a co-morbidity, or mimic, in severe asthma will be explored and the symposium will close with an overview of the role of Circadian Locomotor Output Cycles Kaput (CLOCK) genes, and circadian rhythm, in asthma.

8.30am – 10.30am  
Windsor, 5th Floor  
SYMPOSIUM  
RARE DISEASES AND GeCiP

Chaired by: Professor Eric Alton (London) and Dr Claire Shovlin (London)

8.30am  The role of the GeCiP in rare diseases  
Professor Eric Alton (London)

8.40am  The patients’ perspective of genetic studies in clinical practice  
Fiona Copeland (PCD Support Group UK)

8.50am  Hereditary haemorrhagic telangiectasia (HHT)  
Dr Claire Shovlin (London)

9.15am  Primary ciliary dyskinesia (PCD)  
Dr Claire Hogg (London)

SCIENTIFIC PROGRAMME

9.40am  Bronchiectasis and GeCiP  
Dr Anthony De Soyza (Newcastle upon Tyne)

10.05am  Familial pneumothorax  
Professor Stefan Marciniak (Cambridge)

Learning objectives
1) To understand how Genomics England has embedded genetic medicine into everyday clinical practice.
2) The audience will gain understanding of what genetic medicine means for patients with rare diseases.
3) The audience will get updates on the genetics of four rare diseases: hereditary pneumothorax; primary ciliary dyskinesia; bronchiectasis and haemorrhagic telangiectasia.
4) The audience will have a greater understanding of “who, how and why” to refer patients with rare disease to clinical genetic services.

8.45am – 10.15am  
Moore, 4th Floor  
SPOKEN SESSION: S102 – S106  
Bacteria versus lung: mechanisms of lung infection

Chaired by: Dr James Chalmers (Dundee) and Dr Sarah Walmsley (Edinburgh)

8.50am  S102  
Vitamin D supplementation to prevent acute respiratory infections: systematic review and meta-analysis of individual participant data  
AR Martineau, DA Jolliffe, RL Hooper, L Greenberg, JF Aloia, P Bergman, G Dubnov-Raz, S Esposito, D Ganmaa, EC Goodall, C Grant, W Janssens, I Laaksi, S Manaseki-Holland, D Murdoch, RE Neale, JR Rees, S Simpson, I Stelmach, G Trilok Kumar, M Urashima, CA Camargo

9.05am  S103  
Non-typeable haemophilus influenzae down-regulates release of beta-defensin-1 from bronchial epithelial cells  
LJ Tregidgo, JL Cane, M Bafadhel
**SCIENTIFIC PROGRAMME**

**9.20am S104**
Hypoxia preconditions the innate immune response to acute bacterial pulmonary infections
RS Dickinson, AAR Thompson, JP Thomson, F Murphy, HM Marriott, A Tavares, J Willson, L Williams, A Lewis, S Forbes, RH Stimson, AG Hameed, JA Preston, A Lawrie, V Finisguerra, M Mazzone, SJ Foster, ER Chilvers, AS Cowburn, DH Dockrell, RS Johnson, RR Meehan, MKB Whyte, SR Walmsley

**9.35am S105**
Pneumococcal serotypes implicated in adult pneumococcal pneumonia, 9 years following the introduction of the infant vaccine programme in the UK
P Daniel, D Ashton, C Sheppard, S Eletu, P Sandu, D Litt, N Fry, WS Lim

**9.50am S106**
Peripheral blood neutrophils are primed and activated in bronchiectasis and are attenuated by the pro-resolving mediator Lipoxin A4
P Bedi, B McHugh, DJ Davidson, AG Rossi, AT Hill

**10.00am – 11.00am**
**COFFEE/TEA will be served in the Whittle & Fleming and Britten, 3rd floor**

**10.30am – 11.30am**
**Albert, 2nd Floor**
**BTS SPECIALIST ADVISORY GROUP OPEN MEETING**
**Critical Care**

**10.30am – 12.00pm**
**St James, 4th Floor**
**SPOKEN SESSION: S107 – S111**
**Pulmonary hypertension**
*Chaired by: Dr John Cannon (Cambridge) and Dr Jay Suntharalingam (Bath)*

---

**Friday 9 December 2016**

**10.35am S107**
Genotype-phenotype associations in pulmonary arterial hypertension caused by BMPR2 and EIF2AK4 variants
C Hadinnapola, M Haimel, M Bleda, H Bogaard, G Coghlan, P Corris, S Gibbs, D Kiely, A Lawrie, A Peacock, J Pepke-Zaba, L Southgate, M Toshner, R Trembath, A Vonk Noordegraaf, J Wharton, M Wilkins, SJ Wort, S Graf, NM Morrell

**10.50am S108**
Low skeletal muscle strength and physical activity are associated with poor outcomes in pulmonary arterial hypertension
BE Garfield, D Shao, L Parfitt, C Harries, L Price, K Dimopoulos, MI Polkey, P Kemp, SJ Wort

**11.05am S109**
Targeting the prostacyclin pathway in the treatment of connective tissue disease associated pulmonary arterial hypertension (PAH): Insights from the randomised controlled GRIPHON trial with selexipag

**11.20am S110**
2-D segmental longitudinal strain rates correlate with prognostic indicators in idiopathic pulmonary arterial hypertension
TM Crowe, P Sonecki, A Mackenzie, G Jayasekera, AC Church, MK Johnson, AJ Peacock

**11.35am S111**
Differences in characteristics and outcomes in systemic sclerosis-associated and idiopathic pulmonary arterial hypertension
S Ramjug, N Hussain, J Hurdman, C Billings, CA Elliot, DG Kiely, I Sabroe, S Rajaram, AJ Swift, R Condliffe
**Friday 9 December 2016**

10.30am – 12.00pm  
Westminster, 4th Floor  
**SPOKEN SESSION: S112 – S116**  
**Interventional trials**  
Chaired by: Professor Nick Maskell (Bristol) and Professor Moira Whyte (Edinburgh)

10.35am  
**S112**  
Long-term safety and efficacy of Ivacaftor in paediatric patients aged 2-5 years with cystic fibrosis and a CFTR gating mutation  
JC Davies, S Robertson, J Cooke, M Higgins, M Rosenfeld

10.50am  
**S113**  
High-dose vitamin D3 during intensive phase treatment of pulmonary tuberculosis in Mongolia: a double-blind randomised controlled trial  
D Ganmaa, B Munkhsul, S Bromage, B Buyankhishig, AR Martineau

11.05am  
**S114**  
Predictors of primary treatment failure in children with empyema  
ES Ward-Booth, DA Spencer, JY Paton, SP Rushton, M Brodlie, MF Thomas

11.20am  
**S115**  
HOT-HMV UK trial secondary outcome analysis: early readmission is reduced by the addition of home mechanical ventilation to home oxygen therapy in COPD patients with chronic respiratory failure following a life-threatening exacerbation  
PB Murphy, G Arbane, S Bourke, P Calverley, A Crooks, L Dowson, N Duffy, GJ Gibson, P Hughes, JR Hurst, K Lewis, R Mukherjee, A Nickol, N Oscroft, J Pepperell, S Rehal, I Smith, J Stradling, W Wedizcha, ML Polkey, M Elliott, N Hart

11.35am  
**S116**  
HoT DECAF: a RCT comparing home treatment and inpatient care in COPD exacerbations selected by low risk DECAF score  

**SCIENTIFIC PROGRAMME**

10.30am – 12.00pm  
Abbey, 4th Floor  
**SPOKEN SESSION: S117 – S121**  
**Occupational lung disease**  
Chaired by: Dr Johanna Feary (London) and Professor David Fishwick (Sheffield)

10.35am  
**S117**  
Work-related symptoms in laboratory animal workers  
J Feary, J Canizales, C Fitzgerald, B Fitzgerald, S Schofield, M Jones, P Cullinan

10.50am  
**S118**  
Can fractional exhaled nitric oxide help predict asthma in British foundry workers?  
RE Wiggans, E Robinson, J Sumner, A Codling, L Lewis, CM Barber

11.05am  
**S119**  
Inducible laryngeal obstruction masquerading as work-related asthma; a new approach  
J Feary, B Fitzgerald, J Szram, J Hull, J Selby, M Mataksori, G Scadding, P Cullinan

11.20am  
**S120**  
Asthma in fire fighter applicants: burden of disease and factors predicting successful application  
J Szram, SJ Schofield, B Fitzgerald, P Cullinan

11.35am  
**S121**  
The occupations at increased COPD risk in the large population-based UK Biobank Cohort  
SDM De Matteis, DJ Jarvis, AD Darnton, LR Rushton, PC Cullinan

10.45am – 11.45am  
Victoria, 2nd Floor  
**BTS SPECIALIST ADVISORY GROUP OPEN MEETING**  
Asthma
SCIENTIFIC PROGRAMME

Friday 9 December 2016

Learning objectives

1) Precision medicine to deliver benefits beyond rare severe asthma phenotypes to generalist practice.
2) Digital health to transform the explosion in personal data into meaningful improvements in personalised care.
3) Learning healthcare systems to transform near-real time analysis of routine health record and other ‘big’ data to deliver organisational change that improves health outcomes that matter to patients.

12.00pm – 2.00pm
LUNCH will be available to purchase in the Cafe in the Pickwick, 1st floor, and the Snack Bar in the Whittle & Fleming, 3rd floor

12.15pm – 1.15pm
Victoria, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Lung Infection

12.45pm – 1.30pm
Churchill, Ground Floor
THE MORRISTON DAVIES LECTURE
The future of medicine
Professor Sir John Bell GBE FRS (Oxford)
Introduced by: Professor Peter Ormerod (Blackburn)

1.00pm – 2.00pm
Albert, 2nd Floor
BTS SPECIALIST ADVISORY GROUP OPEN MEETING
Interstitial and Rare Lung Disease

1.15pm – 3.00pm
Abbey, 4th Floor
SPOKEN SESSION: S122 – S127
Virtual smoking: the risks of the evil weeds
Chaired by: Professor John Britton (Nottingham) and Professor Keir Lewis (Swansea)

1.20pm
S122
Effects of vaped e-cigarette liquid condensate upon human alveolar macrophage function. To vape or not to vape that is the question?
A Scott, ST Lugg, V D’Souza, K Lewis, D Dosanjh, B Naidu, DR Thickett

10.45am – 12.15pm
Churchill, Ground Floor
SYMPOSIUM
LUNG CANCER, COPD AND INTERSTITIAL LUNG DISEASE – BEGINNING TO UNDERSTAND THE INTERACTIONS BETWEEN THESE CONDITIONS
Chaired by: Dr Robert Rintoul (Cambridge) and Dr Elizabeth Sage (London)

10.45am The epidemiology patterns of lung cancer with COPD and ILD
Professor Richard Hubbard (Nottingham)

11.15am Lung cancer and COPD overlap
Dr Avrum Spira (Boston)

11.45am Lung cancer and ILD overlap
Dr Joanna Porter (London)

Learning objectives:
This session is aimed at beginning to better understand how these conditions overlap in terms of the epidemiological patterns and the biological drivers behind the diseases. Understanding how a greater understanding of the disease processes will lead to the development of new treatments for lung cancer in the setting of COPD or ILD.

10.45am – 12.20pm
Mountbatten, 6th Floor
SYMPOSIUM
DELIVERING PRECISION MEDICINE AND PERSONALISED CARE
Chaired by: Professor Chris Griffiths (London) and Professor Sebastian Johnston (London)

10.45am A patient’s perspective
Elisabeth Ehrlich (Edinburgh)

10.50am Precision medicine: impact beyond specialist care and severe asthma
Professor Ian Pavord (Oxford)

11.20am How to use big data
Dr Jennifer Quint (London)

11.50am Can learning health care systems help organisations deliver personalized care?
Professor Aziz Sheikh (Edinburgh)
**Friday 9 December 2016**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.35pm</td>
<td>S123</td>
<td>The effects of electronic cigarette flavourings on macrophage cytokine release and phagocytosis</td>
<td>RL Dacie, KB Belchamber, LE Donnelly</td>
</tr>
<tr>
<td>1.50pm</td>
<td>S124</td>
<td>The effectiveness of “in-clinic” smoking cessation support in the setting of secondary care respiratory outpatient services</td>
<td>I Valero-Sanchez, S Agrawal, S Brij, RA Evans, NJ Greening, M Perry, N Toms, E Wiggins, J Williams, MC Steiner</td>
</tr>
<tr>
<td>2.05pm</td>
<td>S125</td>
<td>Smoking cessation knowledge, beliefs and current practices among UK child health professionals</td>
<td>MJP Robertson, A Gupta, J Arumugam</td>
</tr>
<tr>
<td>2.20pm</td>
<td>S126</td>
<td>How does knowledge, perceptions and attitudes towards shisha pipe smoking vary amongst university students?</td>
<td>JM Matharoo, AA Arshad, SS Sadhra, RNW Norton-Wangford, M Jawad</td>
</tr>
<tr>
<td>2.35pm</td>
<td>S127</td>
<td>Effect of cannabis smoking on the development of bullous lung disease: a structured literature review</td>
<td>L Ribeiro, P Ind</td>
</tr>
</tbody>
</table>

---

**SCIENTIFIC PROGRAMME**

**2.30pm** Should we use biologics or anti-fibrotics in RA-UIP?  
Dr Toby Maher (London)

*Learning objectives*

1) There has been an explosion in our understanding of the genetics of fibrotic lung disease and the audience will receive an update on the latest advances in the genetics of familial pulmonary fibrosis.
2) As the treatment paradigms for idiopathic pulmonary fibrosis evolve, they leave behind a group of interstitial lung diseases where the evidence base and understanding are less clear. The audience will be updated in the latest advances in connective disease related interstitial lung diseases.
3) A key emerging issue in the therapy of patients with rheumatoid arthritis related interstitial lung disease is whether they should be treated with conventional disease modifying anti-rheumatic drugs or novel anti-fibrotic therapy. The final session will help clarify this crucial issue.

---

**1.30pm – 3.00pm**  
Windsor, 5th Floor  
**SPOKEN SESSION: S128 – S132**

**Novel approaches to lung cancer screening**

*Chaired by: Professor David Baldwin (Nottingham) and Dr Matthew Callister (Leeds)*

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.35pm</td>
<td>S128</td>
<td>LungSEARCH: a randomised controlled trial of surveillance for the early detection of lung cancer in a high risk group</td>
<td>S Spiro, P Shah, R Rintoul, J George, S Janes, M Callister, M Novelli, P Shaw, C Griffiths, M Falzon, G Kocjan, R Booton, N Magee, M Peake, P Dhillon, K Sridharan, J Allen, N Chinyanganya, V Ashford-Turner, N Counsell, A Hackshaw</td>
</tr>
<tr>
<td>1.50pm</td>
<td>S129</td>
<td>What proportion of patients with lung cancer would have been eligible for CT screening according to various proposed inclusion criteria?</td>
<td>K Gracie, M Kennedy, D Ellames, B Hawramy, A Al-Ameri, G Esterbrook, P Blaxill, G Smith, P Smith, R Naseer, K Rodgers, J Robson, E Paramasivam, M Callister</td>
</tr>
</tbody>
</table>

---

**1.30pm – 3.00pm**  
Mountbatten, 6th Floor  
**SYMPOSIUM**

**PULMONARY FIBROSIS: STILL SO MANY QUESTIONS TO BE ANSWERED**

*Chaired by: Professor Ann Millar (Bristol) and Dr Hannah Woodcock (London)*

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.30pm</td>
<td>S122</td>
<td>Familial pulmonary fibrosis</td>
<td>Professor Christine Garcia (Dallas)</td>
</tr>
<tr>
<td>2.00pm</td>
<td>S123</td>
<td>Mechanisms of ILD in connective tissue disease</td>
<td>Dr Aryeh Fischer (Denver)</td>
</tr>
</tbody>
</table>
**SCIENTIFIC PROGRAMME**

2.05pm **S130**

The prevalence of undiagnosed COPD on spirometry and emphysema on low-dose CT scans in a lung cancer screening demonstration pilot: a teachable moment?

C Horst, M Ruparel, S Quaife, A Ahmed, M Taylor, A Bhownik, S Burke, P Shaw, A McEwen, J Waller, DR Baldwin, N Navani, R Thakrar, SM Janes

2.20pm **S131**

What proportion of the UK population would be eligible for CT screening for lung cancer according to various proposed inclusion criteria?

K Gracie, M Kennedy, J Robson, M Callister

2.35pm **S132**

A randomised controlled study of lung cancer screening in Scotland using the detection of autoantibodies to tumour antigens (EarlyCDT-Lung test)


---

1.30pm – 3.05pm

Moore, 4th Floor

**POSTER DISCUSSION: P198 – P210**

**Service design and delivery**

*Chaired by: Dr Martin Allen (Stoke on Trent) and Dr Justine Hadcroft (Liverpool)*

**P198**

Anchoring COPD screening to drug services in heroin and crack smokers to improve diagnosis

R Peat, J Furlong, T Byrne, R Young, A Kangombe, T Elkin, S Renwick, D Russell, S Oelbaum, H Burhan, PP Walker

**P199**

A multidisciplinary COPD hyperinflation service: report of decision outcomes

J Chew, J Herre, S Perrott, A Coonar, J Babar, M Scarci, J Parmar, R Mahadeva

---

**Friday 9 December 2016**

**P200**

Large scale implementation of COPD discharge bundle

J Congleton, JP Crofton-Biwer, T D’Auvergne, J Bott

**P201**

Integrating patient support groups into respiratory care pathways

M McKevitt, J Bacon, R Merritt

**P202**

Optimising service delivery in asthma and COPD: consensus-driven recommendations for future service development

M Ledson, L Baskaran, C Dunford, S Gwynn, J Khambh, S Prigmore, J Scullion

**P203**

Acute oncology services and the chest physician

JA Benjamin, K Wingfield, C Garman

**P204**

Quality improvement project for emergency oxygen delivery on a respiratory ward

KE Hutchinson, S Craik, K Srinivasan, H Moudgil, N Ahmad

**P205**

Improving long term oxygen prescribing at hospital discharge: a before and after study

S Forster, G Lowrey, S Smith

**P206**

Achieving responsible oxygen prescribing to improve value: London care homes

C Lock, M Gardner, L Restrick, S Williams, M Buxton, M Hastrup, B Krishke, V Mak, D Roots, I Patel

**P207**

Self-fill oxygen systems – benefits for patients, healthcare providers and the environment

P Murphie, S Little, J Setters, N Hex

**P208**

Behavioural feed-back education intervention to enhance adherence in patients with severe uncontrolled asthma, a randomised clinical trial

I Sulaiman, MC Mokoka, E MacHale, J Seheult, C Hughes, M Holmes, S D’arcy, T Taylor, V Rapcan, D Murphy, E Hunt, SJ Lane, A Sahadevan, G Crispino, GB Diette, A Sartini-Bhreathnach, B Cushen, I Killane, RB Reilly, RW Costello
Friday 9 December 2016

**P209** Specialist respiratory pharmacist case management COPD medicines optimisation clinics: implementation and outcomes
C Jones, R Miller, R Sharkey, A Friel, D Clifford, C Darcy, B Moore, M Hall

**P210** Implementation of electronic COPD discharge care bundles: a quality improvement project
S Santharam, ST Lugg, G Packer, R Colclough, S Gompertz

1.30pm – 3.15pm
St James, 4th Floor
POSTER DISCUSSION: P211 – P224
Patient experiences in COPD
Chaired by: Professor Sally Singh (Leicester) and Dr Laura-Jane Smith (London)

**P211** Using the clinical practice research datalink (CPRD) to recruit participants from primary care to investigate chronic obstructive pulmonary disease (COPD) exacerbations
E Moore, M Hashmi, K Sultana, L Chatzidiakou, RL Jones, S Beevers, FJ Kelly, L Smeeth, B Barratt, M Wright, JK Quint

**P212** Interventions to increase referral to and uptake of pulmonary rehabilitation programmes for people with chronic obstructive pulmonary disease (COPD): a systematic review
F Early, I Wellwood, I Kuhn, T Dickerson, JWard, J Brimicombe, C Deaton, J Fuld

**P213** Positive drivers and potential barriers to implementation of hospital at home selected by low risk DECAF score
L Dismore, C Echevarria, A Van-Wersch, AJ Simpson, GJ Gibson, SC Bourke

**P214** The prevalence of respiratory symptoms and lung disease in a South London “Lung Health in Addictions” service

**P215** The incremental disease burden associated with the persistence of morning, daytime and night-time symptoms in chronic obstructive pulmonary disease patients
A Munoz, J Bailey, R Wood, A Ribera, J Nuevo

**P216** Associations between the psychological health of patients and their informal carers in advanced COPD: what are the risk factors for anxiety and depression in patients, carers and patient-carer dyads?
EZ Mi, EZ Mi, S Mendonca, AC Gardener, MC Farquhar

**P217** Improving care and support in advanced COPD – six recommendations from the population-based Living with Breathlessness study
MC Farquhar, G Ewing, P White, P Burge, R Mahadeva, AC Gardener, C Moore, S Howson, S Booth, C Saunders, T Ling

**P218** The development and psychometric validation of the early morning symptoms of COPD instrument (EMSCI)
A Hareendran, E Zaiser, B Make, E Garcia Gil

**P219** Evaluation of individual activity descriptors of the MRC dyspnoea scale: do they add up?
J Yorke, M Khan, J Vestbo, D Singh, PJ Jones

**P220** Determinants of inhaler adherence in a COPD population
I Sulaiman, B Cusden, G Greene, J Seheult, D Seow, F Rawat, E MacHale, MC Mokoka, CN Moran, A Sartinin-Breathnach, S Tappuni, P MacHale, B Deering, M Jackson, H McCarthy, L Mellon, F Doyle, F Boland, RB Reilly

**P221** Comparing the perception of feedback mechanism of the Breezhaler® device with the Ellipta® device in patients with chronic obstructive pulmonary disease (COPD): the Advantage study
P Altman, MA Bergna, GR Garcia, K Kostikas, T Guerin, AV Pino, J Whiteford
SCIENTIFIC PROGRAMME

P222  Input of a patient advisory group into evaluating the benefit:risk profile of existing and potential COPD therapies
DR Burrage, M Tumilty, S Ruickbie, EH Baker

P223  The patient’s role in the choice of new inhaler devices and dosing regimens for asthma and COPD: a preference study
T Robinson

P224  Towards person-centred care: development of a patient support needs tool for patients with advanced chronic obstructive pulmonary disease (COPD) in primary care
AC Gardener, G Ewing, M Farquhar

1.45pm – 3.15pm
Churchill, Ground Floor

SYMPOSIUM

AVERTING THE ‘ANTIBIOTIC APOCALYPSE’: STEWARDSHIP AND NOVEL STRATEGIES
Chaired by: Dr James Chalmers (Dundee) and Professor Stuart Elborn (Belfast)

1.45pm  Infection control and antibiotic stewardship for respiratory physicians
Speaker to be confirmed

2.15pm  Sugar is good (for bacteria); modulating airway glucose to reduce infections
Professor Emma Baker (London)

2.45pm  Emerging strategies to combat antimicrobial resistance in respiratory disease
Professor David Dockrell (Sheffield)

Learning objectives
1) To recognise the scope of antimicrobial resistance in the community and in hospitals, and the role of antibiotic use in driving the emergence of resistant strains.
2) To evaluate the role of practical infection control and antibiotic stewardship measures, and how they can be implemented in respiratory medicine.
3) To showcase current translational research strategies which aim to reduce respiratory infection frequency and severity.
4) To describe novel research strategies currently in development to combat antimicrobial resistance in respiratory pathogen.

Friday 9 December 2016

2.00pm – 3.10pm
Rutherford, 4th Floor

POSTER DISCUSSION: P225 – P233

Breathlessness
Chaired by: Professor Mary Morrell (London) and Dr Aashish Vyas (Manchester)

P225  Triggers of vocal cord dysfunction and asthma
SHK Chua, J Haines, C Slinger, SJ Fowler

P226  Vocal cord dysfunction; clinical outcomes of speech and language therapy intervention
N Pargeter, AH Mansur

P227  Study of clinical characteristics of patients with vocal cord dysfunction
N Pargeter, AH Mansur

P228  Is the Brompton BPAT a useful tool to assess breathing pattern disorder in asthma?
SJ Todd, R Livingston, L Grillo, A Menzies-Gow, J Hull

P229  Breath-taking outcomes: evaluation of a specialist breathlessness clinic
L Douglas, A English, GP Obita, SP Hart, MG Crooks

P230  Evaluation of a novel dysfunctional breathing service
CPW Winfield, CM Moffat, RH Hurst, JPF Fuld

P231  Breathing pattern disorders in a complex breathlessness service; classification and clinical characteristics
RM Stacey, A Vyas, SJ Fowler, SJ Fowler

P232  Does one model of pulmonary rehabilitation fit all? A modified approach to pulmonary rehabilitation
FM Lang, H Matthews, P Brice

P233  A pilot diagnostic cardio-respiratory breathlessness clinic: can a symptom-based approach achieve an earlier diagnosis?
I Valero-Sanchez, S Khatri, W Nicolson, H Seth, R Walton, DP Jackson, MC Steiner, RA Evans
Friday 9 December 2016
2.00pm – 3.30pm
Cambridge, 5th Floor
MODERATED POSTER DISCUSSION:
M10 – M21
Symptom assessment and investigation of lung disease
Chaired by: Dr Will Elston (Derby) and Dr Liz Gamble (Bristol)

M10 Living with relapsing polychondritis: a patient and carer engagement exploration
J Haines, J Hull, J Swaison, T Clark, R Niven

M11 The impact of respiratory speech and language therapy on patients’ cough related symptoms
J Haines, C Slinger, A Vyas, S Chua, SJ Fowler

M12 TRPV1 polymorphism in chronic cough: no evidence for an effect on objective measurements of cough
RD Turner, E Bourne, CA Mein, SS Birring, SO Shaheen, GH Bothamley

M13 The use of online health forums by chronic cough sufferers
A Sinha, AM Wilson, T Porter

M14 A multi-site online cross-sectional survey assessing influenza vaccination uptake among London medical students and modifiable factors influencing this uptake
GA Pankin, NE Jackson, IS Patel, AS Patel

M15 Evaluation of a novel intervention for patients with bronchiectasis: the bronchiectasis information and education feasibility (BRIEF) study
KLM Hester, J Newton, T Rapley, A De Soyza

M16 Construct validity of the needs assessment tool progressive diseases for interstitial lung disease (NAT: PD-ILD) patients
C Reigada, C Fairhurst, J Yorke, J Ross, J Boland, S Hart, D Currow, G Grande, S Bajwah, A Wells, U Macleod, M Bland, M Johnson

M17 Limited value of baseline chest radiography in adults with non-tuberculous mycobacteria
ME Murphy, NM Shah, T Bharucha, C Cash, JR Cleverley, IM Crompton, S Hopkins, MCI Lipman

2.00pm – 3.35pm
Westminster, 4th Floor
POSTER DISCUSSION: P234 – P246
Understanding airways and blood vessels in the lung
Chaired by: Dr Mona Bafadhel (Oxford) and Dr Robin Condliffe (Sheffield)

P234 Sputum cytokines and clinical biomarkers in severe asthma
R Shrimanker, S Go, S Thulborn, L Xue, ID Pavord

P235 Epigenetic landscape of the asthmatic airways

P236 The role of histone arginine methylation in gene expression of airway smooth muscle cells in asthma
KA Kaczmarek, RL Clifford, JK Patel, DE Shaw, J Dowden, AJ Knox

P237 Lung function decline is associated with serum perioestin level but not fractional exhaled nitric oxide or blood eosinophils in severe asthma
SCIENTIFIC PROGRAMME

P238  Investigating genome wide DNA methylation in airway smooth muscle cells from asthmatic and non-asthmatic donors
RL Clifford, JK Patel, DE Shaw, AJ Knox, MS Kobor

P239  Effects of tiotropium on asthma exacerbations are not explained by airway hyper-responsiveness, exhaled breath nitric oxide or airway geometry
S Jabbar, A Manoharan, BJ Lipworth

P240  Low IgE and NOT blood eosinophils predicts lack of response to omalizumab in UHSM cohort
TB Morris, HV Patel, M Demirbag, LJ Holmes, R Daly, D Ryan, RM Niven

P241  Eosinophil apoptosis is negatively associated with body mass index in asthma
A Thavakumar, AKA Wright, MA Ghebre, T Thornton, CE Brightling

P242  The airway microbiota in human rhinovirus induced asthma exacerbation
EHC Wong, J Dhariwal, L Cuthbertson, P James, M Cox, M Moffatt, W Cookson, S Johnston

P243  Specific antibody deficiency to streptococcus pneumoniae and haemophilus influenzae in asthma and fungal disease
SZ Zaidi, GT Tavernier, DR Ryan, SJF Fowler, RN Niven

P244  Haemoglobin mediated proliferation and IL-6 release in human pulmonary artery endothelial cells: a role for CD163 and implications for pulmonary vascular remodelling
L Ramakrishnan, A Anwar, JS Wort, GJ Quinlan

P245  Whole blood levels of microRNA-34a predict survival and regulate genes associated with pulmonary arterial hypertension
J Lin, J Iremonger, J Pickworth, A Rothman, H Casbolt, N Arnold, C Elliot, R Condliffe, D Kiely, A Lawrie

Friday 9 December 2016

P246  The in vitro effect of commonly used vasodilators on human pulmonary artery
A Hussain, R Bennett, K Kotidis, M Chaudhry, S Qadri, M Cowen, A Morice, M Loubani

2.00pm – 3.35pm
Albert, 2nd Floor
POSTER DISCUSSION: P247 – P259

Respiratory physiology
Chaired by: Dr Adrian Kendrick (Bristol) and Dr Annabel Nickal (Oxford)

P247  Specificity of dyspnoea relief with inhaled furosemide
JC Grogono, C Butler, H Izadi, SH Moosavi

P248  Patient eligibility for anti-fibrotic therapy in idiopathic pulmonary fibrosis can be altered by use of different sets of reference values for calculation of FVC percent predicted
K Ward, L Spurr, NR Goldman, GA Margaritopoulos, M Kokosi, E Renzoni, F Chua, TM Maher, S Ward, AU Wells

P249  Comparison of physiological versus mathematical methods for quality control in MBW normalised phase III analysis
M Arigliani, N Verger, E Raywood, J Duncan, A Bush, P Aurora, on behalf of the London Cystic Fibrosis Collaboration

P250  Real flight SpO2 compares with hypoxic challenge testing in adults with cystic fibrosis
R Peat, J Furlong, E Spencer, D Russell, M Ledson, MJ Walshaw

P251  Does fractional exhale nitric oxide and methacholine challenge test help in the diagnosis of airways disease?
J Cliff, M Hepple, MB Allen

P252  Accurate measurement of lung function in the workplace and potential effects of underestimation
JE Sumner, E Robinson, A Codling, L Lewis, RE Wiggins, LM Bradshaw, CM Barber, N Warren, S Forman, D Fishwick
Friday 9 December 2016

P253  Could application of simple diagnostic algorithm aid onward referral for optimisation of pre-existing conditions in patients being considered for major surgery?  
J Hornsby, P Higgins, A Baker, E Black, D Anderson

P254  Validation of telemedicine spirometry  
R Peat, P Szymczyk, D Russell, D Nazareth, M Shaw, Mj Walshaw

P255  Reproducibility of lung clearance index (LCI) in clinically stable adults with mild cystic fibrosis (CF)  
AR Horsley, A Shawcross, M Oladapo, A Maitra, S Cunningham, AM Jones, J Smith, F Gilchrist, F Gilchrist

P256  Respiratory muscle strength measurements in primary school children  
NTS Gharbawi, EA Gaillard, M Viskaduraki, CS Beardsmore

P257  Understanding the effects on lung function of chest binder use in the transgender population  
RJM Cumming, K Sylvester, J Fuld

P258  Infant lung function testing: a new approach using a rapid, portable system for measuring lung clearance index (LCI) in health and disease  
A Shawcross, CS Murray, J Kirkby, J Miles, K Pike, S Rees, P Aurora, A Horsley

P259  Cost analysis of implementing a PE pathway incorporating 3-level Wells scoring, PERC rules and age-adjusted D-dimers  
A Mahmood, C Durrans, S Naik, M Anwar

3.00pm – 4.00pm  
COFFEE/TEA will be served in the Britten, 3rd floor

3.15pm – 4.45pm  
Moore, 4th Floor  
POSTER DISCUSSION: P260 – P271  
Pneumonia and bronchiectasis: why fore and where to  
Chaired by: Professor Wei Shen Lim (Nottingham) and Dr Elizabeth Sapey (Birmingham)

Scientific Programme

P260  The utility of atypical pneumonia screening in community acquired pneumonia: the Leicester experience  
JA Bennett, S Robinson, R Rupesinge, J Skeemer, D Jenkins, G Woltmann

P261  Development of an extended specificity multiplex immunoassay using human monoclonal antibodies for detection of Streptococcus pneumoniae serotype-specific antigen in urine  
S Eletu, C Sheppard, E Thomas, K Smith, D Litt, N Fry

P262  The relationship between penetration or aspiration of oral intake and chest infections in ataxia telangiectasia patients  
CBR Mossey-Gaston, SG Ellum, AC DeSousae, N Oscroft, P Hales, H Baxendale

P263  Does the use of lactate improve the CURB-65 score in community acquired pneumonia patients admitted to a district general hospital?  
TW Nicholson, S Connaire, V Kronsten, S Black, JES Park

P264  Predicting mortality in hospital acquired pneumonia: a multivariate analysis  
CB Morris, S Valapraya, E McCance, AM Turner, D Dosanjh

P265  Concurrent statin and macrolide use during pneumonia treatment improves survival to hospital discharge and beyond  
FS Grudzinska, R Dancer, D Thickett

P266  Outcomes from the introduction of fungal biomarkers to the neutropenic fever pathway in a tertiary haematology department  
R Swayne, D Enoch, S Aliyu, C Crawley, P Krishnamurthy, J Craig, G Follows, B Uttenthal, J Babar, CR Sander

P267  DLCO predicts disease severity and mortality in bronchiectasis  
MJ McDonnell, M O’Mahony, D Breen, JJ Gilmartin, A O’Regan, RM Rutherford

P268  Is bronchiectasis severity influenced by aetiology or co-morbid airways disease?  
TM Quinn, AT Hill
SCIENTIFIC PROGRAMME

**P269** Acquisition of epidemic Pseudomonas aeruginosa strains in non-CF bronchiectasis patients
C Keil, S Manzoor, S Gossain, K Hardy, JL Whitehouse

**P270** Stenotrophomonas maltophilia infection in a bronchiectasis cohort
E Pigott, S Cowman, R Wilson, MR Loebinger

**P271** Rates of resectable bronchiectasis and introduction of a referral framework for surgical management of bronchiectasis
B Barmayehvar, TC Nguyen, A Sullivan, M Kalkat

3.15pm – 4.50pm
Windsor, 5th Floor

POSTER DISCUSSION: P272 – P284

Clinical characterisation of idiopathic pulmonary fibrosis
Chaired by: Dr Owen Dempsey (Aberdeen) and Dr Muhunthan Thillai (Cambridge)

**P272** Epidemiology of idiopathic pulmonary fibrosis in the UK: findings from the British Lung Foundation’s ‘Respiratory Health of the Nation’ project
N Snell, D Strachan, R Hubbard, J Gibson, T Maher, I Jarrold

**P273** Baseline characteristics of patients with idiopathic pulmonary fibrosis aged over 80 years old
GA Margaritopoulos, A Proklou, D Badenes Bonet, M Kokosi, TM Maher, EA Renzoni, AU Wells, F Chua

**P274** Cognitive function in idiopathic pulmonary fibrosis
C Sharp, HI Adamali, AB Millar, JW Dodd

**P275** Patient understanding, expectations and experiences of an interstitial lung disease specialist centre
ML Lee, MB Bennett, CL Leonard, NC Chadhuri

**P276** Development of patient reported experience measure (PREM) for idiopathic pulmonary fibrosis (IPF)
ML Lee, MB Bennett, CL Leonard, NC Chadhuri

**P277** Measuring sedentary behaviours in patients with idiopathic pulmonary fibrosis using wrist-worn accelerometers
CP Atkins, M Baxter, AP Jones, AM Wilson

**P278** Does the six-minute walk test predict survival at one year and in the longer term in patients idiopathic pulmonary fibrosis (IPF)?
J Herridge, K Yuill, AH Kendrick

**P279** Feasibility of an 8-week out-patient inspiratory muscle training (IMT) programme in patients with interstitial lung disease (ILD)
M Kouloupolou, S Greenwood, C Reilly, F Chua

**P280** Pulmonary rehabilitation (PR) for interstitial lung disease (ILD). Do patients’ perceptions match functional outcomes?
L Stanley, C Cobbett, E Morris, D Gibson, SV Fletcher

**P281** Annual change in pulmonary function in asbestosis
S Clarke, J Hoyle

**P282** Comparative use of NHANES III, ECCS and GLI prediction equations in determining spirometric indices and suitability for anti-fibrotic therapy in patients with idiopathic pulmonary fibrosis
I Cliff, A Ali, M Spiteri, H Stone

**P283** An elevated PEF/FVC ratio is a marker for ILD and is associated with traction bronchiectasis on CT scan imaging
K Cranstone, J Briggs, J Park, T Nicholson, M Unstead

**P284** Identifying patients at risk of acute exacerbation of IPF using the CPI score
E Fraser, V St Noble, R Benamore, R Hoyles, LP Ho
**Friday 9 December 2016**

**3.15pm – 5.05pm**

**Abbey, 4th Floor**

**POSTER DISCUSSION: P285 – P299**

**Drugs and devices in COPD**

*Chaired by: Professor Andrew Greening (Edinburgh) and Professor Paul Jones (London)*

**P285**  The ‘real-life’ COPD patient in the age of LABA/LAMAs: an expansion of the DACCORD study  
CV Vogelmeier, HW Worth, RB Buhl, CPC Criée, CM Mailaender, NL Lossi, PK Kardos

**P286**  Cost-consequence of Fluticasone Furoate/Vilanterol 100/25mcg for the management of COPD in the Spanish NHS: an analysis based on the COPD Salford Lung Study  
A Huerta, II Boucot, MT Driessen

**P287**  Patient preference for inhalation devices in COPD: a comparison of the Breezhaler and Respimat devices  
P O’Hagan, J Dederichs, V Boomi, M Gasser, S Walda

**P288**  COPD patients with varying severity of airflow limitation achieve highest peak inspiratory flow rate via the Breezhaler® inhaler compared to the Ellipta® or the HandiHaler® dry powder inhalers  
P Goyal, L Wehbe, J Dederichs, T Guerin, MC Moronta, AV Pino, K Kostikas, P Altman

**P289**  Drug product performance through inhaler life using a LAMA/LABA combination in a dry powder inhaler  
J Plugge, U Basaldella, B Fyrnys, T Pieper

**P290**  Drug product performance after simulated patient handling of an inhalation powder using a LAMA/LABA combination in a dry powder inhaler  
J Plugge, U Basaldella, B Fyrnys, T Pieper

**P291**  In-use stability of aclidinium bromide 400 μg/formoterol fumarate dihydrate 12 μg inhalation powder in a dry powder inhaler  
S Linne-Geyer, K Stahl, T Pieper

**SCIENTIFIC PROGRAMME**

**P292**  Pilot study to assess bronchodilator response during an acute exacerbation of COPD using a vibrating mesh nebuliser versus jet nebuliser for bronchodilator delivery  
B Cushen, A Alsaid, A Abdulkareem, RW Costello

**P293**  Drug delivery performance of budesonide (BD), glycopyrronium (GP) and formoterol (FF) triple combination (BGF) Co-Suspension™ delivery technology MDIs  
V Joshi, P Mack, J Archbell, G Li, M Arent, K Vang, S Ivatury, R Schultz, D Lechuga-Ballesteros, S Dwivedi, M Riebe

**P294**  Benefits of tiotropium/olodaterol over tiotropium at delaying clinically significant events in patients with COPD classified as GOLD B  
R Buhl, L McGarvey, S Korn, GT Ferguson, L Grönke, C Hallmann, FVoß, KF Rabe, F Maltais

**P295**  Efficacy and safety of tiotropium/olodaterol in patients with COPD by ATS category  
F Maltais, E Pizzichini, L Grönke, FVoß, E Derom

**P296**  Effect of tiotropium/olodaterol therapy on COPD exacerbations in the TONADO® studies  
E Derom, M Fležar, L Grönke, FVoß, R Buhl

**P297**  Lung-function profile before and after the first moderate to severe exacerbation during the WISDOM study  
E Wouters, H Magnussen, R Rodriguez-Roisin, K Tetzlaff, S Bell, PMA Calverley

**P298**  Tiotropium/olodaterol therapy provides symptomatic benefits irrespective of prior maintenance treatment: post hoc analyses of the OTEMTO® studies  
R Abrahams, GT Ferguson, L Bjerner, L Grönke, FVoß, D Singh

**P299**  Effects of symptom severity at baseline on lung-function and SGRQ responses in the OTEMTO® studies  
FJ Martinez, R Abrahams, GT Ferguson, L Bjerner, L Grönke, FVoß, D Singh
SCIENTIFIC PROGRAMME

3.30pm – 5.00pm
St James, 4th Floor
SPOKEN SESSION: S133 – S137
Respiratory science
Chaired by: Professor Edwin Chilvers (Cambridge) and Dr Amanda Tatler (Sheffield)

3.35pm  **S133**
Investigating Genome wide DNA methylation in airway and parenchymal fibroblasts from healthy individuals and individuals with COPD
RL Clifford, N Fishbane, P Rajasekar, AJ Fisher, MS Kobor, AJ Knox, TL Hackett

3.50pm  **S134**
How specific are fluorogenic substrates designed to analyse active protease biomarkers of respiratory disease?
CM Robb, TEG Ferguson, KL Moffitt, DG Downey, DF McCafferty, D Ribeiro, SL Martin, B Walker

4.05pm  **S135**
Circulating metabolites in chronic thromboembolic pulmonary hypertension and chronic thromboembolic pulmonary vascular occlusion
KI Zalewska, EM Swietlik, J Sanchez Hernandez, JE Cannon, D Taboada, M Newnham, C Hadinnapola, NW Morrell, MR Toshner, J Pepke Zaba

Friday 9 December 2016

4.20pm  **S136**
Potential therapeutic benefits of the human amniotic epithelium cell secretome during ex-vivo perfusion of donor lungs
JW Mayes, K Jiwa, B Leaw, J Tan, S Lau, L Borthwick, A Andreasson, J Dark, G Jenkin, R Lim, AJ Fisher

4.35pm  **S137**
De novo Pseudomonas aeruginosa colonisation is associated with increased acute rejection and bronchiolitis obliterans syndrome following lung transplantation
H Yung, J Parmar
For patients with pre-existing lung disease

**COULD NTM BE CAUSING MORE DAMAGE?**

**Targeting Susceptible Patients**
A nontuberculous mycobacterial (NTM) lung infection is a chronic condition that can get progressively worse and be debilitating in some patients. Patients with structural lung disease such as emphysema, asthma, bronchiectasis, cystic fibrosis, and COPD are at a greater risk of being infected.1-6

**More Prevalent Than Thought**
A recent survey identified nearly 20,000 patients in Europe who have been diagnosed with an NTM lung infection. Due to the fact that this infection is under-reported, the number could be higher.7,8

**NTM May Be Masked**
Symptoms, such as coughing and fatigue, are common of other respiratory comorbidities. These overlapping symptoms may mask an NTM lung infection, delaying diagnosis. Due to these factors, NTM lung infections can easily be overlooked, in some cases for months or even years.2,5

SPEAKERS’ BIOGRAPHICAL DETAILS

Dr Sanjay Agrawal is a Consultant in Respiratory Medicine at the University Hospitals of Leicester NHS Trust (UHL) and Chairs the British Thoracic Society (BTS) Tobacco Specialist Advisory Group. During this time with many others, he has promoted the work of ‘Cut Films’ a charity working in schools to reduce the uptake of smoking in children, supported the BTS National Stop Smoking Champions Network, run national smoking cessation conferences and developed the BTS National Tobacco Audit in Secondary Care.

Professor Eric Alton is Professor of Gene Therapy and Respiratory Medicine at Imperial College, London. He coordinates the UK Cystic Fibrosis Gene Therapy Consortium, bringing together Edinburgh and Oxford Universities and Imperial College, London, in a translational programme of gene therapy for CF patients.

Professor Margarida Amaral is full Professor of Molecular Biology at the Faculty of Sciences, University of Lisboa and Coordinator of BioISI Research Centre. She has been an EMBO member since 2014. Her research is focussed on the molecular and cellular mechanisms of the genetic disease cystic fibrosis with a translational perspective.

Dr Joseph Arron, MD PhD has led research at Genentech describing molecular bases for heterogeneity in respiratory disorders, enabling the development of biomarkers predictive of clinical benefit for targeted molecular therapies. He is currently Director of Immunology Discovery, a research group responsible for target discovery and preclinical therapeutic development in inflammatory, autoimmune, fibrotic, and ophthalmic diseases.

Professor Emma Baker is Professor of Clinical Pharmacology at St George’s, University of London. She leads a translational research programme investigating the impact of impaired airway glucose homeostasis on chronic lung infection and has clinical expertise in the management of advanced COPD and bronchiectasis. Research funders include MRC, BLF and Wellcome Trust.

Professor David Baldwin works as a Consultant Respiratory Physician sub-specialising in lung cancer and mesothelioma and interventional procedures. He is Chair of the Clinical Reference Group for Lung Cancer, NHS England and Lead for the East Midlands Expert Clinical Advisory Group on Lung Cancer and Mesothelioma. He is Honorary Professor in the School of Medicine at the University of Nottingham. He has obtained research grants from a variety of charities and NIHR. His primary research interests are in CT screening and lung cancer epidemiology. He is lead respiratory physician on the UK CT Lung Cancer Screening Trial (UKLS). He has published over 140 papers. He has held the positions of Honorary Secretary of the British Thoracic Society, Clinical Lead on the NICE Lung Cancer Guideline Development Group and Chair of the Quality Standards Group on Lung Cancer. He works with Public Health England and the National Cancer Research Institute. He enjoys time with his family and is a keen windsurfer and advanced instructor.

Professor Sir John Bell GBE FRS is Regius Professor of Medicine at Oxford University, and Chairman of the Office for the Strategic Coordination of Health Research. He served as President of the Academy of Medical Sciences (2006-2011).

His research interests are in the area of autoimmune disease and immunology where he has contributed to the understanding of immune activation in a range of autoimmune diseases. In 1993, he founded the Wellcome Trust Centre for Human Genetics, one of the world's leading centres for complex trait common disease genetics. He is a non-executive director of Roche Holding AG, is Chairman of the Gates Foundation Global Health Advisory Board, sits on the board of Genome England Limited and Chairs its Science Advisory Committee. He was responsible for the working party that produced the Academy of Medical Sciences “Strengthening Clinical Research” report, highlighting the need for the UK to focus some of its attention on developing expertise in translational research. In December 2011, Sir John was appointed one of two UK Life Sciences Champions by the Prime Minister.

Dr Rahul Bhatnagar is a Clinical Lecturer at the University of Bristol’s Academic Respiratory Unit. His research interests relate to the management of pleural disease, specifically focusing on clinical trials in malignant effusions, novel technologies, and pleural infection. In addition to his academic role, Dr Bhatnagar is also an ST7 in respiratory and general medicine based in the South West Deanery, and maintains a strong interest in education and skills training relating to pleural disease.
SPEAKERS’ BIOGRAPHICAL DETAILS

Dr Stephen J Bourke MD FRCP FRCPI DCH is a Consultant Physician in Respiratory Medicine at the Royal Victoria Infirmary, Newcastle upon Tyne. He is Director of the Newcastle Adult Cystic Fibrosis Centre. He is Chair of the BTS CF Specialist Advisory Group and has research interests in clinical aspects of cystic fibrosis.

Professor Carolyn S Calfee MD MAS is Associate Professor of Medicine and Anesthesia at the University of California, San Francisco (UCSF) where she attends in the intensive care unit. After training in internal medicine and pulmonary/critical care at UCSF, she joined the faculty in 2007. Her primary academic interests focus on the molecular epidemiology of the acute respiratory distress syndrome (ARDS), including molecular phenotyping of ARDS and the role of environmental exposures in ARDS pathogenesis, and on ARDS clinical trials.

Dr Peter Campbell is Head of Cancer Genetics and Genomics at the Wellcome Trust Sanger Institute, having started a Wellcome Trust Senior Clinical Fellowship in 2010. He completed specialist training in Haematology in New Zealand and Australia in 2002. Following this, he completed a PhD at the University of Cambridge in the molecular pathogenesis of myeloproliferative disorders. Since 2007, Dr Campbell has been employed at the Cancer Genome Project, Wellcome Trust Sanger Institute.

His major interest is cancer genomics, and in particular genome-wide analyses of somatic mutations in tumours. The four major areas of interest have been:

- the discovery of new cancer genes;
- the identification of somatic mutation processes operative in tumours;
- the characterisation of patterns of cancer evolution; and
- the translation of these fundamental insights about cancer biology into better management of patients.

Further details are available at: http://www.sanger.ac.uk/research/faculty/pcampbell/

Dr James Chalmers is a Senior Lecturer and Honorary Consultant at the University of Dundee. His group are focussed on understanding how neutrophils interact with bacteria in chronic airway infection and how they contribute to disease progression. He runs a portfolio of studies in bronchiectasis, COPD and pneumonia funded by the Wellcome Trust, European Union, MRC, Scottish Government and Charities. He is associate editor of the ERJ and a member of the international editor board of The Lancet Respiratory Medicine. He chairs the European Bronchiectasis Registry (EMBARC).

Professor Rachel C Chambers PhD, FRSB is Professor of Respiratory Cell and Molecular Biology and Director of the Centre for Inflammation and Tissue Repair (CITR) at University College London (UCL). Professor Chambers is currently Vice-Dean for Innovation and Enterprise for the Faculty of Medical Sciences. She received her undergraduate degree from King’s College London and completed her PhD studies at the National Heart and Lung Institute in London in 1995. She serves on major peer-review committees and is currently Associate Editor for Thorax. Her research focus is on the elucidation of the cell and molecular mechanisms leading to lung inflammation, remodelling and fibrosis with a view to identifying new targets for therapeutic intervention. Professor Chambers also leads a fibrosis discovery biology group at UCL as part of a major academia-industry strategic alliance with GlaxoSmithKline (GSK). She is also academic lead for an MRC and GSK co-funded multi-institutional open-innovation collaborative research network in the area of fibrosis and immuno-inflammation – the Experimental Medicine Initiative to Explore New Therapies (EMINENT).

Professor Edwin R Chilvers is Professor of Respiratory Medicine at the University of Cambridge and President elect of the British Thoracic Society. His research interests include the molecular basis of neutrophil priming, activation and apoptosis, in particular the role of the phosphoinositide 3-kinase (PI3K) and hypoxia inducible factor (HIF) in signalling these events. Past posts include registrar training at the Hammersmith Hospital, an MRC Research Training Fellowship at the University of Leicester and NHLI Imperial College London, and a Wellcome Trust Senior Research Fellowship at the University of Edinburgh. He has held an Honorary NHS Consultant position since 1992, currently at Addenbrooke’s Hospital, and remains clinically active with a particular interest in interstitial lung disease. He is Deputy Head of the Department of Medicine at the University of Cambridge, Director of the Cambridge Clinical Academic Training Office (CATO), Chair of the Faculty Board of the School of Veterinary Medicine, and past Chair of the Association of Clinical Professors in Medicine. He was awarded a ScD from Cambridge in 2016 and elected a Fellow of the Academy of Medical Sciences in 2007.
SPEAKERS’ BIOGRAPHICAL DETAILS

Dr Deborah Clarke did her PhD in respiratory pharmacology at the National Heart and Lung Institute, Imperial College understanding the role of lipid mediators in airway inflammation and asthma. She went on to study cell signaling at The University of Nottingham and on to Medimmune to head their Cambridge fibrosis research group. She joined Boehringer Ingelheim in 2016 as a medical scientific liaison working in the asthma and COPD disease areas.

Dr Robin Condliffe is a Consultant Physician in the Sheffield Pulmonary Vascular Disease Unit. He has published widely on outcomes in different forms of pulmonary hypertension. He was a member of the 5th World Pulmonary Hypertension Task Force and currently sits on the Pulmonary Hypertension CRG.

Fiona Copeland has two sons who have primary ciliary dyskinesia (PCD). She combines running her own project management business with chairing the PCD Family Support Group. She also represents patients within the Ciliopathy Alliance, NIHR Biomedical Research Unit at the Royal Brompton Hospital, the European Respiratory Society and Bronch UK.

Professor Adnan Custovic is Clinical Professor of Paediatric Allergy at Imperial College London. His professional training consisted of specialist training in paediatrics (University Children’s Hospital Sarajevo, 1987-91) and successive appointments as Clinical Research Fellow and Specialist Registrar in Allergy (University Hospital of South Manchester, 1992-98). This period saw him awarded MSc (1991), MD with Gold Medal (1996) and PhD (2000). He was awarded a prestigious National Asthma Campaign Senior Clinical Research Fellowship (2000-2005). Professor Custovic was promoted to the position of Reader at the University of Manchester in 2000, which was followed by a professorship in 2002. He was a Professor of Allergy at the University of Manchester until September 2015, when he moved to Imperial College.

In 2015 he was awarded the European Respiratory Society Gold Medal for research in asthma. In 2013 he received the BSACI William Frankland Medal for outstanding contributions to clinical allergy, and the CIPP President’s award for distinguished achievements in childhood asthma. He has delivered numerous prestigious keynote/named lectures, including Nemacolin Asthma Conference (2014), Alain De Weck Memorial Lecture (2013), Cas Motala Memorial Lecture (South African Allergy Society, 2013), James Hutchison’s Memorial Lecture (Hong Kong Paediatric Society, 2012), the RSM Priscilla Piper Lecture (2011) and Caspar Weinberg Lecture (2007). He has supervised 17 PhD/MD students to completion, was an Associate Editor of Thorax, and serves on 13 journal editorial boards. He has served as a Secretary of the BSACI for two terms, and as President of the Asthma Section of the EAACI.

Professor Jane Davies is a Professor of Paediatric Respiriology and Experimental Medicine at Imperial College London and Honorary Consultant, Royal Brompton Hospital. Her research focus is cystic fibrosis, in particular two areas of bacterial infection and novel treatments. She is the site lead at the ECFS Clinical Trials Network, where she directs the Core Facility for Lung Clearance Index, a sensitive physiological outcome measure, increasingly adopted in paediatric trials.

Dr Anthony De Soyza is a Consultant Respiratory Physician at Freeman Hospital, Newcastle upon Tyne and Senior Lecturer at Newcastle University. Dr De Soyza runs an academic group at Newcastle University studying host defence and pathogen interactions. He is service lead for the adult bronchiectasis service and provides a tertiary service for the North East. He occasionally sits in front of computers striving to get more funding in bronchiectasis! He serves on the BTS and ERS bronchiectasis guidelines groups. He is also NIHR Specialty Group Co Chair for Respiratory Disorders and has major roles in bronchiectasis clinical trials. He is lead for the MRC funded BronchUK collaborative (www.bronch.ac.uk) and was delighted when bronchiectasis was selected as an eligible condition for inclusion.

Dr Anand Devaraj BSc MD MRCP FRCR is a Consultant Thoracic Radiologist at the Royal Brompton Hospital, London and an Honorary Senior Lecturer at Imperial College, London. His specialist interests are in the areas of lung cancer screening with CT, lung nodule management and the imaging of diffuse lung disease and pulmonary hypertension. Dr Devaraj is widely published in the field of thoracic CT and is regularly invited to speak at both national and international meetings.
SPEAKERS’ BIOGRAPHICAL DETAILS

Professor David Dockrell completed his MB at Trinity College Dublin and post-graduate training at the Mayo Clinic. He is Professor of Infection Medicine at the University of Edinburgh and a Consultant in Infectious Diseases. His research focuses on the pathogenesis of infectious diseases and the innate immune system, focusing on macrophage responses to pathogens such as Streptococcus pneumoniae, Staphylococcus aureus and on HIV. He leads the MRC funded SHIELD consortium combatting antimicrobial resistance through host directed responses.

Professor Louise Donnelly is a Professor of Respiratory Cell Biology, in the Section of Airway Disease at the National Heart and Lung Institute, Imperial College London. Her research interests are primarily focused on the cellular profile of inflammatory lung diseases including asthma and COPD. In particular, her work investigates how inflammatory cells are altered in the disease state and how these changes can be exploited in the development of novel therapeutic strategies. To this end, Professor Donnelly’s group have established a number of human primary cell systems to investigate mechanisms of aberrant inflammation.

Professor Julian Downward trained with Mike Waterfield in London and Bob Weinberg in Boston before setting up his own lab in 1989 at the Cancer Research UK London Research Institute, now the Francis Crick Institute, where he is Associate Research Director. His work focuses on the role played by major oncogenes such as RAS and EGFR in human cancer. He established that EGFR is the product of the erbB proto-oncogene and was responsible for mapping out the signaling pathways linking EGFR to RAS and downstream of RAS to the MAP kinase and PI 3-kinase pathways. He is a Fellow of The Royal Society.

Dr Hannah Durrington is a Senior Clinical Lecturer at the University of Manchester and an Honorary Respiratory Consultant at the University Hospital South Manchester. She holds an Asthma UK Senior Clinical Academic Development Award. Her research investigates the circadian biology of asthma. Currently, she is investigating whether the time of day that an allergen challenge occurs, determines the magnitude of inflammatory response. She also has a clinical study looking at time of day differences in biological parameters in asthmatic subjects compared to healthy controls.

Professor Christopher Dye is Director of Strategy in the Office of the Director-General at the World Health Organization, and has worked at WHO since 1996. He holds a first-class degree in biology from the University of York and a DPhil in zoology from the University of Oxford. From 2006–2009, he was also Professor of Physics at Gresham College in the City of London. He is a Visiting Professor of Zoology at the University of Oxford, a member of the Board of Reviewing Editors for Science, a Fellow of The Royal Society and of the UK Academy of Medical Sciences.

Elisabeth Ehrlich is a patient, retired teacher and a Patient Involvement Lead for the Asthma UK Centre for Applied Research. She collaborates with researchers in grant applications, reviews lay summaries and PhD proposals. She contributed to an npj Primary Care Respiratory Medicine article published in 2014 and Asthma UK’s Forgotten Generation report.

Professor J Stuart Elborn CBE, MD is Professor of Respiratory Medicine at Imperial College London/Royal Brompton Hospital, London and Queen’s University of Belfast. The focus in his research is in chronic suppurative lung disease (cystic fibrosis and bronchiectasis), particularly understanding pathophysiology of infection and inflammation and the translation of new therapies into clinical practice.

Dr Johanna Feary is a Respiratory Physician at the Royal Brompton Hospital and Honorary Clinical Research Fellow in the Department of Respiratory Epidemiology, Occupational Medicine and Public Health, Imperial College, London. She completed a PhD in asthma epidemiology at the University of Nottingham in 2011. Dr Feary is a member of the Group of Occupational Respiratory Disease Specialists (GORDS), and the BTS Occupational and Environmental Lung Disease SAG. Currently, she holds an NIHR postdoctoral fellowship and, as part of this, is undertaking a study into the health of laboratory scientists. Clinical interests include the assessment and management of occupational lung disease and severe asthma.

Dr Aryeh Fischer is Associate Professor of Medicine at the University of Colorado School of Medicine within the Divisions of Rheumatology and Pulmonary Sciences and Critical Care Medicine. His specific area
of clinical and research expertise is within autoimmune associated lung diseases, and autoimmune interstitial lung disease in particular. He has developed clinical expertise with patients referred nationally for evaluation of autoimmune lung disease. Dr Fischer has served as an invited lecturer on autoimmune and interstitial lung diseases at numerous national and international pulmonary and rheumatology conferences and has published extensively within this domain.

Professor David Fishwick MBChB, FRCP(UK), AFOM, Diving Physician 2d, FFOM (hon), MD, is currently a Consultant Respiratory Physician in Sheffield, with a major clinical and research interest in workplace health and particularly in respiratory health. He also works as the Co-Director of the Centre for Workplace Health, the Chief Medical Adviser for HSE and is an Honorary Professor of Occupational and Environmental Respiratory Medicine at the University of Sheffield. He also works within the new Science Division of HSE.

His research interests are focussed around the broad interface between the work environment and respiratory health. This work has led previously to the development of professional standards in this area, including standards of care for asthma and COPD at work. He also retains strong links with his research collaborators in New Zealand, as he lived and worked in Wellington for two years. One of his current main clinical and research interests is exposure to respirable crystalline silica.

Professor Fishwick currently Chairs the British Lung Foundation Northern Regional Group, Chairs the British Thoracic Society Occupational Lung Disease Specialist Advisory Group and sat on the ERS Taskforce for Occupational Specific Challenge Testing, in addition to being a member of the GORDS group. He is currently part of the new ATS/ERS COPD Burden of Occupational Disease Taskforce and he also Chairs the BTS SIGN ERG for occupational asthma.

Professor Christine Kim Garcia MD, PhD is a Professor in the Departments of Human Genetics and Internal Medicine at the University of Texas Southwestern Medical Center. Her research focuses on the discovery of rare mutations in different genes that lead to inherited forms of interstitial lung disease.

SPEAKERS’ BIOGRAPHICAL DETAILS

Dr Adam Giangreco is Principal Research Associate, located within UCL Respiratory, Division of Medicine, University College London. The goal of his research is to increase our understanding of the stem cells and molecular mechanisms driving lung regeneration that are disrupted in chronic lung injury. In particular, his laboratory studies how intercellular adhesion, interactions with the local tissue microenvironment, and downstream signalling pathway activation within stem cells regulates homeostasis, repair, and tumorigenesis. He achieves this using translationally relevant in vitro and in vivo models including human airway stem cell cultures, transgenic mouse models, and high throughput, high content human lung organoid assays.

Dr Robert Gray is a full time clinical academic in cystic fibrosis. He is presently a Wellcome Trust Intermediate Clinical Fellow at the University of Edinburgh, working in the UoE/MRC Centre for Inflammation Research, and an Honorary Consultant Physician in Respiratory Medicine at NHS Lothian. His research aims to understand mechanisms of inflammation in CF with a particular focus on myeloid cells and epithelial cells, and the central role of calprotectin in lung inflammation.

Professor Chris Griffiths is Joint Director of the Asthma UK Centre for Applied Research and a Principal Investigator at the MRC and Asthma UK Centre in Allergic Mechanisms of Asthma.

Dr Mark Griffiths is Consultant Physician in the Adult Intensive Care Unit at St Bartholomew’s Hospital and Professor of Critical Care Medicine at Imperial College London. He is a founder member of the UK and Ireland Acute Lung Injury Research Group and Chair of the Intensive Care Society Guideline Development Group for the Management of ARDS. He has clinical and research interests in acute lung injury, alveolar epithelial cell responses to injury and mechanical stimulation and ICU acquired weakness.

Dr Charles Haworth is Director of the Cambridge Centre for Lung Infection (incorporating the Adult Cystic Fibrosis Centre, the Lung Defence Clinic and the Respiratory Immunology Clinic) at Papworth Hospital. He is also an Honorary Consultant at Addenbrooke’s Hospital in Cambridge. The Lung Defence Clinic oversees the care of >1500 patients with bronchiectasis associated with primary and secondary
SPEAKERS’ BIOGRAPHICAL DETAILS

immunodeficiency syndromes, non-tuberculous mycobacterial disease, aspergillus related lung disease, rheumatoid arthritis, serious childhood infection, chronic aspiration and primary ciliary dyskinesia.

Dr Haworth trained at the Manchester Adult Cystic Fibrosis Centre, the Royal Brompton Hospital and at Hammersmith Hospital, before moving to Cambridge in 2003. He co-authored the US CF Foundation and European CF Society NTM guidelines published in Thorax in December 2015 and is Co-chair of the BTS NTM Guidelines Committee. He is also a member of the BTS bronchiectasis and ERS bronchiectasis guidelines committees. He collaborates with several research groups at the University of Cambridge, is a member of the European Union funded iABC consortium and is co-chief investigator of two current multicentre novel therapy clinical trials in people with bronchiectasis.

Dr Claire Hogg is a Consultant at the Royal Brompton and Harefield Foundation Trust in London, UK. She is the Clinical Lead for the National Primary Ciliary Dyskinesia [PCD] Service in London, for both diagnostics and management of this rare disease. The Royal Brompton is one of three National specialist centres for PCD in the UK where there are an estimated 3,000 patients. The Royal Brompton service cares for over 300 patients and sees around 400 referrals for diagnostics each year. This represents one of the largest PCD cohorts in Europe.

Alongside the clinical service, Dr Hogg runs an active research programme, focussing on chronic suppurative lung diseases, with a specific research and development programme for advances in PCD diagnostics. Foremost of these is their three dimensional electron tomography programme. Development of this technique has allowed for identification of ultrastructural abnormalities in the axoneme of patients with Hydin mutation [published 2012], dynein regulatory complex defects and those with DNAH11 mutations. These genetic variations had no previously known ultrastructural defect as determined by conventional 2D electron tomography. They also have close collaborations with the geneticists at UCL, resulting in several novel gene discoveries. Dr Hogg is UK lead for the first clinical trial in PCD as part of an EU programme grant [BESTcilia FP-7], is Head of the BEAT-PCD Training School [EU COST Action grant] and a member of the EU PCD Taskforce. She also leads the PCD domain for the current Genomics UK Project, tasked with improving genetic diagnosis for all patients with rare diseases.

Professor Richard Hubbard is a Consultant Chest Physician and Epidemiologist based at the University of Nottingham. His is currently the British Lung Foundation Professor of Respiratory Epidemiology. His main clinical interest is the care of people with interstitial lung disease and the short and long term respiratory complications of bone marrow transplantation. Currently his main research projects relate to the aetiology and natural history of idiopathic pulmonary fibrosis and access to care for people with lung cancer, but Professor Hubbard is also interested in the epidemiology of allergic disease and provision of care for all people with lung disease.

Professor Sam Janes won an MRC Training Fellowship to perform a PhD and then a post-doctoral period working in the CRUK Lincoln’s Inn Fields Institute with Fiona Watt working on integrin adhesion molecules and cancer cell survival. He then moved as an MRC Clinician Scientist to UCL leading a group interested in the role of stem cells in lung cancer pathogenesis and treatment of lung disease using cell therapies. He was awarded a Wellcome Trust Senior Clinical Fellowship in October 2010 to work on novel cell therapies for lung cancers resulting in a DPFS first-in-man award and recently won his Wellcome Senior Fellowship renewal to study lung cancer pathogenesis.

Professor Janes works as a Consultant at UCLH with a particular interest in lung cancer, mesothelioma, interventional and diagnostic bronchoscopy and early lung cancer detection. He is Head of the Respiratory Research Department at UCL, Director of the Lung Cancer Board for London Cancer and was Chair of the BTS Winter Meeting 2013-2015.

Professor Gisli Jenkins is Professor of Experimental Medicine at the University of Nottingham. He completed his medical training at the University of Southampton before undertaking postgraduate training in Respiratory Medicine in London. During this time he undertook basic scientific training funded by an ARC Fellowship and obtained a PhD in Biochemistry from UCL before doing post-doctoral studies at UCSF as part of an ARC Clinician Scientist Fellowship.

His clinical and research focus is on interstitial lung disease, and pulmonary fibrosis in particular. He is academic lead at the Nottingham Interstitial Lung Diseases Unit and runs the pulmonary fibrosis work strands for the MRC Nottingham Molecular Pathology Node, and the Genomics England Clinical
Interpretation Partnership in Respiratory Medicine. His research has been published in leading academic journals including the Journal of Clinical Investigation, Lancet Respiratory Medicine and Science Signalling.

Professor Jenkins’ research group has received funding from Academic organisations including the Wellcome Trust, the Medical Research Council, Arthritis Research UK and Asthma UK as well as industrial contracts with Biogen, Galacto, GlaxoSmithKline, MedImmune and Novartis.

Professor Jenkins is joint Editor-in-Chief of Thorax, Chair of the BTS Science and Research Committee and is also a Trustee of the charity Action for Pulmonary Fibrosis.

Professor Simon Johnson is Professor of Respiratory Medicine at the University of Nottingham and Director of the National Centre for LAM. His research group work on proteolytic mechanisms of lung destruction in chronic lung diseases including asthma, lung fibrosis, COPD and LAM.

Lt Col Andy Johnston is a Respiratory Physician and Intensivist at the Royal Centre for Defence Medicine, Queen Elizabeth Hospital Birmingham. He graduated from the University of Dundee in 1993, and trained in Scotland, the North of England and the West Midlands. He has experience in managing high volume, high acuity combat trauma, both in Afghanistan and at QEHB. In his role as a specialist in chemical, biological, radiological and nuclear medicine he was part of the training team for UK military, NHS, and international medical personnel deploying to Sierra Leone to treat Ebola patients. At the beginning of 2015 he worked at the specialised MOD run Ebola Treatment Unit in Sierra Leone, caring for health care workers with suspected and confirmed Ebola infection.

Professor Sebastian L Johnston is Professor of Respiratory Medicine and Allergy at the National Heart and Lung Institute, Imperial College London. He is Director of the MRC and Asthma UK Centre in Allergic Mechanisms of Asthma, is the Asthma UK Clinical Professor and is a UK National Institute of Health Research Senior Investigator. He Edited Thorax from 2002-2010 and serves as Associate Editor or on the Editorial Boards of several other respiratory and allergy journals. He has published >400 scholarly manuscripts and 18 patents.

Notable achievements include establishing the viral aetiology of the majority of asthma and COPD exacerbations, discovering novel mechanisms of susceptibility to virus infection in asthma and COPD, and developing novel treatment approaches for acute exacerbations of these diseases.

Professor Malcolm Kohler is the Chair of Respiratory Medicine at the University of Zurich and Clinical Director of the Department of Pulmonology, University Hospital of Zurich. Professor Kohler’s research has a focus on chronic respiratory disorders and their interaction with the cardiovascular system. More recently he has worked on innovative methods on exhaled breath metabolomics. Professor Kohler has published >180 articles.

Dr Heinke Kunst is a Senior Lecturer at Queen Mary University and Honorary Consultant in Respiratory Medicine at Barts Health. Her main interest is translational research in management of active/latent TB and non-tuberculous mycobacterial disease.

Professor Gary Lee is a Professor at the University of Western Australia and directs the Pleural Services, Sir Charles Gairdner Hospital; and the Pleural Medicine Unit, Institute of Respiratory Health. His pleural programme includes laboratory and clinical arms closely integrated with a tertiary pleural service. He has 200 publications (H-index 37), and has spoken in 26 countries.

Professor Mark Lindsay obtained a degree in Natural Sciences from the University of Cambridge (1986) and his PhD from Nottingham Trent University (1991). In the intervening period, he has worked at Imperial College London, AstraZeneca Pharmaceuticals and the University of Manchester. Since 2011, he has been Professor of Molecular Pharmacology at the University of Bath. Professor Lindsay’s research has been focused upon understanding the role of non-coding RNAs in inflammatory and respiratory diseases including asthma, idiopathic pulmonary fibrosis, lung cancer, osteoarthritis and psoriatic arthritis.

Dr Michael Loebinger is a Consultant Respiratory Physician at the Royal Brompton Hospital, UK, specialising in chronic lung infection. He Chairs the Infection Specialist Advisory Group for the British Thoracic Society (BTS), Co-chairs the BTS Bronchiectasis Guideline Committee and is on the Steering Committee for the BTS Non-Tuberculous Mycobacteria and European Respiratory Society (ERS) Bronchiectasis Guidelines. He is a founding member of the UK and European (EMBARC) Clinical and
SPEAKERS’ BIOGRAPHICAL DETAILS

Research Bronchiectasis Networks and sits on the ERS Respiratory Infection Education Task Force. He also holds an Honorary Senior Lecturer position at Imperial College and supervises PhD, MSc and medical students.

Dr Toby Maher is an NIHR Clinician Scientist and Senior Lecturer at the National Heart and Lung Institute, Imperial College, London where he leads the Fibrosis Research Group. He is also a Consultant Physician at the Royal Brompton Hospital, London. His specific research interests include biomarker discovery, clinical trials in ILD and study of the role of the microbiome and cellular senescence in the pathogenesis of idiopathic pulmonary fibrosis. Dr Maher is current Chair of the Specialised Respiratory Clinical Reference Group. He is an Associate Editor for PLOS One and is on the editorial board of the European Respiratory Journal and European Respiratory Review and the advisory board of Lancet Respiratory Medicine. Dr Maher has authored over 100 papers and chapters on idiopathic pulmonary fibrosis, sarcoidosis and other ILDs.

Professor Stefan Marciniak is Professor of Respiratory Science at the University of Cambridge where his lab studies the role of abnormal protein folding in lung disease. He is an Honorary Consultant Respiratory Physician at Addenbrooke’s Hospital with a clinical focus on pleural medicine including familial pneumothorax. http://www.med.cam.ac.uk/marciniak/

Professor Adrian Martineau is Clinical Professor of Respiratory Infection and Immunity at Barts and The London School of Medicine, Queen Mary University of London. His group researches the effects of vitamin D on human health, with a particular focus on the prevention and treatment of respiratory infections. The work encompasses laboratory investigations, proof-of-concept studies, multi-centre clinical trials and meta-analysis. He is Chief Investigator for the ViDiKids study, an MRC-funded n=5,400 clinical trial investigating whether vitamin D can prevent tuberculosis infection among primary schoolchildren in Cape Town, South Africa.

Professor Nick Maskell is Professor of Respiratory Medicine at the University of Bristol and Honorary Consultant at North Bristol NHS Trust, Bristol. He undertook his DM thesis on pleural diseases in Oxford prior to taking up a consultant post at North Bristol NHS Trust in 2003. His research interests include clinical trials in pleural disease, mesothelioma and patient safety during pleural procedures. He Leads the Pleural Service at North Bristol NHS Trust and the Bristol Pleural Clinical Trials Unit at the University of Bristol. He is the Chief Investigator for a number of UK-CRN multi-centre RCT pleural trials. He Chaired the last BTS Pleural Disease Guideline Group, and is Co-chair of the 2016 BTS Mesothelioma Guideline Group.

Professor Danny McAuley is a Consultant and Professor in Intensive Care Medicine at the Regional Intensive Care Unit at the Royal Victoria Hospital and Queen’s University of Belfast. He undertook his training in Belfast, Birmingham, London and San Francisco. He is Co-Director of Research for the UK Intensive Care Society. He has two main research interests; acute respiratory distress syndrome and clinical trials.

Professor Doug McEvoy is Director of the Adelaide Institute for Sleep Health at Flinders University in South Australia. He is Principal Investigator of the Sleep Apnoea cardioVascular Endpoints (SAVE) study, a large international multi-centre, randomized controlled trial of CPAP treatment in high cardiovascular risk patients with co-morbid OSA, which was completed in 2016.

Professor Susan Michie is Professor of Health Psychology at University College London, UK. She studied Experimental Psychology at Oxford University, followed by Clinical Psychology at the Institute of Psychiatry, London University and a DPhil in Developmental Psychology. She is a chartered clinical and health psychologist, and elected Fellow of the Academy of Social Sciences, the US Society of Behavioural Medicine, the US Academy of Behavioural Medicine Research, the European Health Psychology Society and the British Psychological Society. Professor Michie is Director of the Centre for Behaviour Change (http://www.ucl.ac.uk/behaviour-change) and of the Health Psychology Research Group at UCL. She leads an extensive programme of research developing the science of behaviour change interventions and applying that science to intervention development and evaluation. Areas of application focus on prevention of ill health and implementation of evidence-based practice. Methodological projects include the Wellcome Trust-funded Human Behaviour-Change Project (www.humanbehaviourchange.org) and the MRC-funded Theory and Techniques project (www.ucl.ac.uk/behaviour-change-techniques).
SPEAKERS’ BIOGRAPHICAL DETAILS

Personal website: www.ucl.ac.uk/health-psychology/pages/michie

Professor Ann Millar is Emeritus Professor of Respiratory Medicine at the University of Bristol, having trained in London and Liverpool. She has clinical interests in diffuse parenchymal lung disease, acute lung injury and the immunocompromised lung. Professor Millar’s research interests are in the mechanisms regulating the outcome of acute and chronic lung injury. She is past-President of the BTS.

Professor Alyn H Morice is Foundation Chair in Respiratory Medicine, Head of Respiratory Medicine and Head of Centre for Cardiovascular and Metabolic Research at Hull York Medical School. He qualified at Cambridge University and after House jobs in London undertook research (MD) into the pharmacology of asthma at St Mary’s Hospital. As Clinical Lecturer at Addenbrooke’s Hospital, Professor Morice developed his interest in cough, demonstrating cough hypersensitivity caused by ACE inhibitors. In 1989 Professor Morice was appointed as Senior Lecturer in Sheffield developing a pulmonary vascular service and the first UK Cough Clinic. In 1998, Professor Morice was appointed to the Foundation Chair in Respiratory Medicine in Hull University (now part of Hull York Medical School). The Cough Clinic has become the largest centre within Europe with an international pattern of referral. Unique investigational strategies provide diagnosis and treatment advances which are incorporated into national and international guideline documents. Professor Morice has led the European Respiratory Society and British Thoracic Society Taskforces on Cough.

Dr Ian Mudway is the Head of the Lung Biology Group within the Environmental Research Groups at King’s College London, as well as a member of the MRC-PHE Centre for Environment and Health and the NIHR-PHE HPRU in the Health Impact of Environmental Hazards. He has a long standing interest in the interaction of the human lung with gaseous and particulate pollution, with a strong focus on the impact of diesel exhaust emissions on the health of urban populations.

Dr Andrew Nunn joined the MRC’s Tuberculosis and Chest Diseases Unit in 1966, working with Wallace Fox as part of the team that conducted the landmark trials which led to the worldwide adoption of short course chemotherapy. From 1989 he joined the MRC’s Uganda AIDS programme which initially evaluated the dynamics of the HIV epidemic in a developing country setting. On returning to the UK Dr Nunn became a founder member of the MRC Clinical Trials Unit where he was initially responsible for the development of trials in neglected disease areas. Currently he is co-chief investigator on the multi-centre STREAM phase III trial in MDR-TB.

Professor Paul M O’Byrne obtained his Medical Degree at University College, Dublin. He is the EJ Moran Campbell Professor of Medicine, and Chair of the Department of Medicine at McMaster University. His research interests are on the mechanisms and treatment of asthma. He has published more than 420 peer reviewed papers, 98 book chapters, and edited 12 books. He was elected Fellow of the Royal Society of Canada in 2010 and to the Canadian Academy of Health Sciences. He was appointed Distinguished University Professor at McMaster University in 2015.

Professor Jean-Claude Pairon is Professor of Medicine and Health at Work at Paris-Est Créteil University and Head of the Unit of Occupational Diseases at the Centre Hospitalier Intercommunal of Créteil, France. His research has been developed in the framework of an INSERM team within the Institute of Mondor Biomedical Research (IMRB) 955-Unit (Créteil, France). Research topics include: biological mechanisms involved in the response of the respiratory system to nanoparticles; epidemiological research in the field of occupational respiratory diseases; clinical research applied to occupational respiratory diseases, research on inhaled mineral particles. Professor Pairon is the coordinator of the Asbestos-Related Disease Cohort (ARDCO) programme, a multiregional pilot programme implemented by the French public authorities in the aftermath of a consensus conference held in 1999 on the medical follow-up of retired asbestos-exposed workers.

Professor Ian D Pavord DM FRCP FERS FMedSci, is Professor of Respiratory Medicine at the University of Oxford. Before this he was a Consultant Physician and Honorary Professor of Medicine at the Institute for Lung Health, Glenfield Hospital, Leicester. He is an NIHR Senior Investigator. He is a former joint editor of Thorax and medical advisor for Asthma UK. He has a research interest in the clinical aspects of inflammatory airway diseases and is the author of 350 publications with an H-index of 71. He delivered the Cournand
SPEAKERS’ BIOGRAPHICAL DETAILS

Lecture in 2004 and received the 2016 ERS Gold Medal for his research in asthma.

Dr Charlotta Pisinger MD MPH PhD, works at the Research Center for Prevention and Health, Capital Region of Denmark. She is Associate Professor at the University of Copenhagen (Master of Public Health). Dr Pisinger is former President of the Danish Society of Tobacco Research, is used as a national tobacco expert, has written the national smoking cessation guidelines, published many tobacco-related reports and presented scientific evidence in the EU-Parliament. She has published the first systematic review on electronic cigarettes and health; recently updated on request by WHO. She is a former Vice-President of the Danish Society of Epidemiology and has been investigator in several intervention trials including, among others, one of the world’s largest lifestyle intervention studies.

Dr Sanjay Popat PhD FCRP is a Consultant Thoracic Medical Oncologist at the Royal Marsden Hospital in London, Reader in Cancer Medicine at Imperial College London, and Honorary Faculty at the Institute of Cancer Research in London. He received his MBBS degree with triple distinction and his PhD in 2002 from the University of London. His postdoctoral work included a Clinician Scientist Fellowship at the Institute of Cancer Research. His research has focused on thoracic tumour development and treatment, in particular the identification of biomarkers predictive of therapeutic effect.

Dr Popat is active in numerous professional organisations. He is Chair of the British Thoracic Oncology Group (BTOG), Foundation Council Member of the European Thoracic Oncology Platform (ETOP), Chair of the Advanced Disease Subgroup of the UK National Cancer Research Institute (NCRI) Lung Cancer Clinical Studies Group, as well as active in the European Organisation for Research and Treatment of Cancer (EORTC) Lung Group, and the International Thymic Malignancy Interest Group (ITMIG).

Dr Joanna Porter is a Reader in Respiratory Medicine at University College London. Her clinical interest is in interstitial lung disease (ILD), in particular ILD in the context of autoimmune disorders. She is the Clinical Lead for ILD at UCLH and Medical Director of the UCL partners ILD Consortium, and the Breathing Matters Charity. Her lab works on leucocyte migration into the lung and immune mediated lung disease. She has a translational research interest in novel imaging techniques, in ILD and other inflammatory lung diseases.

Dr Ken Powell PhD is Chairman of ReViral, a company developing anti-viral drugs to treat Respiratory Syncytial Virus (RSV) infection. Prior to his current role Dr Powell was: Executive Chairman of Q-Chip a Cardiff, Wales based life science company developing novel delayed release formulations of drugs (merged with Midatech and listed on AIM); Founder and CEO of Arrow Therapeutics Ltd (a specialised antiviral drug discovery company acquired by AstraZeneca PLC for $150 million in February 2007); Professor at UCL; and a senior Pharmaceutical executive.

Dr Powell has more than 30 years experience of the pharmaceutical industry and the biotechnology sector. He is an expert virologist and has been involved in the development of multiple anti-viral compounds against herpes viruses, HIV, Hepatitis C and RSV.

Dr Jennifer Quint is a Clinical Senior Lecturer in Respiratory Epidemiology at the National Heart and Lung Institute, Imperial College and Honorary Consultant Physician in Respiratory Medicine at the Royal Brompton Hospital, London.

Dr Quint’s research interests centre on the use of electronic health records to study respiratory and cardiovascular diseases, including bronchiectasis, asthma and chronic obstructive pulmonary disease (COPD). In addition, she is involved in clinical work and is active on a number of international committees. She is currently secretary of the Epidemiology Group for the European Respiratory Society.

Professor Najib M Rahman is Consultant and Associate Professor of Respiratory Medicine at the University of Oxford and Oxford Centre for Respiratory Medicine. He leads the Oxford Pleural Unit, is Director of the Oxford Respiratory Trials Unit (ORTU) and is Tutor for Medicine at University College, Oxford.

Professor Rahman is currently involved in randomized and observational studies in pleural infection, mesothelioma and malignant pleural effusion intervention. ORTU currently runs 26 studies in total, in both pleural and non-pleural respiratory areas. He is trained in thoracoscopy, thoracic ultrasound (RCR Level III) and clinical trials methodology. He has published in the fields of pleural disease, clinical trials and thoracic ultrasound.
Dr Robert Rintoul is Lead Clinician for Cancer at Papworth Hospital NHS Foundation Trust and Director of the Papworth Hospital Clinical Trials Unit. The focus of his work is around clinical trials, tissue banking and translational research in malignant mesothelioma and early detection of lung cancer. He holds grants from several major funding bodies and is Chief Investigator for multiple clinical trials and for MesobanK UK, a national mesothelioma bioresource (www.mesobank.com). Dr Rintoul is the research lead for lung cancer for the Clinical Research Network Eastern and a member of the British Thoracic Society Science and Research Committee and NHS England Lung Cancer Clinical Reference Group. Part funded by the Cambridge Biomedical Research Centre, he is co-lead for the Aerodigestive Programme of the Cambridge Cancer Centre.

Dr Elizabeth Sapey qualified as a physician from the Royal London Medical School, UK. She gained her PhD studying neutrophil inflammation with age and in chronic obstructive pulmonary disease (COPD) in 2010 from the University of Birmingham, where she now works as a clinician scientist. Dr Sapey became a Senior Lecturer in Respiratory Medicine and an Honorary Respiratory Consultant in November 2012. She is clinically active, specialising in respiratory medicine (primarily COPD) and general internal medicine in the University Hospital Birmingham NHS Foundation Trust.

Dr Sapey’s research focuses on the role of the neutrophil as a mediator of tissue injury in respiratory disease and infection. She has a particular interest in assessing how and why vital granulocyte cellular functions (including migration and phagocytosis) alter with age and chronic and acute respiratory disease and how these can be modulated to improve health. This includes assessing cell signalling pathways including the phosphoinositide 3-kinase (PI3K) signalling system during neutrophil adhesion and migration. Ongoing laboratory projects include targeting aberrant neutrophil signalling pathways in COPD to improve bacterial killing, understanding drivers of innate immunosenescence in healthy ageing and modulating immunoparesis in sepsis.

Dr Dominick Shaw MD MRCP is an Associate Professor and Honorary Consultant at the University of Nottingham and Nottingham University Hospitals Trust. His research interests include asthma and airways disease, in particular the non-invasive assessment of airway inflammation, asthma therapeutics and the use of novel data sources to understand respiratory disease. His work has been published in peer reviewed journals and he is involved in basic, translational and clinical studies.

Dr Shaw leads the commissioned difficult asthma service in Nottingham and is also a former member of the British Thoracic Society Asthma Advisory Group. He is a keen swimmer despite his advancing years.

Professor Aziz Sheikh OBE is Professor of Primary Care Research and Development and co-Director of the University of Edinburgh’s Centre for Medical Informatics. He is co-Director of the 14-university Asthma UK Centre for Applied Research, and a co-investigator in the MRC/Asthma UK Centre in Allergic Mechanisms of Asthma and the Farr Institute.

Professor Anita Simonds is a Consultant in Respiratory and Sleep Medicine at Royal Brompton and Harefield NHS Foundation Trust. She has a clinical and research interest in sleep disordered breathing and ventilatory support, and manages 2000 adults and children on long term ventilation, and 8000 on CPAP. She is Chief Editor of European Respiratory Journal Open Research, and the new ERS Handbook of Non-Invasive Ventilation.

Dr Elaine Soon read medicine at King’s College in Cambridge after working part-time in a laboratory during school holidays to earn pocket money. She has not managed to escape the gravitational attraction of academia and has gone on to work on the pathobiology and genetics of pulmonary hypertension as an NIHR lecturer after completing a PhD with Professor Nick Morrell in Cambridge.

Dr Avrum Spira, a Professor of Medicine, Pathology and Bioinformatics, and the Alexander Graham Bell Professor in Health Care Entrepreneurship at Boston University, is founding Chief of the Division of Computational Biomedicine in the Department of Medicine and Function Leader for the Bioinformatics and Computational Biology Program at BU’s Clinical and Translational Science Institute. Recently, Dr Spira was named Director of the Boston University-Boston Medical Center Cancer Center. He also is an attending physician in the Medical Intensive Care Unit at Boston Medical Center.

Dr Spira obtained his MD from McGill University in Montreal, and completed his internal medicine residency
at the University of Toronto and his fellowship in Pulmonary and Critical Care Medicine at BMC. During his fellowship, Dr Spira obtained a master’s degree in Bioinformatics from Boston University.

Since his 2003 appointment to the BU faculty, Dr Spira has built a translational research program that focuses on genomic alterations associated with smoking-related lung disease, leading to a molecular test for the early detection of lung cancer that may transform the clinical care of high-risk smokers. His research program is based on the paradigm that smoking and other inhaled carcinogens create a ‘field of molecular injury’ in epithelial cells that line the respiratory tract. Sampling these more accessible tissues allows the detection of lung cancer and other smoking-related lung diseases without assessing the lung itself.

Dr Spira serves as Principal Investigator on grants from the National Cancer Institute (NCI); National Heart, Lung, Blood Institute (NHLBI), National Institute of Environmental Health Sciences (NIEHS) and the Department of Defense (DoD), and has authored close to 100 papers.

Dr Spira is a member of the NIH’s Cancer Biomarker Study Section (CBSS), Senior Editor at Cancer Prevention Research as well as Associate Editor at the American Journal of Respiratory and Critical Care Medicine. He was elected a member of the American Society for Clinical Investigation (ASCI) in 2010. He recently was selected to serve on the NIH/NIEHS Advisory Council.

**Professor Rob Stockley** is currently Professor of Medicine at the University Hospital Birmingham and Director of the Lung Immunobiochemical Research Group. He has a longstanding interest in COPD phenotypes with particular reference to airway inflammation, proteinases and anti-proteinases, and especially the role of the neutrophil, bacteria and exacerbations, and lectures widely on these aspects. He has been a member of the GOLD Scientific Committee since 2010 and member of the Executive Committee and Board of Directors. He is currently involved in the 2016 update. Professor Stockley has published more than 450 peer reviewed papers, reviews and chapters, edited seven books, supervised 35 higher degree theses in clinical and basic science and been a member of the editorial board of more than 15 journals. He has initiated and established the International meeting on COPD held every two years in Birmingham.

**Professor John Stradling** MD, FRCP is Emeritus Professor of Respiratory Medicine at Oxford University having directed the Respiratory Sleep Service in Oxford until 2013. His recent research has concentrated on OSA and cardiovascular consequences, recently using the CPAP-withdrawal model. He has published over 200 original publications in peer reviewed journals, recently receiving the William C Dement award from the AASM, an honorary doctorate from Grenoble University, the BTS Medal, and was a keynote speaker at the ATS in 2016.

**Professor Kelan Tantisira** MD, MPH is an Associate Professor of Medicine at the Channing Division of Network Medicine and in the Division of Pulmonary and Critical Care Medicine, Brigham and Women’s Hospital and Harvard Medical School, Boston. He has clinical and research expertise in asthma, with a focus on asthma pharmacogenomics.

**Dr Amanda Tatler** is a Senior Research Fellow within the Division of Respiratory Medicine at the University of Nottingham. Her fellowship is co-funded by Asthma UK and the Medical Research Foundation. Her research is focused upon understanding the...
mechanisms that drive lung tissue remodelling in the context of disease, particularly asthma and pulmonary fibrosis. She has undertaken periods of post-doctoral research at both the University of California San Francisco and Harvard Medical School. To date she has contributed significantly to our understanding of how cell surface integrins contribute to tissue remodelling in respiratory disease. Her current work aims to develop a “breathing” precision cut lung slice model to investigate the effects of breathing and deep inspirations on lung tissue.

Dr Muhunthan Thillai is a Chest Physician and Clinical Lead of the Cambridge Interstitial Lung Disease Group at Papworth Hospital. He trained at St Mary's Medical School in London and was later a Wellcome Trust Fellow at Imperial College London where he was awarded a PhD in Immunology and Proteomics. He has a specific interest in sarcoidosis and has written a number of research papers and book chapters as well as given presentations at international scientific meetings on the disease.

Dr Steve Turner qualified in medicine from the University of Newcastle upon Tyne in 1992. He trained in general and respiratory paediatrics in the North East of England with extended stays in New Zealand and Australia, holding a research position in the latter. He has been a Senior Clinical Lecturer at the University of Aberdeen since 2003. His research interests are the early origins of chronic respiratory disease and asthma monitoring.

Dr Jakko van Ingen is a Consultant Clinical Microbiologist and Head of the Mycobacteriology Reference Laboratory at Radboud University Medical Center in Nijmegen, the Netherlands. He has authored over 100 papers on mycobacterial disease in peer-reviewed scientific journals and is consulted on diagnosis and treatment of non-tuberculous mycobacterial disease from all over the world.

Professor Onno van Schayck is Professor of Preventive Medicine at the CAPHRI School for Public Health and Primary Care, Maastricht University. His research focuses on the prevention of chronic diseases. He has been acknowledged to be the most cited researcher in the world in his area of expertise. He has co-authored more than 450 international and 100 national peer reviewed articles.

Dr Louise Wain is an Associate Professor of Genetic Epidemiology at the University of Leicester, undertaking research into the genetic architecture of respiratory health and disease. Dr Wain has played a prominent role in the discovery of genetic associations with lung function and COPD, and led the first genetic analyses of lung function and smoking behaviour in UK Biobank.

Professor Daniel Weiss is Professor of Medicine, Pulmonary Medicine, Department of Medicine at the University of Vermont Medical Center. He has a longstanding interest in lung repair and regeneration after injury, notably gene and cell therapy approaches for lung diseases. In particular this has included developing novel techniques with which to investigate and enhance lung gene and cell therapies. Recent published work in cell therapy approaches for lung diseases has included several benchmark publications that have included the first ever trial of cell therapy for COPD and that have helped define whether exogenous cells can engraft in the lung. As such, Professor Weiss views himself as a translational scientist whose work spans from benchtop to clinical trials. He has also instituted a biennial meeting held at the University of Vermont, Stem Cells and Cell Therapies in Lung Biology and Diseases, that is widely viewed by the NIH, FDA, and non-profit Respiratory Disease Foundations as the major meeting in the field. His overall goal is to provide a firm scientific basis for clinical application of cell therapies in lung diseases. Professor Weiss has been funded by the NIH, DOD, non-profit Respiratory Disease Foundations, and by industry sources since 1995. Current work in the laboratory is focused in three major areas: 1) Bioengineering approaches for development of functional lung tissue ex vivo; 2) Immunomodulation of lung inflammation by mesenchymal stromal cells (MSCs); 3) Development of cell therapy-based approaches for lung disease.

Dr Martin Wildman is an Adult Respiratory Physician specialising in CF. He also has an Honorary position at ScHARR where he works as a health services researcher with an interest in complex intervention development and evaluation using approaches that link the MRC complex interventions pathway to improvement science. He also has a post within the Sheffield Microsystems Coaching Academy where he delivers training in improvement science (http://www.sheffieldmca.org.uk/). Dr Wildman spent four years in the Health Services Research Unit at the London School of Hygiene and Tropical Medicine where he completed a Masters in public health and completed a PhD linking registry data within the...
Intensive Care National Audit Research Centre (ICNARC) data to prospectively collected trial data to develop the CAOS model to investigate ICU gate keeping and outcomes for patients with COPD. He is currently Co-PI on the £2 million NIHR programme grant to develop CFHealthHub, a complex intervention designed to support self-management and habit formation in adults with CF (http://www.sheffieldmca.org.uk/).

**Professor Tom Wilkinson** is Professor of Respiratory Medicine at the University of Southampton, Faculty of Medicine and Honorary Consultant at University Hospitals Southampton. He trained at the University of Cambridge and Barts and the London School of Medicine and completed his PhD at UCL studying disease mechanisms driving infective exacerbations of COPD. He is Lead of the Southampton COPD Group, and Respiratory Theme Lead for the Wessex CLAHRC. His research seeks to improve understanding the mechanisms which drive susceptibility to respiratory infections in patients with chronic lung disease, and to develop new vaccines and therapies to impact on these. Professor Wilkinson leads a long term collaborative programme of vaccine development with GSK, is a co-chair of the British Thoracic Society Home Oxygen Guidelines Standards of Care Committee and co-founder of the health technology company myMHealth.

**Dr Hannah Woodcock** qualified from the University of Cambridge and is now a Respiratory SpR in the North East Thames Deanery. She recently completed a PhD at UCL on idiopathic pulmonary fibrosis. Her research focussed on understanding the molecular mechanisms and signalling pathways involved in driving fibrosis, with a particular emphasis on the PI3K/mTOR signalling axis.

**Professor Paul Workman** FRS is Chief Executive Officer and President of The Institute of Cancer Research (ICR), London. From 1997 to 2016 he was Director of the CRUK Cancer Therapeutics Unit at ICR – the world’s largest non-profit cancer drug discovery group. Professor Workman has won numerous awards and was elected as a Fellow of the Royal Society in 2016.
EXHIBITORS’ INFORMATION

Action for Pulmonary Fibrosis
Stand number 68
Action for Pulmonary Fibrosis is a charity established by patients, family members and medical professionals, all with a personal connection to IPF. Our vision is a world in which everyone affected by PF has a better future. We support patients and families, educate the wider audience about the disease and raise money for research. Since APF began the number of support groups in the UK has increased from 5 to 35 with more to come. We are funding training for health care professionals in primary care, sponsoring IPF-specific palliative care rooms and have recently called on NHS England to mandate the collection of data on IPF to improve patient care. To learn about the full range of our work please visit www.actionpulmonaryfibrosis.org. We welcome requests from professionals with ideas and projects that will help us achieve our vision.
Tel: 01543 442152
Email: info@actionpulmonaryfibrosis.org
Website: www.actionpulmonaryfibrosis.org
Twitter: @ActionPFcharity

Adherium Ltd
Stand number 18
Adherium Ltd (ASX:ADR) is a world-leading innovator of patient management systems for inhaled respiratory medications. As the pioneering company to develop Smartinhaler™ technologies and receive FDA clearance to market and CE marking, with more than 15 years’ experience, Adherium has a growing intellectual property portfolio. Smartinhaler™ has been used in over 40 projects spanning 29 countries, resulting in a comprehensive body of peer-reviewed publications that demonstrate the accuracy and effectiveness of the Smartinhaler™ solutions.
Email: contact@smartinhaler.com
Website: www.smartinhaler.com

Aerogen
Stand number 45
Aerogen is a global leader in the design and manufacture of high performance acute care aerosol drug delivery systems. As a market leader in aerosol drug delivery, Aerogen’s innovative technology has changed the science and set a new standard of aerosol drug delivery in critical care which is resulting in better care for the most critical patients from pre-term babies to adults. Innovative products such as Aerogen Ultra and Aerogen Solo containing our palladium vibrating mesh technology, turn liquid medication into a fine particle mist, gently and effectively delivering drugs to your patient’s lungs.
Tel: +353 91 540 400
Website: www.aerogen.com

Airsonett AB
Stand number 15
Airsonett AB is a Swedish born company. Airsonett® offers Temperature controlled Laminar Airflow (TLA) technology, protecting patients from exposure to allergens, spores, bacteria, viruses and other airborne particulates. Positioned at the bedside, it draws air through a filter, capturing them and thus providing patients filtered air to breathe whilst sleeping. Airsonett® is for adults and children with severe allergic asthma with poor disease control despite optimal drug therapy at Step 4 (BTS/SIGN) or above. The device (CE marked; Class 1) is non-invasive and non-pharmacological. It has no side effects and is suitable for adults and children.
E-mail: info@airsonett.com
Website: www.airsonett.com
Facebook: https://www.facebook.com/airsonettinternational

Alere
Stand number 6
Alere believes that when diagnosing and monitoring health conditions, Knowing now matters™. Alere delivers on this vision by providing reliable and actionable information through rapid diagnostic tests, enhancing clinical and economic health outcomes globally. To learn how rapid diagnostics from Alere can help support the differential diagnosis of respiratory diseases, visit us at Stand 6.
Tel: 0161 483 5884
Email: uk.roi.customers@alere.com
Website: www.alere.com

Ambu
Stand number 31
Ambu are dedicated to improving patient safety and determined to advance single-use devices. The manifestations of our efforts range from early inventions like the Ambu bag to our latest landmark solutions such as the aScope™ – the world’s first single-use Videoscope and the AuraGain™ – the only anatomically curved, 2nd generation SGA with integrated gastric access and intubation capability. Millions of patients and healthcare professionals worldwide depend on the functionality and performance of our products. Within the field of anaesthesia, Ambu offers a wide range of products, all of which have their own place in the difficult airway algorithm.
Tel: 01480 498 403
Email: uksales@ambu.com
Website: www.ambu.com
Association for Respiratory Technology and Physiology (ARTP)  Stand number 60
The ARTP is the sole professional organisation in the UK for practitioners working in respiratory and sleep physiology.
ARTP provides nationally, professionally recognised qualifications in lung function testing/spirometry. An important function of the ARTP is the provision for CPD and the writing of standards/guidelines. ARTP organises an annual conference and training courses including blood gas sampling, interpretation, respiratory muscle assessment, sleep disorders and cardiopulmonary exercise testing. ARTP coordinates spirometry training centres throughout the UK and also write/publish textbooks in lung function testing and physiology.
ARTP Sleep represents practitioners working in Sleep Medicine.
Tel: 01543 442 141
Email: admin@artp.org.uk
Website: www.artp.org.uk

The Association of Chartered Physiotherapists in Respiratory Care (ACPRC)  Stand number 63
The Association of Chartered Physiotherapists in Respiratory Care (ACPRC) is a national body of physiotherapists interested in all aspects of respiratory care, with 1000 members. The ACPRC aims to promote health and best practice in respiratory physiotherapy for the benefit of all.
Email: secretary@acprc.org.uk
Website: www.acprc.org.uk
Twitter: @theacprc

Association of Respiratory Nurse Specialists (ARNs)  Stand number 64
ARNS was created in 1997 by respiratory nurses, for respiratory nurses, and this ethos is still very true today as we celebrate our 20th year in 2017. ARNS remains the only nursing-led membership organisation within the UK respiratory specialty field. Today, our organisation benefits from the participation of more than 1,400 members across the UK.
ARNs collaborates with other respiratory care organisations, as well as government and NHS initiatives in order to influence policy and developments for respiratory services, such as the NICE and BTS Guidelines. ARNS is a member of the European Respiratory Nurses Association.
Tel: 07740 117 902
Email: info@arns.co.uk

EXHIBITORS’ INFORMATION
Website: www.arns.co.uk
Twitter: @ARNS_UK  You can also find us on Facebook

AstraZeneca  Stand number 3
AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of diseases in three therapy areas – respiratory and autoimmunity, cardiovascular and metabolic diseases, and oncology. The company is also active in inflammation, infection and neuroscience through numerous collaborations. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide. For more information please visit:
Website: www.astrazeneca.com

Baywater Healthcare  Stand number 40
Baywater Healthcare is a specialist provider of healthcare services to patients with long term conditions, delivering high-quality, cost-effective solutions with care closer to home.
Working exclusively in the health sector, our experienced team provides in-home services for: oxygen, nebuliser and ventilation therapies, CPAP treatment/adherence management, sleep diagnostics and long term condition management through telehealth solutions. Our services help to reduce hospitalisations and other secondary effects.
Our aim is to support patients in their therapy and encourage long term compliance to improve health outcomes.
We offer 24/7 support, first line triage and training at home, alongside advice/support from specialist nurse advisers.
Tel: 0845 602 0776
Email: sales@baywater.co.uk
Website: www.baywater.co.uk

BMJ  Stand numbers 55 & 56
BMJ is a healthcare knowledge provider and a leader in respiratory content. Together with our partner the British Thoracic Society, we publish Thorax (ranked 3rd in the field of respiratory) and its Open Access sister title, British Open Respiratory Research. Visit our stand today to learn more about how to submit your research and access content.
Tel: 020 7387 4410
Email: support@bmj.com
Website: www.bmj.com/
EXHIBITORS’ INFORMATION

Boston Scientific Corporation

Stand number 20

Boston Scientific Corporation is a worldwide developer, manufacturer and marketer of medical devices, investing $876 million in research and development, with 22 million patients treated with our products each year. Our products are used in a range of interventional medical specialties, including interventional radiology, interventional cardiology, peripheral interventions, neuro-modulation, neurovascular intervention, electrophysiology, cardiac surgery, vascular surgery, endoscopy, oncology, urology, gynecology and within pulmonology. Boston Scientific is dedicated to transforming lives through innovative medical solutions that improve the health of patients around the world. Within the respiratory field we are committed to advancing the diagnosis and treatment of pulmonary diseases by focusing on the development of less invasive devices and procedures.

Tel: 07468 708 039
Email: angela.smith@bsci.com
Website: www.bostonscientific.com
www.bronchsuite.com

The British Association for Lung Research (BALR)

Stand number 59

The BALR provides a focus for exchange of ideas between all respiratory researchers, basic scientist and clinician alike. Fostering collaboration and furthering fundamental pulmonary research since 1982, thus fulfilling the initial focus of the Society to promote respiratory research throughout the UK. The BALR has an annual summer meeting and a joint BTS/BALR symposium at the BTS Winter Meeting each year. The BALR provides membership benefits including travel awards to national and international conferences and offers support for seminars and workshop provision.

Email: admin@balr.co.uk
Website: www.balr.co.uk

CareFusion

Stand number 30

At CareFusion, we are united in our vision to improve the safety and lower the cost of healthcare for generations to come. Our Interventional Specialties portfolio offers innovative solutions for acute and chronic drainage including the PleurX® catheter system for compassionate home-management of recurrent pleural effusion and malignant ascites and the Safe-T-Centesis® drainage system for thoracentesis and paracentesis.

Tel: 0114 268 8880
Email: IS-Sales@carefusion.com
Website: www.carefusion.co.uk/our-products/interventional-specialties

Chiesi Ltd

Stand numbers 16 & 23–26

Chiesi Limited is a family-owned company with a reputation for research and innovation. Chiesi specialises in respiratory, neonatal and rare diseases. Chiesi is committed to improving patient outcomes and quality of life.

Tel: 0161 488 5555
Website: www.chiesi.uk.com

Clement Clarke International

Stand number 17

Respiratory specialists Clement Clarke International, have a series of innovative devices to showcase at the BTS Meeting. Among these devices are DispozABLE Spacer, the paper cup spacer for emergency SABA delivery and some new training tools, aimed at standardising pMDI technique training, based on the existing Flo-Tone device, now with improved features. Included in these new training tools are Flo-Check; a simple device to facilitate multi-patient use of pMDI placebos and a positive whistle mask for Able Spacer to enable young children a better experience with their spacer — it also works with Rafi-Tone App, making the whole experience fun!

Tel: 01279 414 969
Email: resp@clement-clarke.com
Website: www.clement-clarke.com

Education for Health

Stand number 65

Education for Health are a leading UK based educational charity, working to transform the lives of people living with long term health conditions. Our vision is for a world where everyone living with a long term condition receives high quality care and can manage their condition to the best of their ability. We firmly believe that the way to achieve this is through a well informed and well educated workforce. If you would like to find out more or work with us, please get in touch.

Tel: 01926 838 969
Email: info@educationforhealth.org
Website: www.educationforhealth.org

European Respiratory Society

Stand number 58

ERS is an international organisation that brings together physicians, healthcare professionals, scientists
and other experts working in respiratory medicine. We are one of the leading medical organisations in the respiratory field, with a growing membership representing over 150 countries worldwide. ERS was founded in London in 1990 from the merger of the Societas Europaea Physiologiae Clinicae Respiratoriae (SEPCR, founded 1966) with the European Society of Pneumology (SEP, founded 1981). Our mission is to promote lung health in order to alleviate suffering from disease and drive standards for respiratory medicine globally. Science, education and advocacy are at the core of everything we do. ERS is involved in promoting scientific research and driving standards through the training of respiratory professionals. It also plays a key role in education and in advocacy – raising awareness of lung disease amongst the public and politicians.

Tel: +41 21 213 01 01  
Website: www.ersnet.org

**General Medicine Group**  Stand number 47

General Medicine Group specialise in placing locum and permanent doctors within the NHS, leading private hospitals and public sector organisations across the UK. We can provide you with long or short-term locum work, ad-hoc shifts, out-of-hours, on call and permanent jobs. As preferred supplier to the NHS, we receive priority access to jobs at all grades before other agencies. We have successfully placed over 40 respiratory consultants into NHS full time contracts as well as sourcing interim cover for departments.

Tel: 020 7456 1254  
Email: MarcusAnderson@generalmedicinegroup.co.uk  
Website: www.generalmedicinegroup.co.uk

**GlaxoSmithKline**  Stand numbers 4 & 5

GSK is a UK-based science-led global healthcare company that makes innovative medicines, vaccines and consumer health products, used by millions of people worldwide. In pursuing our mission to eradicating the patient impact of COPD and asthma, we are taking a patient-centred approach to the development of medicines and devices. GSK has been investing more in respiratory research than any other healthcare company over the past 40 years.

Website: www.gsk.com

**Improving Quality in Physiological Services (IQIPS)**  Stand number 38

Improving Quality in Physiological Services (IQIPS) is a professionally led programme with the aim of improving services, care and safety for patients undergoing physiological tests, examinations and procedures. The programme is owned and hosted by the Royal College of Physicians. IQIPS offers the benefits of sharing best practice and the opportunity to enhance efficiency with evidence for local leverage. Accreditation also brings national recognition to the service with a badge of quality.

Tel: 020 3075 1754  
Email: askiqips@rcplondon.ac.uk  
Website: www.iqips.org.uk

**Insmed**  Stand number 19

Insmed is a global, biopharmaceutical company whose mission is to transform the lives of patients with serious, rare diseases.

Email: medicalinformation@insmed.com  
Website: www.insmed.com

**Life of Breath**  Stand number 67

What does breathlessness feel like? How do thoughts, emotions and beliefs affect our breathing? Would better ways of describing breathlessness help doctors and patients communicate? Life of Breath is a five year (2015-20) research project trying to answer these questions and others through the arts, humanities, social sciences and medicine. We want to understand the personal experience and meaning of breathing and breathlessness. We want to help people with breathlessness live well. Our work is led jointly by Durham University and University of Bristol and funded by the Wellcome Trust.

Tel: 0191 334 8142  
Email: mail@lifeofbreath.org  
Website: www.lifeofbreath.org

**Medela Healthcare**  Stand number 21

Medela Healthcare is a global manufacturer of medical vacuum solutions which are respected and trusted by doctors and healthcare professionals around the world. In close collaboration with medical experts and based on thorough research, Medela continues to set standards in digital chest drainage systems. Thopaz+, the next generation digital chest drainage system allows healthcare professionals to make accurate decisions based on the precise monitoring of air leaks and pressure while directly measuring fluid drainage.

Tel: 0161 776 0400  
Email: info@medela.co.uk  
Website: www.medela.co.uk
EXHIBITORS’ INFORMATION

Mesothelioma UK
In the UK, 2,570 British people were diagnosed with Mesothelioma in 2011 and annual numbers continue to rise. Only six per cent of the UK population have any idea what the disease is, yet this deadly cancer kills one person every five hours in the UK. The rising number of deaths from this condition is linked to the continued use of asbestos in the building industry up until the mid 1980s. Our aim is to support those living with mesothelioma and we achieve this through:

- Our website www.mesothelioma.uk.com
- Our free phone telephone helpline 0800 169 2409
- Our e-mail service mesothelioma.uk@uhl-tr.nhs.uk
- Our Annual Patient and Carer Day
- Our quarterly Newsletters
- Disseminating information leaflets to patients, carers, NHS and healthcare providers (Accredited by Information Standards Board)
- Collating UK clinical trial availability and promoting equitable access
- Working in collaboration with all Mesothelioma interested groups
- Promoting the setting up and ongoing support for local Mesothelioma Support Groups
- Providing funding for 11 dedicated Specialist Mesothelioma Nursing posts around the UK
- Signposting where possible to local Lung Nurse Specialists
- Campaigning to raise awareness about the dangers of asbestos
- Employing a Citizens Advice Bureau, Specialist Mesothelioma Benefits Advisor
- Providing funding for dedicated Mesothelioma Research Projects
- Providing funding for Nurse Led Mesothelioma Research Projects
- Coordinating communication surrounding Action Mesothelioma Day
- Presenting at numerous mesothelioma educational events
- Publishing reports, chapters and articles whenever the opportunity arises relevant to mesothelioma.
- Delivering an accredited course in mesothelioma (in partnership with The Royal Marsden School)

Our vision:
1 To be a ‘Mesothelioma Essential One Stop Shop’ for up to date Mesothelioma support, information and education.
2 Support the NHS to drive up standards and ensure equitable access to world class treatment, trials and care.

3 To help the UK to lead the way in making Mesothelioma history through a world class audit, research and clinical trials.
4 To raise the profile of mesothelioma to prevent future cases of asbestos-related disease.

We are: Dedicated to Making Mesothelioma Matter
Tel: 0800 169 2409 (helpline)
Email: mesothelioma.uk@uhl-tr.nhs.uk
Website: www.mesothelioma.uk.com

Mylan
Mylan ranks among the leading global generic and specialty pharmaceutical companies. Working together around the world to provide 7 billion people access to high-quality medicine, we innovate to satisfy unmet needs; make reliability and service excellence a habit; do what’s right, not what’s easy; and impact the future through passionate global leadership.

In the UK, Mylan has one of the largest portfolios of generic and branded generic drugs, offering an extensive range of dosage forms and delivery systems. At Mylan, we have one global quality standard in everything we do. Our internal teams conduct reviews of all products, start to finish. No matter where in the world they are made.

Why such high standards? Because we truly care about the people who will be helped by the medicines we make. And we believe in earning that trust from physicians, pharmacists, other health care professionals and patients, every day. It’s why we say, “Our Mylan is Your Mylan.”

Tel: 01707 853 000
Email: enquiry@mylan.co.uk
Website: www.mylan.co.uk

Napp Pharmaceuticals Limited
Napp Pharmaceuticals Limited is a UK company with a strong track record in providing medicines for long-term conditions. We support the delivery of real world evidence and education, and provide high-quality asthma medicines that meet genuine needs, make a positive difference to patients and offer value to the NHS.

Tel: 01223 424 444
Website: www.napp.co.uk

National Chronic Obstructive Pulmonary Disease (COPD) Audit Programme, led by the Royal College of Physicians (RCP)

Through an extensive partnership approach, the National COPD Audit Programme brings together primary care,
secondary care, and pulmonary rehabilitation audits in order to comprehensively map the patient’s journey through COPD services. This national audit programme aims to drive improvements in the quality of care and services provided for COPD patients in England and Wales. It is led by the RCP, working closely with a range of key stakeholders, including the British Thoracic Society (BTS), the Primary Care Respiratory Society UK (PCRS-UK), the British Lung Foundation (BLF) and the Royal College of General Practitioners (RCGP). The programme is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit Programme (NCA).

For further information contact: Viktoria McMillan, Programme Manager, or Juliana Holzhauer-Barrie, Project Manager.

Tel: 020 3075 1502
Email: copd@rcplondon.ac.uk
Website: www.rcplondon.ac.uk/COPD
Twitter: @NatCOPDAudit, #COPDaudit, #COPDauditQI

The National Lung Cancer Audit, delivered by the Royal College of Physicians

Stand number 39

The NLCA has been driving improvements in the care of lung cancer patients since 2004. In 2014, the RCP was awarded the contract for the NLCA and it aims to build on the success of the previous audit using cancer registry data while incorporating key advances in the field of lung cancer diagnosis and treatment. The programme is commissioned by the Healthcare Quality Improvement Partnership (HQIP) as part of the National Clinical Audit Programme (NCA) and is delivered in partnership with the National Cancer Registration and Analysis Service, the University of Nottingham, the Society for Cardiothoracic Surgery, the Royal Castle Lung Cancer Foundation, the British Thoracic Oncology Group, the National Lung Cancer Forum for Nurses and the Welsh Lung Cancer Specialist Advisory Group. Independently funded by Mesothelioma UK to produce a mesothelioma audit.

Contact: Rosie Dickinson, Project Manager
Tel: 01702 616 333
Email: info@olympus.co.uk
Website: www.olympus.co.uk

The PCD Family Support Group

Stand number 70

The PCD Family Support Group is a charity that:

• Provides support to patients
• Raises awareness of PCD

EXHIBITORS’ INFORMATION

in growing areas of healthcare. In the UK we are the largest sponsor of commercial clinical trials. We are a global leader in the three core areas of pharmaceuticals, eye care (Alcon) and generic medicines (Sandoz). In the UK, Novartis has over 2000 associates across five sites, working in research and development, manufacturing, marketing, and commercial operations. Our commercial HQ is in Frimley, Surrey.

Website: www.novartis.co.uk

Olympus

Stand numbers 7 & 8

Olympus is one of the world’s leading manufacturers of innovative optical and digital equipment such as endoscopes and microscopes for medical, scientific and industrial use as well as cameras and voice recorders.

Founded in Japan in 1919, Olympus has stood for pioneering spirit and innovation for more than 90 years.

The Olympus Medical Systems Division offers a variety of products and system solutions for the healthcare sector, constantly seeking to improve diagnostic procedures and, consequently, the treatment of many diseases. Olympus is committed to developing new technologies, products, services and financial solutions that comply with the toughest industry standards and offer our customers improved safety, security, quality and productivity.

Tel: 01702 616 333
Email: info@olympus.co.uk
Website: www.olympus.co.uk

PARI Medical Ltd

Stand number 35

PARI Medical Ltd is part of the network of PARI companies worldwide.

Founded in Germany in 1906, PARI has become a global leader in developing solutions for people suffering from respiratory diseases.

PARI’s mission is to improve the lives of those affected by respiratory diseases and those who provide care to them. This is reflected in a comprehensive portfolio of innovative products and services.

Tel: 01932 341 122
Email: info@pari.eu
Website: www.pari.com

The PCD Family Support Group

Stand number 70

The PCD Family Support Group is a charity that:

• Provides support to patients
• Raises awareness of PCD
EXHIBITORS’ INFORMATION

- Promotes research to aid the diagnosis and treatment of patients
- Supports the NHS to ensure patients have access to diagnostic services and on-going care

This year is a special year for us as we are celebrating our 25th Anniversary as well as:-

- Working with our diagnostic and Paediatric Management Teams to improve patient care
- Working with the adult physicians to secure NHS funding for an adult PCD Management Service
- Helping to promote the 100k Genomes Project

Help Line: 0300 111 0122
Email: chair@pcdsupport.org.uk
Website: www.pcdsupport.org.uk

Pfizer and Novartis Stand numbers 9-12
Pfizer and Novartis collaborate as the Novartis-Pfizer alliance to improve the wellbeing of patients living with chronic obstructive pulmonary disease (COPD).

About Pfizer
At Pfizer, we apply science and our global resources to improve health and well-being at every stage of life. We strive to set the standard for quality, safety and value in the discovery, development and manufacturing of medicines. Our diversified global healthcare portfolio includes biologic and small molecule medicines and vaccines, as well as many of the world's best-known consumer products. Every day, Pfizer colleagues work to advance wellness, prevention, treatments and cures that challenge the most feared diseases of our time. For more than 150 years, Pfizer has worked to make a difference for all who rely on us.

About Novartis
Novartis provides innovative healthcare solutions that address the evolving needs of patients and societies. Headquartered in Basel, Switzerland, Novartis offers a diversified portfolio to best meet these needs: innovative medicines, eye care and cost-saving generic pharmaceuticals. Novartis is the only global company with leading positions in these areas. Novartis products are available in more than 180 countries around the world.

Tel: 01304 616 161
Websites: www.pfizer.co.uk www.novartis.co.uk

PneumRx Ltd a BTG International Group Company Stand number 32
PneumRx Ltd develops, manufactures, and sells innovative medical devices to treat pulmonary disease. The PneumRx Endobronchial Coil is a minimally invasive implantable device designed specifically for the treatment of severe emphysema. It is CE Marked and available throughout Europe, The Middle East, South Africa, Canada and Australia. It is approved for investigational use only in the USA.

Tel: +31 73 30 30 599
Email: Info-EU@pneumrx.com
Website: www.pneumrx.com

Primary Care Respiratory Society UK Stand number 62
The Primary Care Respiratory Society UK (PCRS-UK) is the UK-wide professional society supporting primary care to deliver high value patient centred respiratory care. Our ultimate vision is “optimal respiratory health for all”.

Our scientific journal, npj Primary Care Respiratory Medicine, flagship annual national primary care conference and membership magazine Primary Care Respiratory Update underpin our research, campaigning and education work.

Website: www.pcrs-uk.org

Public Health England Stand number 57
Public Health England and NHS England jointly launched the Collaborative TB Strategy for England in 2015. They will be present at the BTS Winter Meeting to show case work that is implementing the Strategy and share materials to support front line staff deliver improved TB control.

Tel: 0208 327 7073
Email: TBStrategy@phe.gov.uk

Pulmonx Stand number 28
Pulmonx is an interventional pulmonology company focused on life-changing, cost-effective technologies that improve the lives of patients suffering from lung disease worldwide.

Pulmonx has developed Endobronchial Valve (EBV) Treatment, a non-surgical approach to treating emphysema which is designed to reduce the volume of the diseased region of the lung by blocking airflow. Likely responders to EBV therapy can be identified using the Chartis Pulmonary Assessment System, as recently demonstrated in the STELVIO study in the New England Journal of Medicine.

Over 10,000 patients have been treated with EBV treatment. Pulmonx products are commercially available in Europe, Australia, Asia, Latin America and other countries worldwide.
Thoracic Science:

Respiratory Futures

www.respiratoryfutures.org.uk engages healthcare professionals across primary, secondary and community fields as well as academic research, innovation and the private sector. Promoting guidance on best-practice relating to long-term respiratory conditions, its resources, features and editorial direction reflect NHS England’s priorities for improved commissioning and value.

Working with stakeholders including NHS Innovation and AHSNs, Respiratory Futures champions entrepreneurship and knowledge-sharing. It encourages open, collaborative debate on current practice and future policy amongst opinion formers and the UK’s professional respiratory community as a whole. The platform is also home to a number of independent national programmes and, specifically, it hosts information on behalf of British Thoracic Society’s Models of Care Committee.

Email: contact@respiratoryfutures.org.uk
Website: www.respiratoryfutures.org.uk

Rocket Medical

Rocket Medical have been working in partnership with the NHS for over 50 years. In this time we have consistently developed well received products. As a UK based Design and Manufacturer we have been able to develop products such as the IPC, Pleural Vent, Portable Suction Unit and others with your help and feedback. So come along to the stand to see what we are developing for you today.

Tel: 0191 419 6988
Emails: Beverley@rocketmedical.com and richardv@rocketmedical.com
Website: www.rocketmedical.com

The Royal College of Physicians

The Royal College of Physicians (RCP) plays a leading role in the delivery of high-quality patient care by setting standards of medical practice and promoting clinical excellence. The RCP provides physicians in over 30 medical specialties with education, training and support throughout their careers. As an independent charity representing 30,000 fellows and members worldwide, the RCP advises and works with government, patients, allied healthcare professionals and the public to improve health and healthcare.

Tel: 0207 378 3000
Email: info@rcslt.org
Website: www.rcslt.org

Sandoz

Sandoz, a Novartis company, prides itself on thinking differently. While developing and manufacturing high-quality affordable medicines is core to who we are and what we do, we continuously endeavour to make these medicines available to everyone, everywhere. Sandoz stands out through its ability to develop and produce complex differentiated products. This differentiated portfolio predominantly focuses on the biosimilar, oncology injectable and respiratory fields, three key pillars to our strategy. Through our best in class patient support solutions and our continuous development programme, we have a long term commitment to patients with respiratory diseases.

Tel: 01276 698 020
Email: mailbox.sandoz-gb@sandoz.com
Website: www.sandoz.com

Teva Respiratory

At Teva, we help improve the health of over 200 million people every day. As the world’s largest generic medicines producer, we offer access to a medicine cabinet of more than 1,000 molecules, delivering a wide range of generic products to people in 100 countries. In specialty medicines, we have a world-leading position in several therapeutic areas, including the central nervous system and respiratory. We operate in 60 countries, producing 100 billion tablets every year. Our R&D pipeline, one of the richest in the industry, integrates generics and specialty capabilities to create new solutions for unmet patient needs, combining drug development with devices, services and technologies.

Website: www.tevauk.com
EXHIBITORS’ INFORMATION

Trudell Medical International

**Stand number 27**

Trudell Medical International (TMI) manufactures **AeroChamber Plus** valved holding chambers (VHCs) for use with pressurised MDIs. **AeroChamber Plus** VHCs are available in small, medium and large mask and mouthpiece variants. TMI has developed the **Aerobika** oscillating positive expiratory pressure (OPEP) device, which helps to clear the lungs of excess mucus and can help improve gas perfusion in chronic bronchitis, COPD, cystic fibrosis and similar conditions. TMI’s **AeroEclipse** breath actuated nebuliser (BAN) delivers medication only when the patient is inhaling, optimising medication delivery to the lung. TMI also offers the **Ombra** mains powered and battery powered compressors, ideal for use with the **AeroEclipse** XL BAN.

**Email:** customerservice@trudellmed.com
**Website:** www.trudellmed.com

Unisoft

**Stand number 13**

Unisoft has developed and been supplying its signature **Bronchoscopy Reporting Tool** for over 20 years. Almost two thirds of UK hospitals use this product. Unisoft is launching its **Endobronchial Ultrasound** (EBUS) add-in module at this year’s BTS. Please come and see us on stand 13. You can also contact us via:

**Tel:** 0208 367 2103
**Email:** support@unisoftmedical.co.uk

Ventmed

**Stand number 37**

Ventmed has earned the well-deserved reputation as a leading UK-based supplier of respiratory and consumable products. Our unwavering ambition is to ensure all patients and clinicians have access to the highest quality products at affordable prices in tandem with the provision of professional clinician training, and customer service. Visit our stand (37) to see our range of acute care CPAP/BIPAP masks, circuits and the highly anticipated disposable CPAP kits for the pre-hospital and acute care settings.

**Tel:** 01732 844 091
**Email:** info@ventmed.com
**Website:** www.ventmed.com

Vertex

**Stand number 48**

Vertex is a global biotechnology company that aims to discover, develop and commercialise innovative new medicines so people with serious diseases can lead better lives. Founded in 1989, Vertex today employs approximately 2,000 people at research and development sites and other offices around the world. Since its inception in 1989, Vertex has invested more than $7 billion in research and development efforts aimed at developing transformative medicines for serious diseases. In addition to our clinical development programme focused on cystic fibrosis, Vertex has more than a dozen research programmes aimed at other serious and life-shortening diseases, including cancer and neurological disorders.

**Website:** www.vrtx.com

Vitalograph Ltd

**Stand number 29**

Our Spirotrac® software turns your PC into a powerful and flexible cardio-respiratory workstation, with the ability to integrate test results with electronic medical record systems. Spirotrac is compatible with many of the market leading Vitalograph spirometers, including the PC-based Pneumotrac, the hand held In2itive, and the desktop Alpha Touch. All Vitalograph spirometers feature a Fleisch Pneumotachograph for ultimate performance in accurate, linear and reliable flow and volume measurement. Spirotrac also enables you to add a growing range of additional diagnostic tests and physiological measurements, including 12 lead ECG, pulse oximetry, blood pressure measurement, challenge testing and more in a flexible, integrated solution.

**Tel:** 01280 827 110
**Email:** sales@vitalograph.co.uk
**Website:** www.vitalograph.co.uk

Wisepress

**Stand number 49**

Wisepress are Europe’s principal conference bookseller. We exhibit the leading books, sample journals and digital content relevant to this meeting. Books may be purchased at the booth, and we offer a postal service. Visit our online bookshop for special offers and follow us on Twitter for the latest news @ WisepressBooks.

**Tel:** 020 8715 1812
**Email:** bookshop@wisepress.com
**Website:** www.wisepress.com
**BTS/BALR/BLF Early Career Investigators Symposium**

**T1**

**CALCINEURIN INHIBITION IMPAIRS THE DENDRITIC CELL TRANSCRIPTIONAL RESPONSE TO ASPERGILLUS FUMIGATUS INFECTION IN LUNG TRANSPLANT RECIPIENTS**

1. A. Adikha, 2DAJ Armstrong-James, 3B Lenhard. 1MRC Clinical Sciences Centre, Imperial College, London, UK; 2NHLI, Imperial College, London, UK

**Background** Lung transplant recipients on calcineurin inhibitor immunosuppression have increased mortality from, invasive aspergillosis. Tacrolimus (FK506) diminishes the innate immune response to 

**A. fumigatus** infection partly by inhibition of the calcineurin-NFAT axis. We investigated the effects of FK506 on transcriptional regulation in dendritic cells (DC’s), and assessed interferon-gamma as a treatment, with a combination of RNA-Seq and histone modification ChIP-seq.

**Methods** Healthy volunteer monocytes were negatively isolated from gradient-centrifugation-selected PBMC’s and differentiated into DC’s with GM-CSF and IL-4. DC’s were treated with FK506, interferon-gamma and/or inoculated with swollen conidia of 

**A. fumigatus** (MOI 1:1). For RNA-Seq, extracted mRNA was poly-A purified and reverse-transcribed to ds-DNA, and for ChIP-seq, DNA was cross-linked, sonicated, then immunoprecipitated with antibodies against histone marks H3k4me1 and H3k27ac. Resultant DNA was PCR-amplified to generate libraries for next generation sequencing on the Illumina HiSeq 2500. Computational sequencing analysis pipelines used open-source C++ and R-based packages (Bowtie, Kallisto, edgeR and MACS).

**Results** 

**A. fumigatus** infection in DC’s elicited upregulation of genes belonging to two key groups of early-phase response transcription factors – the early growth response family (EGR1 – log fold-change 4.90, FDR p-value = 0.0003) and the nuclear receptor family (NR4A2 – logFC 6.96, p = 1.56 × 10^-9). FK506 treatment ablated significant differential expression of these genes whilst subsequent interferon-gamma treatment restored their upregulation (EGR1 – logFC 4.43, p = 0.00093; NR4A2 – logFC 5.56, p = 0.00034).

Active gene enhancers regions were identified by presence of significant peaks of H3k4me1 and H3k27ac antibody binding. Motif analysis of enhancers within regulatory domains around differentially-expressed genes identified enrichment of core binding motifs of NFAT (p = 7.8 × 10^-9) and FOXF2 (p = 8.6 × 10^-10) transcription factors, which was lost after FK506 treatment.

**Conclusions** Transcriptome analysis has revealed the key genes involved in early dendritic cell responses to 

**A. fumigatus** infection, and their ablation by FK-506 treatment suggests a deleterious genome-level effect of calcineurin inhibitors in this context. Furthermore, interferon-gamma treatment restores a more favourable transcriptomic response to infection in FK506-treated DC’s. The condition-dependent differential enrichment of enhancer motifs suggests a role for both suspected (NFAT) and previously unidentified (FOXF2) transcription factors in the DC response to 

**A. fumigatus** infection.

---

**T2**

**EARLY-LIFE RESPIRATORY TRACT INFECTION AND ADULT SUSCEPTIBILITY TO CHRONIC MUCUS HYPERSECRETION – A PROSPECTIVE 64 YEAR NATIONAL BIRTH COHORT STUDY**

1. P. Allinson, 2R. Hardy, 3GC Donaldson, 4SO Shaheen, 5D Kuh, 1JA Wedzicha. 1National Heart and Lung Institute, Imperial College London, London, UK; 2MRC Unit for Lifelong Health and Ageing at University College London, London, UK; 3Barts and the London School of Medicine and Dentistry, London, UK

**Introduction** Smoking commonly triggers Chronic Mucus Hypersecretion (CMH) indicating both accelerated FEV₁ decline and arguably early-phase COPD development. Early-life respiratory infections are proposed as another cause of adult CMH and also lead to impaired adult lung function. We investigated how smoking may modify the relationship between early-life infection and CMH across adult life.

**Methods** The MRC National Survey of Health and Development has prospectively studied a nationally representative sample of men and women since their birth during one week in March 1946 within England, Scotland and Wales. During early-life (ages 0 to 2 years) lower respiratory tract infection presence (EL-LRTI), father’s occupational social class and estimated local pollution exposure were recorded for each study member. Smoking status and MRC questionnaire defined CMH were recorded six times between age 20 and 60–64 years. Random-effects logistic regression models for repeated measures were used to describe CMH trajectories across adult life by smoking status and EL-LRTI adjusting for sex, birth weight, early-life pollution exposure (high vs low) and social class (manual vs non-manual).

**Results** Amongst the 3617 individuals included (52% male; 63% ever-smokers) 25% experienced an EL-LRTI. CMH prevalence increased during adulthood (cumulative prevalence = 12%). Smokers had higher odds of CMH at all ages compared to non-smokers (Figure 1). For smokers and non-smokers, those with EL-LRTI had higher odds of CMH than those without EL-LRTI. There was evidence of an interaction between smoking status and EL-LRTI (Figure 1) such that at age 20 the effect of EL-LRTI
HUMAN RHINOVIRUS IMPAIRS THE INNATE IMMUNE RESPONSE TO BACTERIA IN MONOCYTE DERIVED MACROPHAGES FROM PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

LJ Finney, KBR Belchamber, P Mallia, S. Johnston, LE Donnelly, IA Wdowicha. National Heart and Lung Institute, Imperial College, London, UK

Introduction Exacerbations of Chronic Obstructive Pulmonary Disease (COPD) are associated with accelerated disease progression, hospitalisation and death. Respiratory viruses are identified in approximately half of all exacerbations. We have previously found that human rhinovirus infection leads to a secondary outgrowth of bacteria which is associated increased exacerbation severity. The mechanisms of how HRV increases risk of secondary bacterial outgrowth are unknown.

Hypothesis We hypothesised that HRV infection impairs phagocytosis of bacteria by monocyte derived macrophages (MDM) which may lead to an increased risk of secondary bacterial outgrowth during COPD exacerbations.

Methods Participants were recruited from the London COPD Cohort. MDM were generated by culture in GM-CSF or M-CSF for 12 days. MDM were incubated with HRV 16 for 24 hours at increasing multiplicity of infection (MOI) 0.5–10 for 24 hours or poly-IC at increasing concentrations 0–300 μg/ml.

Phagocytic capacity was then assessed by incubating MDMs with fluorescently labelled heat killed Haemophilus influenzae or Streptococcus pneumoniae for 4 hours and uptake measured by fluorimetry. The pro-inflammatory cytokine CXCL-8 and anti-inflammatory cytokine IL-10 were measured by ELISA according to the manufacturer’s instructions.

Results HRV16 impaired phagocytosis of H. influenzae (HRV (MOI of 5) 2.84 ± 0.92 vs media control 4.36 ± 1.06 RFU x 10³ n = 8, p = 0.01) and S. pneumoniae (p < 0.01) by MDM in a virus-dose-dependent manner without impairing cell viability. HRV16 alone induced CXCL-8 and IL-10 release from MDM compared to media alone. HRV16 (MOI 5) significantly impaired IL-10 response to H. influenzae compared to media alone (0.59 (0.33–0.96) ng/ml vs 1.83 (1.11–3.00) ng/ml respectively, n = 6, p = 0.03) and impaired CXCL-8 response to H influenzae compared to media alone 4.41 (3.45–5.85) ng/ml vs 24.65 (11.63–29.77) ng/ml respectively, n = 5, p = 0.01).

Polyc-IC impaired phagocytosis of H. influenzae in a concentration-dependent manner without significantly impairing cell viability. Polyc IC alone also induced IL-8 release from MDM.

Conclusions HRV impairs phagocytosis of bacteria by MDM in COPD and impairs cytokine response to bacteria which may inhibit neutrophil influx and prevent resolution of inflammation. This may lead to an outgrowth of bacteria and prolonged exacerbations in COPD.

GLOBAL SPREAD OF MYCOBACTERIUM ABSCESSES CLONES AMONGST CYSTIC FIBROSIS PATIENT

1DM Grogono, 2M Bryant, 3D Rodriguez-Rincon, 4E Everest, 5KP Brown, 4P Moreno, 3D Verma, 2E Hill, 1J Drijkoningen, 5CS Haworth, 3SR Harris, 2D Ordway, 1J Parkhill, 1RA Floto, 1University of Cambridge Department of Medicine, Cambridge, UK; 2Wellcome Trust Sanger Institute, Hinxton, UK; 4Cambridge Centre for Lung Infection, Papworth Hospital, Papworth, UK; 3EMBL European Bioinformatics Institute, Hinxton, UK; 5Mycobacteria Research Laboratory, Department of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, USA

Introduction Lung infections with Mycobacterium abscessus, a species of multidrug resistant nontuberculous mycobacteria, have increased in frequency worldwide, emerging as an important global threat to individuals with cystic fibrosis (CF) where they cause accelerated inflammatory lung damage and death. M. abscessus was previously thought to be independently acquired by susceptible individuals from the environment. However, using whole genome sequencing and detailed epidemiological analysis of a cohort of patients attending the CF centre at Papworth Hospital, we found strong evidence for transmission between patients. We therefore sought to examine the mechanism of acquisition of M. abscessus in CF individuals across the world.

Methods We undertook whole genome sequencing on 1080 isolates from 517 patients from the UK, US, the Republic of Ireland, mainland Europe and Australia. This was then correlated with clinical metadata and phenotypic functional analysis.

Results Our genomic analysis revealed that the majority of infections are from densely clustered M. abscessus genotypes with low levels of diversity, indicating a high level of human associated spread. Moreover, the phylogeny reveals the presence of three recently emerged dominant circulating clones that have globally spread. We found that these clones are associated with worse clinical outcomes and show increased virulence in both cell-based and mouse infection models. Within patients we found evidence of genetic diversity and evolutionary adaptation through the processes of convergent evolution and hypermutation.

Conclusions The majority of M. abscessus infections in patients with Cystic Fibrosis are caused by genetically related clusters, indicating recent patient-to-patient transmission despite conventional infection control measures. Transmission appears to have facilitated evolution of M. abscessus from an environmental organism into a transmissible human pathogen.

This work was supported by The Wellcome Trust grant 098051 (JMB, SH, JP) and 107032/A1A (DG, RAF) The Medical Research Council (JMB), The UK Cystic Fibrosis Trust (DMG, DR-R, IE, JP, RAF), Papworth Hospital (DMG, KPB, CSH, RAF), NIHR Cambridge Biomedical Research Centre (RAF), and The UKCRC Translational Infection Research Initiative (JP).
TOWARDS HUMAN LUNG REGENERATION IN END-STAGE RESPIRATORY FAILURE: GENETICALLY-MODIFIABLE 3D ORGANOID CULTURE OF HUMAN EMBRYONIC LUNG STEM CELLS ENABLES FOR THE FIRST TIME THE STUDY OF HUMAN LUNG DEVELOPMENT IN VITRO

1MZ Nikolic, 1JA Johnson, 1D Sun, 1D Carity, 1U Laregolit, 1J Brady, 1G Allen, 2A Giangaspero, 2EL Rawlin, 1Gordon Institute, University of Cambridge, Cambridge, Cambridgeshire; 2University College London, London, UK

10.1136/thoraxjnl-2016-209333.5

Introduction and objectives Regeneration of healthy lung tissue in patients with end-stage respiratory disease (ESRD) would cure disease, rather than treating symptoms. For this a detailed understanding of lung development is needed and the mouse has been used extensively as an in vivo genetically-modifiable model. Differentiation and validation of human induced pluripotent stem cells (hiPSCs) is entirely based on mouse literature. The most important epithelial stem cell population in developing lungs is found in distal branching tips, and these Sox9+ lung epithelial stem cells (LESCs) generate all epithelial lineages. Our objective was to develop a self-renewing, genetically-modifiable epithelial in vitro culture system from human embryonic LESCs and differentiate them into alveolar and bronchiolar cells.

Methods Human embryonic LESCs were characterised using genome-wide transcriptional analysis (RNAseq) and immunohistochemistry (5–20 post-conceptional weeks). LESCs were micro-dissected and self-renewing expansion in 3D organoid culture was established empirically. Using RNAseq and immunohistochemistry, we assessed the similarities between cultured and fresh LESCs. Genetic stability was evaluated by karyotyping. Organoids were differentiated in vitro, or in vivo using xenotransplantation into bleomycin-injured adult mouse lungs or kidney capsule. Gene editing was done using CRISPR-Cas9 to delete SOX9.

Results RNAseq of LESCs identified broad-scale transcriptional differences between mouse and human embryonic lung stem cells. Human LESCs were successfully expanded for over 10 months as karyotypically-stable 3D organoids using a combination of 7 signalling molecules. The LESC stem cell markers, transcriptome and organoid morphology were maintained throughout the culture period. Bronchiolar and alveolar differentiation was achieved in vitro and in vivo. Moreover, xenotransplantation of organoids into bleomycin-injured adult mouse lungs was extremely efficient. Knocking out SOX9 led to a loss-of-self-renewing phenotype.

Conclusions Our novel genetically-modifiable human embryonic lung culture system enables for the first time the in vitro study of human lung development and disease modelling. We anticipate that this work will transform lung regenerative medicine by guiding the development of improved protocols for hiPSC differentiation and manipulation of adult stem cells in vivo, with benefits for patients with ESRD. Additionally, our protocol for xenotransplantation following lung injury provides the first method for efficient future cell therapy.

RANDOMISED SHAM-CONTROLLED TRIAL OF TRANSCUTANEOUS ELECTRICAL STIMULATION IN OBSTRUCTIVE SLEEP APNOEA

1M Pengo, 1X Sichang, 1C Rattanasawaran, 1N Shah, 1K Reed, 1T Chen, 1A Douiri, 1N Hart, 1Y Luo, 1G Raffenetti, 1GP Rossi, 1A Williams, 1M Polkey, 1M Hoath, 1J Steier. 1University of Padua, Department of Medicine (DIMEDE), Padua, Italy; 2State Key Laboratory of Respiratory Disease, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China; 3King’s College London, Faculty of Life Sciences and Medicine, London, UK; 4Guy’s and St Thomas’ NHS Foundation Trust, Lane Fox Respiratory Unit/Sleep Disorders Centre, London, UK; 5King’s College London, Division of Health and Social Care, London, UK; 6NHIR Respiratory Biomedical Research Unit at the Royal Brompton and Harefield NHS Foundation Trust and Imperial College, London, UK

10.1136/thoraxjnl-2016-209333.6

Obstructive sleep apnoea is characterised by a loss of neuromuscular tone of the upper airway dilator muscles while asleep. Continuous positive airway pressure is a well-established long-term treatment, but patient compliance is limited. This study investigated the effectiveness of transcutaneous electrical stimulation in patients with obstructive sleep apnoea.

This was a randomised, sham-controlled cross-over trial using transcutaneous electrical stimulation of the upper airway dilator muscles in patients with confirmed obstructive sleep apnoea. Patients were randomly assigned to two nights, sham stimulation and active treatment. The primary outcome was the 4% oxygen desaturation index, responders were defined as patients with a reduction >25% in the oxygen desaturation index when compared to sham stimulation and/or with an index <5/hour in the active treatment night.

In 36 patients (age mean 50.8 (standard deviation 11.2) years, male/female 30/6, body-mass-index median 29.6 (interquartile range 26.9–34.9) kg/m², Epworth Sleepiness Scale 10.5 (4.6) points, oxygen desaturation index median 25.7 (16.0–49.1)/hour, apnoea hypopnoea index median 28.1 (19.0–57.0)/hour) the primary outcome measure improved when comparing sham stimulation (median 26.9 (17.5–39.5)/hour) to active treatment (median 19.5 (11.6–40.0)/hour; p = 0.026), a modest reduction of the mean by 4.1 (95% CI: −0.6–8.9)/hour. Secondary outcome parameters of patients’ perception indicated that stimulation was well tolerated. Responders (47.2%) were predominantly from the mild-moderate obstructive sleep apnoea category. In this subgroup, the oxygen desaturation index was reduced by 10.0 (95% CI: 3.9–16.0)/hour (p < 0.001) and the apnoea hypopnoea index was reduced by 9.1 (95% CI: 2.0–16.2)/hour (p = 0.004).

Transcutaneous electrical stimulation of the pharyngeal dilators during a single night in patients with obstructive sleep apnoea improves upper airway obstruction and is well tolerated. (TESLA trial registration at NCT01661712)
The Difficult Asthma Patient

S1 BIOMARKERS IN ADULT ASTHMA: A SYSTEMATIC REVIEW OF 8-ISOPROSTANE IN EXHALED BREATH CONDENSATE

1AM Peel, 1CJ Crossman-Barnes, 1J Tang, 2SJ Fowler, 3GA Davies, 1AM Wilson, 1YK Loke. 1University of East Anglia, Norwich, UK; 2University Hospital South Manchester, Manchester, UK; 3Swansea University, Swansea, UK

Introduction The potential of exhaled breath condensate (EBC) as a non-invasive indicator of airways disease has been studied for three decades or more. 8-isoprostane is a product of lipid per-oxidation which can be detected within EBC. Studies have reported this as a potential objective indicator of oxidative stress in asthma. We therefore aimed to assess the evidence for the use of 8-isoprostane in exhaled breath condensate (EBC) as a biomarker in adult asthma.

Design A systematic review and meta-analysis of EBC 8-isoprostane in asthma.

Methods We searched a number of online databases (including PubMed, Embase and Scopus) in January 2016. We included studies of adult non-smokers with EBC collection and asthma diagnosis conducted according to recognised guidelines. We aimed to pool data using random effects meta-analysis and assess heterogeneity using I². Study quality and risk of bias was assessed using QUADAS-2 and GRADE.

Results We included twenty studies, the findings from which were inconsistent. Seven studies (n = 329) reported 8-isoprostane concentrations in asthma to be significantly higher than that of control groups, whilst six studies (n = 403) did not. Only four studies had results appropriate for inclusion in a random effects meta-analysis of mean difference between asthma and controls (see Figure 1). This found a statistically significant between-groups difference of +22 pg/ml in asthma.

Confidence in the result is limited by the small number of studies; by substantial methodological and statistical heterogeneity (I² = 94); and by an inability to assess the risk of bias in key domains of the quality assessment tool.

Conclusion The clinical value of EBC 8-isoprostane as a quantitative assessment of oxidative stress in asthma remains unclear due to variability in results and methodological heterogeneity. It will be essential to develop accurate, reliable and standardised methods of both EBC collection and 8-isoprostane analysis if its use as a biomarker in asthma is to be evaluated.

Abstract S1 Figure 1 Random effects meta-analysis of mean between-group difference (asthma vs controls)
Omalizumab was approved in 81% of cases submitted, and BT in complex clinical issues, often managed across multiple sites.

Results
During this period 17 meetings were held, with 208 case-submissions representing 185 patients, mean (SD) 12 (7) discussions per meeting. Indications for case submission included proposals for use of omalizumab, bronchial thermoplasty (BT), and steroid-sparing therapies, and for the discussion of patients with proposals for use of omalizumab, bronchial thermoplasty (BT), and steroid-sparing therapies, and for the discussion of patients with eosinophilic asthma.

Aim To summarise the experience and case-mix encountered during the first 18 months of operation of our regional virtual severe asthma MDT meeting facilitating expert care across a wide geographical area. This ensures governance in the use of novel and expensive severe asthma therapies, strengthens regional collaborations and ultimately aims to provide better patient care.

Conclusion We describe our early experience of a multi-site virtual severe asthma MDT meeting facilitating expert care across a wide geographical area. This ensures governance in the use of novel and expensive severe asthma therapies, strengthens regional collaborations and ultimately aims to provide better patient care.

Background Severe asthma comprises 5% of all asthma, but over 50% of the asthma healthcare burden. With multi-disciplinary team (MDT) working there is potential to improve patient outcomes and reduce healthcare costs. In 2013 NHS England produced service specifications for severe asthma aiming to develop a limited number of high volume specialist centres. In the North West we have developed a networked approach to specialised severe asthma services; the first Operation Delivery Network for a chronic disease. Representatives from 11 NHS Trusts and a central hub undertake a monthly virtual MDT meeting, with physicians, nurses, physiotherapists, clinical psychologists, speech and language therapists, allergists, pathologists and radiologists represented. All patients being considered for specialised treatments undergo MDT discussion for consensus approval of treatment.

Methods We reviewed all cases discussed at the MDT between January 2015 and June 2016.

Results During this period 17 meetings were held, with 208 case-submissions representing 185 patients, mean (SD) 12 (7) discussions per meeting. Indications for case submission included proposals for use of omalizumab, bronchial thermoplasty (BT), and steroid-sparing therapies, and for the discussion of patients with complex clinical issues, often managed across multiple sites. Omalizumab was approved in 81% of cases submitted, and BT in 39%, with more of the latter requiring multiple discussions (30% versus 2%). The most common reasons for non-approval of omalizumab were insufficient steroid requirement, poor adherence, and lack of allergy to a perennial allergen. Thermoplasty was not approved or listed for re-discussion for a variety of reasons, including 10 (43%) that required further investigation.

Conclusion We describe our early experience of a multi-site virtual severe asthma MDT meeting facilitating expert care across a wide geographical area. This ensures governance in the use of novel and expensive severe asthma therapies, strengthens regional collaborations and ultimately aims to provide better patient care.

Rationale Severe asthma is a heterogeneous disease in which patients have diverse clinical characteristics and biomarkers, like eosinophils and IgE. It is important to understand their relationship in a severe asthma population. The IDEAL (Identification and Description of Severe Asthma Patients in a Cross-Sectional Study) study aimed to identify the proportion of patients with severe asthma who could be eligible for an anti-IL-5 (mepolizumab) or anti-IgE (omalizumab) directed treatment, and those who may be eligible for either therapy.

Methods IDEAL, an observational study included subjects aged ≥12 years with severe asthma defined according to ATS/ERS guidelines by treatment with high-dose ICS plus additional controller(s) for ≥12 months. Assessments included spirometry, a blood sample, and symptom/burden of illness questionnaires. Eligibility to mepolizumab and omalizumab were defined according to SMC advice (2016) and NICE MTA guidance (2013), which has been adopted in Scotland, respectively. Mepolizumab eligibility is defined as per SMC advice: patients who have eosinophils of at least 150 cells per microlitre (0.15 x 10⁹/L) at initiation of treatment and have had at least four asthma exacerbations in the preceding year or are receiving maintenance treatment with oral corticosteroids. Omalizumab eligibility (NICE MTA guidance) is defined as evidence of severe persistent allergic asthma and need for continuous or frequent treatment with oral corticosteroids.
(defined as 4 or more courses in the previous year), and meeting bodyweight and IgE criteria for omalizumab treatment.

**Results** 748 subjects with severe asthma were enrolled in the study of which 670 met analysis criteria. After exclusion of subjects currently treated with omalizumab (n = 168), 502 subjects were included in this post-hoc analysis (mean age = 50.9 years; 62% female). 60 subjects (12% [95% CI: 9.2–15.1%]) were eligible for mepolizumab (SMC advice) and 16 (3% [1.8–5.1]) were eligible for omalizumab (NICE MTA guidance). Among the 60 mepolizumab eligible subjects, 10 (16.7%, [8.3–28.5%]) were also eligible for omalizumab.

**Conclusions** This is the first cross-sectional study providing estimation of the proportion of severe asthma patients eligible for biologic therapy in accordance with Scottish guidance, indicating 12% mepolizumab-eligible and 3.2% omalizumab-eligible patients with limited overlap.

**Funding** GSK; 201722

---

**VITAMIN D FOR THE MANAGEMENT OF ASTHMA: COCHRANE SYSTEMATIC REVIEW AND META-ANALYSIS**

1AR Martineau, 2CI Cates, 3U Harashina, 4M Jensen, 5AP Griffiths, 6U Numatou, 7A Sheikh, 8CI Griffiths, 9Queen Mary University of London, London, UK; 2St George’s University of London, London, UK; 2Nkei University School of Medicine, Tokyo, Japan; 1University of Newcastle, Newcastle, Australia; 6Cardiff University, Cardiff, UK; 6University of Edinburgh, Edinburgh, UK

10.1136/thoraxjnl-2016-209333.11

**Introduction and objectives** Several clinical trials of vitamin D to prevent asthma exacerbation and improve asthma control have been conducted in children and adults, but a meta-analysis restricted to double-blind randomised placebo-controlled trials of this intervention is lacking. We conducted a Cochrane systematic review and meta-analysis to evaluate the efficacy of administration of vitamin D in reducing asthma exacerbations treated with systemic corticosteroids (primary outcome) and improving asthma symptom control.

**Methods** Standard Cochrane collaboration procedures were followed. Double-blind randomised placebo-controlled trials of vitamin D in children and adults with asthma evaluating exacerbation risk and/or asthma symptom control were included.

**Results** Seven trials involving a total of 435 children and two trials involving a total of 658 adults were included in the primary analysis. Administration of vitamin D reduced the rate of exacerbations requiring systemic corticosteroids (Rate Ratio 0.63, 95% CI: 0.45 to 0.88; 680 participants; 3 studies; high quality evidence), and decreased the risk of having at least one exacerbation requiring an emergency department visit and/or hospitalisation (Odds Ratio [OR] 0.39, 95% CI: 0.19 to 0.78; number needed to treat for one additional person to experience a beneficial outcome (NNTB), 27; 963 participants; 7 studies; high quality evidence). There was no effect of vitamin D on % predicted forced expiratory volume in one second (Mean Difference [MD] 0.48, 95% CI: −0.93 to 1.89; 387 participants; 4 studies; high quality evidence) or Asthma Control Test scores (MD −0.08, 95% CI: −0.70 to 0.54; participants = 713; studies = 3; high quality evidence). Administration of vitamin D did not influence the risk of serious adverse events (OR 1.01, 95% CI: 0.54 to 1.89; 879 participants; 5 studies; moderate quality evidence). No participant in any included trial suffered a fatal asthma exacerbation.

**Conclusions** Meta-analysis of a modest number of trials in patients with predominantly mild to moderate asthma suggests that vitamin D is likely to reduce the risk of severe asthma exacerbation and reduce health care use.

---

**Lung Cancer Biology and Mechanisms**

**S5**

**MMP12 AND LMO7, TWO KEY PLAYERS ON OPPOSITE SIDES OF EARLY LUNG SQUAMOUS CELL CARCINOMA DEVELOPMENT**

1A Barrett, 7S Lourenco, 8K Kolluri, 7B Carroll, 2M Falcon, 2E Borg, 2J George, 8SM Janes, 1VH Teixeira; 1University College London, London, UK; 2University College London Hospital, London, UK

**Background** Our laboratory has a unique cohort of patients with pre-invasive lung squamous cell carcinoma (SqCC) lesions, within which there is a clear discrepancy between the prevalence of pre-invasive lesions and the incidence of lung cancer, suggesting that not all pre-invasive lesions progress to cancer. Using gene expression microarrays we identified 1846 genes significantly differentially expressed between progressive and regressive pre-invasive SqCC lesions.

The macrophage metalloelastase MMP12 gene was found to be highly expressed in progressive lesions, and we hypothesised that it plays a role in epithelial-to-mesenchymal transition (EMT). Conversely, the actin binding protein LIM-domain only 7 (LMO7) gene was highly expressed in regressive lesions, and we postulated that it may be protective against EMT due to its role in the maintenance of epithelial architecture.

Initial studies using three SqCC cell lines (A431, H357 and H376) with MMP12-shRNA knockdown showed a significant decrease in migration and invasion compared to non-silencing shRNA controls. LMO7-shRNA knockdown in HBECS was found to significantly increase migration. The aim of this study is to further characterise the function and signalling of MMP12 and LMO7 in lung SqCC development.

**Methods** Eight-week-old NOD/SCID mice were used for tumorigenesis experiments. Adhesion assays were carried out to assess the roles of MMP12-knockdown or LMO7-overexpression on cell adhesion. Cell signalling mechanisms were assessed using western blotting, qPCR and immunostaining.

**Results** We observed that MMP12-knockdown decreases tumorigenicity in an immunocompromised mouse model. Both A431- and H357 MMP12-knockdown cells produced significantly smaller tumours compared with non-silencing shRNA cells. We found that MMP12-knockdown decreases cell adhesion, which is currently being further investigated along with effects on integrin signalling pathways. Levels of EMT markers were assessed in MMP12-knockdown and LMO7 overexpressing cells using qPCR, western blotting and immunostaining. Results indicate that higher MMP12 expression is associated with a mesenchymal phenotype, whereas higher LMO7 expression is associated with an epithelial phenotype.

**Conclusions** Our results suggest that MMP12 is a key driver of migration and invasion in SqCC and its high expression may contribute to EMT, whereas LMO7 is a putative tumour suppressor with a crucial role in maintaining epithelial cell architecture. MMP12 and LMO7 may be potential early stage therapeutic markers for lung cancer.
MOUSE LUNG ADENOCARCINOMA CELL LINES REVEAL PRL2C2 AS A NOVEL LUNG TUMOUR PROMOTER

1N. Kanellakis, 2A. Giannou, 3M. Pepe, 1T. Agalioti, 1D. Zazara, 1M. Vreka, 1S. Lillis, 1G. Gianopoulos, 2M. Spyka, 1A. Marazioti, 1N. Rahman, 1P. Pavord, 1P. Psallidas, 2T. Stathopoulos. 1Laboratory of Pleural Translational Research, Nuffield Department of Medicine, University of Oxford, UK; 2Laboratory Molecular Respiratory Carcinogenesis, University of Patras, Patras, Greece; 3lung Carcinogenesis Laboratory, Comprehensive PneumologyCenter (CPC), University Hospital, Ludwig-Maximilians University and Helmholtz Zentrum München, Munich, Germany; 4Respiratory Medicine Laboratory, Nuffield Department of Medicine, University of Oxford, UK

10.1136/thoraxjnl-2016-209333.13

Background Carcinogen-inflicted human cancers, including lung tumours harbour thousands of mutations per genome, most of which are unknown (Garraway, LA et al, Cell 2013;153:17–37).

Aim To develop a faithful mouse model of human tobacco carcino-nogen-induced lung adenocarcinoma suitable for the identification of novel oncogenic genes and pathways.

Methods We repeatedly managed to obtain several murine lung adenocarcinoma cell lines (MLA) by chronically exposing various mouse strains to different tobacco carcinogens. MLA were characterised for cancer stemness and oncogenes, as well as global gene expression.

Results To date, 12 MLA cell lines have been derived from WT and transgenic mice on the FVB, Balb/c, and C57BL/6 strains by means of urethane or diethylnitrosamine exposure. All MLA were immortal, phenotypically stable, and indefinitely passaged in vitro over a period of over 18 months and/or 60 passages. In addition, all cell lines were oncogenic, transplantable, metastatic, and uniformly lethal in vivo. Interestingly, MLA displayed Kras mutations in codon 61, mono- or bi-allelic Trp53 loss, and expression of lung cancer stemness factors Iggb3 and Lgr6, in amazing similarity to human lung cancers. Microarray revealed that all MLA cell lines heavily overexpressed Prl2c2, encoding proliferin, in comparison to the native lungs. Prl2c2 silencing diminished MLA proliferation and stemness, to a degree comparable with Iggb3 interference.

Conclusions MLA are faithful models of human lung adenocarci-noma that lead to the discovery of Prl2c2 as a candidate lung tumour promoter.

Funding European Research Council Starting Independent Investigator Grant #260524. Respiré 2 European Respiratory Society Fellowship, European Respiratory Society Short Term Research Fellowship.

OSTEOPONTIN AS AN AIRWAY EPITHELIAL TUMOUR PROMOTER

1P. Psallidas, 1N. Kanellakis, 2M. Vreka, 2A. Giannou, 3C. Moschos, 1G. Gianopoulos, 1T. Agalioti, 1S. Lillis, 4S. Magkouta, 1N. Rahman, 1P. Pavord, 2T. Stathopoulos. 1Laboratory of Pleural Translational Research, Nuffield Department of Medicine, Oxford Centre for Respiratory Medicine, Oxford University Hospitals Trust, Oxford, UK; 2Comprehensive PneumologyCentre (CPC) and Institute for Lung Biology and Disease (LLD), Ludwig-Maximilians-Universität, Asklepios Fachkliniken München-Gauting und Helmholtz Zentrum, Munich, Germany; 3Laboratory for Molecular Respiratory Carcinogenesis, Department of Physiology, Faculty of Medicine, Rio, Greece; 4First Department of Critical Care and Pulmonary Medicine, University of Athens School of Medicine, General Hospital Evangelismos, Athens, Greece

10.1136/thoraxjnl-2016-209333.14

Osteopontin (secreted phosphoprotein 1; SPP1) expression has been identified in human lung cancer and has been linked with enhanced tumour progression. To examine its functional role, we induced lung tumours by repetitive urethane or MCA/BHT lung carcinogens in C57BL/6 mice lacking both (Spp1−/−), one (Spp1 +/−), or no (Spp1+/+) copy of the endogenous Spp1 gene. Primary end-points were lung tumour number and size; secondary end-points were SPP1 expression, epithelial cell survival, carcino-gen-induced inflammation, and angiogenesis. Data are presented as mean ± SD.

Compared with Spp1+/+ mice (n = 22), Spp1−/− mice (n = 25) developed dramatically fewer and significantly smaller lung tumours in response to urethane, while Spp1± mice (n = 12) behaved similar to Spp1−/− mice (number/diameter of lung tumours in Spp1+/+, Spp1+−/−, and Spp1−/− mice, respectively: 16.1 ± 12.7/1.2 ± 0.3 mm, 2.4 ± 2.3/0.9 ± 0.2 mm, and 1.3 ± 1.6/0.7 ± 0.2 mm; P < 0.05 for comparison of Spp1+/+ with Spp1−/− and Spp1+/− mice). Spp1−/− mice were also protected from two-hit MCA/BHT-oncogenesis compared with Spp1+/+ controls. Spp1−/− mice displayed decreased epithelial cell survival and reduced numbers of airspace macrophages early after ure-thane, and enhanced tumour cell apoptosis and limited tumour angiogenesis at late stages of lung tumour progression. SPP1 was expressed in the naïve lung by non-ciliated airway epithelial cells and alveolar macrophages and was significantly up-regulated during multi-stage lung carcinogenesis.

Our data indicate that SPP1 is functionally involved in airway epithelial carcinogenesis and may present a target for lung cancer treatment and prevention.

THE ROLE OF LRIG1-DEPENDENT EGFR SIGNALLING IN AIRWAY HOMEOEOSTASIS AND SQUAMOUS CELL LUNG CANCER DEVELOPMENT


10.1136/thoraxjnl-2016-209333.15

Background Aberrations of EGFR signalling drive cancer development. In squamous cell lung cancer (SqCLC), EGFR is overexpressed. LRIG1 is a negative regulator of EGFR and patient pre-invasive SqCLC samples show LRIG1 loss, suggesting involvement in early disease pathogenesis. In skin and gut homeostasis, LRIG1 regulates stem cells. In the upper airway, basal cells act as stem cells and are the putative origin of SqCLC. We hypothesise LRIG1 has a key role in airway homeostasis and its loss promotes pre-invasive SqCLC development.

Methods Lrig1 EGFP-ires-CreERT2 mice were used to delineate airway LRIG1 expression. Flow sorted LRIG1-positive and -negative murine basal cells were used in 2D and 3D colony-forming, spheroid and proliferation assays. A murine SqCLC model was set up through application of N-Nitrososourea (2-chloroethyl)urea (NCTU). Pre-invasive lesions and tumour development were compared between wild-type (WT), heterozygous and LRIG1-knockout (KO) animals. Human basal cells obtained from bronchoscopic samples were sorted according to LRIG1 expression and used directly in colony-forming assays or maintained in primary culture to assess the effect of shRNA knockdown of LRIG1. LRIG1-knockdown cells were assessed in colony-forming and proliferation assays, and differentiation and invasion were assessed using organotypic models.

Results LRIG1 is expressed by 40% of airway basal cells. LRIG1-expressing murine basal cells exhibit increased colony-forming capacity (p = 0.0286), spheroid formation (p = 0.0043) and...
proliferation ($p = 0.0043$) compared with LRIG1-negative cells. Similarly, LRIG1-expressing human airway basal cells isolated from endobronchial brush biopsy samples exhibit increased colony-forming capacity ($p = 0.0469$). Topical application of NTCU to mice recapitulates the development of human pre-invasive and SCLC lesions after 23 weeks. Results show lesions in LRIG1-KO mice to be larger than those of WT animals. Knock down of LRIG1 in cultured human airway basal cells alters cell phenotype, leading to an increased colony-forming efficiency and greater proliferation at cell confluence.

Conclusions LRIG1 has an important role in stem cell homeostasis of the human and murine airway epithelium. Loss of LRIG1 promotes pre-cancerous lesion development in a murine SqCLC mouse model and behaviour of human epithelial cells in culture, indicating a potential target for chemoprevention of SqCLC in humans.

INVESTIGATION OF VESSEL STRUCTURE IN THE VICINITY OF LUNG TUMOURS

N Sadri, D Wertheim, Kingston University, Kingston, Surrey, UK

Lung cancer is considered a major cause of cancer death. We are currently developing methods for detection of vessels in lung CT images. The aim of this study was to investigate the number of vessels in areas of unilateral lung tumours and compare with the equivalent contralateral lung with no tumour. Lung CT images were downloaded from the Cancer Imaging Archive wiki.cancerimagingarchive.net/display/Public/LungCT-Diagnosis. Software was written in MATLAB (The MathWorks Inc., USA) in order to display and analyse the DICOM images. Windowing was performed manually in order to clearly display the tumours as well as surrounding vessel like structures. Using the software eight sets of images were analysed; the number of clearly defined vessel like structures directly attached to the tumour were counted and compared with the corresponding region in the contralateral lung with no evidence of tumour; small vessel like structure and branches were not included. The area of the tumour was manually delineated and calculated in terms of pixels. For each set of CT images, one image was used where the tumour size was greatest. In all eight cases the number of clear vessel like structures in the immediate vicinity of the tumour was greater than that in the corresponding area on the contralateral side, mean (standard deviation) of the difference $5.16$, there was a significant difference $p < 0.001$ (one sample t test). In addition vessel like structures often appeared brighter on the side of the tumour. The results of this pilot study suggest that the number of clear bright vessel like structures in the immediate vicinity of a lung tumour may be higher than in the corresponding area on the contralateral side. We feel this research merits further study in order to investigate if this approach may help enable early detection of lung tumours.

REFERENCES
vitro. Thus, we provide important insights into the changes occurring after prolonged in vitro expansion, underlining the importance of using low passage MSCs in clinical trials for ARDS. In agreement with published data, we also found that MSCs do not induce cellular proliferation in the absence of stimulation.

REFERENCES

S12 PLASMA SYNDECAN-1 LEVEL AS A PREDICTIVE MARKER OF VASOPLEGIA ASSOCIATED WITH SURGERY REQUIRING CARDIOPULMONARY BYPASS AND POSSIBLE INVOLVEMENT OF OXIDATIVE STRESS

1MG Rasiah, 1C Michaeloudes, 1T Svernova, 2Z Nikolakopoulou, 2B Creagh-Brown, 1PK Bhavsar, 1A Burke-Gaffney. 1Imperial College London, London, UK; 2The Royal Surrey County Hospital NHS Foundation Trust, Guildford, UK

Background Vasoplegic syndrome (severe refractory hypotension) is associated with oxidative stress leading to endothelial dysfunction and complicates 10 to 40% of surgery requiring cardiopulmonary bypass (CPB). Whilst operative mortality is low, recovery is often prolonged in patients developing vasoplegia. There are, as yet, no validated biomarkers for vasoplegia that could be used to identify ‘at risk’ patients. We hypothesised that plasma levels of the endothelial surface layer (glycocalyx) protein, syndecan-1, shed during CPB, will be higher in patients who develop vasoplegia and that leukocyte responses to oxidative stress will be altered.

Methods Patients (n = 48) undergoing cardiac surgery requiring CPB were, prospectively, enrolled; blood collected and indices of outcome recorded. A surrogate index of vasoplegia was adopted: requirement for infusion of vasoconstrictor agents for longer than 48h. An enzyme-linked immunosorbent assay was used to measure plasma levels of syndecan-1 at four time-points: after induction of anaesthesia but before CPB (T1); within 30 min of CPB ending (T2); 2h (T3) and 24h (T4) post-CBP. Real time qPCR was used to determine, in patient leukocytes (n = 20), relative expression (to house-keeping gene18S) of mRNA for markers of oxidative stress; NQO1 and SOD2, cytoplasmic and mitochondrial enzymes, respectively; and for comparison, TNFα.

Results Syndecan-1 levels at T2 were significantly higher in vasoplegic patients (110.7 ng/mL, IQR 65.46–155.2) than non-vasoplegic patients (53.8 ng/mL, IQR 40.67–102.2; p < 0.001). ROC curve analysis showed syndecan-1 had significant (p = 0.009) predictive power for onset of vasoplegia, with an area under the curve of 0.766 (95% CI: 0.6019–0.9301); and a cut-off of 63.33 ng/mL (83.33% sensitivity, 69.23% specificity). Syndecan-1 levels were higher in patients whose intensive care unit length of stay (LOS) and hospital LOS were above corresponding medians for the cohort (p = 0.0061 and p = 0.0148, respectively). NQO1 relative expression was significantly higher (p = 0.022) in vasoplegic patients (3.779 ± 1.036) than non-vasoplegic patients (1.3 ± 0.302); whereas, neither SOD2 nor TNFα expression were significantly altered.

Conclusion Plasma syndecan-1 measured immediately post-CBP had good predictive power for patients at risk of vasoplegia. Greater relative expression of leukocyte NQO1 in vasoplegic patients indicates activation of antioxidant defence mechanisms in response to oxidative stress, which could contribute to syndecan-1 shedding.

S13 PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS IN CRITICALLY ILL PATIENTS WITH LOWER RESPIRATORY TRACT INFECTIONS. ARE ‘ONE SIZE FITS ALL’ DOSES APPROPRIATE?

1IB Oldfield, 1K Kipper, 1CI Barker, 1BJ Philips, 2M Cecconi, 2A Rhodes, 1A Johnston, 3JF Standing, 1EH Baker, 1M Sharland, 1DO Lonsdale. 1Institute for Infection and Immunity, St George’s, University of London, London, UK; 2St George’s University Hospitals NHS Foundation Trust, London, UK; 3Infectious Diseases and Microbiology Unit, University College London, Institute of Child Health, London, UK

Introduction Respiratory infection is a common cause of severe sepsis.1 Current therapeutic guidelines emphasise the importance of early initiation of antibiotic therapy, but make no
recommendations on dose. Recent studies have suggested that some critically ill patients fail to achieve sufficient plasma antibiotic concentrations to treat infection effectively.2

We determined whether critically-ill patients with respiratory infection achieved pharmacokinetic/pharmacodynamic (PK/PD) targets during antibiotic treatment and investigated factors associated with failure to meet these targets.

Methods This was a subgroup, interim analysis of an ongoing study, ABDose. Participants were adults in intensive care receiving piperacillin-tazobactam or co-amoxiclav for respiratory infection. Demographics and measures of organ function were recorded. Antibiotic concentrations were measured, at steady-state, in plasma at 50% and 100% of the dosing interval. Efficacy of beta-lactam antibiotics is dependent upon time above minimum inhibitory concentration (MIC). We chose PK/PD targets of antibiotic concentration > MIC and a more conservative >4 × MIC of likely pathogen or microbiological isolate (when available). These targets have been used previously.3 During 28-day follow up, need for additional antibiotics was recorded.

Results 24 participants (median age 61, IQR [50–70] years), received co-amoxiclav (n = 7), piperacillin-tazobactam (n = 15) or both (n = 2). At 100% of the dosing interval, 12 achieved plasma antibiotic concentrations >MIC and 8 achieved >4×MIC. Participants who did not achieve PK/PD targets were younger (48 [39–59] years vs 68 [61–80] years, p = 0.002*) and had a higher eGFR (131 ± 58 ml/min/1.73m² vs 64 ± 28 ml/min/1.73m², p = 0.004*) than those who did. Antibiotic concentrations were correlated with age and negatively correlated with eGFR (Figure 1). All participants failing to achieve antibiotic concentrations >4 × MIC at 100% of the dosing interval required further courses of antibiotics during follow-up compared to 50% of patients achieving this target (p = 0.02*).

Conclusion In critically-ill patients with respiratory infection, uniform dosing of beta-lactam antibiotics does not consistently achieve PK/PD targets required for optimal efficacy. Younger patients, with better renal function may be under-dosed. These interim findings identify a need for further work to determine whether personalised dynamic dosing regimens could improve outcomes for patients with severe respiratory infection. Population PK modelling and further covariate analysis is planned within ABDose.

REFERENCES

$S14$ PATIENTS’ PERCEPTIONS OF AN EXERCISE PROGRAMME DELIVERED FOLLOWING DISCHARGE FROM HOSPITAL AFTER CRITICAL ILLNESS (THE REVIVE TRIAL)

K McDowell, JM Bradley, DF McAuley, B Blackwood, B O’Neill. 1Centre for Health and Rehabilitation Technologies, Ulster University, Newtownabbey, UK; 2School of Medicine, Dentistry and Biomedical Sciences, Queen’s University, Belfast, UK; 3School of Medicine, Dentistry and Biomedical Sciences, Queen’s University and Regional Intensive Care Unit, Royal Victoria Hospital and Clinical Trials Unit, Belfast, UK

Introduction The REVIVE RCT investigated the effectiveness of an individually tailored (personalised) exercise programme for patients discharged from hospital after critical illness.1 By including qualitative methods, we aimed to explore their perceptions of engaging in the 6 week programme to facilitate a better understanding of the intervention and trial outcomes.

Methods Patients allocated to the exercise group were invited to participate in semi-structured interviews following their final outcome assessment (6 months following randomisation). Interviews were conducted by a trained member of the research team not involved in the intervention. Interviews were audio recorded, transcribed verbatim and content analysis used to explore themes arising from the data.

Results Of 30 patients allocated to the exercise group 21 completed interviews. Seven core themes were identified (1) sequelae of critical illness and critical care recovery; (2) satisfaction and endorsement of the exercise programme; (3) beneficial impact of the exercise programme on physical and psychological health; (4) facilitators of beneficial impact; (5) barriers to beneficial impact; (6) challenges to continuing exercise; (7) contrasting views on outcome measures.

Patients provided insight into the physical and mental sequelae they experienced following critical illness. There was a strong sense of patients’ need for the exercise programme and its importance for their recovery following discharge home. The programme was described as invaluable, and provided feelings of motivation and hope. Key facilitators of beneficial impact included supervision, tailoring of the exercises to personal needs, and the manual. Barriers to the beneficial impact of the programme included poor mental health, existing physical limitations and lack of motivation. Patients’ views of the questionnaires and performance based outcome measures in the REVIVE trial varied. Many patients were unsure about what would be the best way of measuring how the programme affected their health.

Conclusion The benefits of physical rehabilitation programmes, needs to be counterbalanced against patients’ mental health status post-ICU and any pre-admission limitations, if they are to be successful. Including this qualitative component improved our understanding of the mechanisms underpinning the impact of the programme and how programmes should be evolved for future trials.

REFERENCE
SIMVASTATIN IMPROVES NEUTROPHIL MIGRATION IN ELDERLY PATIENTS WITH SEPTIC PNEUMONIA AND REDUCES 6-MONTH MORTALITY AND RE-ADMISSIONS: RESULTS OF THE SNOOPI TRIAL

J Patel, H Greenwood, S Lugg, P Howells, F Gao, E Sapey, D Thickett. Institute of Inflammation and Ageing, College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

10.1136/thoraxjnl-2016-209333.22

Introduction and objectives Community acquired pneumonia is a leading infectious cause of death in the elderly and the commonest source of sepsis. Neutrophil functions decline with age, and deteriorate further in sepsis.1 Restoring neutrophil function may improve sepsis outcomes. Recent in-vitro and in-vivo studies suggest simvastatin improves aspects of neutrophil function.2 Adjuvant statin therapy in severely critically ill patients has failed to improve outcomes and may be associated with increased morbidity,4,5 however our ASEPSIS study suggested that early intervention with statins may reduce the progression of sepsis in a ward-based cohort of milder sepsis patients.6 In light of this, we investigated whether oral treatment with simvastatin improved neutrophil function and clinical outcomes in elderly patients with septic pneumonia.

Methods SNOOPI was a phase-4, randomised controlled trial comparing 7-days of 80mg simvastatin with placebo in patients aged 55 years or over admitted to hospital with septic pneumonia.7 The primary outcome was changes in neutrophil extracellular trap (NETs) formation by day3/4 compared with baseline. Secondary outcomes included neutrophil migration, safety and tolerability, length of stay, readmissions and mortality.

Results 61 patients were recruited acute admissions unit at the Queen Elizabeth Hospital Birmingham between 2013 and 2015, with 31 patients randomised to simvastatin and 30 to placebo. Groups were well matched for baseline characteristics, pneumonia and sepsis severity, co-morbidities and biochemical and haematological parameters.

There was no significant difference in the primary end-point of change in NETs at day3/4. Directional neutrophil migration (chemotaxis) was significantly improved in patients who received simvastatin at day 3/4 (0.35 ± 0.16 μm/min vs. −0.15 ± 0.17 μm/min; p = 0.033). Simvastatin was well tolerated with no SUS-ARS, even with the co-prescription of macrolides. At 6-months, patients in the simvastatin group were less likely to have been admitted to hospital or died compared to those in the placebo group (OR: 0.44; 95% CI: 0.21–0.91; p = 0.02) (Figure 1).

Conclusions The current study suggests that early intervention with statins in septic pneumonia patients may improve patient outcomes. We propose that one of the mechanistic drivers may be the restoration of sepsis-associated dysregulated neutrophil function. Further larger studies are warranted to confirm whether early intervention with statins in patients with sepsis confer an overall survival benefit.
Understanding the Clinical Course Of Idiopathic Pulmonary Fibrosis

**S17 THE BURDEN OF IDIOPATHIC PULMONARY FIBROSIS IN THE UNITED KINGDOM: A RETROSPECTIVE, MATCHED COHORT STUDY**

1M Storm, 1T Tran, 1H Strongman, 1J Fredriksson, 1T Maher, 6HLS Life Sciences, Washington DC, USA; 2Roche Products Ltd, Welwyn Garden City, UK; 3Clinical Practice Research Datalink, London, UK; 4Royal Brompton and Harefield NHS Foundation Trust, London, UK

**Background** Idiopathic pulmonary fibrosis (IPF) is a specific form of chronic, progressive fibrosing interstitial pneumonia which primarily affects older adults, for which very few treatments have existed. While attention has been paid to quantifying the rising incidence and prevalence of the disease, little has been done to quantify the impact of this disease on NHS resources and how this impact varies by setting.

**Objective** This study aims to identify health care utilisation patterns in the United Kingdom (UK) following IPF diagnosis.

**Methods** The Clinical Practice Research Datalink (CPRD) GOLD database for general practitioner office visits and the linked Hospital Episode Statistics (HES) datasets were analysed, covering the time period from January 1, 2000 to June 30, 2015. A matched cohort analysis was conducted, and frequency counts and regression analyses were used to quantify raw healthcare resource utilisation and understand the proportion of the utilisation that is attributable to IPF.

**Results** The results of this study indicate that IPF patients have significantly higher healthcare utilisation patterns than non-IPF patients. The regression results indicate that IPF leads to roughly 2.2 times as many GP visits, 8.7 times as many inpatient hospitalizations, and 2.4 times as many outpatient hospital visits per year (all p-values <0.0001), as well as increased referrals, prescriptions, and, in the post-diagnosis period, inpatient stay duration. Additionally, healthcare utilisation amongst these patients is dramatically higher in the year prior to IPF diagnosis, a pattern not witnessed in the matched cohort.

**Conclusions** IPF imposes a significant burden on the NHS despite its rare prevalence. IPF patients experience an across the board increase in healthcare utilisation, but the burden is particularly acute in the inpatient hospital setting. Additionally, the large increase in resource utilisation in the year prior to IPF diagnosis is evidence of the potential benefits to refining the diagnostic procedures.

**REFERENCES**

**Background** High resolution computed tomography (HRCT) scanning is able to detect abnormalities consistent with interstitial lung disease (ILD). However, if only a small proportion of lung is affected, radiologists variously report this as ‘minimal’, ‘minor’ or ‘early’ ILD. There is no definition of what constitutes ‘minimal’ ILD and the natural history of these patients is not known.

**Aims** To define ‘minimal’ ILD, test observer agreement with this definition and describe the characteristics and survival of these patients.

**Hypothesis** Minimal ILD can be defined by subjective quantification and has a benign course.

**Methods** Between 01.01.2002 and 31.12.2014 the Edinburgh Lung Fibrosis Database was prospectively populated with data for 1450 consecutively presenting patients with ILD. Of these, 56 were identified as presenting with ‘minimal’ disease according to HRCT. Three radiologists participated in a modified Delphi exercise and agreed on a definition of ‘minimal’ ILD. A sample (n = 38) of HRCT scans was provided to test inter- and intra-observer agreement according to this definition using Fleiss’ Kappa statistics. Survival was assessed using Kaplan-Meier curves.

**Results** The Delphi exercise resulted in ‘minimal’ disease being defined as ILD involving <5% of the total lung volume and/or <10% of the lung peripheries. Using this definition, inter-observer and intra-observer agreement was moderate (kappa 0.42 and 0.58 respectively). Of the 56 subjects originally deemed as ‘minimal’ ILD, 48 were unanimously described as minimal disease by post-definition criteria. One subject was biopsied (consensus after biopsy, unclassifiable). Forty-seven subjects were not biopsied and none met ATS/ERS consensus criteria for diagnosing IPF. Most subjects had ‘unclassifiable’ disease, but the working diagnoses were; IPF or other fibrotic idiopathic interstitial pneumonia (IIP) (n = 34), IIP without fibrosis (n = 7) and connective-tissue disease associated ILD (n = 7). The median age was 69 yrs, 56% were male and 23% had never smoked. The mean (SD) %pred lung function was; FEV1 91.8% (19), VC 101% (18)
TCO 62% (19). The median survival was 11.6 years, and all deaths (n = 12) were attributable to respiratory disease.

Summary Defining ‘minimal’ ILD is feasible and there was moderate radiological agreement. Minimal ILD is relatively benign, but the associated mortality was of respiratory cause.

S19 THE IMPACT OF CLOTTING ABNORMALITIES ON THE NATURAL HISTORY OF IDIOPATHIC PULMONARY FIBROSIS: AN EXTENDED FOLLOW UP OF A POPULATION BASED COHORT

1V Navaratnam, 1AW Fogarty, 1T Mickleeve, 1T Thompson, 1G Jenkins, 1SR Johnson, 2V Kumarar, 1K Poonton, 1RB Hubbard. 1Division of Epidemiology and Public Health, University of Nottingham, Nottingham, UK; 2Nottingham Respiratory Research Unit, Nottingham, UK; 3Department of Respiratory Medicine, University of Nottingham, Nottingham, UK; 4Department of Radiology, Nottingham University Hospitals NHS Trust, Nottingham, UK

10.1136/thoraxjnl-2016-209333.25

Background We have previously demonstrated that people with idiopathic pulmonary fibrosis (IPF) are more likely to have a prothrombotic state and that people with IPF and a prothrombotic state have a higher risk of death at a year’s follow up. The aim of this study was to establish the impact of clotting abnormalities on the natural history of IPF with respect to median survival and lung function (forced vital capacity (FVC)).

Methods We recruited 211 incident cases of radiologically diagnosed definite or probable IPF and collected longitudinal information on pulmonary function tests done as part of routine care. All participants were tagged with the NHS Information Centre to enable us to collect data on mortality. Blood samples were tested for a prothrombotic state defined as at least one inherited or acquired clotting defect or marker of fibrinolytic dysfunction. Kaplan-Meir methods were used to calculate median survival. Random effects linear regression modelling was used to estimate decline in FVC.

Results Median follow-up was four years, during which 148 (70.1%) people died. Median survival in those with and without prothrombotic state was 2.7 and 3.7 years respectively (see Figure 1). We found evidence of effect modification between risk of death and follow-up time (p = 0.031). There was more than a three-fold increase in risk of death in individuals with IPF and a prothrombotic state in the first half of follow-up (HR 3.36, 95% CI: 1.33 to 8.36), but this was reduced (HR 1.79, 95% CI: 1.08 to 2.94) in the second half. The estimated decline in FVC was 288mls (95% CI: 184 to 392mls) in those with normal clotting and 328mls (95% CI: 269 to 387mls) in those with one or more clotting defects.

Conclusions Coagulation dysfunction has an adverse impact on the natural history of IPF, both in terms of median survival and lung function decline. Our findings suggest that a prothrombotic state may be a useful biomarker to predict prognosis as part of routine care.

S20 KBILD SCORES HAVE SIMILAR POWER TO PREDICT SURVIVAL AS PULMONARY PHYSIOLOGY IN INTERSTITIAL LUNG DISEASE

1C Sharp, 1C Baggott, 1SS Birming, 2HI Adamali. 1Academic Respiratory Group, University of Bristol, Bristol, UK; 3Bristol Interstitial Lung Disease (BILD) Service, North Bristol NHS Trust, Bristol, UK; 4Division of Asthma, Allergy and Lung Biology, King’s College London, London, UK

10.1136/thoraxjnl-2016-209333.26

Background The KBILD questionnaire is an ILD health related quality of life (HRQL) tool. Its relationship with survival has not been assessed.

Aims Assess impact of KBILD scores on survival in a heterogeneous population with interstitial lung disease (ILD).

Methods Patients attending the Bristol ILD service with fibrotic ILDs completed KBILD questionnaires, full lung function and exercise testing. Survival analysis using univariable and multivariable Weibull regression with an accelerated time-failure form was used to assess the significance of KBILD scores to predict all cause mortality. Comparison was made with lung function from the same clinic visit. Results are reported as hazard ratio and time ratio.

Area under receiver operator characteristics (AUROC) curve analysis was used to assess sensitivity of KBILD for predicting 12-month mortality.

Results 175 patients, 58% IPF, 67.4% male, completed a KBILD questionnaire. Mean values were; age 71yrs, KBILD 61, FVC 0.99 0.035 0.553 0.416, DLCO (%) 0.96 <0.001 0.680 0.554, 6MWD (m) 0.99 0.035 0.553 0.416, Desaturation 2.64 0.002 2.00 0.61 0.038, TR 0.96 <0.001 0.96 0.96 0.004 0.674 0.560, Area under receiver operator characteristics (AUROC) curve analysis was used to assess sensitivity of KBILD for predicting 12-month mortality.

Abstract S20 Table 1 Weibull regression results and c-statistic for 12-month mortality for variables

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio</th>
<th>Significance</th>
<th>Hazard Ratio</th>
<th>Significance</th>
<th>Time Ratio</th>
<th>Significance</th>
<th>c-statistic</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>1.05</td>
<td>0.003</td>
<td>1.06</td>
<td>0.99</td>
<td>0.002</td>
<td>0.646</td>
<td>0.511, 0.781</td>
<td></td>
</tr>
<tr>
<td>KBILD</td>
<td>0.98</td>
<td>0.005</td>
<td>0.98</td>
<td>1.01</td>
<td>0.022</td>
<td>0.654</td>
<td>0.531, 0.777</td>
<td></td>
</tr>
<tr>
<td>FVC (%)</td>
<td>0.97</td>
<td>&lt;0.001</td>
<td>0.97</td>
<td>1.02</td>
<td>0.004</td>
<td>0.674</td>
<td>0.560, 0.788</td>
<td></td>
</tr>
<tr>
<td>DLCO (%)</td>
<td>0.96</td>
<td>&lt;0.001</td>
<td>0.96</td>
<td>2.00</td>
<td>0.61</td>
<td>0.038</td>
<td>0.553, 0.416</td>
<td></td>
</tr>
<tr>
<td>6MWD (m)</td>
<td>0.99</td>
<td>0.035</td>
<td>0.99</td>
<td>0.99</td>
<td>0.004</td>
<td>0.680</td>
<td>0.554, 0.807</td>
<td></td>
</tr>
</tbody>
</table>

TR = time ratio, AUROC = area under receiver operator characteristics curve, CI = confidence interval

Time ratio – The factor by which survival time changes for each 1 point change in a variable when all other variables are constant, eg. For each additional year of age, survival changes by a factor of 0.95.
84%, DLCO 50%, walk distance 292m. 48% had oxygen desaturation on 6-minute walk. 47 patients (26.9%) died. Mean follow-up was 19.8 months, median 14.4 months. 156 patients had >12 months follow-up and these were included in the prognostic evaluation.

Univariable survival analysis showed age, KBILD, FVC, DLCO, walk distance and exertional desaturation to have prognostic significance for all cause mortality. Univariable analysis of the sub-categories of the KBILD score showed the psychological (p = 0.003) and breathlessness (p = 0.002) domains to be significant, while the chest symptoms domain was not (p = 0.269).

After backwards stepwise selection the multivariable model contained age, KBILD, FVC and desaturation (Table 1). All included variables had prognostic significance.

AUROC analysis showed KBILD had equivalent sensitivity for 12-month mortality to FVC, DLCO and better sensitivity than walk distance (c-statistic in Table 1). A KBILD score of 34 had 73% sensitivity for 12-month mortality, but only 10.5% specificity. Estimated median survival with KBILD of <34 was 9.7 months, compared to 36.4 months for KBILD > 34 (p = 0.02).

Conclusions In this cohort, the KBILD has equivalent prognostic power in ILD to pulmonary physiology and exercise testing at a single point in time. It is important to assess HRQL to give ILD patients optimal prognostic information.

**Sleep Apnoea: The Big Sleep**

**S22**

Severities of Sleep Disordered Breathing Independently Predicts Metabolic Dysfunction in a Large Population of Severely Obese Subjects: The Esada Study

1BD Kent, 1N Gildeh, 1P Drakatos, 2L Grote, 2J Hedner, 3WT McNicholas. 1Guy’s and St Thomas’ Hospitals, London, UK; 2Sahlgrenska University Hospital, Gothenburg, Sweden; 3St. Vincent’s University Hospital, Dublin, Ireland

10.1136/thoraxjnl-2016-209333.28

Introduction Obstructive sleep apnoea (OSA) has an established independent association with insulin resistance and type 2 diabetes mellitus (T2DM). However, there are few data examining this relationship in severely obese populations, wherein any detrimental effect of OSA on metabolic health may conceivably be drowned out by the impact of morbid obesity. We assessed the relationship of OSA severity and nocturnal hypoxaemia with metabolic health in a cohort of severely obese patients attending sleep units across Europe.

Methods We performed a cross-sectional analysis of 1,434 participants in the European Sleep Apnea Cohort (ESADA) study with a body mass index (BMI) ≥35 kg/m², using multivariate regression analysis to assess T2DM prevalence according to OSA severity indices. Patients with diabetes were identified by history and medication prescription, and by screening for undiagnosed diabetes with glycosylated haemoglobin (HbA1c) measurement. The relationship of OSA severity with glycaemic control was assessed in diabetic subjects. Multivariate linear regression and multivariate analysis of co-variance were used to examine the
relationship of HbA1c levels with OSA severity in both diabetic and non-diabetic patients.

Results In a cohort of predominantly male (63.5%) and severely obese (mean BMI 40.3 kg/m²) individuals, 32.2% had T2DM. Although the likelihood of T2DM was significantly greater in the highest AHI quartile than the lowest (unadjusted OR 1.78; 95% CI: 1.29–2.47), this relationship lost significance following adjustment for anthropometric, demographic, and clinical factors (adjusted OR 1.21; 95% CI: 0.83–1.76; p = 0.33). However, severity of nocturnal hypoxaemia remained a predictor of T2DM prevalence despite adjustment for confounding factors (adjusted OR for most severe mean nocturnal SpO₂ quartile 2.23; 95% CI: 1.50–2.20; p < 0.001), as well as predicting the likelihood of poor diabetic control (adjusted OR 1.87; 95% CI: 1.06–3.30; p = 0.03). In further analyses, HbA1c levels were independently predicted by OSA severity indices and nocturnal hypoxaemia in both non-diabetic and diabetic subjects, while adjusted mean HbA1c levels were significantly higher in patients with more severe sleep disordered breathing.

Conclusion Metabolic health in severely obese sleep patients appears to be significantly worse in those subjects with more severe sleep disordered breathing, with a particularly strong relationship with the degree of nocturnal hypoxaemia.

S23 NEURAL RESPIRATORY DRIVE DURING SLEEP AT HIGH ALTITUDE

1Stein, 2N Cade, 3B Walker, 3Miaoum, 3CI Jolley. 1King’s College London, London, UK; 2Francis Crick Institute, London, UK

Introduction Ventilation at altitude changes due to altered levels of pO₂, pCO₂ and the effect on blood pH. Nocturnal ventilation is particularly exposed to these changes. We hypothesised that increasing neural respiratory drive is associated with the severity of sleep-disordered breathing at altitude.

Subjects and methods British mountaineers were studied at sea level (London, UK), and at altitude at the Aconcagua (Andes, Argentina). Neural respiratory drive (NRD) was measured as electromyogram of the diaphragm (EMGdi) overnight by a transoesophageal multi-electrode catheter (Yinghui Medical Ltd, Guangzhou, China). Following initial assessment with a polysomnography (London, UK), pulse oximetry measured oxygen concentration and oxygen desaturation indices (4%ODI) at altitude.

Results Four healthy subjects (3male, age 31 (3) years, body-mass-index 23.6 (0.9) kg/m², neck circumference 37.0 (2.7) cm, FEV₁ 111.8 (5.1)% predicted, FVC 115.5 (6.3)% predicted) were studied. Inspiratory and expiratory muscle strength were normal (PImax 130.7 (29.8) cm H₂O, PEmax (153.3 (38.4) cm H₂O). No subject had significant sleep abnormalities at sea level (Total Sleep Time 344.4 (30.5) mins, Sleep Efficiency 86.6 (6.4)%), Respiratory Disturbance Index 0.8 (0.4)/hour, mean SpO₂ 97.5 (1.3%). The oxygen desaturation index increased with the development of periodic breathing at altitude (4% ODI 22.0 (7.2)/hour at 3,380m, 61.4 (26.9)/hour at 4,370m). Average nocturnal SpO₂ (84.8 (0.5%)) at 3,380m; 81.0 (4.1%) at 4,370m) and nadir oxygenation (68.1 (8.6%) at 3,380m; 67.4 (7.6%) at 4,370m) dropped with altitude. The average EMGdi was 5.2 (19.1)% max at sea level and increased to 14.1 (3.4)% at altitude when falling asleep at 4,370m, and correlated well with the 4% ODI (r = 0.968, p = 0.032). EMGdi during the last inspiratory effort prior to central apnoea was 5.1 (1.5)% max, while the first inspiratory effort following central apnoea was 10.5 (3.2)% max at 4,370m.

Conclusion The severity of periodic breathing when asleep deteriorates with an increase in altitude, induced by an elevated neural respiratory drive as a response to hypobaric environmental conditions.

S24 A COMPARISON OF PULSE TRANSIT TIME BETWEEN SUBJECTS WITH OBSTRUCTIVE SLEEP APNOEA SYNDROME, NOCTURNAL INSPIRATORY FLOW LIMITATION AND THE ABSENCE OF SIGNIFICANT SLEEP DISORDERED BREATHING

1B Chakrabarti, 2S Emegbo, 1S Craig, 1NDuffy, 1JF O'Reilly. 1Aintree Chest Centre, Liverpool, UK; 2Liverpool Sleep and Ventilation Centre, Liverpool, UK

Introduction Pulse Transit Time (PTT) represents a non-invasive indirect marker of sleep fragmentation in OSAS. Little is known regarding PTT indices in persons presenting with sleepiness where sleep studies exhibit “flow limited” breaths in the absence

<table>
<thead>
<tr>
<th>Abstract S24 Table 1</th>
<th>Key demographics in the IFL, OSAS and NFL “Control” cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cohort</td>
<td>Inspiratory flow limitation (IFL)</td>
</tr>
<tr>
<td></td>
<td>Control group (n = 20; female = 13)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>47 (8.39)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>34.25 (6.63)</td>
</tr>
<tr>
<td>AHI (per hour)</td>
<td>3.84 (1.16)</td>
</tr>
<tr>
<td>RDI (per hour)</td>
<td>17.71 (5.34)</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>95.05 (1.85)</td>
</tr>
<tr>
<td>Epworth Sleepiness Score (ESS) at presentation</td>
<td>16.35 (3.65)</td>
</tr>
<tr>
<td>Presence of Hypertension</td>
<td>5/20</td>
</tr>
<tr>
<td>Presence of Cardiac Disease</td>
<td>1/20</td>
</tr>
</tbody>
</table>

| Cohort                | Obstructive sleep apnoea syndrome (OSAS)                   |
|                       | Control group (n = 20; female = 13)                         |
| Age (years)           | 45 (8.30)                                                  |
| BMI (kg/m²)           | 36.31 (5.62)                                               |
| AHI (per hour)        | 48.93 (16.77)                                              |
| RDI (per hour)        | 57.22 (16.33)                                              |
| Oxygen Saturation     | 93.75 (1.55)                                               |
| Epworth Sleepiness Score (ESS) at presentation | 14.45 (5.52) |
| Presence of Hypertension | 5/20                                                       |
| Presence of Cardiac Disease | 1/20                                                      |

| Cohort                | “NFL*” Control group (n = 20; female = 13)                 |
|                       |                                                           |
| Age (years)           | 47 (8.79)                                                  |
| BMI (kg/m²)           | 29.90 (6.81)                                               |
| AHI (per hour)        | 1.01 (1.05)                                                |
| RDI (per hour)        | 2.63 (1.34)                                                |
| Oxygen Saturation     | 95.90 (1.48)                                               |
| Epworth Sleepiness Score (ESS) at presentation | 7.90 (6.21) |
| Presence of Hypertension | 0/20                                                       |
| Presence of Cardiac Disease | 0/20                                                      |

<table>
<thead>
<tr>
<th>f Value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>F = 0.28</td>
<td>P = 0.76</td>
</tr>
<tr>
<td>F = 7.21</td>
<td>P = 0.002</td>
</tr>
<tr>
<td>F = 152.78</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>F = 159.72</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>F = 10.14</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>F = 12.49</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>F = 3.16</td>
<td>P = 0.05</td>
</tr>
<tr>
<td>F = 0.5</td>
<td>P = 0.61</td>
</tr>
</tbody>
</table>
of clinically significant OSA (a so called Inspiratory “Flow Limitation” (IFL) cohort) and whether PTT indices differ when compared to OSAS subjects and with a “control” group exhibiting no evidence of OSAS or IFL (“Non-Flow Limited” or NFL cohort).

**Methodology** 20 subjects meeting criteria for the IFL cohort (mean AHI = 3.84/hr; RDI = 17.71/hr) were aged (± 2 yrs) and gender matched with 20 OSAS subjects (mean AHI = 48.93 hr) and 20 control “NFL” subjects (no sleep disordered breathing; mean AHI = 1.01/hr; RDI = 2.63/hr) underwent respiratory limited polysomnography, including pulse oximetry and ECG monitoring. PTT was defined as interval between the electrocardiographic R wave and point corresponding to 50% height of the ascending plethysmographic (pulse) waveform; PTT Deceleration (deceleration) defined by decline in PTT signal of ≥15 ms, lasting 5 seconds; PTT Deceleration index (PTT Di) defined by number of PTT arousals per hour.

**Results** Table 1 outlines key demographics in the cohorts. Of the NFL cohort, 14 presented with snoring in absence of sleepiness. 72% and 84% were deemed “responders” to CPAP within the IFL and OSAS cohorts respectively. The PTT Di in the IFL cohort (33.67 ± (23.34)/hr) was significantly higher than that measured in the control NFL cohort (23.89 ± (18.88)/hr) but significantly lower than that measured in the OSAS cohort (55.21 ± (29.30)/hr); 3-way ANOVA; F = 8.76; p < 0.001). PTT Di was positively correlated with AHI within the whole study population (CC = 0.46; p < 0.001). Within the IFL cohort, PTT Di was positively correlated with age (CC = 0.501; p = 0.024) but not with gender and BMI.

**Conclusion** The PTT Deceleration Index increased proportionately with SDB, with significantly higher markers of arousal in sleepy subjects exhibiting nocturnal IFL in comparison to control subjects, but not as high as those with clinically significant OSA. These findings support the relevance of IFL as a potentially significant pathogenic entity in the development of daytime sleepiness. The utility of PTT Deceleration Index as a therapeutic target for CPAP Titration in OSAS requires further evaluation.

---

**FEASIBILITY AND PATIENT TOLERABILITY OF TRANSCUTANEOUS ELECTRICAL STIMULATION IN OBSTRUCTIVE SLEEP APNEOA**

1K I Reed, 1MF Pengo, 1S Xiao, 1C Ratneswaran, 1N Shah, 1T Chen, 1A Douiri, 1N Hart, 2Y Luo, 2GF Rafferty, 2GP Ross, 2A Williams, 2Mi Polkey, 1M Mashan, 1J Steier. King’s College London, London, UK; 3Department of Medicine, Padua, Italy; 4Imperial College London, London, UK.

10.1136/thoraxjnl-2016-209333.32

**Introduction** Transcutaneous electrical stimulation (TES) provides neuromuscular tone to the pharyngeal dilator muscles of the upper airway (UA) while asleep, but feasibility of this method to treat obstructive sleep apnoea (OSA) throughout the whole night has not been tested.

**Patients and methods** We conducted a phase two double-blind, sham-controlled, randomised controlled trial using TES of the UA muscles in 36 patients with confirmed OSA to assess patients’ device acceptance and the side effect profile. Patients were studied using polysomnography during randomly assigned nights of sham-stimulation and active treatment following titration of the current while awake. Assessment of patients’ device acceptance and experience of side effects was measured using a visual analogue scale (0–10 points) where high scores indicated better outcomes.

**Abstract S26 Table 1** Device acceptance and side effect profile of TES and polysomnography data. Variables presented as median and interquartilerange. *p*-value derived from the Wilcoxon test.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Sham- Stimulation</th>
<th>Active treatment</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feeling refreshed</td>
<td>5.7 (2.7–7.2)</td>
<td>6.6 (2.2–8.5)</td>
<td>0.40</td>
</tr>
<tr>
<td>Skin discomfort</td>
<td>9.9 (9.5–10.0)</td>
<td>9.9 (9.7–10.0)</td>
<td>0.95</td>
</tr>
<tr>
<td>Tongue unpleasant sensation</td>
<td>9.9 (9.4–10.0)</td>
<td>9.9 (9.4–10.0)</td>
<td>0.63</td>
</tr>
<tr>
<td>Sleep quality</td>
<td>5.6 (2.9–7.1)</td>
<td>6.4 (2.4–8.0)</td>
<td>0.28</td>
</tr>
<tr>
<td>Morning headache</td>
<td>9.4 (6.3–10.0)</td>
<td>9.9 (8.1–10.0)</td>
<td>0.27</td>
</tr>
<tr>
<td>Mouth dryness</td>
<td>4.4 (2.2–8.5)</td>
<td>7.4 (4.9–9.7)</td>
<td>0.007</td>
</tr>
</tbody>
</table>
Results We included 36 patients (age mean 50.8 (SD 11.2) years, male/female 30/6, body mass index median 29.6 (IQR 26.9–34.9) kg/m², Epworth Sleepiness Scale 10.5 (4.6) points, oxygen desaturation index median 25.7 (16.0–49.1)/hour, apnoea-hypopnoea index median 28.1 (19.0–57.0)/hour). None of the patients reported skin discomfort, unpleasant tongue sensations or morning headache. There was no difference in patients’ perceived sleep quality. There was a 59% reduction in mouth dryness after active treatment compared to sham-stimulation. There were no severe adverse events (Table). Conclusion TES of the UA dilator muscles in OSA can be delivered throughout the night with few side effects and does not lead to arousal from sleep, if appropriately titrated.

Cough Sensation

S27 THE EFFECT OF P2X3 ANTAGONISM (AF–219) ON EXPERIMENTALLY EVOKED COUGH IN HEALTHY VOLUNTEERS AND CHRONIC COUGH PATIENTS

Introduction and objectives Effective therapies for chronic cough are a significant unmet need. Recently a P2X3 antagonist (AF–219), markedly reduced cough frequency in two phase 2 trials, but the role of P2X3 receptors and their ligand (adenosine tri-phosphate, ATP) in chronic cough is not well-understood. This study assessed the effect of P2X3 antagonism on cough evoked by capsaicin and ATP in healthy volunteers and chronic cough patients.

Method We performed a double-blind, placebo-controlled, randomised, 4-period crossover study. During each period (≥48 h apart), cough challenges were performed 2h after single doses of study medication [capsaicin (0.48–1000 μM) periods 1/2 and ATP (0.227–929 μmol/mL) periods 3/4]. Two cohorts were enrolled; cohort (1) 14 healthy volunteers (HV, mean age 37.5 yrs, 100% male) and 12 chronic cough (CC, mean age 60.3 yrs, 17% male) received AF-219 300mg/placebo and cohort (2) 12 HV (mean age 34.8 yrs, 100% male) and 12 CC (mean age 57.8 yrs, 25% male) received AF-219 50 mg/placebo. Cough challenges consisted of four inhalations of each doubling concentration of tussive agent, from a dosimeter 30s apart. Coughs in the first 15s were counted and challenges continued to the maximum tolerated dose. The concentrations evoking at least 2 and 5 coughs, C2 and C5 (from inhalation 1) were analysed using mixed effect models; pharmacodynamic modelling was used to estimate Emax/ED50.

Results AF-219 had no effect on capsaicin C2 or C5 at 300 mg or 50 mg in HV or CC (all p > 0.05). For ATP challenges, AF-219 300 mg significantly increased C2 in CC (AF-219 10.8 μmol/mL vs. placebo 2.3 μmol/mL, p = 0.005) but not HV (p = 0.135), whereas AF-219 50mg significantly increased C2 in both groups (CC 40.4 μmol/mL vs. 2.8 μmol/mL, p = 0.002 and HV 114.4 μmol/mL vs. 20.7 μmol/mL, p = 0.046). AF-219 had no significant effect on ATP C5 at either dose in HV (all p > 0.05), but in CC patients 50mg AF-219 (but not 300mg) increased C5 (70.1 μmol/mL vs. 17.1 μmol/mL, p = 0.027). Of note, ATP inhalation evoked less coughing than capsaicin, limiting the utility of the C5 endpoint.

Conclusions P2X3 antagonism reduced cough responses to ATP, particularly in patients with CC, but did not alter cough responses to an off-target tussive agent.

S28 DETERMINANTS OF COUGH FREQUENCY IN ADULT HEALTHY VOLUNTEERS

K Holt, C Gibbard, JA Smith, University of Manchester, Manchester, UK
10.1136/thoraxjnl-2016-209333.34

Introduction Objective cough monitoring is a useful tool to investigate patterns of cough frequency and to evaluate novel cough treatments. The VitaloJAKTM (Vitalograph Ltd, UK) ambulatory cough monitor is a validated semi-automated system for the quantification of cough over 24 hours. Objective cough rates have yet to be quantified in large groups of healthy controls and the influences of subject factors are unclear.

Objective To assess objective cough frequency in a large group of healthy adults across a range of ages.

Method Objective 24 hour cough monitoring was performed using the VitaloJAKTM in adult healthy volunteers; those with a smoking history of >20 pack years and <6 months abstinence were excluded. The recordings were compressed using custom-written software and cough counted manually by trained cough counters and the daytime, night-time and total cough rates calculated. Daytime and total cough rates were log transformed for analysis. Independent t-tests (daytime and total) and Mann-Whitney U test (night-time) assessed the effect of gender and previous smoking. Spearman’s correlation coefficients evaluated the relationships between cough frequency, age, BMI, and pulmonary function.

Results Sixty healthy volunteers were recruited; 27 (45%) males, median age 40 yrs (range 20–74), median FEV1 103.0% predicted (81–141), median FVC 105.5% predicted (82–151), median BMI 24.6 kg/m2 (16.8–39.8), 48 (80%) of subjects had never smoked, median smoking history in the ex-smokers 2.9 (0.1–17) pack years. Median (IQR) 24 h cough rate was 0.17 c/h (0.05–0.87) with daytime rate of 0.26 c/h (0.63–1.33) and night-time rate of 0.00 c/h (0.00–0.12). Males coughed significantly more than females over 24 hours [median 0.42 c/h (IQR 0.13–1.21) vs. 0.13 c/h (0.04–0.59), p = 0.038] and during the day [0.37 c/h (0.11–1.42) vs. 0.19 c/h (0.0–0.91), p = 0.036], but not during the night (p = 0.852). Cough frequency was not significantly correlated with age, BMI, FEV1 or FVC. Cough frequency was no different between never and ex-smokers for daytime or 24 h (p = 0.46 and p = 0.20) but overnight was slightly lower for ex- than never smokers [median 0.00 c/h (0.00–0.09) vs. 0.12 c/h (0.0–0.64), p = 0.037].

Conclusions In healthy adults, spontaneous cough frequency is unaffected by age, BMI, and pulmonary function. Interestingly, males coughed more frequently than females, in contrast to our current knowledge of gender differences in cough reflex sensitivity.

S29 A RANDOMISED CONTROLLED TRIAL OF OVER THE COUNTER MEDICINE CS1002 FOR ACUTE COUGH

1SS Birring, 1J Brew, 2T Kilbourn, 3AH Morice. 1Division of Asthma, Allergy and Lung Biology, King’s College, London, UK; 2Infinit Healthcare Limited, London, UK; 3Hull York Medical School, Castle Hill Hospital, Hull, UK
10.1136/thoraxjnl-2016-209333.35

Introduction Objective cough monitoring is a useful tool to investigate patterns of cough frequency and to evaluate novel cough treatments. The VitaloJAKTM (Vitalograph Ltd, UK) ambulatory cough monitor is a validated semi-automated system for the quantification of cough over 24 hours. Objective cough rates have yet to be quantified in large groups of healthy controls and the influences of subject factors are unclear.

Objective To assess objective cough frequency in a large group of healthy adults across a range of ages.

Method Objective 24 hour cough monitoring was performed using the VitaloJAKTM in adult healthy volunteers; those with a smoking history of >20 pack years and <6 months abstinence were excluded. The recordings were compressed using custom-written software and cough counted manually by trained cough counters and the daytime, night-time and total cough rates calculated. Daytime and total cough rates were log transformed for analysis. Independent t-tests (daytime and total) and Mann-Whitney U test (night-time) assessed the effect of gender and previous smoking. Spearman’s correlation coefficients evaluated the relationships between cough frequency, age, BMI, and pulmonary function.

Results Sixty healthy volunteers were recruited; 27 (45%) males, median age 40 yrs (range 20–74), median FEV1 103.0% predicted (81–141), median FVC 105.5% predicted (82–151), median BMI 24.6 kg/m2 (16.8–39.8), 48 (80%) of subjects had never smoked, median smoking history in the ex-smokers 2.9 (0.1–17) pack years. Median (IQR) 24 h cough rate was 0.17 c/h (0.05–0.87) with daytime rate of 0.26 c/h (0.63–1.33) and night-time rate of 0.00 c/h (0.00–0.12). Males coughed significantly more than females over 24 hours [median 0.42 c/h (IQR 0.13–1.21) vs. 0.13 c/h (0.04–0.59), p = 0.038] and during the day [0.37 c/h (0.11–1.42) vs. 0.19 c/h (0.0–0.91), p = 0.036], but not during the night (p = 0.852). Cough frequency was not significantly correlated with age, BMI, FEV1 or FVC. Cough frequency was no different between never and ex-smokers for daytime or 24 h (p = 0.46 and p = 0.20) but overnight was slightly lower for ex- than never smokers [median 0.00 c/h (0.00–0.09) vs. 0.12 c/h (0.0–0.64), p = 0.037].

Conclusions In healthy adults, spontaneous cough frequency is unaffected by age, BMI, and pulmonary function. Interestingly, males coughed more frequently than females, in contrast to our current knowledge of gender differences in cough reflex sensitivity.
Introduction CS1002 contains diphenhydramine/ammonium-chloride/levomenthol in a demulcent preparation. We conducted a randomised controlled trial to compare the efficacy of CS1002 with Bell’s Simple Linctus (BSL).

Methods 163 subjects with acute cough associated with upper respiratory tract infection, URTI (onset \(\leq 7\) days and cough severity VAS \(\leq 60\) mm), presenting to pharmacists (64%) or general practitioners were randomised to CS1002 or BSL. The subjects (mean age 39 years, 57% female) were instructed to take their medication four times daily (5/5/10/10 ml) for 7 days or until resolution. Investigators were blinded to the treatment allocation. The primary analysis, cough severity VAS (0–100) was ANCOVA in an intention to treat population.

Results CS1002 (n = 82) compared to BSL (n = 75), after 3 days, was associated with a greater reduction in cough severity (adjusted mean(SE) difference 5.9 (4.3), \(p = 0.18\)), cough sleep disruption VAS (mean diff 11.6 (4.5), \(p = 0.01\)) and cough frequency VAS (mean diff 8.1 (4.1), \(p = 0.05\), Figure 1). There was a greater improvement in QOL (LCQ-acute) with CS1002 compared to BSL after 5 days; mean diff 1.2 (0.6), \(p = 0.04\). The reduction in cough severity with CS1002 was similar in dry/cHESTY/TICKLY categories of cough. Cough resolved after 3 days in 24.4% of CS1002 subjects compared to 10.7% BSL, \(p = 0.02\). CS1002 was well tolerated, similar to BSL.

In conclusion We have conducted the largest RCT in URTI with validated outcome measures. CS1002 reduced the impact of cough associated with URTI with a greater reduction in cough frequency and sleep disruption and improvement in QOL and cough resolution compared to BSL.

Introduction and objectives Cough is generally considered a protective airway reflex, however emerging evidence suggests chronic coughing is provoked by noxious sensations from the airway and serves to relieve these sensations. We have found patients with unexplained chronic coughing identify sensations of irritation, tickle (throat) and the urge to cough (UTC) as important sensations provoking coughing. We hypothesised that inhaling low dose tussive agents would evoke similar sensations and could provide a model for investigating chronic cough.

Methods Twelve chronic cough patients (mean age 61.4 yrs, 75% female, median cough duration 7 yrs) and 10 healthy volunteers (mean age 48.8 yrs, 40% female) inhaled increasing concentrations of citric acid from a dosimeter (0.01–4 M, 18 ascending concentrations). Following each inhalation subjects rated irritation, tickle, UTC and taste on 100 mm visual analogue scales (VAS; 0 mm = none and 100 mm = worst). The experiment continued until subjects coughed at least twice on any concentration of citric acid (C2). Somatosensory amplification score (SSAS) and State Trait Anxiety Index (STAI) were also collected. For the analysis, VAS data were aligned by the C2 concentration and sensation VAS scores compared using Mann-Whitney U tests. STAI scores were also compared with Mann-Whitney U tests and SSAS with an independent T test.
Results The chronic cough patients had a much lower C2 than healthy controls (median 0.094 vs. 0.5M, p = 0.009). The UTC VAS and coughs evoked were similar at C2 and for the preceding concentrations in both groups, Figure 1. However, tickle, irritation and taste were rated more highly in healthy volunteers compared with chronic cough patients at C2 and for several preceding concentrations. For example, at C2, irritation VAS was significantly higher in healthy controls (dp = 0.035) and tickle VAS was borderline significant (p = 0.052) compared with chronic cough patients, however taste differences were not significant (p = 0.29). SSAS, STAI state and trait were not significantly different between the groups (p = 0.23, p = 0.096 and p = 0.62 respectively).

Conclusions These data suggest that as well as differences in cough threshold, chronic cough patients exhibit heightened urge-to-cough rather than other sensations in response to low level tussive agents.

S31 REPRODUCIBILITY OF FOUR CHALLENGE MODALITIES FOR CHRONIC COUGH

1L Douglas, 2HF o w l e s, 1K Arnell, 3S Thackray-Nocera, 2AM o r i c e. 1Castle Hill Hospital, Hull and East Yorkshire Hospitals NHS Trust, Hull, UK; 2Hull York Medical School, Hull, UK

Background Cough challenges are utilised in clinical research to help determine efficacy of treatments for cough. Recently adenosine triphosphate (ATP) has gained interest as a potential tussive agent. Previous research suggests such challenges are reproducible in healthy individuals, but little is known about their reproducibility in chronic cough patients, particularly the use of ATP as a tussive agent. This study aims to clarify if ATP is a reproducible tussive agent in chronic cough patients.

Method Data was collected on subjects undergoing cough challenges in the clinical trials unit. Subjects performed tussive challenges with four agents (capsaicin, ATP, citric acid and fog) in a randomly allocated order (visit 1); C2 and C5 were noted. This test was then repeated a week later (visit 2). Intra-patient variability was analysed using the Bland-Altman method for each tussive agent, presented as mean difference (95% limits of agreement). Inter-patient variability was analysed using paired t-tests. Pearson’s correlation coefficient (r) between ATP and other agents was calculated.

Results 26 subjects were recruited; 21 with chronic cough. Average age of 57.4 ± 12.2, mean BMI of 26.8 ± 5.7, with an 85% female predominance. ATP showed a strong correlation with citric acid (r = 0.76, p < 0.001) and capsaicin (r = 0.66, p < 0.001). Bland-Altman analysis at C5 showed a 95% limit of agreement to be more than a two log dose difference except for fog: citric acid −0.07 (−1.7 to 1.5), capsaicin −0.1 (−1.5 to 1.2), ATP −0.2 (−2.5 to 2.1) (Figure 1), fog −0.01 (−0.3 to 0.3). Comparing visit 1 and visit 2 for each tussive agent showed no significant difference (p-value of 0.58, 0.80, 0.90, and 0.80 for ATP, fog, capsaicin and citric acid, respectively).

Conclusion ATP shows a strong correlation with other agents currently being utilised in cough challenges. This suggests direct
EPIDEMIOLOGY OF CHRONIC OBSTRUCTIVE PHYSICAL ACTIVITY INTERVENTION VERSUS PULMONARY REHABILITATION IN COPD: THE LIVELY COPD PROJECT

Introduction and objectives The format of pulmonary rehabilitation (PR) may not meet the needs of all patients with COPD or lead to improved physical activity (PA) levels. Drop outs from PR can be high. A pedometer driven physical activity intervention (PAI) may offer patients an alternative method for increasing their PA. The aim of this study was to assess the feasibility of a 12 week clinician facilitated PAI versus PR in people with COPD.

Methods The design was a multicenter-randomised, parallel-group, feasibility study. Patients with COPD referred for PR were included. Spirometry and demographics were recorded. The following were assessed at baseline, post-intervention and follow up (12 weeks): PA using an ActiGraph GT3X+ accelerometer, sealed Yamax Digiwalker pedometer and the International Physical Activity Questionnaire (IPAQ) (long form); exercise capacity (Incremental Shuttle Walk Test (ISWT)); COPD Assessment Test (CAT). Recruitment, retention and completion/ rates were recorded. Descriptive statistics and mean differences were used to analyse the data.

Results 50 patients (mean (SD) age 64 (8) years, 24M, FEV1 1.44 (0.63)) were recruited and randomised: PR n = 26, PAI n = 24. Of those screened 50/651, 13% were recruited. One participant randomised to the PAI started PR, a per protocol analysis was conducted; PR n = 27 and PAI n = 23. Completion of the PAI was 74% (17/23) and PR was 48% (13/27), and 66% at follow up (n = 15 PAI; n = 18 PR). There was a mean (95% confidence interval (CI)) change of 972 (441 to 449) in the PAI and PR group respectively; 12 week clinician facilitated PAI versus PR in people with COPD.

Conclusions This study will inform a future large scale randomised control trial (RCT). The LIVELY PAI intervention appears to be feasible and safe within this preliminary study, and enhanced physical activity in people with COPD. While the results require confirmation in a fully powered RCT, the mean increase in step count is in line with a recently published minimally clinically important difference.1

REFERENCE

EFFECT OF 8 AND 12 WEEKS’ ONCE-DAILY TIOTROPIUM AND OLODATEROL, ALONE AND COMBINED WITH EXERCISE TRAINING, ON EXERCISE ENDURANCE DURING WALKING IN PATIENTS WITH COPD

1T Troosters, 2JB Oubreau, 3FM Maltais, 4N Leidy, 5D De Sousa, 6LK Korducki, 6LK Lavoie, 6W Janssens, 6A Hamilton. 1KU Leuven, Department of Rehabilitation Sciences and University Hospital Leuven, Pulmonary Rehabilitation and Respiratory Division, Leuven, Belgium; 2McGill University Health Centre, Montreal, Canada; 3Centre de Recherche, Institut Universitaire de Cardiologie et de Pneumologie de Québec, Université Laval, Laval, Canada; 4Evidera, Bethesda, USA; 5Boehringer Ingelheim Pharma GmbH and Co. KG, Biberach an der Riss, Germany; 6Boehringer Ingelheim (Canada) Ltd, Burlington, Canada; 7Boehringer Ingelheim Pharmaceuticals Inc, Ridgefield, USA; 8Montreal Behavioural Medicine Centre, Research Centre, Hôpital du Sacré-Cœur de Montreal, Montreal, Canada; 9University Hospital Gasthuisberg, Respiratory Division, Leuven, Belgium

10.1136/thoraxjnl-2016-209333.40

Rationale: Physical deconditioning is common in patients with chronic obstructive pulmonary disease (COPD), limiting exercise tolerance. PHYSACTO® (NCT02085161) tested the effects of long-acting bronchodilators alone or combined with exercise training (ExT) on exercise endurance time (EET) in patients with COPD. All patients took part in a standardised physical activity self-modification (BM) programme.

Methods: A 12-week, randomised, partially double-blind, placebo-controlled, parallel-group trial at 34 sites in Australia, New Zealand, USA, Canada and Europe. Interventions (all with 12-week BM) were: BM + placebo; BM + tiotropium (T) 5 μg; BM + T + olodaterol (T/O) 5/5 μg; BM + T/O 5/5 μg with 8 weeks’ ExT (T/O 5/5 μg + ExT). EET (log transformed) during an endurance shuttle-walk test (ESWT) to symptom limitation was assessed after 8 weeks (primary end point) and 12 weeks.

Results: 303 patients (200 men) were randomised and treated (full analysis set n=274). Mean post-bronchodilator forced expiratory volume in 1 second was 1.59 L (57% predicted). EET was significantly increased in patients receiving BM + T/O 5/5 μg

<table>
<thead>
<tr>
<th>Intervention arm</th>
<th>EET, adjusted mean ± SE, seconds</th>
<th>Adjusted mean difference ± SE, seconds</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BM + T/O + ExT</td>
<td>355.73 ± 24.787</td>
<td>1.458 ± 0.147 (p=0.05)</td>
<td>1.196</td>
</tr>
<tr>
<td>BM + T/O</td>
<td>315.32 ± 21.671</td>
<td>1.292 ± 0.129 (p=0.01)</td>
<td>1.777</td>
</tr>
<tr>
<td>BM + T</td>
<td>254.18 ± 18.099</td>
<td>1.041 ± 0.106 (p=0.01)</td>
<td>1.061</td>
</tr>
<tr>
<td>BM + T/O</td>
<td>244.07 ± 21.671</td>
<td>1.051 ± 0.113 (p=0.01)</td>
<td>1.573</td>
</tr>
<tr>
<td>BM + placebo</td>
<td>255.67 ± 18.099</td>
<td>0.847 ± 0.103 (p=0.01)</td>
<td>0.853</td>
</tr>
<tr>
<td>BM + T (n=67)</td>
<td>267.65 ± 14.50</td>
<td>0.65 ± 0.100 (p=0.05)</td>
<td>1.272</td>
</tr>
<tr>
<td>BM + placebo</td>
<td>254.81 ± 13.80</td>
<td>0.65 ± 0.100 (p=0.05)</td>
<td>0.850</td>
</tr>
<tr>
<td>BM + placebo</td>
<td>254.81 ± 13.80</td>
<td>0.65 ± 0.100 (p=0.05)</td>
<td>1.299</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.01; ***p<0.001 SE, standard error; CI, confidence interval.
EFFICACY AND SAFETY OF THE DIRECT SWITCH FROM
VARIOUS PREVIOUS TREATMENTS TO
GLYCOPRYRONIUM OR INDACATEROL/
GLYCOPRYRONIUM IN PATIENTS WITH MODERATE
COPD: THE CRYSTAL STUDY

Introduction and objectives In contrast to clinical trials, changes
to new therapies in clinical practice occur without any washout
period. The CRYSTAL study was designed to mimic clinical prac-
tice. Patients with symptomatic, non-frequently exacerbating,
moderate COPD treated with various drugs were directly
switched to glycopyrronium 50 μg (GLY) or indacaterol/glycopyr-
ronium 110/50 μg (IND/GLY). Lung function and symptoms
were evaluated.

Methods CRYSTAL was a prospective, multicentre, 12-week,
randomised, pragmatic, open-label trial. Patients were recruited
into 4 Groups according to previous medication and symptoms
(mMRC) and randomised to a direct switch to GLY or IND/GLY
vs. continuation of baseline therapy (3:1). Co-primary objectives
were superiority of GLY vs. previous SABA and/or SAMA, non-
inferiority of GLY vs. previous LABA or LAMA, and superiority
of IND/GLY vs. LABA, LAMA and LABA+ICS regarding trough
FEV1 and transition dyspnoea index (TDI) at Week 12. Due to
slow recruitment, Groups A and B were prematurely discon-
tinued at the time of completion of Groups C and D.

Results Of the 4,389 patients randomised, 2,159 patients
received IND/GLY (C2: n = 811; D2: n = 811) or continued
their previous treatment (LABA + ICS C1: n = 269; LABA or
LAMA D1: n = 268). IND/GLY provided superior improvement
in trough FEV1 at Week 12 vs. LABA + ICS (treatment differ-
ence (Δ) = 71 mL, p < 0.0001) and LABA or LAMA (Δ = 101
mL, p < 0.0001). IND/GLY also improved TDI vs. LABA + ICS
(Δ = 1.10 units, p < 0.0001) and vs. LABA or LAMA (Δ = 1.26
units, p < 0.0001). Significantly more patients on IND/GLY
reached the minimally clinically important difference (MCID) of
100 mL for trough FEV1 and 1 point for TDI vs. comparators
(Table 1). In the Groups A and B that were underpowered due to
sample size, GLY was superior to previous SABA and/or SAMA
and was non-inferior to previous LABA or LAMA on trough
FEV1 and TDI (Table 1). GLY and IND/GLY were well tolerated.

Conclusions In the pragmatic CRYSTAL trial, IND/GLY demon-
strated superior improvement in lung function (trough FEV1)
and dyspnoea (TDI) after 12 weeks, in symptomatic patients with
moderate COPD and a history of up to 1 exacerbation in the pre-
vious year, after direct switch from previous treatment with
either LABA+ICS or with a LABA or LAMA.

Abstract S35 Table 1 CRYSTAL Study Results

<table>
<thead>
<tr>
<th></th>
<th>A1 (n = 122)</th>
<th>A2 (n = 369)</th>
<th>B1 (n = 420)</th>
<th>B2 (n = 1254)</th>
<th>C1 (n = 269)</th>
<th>C2 (n = 811)</th>
<th>D1 (n = 268)</th>
<th>D2 (n = 811)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trough FEV1 (L)</td>
<td>1.826</td>
<td>1.892</td>
<td>1.800</td>
<td>1.822</td>
<td>1.685</td>
<td>1.756</td>
<td>1.673</td>
<td>1.774</td>
</tr>
<tr>
<td></td>
<td>[1.780, 1.873]</td>
<td>[1.865, 1.919]</td>
<td>[1.777, 1.824]</td>
<td>[1.808, 1.835]</td>
<td>[1.654, 1.715]</td>
<td>[1.738, 1.774]</td>
<td>[1.646, 1.699]</td>
<td>[1.759, 1.790]</td>
</tr>
<tr>
<td>Differences in trough FEV1 (L)</td>
<td>0.065</td>
<td>0.021</td>
<td>0.071</td>
<td>0.101</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>[0.011, 0.119]</td>
<td>[0.005, 0.048]</td>
<td>0.036, 0.107)</td>
<td>[0.071, 0.132]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with MCID in trough FEV1 (≥100 mL)</td>
<td>1.770</td>
<td>1.401</td>
<td>1.902</td>
<td>2.526</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>[1.150, 2.274]</td>
<td>[0.992, 1.798]</td>
<td>[1.421, 2.546]</td>
<td>[1.863, 3.424]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TDI</td>
<td>0.51</td>
<td>0.70</td>
<td>0.90</td>
<td>0.90</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>[0.011, 1.03]</td>
<td>[0.42, 0.98]</td>
<td>[0.47, 1.23]</td>
<td>[0.51, 1.22]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Differences in TDI</td>
<td>1.10</td>
<td>2.12</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>[1.19, 2.34]</td>
<td>[0.41, 1.66]</td>
<td>[1.17, 1.60]</td>
<td>[1.91, 2.33]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with MCID in TDI (≥1 point)</td>
<td>4.58</td>
<td>2.57</td>
<td>2.609</td>
<td>2.853</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>[2.86, 7.34]</td>
<td>[2.00, 3.29]</td>
<td>[1.94, 3.50]</td>
<td>[2.13, 3.82]</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

All data are LSM Data with [95% CI], unless otherwise stated
*Odds ratios are displayed with 95% CI
Linear mixed model. All primary efficacy analysis are superiority analysis except B1-B2 which are non-inferiority analysis.
Group II: non-inferiority testing (Δ ≤ -40mL for trough FEV1 and -0.6 points for TDI)
* p < 0.05; ** p < 0.0001; ° p < 0.0001 (non-inferiority)
A1 (any SABA and/or SAMA), A2 (GLY), B1 (any LABA or LABA and mMRC = 1), B2 (GLY and mMRC = 1)
C1 (any LABA and ICS), C2 (IND/GLY), D1 (any LABA or LABA and mMRC > 1), D2 (IND/GLY and mMRC > 1)
CI: confidence intervals; LSM: least square means; DR: odds ratio; MCID, minimal clinically important difference.
COIL TREATMENT FOR PATIENTS WITH SEvere EMPHYSEMA AND BilATERALLY InCOMPLETE FISSURES; EFFECTIVENESS AND COMPLICATIONS AFTER ONE-YEAR FOLLOW-UP. A SINGLE-CENTRE EXPERIENCE

K Kontogianni, V Geronaki, D Gompelmann, M Schuhmann, CP Heussel, FJF Herth

Introduction

The aim of this retrospective analysis, was to evaluate the safety and efficacy of Lung Volume Reduction with coils (LVR-Coil) treatment in a single-centre setting in patients with severe heterogeneous emphysema and bilaterally incomplete fissures.

Methods

In this retrospective analysis 86 patients with severe COPD were included. A total of 10 coils were unilaterally implanted in a single lobe. 28 patients received additional treatment, such as corticosteroids. However, little is known about the persistence of higher eosinophils, or its associations with infectious aetiology during clinical stability and exacerbation. We investigated the natural history of eosinophilic inflammation over time and studied eosinophil-associated acute exacerbations of COPD and the impact of seasonality in a cohort of COPD patients.

Results

FEV1 improved significantly at the 90-day follow up but the improvement was not sustained at 180 and 365 days (0.71 ± 0.21 L vs 0.76 ± 0.23 L vs 0.73 ± 0.22 L vs 0.69 ± 0.18 L). FEV1 improved more than 12% minimally significantly change, MCID) in 30 patients (38%). Vital Capacity improved significantly at the 90- and 180-day (p < 0.001) and follow-up changes in pulmonary function tests, 6-Minute-Walk-Test (6MWT) and modified Medical Research Council (mMRC) dyspnea scale, as well as possible complications were recorded.

FEV1 improved significantly at the 90-day follow up (p < 0.001) but the improvement was not sustained at 180 and 365 days. RV improved significantly at 90 days (6.1 ± 1.4 L vs 5.5 ± 1.3 L, p < 0.0001) and at 180 days (6.1 ± 1.4 L vs 5.7 ± 1.2 L, p < 0.0008), but the improvement was not sustained at 365 days. 6MWT improved at 90 days (247 ± 90 m vs 278 ± 81 m, p < 0.0001) and 180 days (247 ± 90 m vs 267 ± 90 m, p:0.02) but the improvement was lost at the 365-day follow up. Forty-two from 71 (59%) patients improved by more than 26 m (MCID) at 90 days while 21 patients (30%) improved more than 54 m. mMRC improved significantly at 90 and 180 days. In a total of 114 procedures no periprocedural deaths occurred. Four patients died in the first 3 months after the treatment (mortality rate 3.5%). Complications observed within the first 90 days included pneumonia requiring hospital admission (28%), pneumothorax with chest tube insertion (6%), significant, persistent hemoptysis was documented in 4 cases (3.5%) and hypoxemia and hypoventilation in 4.4% and 1.75% respectively.

Conclusions

LVR-coil improved PFT, 6MWT and mMRC initially but improvement was lost after 365 days. However, this improvement came at a cost of significant complications and with a 3.5% mortality rate.
Non-Tuberculous Mycobacteria: Passengers or Pathogens?

S38 CLINICAL ISOLATES OF MYCOBACTERIUM AVIUM DRIVE COLLAGENOLYTIC AND ELASTOLYTIC ACTIVITY IN MONONUCLEAR CELLS

SJ McFetridge, R McMullan, CM O’Kane, Queen’s University Belfast, Belfast, Northern Ireland

10.1136/thoraxjnl-2016-209333.44

Background Pulmonary non-tuberculous mycobacterial (NTM) infections are increasing rapidly in the UK. The commonest pulmonary NTM infection outside the setting of cystic fibrosis lung disease is with the mycobacterium avium complex (MAC), consisting of M. avium and M. intracellulare. Patients with pulmonary MAC infection present with cavitatory lung disease or nodular bronchiectasis. Prolonged treatment is required, frequently not tolerated, and often associated with progressive lung destruction. A large body of evidence suggests the tissue damage that occurs in tuberculous lung disease is driven by host derived matrix metalloproteinases (MMPs), in particular MMP-1 and 9. The mechanisms of tissue damage in NTM infection are not understood. We hypothesized that NTM drives MMP secretion and that this drives cavitation and bronchiectasis.

Methods Monocytes isolated from healthy human volunteer blood by density centrifugation were stimulated with M. avium clinical isolates for 24 hours. Human monocyte-derived macrophages (MDMs) were generated from monocytes through 5–7 day incubation with GM-CSF before stimulation with four different clinical isolates of M. avium for up to 72 hours. mRNA expression was investigated using qRT-PCR. Protein in cell supernatants was quantified using ELISA and Luminex array techniques.

Results Stimulation with M. avium does not increase MMP-9 secretion in monocytes or macrophages. M. avium significantly increases gene expression of MMP-1 and induces MMP-1 secretion by MDMs (Figure 1). Additionally, M. avium drives induction of MMP-7, an elastolytic enzyme (Figure 1), and reduces the secretion of TIMP-1; the major in vivo inhibitor of MMP-1.

Conclusions Interestingly, unlike Mycobacterium tuberculosis or other chronic pulmonary pathogens such as Pseudomonas or Haemophilus influenzae, M. avium does not drive secretion of MMP-9 by infected mononuclear cells from healthy donors. Instead it drives functionally unopposed MMP-1, which was previously thought to be an M. tuberculosis-specific response. Data suggest MMP-1 and −7 may drive the destructive pathophysiology that characterises M. avium infection. This will be further investigated with patient sputum samples and inflammatory cells.

RISK OF NTM (NON TUBERCULOUS MYCOBACTERIUM) INFECTION IN PATIENTS ON LONG TERM PROPHYLACTIC MACROLIDE ANTIBIOTICS

JB Adizie, M Qasim, M Pagaria, Russell Hall Hospital, Dudley, UK

10.1136/thoraxjnl-2016-209333.45

Introduction Long term prophylactic macrolide therapy is commonly used in respiratory diseases characterised by persistent airway inflammation and chronic bacterial infection. There is growing evidence that they possess immuno-regulatory and anti-inflammatory effects as well as an antimicrobial action. The development of macrolide resistant bacteria, particularly NTM infection, is a concern because macrolide therapy is the primary treatment of NTM. There is little published data investigating this risk.

Methods We identified the cases, retrospectively, of all adult patients who had been given long term continuous prophylactic macrolide therapy attending the respiratory outpatients clinic until January 2016 at Russell Hall Hospital. The clinic letters were reviewed to get a clinical diagnosis and then data regarding sputum culture results were collected from the electronic reporting system. Approximately 75% of cases were reviewed.

Results 226 patient cases were reviewed. 192 (85%) were on long term Clarithromycin. 86 (38%) had a diagnosis of COPD; 133 (59%) of Non CF Bronchiectasis and 100 (44%) of Asthma. The average starting FEV1 was 1.55. The average change in FEV1 was \( +0.1 \) (range \(-3.22\) to \(+1.07\)). Out of all those who had sputum analysed, not one patient demonstrated evidence of NTM infection in their sputum up to 96 months (Figure 1).

Conclusion Our data suggests that the use of long term prophylactic macrolide therapy in the treatment of respiratory disease does not increase the risk of NTM infection and therefore should not be a concern to limit use in clinical practice. However
randomised controlled trials involving larger populations of patients are required to confirm the benefits and harms.

**Introduction and objectives**

There are in excess of 160 species of non-tuberculous mycobacteria (NTM), the minority of which can cause infection predominantly in patients with an underlying respiratory disease such as bronchiectasis or cystic fibrosis. Isolation of NTM in the respiratory tract does not always signify infection and can represent a transient infection, colonisation or active infection. The American Thoracic Society (ATS) criteria for the diagnosis of NTM lung disease can be used to help assess clinical relevance and the need to treat patients. A retrospective study was conducted to assess the clinical relevance of different species of NTM isolation.

**Methods**

A database of microbiology results at a specialist trust was reviewed for patients with positive NTM isolates between January 2005 and December 2010. These patients were assessed against the ATS diagnostic criteria of NTM lung disease. Patient records for those who met the microbiological criteria records were reviewed for demographics, underlying condition and course of infection. Patients were followed up for a minimum of 5 years, or until discharge/death.

**Results**

Five hundred and fifty-five (555) patients with positive NTM cultures were found, 281 (51%) of whom met the ATS microbiological criteria. 70 (13%) patients met the radiographic criteria and so were likely to have an active infection. This varied by species: *M. Avium Complex* (MAC) (21%), *M. malmoense* (20%), *M. abscessus* (18%) and *M. kansasii* (17%) were most likely to cause changes on CT, and species such as *M. fortuitum* (1.6%) and *M. gordonae* (0%) were less likely. The proportion of patients treated also varied by species, with *M. abscessus* (45%), *M. kansasii* (23%) and MAC (20%) most likely to be treated. Five-year mortality for all patients who met the microbiological criteria was 21.4% and was significantly associated with meeting the full ATS criteria, as shown by Figure 1. Five-year survival and the patient’s underlying condition also varied by species.

**Conclusions**

Clinical relevance of NTM isolation varies by species, clinical symptoms and underlying condition. The decision to treat is influenced by these factors in addition to the ATS criteria.
Background The frequency of clinical isolation of non-tuberculous mycobacteria (NTM) from the respiratory tract is increasing. American Thoracic Society (ATS) criteria aid the identification of clinically relevant isolates causing lung disease.

Objectives (1) to audit diagnostic criteria used when treating NTM at our hospital (2) to identify the most clinically relevant isolates in our region and (3) to identify relevant associated patient demographics and radiological features

Methods records of all patients from whom NTM were isolated from respiratory samples between 2007 and 2014 were reviewed. Microbiological results, radiological findings and symptoms were reviewed to assess adherence to ATS diagnostic criteria and outcomes.

Results NTM were isolated 826 times in 444 clinical episodes during the study period. Of 92 treated episodes, 81 (88%) met diagnostic criteria. If isolated, M. abscessus was most likely to be clinically relevant [Figure 1] and sputum smear positive. Isolation of M. kansasii and M. malmoense also warrant particular attention. Of the cases meeting ATS diagnostic criteria, the most common symptoms were fever, night sweats and weight loss. Concomitant oral steroid use and HIV positive status were common in this group. Cavitation and tree-in-bud were the most common CT radiographic appearances.

Discussion 21% of all clinical episodes with NTM isolation were treated for NTM disease. 88% of cases met ATS diagnostic criteria suggesting good adherence to guidance.

REFERENCE
Results 33 patients grew at least one new isolate of NTM: MABSC (n = 20), 5 of which grew other NTM species in temporally distinct episodes), MAC (n = 12) & other NTMs (n = 5, mainly M. kansasii), 51% female. Median age at 1st isolation 12.3 yrs (range, 4–17.3), and FEV1 79.5% predicted (50–116%). 10 (26%) initial isolates were from BAL. For MABSC: 4 (20%) had ABPA and 6 (30%) CFRD. All patients met ATS/IDSA criteria for diagnosis and were treated in accordance with national consensus guidelines. Spontaneous clearance was seen in 100% of other NTM infections. For data on clearance and treatment of MABSC and MAC, see Table 1. 9/14 who completed NTM treatment showed culture conversion at 3 months. Only 2 children with negative cultures at 3 months went on to have subsequent positive microbiology.

Conclusion This is the first report discussing treatment success for NTM in a large paediatric cohort. Although single centre, there is a similar incidence of NTM to that reported for adult CF populations. Spontaneous clearance is more common with MAC (42%) and other NTM infections compared to MABSC (10%). To date 53% of treated MABSC are considered eradicated 12 months post treatment. Early culture conversion appears to be linked with treatment success. Further studies are needed to identify if a lack of early clearance should identify children appropriate for further inpatient induction therapy.

Innate Immunity in Lung Disease

<table>
<thead>
<tr>
<th>Abstract S42 Table 1 Treatment and eradication of M. abscessus complex (MABSC) and M. avium complex (MAC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
</tr>
<tr>
<td>Spontaneous clearance, n (%)</td>
</tr>
<tr>
<td>Commenced treatment, n (%)</td>
</tr>
<tr>
<td>Days to treatment from 1st isolation, median (range)</td>
</tr>
<tr>
<td>Treatment duration in months, mean (range)</td>
</tr>
<tr>
<td>Completed treatment, n (%)</td>
</tr>
<tr>
<td>Eradication with treatment, n (%)</td>
</tr>
<tr>
<td>Relapsed after treatment, n (%)</td>
</tr>
</tbody>
</table>

Innate Immunity in Lung Disease

HYPOXIA UPREGULATES PI3KINASE-DEPENDENT NEOPTROPH DEGRANULATION AND NEOPTROPH-MEDIATED TISSUE INJURY

1JM Lodge, 1K Hoenderdos, 1AJ Robbins, 1DM Storisteanu, 1ER Chilvers, 1W Li, 2AM Condiffe. 1University of Cambridge, Cambridge, UK; 2University of Sheffield, Sheffield, UK

10.1136/thoraxjnl-2016-209333.49

Introduction Damage to host tissue from persistent neutrophilic inflammation is implicated in the pathogenesis of many diseases, including chronic obstructive pulmonary disease (COPD). Infected/inflamed tissues can be profoundly hypoxic; this state may synergise with inflammatory cytokines to promote a destructive neutrophil phenotype with enhanced potential for tissue damage.

Methods Neutrophils isolated from COPD patients or healthy volunteers were incubated under normoxia (21% O2) or hypoxia (0.8% O2) before treatment with priming (GM-CSF/PAF/TNF-α) and stimulating (FMLP) agents, with/without PI3Kinase inhibitors (pan/β/δ). Neutrophil elastase (NE) activity was measured by Enzcheck® assay, Western blotting for total and phosphorylated Akt was performed using cell lysates. Neutrophil extracellular trap (NET) production was assessed by assays of fluorescence absorbance. Neutrophil supernatants were incubated with primary human pulmonary artery endothelial cells (HPAEC); death and detachment were measured by MTT assay and confocal microscopy. Precipitated neutrophil supernatants were separated by SDS polyacrylamide gel electrophoresis (PAGE) and silver stained. S100A8/A9 homo- and heterodimer content of neutrophil supernatants was assessed by ELISA.

Results Hypoxia increased NE release in an agonist- and PI3K-δ-dependent manner, with more pronounced hypoxic degranulation responses seen in exacerbating COPD patients. Hypoxia augmented resting and cytokine-stimulated Akt phosphorylation; PI3K-δ inhibition abrogated Akt phosphorylation and prevented the hypoxic uplift of NE release. Hypoxia did not increase NET production in resting or GM-CSF/MLP treated cells. Hypoxic neutrophil supernatants induced extensive HPAEC detachment and death, which was prevented by co-incubation with alpha-1 antitrypsin. Silver stained protein bands from precipitated neutrophil supernatants separated by SDS-PAGE were identified by mass spectrometry, suggesting a hypoxic increase in damage associated molecular pattern (DAMP) proteins S100A8 and S100A9. When interrogated by ELISA, there was no difference between the amount of S100A8/A9 hetero- or homodimers in normoxic versus hypoxic supernatants.

Conclusion Hypoxia augments neutrophil degranulation in an agonist- and PI3K-δ-dependent manner, which may be further increased during COPD exacerbations. Hypoxic neutrophil supernatants have enhanced capacity to damage endothelial cells in vitro, likely due to increased release of NE. The contribution of S100A8/A9 proteins to this damage is currently unclear. Hence, hypoxia promotes a destructive histotoxic neutrophil phenotype with potential relevance to diseases such as COPD.
S45 EVALUATING THE SENSITIVITY AND SPECIFICITY OF ACTIVE NEUTROPHIL ELASTASE AS A BIOMARKER FOR BACTERIAL INFECTION IN SUBJECTS WITH COPD

1SJ Thulborn, 2NA Kramer, 3VMistry, 4K Moffitt, 4D Ribeiro, 1M Bafadhel.
1University of Oxford, Oxford, UK; 2Oxford Brookes University, Oxford, UK; 3University of Leicester, Leicester, UK; 4ProAxsis Ltd, UK, Carterton

Introduction COPD is a neutrophilic disease, with the majority of subjects having a sputum neutrophil percentage of >60%. Neutrophil elastase (NE) is a serine proteinase, secreted by neutrophils and macrophages during inflammation and has a role in the destruction of bacteria within the host. New advancements now allow accurate assessment of active protease levels in complex biological samples. We sought to investigate if active NE could be used as a biomarker for bacterial infection in subjects with COPD.

Methods Human neutrophils were purified from healthy volunteers by discontinuous percoll gradients. PAO-1 and PHD-deficient strains were grown in lysogeny broth and equivalent growth curves confirmed. Supernatants from wild-type and PHD-deficient P. aeruginosa were harvested at two hours and then co-cultured with neutrophils in normoxia and hypoxia. Neutrophil viability and apoptosis was then assessed using AnnexinV/To-pro-3 staining on flow cytometry at three and five hours.

Results Control neutrophils in normoxia saw a decrease in viability of 6% between three and five hours. Neutrophils treated with supernatant from the PHD-deficient strain experienced a decrease in viability from 3139 (+ 968) cells at three hours to 2058 (+ 586) at five hours – a decline of 34% (P < 0.05). Normoxic neutrophils treated with the wild-type strain, however, saw a decrease of 21% (P < 0.05).

Discussion These data highlight the relationship between tissue oxygen tensions and host immunity and that bacteria have evolved virulence factors with novel mechanisms of action; namely preventing neutrophil survival at sites of inflammation. Moreover, the potential oxygen-sensing capabilities of prokaryotes are intrinsically linked to bacterial virulence.

Abstract S45 Figure 1 Sputum active NE levels at stable and exacerbation state from 31 paired COPD subjects. Mean and 95% CI

S46 NEUTROPHIL VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) AS A DRIVING FORCE FOR ANGIogenesis IN BRONCHIECTASIS?

1CC Cole, 2SC Carnell, 3KJ Jawa, 4JB Birch, 3KH Hester, 1CW Ward, 1JS Simpson, 2ADS De Soyza. 1Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, UK; 2Newcastle Clinical Trials Unit, Newcastle Upon Tyne, UK; 3Sir William Leech Centre for Lung Research, Freeman Hospital, Newcastle Upon Tyne, UK; 4Institute for Cell and Molecular Biosciences, Newcastle Upon Tyne, UK

Introduction Bronchiectasis (BR) in a pulmonary disease thought to involve a characteristic dilation of the bronchi resulting from a cycle of airway infection and inflammation. This inflammation is believed to be driven by neutrophils, which are present in the BR lung in high number. Vascular endothelial growth factor (VEGF) is a pro-angiogenic cytokine that may be upregulated in BR and could contribute towards creating a pro-angiogenic airway environment by supporting neutrophil migration into the airway tissue, however this has yet to be shown.

Aims 1) Examine the BR airway for any indications of increased angiogenesis, 2) Assess the ability of neutrophils to secrete VEGF upon stimulation in vitro, 3) Evaluate sera/sputa samples VEGF concentration to determine if VEGF could act as a biomarker for BR severity.

Methods Healthy volunteer (HV) and BR endobronchial biopsies were stained with a HRP conjugated anti-CD31 antibody, allowing blood vessels to be counted in a blinded manner. Peripheral blood neutrophils isolated from HV were stimulated (e.g. with TNF-α or bacterial PAMPS) for 4 hours, VEGF levels in supernatants were then quantified using ELISA. A VEGF ELISA was also used to determine VEGF concentration in sera and sputa samples...
from BR patients (n = 115), categorised by bronchiectasis severity index (BSI) scores and sera samples from HV controls (n = 26)

**Results** Endobronchial biopsies from BR airways had a significantly (p < 0.05) higher number of blood vessels per mm of basement membrane than HV samples (18 and 9 blood vessels/mm basement membrane respectively). Stimulation of HV neutrophils with a variety of molecules (PMA, fMLP, LPS, TNF-α etc.) resulted in a significant increase in VEGF secretion compared to unstimulated (p < 0.05). Although elevated VEGF was found in some patient samples there was no significant correlation between sera/spuva VEGF and individual patient BSI scores.

**Conclusion** The increased presence of vascular tissue seen in BR could indicate a pro-angiogenic airway environment in BR. The in vitro data collected also show that a variety of stimulants can initiate secretion of VEGF by neutrophils. However, our data does not suggest that VEGF levels in sera or sputa can be used to predict disease severity.

### Table 1

<table>
<thead>
<tr>
<th>System</th>
<th>Neutrophil:platelet aggregates (mean fluorescence intensity ± SDs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Background</td>
<td>11.24 ± 5.0</td>
</tr>
<tr>
<td>ADP (100 µM)</td>
<td>20.63 ± 5.6*</td>
</tr>
<tr>
<td>Ply (10 ng/ml)</td>
<td>18.90 ± 10.7*</td>
</tr>
<tr>
<td>Ply (20 ng/ml)</td>
<td>27.92 ± 16.08*</td>
</tr>
<tr>
<td>Ply (40 ng/ml)</td>
<td>33.21 ± 17.09*</td>
</tr>
<tr>
<td>Ply (80 ng/ml)</td>
<td>42.09 ± 23.05*</td>
</tr>
<tr>
<td>DeltaPly (80 ng/ml)</td>
<td>14.86 ± 7.49</td>
</tr>
</tbody>
</table>

*p < 0.05 - p < 0.0009

---

**S47** PNEUMOLYSIN PROMOTES NEUTROPHIL: PLATELET AGGREGATION IN VITRO

**Methods** Neutrophil: platelet-enriched buffy coat suspensions were prepared from the heparinised blood of healthy, adult humans by sedimentation (at 37°C) and diluted 1:50 in Hanks’ balanced salt solution. Following 5 min of preincubation, recombinant Ply (10–80 ng/ml), or the pneumolysoid, delta 6Ply (attenuated with respect to pore-forming activity, negative control), or adenosine 5’-diphosphate (ADP, 100 µM, positive control) were added to the cell suspensions. After a further 5 min period of incubation at 37°C, samples were stained with 5 µl of each of the following murine, anti-human, fluorochrome-labelled monoclonal antibodies: CD16-APC (neutrophils), CD42a-PE (platelets), and CD45-Krome Orange, and incubated for 15 min at room temperature in the dark. This was followed by analysis of samples at a slow rate using a Gallios flow cytometer. The relative numbers of platelets interacting with a single neutrophil were determined using the relative mean fluorescence intensities of CD16+/CD42a+/CD45+ neutrophils.

**Results** These are shown in the accompanying table. Addition of Ply to the mixed cell suspension resulted in statistically significant dose-related formation of neutrophil:platelet aggregates which was maximal at 80 ng/ml and greater in magnitude to that observed with ADP, while delta6Ply was ineffective.

**Conclusion** Ply, at pathologically-relevant concentrations, promotes neutrophil:platelet aggregation in vitro, an activity which is dependent on the pore-forming properties of the toxin. Given the increasing recognition of the role played by platelets in driving neutrophilic inflammation, this activity of Ply may exacerbate pulmonary and myocardial injury in severe pneumococcal disease.

---

**S48** TARGETING SIGLECS TO REDUCE PROTEASE-MEDIATED DESTRUCTION IN TUBERCULOSIS

**Methods** Siglec expression at gene and protein level on primary monocytes isolated from blood donation, and in a monocyte derived macrophage (MDM) model was investigated by qPCR, flow cytometry and western blotting in both unstimulated and Mtb-infected cells. Monocytes and MDMs were infected with Mtb and incubated with antibodies to either neutralise or cross-link siglecs -7 and -9. The effect on their secretion of inflammatory cytokines and MMPs or their inhibitors (Tissue Inhibitors of Metalloproteinases (TIMPs)) was measured by ELISA.

**Results** Siglecs -5, -7 and -9 are constitutively expressed on human monocytes and MDMs. Unlike Siglec-E in mice, these siglecs are not upregulated by LPS stimulation, nor by infection with Mtb.
The role of platelet-derived TGFβ in pulmonary fibrosis

Background Pulmonary fibrosis (PF) is characterised by abnormal wound healing involving fibroblast proliferation, myofibroblast differentiation and increased extracellular matrix deposition. TGFβ is an important driving force in fibrotic disease, however the source of this cytokine in PF is ill-defined. Platelets can release large amounts of TGFβ and, we, and others, have shown platelet deposition in the lungs of patients with idiopathic pulmonary fibrosis (IPF), although the role of these cells in PF is unknown.

Hypothesis We propose that platelet aggregation and release of platelet-derived TGFβ contributes to the aberrant wound healing in fibroproliferative lung disease.

Methods We used a double-transgenic mouse with megakaryocyty-specific deletion of TGFβ (PF4-Cre+/Tgfb1fl) and hence platelets lacking TGFβ. Knockout (KO) mice and wildtype (WT) littermate controls were subjected to the experimental model of lung fibrosis induced by oropharyngeal bleomycin administration. Lung tissue and broncho-alveolar lavage fluid (BALF) were investigated at 6, 21 or 28 days post-bleomycin. Complementary in vitro studies were performed on isolated neutrophils to investigate the effects of platelet-derived TGFβ in chemotaxis assays.

Results In vitro: Platelet-derived TGFβ was shown to be a potent neutrophil chemoattractant with maximal effect at 1ng/ml. In vivo: At 6 days after bleomycin treatment, neutrophils and macrophages were significantly elevated in the lung and BALF in both WT and KO animals as measured by flow cytometric analysis. No significant difference in the percentage or total cell numbers was found between WT or KO mice. At 21 days post-bleomycin, the lungs developed large fibrotic lesions when examined by micro-CT. Bleomycin-treated KO mice exhibited an attenuated fibrotic response compared with WT animals (26.9 vs. 19.6%), although not reaching statistical significance. During the wound resolution phase at 28 days post-treatment, the degree of fibrosis between WT and KO animals was similar (9.56 vs. 9.84%) as determined by micro-CT analysis.

Conclusion Our data suggest that despite being a potent neutrophil chemoattractant in vitro, platelet-derived TGFβ in vivo is not a major driving force during the inflammatory or resolution phases of our PF animal model, but may contribute to the development of fibrotic disease. This will be the subject of further study.

Idiopathic Pulmonary Fibrosis: Mechanisms

Abstract S48 Figure 1 Siglec-9 activation upregulates TIMP1 release from Mtb-infested MDM

Introducing the central mechanism in IPF is a dysfunctional alveolar epithelial-fibroblast interaction resulting in an aberrant repair process. This defect is influenced by other immune processes; one of these is the macrophage pathway. Macrophages are heterogeneous immune cells that can control all phases of the repair process. ‘M2’ or ‘reparative’ macrophages have anti-inflammatory and reparative phenotype, with high scavenger activities. We investigate how monocytes (precursors of monocyte-derived lung macrophages) might contribute to fibrogenesis in IPF.

Introduction The central mechanism in IPF is a dysfunctional alveolar epithelial-fibroblast interaction resulting in an aberrant repair process. This defect is influenced by other immune processes; one of these is the macrophage pathway. Macrophages are heterogeneous immune cells that can control all phases of the repair process. ‘M2’ or ‘reparative’ macrophages have anti-inflammatory and reparative phenotype, with high scavenger activities. We investigate how monocytes (precursors of monocyte-derived lung macrophages) might contribute to fibrogenesis in IPF.

Methods 35 IPF patients (23 sampled while stable and 10 with AE-IPF) diagnosed according to the 2011 ATS/ERS/JRS/ALAT guidelines, with ‘definite’ or ‘probable’ IPF and age and gender-matched healthy controls were recruited over a one-year period. Those with emphysma greater than 25%, current smokers and malignancy were excluded. Lung function and CT fibrosis score1 were performed. Phenotype and function of purified monocytes and monocyte-derived macrophages (MDMs) were determined using qPCR and multi-flow cytometry for selected M1 and M2 genes and proteins (M1 – CD64 M2 – CD163 and CD200R by FACS; and 26 M1 and 26 macrophage markers against three house keeping genes). The ability of MDMs to phagocytose...
MTOR REGULATES TGF-β INDUCED PRO-FIBROTIC GENE EXPRESSION IN PRIMARY HUMAN LUNG FIBROBLASTS

HV Woodcock, JD Eley, C Nanthakumar, TM Maher, PF Mercer, RC Chambers. UCL, London, UK
10.1136/thoraxjnl-2016-209333.57

Introduction TGF-β is a major pro-fibrotic cytokine with a critical role in the pathogenesis of idiopathic pulmonary fibrosis (IPF). TGF-β drives fibroblast to myofibroblast differentiation and extracellular matrix synthesis. mTOR plays a critical role in regulating protein translation and is the catalytic subunit of two functionally distinct complexes, mTORC1 and mTORC2, which have differential sensitivities to rapamycin. The aim of this study was to delineate mTOR signalling in response to TGF-β in human lung fibroblasts and investigate the role of the mTOR pathway in TGF-β mediated myofibroblast differentiation and collagen synthesis.

Methods All human samples were obtained with informed, signed consent and with research ethics committee approval. Primary human lung fibroblasts (pHLFs) were grown from explant cultures. Cells were pre-incubated with varying concentrations of inhibitor before stimulation with TGF-β 1ng/ml. Collagen biosynthesis and αSMA expression were measured by a high-content imaging based molecular crowding assay. Gene expression was measured by qPCR. Western blots were performed to assess mTOR substrate phosphorylation.

Results TGF-β was found to stimulate the delayed and sustained induction of mTOR signalling in pHLFs and this signalling pathway was critical for mediating the late peak in TGF-β induced pro-fibrotic gene expression. Actively, anti-site mTOR inhibition exerted pronounced inhibitory effects on pHLF collagen biosynthesis and myofibroblast differentiation. The induction of mTOR signalling in response to TGF-β was dependent on the canonical Smad pathway. In addition, potent and selective pharmacological agents demonstrated that TGF-β induced mTOR signalling was independent of PI3K/Akt activity, suggesting that mTOR is not activated through the prototypical linear PI3K/Akt axis downstream of TGF-β. Moreover, rapamycin-resistant mTOR signalling was found to be critical for TGF-β induced pro-fibrotic gene expression in pHLFs.

Conclusion mTOR is an important pro-fibrotic signalling node downstream of TGF-β and a potential target for therapeutic intervention in IPF.

REFERENCE
**S53** EFFECT OF EPIGENETIC INHIBITORS ON LUNG FIBROBLAST PHENOTYPE CHANGE IN IDIOPATHIC PULMONARY FIBROSIS

A Pasini, OJ Brand, G Jenkins, AJ Knox, L Pang. Division of Respiratory Medicine – University of Nottingham, Nottingham, UK

10.1136/thoraxjnl-2016-209333.59

**Introduction and objectives**

Idiopathic Pulmonary Fibrosis (IPF) is a fatal interstitial lung disease with unknown aetiology. Lung myofibroblasts (activated fibroblasts) are the major effector cells in the pathogenesis of IPF. Transforming growth factor-β (TGF-β 1) is a potent activator of fibroblasts. Lack of effective treatment options necessitates novel therapeutic approaches. Epigenetic drugs, by inhibiting chromatin modifying enzymes involved in gene expression control, represent promising agents capable of modulating the cellular phenotype.

We previously demonstrated that the cyclooxygenase-2 (COX-2) gene is epigenetically silenced in lung fibroblasts from IPF patients (F-IPF)1 and epigenetic inhibitors and restore COX-2 expression. However, whether epigenetic inhibitors can alter fibroblast phenotype remains unknown. This study aimed to investigate the effect of four different epigenetic enzyme inhibitors on fibroblast phenotype change in IPF.

**Methods**

F-IPF and fibroblasts from non-fibrotic lung (F-NL) treated with TGF-β1 were cultured to test the effects of the epigenetic inhibitors BIX01294 (BIX, G9a histone methyltransferase inhibitor), 3-deazaneplanocin A (DZNep, EZH2 histone methyltransferase inhibitor), SAHA (histone deacetylases inhibitor) and Decitabine (DAC, DNA demethylating agent), in comparison with the COX-2 products prostaglandin E2 (PGE2). The expression of COX-2 and myofibroblast markers collagen 1 (COL1) and α-smooth muscle actin (α-SMA) was assessed. The COX-2 DNA promoter methylation level was analysed by bisulfite sequencing.

**Results**

TGF-β1 induced a myofibroblast phenotype in F-NL characterised by COL1 and α-SMA upregulation and COX-2 downregulation, similar to F-IPF. PGE2 and SAHA were able to maintain/restore COX-2 expression in TGF-β1-induced myofibroblasts and F-IPF. DAC demonstrated similar effect in TGF-β1 treated F-NL only. SAHA also reduced COL1 and α-SMA expression. But DZNep and BIX showed no effect. No differences in the COX-2 promoter methylation level was analysed by bisulfite sequencing.

**Conclusions**

Among the epigenetic inhibitors tested, SAHA shows a promising antifibrotic effect by inhibiting fibroblast activation and the underlying molecular mechanisms are currently under investigation.

**REFERENCE**


**Lungs and Inflation**

**S54** CPAP REDUCES EXACERBATIONS IN TRACHEOBRONCHOMALACIA

M Demirbag, G Tavernier, T Morris, K Hince, C Ustabasi, D Jones, S Fowler. University Hospital South Manchester, Manchester, UK

10.1136/thoraxjnl-2016-209333.60

**Overview**

Tracheobronchomalacia (TBM) is increasingly recognised as a significant diagnosis in patients diagnosed with “severe asthma”. Continuous Positive Airway Pressure (CPAP) is used as first line treatment to stent the airway in TBM patients in order to clear mucus and prevent irritation, inflammation and bacterial overgrowth thereby reducing the number of exacerbations experienced by patients. However, there is currently no published data which evaluates whether this intervention has an impact on outcomes in. This study describes a cohort of patients referred to a regional centre for severe asthma patients, who were
using continuous positive airway pressure (CPAP) in excessive dynamic airway collapse (EDAC)

AP Hicks, T Brown, A Chauhan, K Adeniji, M Quint, S Babu. Queen Alexandra Hospital, Romsey, UK

EDAC is a term that refers to the pathological collapse of respiratory airways during expiration as a result of posterior wall muscle laxity leading to a >50% loss of airway cross-sectional area. This muscle laxity leads to a loss of airway patency which results in symptomatic dyspnoea. CPAP has been suggested as a method to ameliorate the difficulties associated with EDAC where standard medical care has failed, ameliorating the need for further invasive treatments such as endobronchial stenting or tracheoplasty. Demonstrating its effectiveness is difficult as many of those who suffer with EDAC have co-morbid disease such as COPD, asthma or EGPA which may mask the impact of CPAP when measuring response with subjective criteria such as the WHO functional impairment scale. We set out to determine whether we could objectively demonstrate improvements in airway diameter using CPAP in patients with EDAC, in addition to COPD and EGPA, using firstly bronchoscopy and secondly dynamic computed tomography (CT). In both cases we used a Philips Respironics Trilogy 200 CPAP device to deliver positive airway pressure at 5 cmH2O increments up to a pressure of 20 cmH2O. Figure 1a shows a bronchoscopic example of this process with an increase in airway volume at 20 cm H2O. Figure 1b shows a CT example with a 52.9% increase in airway area, with the RMB increasing in diameter by 3 mm. CPAP was objectively shown to be an effective, relatively inexpensive, treatment for EDAC via bronchoscopy or CT imaging and it is hypothesised such independent measures enhance existing assessments of improvement.
and 18.6 (6.5)% ns, p = 0.028 and p = 0.035; NRDI 480.4 (256.0)/min, 314.7 (125.6)/min and 379.5 (138.0)/min, p = 0.22 and p = 0.012; Figure 1).

There were no significant differences in cardiac function between baseline and 3M-FU (TAPSE: 2.6 (0.6) mm vs. 2.4 (0.4) mm, p = 1.00) or systolic pulmonary artery pressures (sPAP 36.7 (15.2) mmHg vs. 35.8 (16.2) mmHg, p = 0.50). The TAPSE score in compliant patients seemed to improve (n = 3; 2.3 (0.6) mm vs. 2.7 (0.3) mm) while non-compliant patients experienced a deterioration (n = 3; 2.7 (0.5) mm vs. 2.2 (0.4) mm).

Conclusions NIV improves NRD and respiratory parameters in patients with OHS. However, cardiac function does not improve over a three-month period despite the significant improvements in ventilation. These results are influenced by treatment adherence.

Abstract S56 Figure 1 EMG para%max improves following setup of NIV And at 3 month in OHS: (*) p < 0.05

S57 QUALITATIVE ASSESSMENT OF THE EXPERIENCE OF TELEMONITORING IN VENTILATED PATIENTS WITH MOTOR NEURONE DISEASE

1H Ashcroft, 1H Ando, 1R Halhead, 1B Chakrabarti, 1CA Young, 1R Cousins, 1RM Angus. 1Aintree University Hospital NHS Foundation Trust, Liverpool, UK; 2Docobo Ltd, Leatherhead, UK; 3The Walton Centre NHS Foundation Trust, Liverpool, UK; 4Liverpool Hope University, Liverpool, UK

Background The National Institute for Health and care Excellence (NICE) has recently issued recommendations on the care of people with motor neuron disease (MND), promoting tailored care for each patient, Guideline 42, 2016. Previous studies suggest remote monitoring offers a facility to regularly monitor and interact with patients, providing timely interventions so it may facilitate delivery of the recommendations. The efficacy of this approach is dependent upon acceptability of telemonitoring to patients.

Aim To understand the experiences of using telemonitoring in ventilated patients with MND.

Methods Semi-structured interviews were conducted with seven patients (male = 3; mean age = 63 yrs). The median illness duration was 14 m (range = 7 m–13 yrs 7 m) and the median non-invasive ventilation (NIV) usage was 12 m (range = 0 m–3 yrs). Participants used a telemonitoring device (Docobo CAREPORTAL) for six months, completed weekly nocturnal pulse oximetry and symptom-related questions. Five caregivers were present at the interviews and provided their feedback. Interviews were audio recorded and transcribed verbatim. Thematic analysis was conducted to find overarching themes. The interpretation was reviewed and supported by a multidisciplinary team examination.

Findings Five themes were identified: Technical Challenges, Increased Self-Awareness, Taking Initiative, Benefits of Timely Intervention, and Reducing the Unnecessary.Whilst participants expressed general ease of Careportal use, technical issues included; messaging system challenges, oximetry transmission, device fault, mobile signal loss. No other negative experience of using Careportal was reported. Overall, participants expressed how telemonitoring enabled symptom awareness and interpretation. The device also enabled the participants to raise their concerns and/or requests to the healthcare professionals via the messaging system, and this was depicted as a sharp contrast to current communication with hospitals. Timely interventions were observed as a result of regular monitoring, contributing to both physical and psychological well-being of the participants. It was also suggested that using Careportal could reduce unnecessary cost/time and hassles created by attending hospital appointments.

Conclusions Telemonitoring enabled participants to be actively involved in their care and they felt that the interventions were timely delivered to meet their needs. The findings suggest potential benefits of utilising Careportal in routine care as a contact point to accommodate different individual’s needs.

Supported by an SBRI Grant

S58 THE USE OF REMOTE MONITORING TO ASSESS VENTILATOR ADHERENCE AND OUTCOMES WITHIN A REGIONAL HOME MECHANICAL VENTILATION SERVICE

1YM Gn, 2RM Moses, 2A Vyas. 1Manchester Medical School, Manchester, UK; 2Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK

Introduction Home mechanical ventilation (HMV) is a recognised evidence-based intervention for patients in chronic respiratory failure (CRF). However there is a paucity of evidence on the adherence to this treatment. This study examined the adherence of HMV and evaluated the clinical outcomes associated with adherence in a variety of patient populations – namely neuromuscular disease, chest wall disease, obesity hypoventilation syndrome and chronic obstructive pulmonary disease (COPD).

Methods A retrospective study was carried out between May to June 2016. Adherence data was downloaded through remote monitoring. Primary outcomes included changes in blood gases at 3 and 6 months, and hospital admissions 12 months pre- and post-ventilation. Qualitative outcomes were obtained through a questionnaire conducted via telephone interviews.

Results 62 patients were included in this study. Patients undertaking remote monitoring of HMV demonstrated an adherence rate of 90.3%, defined as more than 4 hours of ventilator use/night (mean [SD] = 7h 17min [2h 53min]). No significant difference in adherence was found between patients of different aetiologies. The blood gases improved significantly at 3 months compared to baseline (p < 0.05). However, there was a universal trend for these parameters to return to baseline at 6 months regardless of the underlying disease. HMV reduced hospital admissions by

Abstract S57

Abstract S58
1.07 (1.27) per individual per annum (p < 0.0001) and was most significant in the COPD group (p = 0.005). All patient groups indicated that HMV improved their quality of life.

**Conclusion** This study has demonstrated that contrary to existing evidence, the adherence to HMV was extremely good across all diseases. Remote monitoring may play a role in this increased adherence. Although HMV contributed to improvements in blood gases at 3 months, there was a universal trend for these parameters to return to baseline at 6 months in all disease states despite good adherence. Our data therefore suggests that early follow-up is essential to detect deterioration and support the need for palliation. Nevertheless HMV remains an effective treatment to reduce hospital admissions and improve quality of life, if patients are adherent to the intervention.

**Background** The prevalence of conditions requiring nocturnal breathing support is increasing. Evidence is accumulating that early delivery of optimised nocturnal non-invasive ventilation (nNIV) improves acceptability and longer term NIV usage. The AVAPS-AE (adaptive volume assured pressure support with auto-EPAP) mode of the Respironics A40 ventilator offers prospects of fully auto-titrated NIV. After obtaining initial experience, we adopted use of this ventilator mode for initial nNIV titration in patients with nocturnal hypoventilation (excluding those with neuromuscular disorders), with aim of improving service efficiency and patient outcomes.

**Methods** Patients with nocturnal hypoventilation disorders (majority obesity-related) attend our tertiary inpatient breathing support service. In early 2014 we established a protocol for auto-NIV setup which consists of first night sleep study with morning capillary blood gases (+ancillary cardiorespiratory investigations if indicated), second night on AVAPS-AE mode NIV and then transition on third night to fixed ST mode bilevel NIV based on the A40 ventilator report, supported by appropriate improvement and then stability in sleep quality, daytime symptoms, ventilator integration, overnight transcutaneous and morning blood gas measurements.

**Results** Between March 2014 and June 2016 103 patients received AVAPS-AE mode ventilation for initial setup or re-titration of nNIV. The majority of patients tolerated auto-NIV setup protocol well, and were discharged on ‘fixed’ NIV using a less expensive generator with the A40 derived settings, and did not subsequently require ventilator adjustments. Auto-NIV derived settings typically indicated higher backup rates and unpredictable IPAP/EPAP requirements compared with previous experience. 21 patients continue on AVAPS-AE mode NIV long term based on high pressure support or labile ventilation requirements with suboptimal clinical parameters on fixed NIV. Mean length of stay for breathing support assessment has been reduced by >1 day since the adoption of auto-NIV setup protocol, and clinic follow up has also been rationalised.

**Conclusions** Auto-NIV setup protocol achieves significant service efficiencies. This patient cohort will continue to be studied to judge other clinical benefits, but prospective clinical trials with AVAPS-AE or similar ventilator modes for acute NIV and elective outpatient nNIV are justified.

**Introduction** The National Lung Cancer Audit has collected data for over 10 years demonstrating gradually rising resection rates in the UK. The Clinical (formerly Consultant) Outcomes Programme (COP) is an NHS England initiative, managed by HQIP, using national audit data to publish quality measures at the level of individual consultants. The lung cancer COP focusses on activity at individual surgeon level, and on survival at unit level. The first lung cancer COP in 2014 demonstrated overall 30 and 90-day survival of 97.8% and 95.5%.

**Methods** Data submitted to the NLCA for patients having curative-intent surgery who underwent surgery in 2013 was sent to the clinical lead at each surgical unit for validation and addition of responsible surgeon GMC number, with the option to add surgical cases if they were not included in the supplied dataset. Date of death was derived by a link to the Office of National Statistics. Units reporting unadjusted survival proportions more than three standard errors outside the national mean (“alarm” level) at 30 or 90 days were identified as statistical outliers.

**Results** All of the 28 surgical units in England participated in the audit, submitting a total of 4892 cases. Median annual unit activity was 136 resections (IQR 99–221, range 39–481). Median annual activity for individual surgeons was 39 (IQR 20–52, range 1–132). Overall 30-day survival was 98% and 90-day survival was 96%. There were no units with statistical outliers at the alarm level at 30-days and 90-days (see Figure).

**Conclusion** Volume of activity varies widely by unit and individual surgeon. Survival after lung cancer surgery is very high, is improving, and is not statistically significantly different across the surgical units in England. This suggests that lung cancer teams may still be risk averse when considering surgical treatment of their patients. Reasons why patients die between 30 and 90 days is worthy of further investigation. Case-mix adjustment will be needed to allow robust comparisons between units.
RISK FACTORS AND SHORT-TERM OUTCOMES OF DEVELOPING POSTOPERATIVE PULMONARY COMPLICATIONS AFTER VATS LOBECTOMY

Introduction

Postoperative pulmonary complications (PPC), such as pneumonia and atelectasis are associated with poor outcomes following thoracotomy and lung resection, with risk factors identified.\textsuperscript{1,2} Video-assisted thoracoscopic surgery (VATS) is increasingly performed, however, there are varying reports regarding the incidence of PPC with little is known about their effect on short-term outcomes or potential risk factors.

Methods

A prospective observational study of consecutive patients undergoing VATS lobectomy was performed in a regional centre (2012–2016). Exclusion criteria included re-do VATS/completion lobectomy. All patients received physiotherapy assessment/intervention as necessary from postoperative day 1 (POD1). The presence of PPC was determined daily using the Melbourne Group Scale. Outcomes included hospital length of stay (LOS), intensive therapy unit (ITU) admission and hospital mortality.
Results 287 patients underwent VATS lobectomy, 2 patients undergoing completion lobectomy were excluded. Of 285 patients; 137 were male (48%), median (IQR) age of 69 years (13) and mean (±SD) FEV1 of 87% (±19). PPC developed in 21 patients (7.4%); the median day that PPC developed was postoperative day 3 (Figure 1). Patients who developed a PPC had a significantly longer hospital LOS (4 vs 3 days), higher rate of ITU admission (25% vs 0%) and higher hospital mortality (14% vs 0%) (p < 0.001). Current smoking and COPD diagnosis were significantly different on univariate analysis (p < 0.05), but on forward stepwise logistic regression, only current smoking was a significant independent risk factor for PPC (p = 0.015). Those with PPC required significantly more physiotherapy contacts/time, with more specific pulmonary therapy and emergency out-of-hours therapy.

Abstract S61 Figure 1 Day PPC detected following surgery

Conclusions Patients undergoing VATS remain at risk of developing a PPC associated with significantly worse short-term morbidity and mortality. Patients that develop a PPC following VATS required increased postoperative physiotherapy compared to non-PPC patients. Current smoking is an independent risk factor for PPC development following VATS, thus vigorous addressing non-PPC patients. Current smoking is an independent risk factor required increased postoperative physiotherapy compared to non-PPC patients. Current smoking is an independent risk factor for PPC development following VATS, thus vigorous addressing

REFERENCES

ADEQUACY OF INTRA-OPERATIVE LYMPH NODE SAMPLING DURING SURGICAL RESECTION OF NSCLC: INFLUENCING FACTORS AND ITS RELATIONSHIP TO SURVIVAL

T Edwards, H Balata, C Tennyson, P Foden, P Bishop, M Jones, P Krysiak, K Rammohan, R Shah, P Crosbie, R Boston, M Evison. University Hospital of South Manchester, Manchester, UK

Background Adequate intra-operative lymph node sampling is a fundamental part of lung cancer surgery but adherence to standards, particularly in the United Kingdom is not well known. The International Association for the Study of Lung Cancer (IASLC) has defined adequate lymph node sampling as: at least 3 mediastinal lymph node stations, station 7 in all cases, station 5/6 with left upper lobe tumours and station 9 with lower lobe tumours; the sampling of at least 3 hilar lymph node stations is also recommended. This study sought to measure the adequacy of intra-operative lymph node sampling at a regional Lung Cancer Centre, the factors which may influence this and impact on survival.

Methods A retrospective review of the pathological reports for all patients who underwent surgical resection for NSCLC at the University Hospital of South Manchester between 2011 and 2014 (n = 1407) was performed. Lung cancer resection specimens are reported in line with the minimum dataset defined by the Royal College of Pathology and contain a record of all lymph node stations sampled intra-operatively and the histological findings from these lymph nodes. The influence of clinical variables on adequacy of lymph node sampling was investigated and survival data was obtained from national death registries.

Results Adequate intra-operative lymph node sampling increased significantly from 13% (23/173) in 2011 to 51% (224/437) in 2014 coinciding with a dramatic increase in the volume of lung cancer surgery (Table 1). Secondary analysis also revealed that patients with a low or high T-stage, undergoing sublobar resections and undergoing left sided resections have significantly higher rates of inadequate lymph node sampling. Overall, there was no statistically significant difference in survival between patients with adequate and inadequate intra-operative lymph node sampling.

Conclusion This study provides a much-needed benchmark of current thoracic surgical practice in lung cancer in the UK and provides important granularity to facilitate changes to improve adequacy of staging. Further improvement is needed to meet the standards as defined by the IASLC, however, what constitutes an “acceptable” level of adequacy is yet to be defined and this impact on survival is not clear.

Abstract S62 Table 1 Intra-operative nodal sampling during resection of NSCLC at UHSM (2011–14)

<table>
<thead>
<tr>
<th>Measure</th>
<th>Year of surgery</th>
<th>2011/12 vs 2013/14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of NSCLC resections</td>
<td>n</td>
<td>173</td>
</tr>
<tr>
<td>Overall proportion of adequate nodal sampling</td>
<td>%</td>
<td>13%</td>
</tr>
<tr>
<td>&gt;3 mediastinal LN stations sampled</td>
<td>%</td>
<td>17%</td>
</tr>
<tr>
<td>Station 7 sampled</td>
<td>%</td>
<td>36%</td>
</tr>
<tr>
<td>Station S6 in LUL tumours</td>
<td>%</td>
<td>72%</td>
</tr>
<tr>
<td>Station 9 in lower lobe tumours</td>
<td>%</td>
<td>40%</td>
</tr>
<tr>
<td>Proportion of multi-station N2</td>
<td>%</td>
<td>5%</td>
</tr>
</tbody>
</table>

10.1136/thoraxjnl-2016-209333.68
S63 POSTOPERATIVE PULMONARY COMPLICATIONS AND PHYSIOTHERAPY REQUIREMENTS AFTER OPEN THORACOTOMY VERSUS VATS LOBECTOMY: A PROPENSITY SCORE-MATCHED ANALYSIS

1P Agostini, 1ST Lugg, 1K Adams, 1N Vartsaba, 1M Kalka, 1B Rajesh, 1H Steyn, 1B Naidoo, 1R Rushton, 2E Bishay. Department of Thoracic Surgery, Heart of England NHS Foundation Trust, Birmingham, UK; 1Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK; 2School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, UK

Introduction Video-assisted thoracoscopic surgical (VATS) lobectomy is increasingly used for curative intent lung cancer surgery compared to open thoracotomy due to its minimally invasive approach and associated benefits. However, the effect of the VATS approach on postoperative pulmonary complications (PPC), rehabilitation and physiotherapy requirements is unclear; our study aimed to use propensity score matching to investigate this.

Methods Between January 2012 and January 2016 all consecutive patients undergoing lobectomy via thoracotomy or VATS were prospectively observed. Exclusion criteria included VATS converted to thoracotomy, re-do thoracotomy, sleeve/hi-lobe lobectomy and tumour size >7 cm diameter (T3/T4). All patients received physiotherapy assessment on postoperative day 1 (POD1), and subsequent treatment as deemed appropriate. PPC frequency was measured daily using the Melbourne Group Scale.1 Postoperative length of stay (LOS), high dependency unit (HDU) LOS, intensive therapy unit (ITU) admission and in-hospital mortality were observed. Propensity score matching (PSM) was performed using previous identified PPC risk factors (age, ASA score, BMI, COPD, current smoking) and lung cancer staging.

Results Over 4 years 736 patients underwent lobectomy with 524 remaining after exclusions; 252 (48%) thoracotomy and 272 (52%) VATS cases. PSM produced 215 matched pairs. VATS approach was associated with less PPC (7.4% Vs 18.6%; p < 0.001), shorter median LOS (4 days vs 6; p < 0.001), and a shorter median HDU LOS (1 day vs 2; p = 0.002) (Table 1). Patients undergoing VATS required less physiotherapy contacts (3 Vs 6; p < 0.001) and reduced therapy time (80 min vs 140; p < 0.001). More patients mobilised on POD1 (84% vs 81%; p = 0.018), and significantly less therapies to treat sputum retention and lung expansion were required (p < 0.05).

Abstract S63 Table 1 Postoperative outcomes following open thoracotomy versus VATS.

<table>
<thead>
<tr>
<th></th>
<th>Thoracotomy (n = 215)</th>
<th>VATS (n = 215)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPC (%)</td>
<td>40 (18.6)</td>
<td>16 (7.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median Hospital LOS (IQR)</td>
<td>6 (4)</td>
<td>4 (3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median HDU LOS (IQR)</td>
<td>2 (2)</td>
<td>1 (1)</td>
<td>0.002</td>
</tr>
<tr>
<td>ITU admission (%)</td>
<td>9 (4.2)</td>
<td>6 (2.8)</td>
<td>0.599</td>
</tr>
<tr>
<td>Hospital mortality (%)</td>
<td>5 (2.3)</td>
<td>3 (1.4)</td>
<td>0.724</td>
</tr>
</tbody>
</table>

VATS, video-assisted thoracoscopic surgery; PPC, postoperative pulmonary complication; LOS, length of stay; HDU, high dependency unit; ITU, intensive therapy unit.

Conclusions This study demonstrates that patients undergoing VATS lobectomy developed less PPC and had improved associated outcomes compared to thoracotomy. Patients were more mobile earlier, required half the physiotherapy resources, having fewer pulmonary and mobility issues.

REFERENCE

S64 RATES AND SITES OF RECURRENT FOLLOWING RADICAL TREATMENT OF STAGE I LUNG CANCER

1MPT Kennedy, 1XL Lumminis, 1K Spencer, 1K Franks, 1M Snee, 1ME Callister. 1Leeds Teaching Hospitals NHS Trust, Leeds, UK; 2Cancer Epidemiology Group, Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK

Introduction Lobectomy is the treatment of choice for medically operable patients with stage I lung cancer, with the best reported overall survival and lowest recurrence rates. Patient selection influences outcomes as demonstrated by wide variations in outcomes and reported recurrence rates for all radical lung cancer treatments. Some studies report recurrence rates following Stereotactic Ablative Radiotherapy (SABR) that are comparable to lobectomy. We aim to analyse the rates and site of recurrence in our patients who were radically treated for stage I lung cancer.

Methods All patients with two years follow-up after radical treatment for stage I lung cancer (2008–2013) were included. Retrospective review of electronic patient records to identify outcomes, including the presence and site of any recurrence.

Results 425 patients were identified. Treatment modalities included lobectomy 187 (44.0%), SABR 99 (23.3%), sub-lobar resection 85 (20.0%) and radical radiotherapy 54 (12.7%). There was pathological confirmation in 56.6% of SABR and 63.0% of radical radiotherapy.

Patients treated with surgical resection were younger (mean age 69.0 vs 75.9 years, p < 0.001) and had a better performance status (PS0–1 83.5% vs 37.9%, p < 0.001), although larger tumours (T2a 53.4% vs 31.3%, p = 0.001). Mortality without cancer recurrence at two years was lower following surgery than non-surgical treatment (10.7% lobectomy and 11.8% sub-lobar resection vs 27.3% SABR and 25.9% radical radiotherapy, p < 0.001).
Overall recurrence rates at two years were 12.3% lobectomy, 11.8% sub-lobar resection, 17.2% SABR and 29.6% radical radiotherapy – differences not significant on uni-variable regression, which may relate to small patient numbers. Figure 1 demonstrates the sites of recurrence. Considering only those with pathological confirmation of cancer, recurrence rates at two years were 17.9% for SABR and 32.4% for radical radiotherapy.

**Conclusions** The lowest recurrence rate was observed following surgical resection. In comparison, recurrence following SABR was non-significantly higher due to more loco-regional recurrence. Radical radiotherapy is associated with higher rates of overall, loco-regional and distant recurrence. Nodal recurrence was comparable between lobectomy, SABR and radical radiotherapy. This data is limited by low numbers as well as the confounding effects of early non-cancer deaths and incomplete pathological confirmation in the non-surgical treatment cohorts.
showed subjective deterioration in symptom trajectory 4 days prior to exacerbation onset (p < 0.01), with re-exacerbators demonstrating a higher baseline symptom burden in the post-treatment period compared to single exacerbators (p < 0.01).

In conclusion, salivary biomarker levels can complement patient self-assessment to provide clinically useful cues to enable earlier identification of exacerbations in COPD; salivary CRP potentially offers additional information on re-exacerbation risk. These results support opportunities for patient-reported events and salivary biomarkers to be used synergistically in future near-patient COPD diagnostics for enhanced self-management and prompt exacerbation intervention.

Mortality in COPD Patients Following Community Acquired Pneumonia: A Population Database Analysis of Linked Healthcare Records

1NW Williams, 2A Coombs, 3M Johnson, 4L Josephs, 5LA Rigge, 6DM Thomas, 7TMA Wilkinson. 1Southampton NIHR Biomedical Research Unit, University Hospital Southampton NHS Foundation Trust, Southampton, UK; 2Primary Care and Population Sciences, University of Southampton, Southampton, UK; 3NIHR CLAHRC Wessex Methodological Hub, University of Southampton, Southampton, UK; 4Department of Respiratory Medicine, University Hospital Southampton NHS Foundation Trust, Southampton, UK; 5Clinical & Experimental Sciences, University of Southampton, Southampton, UK

Introduction Community acquired pneumonia (CAP) is a common occurrence in patients with chronic obstructive pulmonary disease (COPD), yet controversy still remains about its affect on outcome. We therefore investigated the impact of CAP on mortality in a cohort of COPD patients identified from the Hampshire Health Record analytical database, a local NHS database containing linked, anonymised primary and secondary care records.

Methods Patients were defined as having COPD if they had a diagnostic Read code in their primary care record at any time prior to the 1st January 2010 and were aged ≥40 years at the start of the study. CAP episodes occurring over a 5-year period from 1st January 2010 were identified using Read and ICD-10 codes. The outcome measure was all-cause mortality following a CAP diagnosis. Cox proportional hazard modelling was used to estimate hazard ratios (HR) and confidence intervals (CI), adjusting for age, sex, GOLD stage, smoking status and inhaled corticosteroid use (ICS).

Results The cohort comprised 14506 COPD patients. The mean age was 70.3 (±10.8) years and 53.6% were male. 1931 (13.3%) patients had at least one CAP and 2870 (19.8%) deaths occurred over the study period. 28.2% of patients diagnosed with CAP died compared to only 9.7% of those without a CAP diagnosis (p < 0.001). Logistic regression analysis, controlling for potential confounders identified CAP as an independent risk factor for future mortality (odds ratio 2.72; CI 2.37–3.12, p < 0.001). Compared to younger individuals (40–59 years) those aged 60–79 and ≥80 years had the highest mortality risk following CAP (HR 2.65; CI 1.61–4.34, HR 7.03; CI 4.27–11.57 respectively, both p < 0.001). Concurrent use of inhaled Fluticasone or Budesonide were associated with reduced mortality risk following CAP (HR 0.82; CI 0.68–0.98 p = 0.029, HR 0.55; CI 0.39–0.76 p < 0.001, respectively) (Figure 1).

Conclusion CAP in COPD is associated with increased risk of mortality, especially in older individuals. Although known to increase CAP risk, ICS use appears to reduce risk of mortality following CAP. Further research to understand the mechanisms underlying CAP risk in COPD and modulating effects of ICS is key, to guide development of future, targeted preventative strategies.

COPD in the ED: Eosinophils, Treatment and Outcomes, Data from the Pre-Award Study

1REK Russell, 2T Doggett, 1PAcknowled, 2R Pullinger, 1S Beer, 1M Bafadhel. 1University of Oxford, Oxford, UK; 2Oxford University Hospitals NHS Foundation Trust, Oxford, UK

Rationale Acute exacerbations of COPD (AECOPD) are common. Peripheral blood eosinophil count (PBE) predicts outcomes in moderate and severe exacerbations, but little is known about PBE levels and outcomes of AECOPD in the emergency department (ED).

Methods Data for all attendances to ED of a large teaching hospital throughout a 12-month period for patients attending with AECOPD were studied. Anonymised data was cleaned to remove diagnostic and data errors and analysed using GraphPadPrism with statistical methods suitable for the data collected. Data is
presented as mean (SEM). Data collected included: demography, length of stay (LOS), vital status, initial treatment, full blood counts, renal function and CRP.

Results There were 549 patients, with 768 AECOPD events. The mean (SD) age was 71 years and 192 episodes were associated with an eosinophil count >2% (26.6%). There were 403 (56%) AECOPD episodes leading to admission; there was no difference in the eosinophil count between patients admitted or discharged from ED. Absolute and relative PBE levels were increased in patients re-attending ED (Absolute PBE mean difference 0.08, 95% CI: 0.02 to 0.13, p = 0.007; %PBE mean difference 0.6, 95% CI: 0.14 to 1.1, p = 0.001). Patients with a PBE > 2% were readmitted more often (p = 0.002, RR 1.16, 95% CI: 1.05 to 1.26). For patients admitted, mean LOS was reduced if admission %PBE levels were >2% (4.6 (0.5) vs. 5.8 (0.3) days, p = 0.012). In patients known to have received oral corticosteroids in ED, the reduction in LOS was greater still if the %PBE was >2% compared to ≤2% (mean (SD) 4.1 (1.0) vs. 6.5 (0.9), p = 0.046). In-patient mortality occurred in 35 patients and occurred more frequently in patients with a %PBE ≤ 2% (RR 1.16, 95% CI: 1.04 to 1.68, p = 0.012).

Conclusions This real-world data suggests that PBE levels may be a useful marker for predicting important clinical outcomes in AECOPD.

TROPTONIN LEVELS AND RISK OF DEATH FOLLOWING A MYOCARDIAL INFARCTION IN PEOPLE WITH AND WITHOUT COPD

KJ Rothnie, N Ahmed, JK Quint. Imperial College London, London, UK
10.1136/thoraxjnl-2016-209333.75

Introduction Myocardial Infarction (MI) is a common comorbidity and cause of death in people with COPD, and COPD is associated with increased risk of death following acute MI. We aimed to: 1) compare levels of peak troponin following MI between people with and without COPD; and 2) investigate differences in the prognostic value of peak troponin between those with and without COPD.

Methods Patients from the Myocardial Ischaemic National Audit Project (MINAP) database who had linked Office of National Statistics (ONS) mortality data from 2003–2013 were included in the study. COPD was defined as the presence of obstructive airway disease and smoking history. We used linear regression to compare levels of peak troponin I and T between people with and without COPD followed by logistic regression to investigate the prognostic value of peak troponin in predicting 180 day mortality separately for those with and without COPD. All models were adjusted for age, sex, smoking, peripheral vascular disease, cerebrovascular disease, chronic renal failure and previous angina.

Results We included 300,146 patients with a first MI, 34,027 (11.3%) with COPD. Peak troponin T & I was lower for those with COPD following both STEMI (troponin T: 0.51 ng/mL lower, adjusted% 12% lower (95% CI: 6–18%); troponin I: 5.49 ng/mL lower, adjusted% 12% lower (6–18%)) and non-STEMI (troponin T: 0.07 ng/mL lower, adjusted% 20% lower (95% CI: 16–25%); troponin I: 0.34 ng/mL lower, adjusted% 19% lower (15–23%)). The prognostic value of increased peak troponin was higher for COPD patients than those without COPD for troponin T, p-value for interaction = 0.02 (Table 1), but this was not apparent for troponin I p-value for interaction = 0.520.

Abstract S69 Table 1 Risk of death at 180 days after acute MI for those with and without COPD at differing troponin T levels.

<table>
<thead>
<tr>
<th>Troponin level (ng/mL)</th>
<th>COPD adjusted OR (95% CI)</th>
<th>Non-COPD adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.01</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>0.01–0.049</td>
<td>1.71 (0.84–3.47)</td>
<td>0.82 (0.62–1.08)</td>
</tr>
<tr>
<td>0.05–0.099</td>
<td>1.59 (0.79–3.18)</td>
<td>1.28 (1.00–1.65)</td>
</tr>
<tr>
<td>0.1–0.49</td>
<td>2.34 (1.20–4.55)</td>
<td>1.44 (1.34–1.82)</td>
</tr>
<tr>
<td>0.5–1.79</td>
<td>2.36 (1.21–4.60)</td>
<td>1.63 (1.29–2.06)</td>
</tr>
<tr>
<td>&gt;1.8</td>
<td>2.55 (1.31–4.95)</td>
<td>1.94 (1.54–2.45)</td>
</tr>
</tbody>
</table>

Conclusion Cardiac Troponin T appears a better prognostic indicator for long-term outcome amongst COPD patients following an MI compared to COPD patients following an MI. Clinicians should not be reassured by relative lower troponin levels in COPD patients at the time of an MI.

REFERENCES

Infections and the Impact on Childhood Respiratory Diseases

570 NEONATAL AIRWAY EPITHELIAL CELL IL-8 RESPONSES TO INFECTION ARE REDUCED IN THOSE WHO GO ON TO WHEEZE

SW Turner, D Miller, G Walsh, U Power, M Shields, G Devereux. University of Aberdeen, Aberdeen, UK; “Queen’s University Belfast, Belfast, UK
10.1136/thoraxjnl-2016-209333.76

Introduction Airway epithelial cells (AEC) are important contributors to the innate immune system and AEC function in children with asthma differs to that of children without asthma. We recruited a birth cohort to establish whether AEC function was abnormal before the onset of asthma symptoms.

Methods Pregnant mothers were recruited and nasal AEC brushings were collected from neonates within 48 hours of birth. Cells were cultured in a submerged model and stimulated with tumour necrosis factor alpha/interleukin-1 beta (TNFa/IL1b), lipopolysaccharide (LPS) and house dust mite (HDM). The mediators in the culture supernatant were quantified by cytometric bead array or ELISA and included: interleukin (IL)–6, IL–8, granulocyte macrophage colony stimulating factor (GMCSF) and interferon gamma (IFNg). The primary outcome of interest was IL-8 expressed as a median [interquartile range] in pg/mg protein. Parents returned a postal questionnaire when their child was four years old.

Results AEC were successfully cultured in 139 neonates of whom 120 were contacted and 85 questionnaires were returned. The mean age was 3.8 years, 42 were boys and 10 reported wheeze in the previous 12 months. Neonates who had recent wheeze at four years had reduced median AEC IL-8 release after exposure to TNFa/IL1b [33, 71] versus 105 [64, 157], p = 0.002, see Figure 1) or to LPS [2.2 [0, 9.0] versus 10.5 [4.6, 24.0] p = 0.038] compared to those who did not wheeze. Neonatal AEC GMCSF
release was also reduced after exposure to TNFα/IL1β in those who later wheezed compared to non wheezers (0.09 [0.01, 0.72] versus 0.67 [0.32, 1.48] p = 0.014). Neonatal AEC release of IFNγ and IL-6 were not associated with later wheeze. Maternal asthma was not associated with AEC IL-8 release.

Conclusions These results suggest that an abnormality which is present at birth in AEC response to infection is important to asthma causation.

**S70**

**Abstract S70 Figure 1**

**S71**

**DO CHILDREN WITH TROUBLESOME PRESCHOOL WHEEZE HAVE EVIDENCE OF FUNGAL SENSITISATION?**

KA Holden, KG Staley, EA Gaillard. University of Leicester, Leicester, UK

10.1136/thoraxjnl-2016-209333.77

Introduction Preschool wheeze is very common and can be troublesome necessitating frequent hospital admissions and trials of preventer medications. It has been suggested that fungal sensitisation is associated with severe childhood asthma (Vicencio 2014), however it is unclear when this sensitisation occurs and whether fungal sensitisation is associated with preschool wheeze. We aimed to assess whether children attending our clinic due to preschool wheeze were sensitised to fungi and whether fungal sensitisation is associated with troublesome wheezing.

Methods Preschoolers attending our clinic due to wheezing investigated for allergic sensitisation to a panel of aeroallergens (D. pteronyssinus, cat, dog, timothy grass and tree pollen) and fungi were identified. Evidence of sensitisation was determined by a raised specific IgE (sIgE) > 35 kU/L detected by fluorescent enzyme immunoassay. Sensitisation to fungi was determined either by raised sIgE to a ‘mould screen’ (comprising Penicillium notatum, Cladosporium herbarum, Aspergillus fumigatus, Candida albicans, Alternaria alternata and Helminthosporium halodes) or to specific fungi including those in the mould screen and Malassezia spp. Data on the number of hospital-recorded admissions due to wheezing in one year, number sensitised to fungi and whether fungal sensitisation is associated with troublesome wheezing.

Results Table 1 displays the demographic features of the 51 children identified, the number of children with a raised total IgE and evidence of sensitisation to aeroallergens and fungi. Six (24%) children with a raised total IgE and 4 (31%) sensitised to aeroallergens were sensitised to fungi. Whilst we found a positive correlation between age and serum total IgE (0.364, r² = 0.13, p < 0.01 – Spearman’s rank) there was no significant correlation between age and sIgE to the mould screen or specific fungi. We found no significant differences in the age, number of hospital-recorded admissions due to wheeze or BTS treatment step between those preschoolers sensitised and not-sensitised to fungi.

Discussion Our preliminary data suggests that a) few children with preschool wheeze attending clinic have evidence of fungal sensitisation and b) fungal sensitisation does not appear to be associated with hospitalisation frequency or required medications. Further exploration is required to determine, if any, the relationship between fungal sensitisation and preschool wheeze.

### Table 1: Demographic data, evidence of sensitisation and clinical parameters

<table>
<thead>
<tr>
<th>Male, n (%)</th>
<th>30 (59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (range) age in months</td>
<td>39 (9–71)</td>
</tr>
<tr>
<td>Serum makers of allergic sensitisation</td>
<td></td>
</tr>
<tr>
<td>Raised total IgE (&lt; 52 kU/L), n (%)</td>
<td>25 (49)</td>
</tr>
<tr>
<td>Evidence of sensitisation to aeroallergens, n (% of those with raised total IgE)</td>
<td>13 (22)</td>
</tr>
<tr>
<td>Evidence of sensitisation to fungi, n (% of those with raised total IgE)</td>
<td>6 (24)</td>
</tr>
<tr>
<td>Evidence of sensitisation to fungi, n (% of those sensitised to aeroallergens)</td>
<td>4 (31)*</td>
</tr>
<tr>
<td>Number of hospital-recorded admissions due to wheezing in one year</td>
<td></td>
</tr>
<tr>
<td>≥ 2 admissions (n = 14)</td>
<td>2 (14) †</td>
</tr>
<tr>
<td>Number sensitised to fungi, n (%)</td>
<td></td>
</tr>
<tr>
<td>&lt; 2 admissions (n = 37)</td>
<td>4 (11) †</td>
</tr>
<tr>
<td>Number sensitised to fungi, n (%)</td>
<td></td>
</tr>
<tr>
<td>BTS treatment step*†</td>
<td></td>
</tr>
<tr>
<td>BTS step 3 or above (n = 11)</td>
<td>2 (18) †</td>
</tr>
<tr>
<td>Number sensitised to fungi, n (%)</td>
<td></td>
</tr>
<tr>
<td>BTS step below 3 (n = 40)</td>
<td>4 (10) †</td>
</tr>
<tr>
<td>Number sensitised to fungi, n (%)</td>
<td></td>
</tr>
</tbody>
</table>

*Those children sensitised to aeroallergens were more likely to be sensitised to fungi than those not sensitised to aeroallergens, p<0.05 (Pearson chi-square), †There was no statistically significant difference between the number of children sensitised and not-sensitised to fungi and the number of hospital-recorded admissions or required asthma medications, p>0.05 (Pearson chi-square), ‡BTS treatment step (BTS/SIGN 2014 guidelines on the management of asthma).
**Streptococcus pyogenes** in a similar manner to that observed in studies with *Streptococcus pneumoniae*.  

**Methods** Human positively-isolated CD14+ monocyte-derived macrophages (MDM), an established model for alveolar macrophages, were incubated with an optimised dose of carbon particulates. Phagocytosis of *Streptococcus pneumoniae* and pyogenes was assessed by bacterial culture of macrophages lysates. Autologous CD3 + T cells were co-cultured with infected MDM for 24 h. Expression of cell surface markers, T cell activation and uptake of FITC beads were assessed by flow cytometry.  

**Results** Phagocytosis of *Streptococcus pneumoniae* and pyogenes by carbon loaded MDM was impaired compared to non-carbon loaded MDM (18.8% reduction, p = 0.01). Phagocytosis of FITC beads was also shown to be reduced by the carbon loaded MDM (10% reduction, p = 0.03).  

Carbon loading decreased MDM surface expression of the phagocytic receptor CD36 (p < 0.01) and decreased the surface expression of antigen presentation molecules HLA-ABC and HLA-DR (p = 0.04 and 0.03 respectively). Addition of carbon loading decreased MDM surface expression of the phagocytic receptor CD36 (p < 0.01) and decreased the surface expression of antigen presentation molecules HLA-ABC and HLA-DR (p = 0.04 and 0.03 respectively). Addition of carbon loading decreased MDM surface expression of the phagocytic receptor CD36 (p < 0.01) and decreased the surface expression of antigen presentation molecules HLA-ABC and HLA-DR (p = 0.04 and 0.03 respectively).  

**Conclusion** We conclude that carbon exerts immunomodulatory effects on MDM phagocytosis of *Streptococcus pyogenes* and subsequent antigen presentation. Further investigation of this subject in the context of both chronic lung infection and RHD is therefore warranted.  

**REFERENCE**  
INCREASED RESPIRATORY SYNCYTIAL VIRUS BURDEN LEADS TO MORE RAPID CELL DEATH IN PHE508DEL BRONCHIAL EPITHELIAL CELLS

1MS Coates, 2EWFW Alton, 1DW Brookes, 1K Ito, 1C Davies. 1Pulmocide Ltd, London, UK; 2Imperial College, London, UK

10.1136/thoraxjnl-2016-209333.80

Introduction Respiratory syncytial virus (RSV) leads to serious lower respiratory tract disease and prolonged periods of symptoms in cystic fibrosis (CF) patients. This study aims to determine whether RSV viral burden and the level of cytopathic effect (CPE) is higher in CF bronchial epithelial cells.

Methods Paired immortalised bronchial epithelial cell lines, CFBE41o-, expressing either wild type (WT) or Phe508del CFTR were infected with RSV A2 at an MOI of 0, 0.01, 0.1 and 1.0. Cell viability was measured daily by Resazurin assay, and viral burden by plaque assay in HEP-2 cells and RT-PCR. Viral attachment was determined by PCR after incubating RSV with the cells for 2 hrs at 4°C. Intracellular RSV proteins were measured by western blot.

Results Phe508del CFTR cells showed significantly greater and more rapid CPE by RSV (0.1 and 1 MOI) compared to WT cells. Viral burden was increased in the Phe508del cells each day up to 7 days post infection. The levels of intracellular RSV genetic material determined by PCR were also increased by 4.0 ± 0.2 (mean of MOIs ± SD) fold at 12 hours post infection in CF cells compared to WT. It was confirmed that increased levels of viral RNA led to increased intracellular viral proteins. Virus shedding determined by PCR in the supernatant at 24 hours post infection was also increased by 10.7 ± 5.0 fold in CF cells. There was no evidence of increased RSV attachment to CF cells.

Conclusion RSV causes CPE in bronchial epithelial cells expressing Phe508del CFTR more rapidly than in WT cells. This increased CPE was associated with an increased viral burden, which occurs despite similar levels of cell attachment and is therefore likely due to increased viral replication or transcription within the cell, which led to increased levels of intracellular RSV proteins. The mechanism for this is under investigation.

THE T2R38 BITTER TASTE RECEPTOR AS A MODIFIER OF HOST RESPONSE TO PSEUDOMONAS AERUGINOSA IN CYSTIC FIBROSIS: DOES T2R38 GENOTYPE IMPACT ON CLINICAL INFECTION?

1A Turnbull, 1H Lund-Palau, 1R Murphy, 1A Simbo, 1A Shoemark, 1K Wong, 1A Bush, 1E Alton, 1D Davies. 1Imperial College London, London, UK; 2Royal Brompton Hospital, London, UK

10.1136/thoraxjnl-2016-209333.81

Background Pseudomonas aeruginosa (Pa) mediates several virulence factors through quorum sensing (QS). Intriguing in vitro data suggests Pa QS molecules are ‘sensed’ by the T2R38 receptor on airway cilia (J Clin Invest, 2012;122:4145–59), leading to changes in ciliary beat frequency and nitric oxide production, possibly enhancing bacterial clearance. Three polymorphisms occur in the gene coding this receptor, altering the amino acid sequence and receptor function; the functional allele has proline-alanine-valine (PAV); the non-functional allele has alanine-valine-isoleucine (AVI). We hypothesised that the T2R38 receptor may be important in Pa host defence in people with cystic fibrosis (CF) and that T2R38 genotype may modify infection status and clinical outcomes.

Methods Patients over 6 years with CF were genotyped for polymorphisms in the TAS2R38 gene. Pa infection status was determined by review of all respiratory cultures during 2014 and assigned according to Leeds criteria as chronic, intermittent, Pa free or never. Only patients with ≥3 cultures/year were included in analysis. Lung function data was obtained from CF annual reviews during 2014.

Results T2R38 receptor genotypes were obtained for 271 patients: 83 (30.6%) AVI/AVI, 44 (16.2%) PAV/PAV, 116 (42.8%) AVI/PAV and 28 (10.3%) AVI/other or PAV/other. Between AVI/AVI, PAV/PAV and AVI/PAV groups there was no significant difference in median age, gender or p.Phe508del CFTR mutation frequency. By T2R38 genotype, there was no significant difference in the proportion of patients in each Pa infection category. In patients with intermittent or chronic Pa there was no significant difference by T2R38 genotype in mean percent predicted FEV1 or FVC.

Conclusion T2R38 genotype does not appear to modify Pa infection in people with CF, or to modify lung disease severity in people with CF and intermittent or chronic Pa infection. Further work is underway to investigate T2R38-dependant responses to Pa in vitro.

ENDOPLECTIC RETICULUM STRESS CORRELATES WITH FIBROSIS IN INTERSTITIAL LUNG DISEASE

1H Parfrey, 2E Moseley, 1B Beardsley, 2J Knight, 3SJ Marciniak, 2D Rassl. 1Papworth Hospital, Cambridge, UK; 2Department of Pathology, Papworth Hospital, Cambridge, UK; 3Department of Medicine, CIMR, University of Cambridge, Cambridge, UK

10.1136/thoraxjnl-2016-209333.82

In interstitial lung disease (ILD), pulmonary fibrosis is associated with a poor prognosis. Distinct histological features differentiate between the ILDs, however it is unknown if there are shared pathogenic mechanisms for the development of fibrosis. Endoplasmic reticulum (ER) stress has been implicated in the pathogenesis of familial and sporadic idiopathic pulmonary fibrosis (IPF). In response to ER stress, cells trigger the integrated stress response and upregulate chaperones, such as BiP, and the phosphatase GADD34, which can regulate EMT, cell proliferation and survival.

AIMS We hypothesise that ER stress may be involved in the pathogenesis of fibrosis in all interstitial lung diseases.

Paraffin embedded lung biopsy sections from 8 patients with familial pulmonary fibrosis, 11 sporadic idiopathic pulmonary fibrosis (IPF), 12 non-specific interstitial pneumonia (NSIP) and 10 hypersensitivity pneumonitis (HP) were evaluated for BiP and GADD34 by immunohistochemistry. Using light microscopy, 6
high power fields were scored for fibrosis, inflammation, BiP and GADD34 using semi-quantitative analysis by 2 blinded, independent investigators. Data were analysed by linear regression using Prism software.

BiP and GADD34 were localised to reactive type II pneumocytes and columnar epithelium within areas of fibrosis. GADD34 was also evident in the endothelium. No staining was detected in fibroblasts. Epithelial GADD34 correlated with extent of fibrosis in familial pulmonary fibrosis ($r^2 = 0.72, p < 0.001$), IPF ($r^2 = 0.51, p < 0.0001$) and NSIP ($r^2 = 0.46, p < 0.0001$). In contrast, BiP was associated with fibrosis in IPF ($r^2 = 0.49, p < 0.0001$) and HP ($r^2 = 0.59, p < 0.0001$).

These data show that ER stress and the unfolded protein response are associated with fibrosis in ILD. Hence targeting ER stress may be a novel therapeutic option for pulmonary fibrosis.

MODULATORY EFFECTS OF RHEUMATOID ARTHRITIS LYMPHOPAENIA AND INCREASED ACE LEVELS STRATIFY 2016; Thorax UK

Rheumatoid arthritis (RA) is an autoimmune rheumatic disease (ARD) characterised by circulating autoantibodies, including anti-citrullinated protein antibodies (ACPAs). Many RA patients have extra-articular disease, including ~10% with interstitial lung disease (ILD). Risk factors for RA-ILD include: male sex; age; smoking history and ACPA positivity.

Hypothesis We propose that RA-IgG, including ACPA, modulate neutrophil functions including: generation of reactive oxygen species (ROS), neutrophil adhesion and generation of neutrophil extracellular traps (NETs) that may contribute to joint and extra-articular tissue damage, including ILD.

Methods Neutrophils and IgG were isolated from RA patients or healthy controls (HC). Bronchoalveolar lavage (BAL) was performed on ILD patients and controls undergoing bronchoscopy for other reasons. ROS production was measured using an enzymatic assay to assess hydrogen peroxide (H2O2) generation. Neutrophil integrins were quantified by flow cytometry. Effects of purified IgG upon neutrophil adhesion to immobilised fibrinogen (Mac-1/aMß2-dependent) and fibronectin (VLA-4/a4ß1-dependent) were determined using a fluorescent adhesion assay. NETosis was measured using a novel capture ELISA.

Results We demonstrated increased NETs in the BAL of patients with active ILD (n = 3; ARD-ILD) compared to those with inactive disease (n = 2; IPF and ARD-ILD) or controls (n = 1; CLL). In addition, we showed binding of RA-IgG to control neutrophils, which increased with neutrophil activation. Stimulation of HC (n = 12) and RA (n = 7) neutrophils with PMA produced similar rates of H2O2 generation (p = 0.9939). Exposure of HC neutrophils to RA-IgG (n = 9) however, increased H2O2 production compared to HC-IgG (n = 9) (p < 0.0001), which was not blocked by FcR blockade. RA-IgG also enhanced PMA-stimulated adhesion of HC neutrophils to fibrinogen (p = 0.0028) and fibronectin (p = 0.0024), which was inhibited by αMβ2 or β1 integrin blockade respectively. RA-IgG increased both spontaneous (p = 0.0248) and PMA-induced (p = 0.0200) NETosis of HC neutrophils compared to HC-IgG. Immunofluorescence studies demonstrate that αMβ2 activation induces NETosis. Further examination found that NETosis could be suppressed by p38 MAPK inhibition (p = 0.0034).

Conclusion We have shown that RA-IgG modulates several aspects of neutrophil activation and function. In addition, we found increased neutrophil activation in the lungs of patients with active ARD-ILD. Further work is underway to evaluate the contribution of these processes to the pathogenesis of RA-ILD.

LYMPHOPAENIA AND INCREASED ACE LEVELS STRATIFY SARCOIDOSIS PATIENTS TO UNDERLYING INCREASE IN IFN-γ + LYMPHOCYTE AND TNF-α+ MONOCYTES RESPECTIVELY

Sarcoidosis is a heterogeneous disease, and different mechanisms may contribute to disease activity at any one time. Both TH1 lymphocyte (IFN-γ+ , IL-2+ CD4 T cells) and activated tissue macrophages contribute to the formation of granuloma and are established disease pathways. More recently, monocytes (precursors of tissue macrophages) have also been implicated. We reasoned that if we could identify a commonly used clinical test as a biomarker for these disease pathways, it could be used as a disease activity marker, and to guide evaluation of new therapies and repositioning of current drugs. In this study, we question whether serum ACE and circulating lymphocyte count correlated with different cellular immune function.

Methods 44 consecutive patients fulfilling the ATS-WASOG diagnostic criteria for sarcoidosis within a 2-year period were recruited. Patients on treatment, current cigarette smokers, inter-current immune disease and malignancies were excluded. Blood samples from all patients were processed contemporaneously for ACE, lymphocyte counts and CD4 T cell intra-cellular cytokine staining (ICS) for IFN-γ, IL-2 and IL-17 and CD14hi monocytes ICS for TNF-α.

Results and discussion We found no correlation between lymphocyte count and ACE (r = −0.2; p = 0.86) suggesting that these two abnormalities reflected independent processes. Lymphopaenia was significantly correlated with markers of activated CD4 T cells (IFN-γ , IL-2+ and TNF-α+) (r = −0.50, 0.50 and 0.60 respectively; all p < 0.001; Spearman Rank Sum test); while ACE only correlated with level of TNF-α+ monocytes (r = 0.60; p < 0.0001).

Conclusions These results suggest that high ACE and lymphopaenia (i) reflect disease activity (ii) are likely to be endpoints of two different mechanistic pathways, and (iii) that they could potentially stratify patients into those with lymphocytic dominant and monocyte dominant disease processes. Thus a monocyte pathway inhibitor could be used specifically in patients with high ACE levels while drugs that target T cell activity may be targeted to those with lymphopaenia.
Reduced CD200 receptor expression on monocytes in sarcoidosis

Background Sarcoïdosis is characterised by release of pro-inflammatory cytokines in affected tissues. Lung macrophages, derived from blood monocytes, are potent producers of tumour necrosis factor (TNF) and interleukin-6 (IL-6) which contribute to the formation of sarcoïd granulomata. Abnormalities of regulatory pathways that normally act to dampen inflammation could explain the hyper-active immunological state seen in sarcoïdosis. The aim of the study was to assess the role of regulatory receptors in modulating monocyte cytokine production in sarcoïdosis.

Methods Patients with sarcoïdosis and healthy controls were recruited. Whole blood cytokine release in response to stimuli was measured by ELISA. Expression of the regulatory molecules CD47, CD200R, and CD200L was measured by flow cytometry, and functional activity was determined using blocking antibodies.

Results Patients with sarcoïdosis had less than half the number of T-lymphocytes in blood compared with healthy controls (p < 0.0001). Despite this, patients with sarcoïdosis produced higher concentrations of TNF and IL-6 from whole blood in response to stimulation with phytohaemagglutinin. Kinetic analysis of TNF was consistent with release from monocytes. Expression of the monocyte regulatory receptor CD200R in patients with sarcoïdosis showed a bimodal distribution (Figure 1), with 52.9% patients of patients having a CD200Rlow phenotype compared with 11.7% of healthy control subjects (p < 0.0001). CD200Rlow subjects produced more IL-6 in whole blood assays compared with CD200Rhigh subjects (p < 0.05). Experimental blockade of the CD200R axis increased pro-inflammatory cytokine responses, recapitulating the hyperactive monocyte phenotype seen in sarcoïdosis.

Conclusions Reduced expression of CD200R on monocytes may be a mechanism contributing to monocyte and macrophage hyper-activation in sarcoïdosis.
Background In the acute respiratory distress syndrome (ARDS) predominantly neutrophil mediated inflammation causes injury to the alveolar epithelial and capillary endothelial junction. Oncostatin M (OSM) is a pleiotropic IL-6 cytokine, upregulated in the lung in ARDS. We have shown that OSM synergises with other cytokines to drive IL-8 secretion from alveolar epithelial cells, but its role in driving endothelial injury is unknown. CXCL5 is an OSM-dependent neutrophil chemokine that is implicated in driving endothelial cell-mediated neutrophil recruitment to the lung in animal models of pneumonia.

We hypothesised that OSM stimulates the production of neutrophilic chemokines and proteases by the alveolar endothelium in patients with ARDS.

Methods Immunocytochemistry and western blotting were performed respectively on fixed and lysed human pulmonary microvascular endothelial cells (HPMECs). The cells were stimulated with OSM ± TNF-alpha, and chemokine (CXCL5/8) and matrix metalloproteinase (MMP) production measured by ELISA. Conditioned media from LPS-stimulated human macrophages (CoMLPS), pre-incubated with inhibitory antibodies to OSM, was used to stimulate HPMECs, and the effect on endothelial protease and chemokine production measured.

Results

- The OSM receptor (OSMR) was detected in HPMECs by immunocytochemistry and western blot of cell lysates.
- Stimulation of HPMECs with recombinant OSM and TNF-α increased CXCL5 from 32 (5.6) to 739 (166) pg/ml, CXCL8 from 2.2(0.4) to 11.0 (2.9) ng/ml, and MMP-3 from 35.3 (1.8) to 57.6 (10.7) pg/ml. Concentrations of the endogenous inhibitors of MMPs, i.e. Tissue Inhibitors of Metalloproteinases (TIMPs)-2 were decreased from 25.2 (1.7) to 13.7 (3.2) ng/ml while concentrations of TIMP-1 were unchanged.
- CXCL5 levels were decreased from 13.2 (2.2) to 6.5 (1.1) ng/ml and levels of MMP-3 were decreased from 78.7 (16.6) to 41.4 (9.4) pg/ml from HPMEC stimulated with CoMLPS + inhibitory Ab to OSM. Interestingly, CXCL8 was not significantly abrogated by OSM neutralisation.
- CXCL5 was increased in BALF from 20.7 (1.9) to 392.5 (53.5) pg/ml from patients with ARDS (Figure 1).

Conclusions OSM drives induction of neutrophil chemokines, particularly CXCL5, and proteases by the alveolar endothelium. Targeted therapeutic inhibition of OSM may down-regulate neutrophil recruitment and MMP activity in ARDS, and will be further explored in an ex vivo human lung model.
INVESTIGATING THE ROLE OF GCN2 IN THE PATHOGENESIS OF PULMONARY HYPERTENSION

E Soon, A Crosby, M Southwood, S Moore, D Ron, S Marchnik, NW Morrell. University of Cambridge, Cambridge, UK; Papworth Hospital NHS Trust, Cambridge, UK

10.1136/thoraxjnl-2016-209333.89

Background

Mutations in the bone morphogenetic protein type II receptor (BMPR-II) underlie the majority (>80%) of familial and up to 25% of ‘sporadic’ cases of idiopathic pulmonary arterial hypertension (PAH). Recently, homozygous recessive mutations in GCN2 (also known as EIF2AK4) were identified as causative in a rare cause of PAH, pulmonary veno-occlusive disease (PVOD) and pulmonary capillary haemangiomatosis (PCH). The mechanisms by which GCN2 deficiency contributes to the development of PAH remain unknown. GCN2 is a serine/threonine protein kinase, one of a family of 4 kinases that phosphorylate the α-subunit of the translation initiation factor eIF2α. Phosphorylation of eIF2α at serine 51 results in an inhibition of eIF2B (the eIF2 guanine nucleotide exchange factor), which ultimately leads to loss of eIF2α function. This results in inhibition of protein synthesis while enhancing the translation of a small number of mRNAs encoding proteins involved in the response to cellular stress.

Methods

We characterised the pulmonary vascular phenotype of the homozygous null Gcn2 (Gcn2−/−) and wild-type controls at 6 months of age. This mouse was chosen because it mimics the homozygous loss-of-function genotype of patients with familial PVOD/PCH. In addition, we investigated the phenotype of Gcn2−/− mice crossed with bmpr2-deficient mice. In complementary in vitro studies, pulmonary artery smooth muscle cells (PASMCs) were extracted from patients with PVOD and idiopathic/heritable PAH and studied with wild-type controls.

Findings

The Gcn2−/− mouse displayed mild pulmonary hypertension. Mean right ventricular systolic pressure (RVSP) was 28.3 ± 1.2 mmHg in Gcn2−/− mice compared with 24.7 ± 1.1 mmHg in wild-type mice. Gcn2−/− mice crossed with bmpr2-deficient mice demonstrated a further increase in RVSP (32.8 ± 4.1 mmHg). Exposure of human PASMCs derived from a PVOD patient, and patients with mutations in BMPR2, to L-histidine, which increases the phosphorylation of eIF2α, resulted in proliferation of these cells but had no effect on control PASMCs.

Conclusions

GCN2 deficiency promotes the development of pulmonary hypertension in mice, an effect that is exaggerated by BMPR2 deficiency. Increased phosphorylation of eIF2α resulted in PASMC proliferation. Further elucidation of these mechanisms may reveal new treatments for this devastating disease.

IDENTIFICATION OF MIR-124A AS A MAJOR REGULATOR OF ENHANCED ENDOTHELIAL CELL GLYCOLYSIS IN PULMONARY ARTERIAL HYPERTENSION

PC a r u s o , BJ Dunmore, K Schlosser, Schoors, Dos Santos, Perez-Iratxeta, Lavoie, Long, Hurst, Ormiston, Hata, Cameli, Stewart, NW Morrell. University of Cambridge, Cambridge, UK; Ottawa Hospital Research Institute and the University of Ottawa, Ottawa, Canada; Laboratory of Angiogenesis and Neurovascular Link, Vesalius Research Centre, Leuven, Belgium; Queen’s University, Kingston, Canada; Cardiovascular Research Institute, University of California, San Francisco, USA

10.1136/thoraxjnl-2016-209333.90

Introduction

Pulmonary arterial hypertension (PAH) is a rare disease characterised by profound vascular abnormalities in the peripheral arteries of the lung, leading to a progressive increase in pulmonary vascular resistance, right heart failure and death. The disease exists in several forms including a heritable form (HPAH) caused primarily by mutations in bone morphogenetic protein receptor type 2 (BMPR2) and an idiopathic form (IPAH). Endothelial cell (EC) dysfunction is considered a critical initiating factor in the pathobiology of PAH, manifested by increased...
susceptibility to apoptosis, heightened permeability and enhanced endothelial proliferation. Substantial changes in bioenergetics of ECs, including higher rates of glycolysis, have been reported in PAH patients. However, the mechanisms underlying alterations in energy production have not been identified.

**Methods** We measured glycolysis in blood outgrowth endothelial cells (BOECs) from HPAH patients carrying mutations in BMPR2 and IPAH patients to confirm the metabolic abnormalities previously. We also employed an unbiased genome-wide microarray and proteomic screening approach to detect miRNAs and proteins dysregulated in the same groups to determine the mechanisms underlying abnormal endothelial glycolysis.

**Results** HPAH and IPAH BOECs recapitulated the metabolic phenotype previously observed in PAECs. These alterations were found to be associated with the downregulation of miR-124 and the upregulation of its known target, splicing factor polyuridyline-tract-binding protein (PTBP1). We also demonstrated that increased PTBP1 promotes the switching in expression of two forms of pyruvate kinase, PKM1 and PKM2, resulting in an increase of aerobic glycolysis, consequently increasing cell proliferation (mechanism schematized in Figure 1). Overexpression of miR-124, or siRNA silencing of PTBP1, restoring normal expression levels of PKM2, also restored normal proliferation and glycolysis in HPAH BOECs. Finally, we observed reduced miR-124 and increased PTBP1 and PKM2 expression in a well-established rat model of PAH, characterised by endothelial proliferation, supporting the presence of this mechanism in vivo.

**Conclusions** Loss of function of BMPR2 results in the downregulation of miR-124 and consequently in the glycolytic abnormalities reported in PAH ECs. Therefore, the manipulation of this miRNA, or its targets, could represent a novel and effective strategy to achieve clinical benefits in the treatment of PAH.

**Results** Interestingly male but not female MacLow mice developed a PAH phenotype compared to controls (RVSP of 66.1 mmHg vs 24.5 mmHg, p < 0.0001, n = 5–8), associated with increased right ventricular Hypertrophy (RVH 0.264 vs 0.226, p < 0.001, n = 8) and pulmonary vascular remodelling. IHC analysis of diseased lungs demonstrated increased iNOS- |CD206+ |F4/80+ macrophages suggesting a M2-like macrophage population drive the PAH phenotype in these mice. The bone marrow transplant studies shows that bone marrow (BM) derived cells contribute in the development of the disease phenotype as wild type BM cells attenuate disease progression. Moreover, female BM transplanted into male mice alleviate but does not protect them from developing PAH.

**Conclusion** Development of PAH in male MacLow mice suggests that macrophages play a causal role in pulmonary vascular remodelling. Results suggest that the phenotype is driven by lung resident M2-like macrophages with a contribution from bone marrow derived cells. A study to examine the probable protective effect of Oestrogen is now underway to further investigate the implication of gender difference in the incidence of PAH in this model.

**Introduction** Macrophages are proposed to play an important regulatory role in the pathogenesis of pulmonary arterial hypertension (PAH) as excessive infiltration detected around vascular lesions in patients and animal models. The exact ‘causal’ role for macrophages, and whether their presence or absence is required for the vascular remodelling seen in PAH remains unclear.

**Objectives** Using a novel inducible macrophage depletion model (MacLow mouse) we aimed to determine the role of macrophages in pulmonary arterial remodelling associated with PAH.

**Methods** Macrophage depletion was induced in MacLow mice by administration of doxycycline, where macrophage-specific induction of the cytotoxic diphtheria toxin A chain (DTA) is driven by the CD68 promoter. Mice were phenotyped for PAH by echocardiography, closed chest cardiac catheterization and immunohistochemistry (IHC) after 6 weeks. To investigate the origin of the effector cells, male chimeric mice were generated, and the disease stimulated by inducing macrophage ablation with doxycycline. Furthermore, to study gender-specificity of the disease phenotype, MacLow mixed gender chimeric mice were produced, and macrophage ablation induced as previous.

**Results** Interestingly male but not female MacLow mice developed a PAH phenotype compared to controls (RVSP of 66.1 mmHg vs 24.5 mmHg, p < 0.0001, n = 5–8), associated with increased right ventricular Hypertrophy (RVH 0.264 vs 0.226, p < 0.001, n = 8) and pulmonary vascular remodelling. IHC analysis of diseased lungs demonstrated increased iNOS- |CD206+ |F4/80+ macrophages suggesting a M2-like macrophage population drive the PAH phenotype in these mice. The bone marrow transplant studies shows that bone marrow (BM) derived cells contribute in the development of the disease phenotype as wild type BM cells attenuate disease progression. Moreover, female BM transplanted into male mice alleviate but does not protect them from developing PAH.

**Conclusion** Development of PAH in male MacLow mice suggests that macrophages play a causal role in pulmonary vascular remodelling. Results suggest that the phenotype is driven by lung resident M2-like macrophages with a contribution from bone marrow derived cells. A study to examine the probable protective effect of Oestrogen is now underway to further investigate the implication of gender difference in the incidence of PAH in this model.
suggesting a mechanism for the crosstalk between BMP and GCN2.

**Conclusion** We have discovered in Drosophila that GCN2 activation modulates BMP signalling. This effect is mediated, at least in part, by the downstream transcription factor ATF4, which inhibits the phosphorylation of MAD (insect SMAD1). Our findings indicate that this pathway is conserved between insects and mammals and this model may shed light on the pathogenesis of PAH and PVOD.

Deficiency of Toll-like receptor 3 (TLR3) Exacerbates Pulmonary Hypertension in Mice

AAR Thompson, ND Arnold, AT Braithwaite, HL Casbolt, JI Iremonger, JA Pickworth, E Cole, Sabroe, A Laurie. University of Sheffield, Sheffield, UK

**Introduction** The mechanisms regulating aberrant vascular remodelling in pulmonary arterial hypertension (PAH) are poorly understood and treatments targeted at halting or reversing this process are lacking. Toll-like receptor 3 (TLR3) is a viral sensor and more recently has been established as a sensor of endogenous damage signals, responding to mRNA released by damaged cells. TLR3 signalling induces pro- and anti-inflammatory cytokine production and regulates inflammation-associated apoptosis and tyrosine kinase signalling. In a model of systemic arterial injury, TLR3 signalling was shown to modulate neointimal remodelling in a protective manner. TLR3 is also expressed in pulmonary artery smooth muscle (PASMCs) and endothelial cells (PAECs). We therefore hypothesised that TLR3 would play roles in pulmonary vascular remodelling.

**Methods** TLR3-deficient (TLR3−/−) or wild-type C57BL/6 (WT) mice were exposed to hypoxia (10% Oxygen) and given Sugen 5416 (weekly 20 mg/kg subcutaneous injections) or maintained in normoxic conditions for 3 weeks. Haemodynamic (cardiac catheterisation and echocardiography) and histological assessments were performed after 3 weeks. Human PASMCs were serum-starved before stimulation with PDGF or poly(I:C) and proliferation was assessed after 72 hours.

**Results** TLR3−/− mice developed a markedly exaggerated phenotype of PAH in response to Sugen/Hypoxia with increased right ventricular systolic pressures (WT 51.6 mmHg ± 4.6 vs. TLR3−/− 73.0 mmHg ± 6.8; p < 0.05, mean ± SEM, n = 6), increased muscularisation of small pulmonary arteries and reduced right ventricular cardiac output (WT 424.2 RVUmin−1 ± 84.2 vs. TLR3−/− 283.3 RVUmin−1 ± 18.4, mean ± SEM, min n = 6) after 3 weeks. Poly(I:C) suppressed PDGF-induced PASMC proliferation in a dose-dependent manner.

**Conclusions** We have shown that mice deficient in TLR3 develop a markedly exaggerated haemodynamic pulmonary hypertension phenotype and human PASMC proliferation is suppressed by the TLR3 ligand, poly(I:C). Together these data imply that TLR3 signalling in disease mediates a protective phenotype in keeping with that observed in systemic vascular remodelling, and identify a protective pathway potentially amenable to therapeutic targeting.

**Tuberculosis: From Screening to Side Effects**

**Results**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Total cost of strategy per 10,000 people living with HIV</th>
<th>Cases TB prevented (discounted)</th>
<th>QALYs gained compared to no testing (discounted)</th>
<th>Cost/case averted</th>
<th>Cost/QALY compared to no testing</th>
<th>Incremental cost/QALY compared to last strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>BHIVA 2011</td>
<td>£749,274</td>
<td>2.28</td>
<td>1.28</td>
<td>£21,371</td>
<td>£17,952</td>
<td>EXTENDED DOMINANCE</td>
</tr>
<tr>
<td>TST in BA</td>
<td>£749,660</td>
<td>3.9</td>
<td>2.09</td>
<td>£12,566</td>
<td>£23,429</td>
<td>£23,429</td>
</tr>
<tr>
<td>TST in BA and MI</td>
<td>£761,797</td>
<td>4.49</td>
<td>2.43</td>
<td>£13,614</td>
<td>£25,218</td>
<td>EXTENDED DOMINANCE</td>
</tr>
<tr>
<td>NICE 2011</td>
<td>£789,037</td>
<td>1.11</td>
<td>0.63</td>
<td>£78,429</td>
<td>£139,281</td>
<td>DOMINATED</td>
</tr>
<tr>
<td>IGRA in BA</td>
<td>£812,048</td>
<td>6.83</td>
<td>3.85</td>
<td>£16,314</td>
<td>£28,971</td>
<td>EXTENDED DOMINANCE</td>
</tr>
<tr>
<td>IGRA in BA and MI</td>
<td>£865,959</td>
<td>9.06</td>
<td>5.1</td>
<td>£18,250</td>
<td>£32,410</td>
<td>EXTENDED DOMINANCE</td>
</tr>
<tr>
<td>IGRA in all</td>
<td>£1,056,702</td>
<td>10.17</td>
<td>5.72</td>
<td>£35,030</td>
<td>£62,209</td>
<td>EXTENDED DOMINANCE</td>
</tr>
<tr>
<td>NICE 2016</td>
<td>£1,058,522</td>
<td>10.17</td>
<td>5.72</td>
<td>£35,234</td>
<td>£62,571</td>
<td>DOMINATED</td>
</tr>
<tr>
<td>TST&amp;IGRA in all</td>
<td>£1,219,154</td>
<td>10.99</td>
<td>5.88</td>
<td>£47,166</td>
<td>£88,139</td>
<td>EXTENDED DOMINANCE</td>
</tr>
<tr>
<td>TST&amp;IGRA&amp;CXR&amp;IS in all</td>
<td>£1,999,789</td>
<td>20.58</td>
<td>10.44</td>
<td>£63,142</td>
<td>£124,393</td>
<td>EXTENDED DOMINANCE</td>
</tr>
</tbody>
</table>

We sought to determine the cost-effectiveness of each UK guideline from an NHS perspective, plus alternatives, using prospective data.

All patients with a new HIV diagnosis attending an ambulatory HIV clinic, plus a sample of those with known HIV were approached, and offered a symptom questionnaire, chest radiograph (CXR), tuberculin skin test (TST), blood interferon gamma release assay (IGRA) and induced sputum for mycobacterial culture (IS). The uptake and results were used to calculate the cost-effectiveness of three different testing strategies using univariate, multivariate and probabilistic sensitivity analyses (PSA).

219 subjects, representative of the total clinic population, took part. 73% were male, 28% black African and 95% on antiretroviral treatment (ART). During testing, 2 cases (0.9%) of subclinical TB and 14 (6%) of LTBI were detected. Half the patients with LTBI completed preventive treatment. Over a median of 28 months follow up, no new cases of active TB were identified.

When compared to no testing, only three of the thirty strategies were below the maximum NICE threshold for cost-effectiveness. Testing black Africans with just TST or IGRA cost £23,429/QALY and £28,971/QALY respectively, whilst testing black Africans plus those from countries with a TB incidence of >20/100,000 (‘middle incidence’), MI cost £25,218/QALY and £32,410/QALY using TST alone or IGRA alone respectively. NICE, BHIVA, or more extensive strategies, were not cost-effective. (Table)

Using PSA, no testing was most likely cost-effective up to £30,000/QALY.

In a contemporary HIV population with very high uptake of ART, neither current UK guideline is cost-effective. Testing black Africans, or black Africans and people from middle TB incidence countries appear at best marginally cost-effective. Future UK guidance needs to reflect changing health demographics, improved outcomes for people in HIV care, and clinical pragmatism.
LIVER FUNCTION TESTS DURING TUBERCULOSIS TREATMENT AND THE IMPLICATIONS ON MONITORING FOR HEPATOTOXICITY

1CD Tweed, 2G Wills, 3AM Cook, 3SK Meredith, 4AJ Nunn, 5CM Mendel, 6SR Murray, 4The TB Alliance, New York, USA; 5Division of Infection and Immunity, University College London, London, UK; 6University of St Andrews Medical School, St Andrews, UK.

Abstract S90 Table 1

<table>
<thead>
<tr>
<th>Symptoms at presentation (all patients)</th>
<th>Younger Patients (18–40)</th>
<th>Older Patients (over 65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough N (%)</td>
<td>186 (38)</td>
<td>38 (52.0)</td>
</tr>
<tr>
<td>Haemoptysis N (%)</td>
<td>27 (5.5)</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Fever N (%)</td>
<td>162 (3.3)</td>
<td>18 (24.7)</td>
</tr>
<tr>
<td>Drenching night sweats N (%)</td>
<td>129 (26.3)</td>
<td>12 (16.4)</td>
</tr>
<tr>
<td>Weight loss N (%)</td>
<td>187 (38.2)</td>
<td>43 (58.9)</td>
</tr>
<tr>
<td>Dyspnoea N (%)</td>
<td>24 (4.9)</td>
<td>28 (38.4)</td>
</tr>
<tr>
<td>Lethargy N (%)</td>
<td>25 (5.1)</td>
<td>11 (15)</td>
</tr>
<tr>
<td>Reduced Appetite N (%)</td>
<td>28 (5.7)</td>
<td>16 (21.9)</td>
</tr>
<tr>
<td>Neck Lymphadenopathy N (%)</td>
<td>131 (26.8)</td>
<td>15 (20.5)</td>
</tr>
<tr>
<td>Pulmonary TB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Symptom duration at presenting to secondary care in days. Median (IQR)</td>
<td>45 (30–90)</td>
<td>90 (26.25–180)</td>
</tr>
<tr>
<td>Time from secondary care to starting treatment in days. Median (IQR)</td>
<td>2 (1–5.5)</td>
<td>7 (2.25–41.5)</td>
</tr>
<tr>
<td>Pulmonary TB</td>
<td>N = 137</td>
<td>N = 37</td>
</tr>
<tr>
<td>Total time from symptom onset to starting treatment in Months. Median (IQR)</td>
<td>2.0 (1–3)</td>
<td>3.0 (1.5–6.5)</td>
</tr>
<tr>
<td>Proportion starting within 2 months of symptom onset N (%)</td>
<td>82 (59.9)</td>
<td>13 (35.1)</td>
</tr>
<tr>
<td>Proportion starting within 4 months of symptom onset n (%)</td>
<td>119 (86.9)</td>
<td>25 (76.8)</td>
</tr>
<tr>
<td>Proportion starting more than 4 months of symptom onset n (%)</td>
<td>18 (13.1)</td>
<td>12 (24.4)</td>
</tr>
</tbody>
</table>

Biases in this work including recording bias due to the retrospective nature of symptom recording, the effect of selecting younger patients from more recent years (to improve data availability) and the low proportion of patients over 65 which had symptom and treatment data available.

**LIVER FUNCTION TESTS DURING TUBERCULOSIS TREATMENT AND THE IMPLICATIONS ON MONITORING FOR HEPATOTOXICITY**

1CD Tweed, G Wills, AM Cook, SK Meredith, AJ Nunn, CM Mendel, SR Murray, The TB Alliance, New York, USA; Division of Infection and Immunity, University College London, London, UK; University of St Andrews Medical School, St Andrews, UK.

10.1136/thoraxjnl-2016-209333.97

Introduction and objectives Drug-induced hepatotoxicity is a common complication of tuberculosis treatment. Guidelines based on expert opinion are available, but the natural history of liver enzyme measurements over the course of treatment and the most effective approach to monitoring on treatment remains unclear.

We investigated the pattern of liver enzyme levels in the REMoxTB trial to describe the magnitude and timing of elevations, along with factors that could influence enzyme patterns, and related this to liver function monitoring.

Methods Patients received either standard tuberculosis treatment (2EHRZ/4HR), or a four-month regimen with moxifloxacin substituted for ethambutol (isoniazid arm, 2MHRZ/2MHR) or isoniazid (ethambutol arm, 2EMRZ/2MR). Liver function tests were performed at weeks 0, 2, 4, 8, 12, 17, and during adverse events. The Chi Square or Fisher’s exact test was used for testing proportions among groups, log rank test for comparison of time, and Students t test for comparison of means.

Results 639 patients were allocated to receive standard therapy as controls, 654 to the isoniazid arm, and 635 to the ethambutol arm (see Table 1). 60 patients (9.4%) taking standard therapy developed a peak ALT/AST ≥ 3 × ULN at median time 28 days (IQR 14–56). The mean difference in time to reach peak ALT was 7 days between isoniazid-containing regimens and the ethambutol arm, and a higher proportion of Asian patients elevated ALT/AST ≥ 3 × ULN in isoniazid-containing arms (51.0% vs 26.3%, p < 0.001). Of the 40/421 (9.5%) HIV positive in Africa, 24/421 elevated ALT/AST ≥ 3 × ULN compared to 25/121 (5.7% vs 20.7%, p < 0.001) in India elevating ALT/AST ≥ 3 × ULN where 2/121 (1.7%) were HIV-positive.

Discussion Monitoring liver function routinely for the first two months of HRZE therapy would have detected approximately 75% of patients with a peak enzyme elevation of ≥3 × ULN, and we would recommend this as a standard of care based on these results. However, there is reassurance that over 90% of patients completed therapy without an ALT/AST result ≥3 × ULN. HIV positive and Asian patients were at higher risk of liver enzyme elevation and there was a shorter time to peak ALT/AST within the first two months of HRZE therapy would have detected approximately 75% of patients with a peak enzyme elevation of ≥3 × ULN, and we would recommend this as a standard of care based on these results. However, there is reassurance that over 90% of patients completed therapy without an ALT/AST result ≥3 × ULN. HIV positive and Asian patients were at higher risk of liver enzyme elevation and there was a shorter time to peak ALT/AST ≥ 3 × ULN.

**REFERENCE**

Predicting Risk in Pleural Disease

**S92**

**NON-MALIGNANT PLEURAL EFFUSIONS (NMPE): A PROSPECTIVE STUDY INTO 355 CONSECUTIVE UNSELECTED PATIENTS**

S Walker, A Morley, L Stadon, D De Fonseka, A Medford, N Maskell. Academic Respiratory Unit, Bristol, UK

10.1136/thoraxjnl-2016-209333.98

**Introduction and objectives**

Non-Malignant Pleural Effusions (NMPE) have an estimated annual incidence of 200,000 in the UK.\(^1\) They are often secondary to underlying organ dysfunction, with congestive heart failure (CHF) the leading cause. CHF itself carries a high mortality risk, with 28% of patients with New York Heart Association (NYHA) class IV dying within a year.\(^2\) Despite this, information on baseline characteristics, prognostic features and mortality in NMPE is sparse. Our aim is to determine the mortality rates in NMPEs in a prospective observational trial.

**Methods**

We recruited 784 consecutive patients presenting to a pleural service, between 03/2008 and 03/2015, with an undiagnosed pleural effusion. Further analysis was conducted on the 355 patients with NMPE.

Pleural biochemistry, cytology, thoracic USS and chest radiograph were performed. Echocardiogram, CT scans, radiological-guided biopsy and medical thoracoscopy were undertaken as clinically indicated. Patients were followed-up for a minimum duration of 12 months with final diagnosis decided by independent review by 2 respiratory consultants. Survival data was calculated from study entry to death. Surviving patients were censored on 07/2016.

**Results**

Of the 784 patients, 355 (45%) were diagnosed with a NMPE. These patients had a mean age of 68 (SD 17) with 69% of patients male. Patients with CHF (HR 4.7 CI: 2.3–9.5) had a 50% 1-year mortality and a mean age of 79. Renal failure (HR 5.2 CI: 2.1–12.9) and liver failure (HR 4.8 CI: 1.9–11.8) patients had 1-year mortality rates of 31% and 25% respectively (HR c/w inflammatory pleuritis). Bilateral effusions (HR 2.6 CI: 1.7–3.9) and transudative effusions (HR 3.1 CI: 2.2–4.3) were associated with a worse prognosis in patients with NMPE, with a 57% and 44% 1-year mortality respectively.

**Conclusion**

This is the largest prospectively collected series in patients with NMPE, demonstrating that those secondary to organ dysfunction have an extremely high 1-year mortality. The presence of a pleural effusion in patients with CHF is a marker of severe disease, almost doubling the mortality risk compared to patients with NYHA class IV CHF.

**REFERENCES**


---

**Abstract S91 Table 1**

<table>
<thead>
<tr>
<th>ALT RESULT</th>
<th>n</th>
<th>2EHRZ/4HR</th>
<th>2MHRZ/2MHR</th>
<th>2EMRZ/2MR</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median peak value as xULN (IQR)</td>
<td>634</td>
<td>649</td>
<td>634</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Median time to peak value in arm (days)</td>
<td>0.83</td>
<td>0.78</td>
<td>0.73</td>
<td>0.046*</td>
<td></td>
</tr>
<tr>
<td>No with peak ≥3 xULN (%)</td>
<td>28</td>
<td>28</td>
<td>55</td>
<td>0.972*</td>
<td></td>
</tr>
<tr>
<td>No with peak ≥5 xULN (%)</td>
<td>41</td>
<td>35</td>
<td>25</td>
<td>0.130</td>
<td></td>
</tr>
<tr>
<td>No with peak ≥10 xULN (%)</td>
<td>(6.5%)</td>
<td>(5.4%)</td>
<td>(3.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AST RESULT</td>
<td>n</td>
<td>2EHRZ/4HR</td>
<td>2MHRZ/2MHR</td>
<td>2EMRZ/2MR</td>
<td>p value</td>
</tr>
<tr>
<td>Median peak value as xULN (IQR)</td>
<td>639</td>
<td>654</td>
<td>635</td>
<td>***</td>
<td></td>
</tr>
<tr>
<td>Median time to peak value in arm (days)</td>
<td>1.02</td>
<td>0.93</td>
<td>0.90</td>
<td>0.026†</td>
<td></td>
</tr>
<tr>
<td>No with peak ≥3 xULN</td>
<td>52</td>
<td>28</td>
<td>55</td>
<td>0.160*</td>
<td></td>
</tr>
<tr>
<td>No with peak ≥5 xULN</td>
<td>46</td>
<td>41</td>
<td>27</td>
<td>0.074</td>
<td></td>
</tr>
<tr>
<td>No with peak ≥10 xULN (%)</td>
<td>(0.2%)</td>
<td>(6.3%)</td>
<td>(4.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No of liver-related withdrawals</td>
<td>21</td>
<td>17</td>
<td>12</td>
<td>0.292</td>
<td></td>
</tr>
<tr>
<td>(3.3%)</td>
<td>(2.6%)</td>
<td>(1.9%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1.3%)</td>
<td>(0.8%)</td>
<td>(0.8%)</td>
<td>0.668§</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Some patients not included due to missing ALT results
† Isoniazid arm against standard therapy
‡ Ethambutol arm against standard therapy
§ Fisher’s exact test
NOVEL BIOMARKERS IN PROGNOSTICATION AND TREATMENT MONITORING OF MALIGNANT PLEURAL MESOTHELIOMA – A SYSTEMATIC REVIEW

1DT Arnold, 1D De Fonseka, 2FW Hamilton, 1NA Maskell. 1Academic Respiratory Unit, Bristol, UK; 2Southmead Hospital, Bristol, UK

Introduction Pemetrexed with cisplatin is the only UK licensed treatment for malignant pleural mesothelioma (MPM) following an RCT that demonstrated a survival advantage of 2–3 months and response rate of 30–40% (Vogelzang, 2003). Radiological markers of treatment response and prognostication have significant limitations due to the morphology of the disease. Therefore, serum or pleural fluid biomarkers that could act as an adjunct to radiological assessment would be of significant value. The aim of this systematic review was to collate and summarise the literature relating to this topic.

Methods The PubMed and EMBASE databases were interrogated using pre-defined search strings (with English language restrictions) up to 30 June 2016, with no early date limit applied. Two independent researchers (DA and FH) read the abstracts and, using the Quality in Prognostic Studies (QUIPS) tool, selected the studies to be included in the final review.

Results From the 795 abstracts generated by the search strategy, 41 relevant studies were identified. Serum mesothelin was the most studied biomarker with 20 studies assessing its role in prognostication. A high serum mesothelin at baseline was thought to be an independent marker of poor prognosis in epithelioid MPM, however, recent studies suggest this is because levels increase with tumour stage and bulk. Six studies assessed serial serum mesothelin measurements during chemotherapy and all showed that it can be a proxy for treatment response and prognosis (see table). Pleural fluid mesothelin was not a useful prognostic biomarker in the 4 relevant studies. Serum Osteopontin (OPN) was the topic of 5 studies and appeared to offer prognostic information at baseline even after adjustment for covariates. Other serum or pleural fluid biomarkers such as fibulin-3, megakaryocyte-potentiating factor, hyaluronic acid and VEGF have shown prognostic utility in individual papers but are yet to be reproduced in large cohort studies.

Discussion The literature suggests that a falling serum mesothelin following chemotherapy correlates with treatment response and improved overall survival. This could be of significant value to clinicians in deciding ongoing treatment, but a larger prospective study is required before its inclusion in routine clinical practice.

BIOLOGICAL MARKERS OF FAVOURABLE PROGNOSIS AND SUCCESSFUL PLEURODESIS FOR MALIGNANT PLEURAL EFFUSION

1PSallidas, 1N Kanellakis, 3MT zezenia, 3P Charles, 3IP Corcoran, 3RHallifax, 3A Talwar, 3CC Pascaull, 3A Kesler, 1NM Rahman. 1Laboratory of Pleural Translational Research; Nuffield Department of Medicine, University of Oxford, Oxford, UK; 3TDI Mass Spectrometry Laboratory, University of Oxford, Oxford, UK; 3Oxford Centre for Respiratory Medicine, Oxford, UK

Abstract S92 Figure 1 Kaplan-meier survival curve according to disease type
Introduction and objectives Malignant pleural effusion (MPE) is a rapidly rising healthcare burden and critically hampers the patients’ survival and quality of life. Current treatments aim to symptoms’ palliation and talc pleurodesis remains a standard therapeutic modality. There is relatively little high quality research data in prediction of patients’ survival and successful pleurodesis. Therefore prognostic and therapeutic biomarkers are desperately needed.

Aim To identify and validate novel prognostic and therapeutic biomarkers in MPE.

Methods Clinical data and pleural fluids from MPE patients, prior to treatment have been prospectively collected for TIME2 trial. According to the trial database patients have been classified in two different groups: survival cohort (poor, n = 20/good, n = 14) and treatment outcome cohort (success, n = 15/failure, n = 11). Pleural fluids on enrolment were assessed with mass spectrometry profiling after depletion of the 12 most abundant proteins. Full protein profile analysed with R software and ELISA technique was performed for the validation of the results. Pathway analysis on samples performed with Ingenuity Pathway Analysis software.

Results With the use of mass spectrometry we identified 1,154 proteins in the pleural fluid, 167 of which were statistical significant (two tailed T-Test, p < 0.05) between survival groups and 97 of which were statistically significant (two tailed T-Test, p < 0.05) between the pleurodesis groups. Analysis of the data (cross validated by 3 independent core bioinformatic groups) identified 10 survival and 3 pleurodesis biomarkers that were differentially expressed in the favourable prognosis and treatment success group respectively. Exploration of the mass spectrometry data identified pathways that were upregulated on patients with favourable survival that could be used for targeted therapies.

Conclusions Based on unique database survival and therapeutic biomarkers were identified that can potentially stratify patients’ management. The results are currently validated on a different retrospective dataset (TIME1 trial) and with a prospective clinical trial (SIMPLE study).

AMBULATORY MANAGEMENT OF PNEUMOTHORAX: IS THERE A NEED FOR A DEDICATED PLEURAL TEAM-LED SERVICE?

A Fawzi, N Maddekar, S Khan, S Bikmalia, W Osman, U Maqsood, M Haris. Royal Stoke University Hospital, Stoke-on-Trent, UK

Introduction Small, asymptomatic pneumothoraces may be managed as outpatients. Several studies show that small-bore catheters and Heimlich valves may be used in the treatment of pneumothoraces. A systematic review of the literature\(^1\) showed successful outpatient management of pneumothorax. Despite good evidence to support ambulatory approach, there has been slow development of this service across the UK. We wished to assess the number of potential primary spontaneous pneumothorax patients that could be managed as outpatients in a large teaching hospital.

Methods Hospital attendances of pneumothorax at a large teaching hospital between 2012–2015 were reviewed. Type of
pneumothorax was characterised: primary spontaneous (PSP), secondary spontaneous (SSP), iatrogenic (IP) and traumatic/post-operative. The data for PSP was then correlated against the data retrieved from the systematic review of outpatient pneumothorax management.1

Results Total number of pneumothorax episodes were 877; PSP 266, SSP 229, IP 41 and traumatic/post-operative 341. Average length of stay (LOS) for all episodes of pneumothorax was 12.39 days. LOS for PSP was 6.9 days. Total number of hospital admissions for PSP (266/3 =) 88.7 patients/year. Extrapolated from systematic review1: Successful outpatient PSP management (88.7*78% =) 77.1 patients/year. Potential bed days saved for PSP: (77.1*6.9 =) 532 beds/year.

Conclusions Studies show both spontaneous and iatrogenic pneumothorax may be managed safely as outpatients. Dedicated pleural services will result in correct stratification of patients requiring appropriate interventions. Ambulatory chest drains could be used and inserted by professionals trained in their use.

Advantages to patients: reduced need for hospital admission, greater patient autonomy, improved patient experience, no need to carry chest drain bottle, reduced likelihood of accidental dislodgement of chest drain, reduced time to discharge.

Advantages to trust: admission avoidance, early discharge, reduced costs, reduced complications from chest drain insertions, reduced hospital associated complications, optimised patient care with increased patient satisfaction.

Although we would not advocate the use of ambulatory pneumothorax devices in trauma patients, there is scope to establish whether they can be used post procedural (e.g. pneumothorax following pacemaker insertion).

Introduction To compare the effectiveness of ambulatory management of primary (PSP) and selected secondary spontaneous pneumothoraces (SSP)

Methods Large PSP and selected SSP patients (WHO performance score 0–1) aged between 16–80 presenting between May 2013 and January 2016, were deemed eligible for the ambulatory pathway. They were reassessed every two days with a chest x-ray in the ambulatory care unit. The patients with Pneumostat valve (Atrium Medical Corporation) were taught to check for air-leak every day. Patient outcomes and complications were recorded. Patients with tension, iatrogenic or traumatic pneumothorax were excluded from the study.

Primary outcome measure
Success rate at day 5 defined as sustained complete re-expansion of lung with no air leak.

Secondary Outcome measures
Number of days spent with the chest drain in situ.
Complications like drain falling out, drain blockage, Infection
Number of patients requiring surgical treatment due to persisting air leak.

Results A total of 110 patients were reviewed with spontaneous pneumothorax, of which 54 were managed on the ambulatory pathway. (Table 1) The pneumothorax resolved successfully in 77% of the primaries pneumothoraces and 67% of the secondaries, with an overall resolution of 72%. In the PSP, five patients (16.7%) went on to have surgery due to non-resolution. Of the 24 SSP eight (33.3%) patients went on to have surgery due to non-resolution. Complications other than pain were minimal. The mean duration of drainage was 3.8 days in PSP and 5.9 days in SSP. This compares well with the median drainage of 6–8 days for inpatient management of PSP (BTS guidelines).1

Conclusion The success rate was 72% for all spontaneous pneumothorax patients managed almost exclusively as outpatients, which compares well with the 78% suggested in the meta-analysis by Brimms and Maskell.2 This study confirms that the use of chest drain with one-way valves in the ambulatory management of primary and selected secondary spontaneous pneumothoraces is safe with very few complications. This procedure clearly decreases the number of hospitalisation days and is thus cost saving.

REFERENCES
Idiopathic Pulmonary Fibrosis Therapy

ANNUAL RATE OF FVC DECLINE IN VARIOUS PATIENT SUB-GROUPS WITH IDIOPATHIC PULMONARY FIBROSIS TREATED WITH PIRFENIDONE: POOLED ANALYSIS FROM 3 PIVOTAL STUDIES

Introduction Pirfenidone has been shown to decrease the annual rate of decline in forced vital capacity (FVC) volume in patients with idiopathic pulmonary fibrosis (IPF). This analysis explored this effect in various patient subgroups.

Methods Patients randomised to pirfenidone 2403 mg/d or placebo in the CAPACITY or ASCEND studies were included. The annualised rate of decline in FVC volume from baseline through 12 months was estimated using a mixed-effects model, with study, time-by-treatment, age-by-sex and height-by-sex as fixed effects and patients and time-by-patient (slope) as random effects. The annual rate of FVC decline was estimated from the slope within the subgroups, defined by demographics and baseline disease activity measures.

Results A total of 623 patients in the pirfenidone group and 624 in the placebo group were included in the pooled analysis. Overall, the adjusted annual rate (SE) of FVC decline from baseline to 12 months was $-109.0$ (13.6) mL for pirfenidone vs $-207.5$ (13.7) mL for placebo, a difference of 98.5 (17.5) mL. The annual rate of FVC decline favoured pirfenidone over placebo across various baseline demographic and lung function subgroups (Figure 1).

Conclusions Patients with IPF treated with pirfenidone, regardless of baseline demographic or lung function, had a significantly lower annual rate of decline in FVC volume vs those treated with placebo after 12 months.
Introduction

On the basis of retrospective and post-hoc analyses the current IPF guideline suggests the use of anti-acid therapy (AAT, i.e., proton pump inhibitors and H2-blockers) as a treatment option in patients with IPF. While recent post-hoc analyses do not support a protective effect of AAT on IPF progression in patients receiving placebo, the impact of AAT on disease progression in patients treated with pirfenidone is unknown.

Methods

Patients with IPF randomised to pirfenidone in 3 trials (CAPACITY studies 004 and 006, and ASCEND) were included. Changes in pulmonary function, exercise tolerance, survival, hospitalisations, and adverse events (AEs) over 52 weeks were analysed for all subjects, based on AAT status at baseline, by bivariate and multivariate analyses. Disease progression was defined as an absolute decrease of forced vital capacity (FVC) ≥10% predicted, a decrease of ≥50 m in the 6-minute walk distance (6MWD) or death.

Results

Of 623 patients, 44% received AAT. Patient characteristics were comparable between groups with the exception of gastrointestinal (GI) comorbidities. In bivariate analyses, there were no significant differences at 52 weeks in disease progression (AAT vs non-AAT: 24.9% vs 30.6%; P = 0.12), all-cause or IPF-related mortality (2.9% vs 4.0%; P = 0.47 and 1.1% vs 2.0%; P = 0.37, respectively), all-cause hospitalisation (16.1% vs. 18.3%, P = 0.48) or observed mean FVC decline (−2.7% vs −3.1%, P = 0.44). Relative but not absolute FVC decline ≥10% was slightly in favour of AAT (15% vs 22%; P = 0.03). In multivariate analyses, hazard ratios across study outcomes ranged from 0.3–0.9 for AAT (vs. non-AAT), although differences were not statistically significant (including relative FVC decline ≥10%).

AEs were generally similar between groups; however, severe GI AEs (3.7% vs. 0.9%, P = 0.015) and severe pulmonary infections (3.7% vs. 1.1%, P = 0.035) were more frequent in AAT users.

Conclusion

In this post-hoc analysis of three randomized-controlled trials, there was no clear evidence of benefit of the combination of AAT and pirfenidone compared to pirfenidone alone. However, AAT use appeared to increase the risk of severe GI and infectious AEs. AAT should be prospectively assessed in a randomised controlled trial before being considered as a specific treatment for IPF.
Introduction The two 52-week Phase III INPULSIS® trials assessed the efficacy and safety of nintedanib in patients with IPF. In both trials, nintedanib significantly reduced the annual rate of decline in forced vital capacity (FVC) versus placebo.

Methods We assessed the cumulative distribution of patients by absolute changes from baseline to week 52 in FVC% predicted using thresholds of ≥0%, ≥5% and ≥10% in the individual INPULSIS® trials and pooled data. Missing data (due to death, loss to follow-up, or censoring before week 52) were imputed using the worst decline from baseline at week 52 observed in all patients with available data regardless of treatment.

Results 1061 patients were treated in the INPULSIS® trials (n = 638 nintedanib; n = 423 placebo). In INPULSIS®–1, a smaller proportion of patients treated with nintedanib than placebo had any decline in FVC% predicted (absolute decline in FVC ≥ 0% predicted) (71% versus 82%; p = 0.002), an absolute decline in FVC ≥ 5% predicted (47% versus 62%; p = 0.001) and an absolute decline in FVC ≥ 10% predicted (29% versus 43%; p < 0.001) from baseline to week 52 based on the cumulative distribution of patients. In INPULSIS®–2, a smaller proportion of patients treated with nintedanib than placebo had any decline in FVC% predicted (70% versus 88%; p < 0.001), an absolute decline in FVC ≥ 5% predicted (47% versus 61%; p = 0.001) and an absolute decline in FVC ≥ 10% predicted (30% versus 36%; p = 0.18) from baseline to week 52. In pooled data, the proportions of patients treated with nintedanib and placebo, respectively, who had any decline in FVC% predicted (70% versus 88%; p < 0.001), an absolute decline in FVC ≥ 5% predicted and an absolute decline in FVC ≥ 10% predicted were 70% versus 85% (p < 0.001), 47% versus 61% (p < 0.001) and 30% versus 39% (p < 0.001) (Figure). The proportion of patients with no decline or an improvement in FVC% predicted were 30% in the nintedanib group versus 15% in the placebo group.

Conclusion In the INPULSIS® trials, a higher proportion of patients with IPF treated with nintedanib than placebo had no decline or an improvement in FVC. Smaller proportions of patients had absolute declines in ≥5% and ≥10% predicted over 52 weeks.
Single Centre Experience of Switching Patients with Idiopathic Pulmonary Fibrosis from Pirfenidone to Nintedanib

A Rathnapala, A Fries, C Ruggiero, LP Ho, RK Hoyles. Oxford Centre for Respiratory Medicine, Oxford, UK

10.1136/thoraxjnl-2016-209333.107

Background Idiopathic Pulmonary Fibrosis (IPF) is a progressive disease with an average life expectancy of 2–4 years. The anti-fibrotic agents Nintedanib and Pirfenidone slow disease progression, and are routinely prescribed by specialist ILD centres. Choice of agent is guided by patient and physician preference, and potential tolerance of side effects. Our centre has prescribed Nintedanib since March 2015, and Pirfenidone since 2013.

Objectives To identify the reasons driving a change of anti-fibrotic from Pirfenidone to Nintedanib, and the frequency of reported side effects and specialist nursing input before and after the switch.

Methods This retrospective study examined patients who had been switched from Pirfenidone to Nintedanib (March 2015–July 2016), including patients with >1 month duration of each agent. Data was taken from patient records including nursing advice via the ILD nurse-led helpline.

Results We identified 16 patients, with a mean duration of Pirfenidone 9 (1–30) months prior to the switch, and 8 (2–15) months Nintedanib use. Average age 73 (65–84) years, male: female 14:2, definite: probable IPF 11:5, median duration since IPF diagnosis 27 (8–65) months, median %FVC 75 (62–90) at initiation of Pirfenidone, and 68 (53–85) %FVC at initiation of Nintedanib.

Rationale for switch. Disease progression (n = 5): decline in FVC ≥ 10% over one year (n = 3), acute exacerbation (n = 2). Intolerable side effects (n = 11): fatigue (3), diarrhoea (2), nausea (2), appetite or weight loss (2), skin rash (1), mood disturbance (1).

Impact of switch on side effects and nursing contact. In 9 months before the switch, 13 patients made 1.5 (mean) calls (range 1–3) to the ILD helpline for advice on Pirfenidone side effect management. After the switch, over 8 months, 3 patients made 2 (mean) contacts (range 1–3) for Nintedanib related side effects (diarrhoea).

Of 5 patients switched to Nintedanib for disease progression, 3 had follow up for six months, showing >10% improvement in %FVC (n = 1), stability (n = 1), persistent mild decline (< 5%) %FVC (n = 1).

Conclusions This study illustrates the potential of Nintedanib as an alternative for those who have disease progression despite Pirfenidone; there is good tolerance to Nintedanib with none of this cohort having to stop treatment due to side effects.

Bacteria versus Lung: Mechanisms of Lung Infection

Vitamin D Supplementation to Prevent Acute Respiratory Infections: Systematic Review and Meta-Analysis of Individual Participant Data

1AR Martineau, 1DA Jolliffe, 1L Hooper, 1L Greenberg, 1P Bergman, 1G Dubnov-Raz, 2S Esposito, 3D Gammia, 4EC Goodall, 5E Grant, 5W Janssens, 6J Laakso, 7S Manaseki-Holland, 8D Murdoch, 9RE Neale, 10S Simpson, 11IS telmac, 12G Trilok Kumar, 13M Urashima, 14CA Camargo.

1Queen Mary University of London, London, UK; 2Winthrop University Hospital, New York, USA; 3Karolinska Institute, Stockholm, Sweden; 4Edmond and Lily Safra Children’s Hospital, Tel Hashomer, Israel; 5Universita degli Studi di Milano, Milan, Italy; 6Harvard School of Public Health, Boston, USA; 7McMaster University, Ontario, Canada; 8University of Auckland, Auckland, New Zealand; 9Universitat Ziekenhuis Leuven, Leuven, Belgium; 10University of Tampere, Tampere, Finland; 11University of Birmingham, Birmingham, UK; 12QIMR Berghofer Medical Research Institute, Brisbane, Australia; 13Geisel School of Medicine at Dartmouth, Lebanon, USA; 14University of Tasmania, Hobart, Australia; 15Medical University of Lodz, Lodz, Poland; 16University of Delhi, Delhi, India; 17Jikei University School of Medicine, Tokyo, Japan; 18Harvard Medical School, Boston, USA

10.1136/thoraxjnl-2016-209333.108
Introduction and objectives Randomised controlled trials of vitamin D to prevent acute respiratory infection have yielded mixed results. We conducted an individual patient data (IPD) meta-analysis to identify factors that may explain this heterogeneity.

Methods We performed an IPD meta-analysis of 25 trials of vitamin D supplementation with incidence of acute respiratory infection as a pre-specified outcome (total 11,321 participants, aged 0 to 95 years). We used one-step logistic regression with random effects adjusting for age, sex, study duration and clustering by study. Pre-specified sub-group analyses were done to determine whether effects of vitamin D on risk of acute respiratory infection varied according to baseline 25-hydroxyvitamin D (25(OH)D) concentration or dosing regimen.

Results IPD were obtained for 10,933/11,321 (96.6%) participants. Vitamin D supplementation reduced risk of acute respiratory infection among all participants (adjusted Odds Ratio [aOR] 0.88, 95% CI: 0.81 to 0.96, P = 0.003; P for heterogeneity < 0.001). Sub-group analysis revealed a strong protective effect among individuals with baseline 25(OH)D < 25 nmol/L (aOR 0.62, 95% CI: 0.45 to 0.83, P = 0.002), not seen among those with higher levels (aOR 0.91, 95% CI: 0.78 to 1.05; Pinteraction = 0.01). A protective effect was also seen in individuals receiving daily or weekly vitamin D without additional bolus doses (aOR 0.81, 95% CI: 0.72 to 0.91, P < 0.001), but not in those receiving one or more bolus doses (aOR 0.97, 95% CI: 0.86 to 1.10, Pinteraction = 0.05). Vitamin D did not influence the proportion of participants experiencing at least one serious adverse event (aOR 0.98, 95% CI: 0.80 to 1.20, P = 0.83). The body of evidence contributing to these analyses was assessed as being of high quality.

Conclusions Vitamin D supplementation was safe, and it protected against acute respiratory infection overall. Very deficient individuals and those not receiving bolus doses experienced the most benefit.

**NON-TYPEABLE HAEMOPHILUS INFLUENZAE DOWNREGULATES RELEASE OF BETA-DEFENSIN-1 FROM BRONCHIAL EPITHELIAL CELLS**

LJ Tregidgo, JL Cane, M Bafadhel. Respiratory Medicine Unit, NDM, University of Oxford, Oxford, UK

Introduction Beta defensin-1 is an antimicrobial peptide released from epithelial cells, acting to defend the host against microbial activity and colonisation. It is possible that reduction in release of this antimicrobial peptide contributes to the host inability to remove bacteria from the airway. We investigated the release of beta-defensin-1 from the bronchial epithelium, with and without Non-Typeable Haemophilus influenzae (NTHi) infection and studied the effects of corticosteroids on this.

Method Human bronchial epithelial cells from three healthy donors were grown to 90% confluence. Cells were treated with 16 nM, 1.6 nM and 0.16 nM Budesonide or 10 nM, 1 nM and 0.1 nM Fluticasone propionate as per clinical equivalence, for two hours prior to addition of 1 x 106 CFU of NTHi. Cells were incubated for a further two hours. Beta-defensin-1 was measured in supernatants by ELISA.

Results NTHi infection downregulated beta-defensin-1 release by 42% (mean basal release: 133.6 pg/ml, SD: 61.6, mean release with NTHi infection: 77.6 pg/ml, SD: 50.6. p = 0.0084). Addition of Budesonide or Fluticasone propionate to bronchial epithelial cells decreased beta-defensin-1 release from mean basal level to 106.2 pg/ml (SD: 79.4, p = 0.023) and 100.6 pg/ml (SD: 50.0, p = 0.083) respectively. This release is synergistically decreased upon NTHi infection with Budesonide and Fluticasone propionate treatment (mean with NTHi: 67.3 pg/ml, SD: 38.7. p = 0.039 and 64.4 pg/ml, SD: 26.1. p = 0.048) respectively compared to corticosteroid treatment only. No difference in beta-defensin-1 level was seen between low and high dose of either corticosteroid tested.

Conclusion NTHi inhibits beta-defensin-1 release from healthy bronchial epithelial cells. This release is dampened further by corticosteroid treatment and may be implicated in NTHi persistence in the airway in patients with chronic lung disease such as COPD.

**HYPOXIA PRECONDITIONS THE INNATE IMMUNE RESPONSE TO ACUTE BACTERIAL PULMONARY INFECTIONS**

1RS Dickinson, 2AA Thompson, 1JP Thomson, 1F Murphy, 1HM Marriott, 1A Tavares, 1J Willson, 2L Williams, 2A Lewis, 2F Forbes, 1RH Stimson, 2AG Hameed, 1JA Preston, 2A Lawrie, 1V Finiguerra, 2M Mazzone, 1SI Foster, 1ER Chivin, 1AS Cowburn, 2DH Doddrell, 2RS Johnson, 1RN Meehan, 1MB Whyn, 2SR Walmley. University of Edinburgh, Edinburgh, UK; 1University of Sheffield, Sheffield, UK; 2Vesalius Research Centre, Leuven, Belgium; 1University of Cambridge, Cambridge, UK

Introduction Systemic hypoxaemia and recurrent bacterial infections frequently co-exist in patients with acute and chronic lung disease and correlate with poor clinical outcomes. Inappropriate neutrophilic inflammation is regularly seen in these circumstances and the HIF/PHD pathway is implicated in the response of the innate immune system to both hypoxia and bacteria. Here we aimed to dissect and modify the interactions between hypoxia and innate host-pathogen response in the lung.

Methods C57BL/6 mice were either housed in room air or ‘pre-conditioned’ by being housed in 10% oxygen for 7 days. They then received intratracheal 1x10⁵ type 2 S. pneumoniae under recovery anaesthesia with subsequent exposure to hypoxia (10% O₂) or room air (21% O₂). Mice were assessed clinically, rectal temperatures recorded and culled for broncho-alveolar lavage (BAL) and tissue sampling (blood and lung) at various time points. Peripheral blood glucose was measured from tail vein venepuncture using a handheld blood glucose monitor. RNA from peripheral blood leukocytes was isolated and analysed using RNAseq. 18FDG-PET was performed on animals 14 h following infection to observe glucose utilisation. Histology was performed on formalin fixed sections for glycogen storage.

Results Exposure to acute hypoxia resulted in significant morbidity (sickness (5.7 vs 2.1, p < 0.02) and hypothermia (31.8 vs 36.0°C, p < 0.05)) and rapid 100% mortality by 48 h post infection. This response was independent of bacterial burden, and leukocyte recruitment. In keeping with a negative energy state, preconditioned mice showed marked protection from both the acute hypoxia-associated systemic phenotype and the negative energy state. Transfer of preconditioned bone marrow to naïve mice also rescued the pathophysiological response. RNAseq analysis of the circulating leukocyte population identified signal-induced suppression of HIF-1α pathway genes, which were linked to reduced leukocyte glucose utilisation in vivo by 18FDG-PET.
Conclusions Hypoxic preconditioning reverses the morbidity and mortality associated with acute hypoxia following intrapulmonary bacterial challenge. This response is dependent on the preconditioning of the innate immune system by suppressing HIF1 alpha and altering circulating leukocyte metabolism.

Support RSD is funded by the MRC. SRW is funded by the Wellcome Trust.

S105 PNEUMOCOCCAL SEROTYPES IMPLICATED IN ADULT PNEUMOCOCCAL PNEUMONIA, 9 YEARS FOLLOWING THE INTRODUCTION OF THE INFANT VACCINE PROGRAMME IN THE UK

P Daniel, D Ashton, C Sheppard, S Eletu, D Sandu, D Litt, N Fry, WS Lim.
Department of Respiratory Medicine, Nottingham University Hospitals, Nottingham, UK;
Respiratory and Vaccine Preventable Bacterial Reference Unit, London, UK
10.1136/thoraxjnl-2016-209333.111

Background The introduction of the pneumococcal conjugate vaccines into infant vaccination schedules, has led to a change in the serotype prevalence causing adult pneumococcal disease, through the process of herd immunity. Whilst there are national surveillance programmes informing the changes in serotype in invasive pneumococcal disease, there are no comparable data to demonstrate the ongoing vaccine effect on non-invasive pneumococcal community acquired pneumonia (CAP), the most common clinical manifestation of pneumococcal disease in adults.

Methods Consecutive adult patients admitted to 2 hospitals, covering the catchment area of a large UK city, with a diagnosis of CAP were studied prospectively, over a 1 year period between September 2014 and 2015. A novel multiplex assay capable of detecting 24 serotypes/serogroups of Streptococcus pneumoniae was performed on patient urine. Pneumococcal infection was determined by identification of the organism from either sterile sites and/or detection of pneumococcal antigen or serotype in urine samples.

Abstract S105 Figure 1 Serotypes isolated in adult pneumococcal CAP

Results Of 478 individuals admitted with CAP pneumococcal disease was diagnosed in 166 (34.7%) cases. Pneumococcal CAP diagnosis was made by blood culture, pneumococcal urinary antigen detection and urinary serotype detection in 23 (13.9%), 61 (36.8%) and 149 (89.8%) cases respectively. A definitive single serotype was identified in 116 individuals; the most commonly observed were serotypes 3 and 8 (31 cases each, 26.7%), followed by serogroup 15 (14 cases, 12.1%), 17F (10 cases, 8.6%) and 33A/B/D/E (9 cases, 7.8%).

Conclusion This is the first report on extended serotype distribution implicated in adult pneumococcal CAP, 9 years after the introduction of the UK infant vaccination programme. In this era of high infant vaccine coverage, whilst the majority of isolates are non-vaccine types due to the effects of serotype replacement, serotype 3 remains a common cause of adult pneumococcal CAP and may reflect inadequate serotype specific vaccine effectiveness.

S106 PERIPHERAL BLOOD NEUTROPHILS ARE PRIMED AND ACTIVATED IN BRONCHIECTASIS AND ARE ATTENUATED BY THE PRO-RESOLVING MEDIATOR LIPOXIN A4

P Bed, B McHugh, DJ Davidson, AG Rossi, AT Hill. MRC Centre for Inflammation Research, Edinburgh, UK
10.1136/thoraxjnl-2016-209333.112

Introduction Excessive neutrophilic airways inflammation is the central feature of bronchiectasis but little is known about the role of serum neutrophils in bronchiectasis. Lipid mediators derived from arachidonic acid such as Lipoxin (LXA4) are known to regulate the inflammatory process and generate pro-inflammatory, anti-inflammatory and pro-resolving mediators. In this research work, we propose to describe the function of peripheral neutrophils in bronchiectasis and the effect of LXA4.

Methods Three study groups were included in this study when clinically stable: 6 healthy volunteers; 6 patients with mild bronchiectasis with a Bronchiectasis Severity Index (BSI) score 0–4; 6 with severe bronchiectasis (BSI scores >9). Freshly isolated peripheral neutrophils from the groups were treated with LXA4 or vehicle control and we assessed spontaneous neutrophil apoptosis at 20 hours, neutrophil activation, neutrophil degranulation, phagocytosis of GFP labelled Pseudomonas aeruginosa and expression of LXA4 receptor formyl peptide receptor (FPR)2.

Results In vehicle treated neutrophils, there was increased viability and less apoptosis in bronchiectasis patients compared to healthy volunteers; Figure 1. There was a significant increase in CD11b upregulation; p = 0.01 and CD62L shedding; p = 0.01 in bronchiectasis patients compared to healthy volunteers. There was a significant increase in neutrophil degranulation with myeloperoxidase (MPO) release, in bronchiectasis patients; p = 0.04. There was an increase in neutrophil phagocytosis of GFP labelled Pseudomonas aeruginosa by neutrophils from bronchiectasis patients, p = 0.03, compared to healthy volunteers; Figure 1.

In LXA4 treated neutrophils, there was no effect of LXA4 on spontaneous neutrophil apoptosis. There was a significant reduction in n-formyl-methyl-leucyl-phenylalanine (fMLF)-induced CD11b upregulation and CD62L shedding by LXA4 in a dose dependent manner in all three groups. There was a significant reduction in cytochalasin-B and fMLF-induced activation of neutrophils and release of MPO, by LXA4 in all three groups. There was significant improvement in neutrophil phagocytosis of GFP labelled Pseudomonas aeruginosa in a dose dependent manner in all three groups. There was a statistically significant increase in FPR2 receptor expression in healthy volunteers compared to bronchiectasis patients when treated with LXA4 100nM, p = 0.03.
Conclusion Serum neutrophils in bronchiectasis are primed and activated compared to healthy volunteers. The pro-resolving mediator LXA4 stabilised the neutrophil whilst promoting neutrophil phagocytosis.

Pulmonary Hypertension

**GENOTYPE-PHENOTYPE ASSOCIATIONS IN PULMONARY ARTERIAL HYPERTENSION CAUSED BY BMPR2 AND EIF2AK4 VARIANTS**

1C Hadinnapola, 1M Haimel, 1M Bleda, 2H Bogaard, 3G Coghlan, 4P Corris, 5S Gibbs, 6D Kiely, 7A Lawrie, 8A Peacock, 9J Pepke-Zaba, 10R Trembath, 11J Wharton, 12SJ Wort, 13JGraff, 1NM Morrell.

1Cambridge University, Cambridge, UK; 2VU Medical Centre, Amsterdam, Netherlands; 3Royal Free Hospital, London, UK; 4Newcastle University, Newcastle, UK; 5Hammersmith Hospital, London, UK; 6Royal Hallamshire Hospital, Sheffield, UK; 7Sheffield University, Sheffield, UK; 8Golden Jubilee Hospital, Glasgow, UK; 9Papworth Hospital, Cambridge, UK; 10Kings College, London, UK; 11Imperial College, London, UK; 12Royal Brompton Hospital, London, UK

10.1136/thoraxjnl-2016-209333.113

**Introduction**

Idiopathic pulmonary arterial hypertension (IPAH) is a rare and incurable disease. Causal mutations in BMPR2 are found in 17% of patients. Pulmonary veno-occlusive disease (PVOD) and pulmonary capillary haemangiomatosis (PCH) are rarer forms of pulmonary hypertension and have a worse prognosis. Biallelic mutations in EIF2AK4 have been described in PVOD and PCH. We hypothesised that mutations in these genes are associated with specific phenotypes or endotypes.

**Methods**

Whole genome sequencing was performed on genomic DNA from PAH patients recruited to the NIHR BRIDGE Study (n = 679). Rare (absent from BRIDGE control cohorts [n = 5906] and minor allele frequency < 0.0001 in the ExAC database [http://exac.broadinstitute.org]) and predicted deleterious (CADD score >15 and Polyphen not benign) variants were selected for association testing with phenotypic and metabolomic data. Plasma samples from 288 patients were sent to Metabolon (USA) for a high-throughput metabolomic screen.

**Results**

Mutations in BMPR2 (82 single nucleotide variants and 13 deletions) were identified in 14% of PAH patients. Unexpectedly, 22 rare and predicted deleterious EIF2AK4 variants were found in 17 patients with IPAH. Biallelic EIF2AK4 variants were found in 1% of patients (5 homozygous variant carriers and 4 potential compound heterozygotes). Additionally, there were 8
heterozygous EIF2AK4 variant carriers in the cohort (1%), suggesting a 3-fold over-representation of heterozygous EIF2AK4 variants compared to ExAC ($p = 0.005$).

BMPR2 mutation carriers presented at a younger age and with more severe pulmonary haemodynamics compared to those without identified variants in the known PAH genes. Biallelic EIF2AK4 variant carriers had a significantly reduced transfer coefficient for carbon monoxide compared to patients with BMPR2 mutations or no identified variants. Heterozygous EIF2AK4 variant carriers were similar to patients with no identified variants. There were no differences between groups in functional class or walk test distances assessed longitudinally.

BMPR2 and EIF2AK4 genotype did not influence the plasma metabolome.

**Discussion** Biallelic EIF2AK4 variants are the second most common genetic defect in patients with apparent IPAH, after BMPR2. Variants in both genes are associated with characteristic phenotypes. Additional, non-coding variants may be present in heterozygous EIF2AK4 variant carriers. These findings have important implications for the clinical and molecular classification of PAH.

**Abstract S107 Table 1**

<table>
<thead>
<tr>
<th>BMPR2 mutation carriers</th>
<th>EIF2AK4 biallelic variant carriers</th>
<th>EIF2AK4 heterozygous variant carriers</th>
<th>Patients with no identified variants</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>68</td>
<td>44</td>
<td>80</td>
<td>72</td>
</tr>
<tr>
<td>Caucasian (%)</td>
<td>81</td>
<td>22</td>
<td>80</td>
<td>85</td>
</tr>
<tr>
<td>Age (years)</td>
<td>39.79 ± 12.97</td>
<td>30.10 ± 9.26</td>
<td>54.43 ± 21.04</td>
<td>51.30 ± 16.57</td>
</tr>
<tr>
<td>mPAP (mmHg)</td>
<td>60.71 ± 11.54</td>
<td>54.11 ± 16.29</td>
<td>48.25 ± 19.57</td>
<td>52.65 ± 13.6</td>
</tr>
<tr>
<td>CO (L/min)</td>
<td>3.55 ± 1.15</td>
<td>4.39 ± 1.48</td>
<td>4.25 ± 2.17</td>
<td>4.26 ± 1.47</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>88.66 ± 15.77</td>
<td>92.00 ± 13.83</td>
<td>82.98 ± 22.26</td>
<td>82.36 ± 17.93</td>
</tr>
<tr>
<td>FEV1/FVC (pred)</td>
<td>0.78 ± 0.08</td>
<td>0.79 ± 0.07</td>
<td>0.78 ± 0.12</td>
<td>0.74 ± 0.10</td>
</tr>
<tr>
<td>KCO (%)</td>
<td>83.54 ± 16.86</td>
<td>33.84 ± 6.48</td>
<td>60.99 ± 41.77</td>
<td>67.76 ± 22.91</td>
</tr>
</tbody>
</table>

Phenotypic characteristics of patients with idiopathic pulmonary arterial hypertension by genotype. Data presented as mean ± sd unless stated. mPAP = mean pulmonary artery pressure; CO = cardiac output; FEV1 = forced expiratory volume 1 second; FVC = forced vital capacity; KCO = transfer coefficient for carbon monoxide.

**S108**

**LOW SKELETAL MUSCLE STRENGTH AND PHYSICAL ACTIVITY ARE ASSOCIATED WITH POOR OUTCOMES IN PULMONARY ARTERIAL HYPERTENSION**

BE Garfield, D Shao, T Parfitt, C Harries, L Price, K Dimopulos, M Polkey, P Kemp, SJ Wort, Imperial College London, London, UK; Royal Brompton Hospital, London, UK; 3NIHR Respiratory BRU Royal Brompton and Imperial, London, UK

10.1136/thoraxjnl-2016-209333.114

**Introduction** Skeletal muscle wasting and low physical activity are emerging as important potentially modifiable complications of pulmonary arterial hypertension (PAH). In other conditions, such as COPD and heart failure, low muscle strength and low levels of activity have been shown to be associated with poor outcomes. We aimed to define the association of muscle strength and physical activity with hospital admission rates, long term quality of life and mortality in patients with PAH.

**Methods** Twenty-eight patients with PAH had their quadriceps maximal volitional capacity (QMVC), step count, BNP and 6MWD measured. At least 1 year later, these patients’ records were reviewed and data were collected on mortality, transplantation, admission to hospital and quality of life using the EMPHASIS 10 questionnaire. QMVC was normalised to BMI and 24 patients with valid step count data were included in the analysis of activity. Kaplan-Meier plots were constructed to define mortality and ROC analysis was used to demonstrate which factors most closely predicted hospital admission. Pearson correlation was used to define the associations with follow-up quality of life.

**Results** Kaplan-Meier plots demonstrated that patients with a QMVC/BMI < 1.1 and those with a step count < 2500 per day were significantly more likely to die or undergo transplant than those above these cut-offs (Figure 1 A and B). ROC analysis showed that a QMVC/BMI <1.5 predicted hospital admission over the follow up period with a sensitivity of 93% and a specificity of 62%. It also demonstrated that QMVC was superior to the 6MWD in predicting hospital admission (AUC 0.83, $p = 0.003$ vs. AUC 0.73, $p = 0.017$). Finally QMVC/BMI was significantly correlated to quality of life at follow-up in this cohort ($r = -0.47$, $p = 0.018$).

**Discussion** Our data suggests that, like in other chronic conditions, low muscle strength and low physical activity in PAH are associated with poor outcomes. Treatment strategies targeting the muscle and physical activity levels may improve outcomes in terms of both quality of life and mortality.

**Abstract S108 Figure 1** Kaplan-Meier plots showing survival (end points being death or transplant) in patients with PAH with a: A. QMVC/BMI <1.1 and >1.1; B. step count < 2500 and > 2500
TARGETING THE PROSTACYCLIN PATHWAY IN THE TREATMENT OF CONNECTIVE TISSUE DISEASE ASSOCIATED PULMONARY ARTERIAL HYPERTENSION (PAH): INSIGHTS FROM THE RANDOMISED CONTROLLED GRIPHON TRIAL WITH SELEXIPAG

Coghlan, Gaine, Channick, Di Scala, Galé, Ghafriani, Hooper, Lang, McLaughlin, Preis, Rubin, Simoneau, Sibon, Tapson, Chin.

National Pulmonary Hypertension Service, Royal Free Hospital, National Health Foundation Trust, London, UK; National Pulmonary Hypertension Unit, Mater Misericordiae University Hospital, Dublin, Ireland; Massachusetts General Hospital, Boston, MA, USA; Actelion Pharmaceuticals Ltd, Allschwil, Switzerland; Istituto di Malattie dell’Apparato Cardiovascolare, University of Bologna, Bologna, Italy; University of Giessen and Marburg Lung Centre (UGMCL), member of the German Centre of Lung Research (DZL), Giessen, Germany; Department of Medicine, Imperial College London, London, UK; Department of Respiratory Medicine, Hannover Medical School and German Centre of Lung Research, Hannover, Germany; Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Allgemeines Krankenhaus, Vienna, Austria; University of Michigan Health System Division of Cardiovascular Medicine, Ann Arbor, MI, USA; Division of Pulmonary and Critical Care Medicine, University of California, San Diego, CA, USA; Hôpital Universitaire de Bicêtre, Université Paris-Sud, Le Kremlin Bicêtre, France; Cedars-Sinai Medical Centre, Los Angeles, CA, USA; UF Southwestern Medical Centre, Dallas, TX, USA.

Rationale Despite available therapies, patients with connective tissue disease-associated PAH (PAH-CTD) have a poor prognosis. The global phase III GRIPHON study (NCT01106014) enrolled 1,156 patients including 334 with PAH-CTD. Compared with placebo, selexipag reduced the risk of the primary composite outcome of morbidity/mortality up to end of treatment by 41% (hazard ratio [HR] 0.59; 99% CI: 0.37–0.96) among patients with PAH-CTD. We examined the effect of selexipag vs placebo in the PAH-CTD subgroups: PAH associated with systemic sclerosis (PAH-SSc), systemic lupus erythematosus (PAH-SLE) and mixed CTD (PAH-MCTD).

Methods Patients (18–75 years) were randomised 1:1 to placebo or selexipag. HRs (95% CI) were calculated using Cox regression models to determine the effect of selexipag vs placebo on morbidity/mortality.

Results Of the 334 patients enrolled with PAH-CTD, 170 had PAH-SSc, 82 PAH-SLE, and 47 PAH-MCTD; CTD sub-classification was not reported in 35 patients. Across the subgroups, the majority of patients were female (84–99%) and were receiving an endothelin receptor antagonist, a phosphodiesterase type-5 inhibitor or both at baseline (73–83%). In the PAH-SSc, PAH-SLE and PAH-MCTD subgroups, the mean (SD) age was 60.0 (10.6), 39.0 (11.3) and 48.0 (14.7) years, respectively, and 65%, 33%, and 45% were in WHO functional class III, respectively. Selexipag reduced the risk of morbidity/mortality events by 44% (HR 0.56; 95% CI: 0.34–0.91) in PAH-SSc, 34% (HR 0.66; 95% CI: 0.30–1.48) in PAH-SLE, and 53% (HR 0.47; 95% CI: 0.15–1.48) in PAH-MCTD (Figure). The treatment effect was consistent across the subgroups (interaction test indicated no heterogeneity; p = 0.6737). By the end of study, 22 PAH-SSc, 7 PAH-SLE and 3 PAH-MCTD patients in the placebo, and 17 PAH-SSc, 4 PAH-SLE, 8 PAH-MCTD patients in the selexipag group had died. Common prostacyclin-associated side effects observed with selexipag in PAH-CTD patients generally occurred at a similar incidence to PAH-non-CTD patients and within the PAH-CTD subgroups.

Conclusion GRIPHON included the largest randomised cohort of patients with PAH-CTD to date. The treatment effect of selexipag on time to first morbidity/mortality event was consistent across the subgroups, suggesting that selexipag is an effective therapeutic option in these difficult-to-treat patients.

Please refer to page A270 for declarations of interest in relation to abstract S109.

2-D SEGMENTAL LONGITUDINAL STRAIN RATES CORRELATE WITH PROGNOSTIC INDICATORS IN IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION

Crowe, Sonecki, Mackenzie, Jayasekera, Church, Johnson, Peacock.

Scottish Pulmonary Vascular Unit, Glasgow, UK; Golden Jubilee National Hospital, Glasgow, UK

Abstract S109 Figure 1
Background/objectives  Speckle tracking echocardiography (STE) has added to the assessment of right ventricular function by providing off-line measurements of strain and strain rate. Worsening right ventricular function is associated with poorer outcomes in idiopathic pulmonary arterial hypertension (IPAH). Global right ventricular free wall (RVFW) longitudinal strain and strain rate have been reported as markers of prognosis. Differences in degree of regional RVFW deformation will affect the global RVFW analysis. We assessed whether RVFW segmental analysis using STE identified specific regional associations with proven prognostic markers.

Method Using our database, we identified newly diagnosed cases of IPAH between January 2012 and May 2016. 25 cases had echocardiograms accessible for retrospective analysis. Using 2D-STE software (EchoPAC, GE Healthcare), we measured longitudinal strain and strain rate of the RVFW basal, mid and apical segments. Data on established prognostic markers, NT-proBNP, cardiac index (CI), WHO functional class (FC), six-minute walk distance (6MWD) and mixed venous saturations (SvO2) were retrieved from the patient database. All data was anonymised for analysis.

Results  Basal peak systolic longitudinal strain rate (PSSLR) of the RVFW correlated very strongly with NT-proBNP (r = 0.82, p < 0.001) and moderately with CI: (r = −0.53, p < 0.007), WHO FC (r = 0.52, p < 0.008) and SvO2 (r = −0.50, p < 0.02). Basal late diastolic longitudinal strain rate (LDLSR) correlated strongly with SvO2 (r = 0.61, p < 0.002), and moderately with NT-proBNP (r = −0.58, p < 0.005), CI: (r = 0.57, p < 0.004), 6MWD (r = 0.5, p < 0.02), and WHO FC (r = −0.49, p < 0.02). Mid PSSLR and LDLSR moderately correlated with SvO2 (r = −0.53 and 0.56), NT-proBNP (r = 0.5 and −0.5) and CI (r = −0.48 and 0.42), (all p < 0.04). The apical segment showed no significant correlations. Peak systolic longitudinal strain demonstrated only one significant segmental correlation between the mid-segment and NT-proBNP (r = 0.44, p < 0.05).

Conclusion We have demonstrated that analysing RVFW longitudinal segments provides significant regional correlations with known prognostic markers in an IPAH population group. We have shown the significant advantage of longitudinal strain rate over strain in its strength and consistency of correlation with these markers. We have acknowledged basal and mid segments as significant regions of interest. This study shows that further exploration of right ventricular function in pulmonary hypertension by RVFW segmental analysis is indicated.

S111 DIFFERENCES IN CHARACTERISTICS AND OUTCOMES IN SYSTEMIC SCLEROSIS-ASSOCIATED AND IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION

S Ramjug, N Hussain, J Hurdman, C Billings, CA Elliot, DG Kiely, I Sabroe, S Rajaram, AJ Swift, R Condiffe. Royal Hallamshire Hospital, Sheffield, UK

Background Previous studies have demonstrated survival in systemic sclerosis (SSc)-associated pulmonary arterial hypertension (SSc-PAH) to be worse than in idiopathic pulmonary arterial hypertension (IPAH). Possible explanations include age, differences in the underlying pulmonary vasculopathy and the ability of the right ventricle to compensate for the increased afterload. We investigated differences between these conditions by comparing demographic, haemodynamic and cardiac magnetic resonance imaging (MRI) characteristics and outcomes in a large cohort of incident, treatment-naive patients.

Methods 183 patients with IPAH and 192 patients with SSc-PAH were identified from departmental databases including the ASPIRE registry. Sub-group analysis in 83 patients who had undergone cardiac MRI within 14 days of right heart catheterisation was performed.

Results Median survival in IPAH was 7.8 years and in SSc-PAH was 3 years (p < 0.001). Patients with SSc-PAH were older with milder pulmonary haemodynamics but lower gas transfer (DLCO). Independent prognostic factors at multivariate Cox regression analysis were age, presence of systemic sclerosis, DLCO, pulmonary artery saturation and stroke volume. For a given resistance (R), pulmonary arterial compliance (C) was reduced (lower RC) in SSc-PAH (Figure). The relationship between mean pulmonary arterial pressure (mPAP) and systolic pulmonary arterial pressure (sPAP) in IPAH was identical to that previously reported (mPAP = 0.61 sPAP + 2 mmHg). The relationship in SSc-PAH was found to be: mPAP = 0.58 sPAP + 2 mmHg (p-value for difference with IPAH = 0.095). There was
no significant difference in compensatory right ventricular hypertrophy when corrected for afterload while the correlation between ventricular mass index (right ventricular mass/left ventricular mass) and pulmonary vascular resistance was stronger in SSc-PAH.

Conclusion The reasons for poorer outcomes in SSc-PAH are likely to be multifactorial including, but not limited to, older age, increased pulmonary arterial stiffness and reduced gas transfer.

REFERENCES

Interventional Trials

LONG-TERM SAFETY AND EFFICACY OF IVACAFTOR IN PAEDIATRIC PATIENTS AGED 2–5 YEARS WITH CYSTIC FIBROSIS AND A CFTR GATING MUTATION

1JC Davies, 1S Robertson, 1JC Cooke, 1M Higgins, 1M Rosenfeld. 2Vertex Pharmaceuticals Incorporated, Boston, MA, USA; 3Vertex Pharmaceuticals (Europe) Limited, London, UK; 4Seattle Children’s Hospital, Seattle, WA, USA

Methods Patients who completed KIWI Part B enrolled in KLIMB and received ivacaftor for an additional 84 weeks. Patients aged 2–5 years received weight-based dosing (50 mg q12h for weight < 14 kg; 75 mg q12 h for ≥14 kg); patients who turned 6 received 150 mg q12h. The primary endpoint was safety. Secondary endpoints included change from baseline (at the start of KIWI) in sweat chloride, weight, and body mass index (BMI). Exploratory endpoints included faecal elastase-1 (FE-1) and immunoreactive trypsinogen (IRT) levels.

Results Of 34 patients in KIWI Part B, 33 enrolled in KLIMB (mean age at KLIMB baseline, 3.7 years). Five patients discontinued study drug (1 for elevated alanine transaminase/aspartate transaminase [ALT/AST] levels, 2 switched to commercial ivacaftor, 2 for noncompliance). The most common adverse event (AE) of any grade was cough (73%). Eleven patients had serious AEs; ten patients had elevated ALT/AST levels ≥3 × upper limit of normal (ULN). Of these, 4 had elevated ALT/AST levels > 8 × ULN in KIWI; ivacaftor was maintained or resumed in all patients except 1 who discontinued. Significant improvements in sweat chloride, FE-1 and IRT levels, and BMI z scores were observed at week 84 (Table 1).

Conclusion Ivacaftor demonstrated a stable safety profile during an extended 84-week follow-up period in patients with cystic fibrosis aged 2–5 years with a CFTR gating mutation. Reported AEs were consistent with the known safety profile; the incidence of elevated ALT/AST levels per 24-week period was consistent with that observed in KIWI. The improvements seen in KIWI are maintained at the end of KLIMB.
P = 0.39). Allocation to vitamin D was associated with accelerated sputum smear conversion (adjusted HR 1.47, 95% CI: 1.09 to 1.98, P = 0.01) and a small but statistically significant reduction in the mean number of zones affected on chest radiograph at 8 weeks (5.48 vs. 5.69, 95% CI: for difference 0.06 to 0.77 zones, p = 0.02).

Conclusions This is the largest randomised controlled trial to investigate effects of adjunctive vitamin D on time to sputum culture conversion in pulmonary tuberculosis conducted to date. Adjunctive high-dose vitamin D was effective in elevating serum 25(OH)D concentrations to high-physiological levels, but did not influence time to sputum culture conversion.

### Table S114

<table>
<thead>
<tr>
<th>Covariant</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drainage and fibrinolysis</td>
<td>Standard for comparison</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Drainage alone</td>
<td>3.04</td>
<td>1.47–6.27</td>
<td>0.003*</td>
</tr>
<tr>
<td>Video-assisted thoracoscopic surgery</td>
<td>1.14</td>
<td>0.32–3.20</td>
<td>0.821</td>
</tr>
<tr>
<td>Decortication</td>
<td>1.53 X 10–7</td>
<td>N/A</td>
<td>0.987</td>
</tr>
<tr>
<td>Other procedure</td>
<td>1.53 X 10–7</td>
<td>N/A</td>
<td>0.987</td>
</tr>
</tbody>
</table>

OR = Odds ratio CI = Confidence interval *p-value > 0.05
N/A 95% CI values were too small to compute

### Table S115

**HOT-HMV UK TRIAL SECONDARY OUTCOME ANALYSIS: EARLY READMISSION IS REDUCED BY THE ADDITION OF HOME MECHANICAL VENTILATION TO HOME OXYGEN THERAPY IN COPD PATIENTS WITH CHRONIC RESPIRATORY FAILURE FOLLOWING A LIFE-THREATENING EXACERBATION**


Introduction
Hospital readmission following treatment for a life-threatening exacerbation of COPD with acute NIV is frequent and associated with an adverse impact in terms of lung function and health related quality of life. They have been identified as a priority area in the NHS with financial penalties for any patient readmitted within 28 days following discharge.

Method
A multicentre open labelled randomised controlled trial recruited patients with persistent hypercapnia (PaCO2 > 7 kPa) 2–4 weeks following resolution of acute acidosis. Patients were randomised to either home oxygen therapy (HOT) or HOT and home mechanical ventilation (HOT-HMV). HMV was titrated overnight to control nocturnal hypercapnia. Follow up was for 12 months. The primary outcome, 12-month admission free survival, has been reported previously demonstrating a significant treatment effect (ERS 2016). Secondary outcome analysis included 28-day all-cause hospital readmission and 12 month exacerbation rate.

Results
116 patients were randomised (HOT = 59, HOT-HMV = 57), age 67 ± 10 years, FEV1 0.6 ± 0.2 L, PaCO2 7.9 ± 0.9 kPa. 28-day readmission was 22 (37%) in the HOT and 7 (12%) in the HOT-HMV arm (unadjusted HR 0.27, 0.12 to 0.63, p = 0.003; adjusted HR 0.26, 0.11 to 0.61, p = 0.002) (Figure 1). 12 month exacerbation rate was reduced from median 5 (1 to 9) per year in the HOT arm to 4 (2 to 6) in the HOT-HMV arm (unadjusted HR 0.64 (0.44 to 0.94); p = 0.022; adjusted HR 0.66, 0.46 to 0.95, p = 0.026).

Conclusion
The addition of HMV to HOT in patients with persistent hypercapnia following an acute life-threatening exacerbation of COPD reduces both 28-day readmission and 12 month exacerbation frequency. These data strongly support a change in
Results: Between June 2014 to January 2016 118 of 207 eligible patients were randomised: female = 56/118 (52.5%), mean age (SD) = 69.8 (10.2), mean FEV1% predicted (SD) = 43.9 (17.6) and coexistent pneumonia = 24/118 (20.3%).

At 14 days, 105/117 (90%) patients expressed a preference for HAH. Median bed days were 4 days lower in the HAH arm (p = 0.001), with no difference in mortality or readmissions.

Conclusions: Selection for HAH by low risk DECAF score is safe, clinically effective, preferred by most patients, reduces total bed days and is a suitable option for up to 50% of admitted patients.

REFERENCES
2. BTS national audit report 2015.

**S117** WORK-RELATED SYMPTOMS IN LABORATORY ANIMAL WORKERS

**J Feary, J Canizales, C Fitzgerald, B Fitzgerald, M Schofield, M Jones, P Cullinan.**

1 Royal Brompton and Harefield NHS Foundation Trust, London, UK; 2 Imperial College, London, UK

Introduction Laboratory animal workers frequently report ocular, nasal and respiratory symptoms which occur in the workplace and improve away from work. A proportion of these will be sensitised to animal proteins on the basis of skin prick tests (SPTs) or serum specific IgE testing and will have laboratory animal allergy. The remainder will have work-related symptoms due to other (unknown) causes.

Methods We performed a cross-sectional study (SPIRAL (Safe Practice In Reducing Allergy in Laboratories)) of laboratory animal workers exposed to mice across six UK research institutions. Participants completed a self-administered questionnaire, which included detailed questions about symptoms, and underwent SPT to common aeroallergens and mouse epithelium, and specific IgE testing to mouse proteins (epithelium and urine). Those participants reporting ocular, nasal or respiratory symptoms which were worse at work were compared with those with no association between their symptoms and work.

Results 685 laboratory workers were recruited (response rate 88%). 187 (28%) reported at least one symptom and of these, 45% (n = 85) were work-related (WR). 56/105 (53%) reported work-related conjunctivitis; 67/156 (43%) reported WR nasal symptoms and 22/44 (50%) reported WR respiratory symptoms. There were no differences between the two groups in sex, smoking status, atopy to a common aeroallergen or job title. Those with at least one WR symptom were significantly more likely to be sensitised to mouse proteins (32 (37.7%) vs 10 (9.8%) p < 0.001 (Table). WR symptoms were significantly more common in those working with mice housed in open cages compared with those housed in Individual Ventilated Cages (IVCs). Prevalence of sensitisation to a common aeroallergen was similar in both groups.

Conclusion In this large study population, prevalence of WR symptoms is reasonably high in all laboratory animal workers and is attributable to mouse allergy in around 50% of cases, consistent with other previous studies. Symptoms are less prominent in people working with IVCs compared with conventional open cages. Exposure to airborne endotoxin may be a cause for nasal and respiratory symptoms on exposure to mice in non-mouse cages.

Abstract S116 Table 1 Outcome by allocated group

<table>
<thead>
<tr>
<th>Outcome</th>
<th>UC n = 58</th>
<th>HAH n = 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bed days, n (IQR)</td>
<td>5 (2–12)</td>
<td>1 (7–7)</td>
</tr>
<tr>
<td>Readmission*†</td>
<td>23 (39.7%)</td>
<td>22 (36.7%)</td>
</tr>
<tr>
<td>14 day mortality*</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>90 day mortality*</td>
<td>1 (1.7%)</td>
<td>1 (1.6%)</td>
</tr>
<tr>
<td>Preference for HAH</td>
<td>51/57</td>
<td>54/60</td>
</tr>
</tbody>
</table>

*All cause. †One or more readmissions.
sensitised animal workers. Measurement of exposure to endotoxin levels in these workers is in progress.

CAN FRACTIONAL EXHALED NITRIC OXIDE HELP PREDICT ASTHMA IN BRITISH FOUNDRY WORKERS?

1RE Wiggans, 1E Robinson, 1J Sumner, 1A Codling, 2L Lewis, 1CM Barber. 1Health and Safety Laboratory, Buxton, UK; 2Northern General Hospital, Sheffield, UK

10.1136/thoraxjnl-2016-209333.124

Background Foundry work may involve exposure to respiratory sensitisers and irritants. There is limited evidence for the use of FENO in occupational settings, and particularly in foundries.

Aim To examine the usefulness of FE NO in identifying foundry workers at risk of asthma.

Methods Foundry workers undertook a respiratory questionnaire. Spirometry (Ndd Easy on-PC Spirometer, Zurich) and FENO (NOBreath, Bedfont Scientific, Kent) were measured to ATS/ERS standards. The ATS upper limit of normal (ULN) of 50 parts per billion (ppb), or 45.9 ppb for current smokers, determined the high FENO category (FE NO >ULN). Workers with FENO >ULN were compared with those with at least one work-related respiratory symptom (WRRS) and those with obstructive lung function (FEV1/FVC <0.7) using Chi Square and Fisher’s Exact Tests.

Results 351 workers (350 men, 99%) participated. 350 workers had a valid FE NO performed. Arithmetic mean FE NO was 30.2 ppb (95% CI: 27.3–33.2); geometric mean (GM) FE NO 20.8 (18.9–22.9) ppb.

FE NO exceeded the ULN in 61 (17%) workers. Average age for the FE NO >ULN group was 41.5 (95% CI: 38.3–44.7), with a mean of 15.8 (12.4 – 19.2) years working in the foundry industry.

Workers in the FE NO >ULN group were significantly more likely to have a current diagnosis of asthma (12% vs 5%, p < 0.05), have ever suffered allergies (55% vs 31%, p < 0.01), or report work-related shortness of breath (3% vs 0%, p < 0.05).

Fourteen workers (4%) had a FE NO >ULN and WRRS (Figure 1). Of these 14, only 2 (14%) had a current diagnosis of asthma (Fisher’s p = 0.20). Eight (2%) workers had a FE NO > ULN and FEV1/FVC <0.7, though only 2 (25%) had a current asthma diagnosis (Fisher’s p = 0.08).

Conclusion A significant proportion of foundry workers have FE NO levels that exceed the ATS cut point for likely cosinophilic airway inflammation. Of these workers, most had a raised FE NO but no WRRS or obstructive lung disease. Only a minority of workers with FE NO >ULN and either WRRS or obstruction had a current diagnosis of asthma. FE NO may be useful in identifying foundry workers at risk of asthma and warrants further study.

Abstract S118 Figure 1 Overlap between FE NO >ULN, work-related respiratory symptoms and obstructive spirometry in foundry workers. Total numbers in each group (%of total): FE NO >ULN: n=61 (17%); >1 WRRS: n=69 (20%); FEV1/FVC <0.7 = n = 34 (10%). FE NO>ULN = FE NO above 50 ppb or 45.9 ppb in current smokers; WRRS = at least one work-related respiratory symptom.
**S119** INDUCIBLE LARYNGEAL OBSTRUCTION MASQUERADING AS WORK-RELATED ASTHMA: A NEW APPROACH


10.1136/thoraxjnl-2016-209333.125

**Introduction** The specific inhalation challenge (SIC) is the reference standard test for diagnosis of occupational asthma in people with immunological sensitisation to a specific agent. In our occupational lung disease clinic, we recognise a separate group of patients who report symptoms consistent with inducible laryngeal obstruction (ILO) triggered by one or more agents which are generally not recognised sensitisers. Symptoms, which include throat and chest tightening, voice change, dysphonia and wheeze, are frequently misdiagnosed as work-related asthma, “allergy” and even anaphylaxis. In such cases securing the correct diagnosis can avoid unnecessary medication use, excessive health care utilisation and occasionally loss of employment. We have designed a SIC to provide objective confirmation of the diagnosis of ILO in the occupational setting.

**Method** Patients are carefully selected to undergo ILO-SIC. After histamine challenge testing, spirometry and direct laryngoscopy, they are exposed, in a specialist exposure chamber, to the agent(s) which provoke their symptoms. Each challenge is bespoke according to the patient’s triggers, work environment and comorbidities. Exposure is usually continued until the symptoms experienced in the workplace are reproduced, or to a level expected to cause airway irritation in a control individual. Direct laryngoscopy and measurement of spirometry is repeated and any anatomical and physiological changes noted.

**Results** We have carried out 30 such challenges (90% women; mean age 45 years (SD 9.4)) to date. Agents have included fumes, household paint and hospital cleaning products. In 87% of cases, we replicated symptoms experienced in the workplace. In 53% of cases, clear changes of ILO were seen. In those with normal laryngoscopy, the SIC is equally useful in reassuring patients that symptoms experienced are not dangerous, nor consistent with anaphylaxis or similar. Following careful explanation of the diagnosis, patients are managed conservatively or referred to specialist physiotherapists or voice therapists if indicated. Asthma treatment can often be withdrawn over time.

**Conclusion** A precise diagnosis in cases of occupational asthma is key to successful outcome; in this setting, we increasingly see patients with occupational (or other environmental) ILO. ILO-SIC testing in specialist centres can provide objective evidence to assist diagnosis avoiding unnecessary investigation and treatment of other conditions.

---

**S120** ASTHMA IN FIRE FIGHTER APPLICANTS: BURDEN OF DISEASE AND FACTORS PREDICTING SUCCESSFUL APPLICATION

1) Szram, 2) Schofield, 3) Fitzgerald, 4) Cullinan. 1) Royal Brompton and Harefield NHS Foundation Trust, London, UK; 2) NHLI Imperial College, London, UK

10.1136/thoraxjnl-2016-209333.126

Asthma is of concern to UK fire services that need to maintain maximal operational capability; current guidance suggests specialist respiratory review of applicants with a history of asthma, including tests of non-specific airway responsiveness. We present data from our occupational lung disease clinic over a 17 year period.

Between March 1999 and January 2016, 112 firefighters were assessed; 90 of these completed histamine provocation testing allowing measurement of non-specific bronchial hyper-responsiveness using PC20 to histamine. Retrospective case note review was undertaken to look for predictors of PC20 from clinical history in this cohort. Subsequent follow up included recorded outcome of application and reported symptoms on future employment in the fire service.

Unsurprisingly the majority of applicants were male (87.8%, n = 79) and atopic (78.6% n = 66). Around one third had experienced symptoms 27 (31.8) or taken treatment 32 (38.0) in the last year. Most patients were taking no asthma therapy at the time of assessment (64.4%, n = 58) with the majority of those on therapy taking a reliever only (n = 20, 22.2%). Three quarters (75.6%) had normal bronchial reactivity at the time of assessment (PC20 > 16 mg/ml histamine; n = 68) and 85.6% borderline normal airway responsiveness (PC20 > 8 mg/ml histamine; n = 77).

Complete data on follow up was available for 86% of those assessed (n = 90); 64 of these had a recorded PC20. Table 1 shows the predictive factors for successful application in this cohort. Applicants were more likely to be rejected if they were older at time of application; reported recent asthma symptoms or use of treatment in the last year, had a history of childhood asthma or a measured PC20 of less than 16 mg/ml.

The findings of this study suggest that a history of asthma in this occupational group remains a concern to occupational health teams focusing on operational capability of workforces with safety critical roles. Further follow-up of this cohort or a wider prospective study could provide applicants with asthma and their recruiters with useful guidance on individual suitability for employment as a fire fighter.

**Abstract S120 Table 1** Characteristics of 64 fire service applicants with asthma who had a known recruitment outcome (excluding those who withdrew application)

<table>
<thead>
<tr>
<th></th>
<th>Accepted n = 57</th>
<th>Not accepted (health grounds) n = 7</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>51 (89.5)</td>
<td>5 (71.4)</td>
<td>0.209</td>
</tr>
<tr>
<td>PC 20 ≥ 8</td>
<td>53 (93.0)</td>
<td>3 (42.9)</td>
<td>0.003</td>
</tr>
<tr>
<td>PC 20 ≥ 16</td>
<td>47 (82.5)</td>
<td>3 (42.9)</td>
<td>0.036</td>
</tr>
<tr>
<td>Recent symptoms</td>
<td>18 (34.6)</td>
<td>6 (85.7)</td>
<td>0.015</td>
</tr>
<tr>
<td>Recent treatment</td>
<td>20 (38.5)</td>
<td>6 (100.0)</td>
<td>0.006</td>
</tr>
<tr>
<td>Atopic</td>
<td>42 (79.3)</td>
<td>4 (57.1)</td>
<td>0.337</td>
</tr>
<tr>
<td>Adult asthma</td>
<td>25 (46.3)</td>
<td>5 (71.4)</td>
<td>0.255</td>
</tr>
<tr>
<td>Childhood asthma</td>
<td>42 (77.8)</td>
<td>4 (32.9)</td>
<td>0.070</td>
</tr>
<tr>
<td>Age at application</td>
<td>24 (18–46)</td>
<td>31 (24–40)</td>
<td>0.032</td>
</tr>
</tbody>
</table>

---

**S121** THE OCCUPATIONS AT INCREASED COPD RISK IN THE LARGE POPULATION-BASED UK BIOBANK COHORT

1) De Matteis, 2) Jarvis, 3) A Darnton, 4) Rushton, 5) Cullinan. 1) Imperial College London, London, UK; 2) Health and Safety Executive, Merseyside, UK

10.1136/thoraxjnl-2016-209333.127
**Background** Occupational exposures are important and preventable causes of COPD. In a cross-sectional study of current occupation among over 220,000 workers in the UK Biobank cohort (over 500,000 subjects) we previously reported that 14 jobs were associated with increased COPD risk (De Marteis S, et al., OEM, 2016). To progress these findings we developed OSCAR, a new web-based tool for efficient self-reporting and automatic coding of job-histories in large population-based studies. Our aim was to identify the occupations at increased COPD risk taking into account lifetime job-histories in the UK general population.

**Methods** We administered OSCAR to all UK Biobank participants with an available email address (n = 324,653) between June-February 2016. Paid jobs held for at least six months were collected and coded by OSCAR using the UK Standard Occupational Classification (SOC), v.2000. COPD was defined as FEV1/FVC<LLN based on spirometry performed at recruitment. Prevalence ratios (PRs) for ever-exposure to each of the 353 SOC-coded jobs using lifetime office workers as reference category were estimated using Poisson regression with adjustment for age, sex, recruitment centre and lifetime tobacco smoking. In addition, we used lifetime cumulative job durations to test for exposure-response trends.

**Results** Among the 116,375 participants who completed OSCAR (response rate: 34%), 94,551 had acceptable and repeatable spirometry data (according to ERS/ATS criteria) and smoking information and were included in the analyses. Taking into account individual lifetime job-histories, 19 jobs significantly increased COPD risk (e.g. ‘fishing and agriculture related occupations’: PR: 1.69; 95% confidence interval (CI): 1.18–2.42, and ‘food, drink and tobacco process operatives’: PR: 1.42; 95% CI: 1.02–1.97). The majority were also confirmed by positive exposure-response trends for cumulative years of employment in each job/lifetime.

**Conclusions** Compared to our previous cross-sectional study, some jobs were confirmed (e.g. ‘food, drink and tobacco process operatives’, and ‘horticultural trades’) while others were not (e.g. ‘coal miners’), likely due to the few employed in these jobs among the OSCAR responders. OSCAR is still collecting job-histories in the UK Biobank cohort; further analyses on a larger sample, as well analyses restricted to never-smokers and never-asthmatics to investigate the possibility of residual confounding, are planned.

---

**Virtual Smoking: The Risks of the Evil Weeds**

**S122**

**EFFECTS OF VAPED E-CIGARETTE LIQUID CONDENSATE UPON HUMAN ALVEOLAR MACROPHAGE FUNCTION. TO VAPE OR NOT TO VAPE THAT IS THE QUESTION?**

A Scott, ST Lugg, V D’Souza, K Lewis, D Dosanjh, B Naidu, DR Thickett. University of Birmingham, Birmingham, UK

10.1136/thoraxjnl-2016-209333.128

**Introduction and objectives** Electronic cigarette usage or “vaping” has risen exponentially in recent years in smokers and ex-smokers. Published data suggests that vaping e-cigarette liquid (ECL) may not be as benign as propounded by e-cigarette companies which are increasingly owned by “big tobacco”. Much of the current literature has focused on the effect of non-vaporised ECL – such studies do not fully reflect the exposure of the user, as the process of vaping causes chemical changes in ECL. To investigate the effect of unvaped ECL and vaped e-cig condensate (ECVC) using our novel system, with and without nicotine, on alveolar macrophage (AM) viability and immune responses.

**Methods** We developed a novel method to produce ECVC to allow direct comparison with unvaped ECL. Nicotine concentration as assessed by GFID was 31 mg/ml in ECL and 26 mg/ml in ECVC. AMs were obtained from lung resection tissue and treated with ECVC/ECL ± nicotine. Cell viability was assessed by cell titre aqueous assay, apoptosis, necrosis and markers of macrophage phenotype (CD68, CD80, CD163, CD206) were assessed by flow cytometry. IL-8 release by AMs was assessed by ELISA.

**Results** AM culture with ECL or ECVC resulted in dose dependent reduction in cell viability, ECVC was cytotoxic at lower concentrations than ECL (0.8% ECVC vs 5 %ECL, n = 6). 24 hour culture with 1% ECVC resulted in a 5 fold increase in AM apoptosis and 2 fold increase in necrosis compared with 1%ECL (p = 0.079, n = 5). Nicotine containing ECVC caused more apoptosis vs nicotine free ECVC (27.2% vs 13.4%, (p = 0.0079, n = 4)). Culture with 0.6%ECVC significantly increased supernatant levels of IL-8 compared with 1% ECL (p = 0.015, n = 4). ECVC was also found to affect macrophage phenotype, showing both nicotine dependent/independent regulations of markers of macrophage m1/m2 polarisation (CD80 p = 0.0357, CD163 p = 0.0179, CD206 p = 0.0357, n = 6).

**Conclusions** Our novel system creates ECVC which is sterile, minimises loss of nicotine and prevents dilution of the vapour. Vaped E-cigarette condensate is significantly more toxic to AMs than non-vaped e cigarette liquid. Furthermore, ECVC with nicotine is significantly more toxic than ECVC without Nicotine. Effects shown on inflammatory cytokine production and markers of macrophage polarisation indicate both nicotine dependent and independent effects of ECVC on alveolar macrophages.
phagocytosis was quantified using fluorimetry. Release of TNFα, CXCL8 and IL-6 was measured by ELISA. Expression of macrophage receptor with collagenous structure (MARCO) and toll-like receptors (TLRs) 2 and 4 was measured by flow cytometry.

**Results** Neither CSE nor any of the e-CVEs had any significant effect on cell viability. In addition, none of the exposures produced any significant effect on phagocytosis, though higher concentrations of CSE displayed a trend towards reduced phagocytosis.

CSE significantly reduced TNFα release (by approximately 70%; p < 0.05). Tobacco- and banoffee pie-flavoured e-CVEs also caused significant reductions in TNFα release (by 30–50%; p < 0.05), while nicotine and the e-liquid vehicle had no effect. Minimal effects were observed on CXCL8 and IL-6 release (0–30% reduction; p > 0.05) with CSE and e-CVEs. Expression of MARCO and TLR4 were unaffected by all cell treatments. TLR2 expression appeared to be slightly increased by e-CVEs, but was not statistically significant.

**Conclusion** Effects of e-CVEs on MDMs differed from those of CSE. E-liquid flavourings appeared to be responsible for changes in MDM function, while the e-liquid vehicle and nicotine solution had minimal effects. More research is needed to improve understanding of the biological effects of e-cigarette flavourings.

---

**S124 THE EFFECTIVENESS OF “IN-CLINIC” SMOKING CESSATION SUPPORT IN THE SETTING OF SECONDARY CARE RESPIRATORY OUTPATIENT SERVICES**

1Valero-Sanchez, 1Agrawal, 5Brij, 8RA Evans, 1NJ Greening, 1N Toms, 4E Wiggins, 5J Williams, 1MC Steiner, 1University Hospitals of Leicester, Leicester, UK; 2Peterborough City Hospital, Peterborough, UK; 3Leicester City Council, Leicester, UK; 4Peterborough City Council, Peterborough, UK; 5Cambridge and Peterborough Foundation Trust, Peterborough, UK.

**Introduction and aims** Although two thirds of smokers wish to quit, referral, uptake and engagement with smoking cessation (SC) services are frequently poor. In Leicester, uptake of smoking cessation referred from secondary care is approximately 20% with successful quit rate at four weeks of 10%. Provision of immediate support through smoking cessation specialist advice provided at the point of clinical assessment in outpatients might enhance referral uptake and quit rates. We assessed the value of this “in-clinic” approach in specialist respiratory outpatient clinics in two secondary care centres.

**Methods** Provision of immediate smoking cessation advice was implemented in two outpatient clinic services providing specialist care for patients with complex, chronic obstructive pulmonary disease (COPD); an Acute General Hospital (Peterborough City Hospital, PCH) and a Tertiary Care Hospital (Glenfield Hospital, GH). All current smokers were referred to an on-site smoking cessation specialist advisor by the physician, or clinic nurse, as part of their outpatient review on the same day of their clinic visit.

In the Glenfield service SC was provided by a smoking cessation specialist, using a harm reduction approach with a guided patient-led tailored programme and the possibility of direct supply treatment at the initial assessment.

In the PCH service, SC using psychosocial and/or pharmacological therapy was undertaken by a dedicated smoking cessation officer.

Follow-up visits and telephone calls were arranged separately by the smoking service and data including demographics, treatment uptake and quit rates after 4 weeks were analysed.

**Results** A population of 122 smokers with a diagnosis of COPD were assessed for in-clinic SC over a period of twelve months in both centres.

Demographic details of both cohorts, outcomes of both SC strategies including treatment uptake and quit rates are disclosed in Table 1.

**Conclusions** Providing “in-clinic”, expert smoking cessation advice results in favourable referral uptake and four week quit rates when compared with locally available data from paper based referral routes. Reinforcing physician delivered smoking cessation advice through immediate provision of proactive cessation support may be an effective means to enhance quit rates in secondary care.

**Abstract S124 Table 1 Smoking cessation outcomes**

<table>
<thead>
<tr>
<th>In-Clinic SC Approach at Peterborough hospital</th>
<th>In-Clinic SC Approach at Glenfield hospital</th>
</tr>
</thead>
<tbody>
<tr>
<td>N patients referred</td>
<td>65</td>
</tr>
<tr>
<td>Age (years) (mean, SD)</td>
<td>61.3 [9]</td>
</tr>
<tr>
<td>Gender</td>
<td>53% Male</td>
</tr>
<tr>
<td>Approach to SC</td>
<td>Conventional</td>
</tr>
<tr>
<td>Treatment Uptake (% of N)</td>
<td>32 (49%)</td>
</tr>
<tr>
<td>SC managed after 4 weeks (% of N)</td>
<td>29 (44%)</td>
</tr>
</tbody>
</table>

10.1136/thoraxjnl-2016-209333.130

---

**S125 SMOKING CESSATION KNOWLEDGE, BELIEFS AND CURRENT PRACTICES AMONG UK CHILD HEALTH PROFESSIONALS**

1MJP Robertson, 1AG Gupta, 1A Summugam, 1Department of Paediatric Respiratory Medicine, King’s College Hospital, London, UK; 2Department of Paediatrics, Basildon and Thurrock University Hospitals, Basildon, UK.

**Introduction and objectives** Two million children in the UK are regularly exposed to second-hand smoke (SHS) in the home and many more are exposed in other settings. The consequences of this are well recognised and include higher incidences of: numerous acute illnesses; hospital admissions; school absences and increased smoking rates in later life. Together these result in significant costs to the NHS and wider economy.

Barriers to improved practice have been reported in other professional groups in the UK and in Child Health Doctors and Nurses in other countries. We could find no previously published data from the UK on this topic with which to inform and improve our own staff training and support.

**Methods** An electronic questionnaire was developed, covering beliefs, knowledge and current practice. The survey was distributed through professional groups, training and healthcare delivery organisations.

**Results** 140 responses were received, from Consultants (22%), trainee Paediatricians (32%), Nurses (34%) and others (11%), including Physiotherapists, Pharmacists, Healthcare Assistants and Play Therapists. Respondents came from 19/21 UK regions.
Spoken sessions

Respondents believe it is important to support smoking cessation for the parents of their patients but are likely to perceive the barriers to this as arising from the smokers more than from deficiencies in their own knowledge and skills (see Table 1). However, we identified significant knowledge gaps. When asked if 7 facts about SHS and cessation were true or false, incorrect answers ranged from 2–41% and ‘don’t know’ from 10–46%. Only 41% knew how to make a referral to their local cessation service. 63% of respondents last had training about smoking cessation more than 5 years ago.

Abstract S125 Table 1 Respondents’ assessment of the impact of parental smoking and barriers to aiding with smoking cessation, where 0 = no impact or not a barrier and 10 = very significant impact or barrier

<table>
<thead>
<tr>
<th>Impact assessed</th>
<th>Mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>How much of an impact do you think parental smoking has on children’s current respiratory health?</td>
<td>8.54 (5–10)</td>
</tr>
<tr>
<td>How significant is the impact of parental smoking on a child’s overall health later in life?</td>
<td>8.20 (3–10)</td>
</tr>
<tr>
<td>How significant do you think is the impact of a parent stopping smoking on their child’s current respiratory health?</td>
<td>8.59 (2–10)</td>
</tr>
<tr>
<td>It is not worthwhile to try and change smoking behaviours as the chance of making an impact is so small</td>
<td>2.64 (0–9)</td>
</tr>
<tr>
<td>You lack knowledge or information to explain to parents how SHS exposure can affect their child’s health</td>
<td>3.10 (0–10)</td>
</tr>
<tr>
<td>You lack motivational interviewing (or similar) skills to help smokers see how they could change their behaviour</td>
<td>5.21 (0–10)</td>
</tr>
<tr>
<td>Smokers may become defensive or aggressive if given advice about the consequences of smoking or the benefits of stopping smoking</td>
<td>6.28 (0–10)</td>
</tr>
<tr>
<td>Smokers are not willing to accept that their behaviour has health consequences</td>
<td>6.16 (0–10)</td>
</tr>
<tr>
<td>Smokers are not motivated to stop smoking</td>
<td>6.28 (0–10)</td>
</tr>
<tr>
<td>Many smokers have other, more significant challenges, to deal with such as: mental health problems, social isolation, poverty, under-employment, insecure housing etc.</td>
<td>6.47 (0–10)</td>
</tr>
</tbody>
</table>

Conclusions Our findings show that Child Health Professionals’ beliefs about the impact of smoking and the importance of smoking cessation are not borne out in their practice. This is likely to be due to a lack of knowledge and training, despite the existence of high quality and easily accessible national resources. We believe that every Child Health organisation should appoint smoking cessation champions who can build links with local specialist services in order to promote training and good practice among their colleagues.

REFERENCE

1 National Centre for Smoking Cessation and Training (NCSCT). http://www.ncsct.co.uk

S126 HOW DOES KNOWLEDGE, PERCEPTIONS AND ATTITUDES TOWARDS SHISHA PIPE SMOKING VARY AMONGST UNIVERSITY STUDENTS?


10.1136/thoraxjnl-2016-209333.132

Background and introduction Despite clear evidence for the harms of shisha pipe smoking (SPS) its use is increasing amongst university students worldwide. This review explores the evidence for the reasons behind this trend by considering students’ perceptions, attitudes towards and knowledge of SPS.

Review question ‘How does knowledge, perceptions and attitudes towards SPS vary amongst university students?’

This question will examine the rationale for students’ shisha use and address their perceptions regarding its addictive properties.

Literature searches Three electronic databases were accessed: MEDLINE, EMBASE and CINAHL. Examples of search terms included “shisha” (and its alternatives), “university”, “perceptions”.

Inclusion criteria

2. English language
3. Human studies

57 articles were initially identified, with 21 articles included in the final review after abstract and full-text screening.

Throughout this process, three common themes emerged Reasons for and attitude towards SPS.

Perceptions regarding health hazards of SPS.

Perceptions regarding addictive properties and ability to quit SPS.

Each theme was explored in detail, in order to answer the review question.

Review findings

Socio-cultural and peer influences are major contributors in students initiating SPS.

SPS ‘addiction’ has two components: physiological and social. This is compounded by the general perception that SPS is a safer, i.e., less harmful and addictive, and sociable alternative to cigarette smoking.

Students believe quitting SPS is ‘easy’, yet few are able to do so successfully.

Conclusion Policy change is fundamental in tackling the SPS pandemic amongst university students. Interventions, within institutions directly or via social media campaigns, must de-glamorise shisha and highlight its harmful effects. Prior to this, additional longitudinal studies are necessitated to build on existing cross-sectional data and understand temporal changes in students’ beliefs to allow better, targeted health promotion.

S127 EFFECT OF CANNABIS SMOKING ON THE DEVELOPMENT OF BULLOUS LUNG DISEASE: A STRUCTURED LITERATURE REVIEW

L Ribeiro, P Ind. Imperial College London, London, UK

10.1136/thoraxjnl-2016-209333.133

Background With increasing cannabis use, physicians need to know more about its respiratory effects. However, there are few long term studies of cannabis smoking, mostly due to legality issues and the confounding effects of tobacco.

Aims We reviewed the effect of chronic cannabis use on bullous lung disease.

Methods 18 out of 69 English-language publications, prior to April 2016, from MEDLINE, Scopus, and Web of Science
databases, which reported bullous lung disease in cannabis users, were examined. Case reports and case series were included.

**Results** The only cross-sectional study reported an increase in the rates of macroscopic emphysema in tobacco only (17 of 92) and tobacco + cannabis smokers (15 of 91), but not in cannabis only smokers (1 of 75) compared to non-smokers.1

The remaining case series and case reports described a total of 56 marijuana smokers presenting with bullous lung disease, often with pneumothorax and predominantly upper lobe involvement (Table 1). Concurrent tobacco smoking was present in all but 3 cases. The majority of cases reported heavy cannabis use, though direct comparison was difficult due to variation in usage measurements. All 4 case series that measured lung function reported normal findings.

**Conclusions** While the clinical association of cannabis smoking and peripheral lung bullae is well recognised (and consequently often not reported) there is scant documentation in the literature correlating marijuana smoking with bullous lung disease.

**REFERENCE**

Novel Approaches to Lung Cancer Screening

**LUNGSEARCH: A RANDOMISED CONTROLLED TRIAL OF SURVEILLANCE FOR THE EARLY DETECTION OF LUNG CANCER IN A HIGH RISK GROUP**

S128


1UCL, London, UK; 2Royal Brompton Hospital, London, UK; 3Papworth Hospital, Cambridge, UK; 4UCH, London, UK; 5St James’s University Hospital, Leeds, UK; 6St James’s University Hospital, Leeds, UK; 7University Hospital South Manchester, Manchester, UK; 8Queens University Belfast, Belfast, UK; 9Glenfield Hospital, Leicester, UK; 10University Hospital Coventry, Coventry, UK; 11Sunderland Royal Hospital, Sunderland, UK.

10.1136/thoraxjnl-2016-209333.134

Screening for the early detection of lung cancers should increase the percentage of operable tumours, thus improving cure rates. A large randomised US trial showed that CT screening moderate/heavy smokers is effective but expensive, with a high false-positive rate. We designed LungSEARCH in 2006 to target screening in higher-risk subjects. Because most tumours in the UK were of squamous-histology, we hypothesised that sputum cytology plus autofluorescence bronchoscopy (AFB) would be an effective initial screen, only offering more intensive/expensive tests to those with abnormal sputum.

Eligibility criteria were: current/former smokers (≥20 pack-years and/or smoked ≥20 years), GOLD-defined COPD, no prior cancer. Subjects were randomised to surveillance or a control group, and each followed for 5 years. Screened subjects provided sputum for central assessment, and those with abnormal results (cytology: low/high-grade squamous intraepithelial lesions, and/or cytometry: abnormal ploidy) were referred for annual low-dose CT and autofluorescence bronchoscopy (AFB) for the remainder of the trial, with diagnostic investigations when cancer suspected by abnormal CT/AFB.

Sputum-negatives provided annual sputum samples only. Control subjects had a chest X-ray when they reached 5 years. Primary objective: to show a higher proportion of early stage cancers using surveillance than controls.

1568 subjects were recruited (target 1300) from GPs or chest clinics across 10 UK centres (August 2007–March 2011): 785 screened, 783 controls. Mean age 63 years; males 52%; current (56%), former (44%) smokers; mild (25%), moderate (75%) COPD; from GPs (79%). >90% screened subjects provided sputum samples in their first year. After 5 years, the overall sputum-negative rate is 33%; 30% (236/785) had a CT scan and 25% (193/785) had an AFB at any time. Of those who had a CT scan 3% (5/193) had severe dysplasia or worse.

79 lung cancers have been identified to date via the centres/national registry: 43 surveillance and 36 control. But awaiting staging details for 6 surveillance and 14 control cases. Preliminary results are promising: 57% (surveillance) versus 41% (controls) of cancers were diagnosed with stage I/II non-small-cell-lung cancer or limited disease small-cell-lung cancer. Final data available later in 2016.
Introduction and objectives Chronic obstructive pulmonary disease (COPD) and emphysema are considerably under-diagnosed conditions. Low dose CT (LDCT) for lung cancer screening, if implemented, may provide an opportunity for earlier diagnosis of smoking-related conditions, in addition to lung cancer. Data gathered in a lung cancer screening demonstration pilot was analysed to look at COPD-related radiological changes and their relationship with patients’ pre-existing diagnoses, spirometry results and smoking status. The aims were to better understand these interlinked conditions and identify the potential for earlier diagnosis and management of smoking cessation interventions for these conditions.

Methods Data were collected as part of the Lung Screen Uptake Trial. Smokers and recent former smokers (quit <5 years) aged 60–75 were invited to a ‘lung health check’ via their general practitioner (GP). Data on pre-existing diagnoses, smoking status and pre-bronchodilation spirometry, categorised according to the National Institute for Clinical Excellence (NICE) criteria, were collected. Patients who met the eligibility criteria for screening went on to have LDCT. Results were analysed for frequencies, and confidence intervals calculated for the most significant results.

Results 275 patients responded to an invitation to attend a ‘lung health check’ in the first six months of recruitment. 149 (54.2%) had values consistent with COPD on spirometry. 106 (71.1% (95% CI: ± 7.3%)] of these individuals were not aware of a diagnosis of COPD, and 81 (76.4%) were current smokers (Figure 1). Of the 103 individuals who had emphysema and no suspicious lesion on LDCT, 74 (71.8%, (95% CI: ± 8.7%)] were not aware of a diagnosis of COPD or emphysema. 55 (74.3%) of these were current smokers, and 33 (44.6%) had preserved spirometry (Table 1).

Conclusion Our data demonstrate the considerable burden of undiagnosed COPD in at-risk groups (38.5% of all screened individuals), and show the prevalence of emphysematous change in those patients without a pre-existing, self-reported diagnosis of COPD or with preserved spirometry. Early diagnosis and CT evidence of smoking damage may provide the opportunity to implement supportive smoking cessation interventions, earlier...
medical intervention and prevention of further progression of disease through improved management of these conditions.

WHAT PROPORTION OF THE UK POPULATION WOULD BE ELIGIBLE FOR CT SCREENING FOR LUNG CANCER ACCORDING TO VARIOUS PROPOSED INCLUSION CRITERIA?

K Gracie, M Kennedy, J Robson, M Callister. Leeds Teaching Hospitals NHS Trust, Leeds, UK

Introduction Low dose CT screening reduced lung cancer mortality by 20% in the National Lung Screening Trial (NLST) using eligibility criteria of age 55–74 yrs, ≥30 pack year smoking history, and quit time < 15 years. The US Preventative Services Task Force (USPSTF) has proposed using the NLST criteria extending the upper age limit to 80 years. Alternative proposed eligibility criteria use thresholds from composite risk prediction scores such as a 1.51% lung cancer risk over 6 years using the PLCO M2012 model (derived from the Prostate Lung Colorectal and Ovarian Study) and a 5% lung cancer risk over 5 years using the Liverpool Lung Project (LLP) model (used in the UK Lung Screening trial). We sought to compare the proportions of patients in the UK who would be eligible for screening according to these criteria.

Methods We commissioned an anonymous telephone survey in Yorkshire (Hull, Leeds and Wakefield) to collect parameters to calculate lung cancer risk (PLCO M2012 and LLPv.2) and likelihood of participation in a future programme. Index of multiple deprivation (IMD) was recorded based on postcode and used to ensure a representative cohort. No patient identifiable information was entered into the research database.

Results 2,424 persons 55–80 years agreed to participate in the telephone survey, of which 1,335 were ever-smokers. The proportion of patients (95% CI) eligible according to various criteria were as follows; NLST 11.9% (10.6%–13.2%), USPSTF 13.3% (12.0%–14.7%), PLCO M2012 ≥1.51% 20.7% (19.1%–22.3%) and LLP ≥5% 15.8% (14.4%–17.3%). The proportions eligible by USPSTF, PLCO and LLP criteria by IMD and age cohort are shown in Figure 1. When asked how likely they would be to attend an NHS lung cancer screening programme, 62.6% indicated ‘very likely’. This proportion was similar between those eligible for screening by any criteria and those not (62.5% and 62.7% respectively) and current and ex-smokers (61.4% and 63.0% respectively).

Discussion The proportions of the population eligible for screening differ considerably between various eligibility criteria, and according to deprivation and age. The criteria selected to determine screen-eligibility in a future national screening programme will have a significant impact on the cost and cost-effectiveness of such a programme.

A RANDOMISED CONTROLLED STUDY OF LUNG CANCER SCREENING IN SCOTLAND USING THE DETECTION OF AUTOANTIBODIES TO TUMOUR ANTIGENS (EARLYCDT-LUNG TEST)

A Dorward, F Frances, F Sullivan, K Vedhara, D Kendrick, T Trewick, C McCowan, A McConnachie, M Sproule, A Briggs, L Ritchie, R Milroy, T Taylor, R Littleford, D Brewer, S Schmelt. NHS Greater Glasgow and Clyde, Glasgow, UK; University of Toronto, Toronto, Canada; University of Nottingham, Nottingham, UK; University of Aberdeen, Aberdeen, UK; University of Glasgow, Glasgow, UK; Scottish Cancer Registry, Edinburgh, UK

Abstract S131 Figure 1 The proportion of 55–80 year old population eligible for screening by various criteria by IMD quintile and age
Background EarlyCDT®-Lung Test detects autoantibodies to abnormal cell surface proteins from the early stages of lung cancer with a specificity of 93%. This may allow earlier tumour detection thus altering prognosis.

The primary research question is: Does using the EarlyCDT®-Lung Test to identify those at high risk of lung cancer, followed by xray and CT scanning in the test positive group, reduce the incidence of patients with late-stage lung cancer (III and IV) or unclassified presentation (U) at diagnosis, compared to standard practice? Recruitment was completed in June 2016 with 12,018 subjects randomised.

Methods A RCT in Scotland recruiting from the most socially disadvantaged quintiles. Adults aged 50 to 75 (ECOG 0–2) who were at high risk for lung cancer (>20 pack years or relevant family history) were eligible. The intervention was the EarlyCDT®-Lung Test, followed by chest xray and CT in those with a positive result. The comparator is standard clinical practice in the UK. The primary outcome is the difference, after 24 months, between the rates of patients with stage III, IV or unclassified lung cancer at diagnosis in test v no-test group. Secondary outcomes include: all-cause mortality; cancer specific mortality; a range of morbidity outcomes; cost-effectiveness and measures examining the psychological and behavioural consequences of screening.

Participants with a positive test result had an initial chest xray which was used to determine the urgency and the need for contrast in the initial screening CT. Those in whom the initial CT scan did not lead to a lung cancer diagnosis were offered biannual chest CTs for 24 months. Participants who are found to have lung cancer will be followed-up to assess both time to diagnosis and stage of disease at diagnosis.

Results 575/6120 (9.8%) of the test group had a positive test with 207 found to have lung nodules >8 mm, 16 cancers have been detected so far, 12 of which are at early stage. Eleven have abnormalities undergoing current investigation. At this stage of the trial we have no outcome data for the comparison group.

Conclusion The study will determine EarlyCDT-Lung test’s clinical and cost effectiveness.

Respiratory Science

INVESTIGATING GENOME WIDE DNA METHYLATION IN AIRWAY AND PARENCHYMAFIBROBLASTS FROM HEALTHY INDIVIDUALS AND INDIVIDUALS WITH COPD

RationalE Lung fibroblasts are implicated in respiratory disease pathology including chronic obstructive pulmonary disease (COPD). Phenotypic differences between fibroblasts isolated from the airway versus the parenchyma have been described but no studies have compared the cell types on a genome wide scale. DNA methylation is a reversible modification of the DNA structure with the ability to affect cell function via the alteration of gene expression. Here we compared genome wide DNA methylation profiles from airway and parenchymal fibroblasts and assessed modification to these profiles in cells isolated from individuals with COPD.

Methods DNA was isolated from parenchymal and airway fibroblasts at passage 4, and bisulphite treated. Site specific, quantitative genome wide methylation was determined using the Illumina 450K Infinium Methylation BeadChip array. Linear modelling and DMRcate functions identified differentially methylated sites and regions respectively between airway and parenchymal fibroblasts isolated from individuals with normal lung function versus those with COPD.

Results 3980 CpG (methylation) sites significantly differed after Bonferroni correction between airway and parenchymal fibroblasts isolated from healthy individuals. These sites had a broad distribution of effect size, with 240 CpG sites displaying a difference in methylation of >50%. 78 of these sites validated in a second cohort of 7 sets of paired airway and parenchymal fibroblasts isolated from the same individual. There was genomic proximity to these sites and DMRcate was used to refine the individual CpG sites to 5 regions of interest associated with 5 genes; HLX, TWIST1, CREB5, SKAP2 and PRDM16. Differences in methylation were less pronounced when comparing cells isolated from healthy individuals to those with COPD. In airway fibroblasts 47 DMRcate regions were identified with a maximum difference in methylation of at least 20%. In parenchymal fibroblasts 3 DMRcate regions were identified with a maximum difference in methylation of at least 20%.

Conclusions DNA methylation profiles are significantly different between airway and parenchymal fibroblasts but only small modifications are associated with COPD. Future work will focus on validating a methylation based markers of parenchymal versus airway fibroblasts and associating our differential observations with gene/protein expression.

HOW SPECIFIC ARE FLUOROGENIC SUBSTRATES DESIGNED TO ANALYSE ACTIVE PROTEASE BIOMARKERS OF RESPIRATORY DISEASE?

Introduction Active proteases, such as neutrophil elastase (NE) and matrix metalloproteinases (MMPs), have been established as inflammatory biomarkers in lung diseases such as cystic fibrosis (CF), chronic obstructive pulmonary disease (COPD) and pulmonary fibrosis. Therefore, biological samples collected during clinical investigations are often analysed using fluorogenic substrates to determine protease activity and identify correlations with clinical and/or demographic parameters. Due to the nature of these diseases, samples often contain numerous active proteases from both human and bacterial origins which collectively have significant substrate crossover. This study investigates the ability of fluorogenic substrates to distinguish between proteases in complex clinical samples and provide an indication of the predictive capability of this assay type.

Methods Expectorated sputum was randomly collected from patients with CF who were hospitalised for an acute exacerbation. Samples were processed within 30 minutes of collection, and the aqueous sol recovered, pooled, aliquoted and stored at −80°C until analysis. The capacity of sputum proteases to hydrolyse fluorogenic substrates with and without the presence of inhibitors specific for serine (multiple subclasses), metallo
Circulating metabolites in chronic thromboembolic pulmonary vascular occlusion

Introduction
Recent studies have demonstrated that metabolomic profiling can identify metabolites and pathways which may have importance in the pathobiology of pulmonary arterial hypertension. However, the plasma metabolome in chronic thromboembolic pulmonary hypertension (CTEPH) and chronic thromboembolic vascular occlusions without pulmonary hypertension (CTED) has not been well characterised.

Objective
To profile circulating metabolites in CTEPH and CTED and assess metabolite gradients across the pulmonary circulation.

Methods
In the patient group, multisite blood sampling was performed at the time of right heart catheterisation. Blood samples were collected from the superior vena cava, pulmonary artery and radial artery. Venous blood samples from patients were compared to healthy controls to identify the metabolites present and to assess the difference between health and disease. Additionally, in the disease group, transpulmonary gradients were assessed by analysis of fold change in metabolite concentration between paired samples from the pulmonary artery and radial artery.

Untargeted, semi-quantitative metabolic profiling of plasma was performed using the Metabolon DiscoveryHD™ platform (Metabolon, NC, USA), utilising 2 ultra-high performance liquid chromatography methods, coupled with tandem mass spectrometry. Kruskal-Wallis analysis was used to compare metabolites between disease and control, with false discovery rate correction for multiple testing.

Results
The disease group included patients with a spectrum of chronic pulmonary vascular occlusions (Table 1). A total of 1375 metabolites were detected in 70 venous plasma samples analysed from 43 patients and 27 healthy controls. Amongst endogenous metabolites, 266 showed a significant difference between disease and control. In the disease group there were increases in acylcarnitine metabolites, long chain fatty acids, polyamines, glycosgen metabolites and primary bile acid metabolites compared to healthy controls. There was a reduction in lysolipids, plasmalogens, aminosugars, branched chain amino acid metabolites, glutathione metabolites and a number of steroids (Table 1). Analysis of transpulmonary gradients revealed primarily a reduction in metabolite concentration across the pulmonary circulation. This included depletion of energy substrates, lysolipids, lysoplasmalogens and acylcholines.

Conclusions
This pilot study of circulating metabolites in patients with CTEPH, CTED and healthy controls reveals differences between health and disease in several biological pathways. Measurement of the transpulmonary gradient of metabolites indicated predominant clearance of circulating metabolites associated with energy metabolism and cell turnover. These findings require confirmation in a larger population.

Abstract S135 Table 1 Study population and changes in metabolite groups in venous blood of patients compared to healthy controls

<table>
<thead>
<tr>
<th>Chronic pulmonary vascular occlusions (n = 43)</th>
<th>Controls (n = 27)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group demographics</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>58 (22–77)</td>
<td>44 (18–75)</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td></td>
</tr>
<tr>
<td>64</td>
<td>60</td>
</tr>
<tr>
<td>Patient group</td>
<td></td>
</tr>
<tr>
<td>Proximal CTEPH- treatment naive (n)</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Distal CTEPH (n)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Proximal CTEPH- previous pulmonary</td>
<td></td>
</tr>
<tr>
<td>endarterectomy- residual PH (n)</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Proximal CTEPH- previous pulmonary</td>
<td></td>
</tr>
<tr>
<td>endarterectomy, no residual PH (n)</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Chronic thromboembolic vascular occlusions</td>
<td></td>
</tr>
<tr>
<td>without PH (n)</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Changes in metabolites in disease</td>
<td></td>
</tr>
<tr>
<td>Acylcarnitines</td>
<td></td>
</tr>
<tr>
<td>Long chain fatty acids</td>
<td></td>
</tr>
<tr>
<td>Polyamines</td>
<td></td>
</tr>
<tr>
<td>Glycogen metabolites</td>
<td></td>
</tr>
<tr>
<td>Primary bile acid metabolites</td>
<td></td>
</tr>
<tr>
<td>Lysolipids</td>
<td></td>
</tr>
<tr>
<td>Plasmalogens</td>
<td></td>
</tr>
<tr>
<td>Aminosugars</td>
<td></td>
</tr>
<tr>
<td>Branched chain amino acids</td>
<td></td>
</tr>
<tr>
<td>Glutathione metabolites</td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td></td>
</tr>
</tbody>
</table>

Potential therapeutic benefits of the human amniotic epithelium cell secretome during ex-vivo perfusion of donor lungs

Introduction
Ex-vivo lung perfusion (EVLP) is used to assess and potentially recondition donor lungs that are not initially suitable for transplantation. In a recent UK study, EVLP was associated...
Discussion EVLP reduces the intravascular leucocyte content of the donor lung, probably due to the presence of a leucocyte filter in the perfusion circuit. However, the endothelium remains primed to activation with IL-1 receptor expression increasing during EVLP. The secreted products of hAECs reduce endothelial activation and limit leucocyte-endothelial interactions. Further studies are required in a suitable in-vivo model to determine if hAECs, or their secretome, are a potential therapeutic option during EVLP to protect against primary graft dysfunction after reperfusion of the transplanted lung.

Abstract S136 Figure 1 Leukocyte adhesion to HUVECs stimulated with 5ng/ml IL-1β; untreated control, treated with human amnion epithelial cell (hAEC) term conditioned media (T-CM), and hAEC preterm conditioned media (PT-CM)
Abstract S137 Figure 1  BOS rates analysed using the competing risks survival model. The cumulative incidence function for all three subgroups are shown following multivariate adjustment. BOS rates are higher in de novo group compared to the persistent PsA group (pvalue 0.043).
Pleural Disease Assessment and Outcomes

P1 PLEURAL EFFUSION SIZE ESTIMATION: US, CXR OR CT?
C Brockelsby, M Ahmed, M Gautam. Royal Liverpool University Hospital, Liverpool, UK
10.1136/thoraxjnl-2016-209333.144

Introduction and objectives Chest X-ray (CXR), CT and Ultrasound (US) are commonly used to evaluate the size of pleural effusions. Accurate description of size is important in the communication of findings and urgency of intervention. With currently no standardised measurement system, significant variation in description of size by CXR, CT or US exists. The use of terms ‘small’, ‘moderate’, and ‘large’ is common, with no consensus on the limits of these sizes.

This study looked at correlation between descriptive definition of effusion size by different imaging modalities and volume of effusion recorded following aspiration.

Methods This was a retrospective analysis of patients referred for pleural tap and/or drain after CXR and/or CT. CXR/CT reports were collected from PACS, US reports from the local US database, accessed by at least two US-trained Respiratory physicians.

Effusion size was estimated by the recognised method of counting intercostal spaces (ICS) from costophrenic angle (small-localised to 1 ICS, medium 2–3 ICS, large ≥4 ICS). Effusion size reported was compared to actual volume of fluid drained (full ‘dry’ or ‘safe aspiration’). For the purpose of this study, effusions <500 mL were characterised as small, 500–1000 mL moderate and >1000 mL large. Correlation was analysed using Spearman’s correlation.

Results 312 patients were referred April 2014–December 2015. 133 patients were excluded due to insufficient data, 179 patients’ data analysed. US pleural effusion size estimation correlated most closely with actual volume of fluid drained (r = 0.833, N = 179, P < 0.0001) vs. CXR (r = 0.548, N = 129, P < 0.001) and CT (r = 0.489, N = 107, P < 0.001). The error rate in size estimation was 41% (53/129) for CXR, 57% (61/107) for CT and 16% (r = 0.489, N = 107, P < 0.001) vs. CXR (r = 0.548, N = 129, P < 0.001) and CT (r = 0.489, N = 107, P < 0.001). The error rate in size estimation was 41% (53/129) for CXR, 57% (61/107) for CT and 16% (28/179) for US. In particular, 29% (31/107) patients with ‘small’ tapped effusions were reported to be ‘medium/large’ effusions by CT scan. CT most commonly overestimated fluid present; whilst US tended to underestimate the few cases where it was inaccurate.

Conclusions This study demonstrates that US may be the most accurate modality when assessing the size of pleural effusions. CT imaging may over represent the volume of fluid present. Where imaging reports guide further management, reliability and consistency is essential to avoid unnecessary/urgent intervention and patient anxiety.

P2 INCORPORATION OF AN IN-DEPTH THORACIC ULTRASOUND ASSESSMENT INTO ROUTINE PREPROCEDURAL EVALUATION OF PATIENTS WITH PLEURAL EFFUSIONS
10.1136/thoraxjnl-2016-209333.145

Background Pleural disease affects 1 in 300 people annually; furthermore, the incidence of malignant pleural effusion (MPE) is increasing with over 40,000 cases each year in the UK alone. A significant minority of patients will have non-expandable lung (NEL) secondary to underlying disease. At present, there is no way of pre-emptively identifying these individuals; with current strategies such as pleural manometry requiring invasive intervention. Early recognition of patients with NEL would streamline care and allow them to be offered appropriate treatment; i.e., indwelling pleural catheter insertion rather than chemical pleurodesis. Recent research1 has described the novel use of thoracic ultrasound (TUS) to identify NEL by assessing mobility and compliance of the atelectatic lung within an effusion. However, this work has not been replicated and was delivered by researchers with expertise and facilities not used by or available to most practitioners.

Method We incorporated an in-depth TUS protocol into the pre-procedural assessment of patients undergoing intervention for suspected MPE, where ≥500 mL of fluid was expected to be drained. TUS images were acquired by two chest physicians with RCR level 1 competence or above. Data recorded included size and characteristics of the effusion; presence of pleural thickening; behaviour of the lung and diaphragm; and M-mode displacement with cardiac impulse of the atelectatic lung during breath hold manoeuvres. NEL was determined using post-drainage imaging (chest X-ray and/or CT) and clinical notes.

Results 34 patients underwent in-depth TUS evaluation (Table 1). Image acquisition and measurements took no more than five minutes in any patient. Poor M-mode displacement (<0.8 mm) was only seen with NEL, whilst good movement (>1.2 mm) was

Abstract P2 Table 1 In-depth thoracic ultrasound (TUS) findings in 34 patients undergoing pleural drainage for suspected malignant disease

<table>
<thead>
<tr>
<th>Feature</th>
<th>NEL (p = 23)</th>
<th>Indeterminate (p = 5)</th>
<th>Non-expandable (p = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effusion side</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right</td>
<td>11/23</td>
<td>5/5</td>
<td>5/6</td>
</tr>
<tr>
<td>Left</td>
<td>12/23</td>
<td>0/5</td>
<td>1/6</td>
</tr>
<tr>
<td>Effusion size</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>10/23</td>
<td>2/5</td>
<td>4/6</td>
</tr>
<tr>
<td>Large</td>
<td>13/23</td>
<td>3/5</td>
<td>2/6</td>
</tr>
<tr>
<td>Septations evident</td>
<td>2/23</td>
<td>2/5</td>
<td>4/6</td>
</tr>
<tr>
<td>Parietal pleural thickening evident</td>
<td>0/23</td>
<td>0/5</td>
<td>3/6</td>
</tr>
<tr>
<td>Visceral pleural thickening evident</td>
<td>0/23</td>
<td>0/5</td>
<td>3/6</td>
</tr>
<tr>
<td>Distinct pleural nodularity evident</td>
<td>5/23</td>
<td>4/5</td>
<td>2/6</td>
</tr>
<tr>
<td>Dynamic TUS features</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paradoxical motion of diaphragm evident</td>
<td>9/23</td>
<td>2/5</td>
<td>3/6</td>
</tr>
<tr>
<td>Free movement of atelectatic lung evident</td>
<td>22/23</td>
<td>3/5</td>
<td>2/6</td>
</tr>
<tr>
<td>Clear inspiratory expansion of atelectatic lung evident</td>
<td>7/23</td>
<td>0/5</td>
<td>0/6</td>
</tr>
<tr>
<td>M-mode motion of atelectatic lung</td>
<td>&lt;0.8 mm; n (%)</td>
<td>0/23</td>
<td>0/5</td>
</tr>
<tr>
<td>Inspiratory hold, near or approaching TLC</td>
<td>0.8–1.2 mm; n (%)</td>
<td>7/23</td>
<td>3/5</td>
</tr>
<tr>
<td>M-mode motion of atelectatic lung</td>
<td>&gt;1.2 mm; n (%)</td>
<td>16/23</td>
<td>2/5</td>
</tr>
<tr>
<td>Inspiratory hold, near or approaching RV</td>
<td>&lt;0.8 mm; n (%)</td>
<td>0/23</td>
<td>0/5</td>
</tr>
<tr>
<td>M-mode motion of atelectatic lung</td>
<td>0.8–1.2 mm; n (%)</td>
<td>2/23</td>
<td>1/5</td>
</tr>
<tr>
<td>M-mode motion of atelectatic lung</td>
<td>&gt;1.2 mm; n (%)</td>
<td>21/23</td>
<td>4/5</td>
</tr>
</tbody>
</table>
highly predictive of free lung. The presence of visceral thickening on TUS may also predict NEL, although there was only limited data to support this finding.

**Conclusion** In-depth TUS assessment can be delivered and interpreted quickly in the day-case setting using widely available portable ultrasound equipment, with potential implications for patient care and non-invasive diagnosis of NEL. Further research is needed to evaluate the ability of M-mode and other TUS parameters to predict NEL and symptom response prior to invasive intervention.

**REFERENCE**

**P3 THORACIC ULTRASOUND EXPERIENCES AMONGST RESPIRATORY TRAINEES – A NATIONAL SURVEY**
P Sivakumar, MKamalanathan, A Collett, L Ahmed. St Thomas’ Hospital, London, UK

10.1136/thoraxjnl-2016-209333.146

**Introduction** Level 1 proficiency in thoracic ultrasound is a mandatory curriculum requirement for respiratory specialty trainees in the UK. Guidance on attaining and maintaining this competency is outlined by The Royal College of Radiologists (RCR). This has been a focus of the GMC survey specialty specific questions.

**Aims** To further evaluate thoracic ultrasound competencies and training experiences amongst respiratory registrars in England.

**Methods** We invited all respiratory trainees in England to complete an online survey. Responses were collected between October 2015 and June 2016.

**Results** 202 (of approximately 600) respiratory trainees completed the survey from 14 deaneries.

65.8% (131/199) trainees are level 1 accredited with 20.6% (22/107) of these performing fewer than 20 ultrasounds in the past year. Figure 1 illustrates the self-reported confidence in identifying pathology.

59% (107/171) of all respondents are never or rarely supervised. 60% (102/169) of queries are answered by real time evaluation or review of stored media. The remaining 40% reported that advice was based on verbal descriptions.

29.2% (50/171) of trainees reported that access to an ultrasonographer for advice was either “not easy” or “impossible”. 9% (15/167) reported that there were no level 1 or level 2 accredited consultants at their current hospital.

**Conclusion** Most trainees are level 1 accredited, but many do not perform the minimum 20 scans/year to maintain their competency. Access to supervision is also limited. Though not a requirement, trainees are less confident in identifying pathology pertinent to acute and respiratory medicine, particularly pulmonary oedema and pneumothorax.

Encouragingly ultrasound training has evolved considerably in recent years, but ongoing work needs to focus on improving supervision and training. There is a case for reviewing current guidance and to consider tailoring training and expectations to align with the specific needs of respiratory registrars.

**REFERENCE**

**P4 A PROSPECTIVE ASSESSMENT OF THE CLINICAL UTILITY OF INTERCOSTAL ARTERY IDENTIFICATION IN PLEURAL INTERVENTION**

10.1136/thoraxjnl-2016-209333.147

**Background** Respiratory Specialists perform an increasing number of complex pleural procedures. With this comes a greater focus on patient safety and risk reduction. There is strong evidence that ultrasound guidance in procedure site selection for pleural effusion reduces organ puncture and pneumothorax, but
it remains important to choose intervention sites to avoid the intercostal arteries (ICA). Previous data suggest that the ICA can follow a tortuous course especially in the elderly. The use of colour Doppler to identify intercostal and collateral arteries has been shown to be accurate in research studies and may assist in selecting a safe intervention site.

This study aimed to prospectively assess identification of the ICA in routine practice and the effect on procedure site selection. **Methods** Data on identification of the ICA was prospectively collected as part of routine clinical care and documented in the pleural procedure records in a tertiary centre between July 2015 and July 2016. Successful identification of the ICA and its influence in choosing the procedure site was recorded. **Results** 404 procedures were carried out over the study period. The mean age of the patients was 69.3 years (sd 14.2). Identification of the ICA was attempted in 386 (95.5%) procedures and the ICA was identified within the intercostal space in 192 (49.7%) of cases.

The site of the procedure was altered after ICA detection in 56/192 (29.2%) of procedures and in 16/32 (50.0%) of image guided pleural biopsies.

In 7/192 (3.6%) procedures the ICA was identified in all rib spaces at potential intervention sites, leading to the procedure not being attempted. No complications related to post procedure haemorrhage were reported.

A more detailed analysis of the identification of the ICA and its influence on practice by procedure type is shown in Table 1. **Conclusion** Screening for the ICA in routine clinical practice influences procedural site selection.

In some cases identification can result in abandoning a procedure, which may have led to intercostal bleeding. Patient position and potential rib crowding may explain differences in the rates of successful identification between procedures.

If these findings are replicated in larger prospective studies, identification of the ICA may become routine practice to maximise safety.

## Abstract P4 Table 1

Comparison of pre-pleural procedure bleeding risk variables for blood stained versus non-blood stained pleural effusions

<table>
<thead>
<tr>
<th>Potential pre-procedure bleeding risk variable</th>
<th>Blood-stained (n = 60)</th>
<th>Non-blood-stained (n = 147)</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean anti-thrombotic medication score</td>
<td>1.21 (0–4)</td>
<td>1.19 (0–4)</td>
<td>p = 0.91</td>
</tr>
<tr>
<td>Mean pre-procedure INR</td>
<td>1.24 (1–4.2)</td>
<td>1.21 (1–3)</td>
<td>p = 0.63</td>
</tr>
<tr>
<td>Mean pre-procedure APTT</td>
<td>30.74 (19–93.8)</td>
<td>31.74 (19.6–56.2)</td>
<td>p = 0.50</td>
</tr>
<tr>
<td>Mean pre-procedure platelet count</td>
<td>341 x 10^9 (72–614)</td>
<td>293 x 10^9 (44–1156)</td>
<td>p = 0.06</td>
</tr>
</tbody>
</table>

**Conclusion** Deranged coagulation or prescribed antithrombotics pre-pleural procedure do not appear to significantly increase the likelihood of obtaining a blood-stained pleural effusion. The aetiology of blood stained pleural effusions is more likely multifactorial and should not always be attributed to a coagulation results or medication related increased bleeding risk. Further study could help determine how to better assess bleeding risk prior to pleural procedures.
Introduction and objectives Recent publications report a significant survival disadvantage associated with minimal pleural effusion (MiniPE) at presentation of non-small cell lung cancer (NSCLC). MiniPE is defined when an effusion is too small for thoracentesis or where aspiration cytology is negative. Occult pleural metastases (OPM), indirect pathophysiology or comorbidity may cause MiniPE, but staging beyond thoracentesis is rarely performed. Assumption of OPM and therapeutic nihilism may contribute to poor outcomes. We assessed the prognostic impact of MiniPE in potentially radically-treatable NSCLC (Stage I-IIIA), oncologists’ attitudes to treatment planning and the final treatment delivered.

Methods Electronic records and baseline imaging were reviewed retrospectively in 441 consecutive diagnoses of NSCLC made over 6 months in 2009. Stage I-IIIA patients were dichotomized into: No effusion and MiniPE. Malignant effusion (Stage IV) cases were recorded for comparison. The impact of effusion status on overall survival (OS) was estimated using Kaplan-Meier methodology. The probable cause of MiniPE was assessed indirectly using follow-up imaging/records. 3 Clinical Oncologists were surveyed for theoretical treatment plans in 8 randomly-selected MiniPE Stage I-IIIA cases based on anonymised imaging and history. These 24 plans were compared to the treatment delivered in MiniPE patients.

Results 103/441 (23%) patients had MiniPE. 167/441 (38%) were Stage I-IIIA; 26/167 (16%) of these had MiniPE. OS based on effusion status (Stage I-IIIA) is shown in Figure 1. 28/103 (17%) MiniPE patients survived 30 days and had limited post-diagnosis imaging. These were excluded from probable cause analyses. Of the remaining 75/103, 20 (27%) had radiological evidence of progressive pleural malignancy. Radical treatment was delivered in 4/26 (15%) Stage I-IIIA MiniPE cases but advocated in 17/24 (71%) theoretical plans, which showed significant inconsistencies.

Conclusions These retrospective data confirm the negative prognostic impact of MiniPE and suggest the prevalence of OPM is at least 27% in Stage I-IIIA NSCLC. This is likely an underestimate given our limited data in poor prognosis patients. Radical treatment was rarely delivered despite aggressive treatment plans. A prospective study utilising thoracoscopic staging could define the true prevalence of OPM in MiniPE. Objective staging might improve decision-making, radical treatment rates and OS in this context.

P6 SIGNIFICANCE OF MINIMAL PLEURAL EFFUSION IN NON-SMALL CELL LUNG CANCER

GA Martin, 2S Tam, 1JC MacLay, 1C Stewart, 1KG Blyth. 1Queen Elizabeth University Hospital, Glasgow, UK; 2Institute of Cancer Sciences, University of Glasgow, Glasgow, UK; 3Glasgow Royal Infirmary, Glasgow, UK

10.1136/thoraxjnl-2016-209333.149

Introduction Malignant pleural effusion (MPE) management has dramatically changed in the last decade with the increasing use of indwelling pleural catheters (IPC) and thoracoscopy. Although treatment is aimed at improving health related quality of life (HRQOL), data on outcomes are limited, with management guided by clinician perspectives and experiences. Aims We sought clinician perspectives of HRQOL for patients with MPE and its impact on decision making worldwide. We present the UK data.

Methods We invited all respiratory doctors in the UK to complete an online survey advertised in the British Thoracic Society newsletter and by e-mail. Responses to questions with ranked options were assigned consecutive integers with lower values indicating a more favoured or higher prioritised response. Responses to best answer questions are presented as frequencies and percentages.

Results 121 UK-based doctors (104 consultants, 1 associate specialist, 16 respiratory registrars) completed the survey.

Factors determining HRQOL (rank 1) were: breathlessness ranked highest (mean rank 1.48) and functional status (mean rank 2.57) were ranked the most important. Social set up – mean rank 5.78, distance to travel for medical care – mean rank 8.27. Factors determining HRQOL (rank 2) were: shortness of breath and chest pain – mean rank 5.16, depression/anxiety – mean rank 5.22, tamour type and stage – mean rank 5.78, distance to travel for medical care – mean rank 5.86, age – mean rank 6.59, financial difficulties from treatment – mean rank 8.27.

Conclusions These retrospective data confirm the negative prognostic impact of MiniPE and suggest the prevalence of OPM is at least 27% in Stage I-IIIA NSCLC. This is likely an underestimate given our limited data in poor prognosis patients. Radical treatment was rarely delivered despite aggressive treatment plans. A prospective study utilising thoracoscopic staging could define the true prevalence of OPM in MiniPE. Objective staging might improve decision-making, radical treatment rates and OS in this context.
NEGATIVE PLEURAL BIOPSIES – DO WE NEED EARLY FOLLOW UP AND IMAGING?

1 Leyakathali Khan, 2 Ganaie, 1 Haris, M Munavvar. 1Royal Stoke University Hospital, Stoke on Trent, UK; 2Lancashire Teaching Hospital NHS trust, Preston, UK

Background Primary pleural or secondary malignancy is a common cause of pleural effusion. The incidence is about 200000 cases per year. Pleural biopsy remains gold standard investigation of choice. Those with negative biopsies are either discharged or have follow up depending on the multidisciplinary team decision.

Objective To review the outcome of all patients with negative pleural biopsy including any follow up imaging for up to two years.

Methods Retrospective analysis of 162 consecutive patients who underwent video-assisted thoracoscopic surgery (VATS) (100) and local anaesthetic thoracoscopy (62) between January 2011 and December 2012 across two large UK tertiary referral centres. Patients referred from peripheral centres were excluded.

Results Of the 162 patients, male:female ratio was 109/53; average age was 69. Pleural biopsy histology was malignant in 63% (100); mesothelioma 43%, lung cancer 35%, extra pulmonary 22%, Granulomatous inflammation 6% (9), Benign 31% (53); chronic inflammation 28, fibrosis/thickening 8, reactive 13 and others 4. See Table 1.

Of the 53 benign, 11 (21%) developed malignancy before 2 years. 6 (53%) required repeat biopsy. Patients alive at the end of 2 years – 1 Malignant and 26 benign of the 53.

Conclusion Shortness of breath and chest pain ranked highly in the perspective of HRQOL with shortness of breath a key factor in offering intervention. There is a lack of consensus on the ideal treatment to maximise HRQOL, which may reflect the paucity of data. Robust clinical trial evidence on HRQOL outcomes is therefore required to guide management decisions of patients with MPE. This should be complemented by a patient survey to ascertain differences in clinician and patient perspectives of quality of life and care.

REFERENCE


THE UTILITY OF P16 FISH IN DIFFERENTIATING MALIGNANT MESOTHELIOMA AND BENIGN MESOTHELIAL PROLIFERATIONS

A Chaturvedi, J Holme, R Shah, P Taylor, M Evison. University Hospital of South Manchester, Manchester, UK

Introduction One of the commonest genetic abnormalities in malignant mesothelioma is deletion of the 9p21 locus which harbours the p16/CDKN2A gene. Homozygous deletion of p16/CDKN2A can be identified with Fluorescence in situ hybridization (FISH) and may be a useful diagnostic tool where there is difficulty separating malignant from benign mesothelial cell proliferations, e.g. where a lack of invasion into adipose tissue prevents a confident diagnosis of mesothelioma.

Methods The University Hospital of South Manchester is a regional mesothelioma centre in the North West of England. p16 FISH has been in clinical use since 2013 for cases of abnormal mesothelial cell proliferation without conclusive evidence of malignancy. This retrospective study analysed the diagnostic performance of p16 FISH using clinical follow-up and post-mortem studies to clarify final diagnoses.

Results 75 pathological samples underwent p16 FISH analysis 2013–2015; 16 cytology samples (14 pleural fluid, 2 ascitic fluid), 36 VATS pleural biopsies, 16 local anaesthetic thoracoscopic pleural biopsies and 7 percutaneous pleural biopsies. There was one failed test. A final diagnosis based on subsequent definitive pathological sampling, definitive radiological surveillance or post-mortem findings were available for 99% of patient (74/75). 71 patients were ultimately proven to have mesothelioma (39 epithelioid, 13 sarcomatoid, 7 biphasic and 12 NOS), 2 patients were diagnosed benign pleural disease and 1 with metastatic lung cancer. The diagnostic performance of p16 FISH was as follows:

Imaging performed during 2 years follow up at 6, 12, and 24 months: plain chest radiograph 22 (42%), 12 (23%), 13 (25%) and CT scan was done at 5 (9%), 8 (16%), 2 (4%) respectively.

Conclusion Our data suggests that 21% of patients were diagnosed as malignant within 2 years of initial negative biopsy, which is higher than expected.1 There is a need for early follow up and imaging in patients with negative pleural biopsy. Further studies are required to establish the follow up interval and imaging modality.

REFERENCE

sensitivity 69%, specificity 100%, positive predictive value 100%, negative predictive value 8%, and diagnostic accuracy 69%. All positive p16 FISH results were in cases of mesothelioma. The sensitivity of p16 according to specimen type was as follows: fluid cytology 88%, VATS 59%, medical thoracoscopy 57% and percutaneous biopsy 50%. The sensitivity as per histological subtype for p16 FISH was 66% in epithelioid mesothelioma and 73% in sarcomatoid mesothelioma.

Discussion p16 FISH is a useful diagnostic tool to confirm cases of suspected malignant mesothelioma. A positive result is consistent with mesothelioma but a negative result does not exclude it. This data shows promising diagnostic yield in fluid cytology which may be especially relevant in those patients unsuitable for invasive biopsies due to technical or clinical reasons.

**Poster sessions**

**P10 LIGHT MAY BE USED TO DIFFERENTIATE MESOTHELIOMA FROM BENIGN PLEURAL DISEASE AT THE BEDSIDE**

NK Oswald, A Robertson, P Rajeoh, R Steyn, M Kalkat, B Naidu. University of Birmingham, Birmingham, UK; Heart of England NHS Foundation Trust, Birmingham, UK

10.1136/thoraxjnl-2016-209333.153

**Introduction** Monitoring patients at risk of mesothelioma, earlier diagnosis and improving diagnostic tests are top research priorities set by the James Lind Alliance. Chest wall motion (CWM) can be quantified using structured light plethysmography (SLP). During SLP a single source of visible light projects a chequerboard grid onto the anterior chest wall of a patient; two spaced cameras record changes in the contours of the grid to calculate thoracic volume changes. This study aimed to assess whether there are quantifiable differences in CWM between benign pleural disease and mesothelioma using SLP.

**Methods** Patients attending the preoperative assessment clinic for an elective diagnostic pleural biopsy were prospective recruited. After giving consent, patients underwent a timed 5 minute SLP recording of tidal breathing whilst resting in an upright seated position. Recordings were done prior to surgery and analysis of the SLP recording was performed by a blinded technician. Histology results were collected after surgery and Mann Whitney U two tailed tests of SLP values performed.

**Results** Fifteen patients were recruited with a median age 71 (23–93 range), 90% were male. Patients subsequently diagnosed with mesothelioma (n = 4) had significantly different values in three measurements: the inspiratory to expiratory time ratio (Ti/Te, p = 0.009), breath phase between ribcage and abdomen (breath phase RC2AB, p = 0.013) and the variation in ratio of inspiratory flow at 50% of tidal motion to expiratory flow at 50% of tidal motion (IE50 IQR, p = 0.004). Median and interquartile ranges for breath phase (a measure of CWM synchrony) are shown in Figure 1. The recording process was highly acceptable to patients.

**Conclusions** Mesothelioma affects the ratio of time for inspiration and expiration as well as synchrony in CWM and variability of the breathing pattern. SLP is rapid, portable, non-invasive, requires minimal operator training and involves no radiation. The differences found indicate that CWM measurement is a promising tool to diagnose or exclude mesothelioma and potentially to monitor patients at risk of mesothelioma, further studies using SLP in this context are indicated.

Abstract P10 Figure 1 Difference in ribcage to abdomen movement synchrony between benign pleural disease and mesothelioma
Introduction Malignant pleural mesothelioma (MPM) has a poor, but heterogeneous prognosis. Previously developed prognostic scores have been derived from patient cohorts not typical of routine UK practice. Recently, a novel prognostic tool, validated in unselected UK patients was published.1

Objective To evaluate the utility of a novel prediction model by Brims et al.,1 to predict prognosis in mesothelioma patients presenting to a two-site UK district general hospital.

Methods Consecutive patients diagnosed with mesothelioma between January 2010 and December 2015 were identified. Data were collected from electronic records at diagnosis (age, gender, histology, performance score, haemoglobin, albumin, weight loss) as well as dates of diagnosis and of death or last follow-up. Patients were allocated to prognostic groups as described by Brims et al. Groups were compared using Kaplan-Meier survival analysis. The proportion of patients whose survival fell within ±33% of the survival predicted from the validation cohort of Brims et al. was calculated.

Results 71 patients (60 male) were diagnosed with MPM during the study period, median age 74 (interquartile range (IQR) 15). Histological diagnosis was available in 66 (93%) patients (43.9% epithelioid, 21.2% undefined mesothelioma, 18.2% sarcomatoid, 13.6% biphasic, 3.0% atypical/mixed). Median overall survival was 262 days (IQR 284 days). 97% of patients could be allocated to a prognostic group. Median survival by Brims group, compared with predicted survival, is shown in Table 1.

Conclusions The “Brims Score” can be retrospectively calculated in a high proportion of patients, using routinely collected data. It appears reliably to separate patients into cohorts with statistically significant difference in survival. The large within-group variation in survival, however, limits the utility of the score as a means of answering the question, “How long have I got, doc?” for individual patients.

Abstract P11 Table 1 Comparison of median survival by Brims group with predicted survival

<table>
<thead>
<tr>
<th>Brims Group</th>
<th>Median survival (days)</th>
<th>IQR (days)</th>
<th>Median predicted survival (days)</th>
<th>% of group within ±33% predicted survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>12 419</td>
<td>312</td>
<td>444</td>
<td>33.0</td>
</tr>
<tr>
<td>3</td>
<td>33 319</td>
<td>216</td>
<td>334</td>
<td>48.5</td>
</tr>
<tr>
<td>4</td>
<td>24 131</td>
<td>247</td>
<td>210</td>
<td>21.7</td>
</tr>
</tbody>
</table>

*Log-rank test
*P = 0.02

REFERENCE

EXPLORING THE CHARACTERISTICS OF PATIENTS WITH MESOTHELIOMA WHO DECLINE CHEMOTHERAPY: A PROSPECTIVE COHORT OF 200 PATIENTS

Introduction Malignant pleural mesothelioma (MPM) is an aggressive cancer with a poor prognosis. Treatment options are limited, and pemetrexed and cisplatin chemotherapy is the only intervention shown to extend life. Promising new therapies may provide alternate treatment options in the future.

Chemotherapy uptake varies in MPM. Some centres report rates as low as 46% in eligible patients. The aim of this study was to explore the characteristics of patients who declined chemotherapy, and to determine which factors were associated with chemotherapy refusal.

Methods Prospective data were collected on all patients diagnosed with MPM in one UK tertiary referral centre. Diagnosis of MPM and eligibility for chemotherapy were determined at the regional MPM multidisciplinary meeting. Patients were followed up until death or censored on 13/7/16.

Patient characteristics were compared using chi-squared, Fishers Exact and unpaired T-tests. Kaplan Meier curves were drawn to compare survival between patients who accepted and declined chemotherapy. Logistic regression was used to assess associations between patient characteristics and chemotherapy uptake.

Results 200 patients were diagnosed with MPM between 1/3/08 and 8/6/16. 150 (75%) were eligible for chemotherapy. 93/150 (62%) patients received chemotherapy, 46/150 (31%) declined and 11/150 (7.3%) patients did not receive it for other reasons.

Patient characteristics are shown in Table 1. The group who declined chemotherapy were older (mean age 74.4 vs 68.4, p < 0.001), with a higher proportion of females (23.9% vs 10.8%, p = 0.041) and fewer patients with performance status (PS) 0 (17.4% vs 43%, p = 0.005). Patients who received chemotherapy had longer median survival (426 days vs 203 days, p = 0.001, HR 0.519, p = 0.015).

The factors associated with chemotherapy refusal were age (regression coefficient 0.144, p < 0.001) and PS ≥ 1 (coefficient 1.052, p = 0.027).

Conclusion This is the first study to report the characteristics of MPM patients who declined chemotherapy. Significant differences were seen compared with patients who received chemotherapy. Further research is needed to determine whether similar patterns are seen in other centres.

Reasons for refusal were not collected, but the association with age and worse performance status may reflect concerns about chemotherapy toxicity. Qualitative research could explore patients’ reasons for refusing chemotherapy.
Introduction and objectives

Pleural disease contributes to a significant proportion of acute admissions and hospital bed-days. Traditionally, patients presenting with pleural effusion were admitted for management, including patients with terminal disease.

In May 2014, we designed one of the first dedicated pleural procedure lists regionally allowing patients to undergo procedures on a day-case basis.

A dedicated pleural procedure room was established for a weekly session to accommodate a maximum of 5 pleural procedures. The list was consultant-delivered by a level 2 thoracic ultrasound-trained Consultant, with built in consultant crossover to prevent cancellation. An electronic referral system, pleural procedure patient pathway and WHO procedural checklist was designed to be completed for each case to maximise patient safety and efficiency. Dedicated nursing was provided to enhance patient experience and multi-professional development. The list provided weekly opportunity for education/training for those wishing to gain ultrasound certification and procedural competency-based assessment.

This study looked at the impact of acute service redesign.

Methods

This was a review of a prospectively maintained data-base of a weekly pleural procedure list, from May 2014–May 2016. Comparison was made with data obtained from previous local audit, including LOS pre and post introduction of the new service.

Results

398 patients were referred over 2 years; 178 outpatients, 200 inpatients. On average, 4 pleural procedures/ultrasound were performed per session. A total of 3738 bed days were saved, based on an average LOS of 22 days for patients previously admitted with pleural effusions, demonstrated by audit pre-2014. In 178 cases, due to the ambulatory nature of the introduced service, average LOS was reduced from 22 to 1 day. There have been no reported adverse events since set-up, and additional income has been generated by receiving a day-case best practice tariff (BPT), introduced in 2013/14.

Conclusion Service innovation resulting in a dedicated hospital pleural procedure list has resulted in demonstrable benefits for patients in terms of LOS, patient safety and experience. Our set up has generated recurrent financial gains through bed day savings, created a regional hub for US training and confirmed the commendable merits of ambulatory care for patients requiring pleural procedures.

**Abstract P13 Table 1**

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of outpatients attended</th>
<th>Number of bed-days saved</th>
<th>Additional income generated by receiving the improved BPT (HRG Code D2602)</th>
<th>(BPT minus standard tariff) x day case</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 2014</td>
<td>83 patients x 22 = 1,826 bed</td>
<td>95 patients x 22 = 2,090 bed</td>
<td>£ 80,925</td>
<td>£ 75,240</td>
</tr>
<tr>
<td></td>
<td>days minus 83 bed days (one day case spell) = 1,743</td>
<td>days minus 95 bed days (one day case spell) = 1,995</td>
<td>BPT Day case tariff = £1,511</td>
<td>BPT Day case tariff = £1,328</td>
</tr>
<tr>
<td>May 2015</td>
<td>95 patients x 22 = 2,090 bed</td>
<td>95 patients x 22 = 2,090 bed</td>
<td>£ 75,240</td>
<td>£ 75,240</td>
</tr>
<tr>
<td></td>
<td>days minus 95 bed days (one day case spell) = 1,995</td>
<td>days minus 95 bed days (one day case spell) = 1,995</td>
<td>BPT Day case tariff = £1,328</td>
<td>BPT Day case tariff = £1,328</td>
</tr>
</tbody>
</table>

**P13 THE RATIONALE FOR SETTING UP A DEDICATED PLEURAL PROCEDURE LIST: BENEFITS FOR PATIENTS AND TRUSTS**

C Brockelsby, A Wells, P Deegan, W Kent, C Houghton, M Gautam. Royal Liverpool University Hospital, Liverpool, UK

10.1136/thoraxjnl-2016-209333.156
EXAMINING THE OUTCOMES OF A PLEURAL DISEASE CLINIC

1DT Whitehall, 2JB McCafferty. 1The University of Edinburgh, Edinburgh, UK; 2NHS Lothian, Edinburgh, UK

10.1136/thoraxjnl-2016-209333.157

Background Pleural effusions, the result of the accumulation of fluid in the pleural space, are a common medical problem. Patients with symptoms of cough and breathlessness with associated signs and chest x-ray (CXR) changes suggestive of a pleural effusion commonly present acutely to the medical assessment unit or to the respiratory outpatient department. Pleural effusions may also develop during admission. Advances in the availability of pleural diagnostic techniques, including thoracic ultrasound, thoracocentesis kits, and medical thoracoscopy means that pleural expertise can be concentrated in a dedicated clinic with the aim of facilitating ambulatory care, reducing hospital admissions and rationalising the use of laboratory services. This study aimed to assess the impact of a dedicated pleural clinic on these factors.

Methods A retrospective analysis of the hospital electronic patient records was carried out on patients attending the pleural clinic from 2014 to 2016. 146 patients were identified. Hospital admission data was also evaluated to assess inpatient admission for pleural effusion before and after the pleural clinic was instituted. In addition, quantification of laboratory samples sent pre- and post-pleural clinic was carried out.

Results Malignant disease was diagnosed in 44% of cases versus 46% for benign disease. A 29% reduction in ward admissions for pleural effusion was seen over 2 years. With a median length of stay of 5 days this resulted in 175 bed days saved in 205 with an associated annual cost saving of approximately £87,000. The number of diagnostic samples sent for cytology dropped by 11% following the introduction of the pleural clinic with estimated annual cost savings of around £3000.

Conclusions The introduction of a pleural clinic is not only cost effective in reducing hospital admissions and optimising diagnostic costs but also improves the patient journey by facilitating ambulatory care wherever possible.

A PILOT STUDY OF A DEDICATED BALLOONED INTERCOSTAL DRAIN


10.1136/thoraxjnl-2016-209333.158

Introduction Intercostal tube drainage of pleural air or fluid is an essential tool in the management of respiratory patients. A common complication of drain insertion is accidental removal of the drain, usually as a result of inadequate securing techniques, with rates of up to 21% quoted in the literature.1,2 This often results in the need for further pleural procedures (including drain re-siting), with associated additional risk to the patient and an increase in hospital costs.

Conclusions The introduction of a dedicated balloon-ended intercostal drain reduces the incidence of accidental removal, resulting in a lower number of further pleural procedures and associated lower costs to the patient and healthcare services.

Abstract P15 Figure 1

Abstract P14 Figure 1 Pleural effusion inpatient admissions at three different hospitals.

Arrows = Pleural clinic established at hospital

Abstract P15 Figure 1
Lung Cancer Investigations

P16 RADIAL EBUS BIOPSY WITH GUIDE SHEATH FOR PERIPHERAL PULMONARY LESIONS
K Srikanthan, C Drouot, B Sukumaran, V Johnson, M Walshaw, K Mohan. Liverpool Heart and Chest Hospital, Liverpool, UK
10.1136/thoraxjnl-2016-209333.159

Introduction The aim of lung cancer screening programs is the detection of early lung cancer, which may appear as small peripheral pulmonary lesion (PPL). Although radial EBUS guided biopsy is recommended by NICE to obtain tissue diagnosis in PPL which cannot be seen by conventional bronchoscopy, there is a paucity of published data within the UK regarding this technique. We looked at our 4-year radial EBUS results at our tertiary centre.

Methods We reviewed 71 consecutive patients who underwent radial EBUS guided biopsy for investigation of a PPL, performed using a guide sheath (K201 or K203) by a consultant operator assisted by a respiratory trainee. We assessed the diagnostic rate, yield from sampling techniques (biopsy vs brushings), whether the diagnosis correlated with other procedures/management, and any complications.

Results Mean patient age was 70 years (range 44–89), 38 female, and 41 (58%) had undergone 1 or more unsuccessful investigations at their local hospital. We were able to visualise the lesion by ultrasound leading to subsequent sampling in 62/71 (87%) patients. A diagnosis of malignancy was confirmed in 41/62 (66%) patients. Of the 21 biopsies which did not demonstrate malignancy, 11 were subsequently shown to have cancer (false negatives—pathological diagnosis by other methods or clinical radiological diagnosis or awaiting follow up) but were 10 true negative (resolution or 2 year stability on CT scan). The yield for malignancy was superior with brushings (88%) compared to biopsy (73%). The overall sensitivity for cancer was 72% (N = 71, whole cohort) and 82% (N = 62, lesion was visualised by ultrasound) respectively. Two patients developed a pneumothorax which did not require intervention.

Conclusion Radial EBUS is a safe and effective technique in obtaining tissue diagnosis in PPL not amenable to other biopsy methods. We visualised the lesion in 87% of patients and our diagnostic yield for malignancy is similar to current standards. Radial EBUS should take a more prominent role in diagnostic pathways for PPL within the UK, particularly in the context of future lung cancer screening programmes.

P17 A RETROSPECTIVE ANALYSIS COMPARING THE USE OF PROCORE WITH STANDARD FINE NEEDLE ASPIRATION IN ENDOBRONCHIAL ULTRASOUND GUIDED TRANSPERSONIAL NEEDLE ASPIRATION (EBUS-TBNA)

DJ McCracken, TE McManus, A Shamboul. South West Acute Hospital, Enniskillen, UK
10.1136/thoraxjnl-2016-209333.160

Endobronchial ultrasound has become first line in the investigation of mediastinal lesions suspicious for malignancy in keeping with NICE guidelines, however needle size and type, along with number of passes required to maximise diagnostic sensitivity remains unclear.

Previous meta-analyses, the largest of which included 576 patients,1 have compared the use of ProCore with standard fine needle aspiration in the assessment of pancreatic masses with differences noted only in the number of passes required.

We aim to assess whether a ProCore needle improves diagnostic sensitivity in EBUS-TBNA.

Complete follow up data regarding all 235 patients undergoing EBUS-TBNA in a district general hospital has been collected since the service’s inception in 2012. Results were collated and retrospectively analysed allowing for calculation of test sensitivity and specificity. Comparison was then made between procedures where standard fine needle aspiration was performed and those using a ProCore needle.

Overall sensitivity of EBUS-TBNA was shown to be 85% with a specificity of 100% in keeping with quoted figures from other centres. Standard fine needle aspiration produced a sensitivity of 77% (85/110) versus ProCore sensitivity of 92% (115/125) with a p value of 0.0016. 30% (33/110) of patients undergoing standard fine needle aspiration required an appropriate crossover technique such as mediastinoscopy or CT guided FNA in order to either obtain or confirm the diagnosis compared with 15% (19/125) of the ProCore group with a p value of 0.0064.

Our retrospective analysis shows a statistically significant difference in the diagnostic sensitivity of sampling mediastinal lymphadenopathy using a ProCore needle compared with standard fine needle aspiration. It also shows that a significantly fewer number of patients required further procedures in order to obtain or confirm the diagnosis. This could potentially be confounded by the retrospective nature of the study design, however due to
the statistical significance demonstrated, further study is required in the form of a randomised control trial.

REFERENCE

P18 DO BRONCHIAL WASHINGS IMPROVE DIAGNOSTIC YIELD IN PATIENTS UNDERGOING EBUS-TBNA
K Srikanthan, C Drouet, C Smyth, T Giles, M Walshaw, K Mohan. Liverpool Heart and Chest Hospital, Liverpool, UK

Introduction EBUS is increasingly used in the diagnosis and staging of lung cancer, particularly where there are no endobronchial lesions. Despite this, in these cases referring physicians often request bronchial washings to be performed at the same time, in the hope of increasing diagnostic yield. We wished to investigate whether this added to the information provided by EBUS-TBNA in such patients.

Methods We looked at all patients who underwent EBUS procedures at our tertiary centre in the last six months, who also had washings taken for cytology at the same sitting where there were no visible endobronchial lesions. We compared the diagnostic yield from EBUS-TBNA with that from the bronchial washings.

Results Of the 111 EBUS patients, 40 underwent concurrent bronchial washings for cytology (mean age 70 years (range 23–89), 23 (58%) male). EBUS-TBNA samples were diagnostic in 39 (98%): 31 malignancy (12 adenocarcinoma, 11 squamous cell carcinoma, 3 small cell carcinoma, 2 carcinoid, 2 breast adenocarcinoma, 1 renal cell carcinoma) and 8 were benign disease. Although bronchial washings were also diagnostic for malignancy in 7 (18%) (4 squamous cell carcinoma, 3 adenocarcinoma), all these cases also had positive EBUS-TBNA samples. There were no cases in which bronchial washings provided the diagnosis in the context of a negative EBUS-TBNA sample.

Conclusions This is the first study to evaluate the effectiveness of bronchial washings in addition to EBUS-TBNA sampling, where there is no visible endobronchial disease. Since each cytological sample analysis costs £75, elimination of bronchial washings in our patients could have saved £3000 over this 6-month period. We conclude that in those patients undergoing EBUS-TBNA, who also have peripheral pulmonary lesions, bronchial washings do not improve the diagnostic yield, and should not constitute routine practice.

P19 CENTRAL AIRWAY OBSTRUCTION IN BRONCHOCARCINOMA
M Hindle, A Silby, MG Aldik, A Marchbank, C Daneshvar. Plymouth Hospitals NHS Trust, Plymouth, UK

Background Endobronchial compromise with central airways obstruction (CAO) is a life threatening complication of lung cancer. Endobronchial treatments provide immediate symptom relief, while allowing other treatment modalities to begin. Yet the prevalence of this condition is poorly defined. We set to identify the prevalence of CAO to inform the development of an intervention service.

Method Between 11/2014–11/2015, we reviewed the index computer tomography (CT) scans of all patients diagnosed with a thoracic malignancy. Data collected included staging and the presence of endobronchial involvement. In patients with reported endobronchial involvement, images were reviewed for suitability of airway treatment.

Results Over the study period 434 patients were diagnosed with a thoracic malignancy. In 51 non-primary bronchogenic malignancies were identified, including 41 mesotheliomas. Of the remaining 383 patients with lung cancer, 359 underwent an index CT scan. Staging by CT was reported in 291 (81.0%) patients. Of the 359 patients with CT imaging available, endobronchial disease was present in 111 (30.9%) (95% confidence intervals (CI) 26.1–35.7%), with 29 (8.0%; 95% CI: 5.2–10.8%) patients having CAO. Of these, the commonest site was the bronchus intermedius (62.1%). The median degree of obstruction was 71.4% (interquartile range 50–100). Extrinsic compression was dominant in 8 (27.6%) patients. By cell type, squamous cell carcinoma, NSCLC-NOS, small cell lung carcinoma, and adenocarcinoma accounted for 9 (31.0%), 5 (17.2%), 4 (13.8%), and 4 (13.8%) cases respectively. In 9 (31.0%) no histology was available. Of those patients with CAO, 26 (89.7%) could be considered for airway treatments, however only 3 (12%) had a therapeutic procedure performed. Of 18 patients with follow up imaging, 8 (44%) developed obstructive complications.

Conclusions CAO affects nearly 1 in 10 lung cancer patients at the time of diagnosis and services should be developed to evaluate and offer timely intervention. Further longitudinal data will help predict the risk of developing central airways obstruction.
abnormal findings included nasal bleed-2%, haemangioma/telangiectasia-3%, purulent secretions-2%, dynamic airway collapse-1%, aberrant anatomy-1% and possible tumour-1%. The two cases of possible tumour were further evaluated with nasendoscopy and rigid bronchoscopy and no cancers were identified on biopsies. A single case of oral cancer was identified 1 year post bronchoscopy on follow up review of these cases.

**Conclusion** In conclusion our study shows that in patients with haemoptysis with no relevant finding identified on CT and irrespective of their smoking status, flexible bronchoscopy does not reveal any significant serious pathology. We would recommend that further studies are required to evaluate the investigative pathway for haemoptysis particularly if CT thorax does not identify a cause for haemoptysis.

---

**P21** PULMONARY NODULES: ASSESSING THE REPEATABILITY OF IMAGING BIOMARKERS OF MALIGNANCY

1AT alw ar, 2MY Willaime, 2LC Pickup, 2M Enescu, 2D Boukerroui, 1W Hiches, 2MJ Gooding, 1NM Rahman, 2T Kadir, 1FV Gleeson. 1Oxford University Hospitals NHS Foundation Trust, Oxford, England UK; 2Mirada Medical Ltd, Oxford, UK

10.1136/thoraxjnl-2016-209333.164
Introduction The BTS Pulmonary Nodule Guidelines recommend the use of nodule volumetry as a biomarker of malignancy in pulmonary nodules (PNs). Unfortunately, there is significant inter-scan volumetry measurement variability not representing true growth, of up to 25% (Gietema et al., 2007), with reliable growth detection requiring a scan time interval of up to 12 months. CT Texture analysis (CTTA) does not require volumetry detectable growth to detect change and may be a useful biomarker of malignancy.

Aims and objectives To assess the repeatability of texture features extracted from PNs and compare this to the inter-scan variability of volume measurements.

Materials and methods 40 patients, (20 with an indeterminate PN and 20 with pulmonary metastases) underwent two Low Dose Volumetric CT scans within a 60 minute period.

20 texture features previously used in combination to predict nodule probability of malignancy (BTS 2015) were extracted from each automatic contoured region surrounding the PN.

The variability of texture measurements within individual nodules was assessed by computing the relative differences between baseline and validation scans. Mean and standard deviation (sd) were estimated from the relative differences. Lower and upper limits of repeatability (LLR and ULR) were calculated as mean ± 1.96 × sd. The intra-class correlation coefficient (ICC) was also used to assess the repeatability of the image features for this group of patients.

Results Nodule volumes ranged from 76 to 8130 mm³ (mean 2D diameter 8.7 mm; sd 3.2) and were not statistically different between baseline and validation scans (p = 0.92, Wilcoxon rank sum test).

The mean difference in volume between the two scans was 37.4 mm³ (6.2%, sd 30.4).

18 out of 20 textural features displayed ULR and LLR below ± 26.2% (sd ± 12.3%). These were less variable than nodule volume (mean = 1.2%; sd = 14.4%; LLR = −27.0%; ULR = 29.5%). All features had high repeatability (0.87 ≤ ICC ≤ 0.99), see Figure 1.

Conclusion The repeatability of CTTA was comparable to automatic volumetric measurements that are currently recommended for use in clinical practice. To our knowledge this is the first study to assess CTTA repeatability, a promising biomarker of malignancy.

Abstract P22 Table 1

<table>
<thead>
<tr>
<th></th>
<th>&lt;5 mm</th>
<th>≥5-7.9 mm</th>
<th>≥8 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>22</td>
<td>22</td>
<td>1</td>
</tr>
<tr>
<td>Volume &lt; 80 mm³</td>
<td>22</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Benign features</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Static volume at 1 year</td>
<td>8</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>VDT &gt; 800 days at 1 year</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Total discharge</td>
<td>22</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Scans saved</td>
<td>28</td>
<td>10</td>
<td>15</td>
</tr>
</tbody>
</table>

For patients with larger nodules and CT scans at least a year apart, serial volumetry identified 17 patients with nodules 6–7.9 mm of which 15 were either morphologically benign, <80 mm³, static in volume or VDT >800 days, and thus dischargeable saving 15 future CT scans; and 9 patients with >8 mm nodules of which static volumetry was noted in 6, saving 8 future scans.

All patients with a CT follow up period of between 3 months and 1 year (n = 44) had static linear measurements and volumetry was not retrospectively performed on these.

Total discharges were 51 (see table), with a saving of 61 scans compared to historical protocol. Discharge of patients with nodules < 5 mm is a one off gain as these will not enter follow up in the future. Excluding these, results in an ongoing saving of 33 scans if 34 patients undergo either paired or one off volume measurements, taking an average of 5 minutes to perform. Additional volumetry at 3 months would add a further 5 minutes to analysis of these patients CTs. We believe the ‘trade off’ between time for volumetry versus reduced CTs (radiology time, radiation exposure and patient inconvenience) is favourable and should provide an incentive for units to offer volume measurements, performed as in this study by either chest radiologist or trained chest physician, if they are not already doing so.
Results Of the 42 reports included, only fourteen of these (33%) provided any guidance on follow-up. Of these, nine (21% of reports) complied with BTS or Fleischner Society recommendations. The reasons for non-compliance with guidelines when advice was provided were no timescales or follow-up modalities suggested (four of five) and incorrect follow-up time (one of five). Results are summarised in Figure 1.

Conclusions From our results it is evident that no or incorrect follow-up advice is being given, based on radiological appearances, for the majority (79%) of pulmonary nodules seen on CT imaging. Clearly the potential consequences of this may include malignancy not being detected and managed in a timely fashion. It is therefore fundamental that each unit has a system, based on existing guidelines, to ensure correct advice is provided based on radiological findings.

Clinical Aspects of Pulmonary Vascular Disease

P24 SHORT TERM OUTCOME OF PATIENTS WITH ACUTE PULMONARY EMBOLISM AND HIGH LACTATE AT A DISTRICT GENERAL HOSPITAL

JB Adzie, ZD Momoh, B Soliman, A Macduff. The Royal Wolverhampton NHS Trust, Wolverhampton, UK

10.1136/thoraxjnl-2016-209333.167

Introduction The risk stratification of haemodynamically stable patients presenting with pulmonary embolism (PE) is currently focussed on evidence of right ventricular (RV) dysfunction and myocardial necrosis (elevated Troponin). However these single markers have insufficient evidence to definitively guide treatment decision making. Plasma lactate has been shown to be potentially useful in identifying normotensive PE patients at high risk of PE related adverse events. The aim of this retrospective cross sectional study is to assess the role of serum lactate in the risk assessment of patients presenting with acute PE in a “real world” setting.

Methods We reviewed the cases of all patients with a radiologically confirmed PE on CTPA from Royal Wolverhampton Hospital between June 2014 and June 2015. The primary outcome was PE related complications within 7 days of diagnosis. This comprised of shock (systolic blood pressure <90 mmHg or pressure drop of ≥40 mmHg for ≥15 min), RV dysfunction, or need for cardiopulmonary resuscitation/mechanical ventilation.

Results 172 patients were diagnosed with acute PE during this time. 169 cases were analysed (insufficient information recorded in 3). Serum lactate was recorded in 92 (54.4%). Out of the 92 patients, 38 (41.3%) had a PE related complication with a higher average lactate (2.40 mmol/L) than the 54 (58.7%) who did not (lactate of 1.73 mmol/L) (p < 0.018 using the unpaired t test). PE related complications occurred in 33 (38.8%) of the 85 normotensive patients that had a lactate recorded. These patients also had a higher average lactate (2.24 mmol/L) than the 52 (61.2%) patients without complications (lactate 1.72 mmol/L) (p < 0.05). The positive predictive value of lactate as a single marker for a PE related complication is 53.1%. However the combination of a lactate ≥2, evidence of RV dysfunction and positive Troponin had a positive predictive value of 100%.

Conclusions This study adds to the evidence that a high serum lactate used in combination with a positive troponin and RV dysfunction can be a useful predictor of early adverse PE related events and may aid treatment decision making.

P25 RETROSPECTIVE ANALYSIS OF PATIENTS PRESENTING WITH ACUTE PULMONARY EMBOLISM (PE) AS THE FIRST MANIFESTATION OF MALIGNANCY

A Murchison, A Asher, A Van Manen, H Ellis. Milton Keynes University Hospital, Milton Keynes, UK

10.1136/thoraxjnl-2016-209333.168

Introduction A link between development of PE and presence of malignancy has long been established. NICE recommends patients presenting with PE should be offered: history, examination, chest x-ray and urinalysis. Further investigation for cancer with abdomino-pelvic CT (CT A/P) scan in patients over 40 with a first unprovoked PE should be considered. CT screening has not been shown to improve occult cancer diagnosis or mortality from cancer.
Methods We conducted a retrospective review of patients diagnosed with new PE at Milton Keynes hospital between August 2014 and 2015 to determine the proportion of patients found to have malignancy after CT. Selected patient notes were interrogated for clinical and laboratory findings at the time of diagnosis, and for details of subsequent management.

Results 177 patients were included in our study. 102 received a CT A/P, 88 of whom did not have an established diagnosis of cancer. Out of the 88, 5 new diagnoses of cancer were made. In 10 cases, CT revealed incidental findings. 8 patients received further imaging, and 2 investigated with invasive procedures. 4 of the 5 new cancer diagnoses had abnormal findings after basic screening.

Standardised incidence ratios were calculated to assess the probability of presence of undiagnosed cancer in patients presenting with PE. Our data showed no significant increase in the incidence of cancer in patients presenting with PE compared to national cancer statistics (SIR of 0.75 in males (CI: 0.2-0.64) and 1.0 in females (CI: 0.23-0.56) aged 70–79).

Discussion Our data suggests that in patients presenting with acute PE, clinical acumen (as outlined by NICE) can be used to identify patients with potential malignancy. Our data would support limiting CT A/P to patients with significant clinical features or deranged tests.

REFERENCES
1 National institute for Health and Clinical Excellence. Venous thromboembolic disease: diagnosis, management and thrombophilia testing. CG144. NICE 2015.

P27 EVALUATION AND BASELINE CHARACTERISTICS OF PATIENTS WITH CHRONIC THROMBOEMBOLIC DISEASE IN A SINGLE REFERRAL CENTRE


Introduction Chronic thromboembolic disease (CTED) is a consequence of failure of thrombus resolution following pulmonary embolism. Thrombotic material becomes fibrosed, resulting in chronic vascular occlusion without pulmonary hypertension. The prevalence and incidence of the condition is unknown and the mechanisms behind exercise intolerance are poorly understood. Surgical management in selected cases may significantly improve symptoms and patient functioning.

Methods We prospectively evaluated baseline characteristics of patients with CTED in a single referral centre between January 2015 and June 2016. Newly referred patients with suspected CTED underwent a standard assessment as delineated in international guidelines with a minimum of 2 imaging modalities, resting and exercise right heart catheterisation and additionally incremental cardiopulmonary exercise testing (CPET). All patients were assessed in a pulmonary endarterectomy (PEA) MDT.

Results 128 patients were diagnosed with CTEPH or CTED from our referral centre. 28 patients were referred with suspected CTED due to ECHO findings. Of these 21 patients were confirmed to have CTED at right heart catheterization and 16 underwent full investigation protocol and were analysed. Patients with CTED were younger than contemporary cohorts of CTEPH and were more likely to have a past medical history of VTE (94%). Patients with CTED had normal resting haemodynamics, resting and exercise right heart catheterisation and additionally incremental cardiopulmonary exercise testing (CPET).

Conclusions Patients with CTED represent a significant proportion of the new referrals to our specialist centre. Surgery is deemed an appropriate therapeutic approach in a small subset of patients with significant functional and symptomatic impairment. The natural history of CTED is unclear so any discussion of surgery needs to carefully consider surgical risk of death and morbidity against the potential for symptomatic improvement.
Chronic thromboembolic pulmonary hypertension (CTEPH) is commonly associated with a history of venous thromboembolism. Pulmonary endarterectomy (PEA) offers a potential cure in surgically accessible disease. However, a significant proportion of patients with CTEPH may not undergo surgery due to various reasons including disease distribution, comorbidities and patient choice. This group of patients have previously been considered to have a poor outcome although an international registry has recently reported on improved medium term outcomes in this patient population.

Aims and objectives
To compare long term survival of patients with CTEPH undergoing pulmonary endarterectomy (CTEPH-surgical-operated), surgically accessible disease not undergoing pulmonary endarterectomy (CTEPH-surgical-not-operated), surgically inaccessible disease (CTEPH-non-surgical).

Methods
Data was retrieved from hospital records and departmental database for consecutive, treatment-naïve patients with CTEPH diagnosed between 1st January 2001 and 30th November 2015 at the Sheffield Pulmonary Vascular Disease Unit and collected in the ASPIRE registry. Patients with suspected CTEPH undergo systematic evaluation but formal pulmonary angiography is only performed when other imaging modalities such as CTPA, MR imaging and nuclear medicine imaging are non-diagnostic.

Results
592 patients, mean age (± standard deviation), 65 ± 22 years, mean pulmonary arterial pressure 48 ± 13 mmHg and median pulmonary vascular resistance 480 ± 463 dynes/sec/cm⁵ were identified and followed for 4.3 ± 3.2 years. 5 year survival was significantly (p < 0.001) better in CTEPH-surgical-operated (n = 279) at 82.9 ± 3.1% compared to CTEPH-surgical-not-operated (n = 206) at 44.4 ± 5% (66.7 ± 9.1% patient choice, 39.4 ± 6% comorbidities) and 53.4 ± 5.8% in CTEPH-non-surgical (n = 107). Only 4% of the patients in our study were investigated with conventional pulmonary angiography. The median time to PEA surgery from diagnosis was 10.2 months and did not affect long term survival (p = 0.52).

Conclusions
For operable patients with CTEPH pulmonary endarterectomy is associated with an excellent long term outcome, the long-term survival of patients with surgical disease who decline surgery is significantly better than historically reported and that a non-invasive multimodality imaging approach can be used to assess patients with suspected CTEPH. Furthermore there is no time from diagnosis to surgery which predicts outcome.
Abstract P29 Table 1 Exercise intolerance in chronic thromboembolic disease

| Gender | M/F number (%) | 11 (69)/5 (31) |
| Age [years] Median, IQR | 53, 46.6–61.5 |
| Camphor score Median, IQR | 9.5, 5–12.3 |
| • Symptoms | 3, 1.8–6.8 |
| • Activity | 5, 0.8–12 |
| • QoL |  |
| mPAP [mmHg] Median, IQR | 20.5, 18–23 |
| PVR [dyn·cm⁻²] Median, IQR | 158, 112–195.7 |
| PAWP [mmHg] Median, IQR | 10.5, 8–12 |
| Cardiac Output [L/min] Median, IQR | 5.35, 4.1–5.8 |
| Cardiac Output fold increase on exercise* | 2.4 ± 0.5 |
| mPAP on exercise [mmHg]* | 30, 25.8–32.8 |
| TPR on exercise [WU] | 2.6, 2.1–3.9 |
| Peak VO₂ [%pred.] Mean ± SD | 90 ± 19.5 |
| VE/VCO₂ at AT Median, IQR | 36, 31–44.9 |
| Peak O₂ pulse [% pred.] Median, IQR | 84.5, 71–103 |

* Exercise at 40% of peak workload achieved during incremental CPET

Results Of 21 patients with confirmed CTED, 16 have completed the full assessment protocol (median age 53, 47–62). 14 (87%) were in functional class II/III. All patients had normal right ventricular function on echocardiography. Airway obstruction was present in 7 patients (44.5%). In majority of patients peak VO₂ and oxygen pulse were decreased and VE/VCO₂ at anaerobic threshold (AT) was increased (Table 1). CPET revealed 3 types of exercise limitation: combined cardiovascular and ventilatory limitation (n = 12), ventilatory limitation (n = 2) and limitation due to other reasons (n = 2). Peak oxygen consumption correlated with the symptoms domain of CAMPHOR (pulmonary hypertension specific quality of life measure) (p = 0.0242, R 0.56), cardiac output increase on exercise (p = 0.03, R 0.569) and VE/VCO₂ at anaerobic threshold (p = 0.012, R 0.608). Resting mPAP and PVR did not correlate with peak VO₂ or symptoms.

Conclusions We confirm the limited utility of resting measurements, including RHC in CTED for understanding exercise and functional limitation. CPET identified alternative causes for breathlessness and clarifies that patients with CTED are limited on exertion because of inability to increase cardiac output and hyperventilation.

REFERENCE

P30 AN EVALUATION OF THE USE OF QUALITY-OF-LIFE (QOL) SCORES IN PULMONARY ARTERIAL HYPERTENSION

Introduction Pulmonary Arterial Hypertension (PAH) is a severe, progressive condition leading to increased pulmonary vascular resistance, right ventricular failure and death. PAH is associated with poor prognosis and WHO functional class (FC) is strongly predictive of mortality. Living with PAH has significant physical, psychological and social impact on the lives of patients and carers. Symptoms of depression and anxiety are common and may contribute to poor quality of life (QOL) and social isolation.

Although QOL scores have been developed and validated in PAH, the psychological impact of living with PAH is often overlooked. Current guidelines advocate appropriate psychological and social support for patients, however, no formal recommendations exist currently to guide clinicians with regard to the timing and involvement of appropriately skilled professionals.

Methods QOL questionnaire data (Emphasis-10) was collected retrospectively from PAH patients attending routine appointments at PAH nurse and physician-led clinics over a 5 week period (June–July 2016).

Results
- 56 patients
- Median age: 62 (31–88)
- Sex: Male 17 (30%); Female 39 (70%)
- WHO FC: II: 24 (43%) III: 26 (46%) IV: 6 (11%)
- Aetiology: Familial: 2 (3%) Portal hypertension: 2 (3%)
- Scleroderma: 8 (14%)
- Connective tissue disease: 8 (14%)
- Congenital heart disease: 1 (2%)
- Marfan syndrome: 2 (3%)
- Pulmonary Fibrosis: 2 (3%)
- Pulmonary Embolism: 2 (3%)
- NYHA: I: 24 (44.5%)
- WHO FC: II: 24 (44.5%) III: 26 (46%) IV: 6 (11%)

Conclusion Anxiety and depression are common in PAH and can lead to reduced physical and social functioning and poor QOL. The management of physical and psychological symptom burden is important for holistic patient care.

Patients with advanced PAH are known to have significantly impaired QOL and this is supported by our data. Whilst QOL scores are recommended in current guidelines and frequently used in clinical practice, there remains uncertainty around the identification and referral of suitable patients to colleagues skilled in psychological interventions and the role for supportive (palliative) care.

Our data shows a wide variation in QOL scores within each FC. This shows that psychological support should be considered on an individual patient basis and not only reserved for patients with a poor FC.

P31 PHA-UK LIVING WITH PULMONARY HYPERTENSION 2016 SURVEY

1. Armstrong, 2C Billings, 3C Harries, 4J Yorke. 1Pulmonary Hypertension Association UK, Sheffield, UK; 2Sheffield Pulmonary Vascular Disease Unit, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; 3Pulmonary Hypertension Unit, Royal Brompton and Harefield NHS Foundation Trust, London, UK; 4School of Nursing, Midwifery and Social Work, University of Manchester, Manchester, UK.

10.1136/thoraxjnl-2016-209333.174

Background Pulmonary Hypertension Association UK (PHA-UK) is the only charity in the UK especially for people affected by pulmonary hypertension (PH). To gain information on the patient journey and how PH impacts on daily living, surveys have been conducted by PAH-UK in 2007, 2010 and more recently in 2016. This paper reports the 2016 survey and provides comparisons with previous survey results.

Method A quantitative survey consisting of 4 sections regarding diagnosis, management, ongoing quality-of-life and treatment was available to complete online via PHA-UK’s website or by hard copy sent to PHA-UK members and to patients on PH-specific targeted therapy.
Poster sessions

Results 551 responses were received. Participant mean age was 58.3 ± 16.6 years and age at diagnosis was 52.3 ± 18.8 years. 49% of patients had symptoms for >6 months before going to see a doctor and 22% were seen by 4 or more doctors before diagnosis. Time from first symptoms to diagnosis was >1 year in 49% with 31% of patients admitted as an emergency because of their symptoms. After diagnosis, 48% see a specialist at least every 6 months, 87% at least every 12 months. 62% think the support they receive is excellent and 26% good. 90% thought it was better to travel to a Specialist PH Centre rather than to be under the care of a non-PH specialist at a more local hospital.

Discussion This survey found that care of patients with PH is generally good or excellent and patients were keen to travel to Specialist PH Centres for their care. The early symptoms of pulmonary hypertension can be mild and are common to many diseases so it is often a lengthy process to arrive at the diagnosis. Compared with the previous survey the percentage of patients seeing >4 doctors before diagnosis was reduced (22% vs 47%) suggesting an increasing awareness of pulmonary hypertension amongst physicians. However, 49% of patients had symptoms for >6 months before presenting, which has not improved since previous surveys. As earlier diagnosis of patients results in better long-term survival, further work should be undertaken to continue to raise awareness in the UK of pulmonary hypertension.

In 2015 Dr R Limbrey (Respiratory Physician) and Sr S Good-
man (CNS Pulmonary Vascular Service) set up a Nurse Led (new patient) Pulmonary Embolism (PE) clinic to support increasing demand on the traditional model of consultant care.
We aim for a CNS review of all new patients with PE at 3 weeks following diagnosis, and provide follow up for 2 years. Previously a CNS led follow up clinic was in place.
We aim to provide our patients with early high quality education and information to reduce anxiety, improve physical functioning and quality of life. We suggest that this will reduce perceived ongoing symptoms and lessen follow up requirement.

Referral is made electronically. The referral system has been developed as a learning opportunity to enable medical referrers to identify provoking factors and quantify risk associated with the event. The data obtained from referrals provides support for service provision.

In 2015, 260 patients were reviewed in the Nurse led clinic, 95 of these were new referrals.
Of the 95 new referrals to the service 54 (57%) were provoked by an identifiable transient provoking factor. ESC (2014). Of these 42 (78%) also had persistent risk factors by ESC.

Unprovoked group:

In the unprovoked group 12 patients have been discharged to date with an average of 3.3 appointments per person with an additional telephone review planned for the 2 year mark.

The remainder of these patients can reasonably be expected to be discharged from follow up with similar levels of review.

Feedback from our patients has been overwhelmingly positive, most commonly expressed as a significant reduction in anxiety and improvement in quality of life.

Abstract P32 Table 1

<table>
<thead>
<tr>
<th>Persistent provoking factors (new patients)</th>
<th>No of patients seen in Nurse led P.E clinic 2015 by identified transient provoking factors (new patients)</th>
<th>No of patients</th>
<th>Persistent provoking factors identified</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post operative</td>
<td>17/54</td>
<td>Obesity</td>
<td>26/54</td>
<td></td>
</tr>
<tr>
<td>Travel</td>
<td>11/54</td>
<td>Hypertension</td>
<td>12/54</td>
<td></td>
</tr>
<tr>
<td>Immobility</td>
<td>8/54</td>
<td>Previous VTE</td>
<td>6/54</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2/54</td>
<td>A.F</td>
<td>2/54</td>
<td></td>
</tr>
<tr>
<td>Oral Contraceptive Pill</td>
<td>4/54</td>
<td>Age &gt; 80yrs</td>
<td>2/54</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>3/54</td>
<td>Known</td>
<td>2/54</td>
<td></td>
</tr>
<tr>
<td>Cancer (identified prior to diagnosis of VTE)</td>
<td>1/54</td>
<td>Thrombophilia</td>
<td>2/54</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>3/54</td>
<td>Diabetes</td>
<td>1/54</td>
<td></td>
</tr>
</tbody>
</table>

Unprovoked group:

Persistent risk factors identified in Nurse led P.E clinic 2015 in unprovoked group

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Persistent provoking factors identified</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>16/41</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>13/41</td>
<td></td>
</tr>
<tr>
<td>Previous VTE</td>
<td>7/41</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 80 yrs at time of event</td>
<td>8/41</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>5/41</td>
<td></td>
</tr>
<tr>
<td>Known Thrombophilia</td>
<td>2/41</td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1/41</td>
<td></td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>1/41</td>
<td></td>
</tr>
</tbody>
</table>

P32 A NEW NURSE LED P.E CLINIC 2015

5 Goodman, University Hospital Southampton, Southampton, UK

10.1136/thoraxjnl-2016-209333.175

In 2015 Dr R Limbrey (Respiratory Physician) and Sr S Goodman (CNS Pulmonary Vascular Service) set up a Nurse Led (new patient) Pulmonary Embolism (PE) clinic to support increasing demand on the traditional model of consultant care.

We aim for a CNS review of all new patients with PE at 3 weeks following diagnosis, and provide follow up for 2 years. Previously a CNS led follow up clinic was in place.

We aim to provide our patients with early high quality education and information to reduce anxiety, improve physical functioning and quality of life. We suggest that this will reduce perceived ongoing symptoms and lessen follow up requirement.

Referral is made electronically. The referral system has been developed as a learning opportunity to enable medical referrers to identify provoking factors and quantify risk associated with the event. The data obtained from referrals provides support for service provision.

In 2015, 260 patients were reviewed in the Nurse led clinic, 95 of these were new referrals.
Of the 95 new referrals to the service 54 (57%) were provoked by an identifiable transient provoking factor. ESC (2014). Of these 42 (78%) also had persistent risk factors by ESC.

Unprovoked group:

The remaining 41 (43%) had no identifiable transient provoking factor. Of these 32 (78%) did have persistent risk factors as per ESC 2014.

We note that 44% of all identified PE patients in this cohort, provoked and unprovoked, had a BMI ≥ 30kg/m².

In the provoked group 16 new patients were reviewed and discharged after an average of 2.62 appointments per person with an additional telephone review planned at the 2 year point.

In the unprovoked group 12 patients have been discharged to date with an average of 3.3 appointments per person with an additional telephone review planned for the 2 year mark.

The remainder of these patients can reasonably be expected to be discharged from follow up with similar levels of review.

Feedback from our patients has been overwhelmingly positive, most commonly expressed as a significant reduction in anxiety and improvement in quality of life.

Abstract P32 Table 1

<table>
<thead>
<tr>
<th>No of patients seen in Nurse led P.E clinic 2015 by identified transient provoking factors (new patients)</th>
<th>No of patients</th>
<th>Persistent provoking factors identified</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post operative</td>
<td>17/54</td>
<td>Obesity</td>
<td>26/54</td>
</tr>
<tr>
<td>Travel</td>
<td>11/54</td>
<td>Hypertension</td>
<td>12/54</td>
</tr>
<tr>
<td>Immobility</td>
<td>8/54</td>
<td>Previous VTE</td>
<td>6/54</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2/54</td>
<td>A.F</td>
<td>2/54</td>
</tr>
<tr>
<td>Oral Contraceptive Pill</td>
<td>4/54</td>
<td>Age &gt; 80yrs</td>
<td>2/54</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>3/54</td>
<td>Known</td>
<td>2/54</td>
</tr>
<tr>
<td>Cancer (identified prior to diagnosis of VTE)</td>
<td>1/54</td>
<td>Thrombophilia</td>
<td>2/54</td>
</tr>
<tr>
<td>Other</td>
<td>3/54</td>
<td>Diabetes</td>
<td>1/54</td>
</tr>
</tbody>
</table>

Unprovoked group:

Persistent risk factors identified in Nurse led P.E clinic 2015 in unprovoked group

<table>
<thead>
<tr>
<th>No of patients</th>
<th>Persistent provoking factors identified</th>
<th>No of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>16/41</td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>13/41</td>
<td></td>
</tr>
<tr>
<td>Previous VTE</td>
<td>7/41</td>
<td></td>
</tr>
<tr>
<td>Age &gt; 80 yrs at time of event</td>
<td>8/41</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>5/41</td>
<td></td>
</tr>
<tr>
<td>Known Thrombophilia</td>
<td>2/41</td>
<td></td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>1/41</td>
<td></td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>1/41</td>
<td></td>
</tr>
</tbody>
</table>

P33 PATIENTS WITH PULMONARY ARTERIOVENOUS MALFORMATIONS AND HEREDITARY HAEMORRHAGIC TELANGECTASIA REPORT FORCED EXPIRATORY MANOEUVRES DURING PULMONARY FUNCTION TESTS PROVOKE NOSEBLEEDS AND MIGRAINES

1HC Tighe, 1H McKerman, 1JT Springett, 1L Babawale, 1Y Perks, 2Y Patel, 3CL Shovlin.
1St George’s Hospital, London, UK; 2Imperial College London, London, UK; 3Imperial College Healthcare NHS Trust, London, UK

10.1136/thoraxjnl-2016-209333.176

Introduction and objectives Forced expiratory manoeuvres during lung function testing produce major pressure swings that are often overlooked by referring clinicians. Standard tests use a noseclip to prevent air leakage through the nose. Our goal was to examine how often the tests caused clinical sequelae such as nosebleeds in people with abnormal nasal and pulmonary vasculature due to hereditary haemorrhagic telangiectasia (HHT).

Methods With ethical approval, self-reported migraine features and exacerbations were examined in HHT subjects with and
LONG TERM OUTCOMES FOR PATIENTS WITH PULMONARY ARTERIOVENOUS MALFORMATIONS CONSIDERED FOR LUNG TRANSPLANTATION

1CL Shoulmin, 1MB Hughes, 2MT Layton, 1E Bootheer, 1D Allison, 1JE Jackson, 2IC Shoulmin. 1Imperial College School of Medicine, London, UK; 2Imperial College Healthcare NHS Trust, London, UK

Introduction and objectives Pulmonary arteriovenous malformations (PAVMs) are abnormal vessels that provide anatomic right-to-left shunts, and frequently result in severe hypoxaemia. Lung transplantation is sometimes considered if PAVMs are not amenable to treatment by embolization or surgical resection.

Methods A retrospective review was performed of patients with PAVMs assessed between 1999 and 2016 at a single UK institution. Characteristics of those considered and referred for lung transplantation assessment were examined.

Results Between May 1999 and July 2016, 707 patients with PAVMs were reviewed. Six were or had been formally considered for lung transplantation purely for PAVMs, 4 as adults (3 at our institution between 1989–1995), 2 as children. Ages ranged from 2–47 (median 22) years. Four were from the UK, two had been assessed in non UK countries. All had hereditary haemorrhagic telangiectasia (HHT). Three had suffered a cerebral abscess due to their PAVMs. The adults had undergone maximal embolisation of PAVMs, and the children were considered to have untreatable PAVMs assessed between 1999 and 2016 at a single UK institution.

Three had suffered a cerebral abscess due to their PAVMs. The adults had undergone maximal embolisation of PAVMs, and the children were considered to have untreatable PAVMs assessed between 1999 and 2016 at a single UK institution.

Conclusion Noseclip use should be restricted in people already experiencing regular nosebleeds, and further pretest information may be required.
Abstract P35 Table 1 A list of the bacterial organisms that were cultured from cerebral abscesses in the 2005–2016 cohort

<table>
<thead>
<tr>
<th>Bacterial organisms from cerebral abscesses in PAVM patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actinomycyts spp.</td>
</tr>
<tr>
<td>Alpha haemolytic streptococci</td>
</tr>
<tr>
<td>Streptococcus intermedius</td>
</tr>
<tr>
<td>Streptococcus Milleri</td>
</tr>
<tr>
<td>Streptococcus Anginosus</td>
</tr>
<tr>
<td>Actinomycyts larreni</td>
</tr>
<tr>
<td>Streptococcus Constantian</td>
</tr>
<tr>
<td>Non-haemolytic streptococci</td>
</tr>
<tr>
<td>Non specified streptococcal spp</td>
</tr>
<tr>
<td>Non specified anaerobic species</td>
</tr>
</tbody>
</table>

REFERENCE

P36 INJECTIONS OF INTRAVENOUS CONTRAST FOR COMPUTED TOMOGRAPHY SCANS PRECIPITATE MIGRAINES IN HEREDITARY HAEMORRHAGIC TELANGIECTASIA SUBJECTS AT RISK OF PARADOXICAL EMBOLI: IMPLICATIONS FOR RIGHT-TO-LEFT SHUNT RISKS

Introduction and objectives Migraine headaches commonly affect people with pulmonary arteriovenous malformations (PAVMs) that provide right-to-left shunts. The majority of PAVMs are due to underlying hereditary haemorrhagic telangiectasia (HHT). In our clinic practice, patients occasionally reported acute precipitation of migraine headaches following injection of technetium-labelled albumin macroaggregates for nuclear medicine scans. Our goal was to evaluate if injection of intravenous particles may provoke migraines in the cohort.

Methods Self-reported migraine features and exacerbations were examined in HHT subjects with and without pulmonary AVMs, for a series of noninvasive and invasive investigations, using an unbiased online survey. With ethical approval, the study recruited 166 subjects were classified as having both HHT and migraines. HHT subjects with migraines were more likely to have pulmonary AVMs (p < 0.0001). Pulse oximetry, x-rays, ultrasound and computerised tomography (CT) scans without intravenous contrast medium rarely, if ever, provoked migraines, but unenhanced magnetic resonance imaging (MRI) was reported to exacerbate migraines by 14/124 (11.2%) subjects. 114 had both enhanced and unenhanced CT examinations: studies with contrast media were more commonly reported to start (9/114 [7.8%]), and/or worsen migraines (18/114 [15.7%]) compared to those undertaken without contrast medium (p < 0.01), or after simple blood tests (p < 0.05). Additionally, migraine exacerbation was reported by 9/90 (10%) after contrast echocardiography, 2/44 (4.5%) after nuclear medicine scans, and 10/154 (6.5%) after blood tests.

Conclusions In this population, MRI studies, blood tests, contrast echocardiograms, and intravenous injection of iodinated contrast medium associated with CT examinations were reported to provoke or exacerbate migraines. Since air emboli are recognised to complicate intravenous injections, particularly following pressurised pump injections of CT scan contrast, evaluation of migraines as a potential read-out for paradoxical emboli is recommended. In the meantime, for people with HHT and migraines, pre-test counselling may helpfully include advice to bring migraine preventers or treatments to help alleviate symptoms promptly.

Abstract P37 Table 1 SLP Tidal Breathing Parameters for adult male and female normals aged 18-69 years

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Males 18–39 yrs (n = 32) Mean±SD</th>
<th>Males 40–69 yrs (n = 25) Mean±SD</th>
<th>Young vs older males, t (p)</th>
<th>Females 18–39 yrs (n = 21) Mean±SD</th>
<th>Females 40–69 yrs (n = 29) Mean±SD</th>
<th>Young vs older females, t (p)</th>
<th>Males vs. Females (all ages), t (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAA</td>
<td>5.7 ± 23.3</td>
<td>4.7 ± 2.69</td>
<td>1.18 (0.24)</td>
<td>4.85 ± 2.45</td>
<td>4.8 ± 1.83</td>
<td>0.08 (0.94)</td>
<td>0.92 (0.36)</td>
</tr>
<tr>
<td>LRVTA</td>
<td>2.24 ± 2.13</td>
<td>2.39 ± 1.64</td>
<td>-0.29 (0.77)</td>
<td>1.58 ± 0.69</td>
<td>2.04 ± 1.42</td>
<td>-1.36 (0.18)</td>
<td>1.47 (0.14)</td>
</tr>
<tr>
<td>%ARE</td>
<td>45.87 ± 13.07</td>
<td>56.29 ± 11.03</td>
<td>-3.2 (0.01)</td>
<td>60.23 ± 8.55</td>
<td>61.31 ± 10.33</td>
<td>-0.29 (0.70)</td>
<td>-4.62 (0.001)</td>
</tr>
<tr>
<td>%E5O</td>
<td>1.34 ± 0.27</td>
<td>1.25 ± 0.18</td>
<td>1.48 (0.14)</td>
<td>1.37 ± 0.2</td>
<td>1.42 ± 0.29</td>
<td>-0.64 (0.52)</td>
<td>-1.94 (0.06)</td>
</tr>
<tr>
<td>PTERIE</td>
<td>0.34 ± 0.09</td>
<td>0.26 ± 0.07</td>
<td>3.67 (&lt;0.001)</td>
<td>0.32 ± 0.09</td>
<td>0.26 ± 0.06</td>
<td>2.62 (&lt;0.05)</td>
<td>0.91 (0.36)</td>
</tr>
<tr>
<td>PTERIVI</td>
<td>0.49 ± 0.09</td>
<td>0.55 ± 0.09</td>
<td>-2.69 (&lt;0.01)</td>
<td>0.5 ± 0.08</td>
<td>0.52 ± 0.07</td>
<td>0.88 (0.38)</td>
<td>-1.13 (0.26)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parameter</th>
<th>(all ages)</th>
<th>Males vs. Females (all ages)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAA</td>
<td>5.7 ± 23.3</td>
<td>4.7 ± 2.69</td>
</tr>
<tr>
<td>LRVTA</td>
<td>2.24 ± 2.13</td>
<td>2.39 ± 1.64</td>
</tr>
<tr>
<td>%ARE</td>
<td>45.87 ± 13.07</td>
<td>56.29 ± 11.03</td>
</tr>
<tr>
<td>%E5O</td>
<td>1.34 ± 0.27</td>
<td>1.25 ± 0.18</td>
</tr>
<tr>
<td>PTERIE</td>
<td>0.34 ± 0.09</td>
<td>0.26 ± 0.07</td>
</tr>
<tr>
<td>PTERIVI</td>
<td>0.49 ± 0.09</td>
<td>0.55 ± 0.09</td>
</tr>
</tbody>
</table>

TAA: Thoraco-abdominal asynchrony (TAA), LRVTA:left vs Right Hemithoracic asynchrony, %E5O: Inspiratory to expiratory flow at 50% of tidal volume calculated from thoraco-abdominal wall displacement, PTERIE: normalised time to reach peak tidal expiratory flow, PTERIVI: normalised time to reach peak tidal inspiratory flow

Imaginative Imaging in Lung Disease

P37 PRELIMINARY NORMAL VALUES FOR STRUCTURED LIGHT PLETHYSMOGRAPHY TIDAL BREATHING PARAMETERS AND AGE AND GENDER DIFFERENCES

Introduction This is the first report from an ongoing study to define normal values for Structured Light Plethysmography (SLP) tidal breathing parameters in adults. Structured Light Plethysmography (SLP) is a non-contact, non-invasive respiratory measurement technology that utilises the movement of thoraco-abdominal (TA) wall to measure a range of tidal breathing parameters. Various studies have been using SLP but lack of normative values can make any clinical judgement difficult.
Methods: As a part of an on-going collaboration between Pneumacare Ltd. and Queen Elizabeth (QE) Hospital (Birmingham, UK), 107 healthy adult subjects between ages of 18 to 69 were measured with SLP during 4 to 5 minutes of seated tidal breathing. Parameter means and standard deviations for males and females aged 18–39 and 40–69 were calculated and gender and age related comparisons were made (t-test).

Results: Tables 1 summarises the normative values for males and females older and younger than 40 years. Three parameters showed age related differences and one parameter showed a gender related difference.

Conclusion: Preliminary normal values for SLP derived tidal breathing parameters are reported. Some gender and age related differences are apparent. It is interesting that tPTEF/tE was significantly lower in the older participants, possibly a sign of natural airway obstruction associated with age.

References
via their N-terminus or side chain amino group with a 6-amino- or a 6-azidohexanoic acid spacer to provide a convenient attachment site for either 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA) or an 2-ethyl-6-[18F]-fluoropyridine prosthetic group for radiolabelling with 68Ga or 18F, respectively. The $\alpha_6\beta_1$-binding capability of these peptide derivatives was assessed by competitive binding enzyme-linked immunosorbent assay (ELISA) and flow cytometry. Peptide derivatives that displayed strong affinity for $\alpha_6\beta_1$ were taken forward to “hot” cell surface binding experiments to evaluate their selectivity for the target. Stability of radiolabelled peptides was measured in human serum.

Competitive binding ELISA experiments (Figure 1) and flow cytometry experiments, showed that cRGD1 and cRGD4 were able to inhibit the binding of $\alpha_6\beta_1$-specific 10D5 mAb to $\alpha_6\beta_1$ with IC50 values of 6.6 nM and 1.6 nM, respectively. Labelling cRGD1 and cRGD4 with fluorine and gallium resulted in IC50 values of 1.2 nM and 1.2 nM for 18F-Pyr-cRGD1 and 68Ga-DOTA-cRGD4, respectively. Serum stability studies of 68Ga-DOTA-cRGD4 have shown that this tracer is >90% stable after 2 half-lives of 68Ga (136 min).

Radiolabelled cyclic RGD peptides have shown favourable binding and stability characteristics to warrant their investigation by PET imaging in vivo. A xenograft murine model using $\alpha_6\beta_1^+\text{ and }\alpha_6\beta_1^–$ tumours is currently under development to validate tracer uptake and biodistribution in vivo.

**Abstract P40 Figure 1** $\alpha_6\beta_1$ competitive binding ELISA between labelled/non-labelled cyclic peptides and the $\alpha_6\beta_1$-specific mAb (clone10D5)

**P41 A PROSPECTIVE COHORT STUDY TO MEASURE IN-VIVO CHANGES IN LUNG GLUCOSE METABOLISM IN PATIENTS WITH SSc-ILD USING FDG-PET**


10.1136/thoraxjnl-2016-209333.184

**Background** Systemic sclerosis (SSc) is a chronic inflammatory autoimmune rheumatic disease with a UK prevalence of 2–10 per 100,000. It is a heterogenous disease characterised by varying degrees of dermal and organ fibrosis. Interstitial lung disease (ILD) occurs in 60–80% of patients and ranges from mild, clinically trivial disease to extensive fibrosis that results in respiratory failure and premature death. Therapeutic options include cyclophosphamide, mycophenylate mofetil and rituximab. Clinical decisions are complex and decisions to treat or not have historically been based on radiology and lung function tests, neither of which (at a single time point) give a dynamic view of disease progression. Novel biomarkers are urgently needed to predict disease activity, progression and response to treatment in patients with SSc-ILD.

**Aims** To investigate the potential of 18F-fluoro-deoxyglucose Positron Emission Tomography (FDG-PET)/CT to act as a prognostic and response biomarker in patients with SSc-ILD.

**Methods** 35 SSc-ILD patients were prospectively recruited for 18F-FDG-PET/CT. Patients were screened for lung involvement using clinical assessment, chest X-ray and pulmonary function testing (PFT). Those with confirmed SSc-ILD underwent combined high resolution CT scan (HRCT)/PET scanning. The imaging signal and clinical findings were correlated with the need for, and response to, therapy. Follow up was with clinical assessment, PFT and when a change in treatment was indicated, repeat imaging.

**Results** The overall maximum pulmonary uptake of 18F-FDG (SUVmax), the minimum pulmonary uptake or background-lung activity (SUVmin) and target-to-background (SUVmax/SUVmin) ratio (TBR) were quantified using routine region-of-interest analysis. Kaplan-Meir analysis was used to identify associations with disease progression and response to treatment.

**Conclusions** We have shown that high pulmonary uptake of 18F-FDG is associated with disease activity and progression in patients with SSc-ILD. These PET findings can be used to give additional information, supplemental to PFTs, which may then aid clinical treatment decisions.

**P42 INCREASED FDG UPTAKE IN AREAS OF ‘NORMAL’ LUNG IN IDIOPATHIC PULMONARY FIBROSIS**

1SA Aliyu, 2G Avery, 1AH Morice, 2SP Hart, 2MG Crooks. 1University of Hull, Hull, UK; 2Hull and East Yorkshire NHS Trust, Hull, UK

10.1136/thoraxjnl-2016-209333.185

**Background** Idiopathic pulmonary fibrosis (IPF) has a variable disease course and we lack biomarkers that accurately predict prognosis or treatment response. Positron Emission Tomography-Computed Tomography (PET-CT) provides structural and functional information about the lung. A study of 25 IPF patients reported increased 18[Fl]-FDG uptake in areas of normal lung compared to controls. If confirmed, this raises the possibility that PET-CT can identify ‘microscopic fibrosis’ with prognostic implications. We assess 18[Fl]-FDG uptake in areas of lung with normal CT appearance in a second IPF cohort.

**Methods** PET-CT scans undertaken for cancer staging at an interstitial lung disease tertiary referral centre were reviewed. IPF patients and controls without lung disease were identified. 18[Fl]-FDG uptake was assessed using manual region of interest (ROI) placement in areas of lung with normal CT appearance. ROI placement was quantified using routine region-of-interest analysis. SUV normalised by body weight. Mean Hounsfield Units (HU) were evaluated to assess subtle differences in radiodensity within ROI. Data are presented as mean ± SD. Unpaired, 2-tailed T-tests were used to compare between group differences with a P value < 0.05 considered significant.

**Results** Forty-five subjects were included in this study (15 IPF and 30 controls). Lung cancer was the most common concomitant malignancy in both groups.

There was no difference in mean HU within ROI between IPF and controls (~719 ± 79 HU in IPF and ~723 ± 147 HU in...
controls, $P = 0.92$), Areas of normal lung in IPF patients exhibited increased 18\textsuperscript{F}-FDG uptake compared to controls measured by maximum SUV (0.98 ± 0.32 in IPF and 0.70 ± 0.20 in controls, $P < 0.01$) and mean SUV (0.80 ± 0.29 in IPF and 0.57 ± 0.18 in controls, $P < 0.01$).

**Conclusions** We confirm that in IPF, areas of normal appearing lung exhibit increased 18\textsuperscript{F}-FDG uptake compared with corresponding areas in controls. A longitudinal study is required to establish the relationship between 18\textsuperscript{F}-FDG uptake, disease progression and treatment response.

**REFERENCE**


**Introduction** Conventional proton MRI, although non-invasive and non-ionising, is of little value in imaging the lungs due to poor signal intensity. Hyperpolarised xenon-129 MRI (129Xe-MRI) is a novel technique developed to enhance the applicability of MRI in lung imaging. It has the potential to provide not only anatomical data but also regional lung function data, particularly as xenon is highly lipophilic, and can be use as a gas exchange probe.

**Aim** We aimed to assess the feasibility and tolerability of 129Xe-MRI in healthy adult volunteers.

**Method** This was a single centre prospective observational study. Ethical approval had been obtained. The volunteers had provided written informed consent. A GE 2000 polariser was used for production of hyperpolarised 129Xe, with a 1.5T GE MRI scanner for imaging.

The volunteers underwent a conventional MRI thorax, followed by 129Xe-MRI of lungs. The inhaled volume of hyperpolarised 129Xe ranged 0.6–1.0L. There was 30 minutes of observation with recording of vital signs, i.e., oxygen saturations (O2 sats), heart rate (HR), and blood pressure (BP) at 5, 10, 15, and 30 minutes post-inhalation of xenon, after each scan. Each visit comprised of a maximum of four scans.

**Results** Nine volunteers (male: female 8:1, aged 20–34) underwent 28 scan visits, comprising of 102 scans. 129Xe-MRI was well-tolerated, with no serious adverse events. The polarisation achieved ranged 4.10–10.57%.

To assess the impact of inhaling xenon on vital signs as a safety measure, the recorded vital signs were analysed using student’s t-test. There was no significant change in O2 sats or BP. The most notable change was noted in HR, which was persistently reduced following inhaling xenon ($p < 0.001$). These changes were not deemed clinically significant.

We achieved good image quality (Figure 1). Spectroscopy distinguished lung tissue-dissolved xenon from blood-dissolved. Dissolved phase imaging (DPI) was obtained. The technique was reproducible.

**Discussion** The data demonstrates satisfactory feasibility and tolerability of 129Xe-MRI. DPI can image regional gas exchange. 129Xe-MRI may be used to develop biomarkers of disease progression, and assess drug efficacy, to personalise medicine, reduce healthcare costs, and lower cost and duration of drug development.

**Abstract P43 Figure 1** 25 mm corona plane (top row) and axial plane 129Xe-MRI of a healthy volunteer
within the last year (stable) and 23 healthy age-matched controls, were recruited. Exclusion criteria included neurological or psychiatric disorders, cerebrovascular disease or hypertension. Cognition was measured using the Montreal Cognitive Assessment. T1-weighted (T1W), diffusion tensor (DTI) and Fluid Attenuated Inversion Recovery (FLAIR) were acquired using a Philips 3T scanner. The following brain indicators were calculated: normalised whole brain and ventricular volumes (scan: T1W, software: SITENAX), white matter microstructural fractional anisotropy and increased mean diffusivity throughout the white matter skeleton, compared to controls (\(p=0.028\)). Hospitalised and stable COPD patients had widespread significant reductions in fractional anisotropy and increased mean diffusivity – compared voxelwise using tract-based spatial statistics (DTI, FSL), and white matter lesion volume (FLAIR, distanced). Ethical approval was obtained (15/LO/0425).

**Results**

Cognition was clinically impaired in hospitalised COPD (median (IQR): 23.0 (5)) but not in stable patients (27.0 (2)) or controls (28.5 (3)), with a significant difference only between hospitalised patients and controls (\(p<0.0001\)). No significant differences were found in normalised whole brain volume, however, normalised brain ventricular volume was significantly greater in hospitalised COPD, compared to stable COPD (\(p=0.046\)) and controls (\(p=0.028\)). Hospitalised and stable COPD patients had widespread significant reductions in fractional anisotropy and increased mean diffusivity throughout the white matter skeleton, compared to controls (\(p<0.001\)). Hospitalised patients had the highest white matter lesion volume, however this was not significantly different between groups.

**Conclusions**

Hospitalised COPD patients have greater cognitive impairment compared to stable COPD and controls with evidence of greater ventricular and white matter lesion volumes and damaged white matter microstructure. Mechanisms behind these neuropathological processes and possible links to observed cognitive dysfunction remain unclear, but may involve ischaemic small-vessel disease.

**Background**

Pulmonary hypertension (PH) is important in COPD as it predicts death and hospitalisation. The diagnosis is made by right heart catheter (RHC). Several predictive cardiac MRI (CMR) models have been proposed to estimate mean pulmonary artery pressure (mPAP):

1. VMI/IVS: \(-4.6 + (\text{interventricular septal angle (IVS) \times 0.23}) + (\text{ventricular mass index (VMI) \times 16.3})\)
2. PA/RV: \(21.806 + (\text{IVS} \times 0.31) + (\text{VMI} \times 11.5)\) + (Diastolic pulmonary artery (PA) area \(\times 0.01) – (\text{PA relative area change} \times 0.22)\)
3. Alpha-index: minimum PA area/right ventricular ejection fraction

The predictive value of these models in a COPD population with suspected PH remains unknown, so we aimed to assess their diagnostic accuracy.

**Methods**

All consecutive patients referred to a PH centre from April 2012 to October 2015 with suspected PH were assessed. Any patient with a formal diagnosis of COPD was included. Sensitivity and specificity were calculated using diagnostic cut-offs published in the literature (VMI/IVS = 32, PA/RV model = 25, alpha index = 7.2). Ethical approval was granted.

**Results**

1864 patients were referred to the PH centre, 145 had a documented diagnosis of COPD, 102 had MRI and RHC within 90 days. All CMR models showed good correlation with RHC measured mPAP (Pearson’s R for (i) VMI/IVS = 0.689, (ii) PA/RV model = 0.732 and (iii) Alpha-index = 0.527). Sensitivity and specificity for (i) VMI/IVS were 92% and 79%, (ii) PA/RV model 80% and 93% and (iii) for Alpha index 100% and 13% respectively. An ROC curve for the diagnosis of PH for each of the models is provided.

**Conclusion**

VMI/IVS and PA/RV models both have good accuracy in the detection of PH in COPD patients. Alpha-index had a low specificity, largely due to a low diagnostic threshold. As such these models are useful in the assessment of PH, and likely prognosis in patients with COPD.
**Abstract P45 Figure 1** ROC comparing all CMRI mPAP predictive models for making a diagnosis of PH

**REFERENCES**


---

**P46 ASSESSMENT OF AORTIC STIFFNESS AND CORRELATION WITH LUNG FUNCTION IN PATIENTS WITH COPD USING CARDIAC MAGNETIC RESONANCE**

1. E De Garate, 2G Biglino, 1A Wilson, 2P Jones, 1C Bucciarelli-Ducci, 1J Dodd. 1NIHR Bristol Cardiovascular Biomedical Research Unit, Bristol Heart Institute, Bristol, UK; 2Division of Clinical Sciences St. George’s University of London, London, UK; 3Academic Respiratory Unit University of Bristol, Southmead Hospital, Bristol, UK

**Introduction:** COPD has been associated with increased cardiovascular risk, although the mechanisms for this are still unclear. Proposed theories include increased systemic inflammation and accelerated ageing resulting in arterial stiffness. We aimed to evaluate aortic distensibility using cardiac MRI in patients with COPD compared to an age-matched non COPD, ‘healthy’ smoker control group.

**Methods** we recruited 49 subjects, of which 27 had diagnosis of COPD and FEV1/FVC < 70%; and 21 age-matched normal smoker controls (mean age 64 years ± 10). We acquired data including age, gender, smoking status, number of packs of cigarettes per year, and FEV1/FVC ratio. MRI images were acquired using a 3.0T scanner, and analysed using CVI42 software. Left ventricle and right ventricle function and volumes were evaluated using short axis SSFP cine. Aortic distensibility was measured using a validated method that takes in consideration aortic maximal and minimal areas from axial SSFP cine acquired perpendicular to the vessel.

**Results** Aortic distensibility was reduced in the COPD patients compared to control (0.0022610 × 10⁻³ mm Hg⁻¹ vs 0.004337 × 10⁻³ mm Hg⁻¹, p = 0.003). The distensibility of descending aorta was similar in both groups (p = 0.06). Ejection fraction and biventricular volumes were also similar in the two groups. Univariate analysis demonstrated a significant relationship between ascending aorta distensibility and FEV1/FVC ratio. There was no difference when comparing distensibility with smoking status or number of packs per year. Linear regression demonstrated that the degree of aortic distensibility was directly proportional to FEV1/FVC ratio

**Conclusion** Patients with COPD have significantly increased aortic stiffness measured by cardiac magnetic resonance. This was observed in the presence of normal LV/RV systolic function in both groups. This difference was related to FEV1/FVC, and was independent of smoking. Preserved FEV1/FVC showed more elastic ascending aortas. Reduced aortic distensibility could represent the early phase changes in cardiovascular function but further research is needed.

---

**Abstract P46 Figure 1** Contouring of ascending and descending aortic area on axial SSFP cine

---

**P47 THE INFLUENCE OF MUSCLE MASS IN THE ASSESSMENT OF LOWER LIMB STRENGTH IN COPD**

1. R Trethewey, 1D Ediger, 1E Petherick, 2R Evans, 3N Greening, 4B James, 1A Kingsnorth, 2M Morgan, 1M Omre, 5S Singh, 3L Sherar, 1N Toms, 6M Steiner. 1WCEM, Loughborough University, Loughborough, UK; 2Respiratory Biomedical Research Unit, Glenfield Hospital, Leicester, UK; 3Institute of Lung Health, Leicester, UK; 4Leicester University, Leicester, UK

**Introduction and objectives** Lower limb muscle strength measured by Quadriceps Maximal Voluntary Contraction (Q MVC) provides valuable functional and prognostic information in people with COPD. Reference equations providing normal values for QMVC have been reported, some requiring measurement of muscle mass. It is unclear whether including muscle mass in the calculation significantly alters predicted values in COPD. We addressed this question by deriving reference equations for QMVC with and without the inclusion of whole body assessment of muscle mass in a cohort of healthy volunteers and
Poster sessions

subsequently comparing QMVC assessment using these reference equations in two separate cohorts of patients with COPD.

Methods Prediction equations were derived through multiple linear regression in a healthy control (HC) group. Age, gender, height and weight were inputted into the first model (FFM–model) and fat-free mass (FFM) added for the other (FFM+ model). The prediction equations were then applied to a Primary Care COPD (PCC) group and Complex Care COPD (CCC) group of patients where percentage predicted values were calculated and weakness determined using a threshold of the lower limit of normal.

Results 175 HC subjects (median (IQR) age: 54 (14) years, 31% male) were recruited. The PCC group comprised 87 patients (median (IQR) age: 68 (9) years, 71% male, FEV1 62 (20)% predicted) and the CCC group 189 patients (median (IQR) age: 68 (9) years, 71% male, FEV1: 29 (16)% predicted).

Prediction values for the HC and PCC were similar between the FFM– and FFM+ models as shown in the table. In the CCC percentage predicted values were lower and there were 11.9% more classed as weak by the FFM– model compared to the FFM+ model.

### Abstract P47 Table 1 QMVC values expressed as percent predicted values and number classed as weak using the FFM– and FFM+ models for the COPD cohorts

<table>
<thead>
<tr>
<th></th>
<th>Healthy control</th>
<th>Primary care COPD</th>
<th>Complex care COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>FFM– Model (%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%pred QMVC:</td>
<td>100.3 (24.1)</td>
<td>86.0 (22.0)</td>
<td>54.0 (16.4)</td>
</tr>
<tr>
<td>Number classed as weak (%):</td>
<td>6 (3.4%)</td>
<td>14 (16.3%)</td>
<td>101 (53.2%)</td>
</tr>
<tr>
<td>FFM+ Model (%):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% pred QMVC:</td>
<td>100.2 (24.1)</td>
<td>86.7 (20.6)</td>
<td>59.2 (17.8)</td>
</tr>
<tr>
<td>Number classed as weak (%):</td>
<td>8 (4.6%)</td>
<td>10 (11.6%)</td>
<td>78 (41.3%)</td>
</tr>
</tbody>
</table>

Mean (SD) values presented as a percentage of the values predicted (%pred) using the FFM– and FFM+ models. Abbreviations: FFM+: fat-free mass included, FFM– fat-free mass not included.

Conclusion The inclusion of fat-free mass did not significantly alter prediction of muscle weakness in the healthy cohort. In the COPD cohorts, including FFM in the model altered the proportion classified as having muscle weakness, most notably in the CCC cohort. This is likely to be due to a higher prevalence of muscle wasting in this population which resulted in an underestimate of predicted strength when muscle mass is included in the model.

P48 RESEARCH BAL USING SINGLE USE DISPOSABLE BRONCHOSCOPE

S Zaidi, A Collins, K Davies, A Wright, E Mitsu, J Reine, J Owohga, S Gordon, O Ferreira, J Rylander, Liverpool School of Tropical Medicine, Liverpool, UK; Royal Liverpool University Hospital, Liverpool, UK; Malawi-Liverpool-Wellcome Trust, Clinical Research Programme, Blantyre, Malawi

Background Broncho alveolar lavage (BAL) is widely used for investigative research to study innate, cellular and humoral immune responses, and in early phase drug trials. Conventional (multiple use) flexible bronchoscopes have time and monetary costs associated with cleaning, and may also carry a small risk of cross infection. Single use bronchoscopes may provide an alternative, but have not been evaluated in this context.

Methods Healthy volunteers underwent bronchoscopy on a day-case clinical research unit using the Ambu® Scope single-use flexible intubation bronchoscope. The bronchoscopy protocol was identical to previous studies using multiple-use equipment: fasted volunteers had local anaesthesia to the nasopharynx, and were intubated with further sequential local anaesthetic (2% lidocaine throughout). Lavage was performed from a sub segmental bronchus within the right middle lobe. A total of 200ml of warmed normal saline divided into four aliquots. Fluid was aspirated using handheld suction. Supplemental oxygen was used to maintain saturations above 90% throughout the procedure. The lab processing of BAL was identical to earlier studies. BAL volume was recorded, mucus plugs removed by filtration through a double layered gauze swab into sterile centrifuge tubes. The cells were pelleted by centrifugation and washed by vortexing in 50 mls of cold normal saline, then re-suspended in culture medium for differential counting and viability staining with trypan blue stain.

Results Ten volunteers, (mean age 23 years, 6 male) participated. The procedure was well tolerated by all the participants and all were carried out by two operators. The results were compared to 50 (mean age 23, 14 male) procedures done using the conventional scope by the same two operators. The total volume yield was significantly higher in the disposable group mean (SD) 149 mls (24.6) compared to 123 mls (20.6) p = 0.0007 Mann-Whitney Test. The total cell yield and viability were similar in both groups, with no significant differences.

Conclusions BAL using single use bronchoscopes are safe with no risk of cross infection, and well tolerated, with potentially reduced side effects post procedure such as pleuritic chest pain and cough as the volume yield is better. The cell yield and viability are comparable to the conventional bronchoscopes.
Introduction Multiple complications in CT-guided lung biopsy have been described with pneumothorax known to be the commonest. This often leads to patients being admitted to hospital for observation or even drainage.

We hypothesised that increased intrathoracic pressure may reduce complications and a comparative retrospective cohort study was performed with the types and rates of complications recorded in patients instructed to perform a Valsalva manoeuvre versus those who were not.

Methods Patients who underwent CT-guided lung or pleural biopsies performed by multiple operators between January 2005 and December 2014 at Queens Hospital, Essex, UK, were retrospectively identified. Information from RIS reports and images from PACS were analysed. Patients were stratified into two groups, those who undertook Valsalva at time of biopsy and those who did not. Complication rates were assessed for haemoptysis, haemothorax and pneumothoraces including those requiring chest drain insertion. Statistical analysis was performed using Chi square test.

Results 791 procedures were performed over 10 years, 420 patients undertook Valsalva manoeuvre with mean ages 71.1 years ±SD 12.54: range 21–91. The other 371 patients did not undertake a Valsalva manoeuvre. Their mean ages were 71.1 years ±SD 11.52: range 27–91.

In total, 119 patients had complications post-procedure: 64 in the non-Valsalva group vs 55 in the Valsalva group (17.25% vs 13.10%, p = 0.05).

Rates of haemoptysis were significantly reduced with Valsalva (2.16% vs 0.24%, p = 0.006). Pneumothorax requiring chest drain (2.70% vs 1.43%, p = 0.10) and those managed conservatively (12.40% vs 11.19%, p = 0.30) were higher in the non-Valsalva group.

Rate of haemothorax (0.24% vs 0%, p = 1) was greater in the Valsalva group.

Conclusion Our study shows that Valsalva manoeuvre at the time of biopsy helps reduce the rate of complications, with a statistically significant decrease in rate of haemoptysis. Rates of pneumothoraces requiring chest drain insertion and other pneumothoraces were also reduced.

The differences could be explained by physiological changes in pulmonary wedge pressure and positive end expiratory pressure brought about by increased intrathoracic pressure following Valsalva manoeuvre.

REFERENCE
Clinical Studies in COPD

PS1 CLINICAL EFFECTIVENESS OF PROCALCITONIN BASED PROTOCOLS TO GUIDE THE ADMINISTRATION OF ANTIBIOTICS IN PATIENTS PRESENTING WITH COPD EXACERBATIONS: SYSTEMATIC REVIEW AND META-ANALYSIS

1AG Mathioudakis, 1V Chatzimavridou-Grigoriadou, 1A Corlateanu, 1 Vesto. 1Institute of Inflammation and Repair, University Hospital of South Manchester, Manchester, UK; 1Respiratory Department, General Hospital of Nikola St. Pantleimon, Piraeus, Greece; 1Department of Respiratory Medicine, State University of Medicine and Pharmacy “Nicola Testemițanu”, Chișinău, Moldova

Abstract P51 Table 1 CTPA usage 2009–2014

<table>
<thead>
<tr>
<th>Year</th>
<th>Annual total no. of CTPAs (% change from 2009)</th>
<th>No. of CTPAs in 6-week reference period (% of annual total)</th>
<th>No. of technically inadequate CTPAs (% of reference scans)</th>
<th>No. of scans positive for acute PE (% of technically adequate reference scans)</th>
<th>No. of scans negative for any diagnosis (% of all reference scans)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>1933 (n/a)</td>
<td>242 (12.3%)</td>
<td>19 (7.9%)</td>
<td>51 (22.9%)</td>
<td>29 (16.1%)</td>
</tr>
<tr>
<td>2010</td>
<td>2317 (+17.4%)</td>
<td>249 (10.7%)</td>
<td>11 (4.4%)</td>
<td>41 (17.2%)</td>
<td>42 (16.9%)</td>
</tr>
<tr>
<td>2011</td>
<td>2561 (+29.8%)</td>
<td>320 (12.5%)</td>
<td>20 (6.3%)</td>
<td>60 (20.0%)</td>
<td>42 (13.1%)</td>
</tr>
<tr>
<td>2012</td>
<td>2759 (+39.8%)</td>
<td>329 (11.9%)</td>
<td>25 (7.6%)</td>
<td>57 (18.8%)</td>
<td>43 (13.1%)</td>
</tr>
<tr>
<td>2013</td>
<td>3017 (+52.9%)</td>
<td>348 (11.5%)</td>
<td>18 (5.2%)</td>
<td>67 (20.3%)</td>
<td>52 (14.9%)</td>
</tr>
<tr>
<td>2014</td>
<td>3302 (+67.4%)</td>
<td>394 (11.9%)</td>
<td>20 (6.1%)</td>
<td>77 (20.6%)</td>
<td>55 (14.0%)</td>
</tr>
</tbody>
</table>

Abstract P51 Table 1 Clinical effectiveness of procalcitonin-based protocols to initiate or discontinue antibiotics in patients presenting with acute exacerbations of COPD

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>No of participants (studies) Follow-up</th>
<th>Quality of the evidence (GRADE)</th>
<th>Relative effect (95% CI)</th>
<th>Anticipated absolute effects</th>
<th>Risk with standard care</th>
<th>Risk difference with Procalcitonin-guided protocols</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failure for the index exacerbation</td>
<td>834 (5 RCTs)</td>
<td>LOW (1,2,3)</td>
<td>RR 0.81</td>
<td>206 per 1,000</td>
<td>39 fewer failures per 1,000</td>
<td>78 fewer to 12 more</td>
</tr>
<tr>
<td>Length of hospital stay for the index exacerbation</td>
<td>1062 (8 RCTs)</td>
<td>MODERATE (1,2,3)</td>
<td>MD – 0.76 (–1.95 to 0.43)</td>
<td>Mean length of hospital stay was 8.55 days</td>
<td>MD 0.76 days lower</td>
<td>(1.95 lower to 0.43 higher)</td>
</tr>
<tr>
<td>Proportion of patients who were prescribed antibiotics on admission</td>
<td>964 (7 RCTs)</td>
<td>MODERATE (1,2,3)</td>
<td>RR 0.56</td>
<td>791 per 1,000</td>
<td>348 fewer prescriptions per 1,000</td>
<td>(451 fewer to 214 fewer)</td>
</tr>
<tr>
<td>Mean duration of the course of antibiotics</td>
<td>776 (6 RCTs)</td>
<td>LOW (1,2,3)</td>
<td>MD – 3.83</td>
<td>Mean duration of course of antibiotics was 8.27 days</td>
<td>MD 3.83 days lower</td>
<td>(4.32 lower to 3.35 lower)</td>
</tr>
<tr>
<td>Exacerbation recurrence rate at longest follow-up</td>
<td>496 (3 RCTs)</td>
<td>LOW (1,2,3)</td>
<td>RR 0.96</td>
<td>205 per 1,000</td>
<td>8 fewer recurrences per 1,000</td>
<td>(63 fewer to 72 more)</td>
</tr>
<tr>
<td>Re-hospitalisation rate at longest follow-up</td>
<td>398 (3 RCTs)</td>
<td>LOW (1,2,3)</td>
<td>RR 1.45</td>
<td>116 per 1,000</td>
<td>52 more admissions per 1,000</td>
<td>(9 fewer to 150 more)</td>
</tr>
<tr>
<td>Rate of re-hospitalisation due to an exacerbiation at longest follow up</td>
<td>298 (2 RCTs)</td>
<td>LOW (1,2,3)</td>
<td>RR 1.22</td>
<td>135 per 1,000</td>
<td>30 more admissions per 1,000</td>
<td>(39 fewer to 147 more)</td>
</tr>
<tr>
<td>Overall mortality at longest follow up</td>
<td>1062 (8 RCTs)</td>
<td>LOW (1,2,3)</td>
<td>RR 0.99</td>
<td>41 per 1,000</td>
<td>0 fewer deaths per 1,000</td>
<td>(18 fewer to 29 more)</td>
</tr>
</tbody>
</table>

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI). CI: Confidence interval; RR: Risk ratio; MD: Mean difference.
between 61.3% and 98.1%. Procalcitonin-based protocols decreased antibiotic prescription (RR 0.56 [0.43, 0.73]) and the total antibiotic exposure (MD –3.83 [−4.32, −3.35]), without affecting clinical outcomes such as rate of treatment failure (RR 0.81 [0.62, 1.06]), length of hospitalisation (MD −0.76 [−1.95, 0.43]), exacerbation recurrence rate (RR 0.96 [0.69, 1.35]) or mortality (RR 0.99 [0.57, 1.70]). However, the quality of the available evidence is low to moderate because of methodological limitations and small overall study population.

Conclusion Procalcitonin-based protocols to guide the administration of antibiotics in patients presenting with AECOPD appear safe and clinically effective. The quality of the available evidence is low-to-moderate because of methodological limitations and small overall population. Thus, additional appropriately designed and powered confirmatory randomised controlled trials are required.

**Abstract P52 Table 1** Relationships between clinical indices of periodontitis and lung function in COPD and AATD

<table>
<thead>
<tr>
<th></th>
<th>COPD</th>
<th>AATD</th>
<th>COPD</th>
<th>AATD</th>
</tr>
</thead>
<tbody>
<tr>
<td>% predicted FEV1</td>
<td>0.085</td>
<td>−0.42</td>
<td>−0.03</td>
<td>−0.52</td>
</tr>
<tr>
<td>p = NS</td>
<td>p &lt; 0.01</td>
<td>p = NS</td>
<td>p &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>% predicted TLCO</td>
<td>−0.06</td>
<td>−0.34</td>
<td>0.01</td>
<td>−0.51</td>
</tr>
<tr>
<td>p = NS</td>
<td>p &lt; 0.01</td>
<td>p = NS</td>
<td>p &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>% predicted KCO</td>
<td>−0.10</td>
<td>−0.30</td>
<td>−0.04</td>
<td>−0.42</td>
</tr>
<tr>
<td>p = NS</td>
<td>p &lt; 0.05</td>
<td>p = NS</td>
<td>p &lt; 0.01</td>
<td></td>
</tr>
</tbody>
</table>

Periodontal indices are correlated with lung function parameters in AATD patients which could reflect the inflammatory and predominantly neutrophilic pathophysiology leading to excessive tissue destruction in both diseases.

**REFERENCES**


**Poster sessions**

**P53** PREDICTING POOR OUTCOMES IN COPD PATIENTS DEEMED ‘LOW RISK’ BY DOSE SCORE

1. LA Rigge, NA Coombs, M Johnson, D Culliford, T Josephs, N Williams, M Thomas, T Wilkinson. NIHR CLAHRC Wessex, University of Southampton, Clinical and Experimental Sciences and University Hospitals Southampton Foundation Trust, Southampton, UK; 2. University of Southampton, Primary Care and Population Sciences, Southampton, UK; 3. NHRI CLAHRC Wessex, Methodological Hub, Southampton, UK; 4. NHRI CLAHRC Wessex, University of Southampton, Primary Care and Population Sciences, Southampton, UK; 5. University of Southampton, Clinical and Experimental Sciences and University Hospitals Southampton Foundation Trust, Southampton, UK.

Introduction COPD continues to cause a substantial symptom, mortality and financial burden in the UK. Current treatment strategies are predominantly reactive as insufficient evidence exists to successfully target clinical resource into pre-emptive ‘early interventions’. The DOSE (dyspnoea, obstruction, smoking status and exacerbation) score has been validated as a risk predictor for mortality, hospitalisation and poorer health status. However, only a small proportion of COPD patients with poor outcomes have high DOSE scores. We sought to establish if clinical characteristics can be used to pre-emptively identify those COPD patients vulnerable to future poor health status by using an electronic database of anonymised patient records—the Hampshire Health Record Analytical Database (HHRA).

Methods Within our HHRA database COPD cohort, we identified a cohort of 6890 patients who fell into the ‘low risk’ category by DOSE score (<4). Within this group, a subset met the criteria for poor COPD outcomes over the next four years, defined as; death (all cause), COPD related hospital admission, a DOSE score increase of ≥2 points or a subsequent DOSE score of ≥4 (high risk). We used logistic regression analysis to examine the association between demographic and clinical characteristics documented by Read code at baseline and those who subsequently fell into the poor outcomes subgroup.
Results In our ‘low risk’ cohort of 6890 COPD patients, 5000 held sufficient data to be included in the analysis. After four years, 2211 (44.2%) of those 5000 patients fell into the poor outcomes subgroup. As shown in Table 1, poor future outcomes were significantly associated with age, high deprivation decile, low BMI, certain comorbidities, a raised eosinophil percentage (>2%) and the prescription (in the preceding twelve months) of nebulised bronchodilators, inhaled bronchodilators and an ICS/LABA combination inhaler. A BMI of >25 and rhinosinusitis were associated with a lower risk of poor future outcomes.

Conclusions Poor future clinical outcomes appear to be associated with certain clinical characteristics in a COPD database cohort deemed low risk by DOSE score. These findings warrant further validation in a clinical cohort and investigation into the effect of pre-emptive optimisation of these characteristics on health outcomes.

Abstract P53 Table 1 Associations between clinical characteristics and odds of future poor clinical outcome

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>OR (n = 51)</th>
<th>OR (n = 50)</th>
<th>OR (n = 36)</th>
<th>OR (n = 36)</th>
<th>OR (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤50 (reference)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>50-59</td>
<td>1.01</td>
<td>1.01</td>
<td>1.01</td>
<td>1.01</td>
<td>1.01</td>
</tr>
<tr>
<td>alden decile** BMI &lt;18</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>25-29</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>30-34</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>35+</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>History of pneumonia</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Heart of Heart Failure</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Cerebrovascular Disease</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Peripheral Arterial Disease</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>History of Heart Failure</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>History of Rhinosinusitis</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Abstract P54 Table 1 Features of multi-morbid clusters

<table>
<thead>
<tr>
<th>Cluster</th>
<th>1 (n = 51)</th>
<th>2 (n = 50)</th>
<th>3 (n = 36)</th>
<th>4 (n = 36)</th>
<th>5 (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.3 ± 8.5*</td>
<td>72.4 ± 8.0*</td>
<td>64.2 ± 9.1</td>
<td>62.0 ± 9.0*</td>
<td>65.4 ± 7.4</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>52.9%</td>
<td>68.0%</td>
<td>52.8%</td>
<td>72.2%</td>
<td>53.3%</td>
</tr>
<tr>
<td>FEV1 (% predicted)</td>
<td>36.4% ± 10.5%</td>
<td>34.5% ± 11.2%</td>
<td>35.6% ± 5.6%*</td>
<td>30.2% ± 9.9%</td>
<td>34.2% ± 9.8%</td>
</tr>
<tr>
<td>Participants using home oxygen (%)</td>
<td>35.3%</td>
<td>42.0%</td>
<td>30.0%</td>
<td>25.0%</td>
<td>53.3%*</td>
</tr>
<tr>
<td>COPD Assessment Test (CAT) score</td>
<td>30 ± 5</td>
<td>24 ± 7</td>
<td>26 ± 6</td>
<td>21 ± 7*</td>
<td>27 ± 5</td>
</tr>
<tr>
<td>Eosinophilia (&lt;0.3) in the past 3 years</td>
<td>45.1%</td>
<td>58.0%</td>
<td>44.4%</td>
<td>55.8%</td>
<td>53.3%</td>
</tr>
<tr>
<td>Antibiotic courses in past year</td>
<td>5.0 [2.0 - 7.0]</td>
<td>4.0 [2.0 - 6.0]</td>
<td>5.0 [2.0 - 7.0]</td>
<td>2.0 [1.0 - 5.0]*</td>
<td>3.0 [2.0 - 6.0]</td>
</tr>
<tr>
<td>Steroid courses in past year</td>
<td>4.0 [2.0 - 7.0]</td>
<td>4.0 [2.0 - 6.0]</td>
<td>4.0 [2.0 - 7.0]</td>
<td>2.0 [1.0 - 5.0]*</td>
<td>3.0 [2.0 - 6.0]</td>
</tr>
<tr>
<td>COPD hospitalisations in past year</td>
<td>1.0 [0.0 - 2.0]</td>
<td>0.5 [0.0 - 2.0]</td>
<td>1.0 [0.0 - 1.0]</td>
<td>0.0 [0.0 - 1.0]</td>
<td>0.0 [0.0 - 1.0]</td>
</tr>
<tr>
<td>Total hospitalisations in past year</td>
<td>1.0 [1.0 - 3.0]</td>
<td>1.0 [0.0 - 3.0]</td>
<td>1.0 [1.0 - 2.0]</td>
<td>1.0 [0.0 - 2.0]</td>
<td>1.0 [0.0 - 2.0]</td>
</tr>
<tr>
<td>Framingham risk (%)</td>
<td>7 ± 5*</td>
<td>12 ± 7*</td>
<td>7 ± 5*</td>
<td>11 ± 7</td>
<td>10 ± 7</td>
</tr>
</tbody>
</table>

Abstract P54 Table 1 Features of multi-morbid clusters

Introduction and objectives Comorbidities have a negative effect upon outcomes in patients with COPD, and ‘phenotypes’ of comorbidity have been described. International guidelines recommend that comorbidities “should be looked for routinely”. We aimed to objectively assess comorbidities, and investigate whether comorbidity phenotypes could be described using cluster analysis, in a cohort of patients with advanced COPD.

Methods Patients with advanced COPD were prospectively recruited to undergo a ‘Comprehensive Respiratory Assessment’ (CRA), as previously described. 13 comorbidities were objectively assessed using validated definitions and their prevalence determined. K-means cluster analysis was applied with the objective measurements, and FEV1%predicted. The clusters formed were compared with respect to demographic features, measures of health status, self-reported exacerbation frequency, and future cardiovascular risk.
**Results** Between June 2013 and December 2015, 246 patients with advanced COPD underwent a CRA: 61.0% male, mean (SD) age 66.0 (9.1) yrs, FEV1/predicted 31.1% (10.4%). 98.4% of participants were in GOLD combined assessment group D. The prevalence of the 13 comorbidities ranged from 68.8% (muscle wasting) to 7.7% (renal impairment). 93.9% of participants had at least two of the assessed comorbidities. Cluster analysis was applied to a subsample of 203 participants with sufficient data: five multimorbid clusters were identified according to a significantly higher prevalence of certain comorbidities: Cluster 1 – psychological disease, Cluster 2 – left ventricular systolic dysfunction and anaemia, Cluster 3 – features of cachexia, Cluster 5 – features of metabolic syndrome and vitamin D deficiency. Cluster 4 had a significantly lower prevalence of comorbidities. Table 1 shows the differences between the five clusters in demographics, airflow limitation, health status, hospital admissions, use of antibiotics and steroids, and future cardiovascular risk.

**Conclusions** In this cohort of patients with advanced COPD, five multimorbid phenotypes were identified. The phenotypes differed significantly in comorbidity prevalence, airflow limitation, health status and future coronary heart disease risk; however the number of hospital admissions in the past year was similar.

**REFERENCES**

**Abstract P55 Table 1**

<table>
<thead>
<tr>
<th>Week 12</th>
<th>Bronchitis</th>
<th>Empysema</th>
<th>Both</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1, AUC0–12h</td>
<td>T/O – P</td>
<td>0.306</td>
<td>0.321</td>
</tr>
<tr>
<td>response</td>
<td>T/O – T</td>
<td>0.097</td>
<td>0.121</td>
</tr>
<tr>
<td>Trough FEV1</td>
<td>T/O – P</td>
<td>0.157</td>
<td>0.178</td>
</tr>
<tr>
<td>response</td>
<td>T/O – T</td>
<td>0.024</td>
<td>0.044</td>
</tr>
<tr>
<td>SGRQ</td>
<td>T/O – P</td>
<td>–6.16</td>
<td>–7.67</td>
</tr>
<tr>
<td>TDI</td>
<td>T/O – T</td>
<td>–2.63</td>
<td>–2.24</td>
</tr>
</tbody>
</table>
| Respiratory Questionnaire (SGRQ) and the Mahler Transition Dyspnoea Index (TDI). Comparisons between T/O 5/5 μg, T 5 μg and P at Week 12 are reported here.

**Results** The numbers of patients included in the analysis were as follows: bronchitis, 506; emphysema, 476; both bronchitis and emphysema, 206. The baseline characteristics of these three groups were generally comparable. After 12 weeks of treatment, there were significant improvements in FEV1, AUC0–3h and trough FEV1 in all groups, with similar improvements across the groups. Significant improvements in SGRQ and TDI occurred in all groups at Week 12 and, again, these seemed to be similar (Table). **Conclusions** T/O 5/5 μg resulted in significant improvements in lung function, dyspnoea and health-related quality of life in patients with moderate to severe COPD with bronchitis, emphysema or both bronchitis and emphysema.

**REFERENCE**

**Funding** Boehringer Ingelheim.

Please refer to page A271 for declarations of interest in relation to abstract P55.

**P56**

**EFFICACY AND SAFETY OF LONG-ACTING BETA AGONISTS + LONG ACTING MUSCARINIC ANTAGONISTS VS. LONG-ACTING BETA AGONISTS + INHALED CORTICOSTEROIDS IN COPD: A META-ANALYSIS**

**Background and significance** Current Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines recommend the use of long-acting beta agonists (LABA) plus inhaled corticosteroids (ICS), or long-acting muscarinic antagonists (LAMA) for the treatment of patients with moderate to severe respiratory disease.
The combination of LABA+LAMA is recently indicated for COPD patients with severe symptoms; however, its role in reducing exacerbations is less clear.

Methods We performed a meta-analysis of randomised controlled trials that compared efficacy and safety of LABA+LAMA versus LABA+ICS in moderate to severe COPD patients. The primary outcome is the rate of COPD exacerbations. Other outcome measures include improvement in trough FEV1, St. George Respiratory Questionnaire for COPD (SGRQ-C) scores, transition dyspnea index (TDI) scores, rescue medication use and pneumonia risk. Analysis was performed in accordance with the Quality of Reporting of Meta-Analyses (QUORUM) guidelines.

Results A total of 6 RCTs with 3370 patients were included. Over-all exacerbation rates were 21% lower in those treated with LABA+LAMA versus LABA+ICS (RR 0.79, [95% CI: 0.66–0.94]). This effect is more pronounced in patients who had >1 exacerbation per year, showing 25% lower exacerbation rates (RR 0.75 [0.60–0.95]) compared to those with no history of prior exacerbations (RR 0.85 [0.61–1.14]). Patients given Indacaterol+Glycopyrronium also experienced lower rates exacerbation versus LABA+ICS (RR 0.71 [0.57–0.89]) compared to those given Umeclidinium+Vilanterol (RR 1.16 [0.68–2.00]).

There were also statistically significant improvements in FEV1 (mean difference 70 mL [95% CI: 0.07–0.07 Liters]), improvement in SGRQ-C (mean difference −0.92 points [−0.95, −0.89]), improvement in TDI scores (mean difference 0.24 [0.23–0.25]) and decrease in use of rescue medications (mean difference −0.20 puffs/day [−0.21, −0.20]). Pneumonia risk was 41% lower in patients given LABA+LAMA compared LABA+ICS (RR 0.59 [0.43–0.80]).

Conclusions The combination of LABA+LAMA is safer and more effective in reducing exacerbations and improving clinical outcomes compared with LABA+ICS in patients with moderate to severe COPD.

Abstract P56 Figure 1

The combination of LABA+LAMA is recently indicated for COPD patients with severe symptoms; however, its role in reducing exacerbations is less clear.

Methods

We performed a meta-analysis of randomised controlled trials that compared efficacy and safety of LABA+LAMA versus LABA+ICS in moderate to severe COPD patients. The primary outcome is the rate of COPD exacerbations. Other outcome measures include improvement in trough FEV1, St. George Respiratory Questionnaire for COPD (SGRQ-C) scores, transition dyspnea index (TDI) scores, rescue medication use and pneumonia risk. Analysis was performed in accordance with the Quality of Reporting of Meta-Analyses (QUORUM) guidelines.

Results

A total of 6 RCTs with 3370 patients were included. Over-all exacerbation rates were 21% lower in those treated with LABA+LAMA versus LABA+ICS (RR 0.79, [95% CI: 0.66–0.94]). This effect is more pronounced in patients who had >1 exacerbation per year, showing 25% lower exacerbation rates (RR 0.75 [0.60–0.95]) compared to those with no history of prior exacerbations (RR 0.85 [0.61–1.14]). Patients given Indacaterol+Glycopyrronium also experienced lower rates exacerbation versus LABA+ICS (RR 0.71 [0.57–0.89]) compared to those given Umeclidinium+Vilanterol (RR 1.16 [0.68–2.00]).

There were also statistically significant improvements in FEV1 (mean difference 70 mL [95% CI: 0.07–0.07 Liters]), improvement in SGRQ-C (mean difference −0.92 points [−0.95, −0.89]), improvement in TDI scores (mean difference 0.24 [0.23–0.25]) and decrease in use of rescue medications (mean difference −0.20 puffs/day [−0.21, −0.20]). Pneumonia risk was 41% lower in patients given LABA+LAMA compared LABA+ICS (RR 0.59 [0.43–0.80]).

Conclusions

The combination of LABA+LAMA is safer and more effective in reducing exacerbations and improving clinical outcomes compared with LABA+ICS in patients with moderate to severe COPD.
from UK public sources and encompassed annual drug costs (£268 FF/VI; £491 usual care), and COPD exacerbation management costs (moderate £114; severe £2,053).

Results Substituting usual care with FF/VI is likely to be associated with reduced COPD medication and exacerbation management costs. Total annual savings of £34,000 were obtained for a population of 1000 patients with COPD.

Conclusion In an everyday UK clinical setting, substituting usual care with FF/VI in patients with COPD can result in substantial annual cost savings. These results are relevant for clinicians and health care organisations.
The potentially inappropriate use of inhaled long-acting beta agonist/corticosteroid (LABA/ICS) combinations in COPD patients for whom this treatment is not recommended has clinical and economic implications. This retrospective analysis of anonymized electronic medical records in the UK Health Improvement Network (THIN) database was conducted to identify factors associated with step-up from long-acting muscarinic antagonist (LAMA) to LAMA+LABA/ICS therapy. Secondary objectives included time to step-up, Global Initiative for Chronic Obstructive Lung Disease (GOLD) and Medical Research Council (MRC) classification. Data were included from COPD patients between 1 June 2010 and 4 September 2014, aged ≥35 years at first LAMA treatment, with continuous enrolment >360 days before the index event (date of first LAMA prescription) who received LAMA monotherapy only prior to step-up. Time to step-up was analysed using a Cox regression model with time-varying covariates using a step-wise model selection procedure.

Data from 8773 patients (6199 LAMA [136 deaths]; 2438 LAMA+LABA/ICS) were included. Multivariable analysis revealed that exacerbations (composite), elective secondary care contact, markers of COPD proactive planned care, and reactive COPD care within the primary care setting were clinically and statistically significantly associated with step-up. Statistically significant factors negatively associated with step-up were being female and having diabetes (Table). Univariate analysis revealed FEV1, COPD severity and MRC classification to be significant predictors of step-up. These were not included in the multivariable model due to reduced observations, but sensitivity analyses including each in turn confirmed the above predictors. 28% of the cohort received step-up therapy, the majority (23%) within 2 years of LAMA monotherapy initiation. Assessment per GOLD classification suggests that step-up was appropriate in most patients (group A, 18%; B, 21%; C, 26%; D, 35%). Assessment of MRC score (mean, median) in the step-up group (baseline: 2.45, 2.00; follow-up: 2.74, 3.00) suggests that patients who were stepped-up became more symptomatic prior to step-up.

These results show that COPD exacerbations were the most significant predictor of therapy step-up and that patients with initially stable disease are unlikely to require step-up. Therapy step-up appears to be appropriate in the majority of, but not all patients, and may reflect adherence to national guidelines.

---

**Abstract P59 Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariate Cox Regression Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR</td>
</tr>
<tr>
<td>Composite: exacerbations a</td>
<td>2.380</td>
</tr>
<tr>
<td>Elective secondary care contact</td>
<td>1.445</td>
</tr>
<tr>
<td>Markers of COPD proactive planned care within primary care setting</td>
<td>1.268</td>
</tr>
<tr>
<td>Reactive COPD care within primary care setting</td>
<td>1.155</td>
</tr>
<tr>
<td>Composite: cardiovascular b</td>
<td>1.150</td>
</tr>
<tr>
<td>Number of cough symptoms</td>
<td>1.086</td>
</tr>
<tr>
<td>Number of short-acting bronchodilator prescriptions</td>
<td>1.033</td>
</tr>
<tr>
<td>Age at index date c</td>
<td>0.992</td>
</tr>
<tr>
<td>Sex (female)</td>
<td>0.798</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.685</td>
</tr>
</tbody>
</table>

aExacerbations (COPD emergency admission or AECOPD or lower respiratory tract infection or oral corticosteroid + antibiotic). bCombined comorbidity for cardiovascular risk (heart failure, congestive heart disease, hypertensive disease, cerebrovascular disease, aneural fibrillation). cHR relative to change to every 1 year difference in age.

---

**P60**

**EFFECT OF INDACATEROL/GLYCOPYRRONIUM (IND/GLY) ON PATIENT-REPORTED OUTCOMES IN MEN AND WOMEN WITH COPD: A POOLED ANALYSIS FROM THE IGNITE PROGRAMME**

K Kostikas, A Tisiaggianni, S Fucile, K Mezi, S Shen, D Banerji, R Fogel. Novartis Pharma AG, Basel, Switzerland; cClinic of Social and Family Medicine, University of Crete, Heraklion, Crete, Greece; dNovartis Pharmaceuticals Corporation, East Hanover, NJ, USA

Introduction

Literatures, although limited, suggest differences in the manifestations of COPD in terms of symptoms and health-related quality of life between men and women. Moreover, a
Abstract P60 Table 1  Effects of IND/GLY on PROs in men and women compared with other comparators at Week 26

<table>
<thead>
<tr>
<th>Parameters</th>
<th>IND/GLY vs SFC</th>
<th>IND/GLY vs GLY</th>
<th>IND/GLY vs TIO</th>
<th>IND/GLY vs PBO</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men Women</td>
<td>Men Women</td>
<td>Men Women</td>
<td>Men Women</td>
</tr>
<tr>
<td>TDI total scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.46</td>
<td>0.65</td>
<td>0.23</td>
<td>1.31</td>
</tr>
<tr>
<td></td>
<td>(0.06, 0.85)</td>
<td>(0.12, 1.43)</td>
<td>(0.23, 0.68)</td>
<td>(0.52, 2.10)</td>
</tr>
<tr>
<td>SGRQ total scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.93</td>
<td>-1.93</td>
<td>-1.36</td>
<td>-2.83</td>
</tr>
<tr>
<td></td>
<td>(-2.53, 0.66)</td>
<td>(-4.92, 0.16)</td>
<td>(-2.57, -0.14)</td>
<td>(-4.91, -0.75)</td>
</tr>
<tr>
<td>Symptom scores (total) via e-diary</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.37</td>
<td>0.06</td>
<td>-0.34</td>
<td>-0.40</td>
</tr>
<tr>
<td></td>
<td>(-0.82, 0.09)</td>
<td>(-0.60, 0.73)</td>
<td>(-0.60, -0.08)</td>
<td>(-0.82, 0.02)</td>
</tr>
<tr>
<td>Rescue medication use</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.14</td>
<td>-0.03</td>
<td>-0.01</td>
<td>-1.22</td>
</tr>
<tr>
<td></td>
<td>(-0.45, 0.17)</td>
<td>(-0.74, 0.67)</td>
<td>(-0.89, -0.43)</td>
<td>(-1.66, -0.78)</td>
</tr>
</tbody>
</table>

*p < 0.05; †p < 0.01; ‡p < 0.001; ††p < 0.0001; data presented as LSM (95% confidence interval); e-diary, electronic diary; IND/GLY, indacaterol/glycopyrronium (110/50 µg once daily); SGRQ, St. George’s Respiratory Questionnaire; TDI, transition dyspnoea index; TIO, tiotropium (18 µg once daily)

Introduction Many patients who are prescribed home oxygen are symptomatic from progressive, life-limiting disease. The GMC recommends “if cardiac or respiratory arrest is an expected part of the dying process and CPR will not be successful, making and recording an advance decision not to attempt CPR will help to ensure that the patient dies in a dignified and peaceful manner”. In addition, patients who are at risk of death or declining are identified on the gold standard framework (GSP) and future care planned according to their wishes.

Objectives To investigate whether patients prescribed oxygen in the community had Do Not Attempt CPR (DNACPR) discussed and recorded; and secondly to investigate the length of time these patients were on oxygen and had DNACPR discussed/recorded prior to death.

Methods Patients who died between January and June 2016 on home oxygen were identified from the Stockport Home Oxygen Service records. The Stockport Health Record (SHR) and GP practices were consulted to find patients’ primary diagnoses and DNACPR status.

Results 43 patients (mean age 73.8 ± 1.8) were identified. The overall median (range) length of time on home oxygen was 191 (5–3617) days. 14 (32.6%) had a community DNACPR form.

Conclusion Patients are prescribed home oxygen for many reasons and for variable amounts of time. For many the prescription represents a deterioration in their health. In our cohort of patients only 32.6% had DNACPR discussed/present at death, and median survival after initiation of oxygen was only 191 days.
We propose that the prescription of home oxygen can be used as a trigger for discussion of a community DNACPR form. As well as planning for their death, the hope is that this discussion can also prompt planning for the final weeks and months of life, such as wills, advanced directives and preferred place of care.

REFERENCES

P62 AVOIDING INAPPROPRIATE PRESCRIBING OF HIGH DOSE INHALED CORTICOSTEROID COMBINATION INHALERS – IS THE MESSAGE GETTING THROUGH?

1V Mak, 2G D’Ancona. 1Imperial College Healthcare NHS Trust, London, England – on behalf of London Respiratory Network; 2Gays and St Thomas’ NHS Foundation Trust, London, UK

10.1136/thoraxjnl-2016-209333.205

Introduction In the UK, over a third of asthma patients are treated at BTS step 4 or 5 with similar suggestions of over use of high dose inhaled corticosteroids (ICS), equivalent to ≥1000 micrograms beclomethasone dipropionate, in patients with COPD. This has resulted in the highest dose ICS (HDICS-licensed daily dose equivalent to 2000 micrograms beclomethasone dipropionate) with long-acting Beta_2-agonist combination inhalers consistently appearing in the top five costliest drugs to the NHS. The London Respiratory Team have shared their concerns regarding the potential harm and waste associated with this practice; hence, many prescribing initiatives have been implemented to optimise ICS use through appropriate step down or ICS withdrawal. However cost-saving interventions such as generic prescribing have also been implemented.

Aims To ascertain whether any reduction in spend on HDICS combinations is due to treatment optimisation or generic switches.

Methods Monthly prescription cost analysis data available from the NHBSA website (http://www.nhsbsa.nhs.uk) for the latest 15 months were analysed for the quantities prescribed and associated cost (Net Ingredient Cost) of all of the HDICS combination inhalers currently available.

Results In 2015–16, the monthly spend on all HDICS combination inhalers fell from around £20million/month to £18million/month, and number of items fell from around 400,000/month to 365,000/month. By the last quarter, the switch from high cost HDICS combinations to lower cost ones accounted for 15% of all HDICS combinations, saving around £0.75million/month.

Conclusion The message around inappropriate use of high dose ICS is beginning to filter through. Savings have been made from both switching to lower cost HDICS combination products and reduction in total numbers prescribed. Some of these saving will be offset by some patients being prescribed lower cost, lower dose ICS combinations.

However the reduction in high dose prescribing is less than 10% of the total number prescribed. Given the extent of overuse, further harm and waste reduction can be made by reviewing the appropriateness of high dose ICS combinations prescribing in asthma and COPD with can lead to significant cost savings and improve value.

REFERENCES
Introduction

Endobronchial lung volume reduction with one-way valves (ELVR), in combination with staged unilateral VATS lung volume reduction surgery (LVRS), multiplicates the options of treatment for emphysema. No experience has yet been reported in literature of the use of LVRS after failure of ELVR. We aimed therefore to review our current series.

Methods

7 consecutive patients (3 male, age 68, 59–76) had successful Chartis assessment and ELVR, and subsequently underwent salvage LVRS following failure or complications of primary procedure. All patients were suitable candidates for either approach according to our criteria (average RV/TLC 67 range 56–77, FEV1 32% range 25–38, DLCO 32%, range 24–55), with 4 patients classifying as moderate to high risk for LVRS and the rest as moderate or low. They were offered both options and opted for ELVR on the assumption of reduced risks and shorter hospitalisation. Valves were not removed prior to LVRS, except in one case who was also the first chronological patient in our series.

Results

Delayed collateral ventilation with no lobar collapse and no functional improvement at any time was observed in 3 patients. The remainder had lobar collapse with initial improvement: of these, 1 developed ipsilateral pneumothorax with persisting air leak leading to LVRS, 2 developed contralateral upper lobe compensatory hyperinflation (1R, 1L) and 1 ipsilateral lower lobe compensatory hyperinflation.

No significant morbidity or 30-day/in-hospital mortality. Median length of stay after LVRS was 11 days (4–34), slightly longer (19 days, 4–34) for patients who were operated for contralateral hyperinflation or whose EBV was removed prior to VATS (no valve in situ on the operated side). Duration of drainage was also longer in these patients compared to the whole group, 18 (6–30) vs. 8 (5–30) days. Average EQ-5D score was 49.7 (18.9–71) six months after LVRS, vs. 42 (18.9–81.4) preoperatively, with only one patient reporting further deterioration.

Conclusion

ELVR can be considered as a trial of LVR not precluding salvage LVRS. Removal of endobronchial valves prior to surgery seems unnecessary and may actually be protective against excessive postoperative air leak. Occurrence of compensatory hyperinflation may suggest that single-stage bilateral ELVR could also be considered.

Sleep Apnoea and Non-invasive Ventilation

Introduction

Sleepiness is a subjective symptom, often reported by patients with sleep disorders. We investigated subjective measures of sleepiness, as measured by the Epworth Sleepiness Scale (ESS), and correlated this to objective observations, as recorded by the mean sleep latency (MSL). We related our findings to affect, fatigue, emotion, mood, and quality of life.

Patients and methods

Patients referred to a tertiary referral centre for sleep disorders were assessed regarding their sleep complaint, excessive daytime sleepiness (EDS), sleep routine and night-time symptoms. Age, gender and BMI were recorded. The ESS (0–24 points), the Stanford Sleepiness Scale (SSS; 0–8 points), the Samn-Perrelli fatigue scale (SPS; 0–7 points), the Global Vigour and Affect Scale (GVS and GAS 0–10 points, respectively), the Hospital Anxiety and Depression Scale (HADS-A and HADS-D 0–21 points, respectively), and the Positive and Negative Affect Schedule (PAS and NAS 10–50 points, respectively).
respectively) were recorded. Patients underwent polysomnography (PSG) and multiple sleep latency tests (MSLT).

**Results**

9 patients (5 male/4 female, age 44.1 (14.6) years, BMI 30.5 (6.7) kg/m²; obstructive sleep apnoea (OSA, n = 4), narcolepsy (n = 2), idiopathic hypersomnia (n = 1), insomnia (n = 1), no sleep disorder (n = 1)) were studied. The PSG results showed a short total sleep time (TST 360.1 (69.7) min) with a slightly reduced sleep efficiency (SE 79.6 (11.4)%), there were no relevant periodic limb movements (PLM index 7.3 (4.3)/h) but mild-moderate OSA (apnoea-hypopnoea index (AHI) median 6.4 (interquartile range 0.2–30.5)/h). The ESS was 13.9 (7.2) points, the MSL was 7.6 (5.9) min, the SSS was 3.0 (1.3) points and the SPS was 4.0 (1.3) points. The GVS was 4.8 (2.2) points and the GAS was 5.6 (2.2) points, the HADS-A was 8.7 (6.2) points and the HADS-D was 8.9 (5.9) points, the PAS was 23.9 (10.7) and the NAS was 25.6 (8.0) points. There was a positive correlation between the ESS and the SPS, but no other significant correlations (Table 1).

**Conclusion**

The ESS and the MSL did not correlate well, nor did they relate to measures of affect, emotion, mood, or quality of life. Conversely, there was an interaction between measures of fatigue and the ESS. These findings emphasise the need to develop better scores to characterise EDS, other than the ESS.

**Abstract P65 Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Spearman’s rho correlation coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ESS</strong></td>
<td><strong>MSL</strong></td>
</tr>
<tr>
<td>MSL</td>
<td>r = 0.086 / p = 0.872</td>
</tr>
<tr>
<td>SSS</td>
<td>r = -0.980 / p = 0.802</td>
</tr>
<tr>
<td>SPS</td>
<td>r = 0.675 / p = 0.045*</td>
</tr>
<tr>
<td>GVS</td>
<td>r = 0.160 / p = 0.682</td>
</tr>
<tr>
<td>GAS</td>
<td>r = 0.370 / p = 0.237</td>
</tr>
<tr>
<td>HADS-A</td>
<td>r = 0.479 / p = 0.192</td>
</tr>
<tr>
<td>HADS-D</td>
<td>r = 0.207 / p = 0.594</td>
</tr>
<tr>
<td>PAS</td>
<td>r = 0.172 / p = 0.658</td>
</tr>
<tr>
<td>NAS</td>
<td>r = 0.768 / p = 0.160</td>
</tr>
</tbody>
</table>

*p<0.05.

**Introduction**

In 2013 a BTS survey showed substantial variability in the advice that patients with obstructive sleep apnoea syndrome (OSAS) would be likely to receive from clinicians with regard to whether they were fit to drive or not. Since then the BTS has issued guidance and the DVLA changed its emphasis to sleepiness “likely to impair safe driving”, rather than sleepiness in general. The survey was divided into two parts, the first focusing on patients at presentation and the second after treatment, with the wording of the questions reflecting that used in the DVLA forms. We repeated this study in 2016 to assess whether these changes had resulted in greater consistency. Additional questions about BTS and DVLA guidance were included.

**Methods**

Web based survey of members of BTS, BSS and ARTP.

**Results**

304 respondents. The vignettes at diagnosis are directly comparable between the surveys and the results are very similar (p = NS). In the most contentious case there remains an approximately 50:50 chance of a patient receiving opposing advice.
Significant variation in the assessments of control of patient’s condition, improvement in sleepiness and compliance after treatment remains (Figure 1). 2 36% were not aware that the BTS have issued a statement 63% felt the change in emphasis from excessive sleepiness to sleepiness likely to impair safe driving helpful. 64% of respondents were not aware that DVLA had changed its guidance in January 2016. 18% of respondents advise patients to inform the DVLA when diagnosis felt to be likely based on symptoms. 57% when diagnosis confirmed following investigation, 13% when CPAP first trialled and 12% when CPAP issued to the patient.

Conclusions The results of the 2016 survey confirm the results of the 2013 survey. Disappointingly the guidance from the BTS appears to have had little impact. The change in emphasis from excessively sleepy to sleepiness likely to impair safe driving was felt to be helpful by a small majority. There is a clear need for tools which are felt to be robust by clinicians and patients to help make decisions about fitness to drive and for these to be disseminated to clinicians.

A limitation of this audit is that not all clinicians record discussions about driving even though it is important for medicolegal purposes.

Conclusion Driving safety discussions on referral can be improved by educating GPs/secondary care and introducing an Alert on eReferral. The Sleep Clinic should use a pro forma to remind clinicians to discuss driving regardless of a patient’s ESS or diagnosis.

### FALING ASLEEP WHILE DRIVING: IS DRIVING SAFETY ADVICE GIVEN TO PATIENTS WITH EXCESSIVE DAYTIME SLEEPINESS?

A Khetarpal, K Anderson, S West. Regional Sleep Service, Newcastle upon Tyne Hospitals, Newcastle upon Tyne, UK

10.1136/thoraxjnl-2016-209333.209

**Background** 3.5 million people in the UK have excessive daytime sleepiness and 1 in 5 Road Traffic Accidents are due to sleepiness while driving.

**Aim** To improve Patient and Public safety by auditing whether DVLA’s driving safety advice is given to patients with excessive daytime sleepiness in two settings: (i) at referral as recommended by The Royal Society for the Prevention of Accidents guidelines and (ii) at the Regional Sleep Clinic as recommended by the BTS guidelines.

**Method** Retrospective study between 01/10/15 and 06/01/16 of (i) 100 referral letters to the Regional Sleep Clinic and (ii) 100 sleep clinic letters to patients’ GP. In both cases, patients were included if the letter mentioned ‘Daytime sleepiness’ or if their Epworth Sleepiness Score (ESS) was over 10 (indicating excessive daytime sleepiness).

**Results** Only 19% of referral letters from primary and secondary care had documented giving driving safety advice to patients with daytime sleepiness. Sixteen specialties referred patients to the Sleep clinic. General Practice accounted for three quarters of these referrals and driving safety had only been discussed in 14% of cases. Even with specialties like Respiratory medicine and Neuropathy which see patients with sleep disorders regularly, few had discussed driving safety.

The Sleep Clinic gave DVLA advice to 85% of patients. In the 15% where no advice was given, patients usually had ESS <10 (but symptomatically sleepy) or sleepiness as a secondary consequence of insomnia/non-REM parasomnia.

7 patients reported falling asleep while driving (only 2/7 were discovered at referral). Moreover, the Sleep Clinic noted that 1 had a Road Traffic Accident and 1 had a near miss. Average waiting time from referral to Sleep Clinic appointment was 3 months. Thus driving advice needs to be given at referral.

### IS THERE A DIFFERENCE BETWEEN THE SLEEP PHYSIOLOGY OF OBESE AND SUPER OBESE PATIENTS?

A Rajhan, L Michael, A Bain, A Thomas, M Allen. University Hospital of North Midlands, Stoke-On-Trent, UK

10.1136/thoraxjnl-2016-209333.210

**Introduction** Bariatric surgery is increasingly recommended for managing patients who are both obese and super obese (BMI ≥45 ref. WHO Classification). We have compared if there are physiological and subjective differences between these two categories.

**Methods** Patients assessed for bariatric surgery were split into the super obese and obese group. Their physiological parameters including Apnoea Hypopnoea Index(AHI), Desaturation Index (ODI >4%) and subjective results i.e., Epworth Sleepiness Score (ESS) and STOPBANG Questionnaire were compared.

**Results** 111 patients assessed for bariatric surgery attended for limited sleep studies from a period between July 2013 to December 2014. 57 patients were obese (40 females) and 54 were superobese (37 females) and the results are tabulated below. (Table 1)

The superobese patients had a higher AHI, ODI and time spent desaturated when compared to the obese patients.

**Conclusion** 1) There is more physiological derangement in the super obese patient group so greater caution is needed in the administration of anaesthetic to such patients.

2) Despite the physiological derangement, superobese patients were less sleepy based on their ESS, the reasons for which are not entirely clear.

### Abstract P67 Table 1

<table>
<thead>
<tr>
<th></th>
<th>Obese (n = 57)</th>
<th>Super obese (n = 54)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>ODI &gt; 4%</td>
<td>20.64</td>
<td>18.78</td>
<td>31.46</td>
</tr>
<tr>
<td>Time spent &lt;90%</td>
<td>8.03</td>
<td>14.78</td>
<td>12.93</td>
</tr>
<tr>
<td>Time spent &lt;85%</td>
<td>1.85</td>
<td>7.66</td>
<td>2.99</td>
</tr>
<tr>
<td>AHI</td>
<td>21.71</td>
<td>19.67</td>
<td>31.49</td>
</tr>
<tr>
<td>ESS</td>
<td>8.85</td>
<td>5.2</td>
<td>6.72</td>
</tr>
<tr>
<td>STOPBANG</td>
<td>Median – 3</td>
<td>IQR 2–4</td>
<td>Median – 5</td>
</tr>
<tr>
<td>Mallampatti Score</td>
<td>Median – 3</td>
<td>IQR 2–4</td>
<td>Median – 3</td>
</tr>
</tbody>
</table>

SD – Standard Deviation IQR – Interquartile Range

### TO SCREEN OR NOT TO SCREEN FOR OBSTRUCTIVE SLEEP APNOEA (OSA) PRE-OPERATIVELY?

1CD Turnbull, 2 D Ball, 3 M Estavez, 4 H Du Plessis, 5 M Harding, 6 A Nicol. 1Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Foundation Trust, UK; 2Department of Anaesthetics, Oxford University Hospitals NHS Foundation Trust, UK; 3Hospital Clinico San Carlos, Madrid, Spain

10.1136/thoraxjnl-2016-209333.211
Background Anesthesia worsens OSA, and may lead to respiratory and cardiac complications. Three critical incidents have occurred in the Oxford Hospitals in recent years. OSA is very common at around 5–25%, but half the cases are not diagnosed. So should we screen for OSA pre-operatively?

Audit Over 9 months from July 2015 all patients completed a STOP-BANG questionnaire in a gynaecology pre-operative clinic. Those with snoring and a score of 3 or greater were referred for a sleep study. Data is presented for 102 patients (100 female; 2 transgender) with a mean ± SD age of 55.7 ± 11.4 yrs, BMI 35.8 ± 7.6 kg/m² and collar size 40.0 ± 4.8 cm.

The rate of non-attendance was high at 19/102 (19%), with those with a lower STOP-BANG score being more likely not to attend. Of those undergoing a sleep study, a new diagnosis was made in 53/83 (62%) patients. Symptoms and OSA/hypventilation were sufficient for CPAP to be started in 13 patients and NIV in 1 (29% of those screened), with positive diagnoses more likely with higher STOP-BANG scores. The median (IQR) time to CPAP set-up was 80 (52, 100) days, thus a substantial proportion of patients had surgery before treatment.

How should we ensure anaesthetic safety for patients at risk of OSA?

Completing a sleep study and establishing OSA patients on CPAP prior to surgery would significantly slow the surgical pathway, and there is no evidence that this would improve outcome. However it seems sensible for anaesthesia of all patients deemed at risk of OSA (STOP-BANG 3+) to be managed with special precautions. We pragmatically recommend that all patients found to have a STOP-BANG score of 5+ or strong clinical suspicion of OSA, who are undergoing major surgery AND in whom it is reasonable to delay surgery, are referred for a sleep study prior to surgery. Patients with a STOP-BANG of 3+ not falling into this category should be informed they are at risk of OSA, and advised to seek a referral from their GP to the sleep clinic if they find symptoms of sleepiness troublesome.

Background Undiagnosed Obstructive Sleep Apnoea (OSA) has been associated with a higher perioperative morbidity and mortality. The aim of this study is to prepare a comprehensive review of the STOPBANG score, a pre-operative screening tool for patients with possible OSA. The study investigates if the current STOPBANG threshold of ≥3/8 is appropriate, or if it should be increased to ≥5/8 or ≥4/8 (with 4/8 in the STOP category) to avoid the unnecessary cancellation/postponement of surgery and inappropriate referrals into the sleep service.

Methods This was a retrospective study of patients referred to the Sleep Service following a positive STOPBANG score (≥3). The Research and Development Department of the hospital deemed the study did not require ethical approval. 84 patients were included in the study. The selected patients’ case notes were used to review their STOPBANG score, Epworth Sleepiness Score, type of sleep study performed, Oxygen Desaturation Index (ODI), diagnosis and treatment. If the patient had an ODI ≥ 15, or was successfully started on treatment with a borderline ODI 5 < 15, this was considered an appropriate referral for that threshold.

The sensitivity and specificity of the different STOPBANG thresholds were calculated to assess if the threshold score of STOPBANG ≥3 is appropriate, or if this should be adjusted to more appropriately identify those patients with OSA.

Results For a threshold of ≥3, the sensitivity is very high (100%). The specificity is decreased for the threshold of ≥5 (71%), and further decreased for the ≥4/8 (3 from STOP) threshold (53%). For the ≥3 threshold, the specificity is 0%. The specificity is dramatically increased for the ≥5 threshold (70%), and highest in the ≥4/8 (3 from STOP) category (83%).

Conclusion The statistical analysis confirms that a threshold of ≥3 has a very high sensitivity, but very low specificity. A threshold of ≥5 has a lower sensitivity however is much more specific and may be a more useful way of identifying the high risk of OSA surgical patient. A change in protocol to ≥5 aims to reduce the unnecessary delay or cancellation of surgery and avoid inappropriate referrals into the Respiratory and Sleep department.

P70 CPAP COMPLIANCE IN BARIATRIC PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA

1PSP Cho, 1A Rainey, 1B Mukherjee, 1KK Lee. 1King’s College Hospital NHS Foundation Trust, London, UK, 2Division of Asthma, Allergy and Lung Biology, King’s College London, London, UK

10.1136/thoraxjnl-2016-209333.213

Introduction CPAP compliance is a challenge in the management of obstructive sleep apnoea (OSA). Pre-operative screening with a sleep questionnaire for OSA followed by sleep studies is common in bariatric services. The King’s bariatric service performs overnight pulse oximetry in all patients considered for surgery. Therefore, additional cases may be detected in patients with lower clinical suspicion. We hypothesised that CPAP compliance in bariatric patients with OSA confirmed by routine screening would be lower than that seen in patients referred to the sleep clinic for suspected OSA.

Method Case records of all bariatric patients screened for OSA over a 16-month period were reviewed, and CPAP compliance data retrieved for those with confirmed OSA who commenced CPAP therapy. Retrospective case-control analysis was made against 50 randomly selected patients from the sleep clinic that commenced CPAP for confirmed OSA within the same study.
period. CPAP compliance at 4 weeks was compared between the two groups.

**Results**

409 patients were screened through the bariatric pathway during the study period. 49 (12.0%) patients were diagnosed with OSA and were commenced on CPAP. Baseline characteristics of the bariatric and sleep clinic groups are shown in Table 1. There was no significant difference between gender, baseline overnight desaturation indices and baseline Epworth Sleepiness Scale scores between the two groups.

21 (42.9%) patients in the bariatric group used their CPAP for ≥75% of nights within the 28-day period compared with 25 (50.0%) patients in the sleep clinic group; p = 0.48. There was a trend to significance for proportion of patients who used CPAP for mean ≥4 hours per night (20 (40.9%) patients in the bariatric group vs 29 (58.0%) patients in the sleep clinic group; p = 0.087).

**Conclusion**

Our study suggests that the number of patients who are compliant with CPAP at mean use of ≥4 hours per night may be lower in those with confirmed OSA found on routine screening within a bariatric pathway than in patients referred to a sleep clinic, but our finding was limited by the small sample size. Future study to investigate this trend and its underlying causes could improve the success of intervention in the bariatric patients.

---

**Abstract P70 Table 1** Baseline and compliance data of bariatric and sleep patients. Data presented as median (inter-quartile range) or n(%). BMI: body mass index; ODI: overnight desaturation index; ESS: Epworth Sleepiness Score.

<table>
<thead>
<tr>
<th></th>
<th>Bariatric (n = 49)</th>
<th>Sleep (n = 50)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>49 (42-52)</td>
<td>56 (44-63)</td>
<td>0.012</td>
</tr>
<tr>
<td>Gender (F:M)</td>
<td>29:20</td>
<td>20:30</td>
<td>0.056</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>49.9 (46.4-55.9)</td>
<td>42.3 (33-48.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline ODI</td>
<td>31.1 (22.3-43.7)</td>
<td>41.0 (21.5-61.6)</td>
<td>0.280</td>
</tr>
<tr>
<td>Baseline ESS</td>
<td>12 (8-15)</td>
<td>11 (7.5-15)</td>
<td>0.504</td>
</tr>
<tr>
<td>Proportion of</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>patients with ≥75% of nights</td>
<td>21 (42.9%)</td>
<td>25 (50.0%)</td>
<td>0.476</td>
</tr>
<tr>
<td>CPAP use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>patients with mean use of ≥4 hours per night</td>
<td>20 (40.9%)</td>
<td>29 (58.0%)</td>
<td>0.087</td>
</tr>
</tbody>
</table>

**Discussion**

Our data suggests that patients with lower ODIs are more likely to have supine predominant OSA. At ODI values over 40 it is very unlikely that there is a posturally dependant component to a patient’s OSA. However, the reverse is not the case; although many patients with low ODIs do have a postural component, many do not. It is therefore necessary to objectively assess the degree of supine predominant OSA in future trials of positional therapies, but patients with ODIs over 40 could be excluded at the outset.
The ROSA trial (Retinopathy and Obstructive Sleep Apnoea) is a multi-centre randomised controlled trial conducted in the United Kingdom. The hypothesis is that CPAP (continuous positive airway pressure) will improve visual acuity in people with diabetic macular oedema and concurrent OSA, due to improvements in intermittent hypoxia, blood pressure and catecholamine surges. An uncontrolled study showed visual acuity improved equivalent to one line on the logMAR chart in those people who used CPAP regularly at six months (Mason RH et al. Respiration 2012). We present baseline data from a larger randomised controlled trial.

**Methods**
Patients of Eye Hospitals across the UK with diabetic macular oedema and type 2 diabetes were offered home sleep studies to diagnose OSA. These were posted to them with instructions by the coordinating centre and returned by post after a single night’s recording. Those patients found to have severe OSA (ODI > 20 or AHI > 30), along with visual impairment due to diabetic macular oedema were randomised to usual ophthalmic care (control) or usual ophthalmic care plus CPAP for one year. Anyone with respiratory failure, excessive daytime sleepiness requiring urgent treatment or cataract precluding ophthalmic assessment was excluded. Follow up occurred at three, six and twelve months and included measures of sleepiness, health related quality of life, visual acuity, optical coherence tomography and retinal photography.

**References**

**Abstract P72 Table 1**

<table>
<thead>
<tr>
<th></th>
<th>CPAP N = 64</th>
<th>Control N = 66</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.3 (10.5)</td>
<td>63.7 (8.0)</td>
<td>n.s.</td>
</tr>
<tr>
<td>% male</td>
<td>67</td>
<td>79</td>
<td></td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>34.9 (8.7)</td>
<td>35.1 (6.3)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Neck circumference (cm)</td>
<td>42.2 (4.1)</td>
<td>44.9 (4.0)</td>
<td>0.017</td>
</tr>
<tr>
<td>Duration of diabetes (years)</td>
<td>16.3 (8.7)</td>
<td>15.2 (9.5)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Hba1c (mmol/l)</td>
<td>67.0 (17.5)</td>
<td>66.7 (23.1)</td>
<td>n.s.</td>
</tr>
<tr>
<td>Oxygen desaturation index/hr</td>
<td>37.2 (18.3)</td>
<td>35.9 (15.1)</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

**Results**
There have been 130 patients randomised from 23 UK centres; 64 to CPAP, 66 to control. The groups are well matched at baseline (Table).

**Conclusions**
This novel study demonstrates that it is feasible to conduct a multicentre randomised controlled trial with UK Eye Hospitals and their local Sleep service, all coordinated by a single centre (Newcastle). The UK NHS National Institute for Health Research has facilitated this research via the Local Clinical Research Network at each centre. Minimisation criteria for randomisation has enabled the two groups to be well matched at baseline, essential for this type of study. The results of this trial will determine whether CPAP could form a novel treatment for diabetic macular oedema and visual impairment in people with concurrent obstructive sleep apnoea; these results are eagerly awaited when follow up is completed in 2017.
there were 11 Grade 2 pressure ulcers from 109 admissions; in period 2 there were 5 pressure ulcers from 105 admissions. Benefits of using total face masks for NIV delivery were also noted with those patients who were poorly complaint with the standard NIV full face mask to prevent treatment failure.

Conclusions An early prophylactic pressure-relieving dressing and a reactive change to a pressure-avoidance mask for identified Grade 1 pressure sore, can reduce the chance of developing Grade 2 pressure ulcers for patients using NIV acutely. Further studies including longitudinal data on a proactive prevention approach adjusted for acute NIV duration for NIV-related nasal bridge pressure ulceration are needed to confirm the utility of this approach.

**P74** NON-INVASIVE VENTILATION DELIVERED ON A STANDARD RESPIRATORY UNIT COMPARED TO USE IN LEVEL 2 CARE SETTING: IS THERE AN IDEAL SERVICE DELIVERY MODEL?

1A Jayadev, 2M McEvie, 3I Moonsie. 1The Royal Free Hospital, London, UK; 2North Middlesex University Hospital, London, UK

10.1136/thoraxjnl-2016-209333.217

Introduction BTS guidelines recommend Non-Invasive Ventilation (NIV) should take place in a clinical environment with enhanced monitoring, predicting 20% of all cases may need level 2 or 3 care. However, current practice varies between and within NHS organisations. A management led service change within our Trust in 2013 enabled us to test the null hypothesis that there is no significant difference in mortality of COPD patients requiring NIV on an open respiratory-led unit (level 1 care), compared to a closed, anaesthetist led Level 2 setting (PCU, Progressive Care Unit).

Methods An electronic search was performed to find patients on PCU whom received NIV between 1st January and 30th November 2014. Inclusion criteria were patients that had received NIV for COPD exacerbations solely. Data from the physician led respiratory unit between Jan–Nov 2011 was prospectively collected, and the two datasets compared.

Results In the respiratory unit 75 patients were admitted for NIV of which 54 met the criteria for inclusion in the analysis. In the PCU group 110 patients were admitted between Jan–Nov 2014. of which 55 were included for analysis.

Samples were matched in gender, with no significant difference between groups. The average age of patients treated in PCU was 69.8 years, and 74.4 years on the respiratory unit, which is statistically significant (Mann-Whitney U Test, p = 0.012). The mortality on PCU was 27.2% compared to 20.4% on the respiratory unit, which was not statistically significant. Mean pH on PCU was 7.33 compared to 7.24 on the respiratory unit, which is statistically significant. Mean pCO₂ was 10.06 on PCU, and 10.5 on the respiratory unit, which is statistically significant. Average length of stay of ward patients was 15 days, compared to 11.4 days on PCU, which was not statistically significant.

Conclusions NIV delivered on a physician-led respiratory unit was not inferior in mortality and length of stay compared with a closed, ITU-led service. Interestingly we found a significant difference in age of patients being treated with NIV, with significantly older patients receiving this on ward with no difference in overall mortality.

**REFERENCE**


**P75** PATIENT EXPERIENCE OF NON-INVASIVE VENTILATION: A QUALITATIVE STUDY

N Goldman, L Richardson, S Blakey, L Staveacre, SAA Bloch. Imperial College Healthcare NHS Trust, London, UK

10.1136/thoraxjnl-2016-209333.218

Introduction Non-invasive ventilation (NIV) is an effective treatment for acute type 2 respiratory failure, often avoiding intubation and improving mortality. However many patients struggle to tolerate NIV. There is limited understanding of patients’ or their relatives/carers subjective experience of NIV. As good patient experience is increasingly recognised to reflect high-quality care we conducted an in-depth experience-based questionnaire aiming to identify key concerns of patients, and their relatives/carers, treated with NIV, which would reflect potential targets for service improvement.

Method In a qualitative, exploratory study patients started acutely on NIV were identified. Patients and relatives/carers completed a questionnaire with both free text and Likert style responses. Data were analysed using thematic analysis.

Results 20 questionnaires were completed (15 patients, 5 relatives). From the responses we identified key themes. Emotional responses were positive and negative. Positively - all patients and carers felt that NIV had helped. However whilst all carers would wish their relatives to have NIV again, 2 of the patients felt they would not. Negative emotional responses were related to fear and anxiety of NIV. A significant theme emerged surrounding the physical discomfort of NIV. Descriptions of NIV are represented in Figure 1. Patients and relatives identified that negative feelings were partly due to lack of understanding. Only 9 patients felt that they were involved in decision making and only 6 felt that NIV had been adequately explained. 11 patients and all relatives felt that written information would be beneficial. Finally a further theme described different levels of competence between staff and across wards and the varying degrees of feeling safe that this created.

Conclusion This study enabled us to identify key areas to address when considering quality improvement for NIV service delivery. Whilst our sample size is small, and biased towards survivors, the themes are strong and add significantly to the available literature. Some aspects of NIV are non-modifiable however focus on patient involvement and experience should facilitate improved experience and outcomes. We aim to address these points by expanding on this work in an experience-based co-designed project, funded by CLAHRC.
Abstract P75 Figure 1  Word-cloud to represent patient experience of NIV (n = 15 patients, 5 relatives). (Size of word is proportional to the frequency of use of word in response to being asked to describe NIV. Black association with negative experience grey with positive).

P76 INITIATION OF LONG-TERM NON-INVASIVE VENTILATION (NIV) IN A SPECIALIST RESPIRATORY FAILURE UNIT IN THE UK

SJ Telfow, P5 Marino, PD Murphy, H Pattari, J Steier, N Hart. Lane Fox Respiratory Unit, St Thomas’ Hospital, London, UK
10.1136/thoraxjnl-2016-209333.219

Introduction and objectives There are currently no guidelines for the provision of long-term NIV and little data into the settings and interfaces employed by different centres. Our aim was to assess long-term NIV provision in a Specialist Respiratory Failure Unit (SRFU).

Methods A retrospective observational study was performed of all patients commenced on long-term NIV by the SRFU. Data was collected from electronic patient records and technician databases on all initiations from August 2014 to January 2015.

Results Data was obtained from 113 patients. Oronasal masks were used in 87% of patients, nasal pillows in 10%, total face masks in 2% and nasal masks in 1%. Oronasal masks were used to deliver higher inspiratory positive airway pressures (IPAP) (mean ± SD 23.3 ± 5.3 cm H2O). Nasal interface use was associated with lower IPAPs (mean ± SD 12.5 ± 4.5). A relatively higher IPAP was applied at initiation to the study group (mean ± SD 22.3 ± 6.2 cm H2O) but this varied according to diagnosis; patients with obstructive sleep apnoea (OSA), chronic obstructive pulmonary disease (COPD) and motor neurone disease (MND) received a mean ± SD IPAP of 24.3 ± 5.4 cm H2O, 23.4 ± 4.2 cm H2O and 12.4 ± 3.6 cm H2O respectively.

Conclusions Oronasal masks were predominantly used reflecting the frequent application of IPAPs above 20 cm H2O as high pressures are poorly tolerated with nasal interfaces. High mean IPAPs were used in OSA and COPD patients, whilst lower IPAPs were administered to MND patients. No guidelines exist for long-term NIV use, with practice on the SRFU differing from the British Thoracic Society’s guidelines on acute NIV that recommend a pressure target of 20 cm H2O (Royal College Of Physicians et al. Concise Guidance to Good Practice Series, 11). However, the relevance of these guidelines to long-term NIV provision is unclear, and the lack of data has impeded the development of specific guidance. A database of patients receiving long-term NIV in the UK would facilitate research and the formulation of evidence-based best practice guidelines.

REFERENCE

How can we improve lung cancer pathways?

P78 TACKLING EMERGENCY LUNG CANCER ADMISSIONS

RV Reddy, Y Vali, M Naeem. Kettering General Hospital, Kettering, UK
10.1136/thoraxjnl-2016-209333.221
**Introduction** A significant proportion of lung cancer patients present as an emergency. This is associated with poor one year survival. Many of these patients have had contact with health services before presenting as an emergency. It is estimated that one in five lung cancer patients have an unplanned admission before their urgent clinic appointment.  

**Objective** To reduce the number of emergency lung cancer admissions by providing an effective alternative ambulatory pathway for high risk patients.  

**Methods** Patients referred on the two week wait pathway are veted by the respiratory physicians. Those identified as having a high risk of admission are prioritised and reviewed urgently on the ambulatory care unit usually by the next working day. Patients with the following features were expedited:

1. Superior vena caval obstruction  
2. Liver function abnormalities  
3. Large tumour burden on chest radiograph  
4. Severe symptoms such as pain and breathlessness  
5. Large pleural effusion.  

Patients with suspected lung cancer presenting to the emergency department were also re-directed to the ambulatory care unit whenever feasible. We evaluated the service for a period of 12 months prior to the commissioning of the ambulatory care unit in June 2013. As part of the service, the team developed an innovative lung cancer diagnostic service utilising ultrasound guidance to facilitate early diagnosis.  

**Results** Table 1 demonstrates the resulting drop in unplanned lung cancer admissions and length of stay. We estimate a cost saving of £170,000 based on a 710 bed-day reduction (£300/bed day) after taking into consideration physician time. If rolled out nationally, reducing the admission rate to 34% of the lung cancer incidence will avoid 6800 admissions (>55,000 bed-days) with significant cost savings and benefits to patients.  

**Conclusion** Flexible pathways are cost effective and prevent emergency admission of lung cancer patients which is associated with high mortality. This novel approach is easily adoptable widely and would have a significant impact across NHS.  

**REFERENCE**  

### Table P78 Table 1

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence of lung cancer</th>
<th>Total no. of admissions (% of lung cancer incidence)</th>
<th>Length of stay (Total bed-days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kettering 2012–13</td>
<td>195</td>
<td>108 (55%)</td>
<td>11.6</td>
</tr>
<tr>
<td>England Hospital 2012–13</td>
<td>33,231</td>
<td>18,878 (56%)</td>
<td>8.9</td>
</tr>
<tr>
<td>General 2014–15</td>
<td>195</td>
<td>67 (34%)</td>
<td>8.1</td>
</tr>
<tr>
<td>England Hospital 2014–15</td>
<td>30,765</td>
<td>17,281 (56%)</td>
<td>8.9</td>
</tr>
<tr>
<td>Wales &amp;</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Aim** A new pathway to enable quicker lung cancer diagnosis for the 4 district health boards within one of the cancer networks in New Zealand was developed incorporating rapid access clinics (RACs), with upfront PET-CT scans for those considered potentially curable at initial assessment.  

**Methods** In this 12-week pilot, patients graded as high suspicion of lung cancer were seen in RACs with spirometry, performance status assessment and available radiology (chest X-ray or CT scan). Those considered potentially curable by surgery or radiotherapy (FEV1 >1 litre, ECOG score <2, no evidence of mediastinal lymphadenopathy or metastasis on imaging, no comorbidities precluding radical treatment) received an upfront PET-CT scan; those who were not received a standard CT scan if not already done. These protocols were based on the virtual model proposed by the Gleeson group, Oxford, UK. Time through the pathway was measured and compared with historical data from the regional lung cancer database in a 6 month period the year before the pilot.  

**Results** One hundred and sixty five patients completed the pathway, of which 105 were found to have lung cancer. Forty one patients had upfront PET-CT scans; 30 were confirmed as lung cancer, 7 of which subsequently had palliative treatment. Eleven had non-lung cancer diagnoses (9 not cancer or nodule follow up; 1 metastasis; 1 other cancer). Seventeen patients had PET-CT scans later in the pathway, 4 of which subsequently had curative treatment. Median time from referral to first treatment was reduced by 16.7 days (patients with curative treatment intent 17.2 days and palliative treatment intent 12.7 days), significantly reducing both the time from referral to multidisciplinary meeting (MDM) and MDM to first treatment. Achievement of 62-day target referral to treatment targets was 85.7% compared with 56.6% in the historical data.  

**Conclusion** Regional lung cancer pathway incorporating RACs and upfront PET-CT scans for curative track patients resulted in improvements in diagnostic delays and 62-day treatment targets. These findings subsequently led to implementation of this pathway regionally.  

The study was funded by a New Zealand Ministry of Health project grant.  

**REFERENCE**  

---

**P79** SINGLE POINT OF ACCESS CLINIC (SPOAC): A NEW REGIONAL LUNG CANCER PATHWAY IN NEW ZEALAND

1. P Dawkins, 1J McWilliams, 1R Sullivan, 1Middlemore Hospital, Auckland, New Zealand; 2Northern Regional Alliance, Auckland, New Zealand; 3Auckland City Hospital, Auckland, New Zealand

10.1136/thoraxjnl-2016-209333.222

**Aim** A new pathway to enable quicker lung cancer diagnosis for the 4 district health boards within one of the cancer networks in New Zealand was developed incorporating rapid access clinics (RACs), with upfront PET-CT scans for those considered potentially curable at initial assessment.  

**Methods** In this 12-week pilot, patients graded as high suspicion of lung cancer were seen in RACs with spirometry, performance status assessment and available radiology (chest X-ray or CT scan). Those considered potentially curable by surgery or radiotherapy (FEV1 >1 litre, ECOG score <2, no evidence of mediastinal lymphadenopathy or metastasis on imaging, no comorbidities precluding radical treatment) received an upfront PET-CT scan; those who were not received a standard CT scan if not already done. These protocols were based on the virtual model proposed by the Gleeson group, Oxford, UK. Time through the pathway was measured and compared with historical data from the regional lung cancer database in a 6 month period the year before the pilot.  

**Results** One hundred and sixty five patients completed the pathway, of which 105 were found to have lung cancer. Forty one patients had upfront PET-CT scans; 30 were confirmed as lung cancer, 7 of which subsequently had palliative treatment. Eleven had non-lung cancer diagnoses (9 not cancer or nodule follow up; 1 metastasis; 1 other cancer). Seventeen patients had PET-CT scans later in the pathway, 4 of which subsequently had curative treatment. Median time from referral to first treatment was reduced by 16.7 days (patients with curative treatment intent 17.2 days and palliative treatment intent 12.7 days), significantly reducing both the time from referral to multidisciplinary meeting (MDM) and MDM to first treatment. Achievement of 62-day target referral to treatment targets was 85.7% compared with 56.6% in the historical data.  

**Conclusion** Regional lung cancer pathway incorporating RACs and upfront PET-CT scans for curative track patients resulted in improvements in diagnostic delays and 62-day treatment targets. These findings subsequently led to implementation of this pathway regionally.  

The study was funded by a New Zealand Ministry of Health project grant.  

**REFERENCE**  

---

**P80** SYMPTOMS, DELAY TO PRESENTATION AND SURVIVAL IN LUNG CANCER

1. WY Chan, 2A Clark, 1U Dernedde, 1T Roques, 1M Burton, 1J Kotecha, 1A Wilson, 1C Martin. 1Norfolk and Norwich University Hospital, Norwich, UK; 2University of East Anglia, Norwich, UK; 3James Paget University Hospital, Norwich, UK

10.1136/thoraxjnl-2016-209333.223
**P81**

**STRAIGHT TO CT DELIVERS EARLIER FIRST DEFINITIVE TREATMENT IN LUNG CANCER—EFFECT OF A SIMPLE INTERVENTION**

*P Malhotra, P Murphy, C Dawson, N Hunt, J Hendry. St Helens and Knowsley Teaching Hospitals NHS Trust, Prescot, UK*

10.1136/thoraxjnl-2016-209333.224

**Background** The National Optimal Lung Cancer Pathway (NOLCP) recommends performing a CT scan before a patients first appointment in a rapid access suspected lung cancer clinic. A local audit in 2014 at our hospital which receives over 350 two week rule suspected lung cancer referrals per year found that less than 50% of patients had a CT scan before their first appointment.

**Objective** To determine the effect of a simple cue for physicians stamped on 2 week rule referral forms on the proportion of patients who have a CT scan before their first appointment in a rapid access suspected lung cancer clinic, and its effect on the time to definitive treatment.

**Methods** This was a retrospective analysis of the lung cancer clinic database at a large district general hospital. Two periods were audited: September – November 2014 (pre-intervention), and July – September 2015 (post-intervention). Data on demographic characteristics, date of first clinic, date of performance of CT scan, and time to definitive treatment was collected. From January 2016 onwards, a simple new intervention was put in place: all 2 week rule referrals were stamped with a cue (“Pre-clinic CT: Yes or No?”) for Consultants triaging the referral to prompt them to arrange a pre-clinic CT scan if appropriate. Re-audit was carried out during the period July–September 2015.

**Results** Seventy-six out of 81 two week rule referrals between September–November 2014 had a CT scan during their management pathway. Thirty-six (47%) of these scans were performed before the patients first appointment in clinic. Re-audit between July–September 2015 after introduction of the stamp revealed that 88 CT scans were performed on 101 two week referrals. Of these, 70 (80%) patients had a CT scan before their first appointment.

Time to first definitive treatment improved by 1 week from 38.7 days in the pre-intervention cohort, to 31.5 days in the post-intervention cohort.

**Conclusion** A simple cue stamped on 2 week rule referral forms increased the proportion of patients who had a CT scan before their first appointment in a rapid access suspected lung cancer clinic from 47% to 80%, and reduced the time to definitive treatment by 1 week.

---

**P82**

**OUTCOMES FOR PATIENTS WITH NEGATIVE SCANS ON THE ‘STRAIGHT TO CT’ PATHWAY**

*H Gundersen, A Hufton, R Trafford, MJ Walshaw, M Ledson. Liverpool Heart and Chest Hospital NHS Foundation Trust, Liverpool, UK*

10.1136/thoraxjnl-2016-209333.225

**Introduction** Liverpool has a ‘straight to CT’ service for patients with coded radiology suspicious of lung cancer and for clinicians worried symptoms may indicate malignancy. In our pathway the lung cancer team automatically take patients whose CT suggests lung cancer. For patients whose scan does not suggest cancer the result is forwarded to their GP to act upon as necessary. We have investigated the outcomes for this patient group for the calendar year 2015.

**Method** 387 CT scans were carried out on the 72 hour ‘straight to CT’ pathway. The cancer services took 179 patients. We have reviewed local radiology, result datasets and hospital records for the remaining 208 patients whose CT results were managed by their GP.

**Results** Within the group without suggestions of cancer on CT, indications for 72 hour CT were: 90 patients (43%) had coded radiology and 118 ‘worried clinician’ (57%) (23% haemoptysis; 34% other symptoms). The results of the CT scans showed 42 (20%) nodules requiring follow up, 49 (23.5%) inflammatory changes, 49 (23.5%) nil significant, 20 (10%) emphysema, 11 (5%) bronchiectasis and 37 (18%) combinations of other (fibrosis, PE, atelectasis etc). For follow up 17 (8%) were already under the care of a chest physician, 74 (36%) were referred to a chest physician and 117 (56%) were managed in primary care. 73 patients (35.1%) had repeat CT scans. In total 99 scans have been done, 31.3% of these were ordered by primary care 68.7% by...
secondary care. 4 patients following repeat imaging were diagnosed with cancer. 3 of these had nodules initially, 1 had inflammatory shadowing.

**Conclusion** The ‘straight to CT’ pathway dictates that all patients with a CT scan not suggestive of lung cancer remain under the care of the referring clinician. Only 35% of patients subsequently needed referral for secondary care advice. The ‘straight to CT’ service not only provides prompt action for patients with cancer but empowers primary care to manage non-malignant diseases. Patients are now managed in the most appropriate setting and inappropriate hospital visits minimised.

**Introduction** In 2014 we introduced in conjunction with our primary care colleagues a “straight to CT” protocol for patients with suspected lung cancer, to not only to speed up the diagnostic pathway but also to reassure at an early stage patients without the disease. However, some clinicians suggested that this approach may increase the burden of CT scans performed without improving cancer care.

**Method** “Straight to CT” is available for patients with a CXR coded as concerning for malignancy, or via a general practitioner with concerns based on symptoms and risk factors. Following radiologist review, if appropriate scans are offered within 72 hours: scan positive cases are reviewed by the lung cancer team for onward next investigation, and where the scan is negative the referral is faxed by radiology back to the GP. We compared 2015 data with that for 2014, looking for route of referral, investigations performed, and outcome.

**Results** In 2015 [2014] 464 [468] were eligible for the “straight to CT” pathway. Of these 258 (56%) [246, 53%] coded chest X-rays and 206 (44%) [222, 47%] ‘worried clinician’ referrals.

Of the coded CXRs, 24 [22] patients (9%)[9%] declined further investigation. Of the 234 [224] who accepted a 72hr hour CT scan, 149 (64%) [119, 53%] had confirmed cancer.

Of the 206 [222] ‘worried clinician’ referrals, 21 (10%) [16, 7%] patients declined further imaging or assessment, and 32 (16%) [29, 13%] were deemed inappropriate. Of the 153 [177] remaining who went on to have 72 hour CT scans only 29 (19%) [42, 24%] had cancer confirmed.

Overall, 387 [401] CT scans were carried out. 178 [187] patients were accepted by the cancer services, and 209 [214] patients remained under primary care.

**Cancer conversion rates for accepted patients was 70% [79%]**

**Conclusions** This study has shown that the burden placed on radiological services has remained constant during the two years of our innovative service, and we had previously shown that introducing this protocol did not increase the overall number of scans. We recommend this pathway to other lung cancers units as a way of improving their diagnostic pathway.

---

**P84** THE RELATIONSHIP BETWEEN UNADJUSTED REFERRAL TO TREATMENT TIMES, DISEASE STAGE AND SURVIVAL IN LUNG CANCER

SA Hodgson, KG Blyth. Respiratory Medicine at the Queen Elizabeth University Hospital, Glasgow, UK

10.1136/thoraxjnl-2016-209333.227

**Introduction and objectives** Cancer waiting times (CWT) targets have helped hospital services evolve to meet the needs of Lung Cancer patients. However, these outcomes are adjusted to allow for perceived clinical complexity or deviation from a ‘standard’ diagnostic journey. Few patients breach CWT targets in our unit. We performed a retrospective audit to determine the actual time our patients spent on diagnostic pathways and how this related to disease stage and survival.

**Methods** 377 consecutive patients who presented with Lung Cancer during 2013 were identified from our MDT database. 243/377 (64%) presented as an inpatient and were excluded. 22/134 GP referrals were excluded (insufficient records, aborted investigation (clinical deterioration, patient preference), incomplete staging) leaving 112 cases. Demographics, histology, referral-to-treatment (RTT), referral-to-diagnosis (RTD) and diagnosis-to-treatment (DTT) times were recorded. Overall Survival (OS) based on RTT times and Stage was assessed using Kaplan-Meier methodology.

**Results** 82/112 (73.2%) patients had non-small cell lung cancer, 18 (16.1%) had small cell lung cancer and 12 (10.7%) were radiologically-diagnosed. 48/112 patients (42.9%) had stage I to IIIA disease. Mean RTD, RTT and DTT times were 43 (SD 55), 69 (SD 45) and 26 (SD 51) days, respectively.
RTD time was <31 days in 57/112 cases (50.8%). 31.6% of these were Stage I-IIIA, compared with 54.5% Stage I-IIIA when RTD was >31 days.

RTT time was <62 days in 59/112 cases (52.7%). 25.4% of these were Stage I-IIIA, compared with 62.3% Stage I-IIIA when RTT was >62 days.

RTT time was <62 days in 15/48 (31.3%) Stage I-IIIA patients and <62 days in 44/64 (68.8%) patients with Stage IIIB-IV.

Conclusions Despite few CWT breachers, RTT times were frequently >62 days suggesting pathway adjustments have a major impact. Patients with earlier stage disease, and the most to lose from diagnostic delay had longer diagnostic journeys. The survival disadvantage of short pathways likely reflects stage mix. Pathway redesign to accelerate the complex diagnostics needed for radially-treatable disease should be considered. CWT adjustments may have unintentionally clouded this issue.

**P85 VIRTUAL LUNG CANCER CLINIC: EARLY EXPERIENCE AND FEASIBILITY**

IF Faccenda, LD Calvert, SO Brj. Peterborough City Hospital, Peterborough, UK

10.1136/thoraxjnl-2016-209333.228

**Background** With increased public awareness, cough campaigns and incidental nodules on computed tomography (CT), referrals on a Lung Cancer Pathway (LC) have risen significantly. Safe and effective methods to transfer patients to Respiratory Pathways (RP) are essential.

**Aims** To evaluate a chosen and book, virtual Lung Cancer Clinic (VLCC) to facilitate non-face-to-face “blind” rapid patient assessment, next investigation and appropriate outpatient review.

**Methods** A retrospective review of all referrals during the period March–May 2016 was undertaken to assess whether blind clinical decision-making at point of referral was sufficient to plan ongoing management.

**Results** 60 referrals were reviewed in VLCC by a Lung Cancer Consultant Physician (average time from referral 2 days, range 0–4 days) as their first 2 week wait appointment. 17 (28%) patients had a final diagnosis of Lung Cancer (histological 12, radiological 5).

Only 29/60 (48%) were of an acceptable quality for blind decision making. 16 (27%) referrals did not have sufficient information provided to allow any decision to be made and further information from the GP was requested. 26 referrals (43%) were removed from CP onto RP at VLCC review: 14 did not require a CT; 12 scans were undertaken (7 high resolution CT, 1 CT pulmonary angiogram, 4 staging CT), 8 prior to clinic attendance.

34 referrals (57%) remained on CP: 30 (88%) proceeded to staging CT with average wait 12 days (range 3–17 days) from referral, all performed prior to clinic attendance. 1/34 died prior to clinic attendance. 3/34 were scanned before VLCC. A further 8 referrals were removed from CP after imaging. Thus, only 36/60 (60%) referrals were seen in the Lung Cancer Clinic. There was appropriate pathway change in 30% of referrals to General Respiratory (25%) and Pleural Clinic (5%).

**Conclusion** The VLCC can effectively assess and plan next investigation with appropriate clinic follow-up for suspected Lung Cancer patients. However, blind decision-making relies upon good clinical information from the referrer and administrative time can be wasted chasing this. Our data confirms that the VLCC facilitates efficient use of Out-patient and Radiology Services.

**Abstract P86 Figure 1** Number of patients triages high/intermediate/low with benign or malignant disease
In order to speed up the diagnostic pathway, in January 2014 we set up a “straight to CT” service for patients with suspected lung cancer from primary care, where positive scans undergo immediate chest physician review to decide the next diagnostic test and a lung cancer nurse specialist (CNS) offers the patient a telephone assessment to plan this. We have looked at the utility of this “virtual clinic” in the management of our patients with lung cancer over the first 2 years, in particular paying attention to patient uptake and satisfaction, and outcomes.

Of about 300 patients annually who have been triaged in this way, 82% have chosen the virtual clinic, 13% preferred or the CNS advised an outpatient appointment, 4% required immediate inpatient referral, and the remaining 1% were referred back to the GP as outpatient intervention not felt appropriate (too unwell). Overall, 75% subsequently were diagnosed with lung cancer.

For those patients who chose the virtual clinic consultation, feedback has been overwhelmingly positive. This has been captured qualitatively at the time and at subsequent events e.g. patients report feeling well informed and supported, and quantitatively at an ongoing survey: 98% prefer the telephone clinic versus clinic appointment, 97% felt prepared for next test.

This study has shown that performing a number of diagnostic investigations using a telephone support is not only feasible but preferred by patients with suspected lung cancer. By avoiding unnecessary clinic attendances it improves patient convenience, speeds up the diagnostic pathway and reduces unnecessary costs. This early CNS assessment and interventions reduces the level/scoping of patient concerns prior to the time of diagnosis, this has further significance to the team formalising the Holistic Needs Assessment process.

CNSs are best placed to do the consultations as they have the specialist skills and knowledge of the local clinical pathways, tests, disease symptomology and ultimately provide the continuity throughout the diagnostic pathway through to treatment and we recommend this to other cancer units.

Methods

We surveyed a majority of hospitals (six NHS trusts) in our region about their current follow-up practice. A retrospective study was performed of patients in our trust who underwent curative surgery for NSCLC between March 2013 and December 2014.

Results

None of the surveyed trusts were following ESMO or ACCP guidelines. Only two had a local policy in place. The majority used chest X-ray (CXR) rather than CT follow-up, which reflected our practice.

We identified 79 patients who had undergone surgery with curative intent in our trust. 5 patients were excluded, as notes were unavailable for 2, and 3 died before any follow-up. Amongst the remaining 74 patients, follow-up was for a mean of 19 months. During this time the mean number of CTs and CXRs per patient was 1.3 and 2.7 respectively. Following ESMO guidelines would reduce the number of CT scans compared to our overall current practice, to 1.1 per patient, whilst ACCP guidelines would result in an increase to 2.7 CTs per patient.

Conclusions

Most patients in our region are followed-up by CXR rather than CT. Most hospitals are not using follow-up guidelines, resulting in practice variation. Compared to current practice in our trust, following ESMO guidelines would not result in an increase in CT scans for this purpose, and no CXRs would be required for routine follow-up. Therefore it may be feasible to adopt this more uniform, evidence-based approach.

REFERENCES

pancreatic insufficient and pancreatic sufficient children (−0.05 vs −0.36, p = 0.29) however a significant difference was observed in rate of weight gain from birth to first clinic visit (−0.1 vs −0.33, p = 0.007). Time taken for children to reach a z score of 0 for weight was 65 weeks and length was 90 weeks. Cluster analysis identified two distinct groups of children. Faecal elastase (FE) being the main determinant of class, with a cut off of 212 mg/g. Our models can predict weight z score at 1 and 2 years with a mean absolute error of 0.51 and 0.67 and length z scores at 1 and 2 years with an accuracy of 0.7 and 0.85. The most important factor when predicting future nutritional parameters was birth weight z score.

**Conclusions**

We have developed and validated models that can provide a good estimate of weight and height z scores in the first 2 years of life for children diagnosed with CF by NBS. These models only require data available at the first clinic visit. They can potentially be used by clinicians to identify children at risk of poor nutritional outcomes thus, encouraging closer monitoring and earlier intervention.

---

**P90 THE NORTH-SOUTH DIVIDE: REGIONAL INEQUALITIES IN DEMOGRAPHIC CHARACTERISTICS AND CLINICAL OUTCOMES IN PATIENTS WITH CYSTIC FIBROSIS IN ENGLAND–A POPULATION BASED CROSS-SECTIONAL STUDY USING UK CF REGISTRY DATA**

**1S Nyangoma, 1V Rajabzadeh-Heshejin, 1P Cullinan, 1J Sampton. 1Imperial College, London, UK; 2Staffordshire University, Stoke-on-Trent, UK**

10.1136/thoraxjnl-2016-209333.233

**Background**

For many diseases including cancer, the inequalities in key clinical outcomes are known to be wider in the economically disadvantaged Northern England (NE) compared to the more affluent South England (SE) (Shack, et al, 2008). This study aimed to investigate the North-South divide in demographic characteristics and clinical outcomes in cystic fibrosis (CF) patients in England.

**Methods**

This was a cross-sectional study of patients with CF living in the SE and NE and registered on the UK CF Registry in 2010. Clinical data from Annual Review Encounter (ARE) of that year included demographics, prescription records and clinical outcomes: FEV1%predicted and chronic infections.

Descriptive statistics were adopted to summarise categorical and continuous outcomes. Wilcoxon test and t-test was used to compare continuous outcomes, while two-sample test for equality of proportions was used to compare prevalence of infections and drug use.

**Results**

The study cohort included 1265 children and 1752 adults from SE and 1483 children and 1917 adults from NE. For children: lung function (FEV1%), adjusted for age and sex was

---

**Abstract P89 Figure 1** Schematic representation of the accuracy of the model predicting weight z score at age 1

**Abstract P90 Table 1** Patient characteristics

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Outcome/ Category</th>
<th>South of England N = 3017</th>
<th>North of England N = 3400</th>
<th>P-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 – &lt;16 (Children)</td>
<td></td>
<td>1265 (41.9)</td>
<td>1483 (43.62)</td>
<td>0.1805</td>
</tr>
<tr>
<td>≥16 (Adults)</td>
<td></td>
<td>1752 (58.1)</td>
<td>1917 (56.38)</td>
<td></td>
</tr>
<tr>
<td>Age (Years) Mean ± SD</td>
<td></td>
<td>19.71 ± 13.24</td>
<td>18.81 ± 12.52</td>
<td></td>
</tr>
<tr>
<td>Gender, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>1423 (47.17)</td>
<td>1578 (46.41)</td>
<td>0.5623</td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>1594 (52.83)</td>
<td>1822 (53.59)</td>
<td></td>
</tr>
<tr>
<td>Percent predicted FEV1, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;40</td>
<td></td>
<td>333 (11.04)</td>
<td>341 (10.03)</td>
<td></td>
</tr>
<tr>
<td>40–69</td>
<td></td>
<td>728 (24.13)</td>
<td>846 (24.88)</td>
<td></td>
</tr>
<tr>
<td>≥70</td>
<td></td>
<td>1335 (44.25)</td>
<td>1443 (42.44)</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis, n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;3 months; n (%)</td>
<td></td>
<td>1280 (42.43)</td>
<td>1590 (46.76)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td>629 (20.85)</td>
<td>645 (18.97)</td>
<td></td>
</tr>
<tr>
<td>3–12 months; n (%)</td>
<td></td>
<td>416 (13.79)</td>
<td>474 (13.94)</td>
<td></td>
</tr>
<tr>
<td>≥3 years; n (%)</td>
<td></td>
<td>453 (15.01)</td>
<td>488 (14.35)</td>
<td></td>
</tr>
</tbody>
</table>

| FEV1 percent predicted   |                  |                           |                           |          |
| All patients Mean ± SD   |                  | 70.98 ± 24.66             | 71.23 ± 24.23             | 0.9821   |
| Children Mean ± SD       |                  | 84.51 ± 17.99             | 81.57 ± 19.80             | 0.0061   |
| (Age < 16) adults        |                  | 64.69 ± 24.81             | 66.73 ± 24.61             | 0.0422   |
| (Age ≥ 16)               |                  |                           |                           |          |
significant higher in SE (84.51% vs 81.57%, p < 0.01). However, rates of *Pseudomonas aeruginosa*, Burkholderia cepacia and MRSA were similar. Significantly higher proportions of patients were diagnosed before turning 3 months in the NE compared to SE (46.76% vs 42.43%). In adults: in the NE the BMI was higher 22.35 vs 21.99 (p < 0.01) as was the FEV1%p, adjusted for age and sex (66.73% vs 64.69%, p = 0.04). Patients in SE were more frequently prescribed mucolytics (Dornase Alfa and hypertonic saline). In NE they more frequently used chronic macro-lides. There were higher rates of PA, Bcc and MRSA in NE. The rates of MSSA and NTM were higher in the SE.

Conclusions There is a north-south divide in demographic characteristics and clinical outcomes in cystic fibrosis (CF) patients in England. In SE children have higher lung function. However, adults in the NE seem to have higher lung function compared to adults in SE. A single year cohort is not sufficient to deduce if these differences affect longer-term outcomes, like survival and requires further investigation.

---

**P91**

**TRYPSIN-LIKE PROTEASE ACTIVITY PREDICTS DISEASE SEVERITY AND PATIENT MORTALITY IN ADULTS WITH CYSTIC FIBROSIS**

1JA Reihill, 1KL Moffitt, 1AM Jones, 1JS Elborn, 1SL Martin, 1Queen’s University Belfast, Belfast, UK; 2Manchester Adult Cystic Fibrosis Centre, Manchester, UK

**Introduction** Serine trypsin-like (TL) proteases, which are exclusively active in CF airways, promote activation of the epithelial sodium channel (ENaC) and airways dehydration; a key initiating factor for CF lung disease pathogenesis. Furthermore TL-proteases enhance mucin gene expression and mucus hypersecretion, yet whether there is any relationship between the activity of these enzymes and CF pulmonary disease is unknown.

**Objectives** The primary objective of the current investigation was to determine whether TL-protease activity, measured in adult CF sputum sol, correlates with lung disease and patient outcome (survival). A secondary objective was to compare the strength of any relationships observed with that of neutrophil elastase (NE), an established protease biomarker.

**Methods** In this cross sectional retrospective study we analysed CF sputum sol collected from 30 clinically stable adult CF patients. Protease activity was measured by monitoring the hydrolysis of peptide-based substrates. Biomarkers of inflammation (IL-8 and TNF-α) were measured by ELISA. Lung function was assessed by spirometry (FEV1). Mortality data was retrospectively obtained and time in months until death or transplantation used for subsequent survival analysis.

**Results** TL-protease activity inversely correlated with lung function (FEV1) (r = −0.4, p = 0.031) however, no relationship with IL-8 and TNFα was observed. In contrast, NE was found to correlate with IL-8: r = 0.7, p < 0.001 and TNFα: r = 0.7, p < 0.001 but showed no relationship with lung function, indicating that these serine proteases play very distinct roles within the disease process. Kaplan-Meier analysis demonstrated significantly reduced survival for those individuals with above median TL-protease activity. Levels of NE activity showed no relationship with patient survival. Using a multivariate Cox regression analysis (adjusted for age and BMI) a significantly increased mortality hazard (HR 1.028, 95% CI: 1.007–1.049; p = 0.009) was also identified. These findings are supported by analysis of a validation cohort consisting of samples collected from a separate cohort of 33 adult CF patients.

**Conclusions** TL-protease activity inversely correlates with lung function and patient survival. As such trypsic activity may warrant consideration when modelling CF survivorship and should be investigated further as a biomarker of CF lung disease and as a potential therapeutic target.

---

**P92**

**SYSTEMIC ALKYL QUINOLONES AS NOVEL BIOMARKERS FOR PULMONARY EXACERBATIONS IN CYSTIC FIBROSIS: A VALIDATION STUDY**

1H Barr, 1A Fogarty, 1N Halliday, 1A Knox, 1B Quon, 1P Williams, 1D Barrett, 1M Camara, 1University of Nottingham, Nottingham, UK; 2University of British Columbia, Vancouver, Canada

**Introduction and objectives** There is a clinical need to identify and validate biomarkers that are sensitive to treatment of infection in cystic fibrosis (CF). The aim of this study was to externally validate two novel biomarkers for pulmonary exacerbations in CF of the alkyl quinolone (AQ) class of quorum sensing molecules produced by *Pseudomonas aeruginosa*.

**Methods** Retrospective analysis of 70 plasma samples from thirteen adults with CF obtained during treatment of fifteen discrete exacerbations treated with intravenous antibiotics. Plasma samples were obtained at the start, day five, day ten, at the end of treatment, and at clinical stability. Samples were analysed using liquid chromatography-mass spectrometry. Data were analysed using Spearman’s rank correlations and Wilcoxon matched pairs signed-rank tests using STATA 11 statistical software (Texas, USA). Graphs were produced in EXCEL 2011.

**Results** Plasma 2-heptyl-4-hydroxyquinoline (HHQ) concentration significantly decreased by a median of 221 pmol/L (IQR: 158 to 258 pmol/L) or 73% (IQR 52 to 94%; p = 0.0007) during treatment for a pulmonary exacerbation (Figure 1). In the same interval, there was no significant change in plasma HHQ (median decrease of −3 pmol/L, IQR: −35 to 10 pmol/L; p = 0.65). During treatment for a pulmonary exacerbation, percent predicted FEV1 increased by 4% (IQR: 1 to 7%; p = 0.0086). Following systemic antimicrobial therapy, systemic IL6 concentration decreased by a median of 2.06 pg/mL (IQR: 1.02 to 3.55 pg/mL; p = 0.0022) and systemic calprotectin
decreased by 1687 ng/mL (IQR: 291 to 3992 ng/mL; p = 0.0229).
There was no significant association between change in plasma HHQ and change in FEV1 during treatment of a pulmonary exacerbation (Spearman’s correlation co-efficient, r = −0.42; p = 0.15).

Conclusions: Plasma HHQ declined significantly during treatment of a pulmonary exacerbation and merits further investigation as a biomarker for measuring treatment response in CF. There was no significant decline in plasma NHQ during systemic antimicrobial therapy.

P93 IN-VITRO ACTIVITY OF SEVEN HOSPITAL BIOCIDES AGAINST MYCOBACTERIUM ABSCESSUS

1SC Askew, 2JE Moore, 1JC Rendall. 1Adult Cystic Fibrosis Centre, Belfast City Hospital, Belfast, UK; 2Northern Ireland Public Health Laboratory, Belfast City Hospital, Belfast, UK

Introduction and objectives: Mycobacterium abscessus pulmonary infection in patients with cystic fibrosis (CF) is associated with significant morbidity, and the prevalence is increasing. The cause of the apparent increase is unknown. Contributing factors may include the ageing CF population, and the potential for patient-to-patient transmission. To date, there is a paucity of data describing the activity of common hospital biocides against this organism.

Methods: M. abscessus isolates (n = 13) were recovered from CF and non CF respiratory specimens. Seven commonly employed hospital biocides (Steri-7TM, Difficle-S™, Hydrex™, Cutan™, Stellisept™, Rely+On™ PeraSafe™, Distaclor™) were assayed for their biocidal activity against M. abscessus. Fresh cultures of NTM were exposed to biocide in liquid medium as per manufacturers instruction and were immediately plated following the completion of the contact period. The mean concentration of NTM plated was 9.82 × 10⁶ colony forming units (CFU) (range: 1.63 × 10⁵ – 1.12 × 10⁷). Additionally, the remaining bacteria/biode solution was enriched non-selectively in Mueller Hinton broth (37 °C/1 week). Following this, growth of surviving bacteria was assessed with broth turbidity.

Results: After appropriate exposure of NTM to biocide, all NTM isolates survived in Steri-7™, Difficle-S™, Hydrex™, Stellisept™, Rely+On™ PeraSafe™ and Distaclor™. One out of 13 NTM cultures was killed by Difficle-S™ and 1 by Distaclor™, representing a 5 log kill. Two isolates were killed by Cutan™ again representing a 5 log kill. Following enrichment, Stellisept™ showed the greatest biocidal activity with 11/13 isolates, whereas 2/13 cultures were killed by Distaclor™. All other biocide/culture combinations yielded growth.

Conclusions: These data indicate that M. abscessus may persist after exposure to several commonly employed hospital biocides. Given the importance of effective infection prevention and control, further work is urgently needed to define unequivocal biocide contact treatments to ensure successful eradication.

Acknowledgements: SC is a CF Trust funded Clinical Fellow.

P94 THE MANAGEMENT OF RESPIRATORY TRACT Fungal DISEASE IN CYSTIC FIBROSIS – A UK SURVEY OF CURRENT PRACTICE

M Boyle, JE Moore, DG Downey, Northern Ireland Regional Adult Cystic Fibrosis Centre, Belfast, UK

Aspergillus fumigatus is commonly found in the airways of patients with Cystic Fibrosis, (CF). Allergic Bronchopulmonary Aspergillosis, (ABPA), is the most recognised clinical condition associated with Aspergillus. The most widely used diagnostic criteria are from the Cystic Fibrosis Foundation Consensus Conference 2003. However, diagnosis remains challenging due to the overlap of classical symptoms and radiological features of ABPA and CF. There are a lack of clinical trials with clear outcomes to guide management of fungal disease, leading to variability between CF centres.

The aim of this survey was to assess the variability in current practice across the UK in diagnosis and management of fungal lung disease in CF patients.

A 21 question anonymous online survey was sent to 94 paediatric and adult CF consultants in the UK.

The response rate was 60.6% with 55 full and 2 partially completed surveys. Thirty-two respondents were adult physicians and twenty-five paediatricians. For a first diagnosis of ABPA 20 (35.1%) treat with Prednisolone alone, 19 (33.3%) use Prednisolone with Itraconazole capsules, 19 (33.3%) use Prednisolone with Itraconazole liquid and 2 (3.5%) choose Voriconazole.

Only 5 (8.8%) treat with Prednisolone alone for a 1st relapse, preferring Prednisolone with Itraconazole Liquid (33.3%) or with Itraconazole capsules (24.6%).

To reduce treatment, 21 (36.8%) decrease steroids to zero over time and maintain azole therapy, 18 (31.6%) stop the azole and steroid after a fixed time and 5 (8.8%) stop azole after a fixed time and maintain a small steroid dose. Variations in specific therapies were reported, including the use of pulsed Methylprednisolone, Posaconazole, nebulised Amphotericin and Omalizumab.

Thirty-eight (66.7%) respondents believe Aspergillus colonisation of the airway can cause clinical deterioration and 37 (66.1%) would treat this. Scedosporium apiospermum infection has been diagnosed and treated by 35 (61.4%) of respondents.

Results of this survey highlight significant differences in treatment regimes for ABPA, with increasing variation seen in the management of subsequent relapses. Respondent comments showed a wide range of opinions. This survey highlights the lack of evidence currently available to guide the management of CF fungal disease.

P95 EXPLORING THE TIMING OF HYPERTONIC SALINE (HTS) AND AIRWAYS CLEARANCE TECHNIQUES (ACT) IN CYSTIC FIBROSIS (CF): A CROSS OVER STUDY

1O’Neill, 2FG Moran, 3BR Bradbury, 4DG Downey, 5JC Rendall, 6MM Tunney, 7JS Elborn, 8JM Bradley. 1Queen’s University Belfast, Centre for Experimental Medicine, UK; 2School of Health Sciences, Ulster University, UK; 3Frontier Science (Scotland) Ltd, UK; 4Belfast Health and Social Care Trust, UK; 5Queen’s University Belfast, School of Pharmacy, UK; 6Queen’s University Belfast, Clinical Research Facility, UK

10.1136/thoraxjnl-2016-209333.237

Aspergillus fumigatus is commonly found in the airways of patients with Cystic Fibrosis, (CF). Allergic Bronchopulmonary Aspergillosis, (ABPA), is the most recognised clinical condition associated with Aspergillus. The most widely used diagnostic criteria are from the Cystic Fibrosis Foundation Consensus Conference 2003. However, diagnosis remains challenging due to the overlap of classical symptoms and radiological features of ABPA and CF. There are a lack of clinical trials with clear outcomes to guide management of fungal disease, leading to variability between CF centres.

The aim of this survey was to assess the variability in current practice across the UK in diagnosis and management of fungal lung disease in CF patients.

A 21 question anonymous online survey was sent to 94 paediatric and adult CF consultants in the UK.

The response rate was 60.6% with 55 full and 2 partially completed surveys. Thirty-two respondents were adult physicians and twenty-five paediatricians. For a first diagnosis of ABPA 20 (35.1%) treat with Prednisolone alone, 19 (33.3%) use Prednisolone with Itraconazole capsules, 19 (33.3%) use Prednisolone with Itraconazole liquid and 2 (3.5%) choose Voriconazole.

Only 5 (8.8%) treat with Prednisolone alone for a 1st relapse, preferring Prednisolone with Itraconazole Liquid (33.3%) or with Itraconazole capsules (24.6%).

To reduce treatment, 21 (36.8%) decrease steroids to zero over time and maintain azole therapy, 18 (31.6%) stop the azole and steroid after a fixed time and 5 (8.8%) stop azole after a fixed time and maintain a small steroid dose. Variations in specific therapies were reported, including the use of pulsed Methylprednisolone, Posaconazole, nebulised Amphotericin and Omalizumab.

Thirty-eight (66.7%) respondents believe Aspergillus colonisation of the airway can cause clinical deterioration and 37 (66.1%) would treat this. Scedosporium apiospermum infection has been diagnosed and treated by 35 (61.4%) of respondents.

Results of this survey highlight significant differences in treatment regimes for ABPA, with increasing variation seen in the management of subsequent relapses. Respondent comments showed a wide range of opinions. This survey highlights the lack of evidence currently available to guide the management of CF fungal disease.
Background Streamlining the timing of treatments in CF is important to optimise adherence whilst ensuring efficacy. The optimal timing of HTS and ACTs is unknown.

Objectives This study hypothesised that ACTs after HTS would be more effective than ACTs during HTS as measured by lung clearance index (LCI). FEV1, sputum weight and patient perceptions were also compared.

Methods Adults with CF providing written informed consent were randomised (between days 10–14 of intravenous antibiotic course during a pulmonary exacerbation) to a crossover trial of ACTs after HTS inhalation or ACTs during HTS inhalation on alternate days. ACT treatment consisted of 10 cycles of active cycle of breathing technique using an Acapella8. The physiotherapist collecting the outcome measures was blinded. Patients completed a Multiple Breath Washout (MBW) test to obtain LCI and spirometry at baseline and 90 mins post treatment. Sputum collection during 90 mins, ease of clearance and satisfaction with treatment was also recorded. Wilcoxon test was used and p < 0.05 was considered significant.

Results Fourteen subjects were recruited and 13 completed the study (mean [SD] age 33 [12], FEV1% predicted 51 [22], LCI (no. turnovers) 14 [4]). Comparing the 2 treatments (ACT after HTS vs ACT during HTS), the change from baseline to 90 mins post treatment in LCI (p = 0.71) and FEV1% predicted (p = 0.97) was not significant. There was also no difference in sputum weight expectorated (p = 0.17), patient perceived ease of clearance (p = 0.33) or satisfaction (p = 0.28). The time taken for ACT during HTS was significantly shorter (p = 0.001).

Conclusions In this small study, ACTs after HTS was no more effective than ACTs during HTS.

P96 PHYSIOTHERAPY MANAGEMENT OF ADULT PATIENTS WITH CYSTIC FIBROSIS ON INTENSIVE CARE UNITS (ICU) – A SURVEY OF UK PHYSIOTHERAPISTS

F Cathcart, H Parrott, A Jones, N Simmonds. Adult Cystic Fibrosis Centre, Royal Brompton Hospital, London, UK

10.1136/thoraxjnl-2016-209333.239

Introduction and objectives Currently no guidelines or data exist on the physiotherapy management of adults with CF on the ICU. The aim was to explore the views and experiences of the specialist physiotherapists (SPs) managing adults with CF admitted to an ICU.

Methods An online survey was designed which included questions (open and closed) on staff confidence, communication, learning needs, extracorporeal membrane oxygenation (ECMO) and end of life care. The survey was sent to CF, ICU and transplant SPs across the UK.

Results 42 SPs responded (74% response rate), 52% (n = 22) adult CF, 40% (n = 17) ICU and 7% (n = 3) transplant specialists. 73% (n = 30) had been specialists in their area for >5 years. 27% (n = 11) reported no CF admissions to their ICU in the last year, only 24% (n = 10) had >3 in the last year. Physiotherapy care was shared between the ICU and CF SPs teams in 43% (n = 18) of respondents. 90% (n = 37) felt this joint working was essential to optimise patient care. On a confidence scale of 1 – 10 (1 = low, 10 = high) the median (IQR) confidence score of SPs to manage patients with CF on ICU was 7 (7–9).

43% (n = 17) had experienced pre transplant patients with CF being invasively ventilated and reported that the challenges included airway clearance, weaning, inhalation therapy and nursing staff education. Of the 17 respondents who worked in ECMO centres, 57% (n = 12) had never had a patient with CF on ECMO and 90% had no physiotherapy ECMO protocol. Reported challenges were mobilisation, chest clearance, inhalation therapy and palliative care.

Of respondents 50% (n = 21) had managed a patient with CF who died on ICU. 79% (n = 33) of respondents wanted more education on managing patients with CF on ICU with comments around, joint training, national guidelines being developed and the importance of collaborative care.

Conclusions The number of adults with CF admitted to ICU remains low nationally however SPs need to maintain competence and confidence in managing these complex patients. National, expert consensus guideline development, including a physiotherapy ECMO protocol would assist in ensuring equitable quality care in this setting.

P97 GASTRO-OESOPHAGEAL REFLUX IN CYSTIC FIBROSIS

1RW Lord, 1JS Pearson, 1PJ Barry, 1P Whorwell, 1RB Jones, 1PJ Barry, 1JA Smith, 1AM Jones. 1University Hospital South Manchester, Manchester, Manchester, UK; 2University of Manchester, Manchester, UK; 3Alder Hey Hospital, Liverpool, UK; 4University of Liverpool, Liverpool, UK

Background Initial small studies using combined pH and impedance (pH-MII) have suggested increased gastro-oesophageal reflux (GOR) in adult cystic fibrosis (CF) patients. Reflux episodes frequently reach the proximal oesophagus and occur whilst supine, which may predispose to micro-aspiration.

Aims To investigate the relationship between GOR and CF lung disease.

Methods We conducted a prospective observational study in stable adult CF patients undergoing 24 hour pH-MII. Reflux symptoms (using validated RESQ-7 questionnaire) and spirometry were also recorded.

Results 10/12 subjects recruited completed pH-MII the study (mean age 28.5 years, mean FEV1 48.8%, predicted, 100% male). An increased number of reflux episodes per 24 hours were noted in 80% of participants (median 104.1, IQR 78.6 –164.4, normal range <75 episodes), with increased ‘high-risk’ proximal reflux or supine reflux noted in 60% (Table 1). In this small preliminary patient sample there were no significant correlations between FEV1% and total, proximal or supine reflux episodes, or RESQ-7 heartburn scores and any reflux measure.

7/10 subjects completed the study on a PPI and had data available for acid reflux (pH < 4) parameters. 4/7 had an abnormal acid exposure despite standard dose PPI therapy, 5/7 had prolonged acid reflux events; the longest was 66.5 minutes (see Table 1).

Conclusions In this preliminary data set, CF patients appear to have a pattern of GOR that puts them at risk of reflux micro-aspiration and have significant acid reflux despite antacid therapy. Reflux symptoms and spirometry were not related to reflux parameters.

The clinical implications of these findings are that standard PPI dosing maybe insufficient in CF patients to control acid reflux. In addition silent reflux aspiration may occurring and as such could be a potential area for future therapies.
AN 18 (± 6) MONTH FOLLOW UP STUDY OF COGNITIVE FUNCTION IN ADULTS WITH CYSTIC FIBROSIS RELATED DIABETES (CFRD)

Introduction and objectives Cognitive impairments have been observed in people with type 1 and 2 diabetes. People with cystic fibrosis (CF) who have developed CF related diabetes (CFRD) also show some degree of impairment relative to healthy controls. The aim of this study was to examine cognitive function in people with CFRD after an 18 (± 6) month period to assess any change in performance.

Method Adult (>16 years old), pancreatic insufficient patients with insulin treated CFRD registered to a large UK CF unit who had adequate verbal and written English were eligible. Cognitive performance was assessed using parallel versions of tests from the Cambridge Neuropsychological Test Automated Battery (CANTAB). Subjective ratings of sleep, stress, mood, cognitive performance and minor daily cognitive errors were also collected. At baseline, 67 people were tested; 49 non transplanted and 18 post transplantation patients. Twelve patients were lost to follow-up. To date, 43 people have been retested after an 18 (± 6) month period; 35 non transplanted and 8 post transplantation patients.

Results At follow up, blood glucose levels were significantly lower during testing (reflecting better glycaemic control in some patients) and people reported significantly fewer occurrences of minor daily cognitive errors within the past 6 months. There was no change in performance between baseline and follow up on tests of motor function, visual memory and new learning, immediate pattern recognition, working memory and mental flexibility. On tests of immediate and delayed verbal memory, delayed pattern recognition and processing speed, performance had significantly improved at follow up.

Conclusion Cognitive function is impaired in people with CFRD but remains stable over an 18 (±6) month period. Deficits in cognitive performance may impact upon quality of life and ability to adhere to treatment.

Cystic fibrosis (CF) is a multi-system disease requiring complex, high-burden treatment regimens. Discrepancies can arise between hospital and GP drug lists, in turn impacting patient’s access to required long-term medications. One large adult CF centre has been conducting medicines reconciliation at the point of transition from paediatric care, with the goal of identifying and eliminating such discrepancies.

The objective of this study was to evaluate the accuracy of hospital medication lists versus the GP repeat prescription lists, at the point of transition from paediatric to adult care.

Methods Drug lists were assessed for discrepancies, in drug or dose, as well as non-collection of items. These issues were sub-grouped to evaluate whether frequency varied by drug class.

Results Drug list from 99 patients from a 4.5-year period (2011–2016) were included, featuring a total of 1201 items, with a mean of 12, range 1–22, items per patient. There was a drug discrepancy in 11.7% of total items, with greatest frequency occurring in oral antibiotics (8.7%). It was also found that 9.2% of items had not been collected from GP for ≥6 months, with greatest frequency occurring in nebulised medicines 13.8%.

Conclusions Discrepancies are common across CF medication lists. These may have a detrimental impact on clinical care, as patients are unable to access the required medicines from their GP, and hospitals may prematurely escalate care. Furthermore, a number of items prescribed by GPs are not regularly collected, indicating poor adherence. Medicines reconciliation at transition of care has a significant impact in identifying these issues, and CF centres should consider whether to also routinely include this process during CF annual reviews.
PRE-TRANSPLANT C-REACTIVE PROTEIN (CRP) AS A MARKER OF POST-TRANSPLANT OUTCOMES IN PATIENTS WITH CYSTIC FIBROSIS (CF)

A Fazleen, J Parmar. Papworth Hospital NHS Foundation Trust, Cambridge, UK

Introduction Although novel therapies for CF have been introduced, the condition still has a high rate of complications and early death. Transplantation remains the only hope for extended survival and quality of life. Our study aimed to determine whether pre-transplantation CRP could predict outcomes post-transplantation.

Methods In a retrospective analysis of all lung transplantations performed at our centre between 2001 and 2016, only patients who had complete data were analysed. CRP levels within 72 hours pre-transplantation were compared with length of intubation, ITU and hospital stay, Primary Graft Dysfunction (PGD), pulmonary infection within 3 months post-transplantation and rates of acute cellular rejection.

Results Among 100 patients who underwent lung or heart/lung transplantation, 72 patients had a complete dataset. Average age at transplantation was 28.1 in both groups.

48 patients had CRP < 40 mg/L (24 males, 24 females, median CRP 14), and 24 patients had CRP > 40 mg/L (14 males, 10 females, median CRP 60). Average age of donor was 41.6 in the low CRP group, and 41.8 in the high CRP group.

Average duration of intubation was 66.7 hours in the low CRP group, versus 48.0 hours in the high CRP group, while average length of ITU stay was 6.9 days in the low CRP group, versus 9.3 days in the high CRP group (p 0.76). Average duration of hospital stay was 26.3 days in the low CRP group, and 25.7 days in the high CRP group.

Mean number of infections in the low CRP group was 2.4, and 3.3 in the high CRP group (p 0.52). Mean number of episodes of rejection was 0.4 in the low CRP group, and 0.6 in the high CRP group (p 0.36).

Kaplan-Meier plots showed no evidence of impact on survival to 5 years.

Conclusion CRP within 72 hours pre-transplantation in patients with CF was not a predictor of short- or long-term outcomes in our study. It is important to note that the sample size for this study was quite small, possibly contributing to this finding. Extension of this study to include patients from multiple transplant centres would be beneficial.

Abstract P100 Table 1

<table>
<thead>
<tr>
<th>Postoperative data</th>
<th>Average &lt; 40 (n = 48)</th>
<th>Average ≥40 (n = 24)</th>
<th>p.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGD</td>
<td>4</td>
<td>0</td>
<td>0.29</td>
</tr>
<tr>
<td>Intubation time (hours)</td>
<td>66.7</td>
<td>48.0</td>
<td>0.52</td>
</tr>
<tr>
<td>Blood loss in first 24 hours (mls)</td>
<td>1255.0</td>
<td>1550.8</td>
<td>0.19</td>
</tr>
<tr>
<td>Length of ITU stay (days)</td>
<td>6.9</td>
<td>9.3</td>
<td>0.76</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>26.3</td>
<td>25.7</td>
<td>0.50</td>
</tr>
<tr>
<td>Renal failure</td>
<td>2</td>
<td>1</td>
<td>1.00</td>
</tr>
<tr>
<td>Airway complications</td>
<td>4</td>
<td>1</td>
<td>0.77</td>
</tr>
<tr>
<td>Rejection episodes</td>
<td>0.4</td>
<td>0.6</td>
<td>0.36</td>
</tr>
<tr>
<td>Infection episodes</td>
<td>2.4</td>
<td>3.3</td>
<td>0.52</td>
</tr>
<tr>
<td>1 year survival</td>
<td></td>
<td></td>
<td>0.18</td>
</tr>
</tbody>
</table>

Abstract P101

STRUCTURED HOLISTIC NURSING ASSESSMENT (HNA) IN BUCKINGHAMSHIRE HEALTHCARE TRUST (BHT) FOR LUNG CANCER & MESOTHELIOMA PATIENTS: PROCESS AND FINDINGS

J Mowforth, H Steiner, A Prasad. Buckinghamshire Healthcare NHS Trust, Aylesbury, UK

Aim Lung cancer and mesothelioma patients have complex needs. Without a structured process of screening and assessment these can go undetected. Structured screening and assessment needs considered planning. Our experience of screening and assessment of the holistic needs for lung cancer and mesothelioma patients in BHT is described.

Method All BHT lung cancer and mesothelioma patients are invited to be screened post diagnosis using the Distress Thermometer and Needs checklist (Brennan et al 2012). Participation
rates vary between 55–65% and since 2013, 467 patients have been contacted with 265 patients participating. A database stores all HNA activity. This includes individual overall numerical score for distress (0–10), a breakdown of categories of need including physical, emotional, practical, social and spiritual. It also records specific aspects of distress within each category and where specified the top four aspects of need.

**Results** Of the 265 respondents, 196 (74%) recorded physical problems, 145 (54%) recorded emotional issues with worry, fear, sadness and depression sited as the top four aspects. In addition 63 (24%) reported practical problems e.g. money and transport, 53 (20%) family problems, and 32 (12%) spiritual concerns. Overall tiredness, breathing, getting around and worry are the top four needs recorded by our patients. Of all patients screened to date a third score Distress above 5, these patients are prioritised for a nurse led clinic.

**Conclusion** Through screening issues often not disclosed in doctor led clinics are identified and addressed leading to involvement of other professionals and services. Screening patients away from the clinical setting enables greater disclosure, prevents bias or influence on scoring and allows complex needs that might go undetected to be explored. The process enables care to be patient focused and proactive in managing complex needs before crisis events occur.

**REFERENCE**


---

**P102 THE LIVERPOOL HEALTHY LUNG PROJECT – SEEKING OUT EARLY STAGE LUNG CANCER**

M J Ledson, 2 S Grundy, 3 E Gaynor, 4 R Arvanitis, 3 M Timoney, 4 J Field. 1 Liverpool Heart and Chest Hospital, Liverpool, UK; 2 Aintree Hospital, Liverpool, UK; 3 Liverpool Clinical Commissioning Group, Liverpool, UK; 4 Liverpool University, Liverpool, UK

10.1136/thoraxjnl-2016-209333.245

Liverpool has one of the highest respiratory morbidity rates in England, with double the lung cancer incidence, particularly in lower socioeconomic groups. To tackle this health inequality in February 2016 in conjunction with Liverpool CCG, the primary care sector, public health and Liverpool University we commenced the 3-year £3.3M Liverpool Healthy Lung Project. The project has 2 sequential phases.

**Phase 1** By means of a series of coordinated focused public engagement events throughout the city, starting in areas with higher lung cancer incidence, this aims to promote positive messages around lung health, and address the fear and fatalism surrounding lung cancer.

**Phase 2** All individuals between the ages of 58–70 who have COPD, have smoked, or are asbestos exposed are invited to a face to face lung health check conducted by an experienced respiratory nurse. Positive lifestyle messages are promoted and a 5-year personal lung cancer risk calculated (www.MyLungRisk.org using LLPv2 risk model). Those who trigger the 5% threshold are offered a low dose thoracic CT scan.

The community healthy lung events attracted 1346 interactions and 462 individuals completed spirometry. 90 (19%) of these tests were abnormal which triggered a consultation in primary care.
Projections suggest 34,000 patients will be eligible for phase 2; in the first 12 weeks, in Picton Ward (eligible population 2471) 896 (36%) individuals booked to attend the lung health check, where 230 (31%) triggered the offer of a CT. To date 138 scans have been reported: 24 (17%), had significant findings, of which 9 (6%) require a 3 month and 3 (2%) 12 month repeat scan for nodules. Two individuals had confirmed cancer (both resected), with 2 further cases currently being worked up.

Of 406 patients (45%) without previously diagnosed COPD, 180 (44%) had abnormal spirometry, and have gone on to further diagnostics.

The complete Picton Ward data will be presented at the conference.

This innovative project is already improving access to respiratory healthcare in a deprived area of Liverpool, and should improve outcomes for lung cancer in this disadvantaged population. The project has been adopted by the national ACE program.

**P103 APPLES AND PEARs? A COMPARISON OF TWO SOURCES OF LUNG CANCER DATA IN ENGLAND**

1A Khakwani, 2R Hubbard, 2R Jack, 3N Wood, 2S Vernon, 2P Beckett, 3N Navani, 3S Vernon, 2S Vernon, 3R Jack, 3N Wood, 3B Plewa, 3N Navani, 3I Woolhouse. 1University of Nottingham, UK; 2National Cancer Registration Service, UK; 3Royal College of Physicians, London, UK

10.1136/thoraxjnl-2016-209333.246

**Introduction** In 2014, the contract to deliver the National Lung Cancer Audit (NLCA) was awarded to the Royal College of Physicians. Data were previously submitted using a bespoke dataset (LUCADA), but will now be submitted via the nationally mandated Cancer Outcome and Services Dataset (COSD) and linked to additional cancer registry datasets. For patients diagnosed in 2014, NLCA data were submitted using LUCADA for 132 of 151 English trusts. Trusts also submitted data via COSD and registry data were produced by the National Cancer Registration Service (NCRAS), providing the opportunity to compare both datasets for data completeness and reliability.

**Methods** We have linked the LUCADA and cancer registry datasets at patient level and assessed completeness of key patient variables including age, sex, stage, performance status and pathological confirmation, as well as recording/dates of treatment received. We assessed the inter-rater/data agreement of these variables using Cohen’s kappa statistics (k). Finally, we carried out a qualitative assessment on a subset of cases to explore reasons why patients were represented in one dataset but not the other.

**Results** There were 26,001 patients in both datasets (94% of LUCADA data) with more in the registry dataset and not LUCADA than vice versa. Recorded sex and age were highly congruent, as was trust first seen which was the same in 96%. 56% of the patients had the same date of diagnosis, 74% were ± 7 days and 86% were ± 14 days of each other. The cancer registry data had a larger proportion of patients with missing PS (27% vs 11%) with agreement on PS (where available) being 97% (k = 0.91). Agreement on stage was 94% (k = 0.81). Agreement for surgery, chemotherapy and radiotherapy was 0.86, 0.88 and 0.77 respectively. Details of the qualitative work and trust first seen algorithms will be provided in the presentation.

**Conclusion** Results suggest that cancer registry data accurately describe key patient features. Compared with LUCADA, the national cancer registry:

- has a higher proportion pathological confirmation
- identified more patients with surgery, chemotherapy and radiotherapy
- has a higher proportion of missing data for PS which could be due to data entry transition

**P104 RESULTS OF THE FIRST ANALYSIS OF NATIONAL LUNG CANCER AUDIT DATA BASED ON CANCER REGISTRATION DATA**

1P Beckett, 2A Khakwani, 2R Hubbard, 2S Vernon, 2R Jack, 2N Wood, 2B Plewa, 4N McAndrew, 2R Dickenson, 2N Navani, 3S Vernon, 3R Jack, 3N Wood, 3B Plewa, 3I Woolhouse. 1Royal College of Physicians, London, UK; 2University of Nottingham, UK; 3National Cancer Registration Service, UK; 4Wrexham Maelor Hospital, UK

10.1136/thoraxjnl-2016-209333.247

**Introduction** The National Lung Cancer Audit (NLCA) has collected data for over 10 years, but in early 2015 a transition to using the Cancer Outcomes and Services Dataset (COSD) and cancer registration was begun and has now entirely superseded the legacy LUCADA dataset. An online portal (CancerStats) has
been developed with a bespoke section providing near real time analysis of unprocessed COSD data for the NLCA. This portal currently focuses on data completeness, with plans to add process and treatment data in the near future. We report the results of the first 12 months of data collection using the new system (2015), and have compared this to the last year of LUCADA submissions (2014).

**Methods** The COSD was submitted monthly by English trusts on patients diagnosed with invasive lung cancer throughout 2015. This raw data was used to populate the data completeness tables on the CancerStats portal. An algorithm was developed to allocate “trust first seen” to each patient record. Our presentation will include data from the final processed cancer registration records that have been validated using all available data sources within the National Cancer Registration Service (NCRAS). Welsh data submitted via their CANISC system will be available for our presentation.

**Results** 35,000 individual cases of invasive lung cancer were submitted by English Trusts. Data completeness results are shown in Table 1. Our final presentation will be updated with data from the processed cancer registration records that have been validated using all available data sources within the National Cancer Registration Service (NCRAS), as well as results from Welsh trusts.

**Conclusion** COSD submissions appear to capture more cases of lung cancer than LUCADA. During this transition period, the quality of the data was less good than previous years with significant variation across organisations. However, data completeness for stage and treatment is expected to be better than indicated since final registered cases use data from a variety of other sources. CancerStats offers the opportunity for teams to monitor their data quality and to iteratively improve their internal processes to deliver robust data for future years, in particular patient factors such as performance status which is not available elsewhere.

**Introduction** Despite significant advances in the diagnostic and staging modalities, lung cancer survival remains poor. Accurate staging and stratification of lung cancer is imperative to appropriate management. We reviewed the accuracy of staging in all patients who underwent surgical resection for confirmed or suspected lung cancer.

**Methods** Retrospective study of consecutive surgical resections over 5 year period between January 2010 and December 2014; patients referred from other hospitals were excluded due to lack of pre-operative staging information. Surgical database and pre-operative diagnostic information was reviewed.

**Results** 298 patients underwent surgical resection, mean age 68 years (range 26–91), male 150 (50%). All patients had staging CT. 108 (36%) had EBUS/Bronchoscopy, 9 (3%) had pleural aspiration, 39 (13%) had CT guided lung biopsy, 8 (3%) other tissue sampling (pelvic lesion, subcutaneous lymph node, previous wedge biopsy & exploratory thoracotomy). Mean time from staging CT to resection was 47 days. 48 (16%) had histological confirmation of lung cancer prior to resection. 248 (83%) were primary lung, 17 (6%) metastatic lung tumours from other primaries (breast, colorectal, bladder and renal), 2 (1%) lymphoma and 31 (10%) benign. Of the 248 patients with lung primary (see Figure 1), pre-operative staging was available in 234; 60/234 (26%) were down staged on post-operative staging, 54 (23%) upstaged and 120 (51%) showed concordance.

**Conclusion** Despite the use of combined pre-operative assessment, staging accuracy was only 51% and histological confirmation of lung cancer was only available in a small number of patients. Every effort should be made by the multidisciplinary team to accurately stage lung cancer to guide appropriate therapeutic intervention.

**Abstract P104 Table 1** Comparison of LUCADA (2014) and cancer registration data (2015)

<table>
<thead>
<tr>
<th>Measure</th>
<th>National average (Range by Strategic Clinical Network)</th>
<th>LUCADA 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of diagnoses</td>
<td>33,465</td>
<td>27,995</td>
</tr>
<tr>
<td>Gender</td>
<td>100%</td>
<td>96%</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>86% (70–96)</td>
<td>N/A</td>
</tr>
<tr>
<td>Performance</td>
<td>69% (59–76)</td>
<td>89%</td>
</tr>
<tr>
<td>Status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1%</td>
<td>24% (9–35)</td>
<td>20%</td>
</tr>
<tr>
<td>Smoking status</td>
<td>43% (27–57)</td>
<td>N/A</td>
</tr>
<tr>
<td>Basis of Diagnosis</td>
<td>95% (87–100)</td>
<td>99%</td>
</tr>
<tr>
<td>Pre-treatment</td>
<td>72% (54–77)</td>
<td>92%</td>
</tr>
<tr>
<td>stage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment modality</td>
<td>83% (66–83)</td>
<td>57%</td>
</tr>
</tbody>
</table>

**Abstract P104 Figure 1**

**Poster sessions**

**LUNG CANCER STAGING – ARE WE GETTING IT RIGHT?**

J Ibrahim, A Mukhopadhyay, V Lstorakos, A Mahmood, S Khan, N Maddekar, S Bikmalla, A Lea, C Satur, Q Abd, S Ghosh, M Haris. Royal Stoke University Hospital, Stoke-on-Trent, UK

**Introduction** Despite significant advances in the diagnostic and staging modalities, lung cancer survival remains poor. Accurate staging and stratification of lung cancer is imperative to appropriate management. We reviewed the accuracy of staging in all patients who underwent surgical resection for confirmed or suspected lung cancer.

**Methods** The UK Lung Cancer Coalition (UKLCC) was established in 2005 with the primary goal of doubling five-year survival rates in lung cancer by 2015. Estimates suggest that the UKLCC has met this goal in England, with improvements also seen in Scotland, Wales and Northern Ireland. The UKLCC is now looking to set a new ambition to substantially raise five-year survival rates by 2025.

**Method** The UKLCC surveyed 102 patients and carers, 148 healthcare professionals, and 1,003 general practitioners (GPs) asking questions related to improvement of five-year survival rates for lung cancer.
Predictors of mortality in patients undergoing lung cancer surgery

Introduction: Surgical resection is a treatment of choice for patients with early stage lung cancer and physiological measurements are routinely used to help predict post-operative risk, particularly in the 'high-risk' patient group.

At present, there is a lack of concordance between current available guidelines incorporating the use of such parameters aimed to guide decisions on surgery for high-risk patients with lung cancer. As a result, the decision will differ for a particular patient depending on which guidelines are consulted.

We aim to identify which parameters best predicts post-operative mortality and whether this information can be used to construct a more encompassing pre-operative risk prediction model to help guide these difficult decision processes.

Methods: Retrospective analysis of all patients undergoing CPET (cardio-pulmonary exercise testing) prior to lung cancer surgery between 01/01/2012 and 31/12/2015 was carried out. Age, BMI along with pre-operative and post-operative predicted physiological parameters were reviewed and statistical analysis performed. We also looked at survival based on type of surgery (sub-lobar, lobar, pneumonectomy), histology and cancer staging.

Results: Single variable analysis of the 178 patients identified that low BMI (p = 0.005) and PPO DLCO% (p = 0.004) were associated with greater post-operative mortality risk.

There was a statistically significant difference between different cancer stage and type of surgery as expected.

Using the probabilities from the logistical regression model to predict one-year mortality gives an AUC of 0.764. A probability cut-off of 0.167 used to predict whether a patient will die within one year of surgery provides a sensitivity of 76.5%, specificity 66.4%, PPV 35.1% and NPV 92.2%.

Conclusions: Contrary to current guidelines, CPET data did not seem to carry statistically significant weighting in determining post-operative mortality outcomes in our patient group with BMI and PPO DLCO% showing a stronger, statistically significant association.

Absolute% change between pre and PPO FEV1 values appears to be a good predictor of one-year mortality following surgery.

Further work is required but early analysis suggested that parameters such as BMI, PPO DLCO% and absolute post-operative change in FEV1% can be used to construct a pre-surgical prediction model for 'high-risk' patients undergoing surgery for lung cancer.

Abstract P107 Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Hazard ratio (95% CI)</th>
<th>Cox regression p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>178</td>
<td>0.988 (0.957, 1.020)</td>
<td>0.47</td>
</tr>
<tr>
<td>BMI</td>
<td>178</td>
<td>0.932 (0.887, 0.979)</td>
<td>0.005</td>
</tr>
<tr>
<td>FEV1% predicted (pre)</td>
<td>178</td>
<td>1.008 (0.999, 1.018)</td>
<td>0.088</td>
</tr>
<tr>
<td>FEV1% predicted (post)</td>
<td>177</td>
<td>0.998 (0.987, 1.010)</td>
<td>0.73</td>
</tr>
<tr>
<td>DLCO% predicted (pre)*</td>
<td>137</td>
<td>0.994 (0.976, 1.013)</td>
<td>0.54</td>
</tr>
<tr>
<td>DLCO% predicted (post)</td>
<td>136</td>
<td>0.963 (0.939, 0.988)</td>
<td>0.004</td>
</tr>
<tr>
<td>VO2 max</td>
<td>178</td>
<td>1.035 (0.975, 1.098)</td>
<td>0.26</td>
</tr>
<tr>
<td>VO2 max% predicted (pre)</td>
<td>178</td>
<td>1.003 (0.991, 1.015)</td>
<td>0.66</td>
</tr>
<tr>
<td>VO2 max% predicted (post)</td>
<td>177</td>
<td>0.990 (0.977, 1.003)</td>
<td>0.14</td>
</tr>
<tr>
<td>VE/CO2</td>
<td>176</td>
<td>1.024 (0.996, 1.053)</td>
<td>0.091</td>
</tr>
</tbody>
</table>

Lung Cancer Resection Outcomes in the First Year: A 5 Year Review

Introduction: Lung cancer survival remains poor despite the use of advanced diagnostic and therapeutic interventions. Surgical resection offers the best chance of cure for those with early stage lung cancer. Those who undergo curative resection for non-small cell lung cancer remain at risk of recurrence. We wished to evaluate thoracotomy outcomes in patients undergoing resection with curative intent.

Methods: Retrospective review of consecutive surgical resections for suspected or confirmed lung cancer over 5-year period between January 2010 and December 2014 in a tertiary thoracic unit. Patients referred from other centres were excluded. Surgical database and post-operative follow up information was reviewed. Futile thoracotomies were defined as inoperable lung cancer at the time of surgery, benign lung lesion, incomplete tumour resection margins and recurrence or death in the first year.

Results: 298 patients underwent surgical resection; mean age 68 years (range 26–91); male 150 (50%), 48 (16%) had histo-cytological confirmation of lung cancer prior to resection. Post-operative histology revealed 248 (83%) primary lung cancer; 31 (10%) benign pathology; 17 (6%) metastatic tumour from other
The impact of TB NICE guidance on resource capacity and contact screening outcomes: A retrospective, observational study within a central London TB centre

M O’Donoghue, H Jarvis, J Drey, JH Almond, A Seneviratne, A LaValksi, OM Kon.
Imperial College NHS Trust, London, UK; School of Health Sciences, City University, London, UK; Imperial College, London, United Kingdom.

Introduction and objectives Recently published NICE guidance has significantly expanded the approach to adult tuberculosis (TB) contact screening by recommending tuberculin skin testing (TST) for pulmonary and laryngeal contacts only, increasing the age threshold for screening and treatment to 65 years and defining a positive TST as induration ≥5 mm, regardless of BCG vaccination status. Interferon Gamma Release Assay (IGRA) is recommended only in situations where more evidence of infection is needed.

Our institution has previously adopted an approach comprising a chest radiograph, TST and IGRA.

The aim of our study was to evaluate the impact of NICE guidance on screening outcomes and resource capacity by applying the criteria to a well-defined historic cohort of TB contacts.

Methods This was a retrospective, observational study carried out at a central London teaching hospital. The study population comprised 593 consecutive, adult TB contacts screened between 1/1/2008 and 31/12/2010. Data was collected through a retrospective review of TST and IGRA tests.

Results Of the 593 contacts screened, 358 pulmonary contacts had TST and IGRA results. 56% had a TST ≥5 mm, regardless of BCG status, qualifying them for treatment as per the new NICE guidance. Of these, 61% were IGRA negative (discordant) and may therefore include false positive diagnoses, resulting in the potential for over treatment. In those with TST 5–14 mm, discordance rises to 84%. Conversely, 6% of those with TST < 5 mm are IGRA positive representing potentially missed cases.

16% of screened individuals were contacts of extra pulmonary TB. Not screening this group would reduce the demand for outpatient appointments by 151% in our cohort. In contrast, testing contacts > 35 years would require capacity for an additional 165% appointments. Furthermore, there were 162 additional LTBI cases in comparison to previous guidance requiring an additional 648 appointments. 72% of this group were IGRA negative.

Conclusion Our results show the revised guidance will require increased resource capacity largely due to more patients being classified as having latent TB. In addition to workforce planning to meet these demands, further debate is needed to decide if this new approach truly reduces the incidence of active TB or results in unnecessary treatment.

Poster sessions

P109

THE IMPACT OF TB NICE GUIDANCE ON RESOURCE CAPACITY AND CONTACT SCREENING OUTCOMES: A RETROSPECTIVE, OBSERVATIONAL STUDY WITHIN A CENTRAL LONDON TB CENTRE

M O’Donoghue, H Jarvis, J Drey, JH Almond, A Seneviratne, A LaValksi, OM Kon.
Imperial College NHS Trust, London, UK; School of Health Sciences, City University, London, UK; Imperial College, London, United Kingdom.

Introduction and objectives Recently published NICE guidance has significantly expanded the approach to adult tuberculosis (TB) contact screening by recommending tuberculin skin testing (TST) for pulmonary and laryngeal contacts only, increasing the age threshold for screening and treatment to 65 years and defining a positive TST as induration ≥5 mm, regardless of BCG vaccination status. Interferon Gamma Release Assay (IGRA) is recommended only in situations where more evidence of infection is needed.

Our institution has previously adopted an approach comprising a chest radiograph, TST and IGRA.

The aim of our study was to evaluate the impact of NICE guidance on screening outcomes and resource capacity by applying the criteria to a well-defined historic cohort of TB contacts.

Methods This was a retrospective, observational study carried out at a central London teaching hospital. The study population comprised 593 consecutive, adult TB contacts screened between 1/1/2008 and 31/12/2010. Data was collected through a retrospective review of TST and IGRA tests.

Results Of the 593 contacts screened, 358 pulmonary contacts had TST and IGRA results. 56% had a TST ≥5 mm, regardless of BCG status, qualifying them for treatment as per the new NICE guidance. Of these, 61% were IGRA negative (discordant) and may therefore include false positive diagnoses, resulting in the potential for over treatment. In those with TST 5–14 mm, discordance rises to 84%. Conversely, 6% of those with TST < 5 mm are IGRA positive representing potentially missed cases.

16% of screened individuals were contacts of extra pulmonary TB. Not screening this group would reduce the demand for outpatient appointments by 151% in our cohort. In contrast, testing contacts > 35 years would require capacity for an additional 165% appointments. Furthermore, there were 162 additional LTBI cases in comparison to previous guidance requiring an additional 648 appointments. 72% of this group were IGRA negative.

Conclusion Our results show the revised guidance will require increased resource capacity largely due to more patients being classified as having latent TB. In addition to workforce planning to meet these demands, further debate is needed to decide if this new approach truly reduces the incidence of active TB or results in unnecessary treatment.

P110

THE ROLE OF TB CHEMOPROPHYLAXIS IN RENAL TRANSPLANT RECIPIENTS

JN Periselneris, S Mahendran, P Chowdhury, H Milburn. Guy’s and St. Thomas’ NHS Foundation Trust, London, UK.

Background Rates of tuberculosis infection are increased after solid organ transplant. This is associated with increased mortality and allograft loss in one third of cases. The WHO recommend testing for latent tuberculosis (LTBI) in patients receiving dialysis or preparing for solid organ transplant. BTS and ERS guidelines suggest screening for LTBI where tuberculosis incidence rates are high or in patients with risk factors for developing tuberculosis in low incidence areas. They go on to propose chemoprophylaxis with isoniazid or three months of rifampicin and isoniazid, with above 60% effectiveness at preventing subsequent tuberculosis. Guidelines at a large renal transplant centre advocate isoniazid prophylaxis for 6 months post transplant in all patients of Indo-Asian or African heritage as well as anyone who is from a country with TB incidence rates above 40/100,000 who have been in the UK for less than 5 years.

Methods All patients who underwent renal transplantation between January 2011 and December 2014 were assessed to see if tuberculosis prophylaxis was prescribed as per guidelines. Cases of subsequent TB were then identified.

Results 912 patients underwent renal transplant during this time. 243 (26.6%) received isoniazid prophylaxis, with 88% adherence to trust guidelines. 42 (4.6%) patients who should have received prophylaxis did not. During this time one patient developed tuberculosis post transplant. This individual should have received isoniazid according to guidelines, but did not. Another patient from sub-Saharan Africa was discovered to have abdominal tuberculosis when on the operating table prior to transplant.

Discussion We are not aware of any LTBI screening programme amongst renal transplant units in the UK currently. Many use prophylactic isoniazid in a similar manner to our trust. Pre-emptive screening with interferon gamma release assays costs approximately £60 per test, 6 months of isoniazid £560 and 3 months of rifampicin and isoniazid costs £185. Whilst screening may...
reduce overall costs and may identify patients earlier, protocol based isoniazid prophylaxis is effective in preventing active tuberculosis.

Conclusion While Isoniazid prophylaxis was effective in prevention of subsequent tuberculosis, screening prior to transplantation should have identified both patients who developed TB.

### P111 OLDER PATIENTS WITH TUBERCULOSIS HAVE LESS TYPICAL CHANGES ON CHEST RADIOGRAPHS

1A Abbara, 2Z Mahomed, 3SM Collin, 4OM Kon, 5V Bushell, 6K Buell, 7IAJ Sullivan, 8T Hansel, 9TC o r r a h, 5RN Davidson. London North West Healthcare NHS Trust, London, UK; 2University of Bristol, Bristol, UK; 3Imperial Healthcare NHS Trust, London, UK; 4Imperial College, London, UK; 5NHLI, Imperial College, London, UK

10.1136/thoraxjnl-2016-209333.254

Introduction and objectives It has been suggested that TB has a different phenotype in older patients with age-related changes to the cell-mediated immune response and co-existent organ dysfunction. Older patients with tuberculosis (TB) may have different radiographic features than younger patients; this may lead to less immediate suspicion of TB resulting in delays to diagnosis and starting treatment. We wanted to identify if there are differences in the most common radiological differences in older and younger patients with pulmonary TB (PTB).

Methods Patients with PTB > 65 were noted from the London TB register between 2002 and 2015. A random selection of younger patients aged 18–40 with PTB were also identified. All available chest x-ray (CXR) reports were obtained from online radiology systems. CXR features were classified according to reported features with particular note of cavitation, nodules and miliary changes, consolidation, lymphadenopathy and effusions.

Results The CXR reports of 239 patients with PTB < 65 and 99 patients with PTB > 65 were collated. Demographic details as well as CXR changes are detailed in Table 1. Cavitation, lymphadenopathy and effusions were more common in younger patients whereas consolidation was more evident in older patients. Upper zone involvement was similar in both groups.

Conclusions Studies by other groups have suggested a higher proportion of cavitation and upper zone changes in younger patients with TB with less specific changes in older patients. This may lead to less suspicion of TB and potentially a longer infective period; this is important given that 23% and 19% of younger and older patients have smear positive PTB. In our study, the proportion with upper zone changes are similar though cavitation is more frequent in younger patients. Of note, is the much higher presence of lymphadenopathy and effusions seen in younger patients. This may potentially be related to differences in the immune function of both groups or primary infection versus reactivation. These findings re-enforce the need for clinical suspicion for PTB in both older and younger patients with both specific and non-specific radiographic changes.

### P112 SERUM INFLAMMATORY BIOMARKERS AS PREDICTORS OF TREATMENT OUTCOME IN PULMONARY TUBERCULOSIS

1A Ritchie, 1A Singanayagam, 1K Maranlan, 1D Connell, 1J Chalmers, 1S Sridhar, 1A Lakvari, 1MM Wickremasinghe, 1OM Kon. Imperial College NHS Trust, London, UK; 2Tayside Respiratory Research Group, Dundee, UK

10.1136/thoraxjnl-2016-209333.255

Background The aim of this study was to evaluate C-reactive protein (CRP), globulin and white cell count as predictors of treatment outcome in pulmonary tuberculosis.

Methods An observational study of patients with active pulmonary tuberculosis was conducted at a tertiary centre. All patients had serum CRP, globulin and white cell count measured at baseline and two months following commencement of therapy. The outcome of interest was requirement for extension of therapy beyond 6 months.

Results There were 226 patients included in the study. Serum globulin >45 g/L was the only baseline biomarker evaluated that independently predicted requirement for therapy extension (OR 3.59 (1.79–7.37; p < 0.001)). An elevated globulin level that failed to normalise at 2 months was also associated with increased requirement for treatment extension (63.9% versus 5.1%; p < 0.001) and had low negative likelihood ratio (0.07) for exclusion of requirement for therapy extension. On multivariable analysis, an elevated globulin that failed to normalise at 2 months was independently associated with requirement for therapy extension (OR 6.12 (2.23–16.80); p < 0.001).

Conclusions Serum globulin independently predicts requirement for treatment extension in pulmonary TB and outperforms CRP and white cell count as a predictive biomarker. Normalisation of globulin at two months following treatment commencement is associated with low risk of requirement for treatment extension.
INDETERMINATE IGRA RESULTS PRIOR TO ANTI-TNF THERAPY: STABLE STATE TESTING MAY BE IMPORTANT FOR IMMUNE-MEDIATED INFLAMMATORY DISORDERS

Introduction Screening for active tuberculosis (TB) and latent TB infection (LTBI) is mandatory prior to the initiation of anti-TNF therapy in patients with immune-mediated inflammatory diseases (IMID). In 2010, our local guideline included QuantiFERON®-TB Gold (QFT) as well as clinical risk stratification. However, indeterminate QFT results were increasingly identified in this population, higher than that observed in other published series.

Aims To identify patient and IMID characteristics that may be contributing to indeterminate QFT results and LTBI diagnostic uncertainty.

Methods We conducted a retrospective study of all patients that had received at least one dose of anti-TNF since 2010. Data obtained included patient demographics, TB risk stratification and QFT results.
Abstract P113 Table 1  Patient demographics, disease profile and Quantiferon results

<table>
<thead>
<tr>
<th>Disease</th>
<th>N (%)</th>
<th>Quantiferon result (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD</td>
<td>78 (43.1)</td>
<td>95 (73.6%) reactive</td>
</tr>
<tr>
<td>UC</td>
<td>65 (35.9)</td>
<td>40 (48%) reactive</td>
</tr>
<tr>
<td>RA</td>
<td>20 (11.1)</td>
<td>3 (15%) non-reactive</td>
</tr>
<tr>
<td>Ps</td>
<td>14 (7.7)</td>
<td>6 (42%) reactive</td>
</tr>
<tr>
<td>Other</td>
<td>4 (2.2)</td>
<td>2 (50%) reactive</td>
</tr>
</tbody>
</table>

For 114 colitis patients – was rescue anti-TNF given?

<table>
<thead>
<tr>
<th>Quantiferon result (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>non-reactive</td>
</tr>
<tr>
<td>No</td>
</tr>
<tr>
<td>Yes</td>
</tr>
</tbody>
</table>

Results 181 patients (M:F 87:94; age range 11–83; average age 44.8 years) had received at least one dose anti-TNF and were included in this study (see Table). The majority of patients had colitis (n = 143; 79%), 52 patients (28.7%) did not have a documented QFT or IGRA (interferon gamma release assay) result. LTBI was diagnosed in 8 (6.2%) with reactive QFT of whom 7 completed chemoprophylaxis and 1 was referred for further investigation and treatment elsewhere. 95 (73.6%) were QFT non-reactive. 26 (20.2%) were QFT indeterminate, all of whom had a diagnosis of colitis. Colitis patients were more likely to be QFT indeterminate if they were tested at the time of rescue anti-TNF with or without surgery (RR 5.71; 95% CI: 2.49–13.09; p < 0.0001). 2 patients who received rescue anti-TNF and were subsequently found to be QFT reactive, successfully completed LTBI chemoprophylaxis.

Conclusion The rate of indeterminate QFT results is higher than expected in our cohort of patients with colitis who require rescue anti-TNF therapy and is likely to be related to the timing of testing. If QFT testing is undertaken, this should be performed when patients are at stable state and not at the time of inflammatory crisis.

Introduction NICE 2016 Tuberculosis guidance recommends significant changes in contact screening. Tuberculin Skin Test (TST) is advocated for diagnosis of latent tuberculosis infection (LTBI), with a positive TST redefined as 5mm regardless of BCG status, IGRA only to be used in diagnostic uncertainty, upper age for LTBI treatment raised from 35 to 65, and contact tracing no longer recommended for extra-pulmonary TB.

We use a 2 step test, with IGRA for those with TST > 10 mm in context of BCG, and treat LTBI on basis of IGRA result. We aimed to assess the implications for our service of adopting the new guidance.

Methods We reviewed written and electronic records for all contacts screened in Leeds in 2015. NICE 2016 guidance was applied retrospectively to analyse the impact of each recommendation and the guidance as a whole.

Results 216 contacts were screened. Full records were available for 193. 14 were treated for LTBI, 2 for active TB, and 6 contacts over 35 had X-ray follow up. 34 had TST > 10 mm, an additional 13 had TST 5–9 mm. Of 34 with TST > 10 mm, 14 (41%) had positive IGRA. 97/193 (50%) were contacts of extrapulmonary tuberculosis. 4 of these were treated for LTBI, but 21 had TST > 5 mm.

Using TST > 5 mm cut off would increase the number of IGRA tests from 34 to 46. Treating on basis of TST alone would increase the number given chemoprophylaxis from 14 to 46. Stopping screening for contacts of extrapulmonary cases would reduce the number screened by 50% and the number treated from 46 to 29. However, this would be at the cost of missing at least 4/14 LTBI with positive IGRA.

Conclusion Adopting the new NICE guidance in full would reduce the number screened but significantly increase the numbers treated for LTBI. Using the 2 step test with a TST cut off of 5mm would modestly increase the number of IGRA tests but would be unlikely to have a large impact on the number treated. Stopping screening for contacts of extrapulmonary TB would reduce the screening workload by 50% but reduce the number of LTBI cases diagnosed by 29%.
Methods Close contacts of MDR-TB patients were traced in the cross-sectional study. Different clinical, radiological and bacteriological were performed to rule out the evidence of TB/MDR-TB.

Results Between January 2012 and December 2012, a total of 200 index MDR-TB patients were initiated on MDR-TB treatment, out of which home visit and contacts screening were conducted for 154 index cases. Of 610 contacts who could be studied, 41 (17.4%) were diagnosed with MDR-TB and 10 (4.2%) had TB. The most common symptoms observed were cough, chest pain and fever.

Conclusions The high incidence of MDR-TB among close contacts emphasise the need for effective contact screening programme of index MDR-TB cases in order to cut the chain of transmission of this disease.

REFERENCES
Abstract P117 Table 1

<table>
<thead>
<tr>
<th>Number (%) Declined treatment</th>
<th>Lost to follow-up</th>
<th>Stopped due to side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>105 (90.9)</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Biological therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>71 (44.4)</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>New entrant screening</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 (0.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Occupational health</td>
<td></td>
<td></td>
</tr>
<tr>
<td>120.8</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total number of patients seen</td>
<td>206</td>
<td>8</td>
</tr>
</tbody>
</table>

P118 HOW DO FOREIGN-BORN PATIENTS WITH TUBERCULOSIS ACCESS HEALTHCARE? A COHORT ANALYSIS OF REFERRALS FROM GENERAL PRACTICE AND THE EMERGENCY DEPARTMENT TO A TERTIARY TUBERCULOSIS SERVICE

Introduction More than Seventy percent of active Tuberculosis (TB) cases in England are in patients born outside the United Kingdom (UK). Lack of access to primary healthcare is often cited as a barrier to TB control. We considered how patients with TB referred directly to outpatient services initially access healthcare.

Method A retrospective cohort analysis of all patients with active TB on the London TB register (LTBR) between April 2014 and April 2015 at a large urban tertiary referral centre. The route of referral to TB services was confirmed by a review of electronic patient records. We compared demographic, disease and outcome variables between groups as recorded in the LTBR. We excluded those requiring admission; identified through contact tracing; referrals from other secondary care outpatient services and those with inadequate data. Chi squared or Exact tests were used in the analysis.

Results We compared patients diagnosed with TB who were referred directly to outpatient services from General Practice (GP) (97 patients) and the Emergency Department (ED) (35 patients). There was no significant difference in age or sex between groups.

Of those patients born outside the UK (105), 78 percent (82/105) were referred to clinic from their GP compared to only 56 percent (57/105) of those born within the UK (57/105). This difference was statistically significant (p < 0.05). There was no statistically significant difference between the mean length of stay in the UK amongst migrants that presented via ED or GP (MD 2.33 years, 95% CI: –2 to 7, p < 0.4). There was no statistically significant difference in the number of patients who had at least one social risk factor between groups.

Comparing disease between the groups, there was a higher proportion of multi-site disease amongst those referred from ED compared to GP (23% [8/35] vs 14% [14/97], p < 0.025), there was no statistical difference between the numbers of pulmonary cases identified or smear status between the groups.

Conclusion Amongst patients with active TB referred directly to outpatient services, those born outside the UK were more likely to have been referred by their GP than UK-born patients.

Abstract P119 Table 1

<table>
<thead>
<tr>
<th>Intensive Phase (Month 0–2)</th>
<th>Continuation Phase (Month 3–6)</th>
<th>Follow Up Phase (Month 7–18)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Grade 3 AEs Reported</td>
<td>66</td>
<td>31</td>
<td>19</td>
</tr>
<tr>
<td>No. Grade 4 AEs Reported</td>
<td>19</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>System Organ Class of Reported Grade 3 &amp; 4 AEs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>14</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Metabolism &amp; Nutrition</td>
<td>11</td>
<td>0</td>
<td>6</td>
</tr>
<tr>
<td>General Disorders</td>
<td>7</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>No of Grade 3 or 4 AEs per Patient</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>578</td>
<td>574</td>
<td>554</td>
</tr>
<tr>
<td>1</td>
<td>49</td>
<td>18</td>
<td>9</td>
</tr>
<tr>
<td>2</td>
<td>9</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>≥3</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>No of Patients</td>
<td>32</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>with ≥1 SAE (Considered Related)</td>
<td>(21)</td>
<td>(6)</td>
<td>(2)</td>
</tr>
<tr>
<td>Mean No of SAEs per Patient</td>
<td>1.78</td>
<td>1.39</td>
<td>1.60</td>
</tr>
<tr>
<td>No of Withdrawals</td>
<td>38</td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td>No of Deaths</td>
<td>5</td>
<td>1</td>
<td>10</td>
</tr>
</tbody>
</table>

Conclusion Using adverse events in a tuberculosis trial to describe the tolerability of standard therapy

Introduction and objectives The current standard treatment for pulmonary tuberculosis (TB) has been in use for several decades and the major risks associated with each of the four drugs (HRZE) are well recognised. However, large prospective trials with regular review and documentation of adverse events while taking HRZE are lacking.

We used the incidence of grade 3 and 4 adverse events (AEs) and serious adverse events (SAEs) in patients taking HRZE in the REMoxTB trial to investigate the overall tolerability of the regimen.

Methods Grade 3 or 4 AEs and SAEs (of any grade) for patients taking standard TB therapy were analysed. Events were labelled as occurring in the intensive phase, continuation phase or in follow-up (up to 18 months after enrolment). ANOVA and chi-
square testing was used to test for significant differences in the incidence of events across the treatment phases. Logistic regression was used to investigate associations between baseline characteristics and on-treatment SAEs and withdrawal from treatment, death or relapse/treatment failure.

**Results** 201 (31.5%) of 639 patients taking standard therapy experienced grade 3/4 AEs or SAEs during treatment. AEs, SAEs, and withdrawals from treatment occurred most frequently in the intensive phase (see Table). Of 116 SAEs reported 84 (72.4%) improved or resolved and were most commonly respiratory (16.4%), gastrointestinal (6.9%), and infection (5.2%) related. There were 10 deaths in follow-up due to suicide, trauma, TB relapse, and acute illness. Logistic regression detected a significant association between on-treatment SAEs and withdrawal (p < 0.001) or death (p < 0.001), but not relapse/treatment failure (p = 0.611). HIV-positive status (OR 4.23, p = 0.016) and lower baseline weight (OR 1.46, p = 0.023) were associated with the reporting of on-treatment SAEs.

**Discussion** AEs and SAEs were predominantly reported in the intensive phase, probably due to a combination of TB and effects of medication. However most deaths occurred in follow-up and were unrelated, emphasising the impact that social circumstances have on TB patients. The lack of significant association between SAEs during treatment and relapse/recovery may reassure that a complicated treatment period can end with successful treatment of TB. The association between SAEs on treatment and lower weights at baseline and HIV infection reinforces the need to monitor these patients closely.

**Clinical Studies of Asthma**

**P120 CHALLENGES IN USING HIERARCHICAL CLUSTERING TO IDENTIFY ASTHMA SUBTYPES: CHOOSING THE VARIABLES AND VARIABLE TRANSFORMATION**

1M Deliu, 2S Yavuz, 1M Sperrin, 3T Belgrave, 1C Sackesen, 1U Sahiner, 1M Custovic, 1O Kalyay. University of Manchester, Manchester, UK; 2Hacettepe University, Ankara, Turkey; 3Imperial College, London, UK

**Introduction** The use of unsupervised clustering has identified different subtypes of asthma. Choosing the variables to input into the clustering algorithm is one of the important considerations. The majority of previous studies selected variables based on expert advice, whilst others used dimension reduction techniques such as principal component analysis (PCA). We aimed to compare the results of unsupervised clustering when using raw variables, or variables transformed using dimensionality reduction techniques.

**Methods** We performed our analysis on 613 asthmatics aged 6–23 years from Ankara, Turkey. We conducted extensive phenotyping and recorded 49 variables including demographic data, sensitisation, lung function, medication, peripheral eosinophilia, and markers of asthma severity. We performed hierarchical clustering (HC) using: (1) all variables; and (2) variables transformed using dimensionality reduction techniques.

**Results** PCA revealed 5 components describing atopy and variations in asthma severity, which were then used to infer cluster assignment. The optimal HC solution in both PCA-transformed and raw untransformed data identified five clusters. However, these clusters were not identical. Both identified mild asthma with good lung function, severe atopic asthma and late-onset mild atopic asthma. However, the overlap between children assigned to these three clusters in two HC analyses was modest. Clustering without PCA identified early-onset severe atopic asthma and late-onset atopic asthma with high BMI, whilst early onset non-atopic mild asthma in females was identified in HC with PCA. Using both methods, we identified four features that characterised the clusters. These were age of onset, atopy, asthma attacks, and asthma severity. Using only these four features, we identified early onset mild asthma, early onset non-atopic mild asthma, severe asthma, late onset asthma, and exacerbation prone asthma. Cluster stability increased drastically.

**Conclusion** Different methodologies applied to the same dataset identified differing clusters of asthma. We identified four features that characterised the clusters. We propose that these four features could be more useful in identifying asthma endotypes.

**P121 URBAN FINE AND COARSE MODE PARTICULATE MATTER DIFFERENTIALLY ALTER THE MATURATION OF MONOCYTE-DERIVED DENDRITIC CELLS**

1TR Ho, N Camina, PE Pfeffer, EH Mann, IS Mudway, CM Hawrylowicz. King’s College London, London, UK

**Background** There is considerable evidence linking increased exposure to particulate matter (PM2.5 and PM10) to adverse respiratory outcomes, with patients with asthma and chronic obstructive pulmonary diseases (COPD) prone to more exacerbations and respiratory tract infections during pollution episodes. We have previously shown that peripheral human CD1c+ myeloid DCs, a key orchestrator of the adaptive immune response, promoted naïve CD4+ T lymphocyte proliferation and increased expansion of potent inflammatory Th1 and Th17 effector cells when challenged with standard reference urban PM (SRM-1648a). However, monocyte-derived dendritic cells (MDDCs), which represent an inflammatory subset of DCs, may play a substantial role in lung inflammation. In this study, we investigated the effects of PM on MDDC maturation, focusing on responses to PM samples collected from the contemporary London airshed.

**Methods** PM2.5 and PM10 from a high traffic roadside site in London were collected (2/1/2013 – 15/1/2014) and pooled to generate representative annual samples. SRM-1648a and SRM-2975 (diesel exhaust derived PM) were used as control samples. Differentiated MDDCs, derived from CD14+ monocytes incubated with IL-4 and GM-CSF for 6 days, were challenged with these PM samples, plus control PM samples at various concentrations (2.5–20 μg/ml) for 24 hours. DC expression of CD83, MHC-I and MHC-II were measured by flow-cytometry.

**Results** Roadside PM10 and SRM-1648a exposure significantly increased the expression of MHC-II on MDDCs, whilst Roadside PM2.5 and SRM-2975 had no impact. There was also an increased expression of maturation marker CD83 when cells were exposed to Roadside PM10 and SRM-1648a, as well as Roadside PM2.5 at a higher concentration. However, exposure to all PM samples except for Roadside PM10 led to a significant decrease in MHC-I expression.

**Conclusion** PM fractions containing coarse mode material (SRM-1648a and PM10) appeared more able to stimulate MDDC maturation than fine mode PM (SRM-2975 and PM2.5). There was a clear decrease in MHC-I expression after exposure to most PM samples. This may indicate that MDDCs DCs exposed to PM are less able to stimulate CD8+ T cells, resulting in recurring
respiratory tract infections. Understanding the immunological effects of different particle types will help guide public health interventions.

P122 LOCAL SOURCES RATHER THAN INTERACTIONS WITH OXIDISING CO-POLLUTANT GASES DETERMINE THE GEOGRAPHICAL AND SEASONAL VARIATION IN PARTICULATE MATTER OXIDATIVE POTENTIAL

N Camina, DC Green, FJ Kelly, IS Mudway. King’s College London, London, UK

10.1136/thoraxjnl-2016-209333.265

Background Reactions of ambient particulate matter (PM) with atmospheric radicals and oxidising gases such as nitrogen dioxide (NO₂) and ozone (O₃) may alter their toxicity – often referred to as particle ageing. As concentrations of O₃ dominate in the warmer months, with NO₂ episodes more common in the winter, we investigated whether seasonal differences in the PM oxidative potential (the capacity of inhaled PM to cause damaging oxidation reactions at the air-lung interface) could be attributed to their interaction with these gases.

Methods Daily PM₁₀ and PM₂.₅ filters from 4 sites in Southern England were obtained during summer (21st July – 23rd August) and winter (6th Jan – 11th Feb) campaigns in 2012: two sites in London, roadside (Marylebone Road) and urban background (North Kensington) locations, plus two rural sites to the West (Harwell) and East (Detling) of the city. Ascorbate and glutathione-dependent oxidative potential (OP-AA and OP-GSH, expressed per unit mass of PM) were then determined following incubation in a synthetic respiratory tract lining fluid (4 hours at 37°C, pH 7.0) using a novel on filter methodology.

Results In terms of the OP-AA metric only PM₂.₅ measured at the urban background location demonstrated a seasonal increase (p < 0.05) during the summer, with equivalent seasonal OPs across the remaining 3 sites and no differences apparent in PM₁₀. In contrast, PM₁₀ and PM₂.₅ OP-GSH was significantly (P < 0.001) lower in the summer period at the urban background site. Summer increases in OP-GSH were observed at the rural sites, with evidence that summer PM₂.₅ OP-GSH was increased at the roadside site. This heterogeneous pattern of seasonal contrasts could not be simplistically related to the differences in period, or daily NO₂ or O₃ concentrations.

Conclusions No consistent seasonal pattern in PM₁₀ or PM₂.₅ OP was observed across the four sites and the associations between the measured particulate OPs with O₃ and NO₂ at these locations did not fit with the particle ageing hypothesis. Rather high OP days were often found to be associated with wind speed and direction, suggesting that the differences were driven by a combination of long and short range sources.

P123 WHAT CAUSES OCCUPATIONAL ASTHMA IN CLEANERS?

VC Moore, PS Burge, AS Robertson, ED Parkes, GI Walters. Birmingham Heartlands Hospital, Birmingham, UK; University Hospitals Birmingham, Birmingham, UK

10.1136/thoraxjnl-2016-209333.266

Domestic cleaners show a consistently raised risk of developing asthma in population-based epidemiological studies. The main risks appear to be the use of bleach and sprayed cleaning agents. These risks are now found in other occupations, such as healthcare due to the requirement for disinfection of clinical areas. Since 2000, there has been 26 cleaners and healthcare workers with occupational asthma (OA) reported to Shield (West Midlands registry for OA) thought to be due to cleaning agents. The majority of these were using chlorine-releasing substances containing dichloro-isocyanurate for disinfection purposes. We have carried out 8 specific inhalation challenge tests to chlorine-releasing tablets mixed with cold water but none of these have elicited an asthmatic reaction despite the workers previously showing work-related changes on serial peak flows when exposed. In a

Abstract P123 Figure 1 Specific inhalation challenge testing showed no asthmatic response to hartabs or urine alone. The chlorine urine mixture provoked a dual asthmatic reaction and sustained drop in FEV1 of up to 34% from base line. The grey box denotes the exposure.
AN INVESTIGATION INTO COMORBIDITY ACCUMULATION IN ASTHMA PATIENTS WITH SYSTEMIC STEROID EXPOSURE

LB Barry, JS Sweeney, C O’Neill, CP Patterson, DP Price, LH Heaney. Queen’s University Belfast, Belfast, UK; National University of Ireland, Galway, Ireland; University of Aberdeen, Aberdeen, UK

Introduction Much of the economic cost associated with severe asthma is related to the treatment of comorbidities, several of which arise from systemic steroid exposure related to asthma management. However these comorbidities may not progress equally across age-groups and genders following systemic steroid exposure.

Aim To examine the relationship between age-groups and gender in relation to prevalence of steroid induced comorbidity and the associated costs.

Methods Data for a cohort of 808 patients with severe asthma (SA) matched by age and sex with a cohort of 3,975 patients with a diagnosis of mild asthma and 2,412 non-asthma patients with a diagnosis of rhinitis were extracted from the Optimum Patient Care Research Database (OPCRD). Consultation data were used to identify comorbidities and conditional logistic regression analysis provided odds ratios (95% CI’s) for comorbidity risk between cohorts by age-group and gender. Prescription data for individual comorbidities was costed using Prescription Cost Analysis data from Northern Ireland and regressed upon cohort, age and gender.

Results Results presented below focus on a comparison between the non-asthma and severe asthma cohorts. Compared to older patients, younger patients in the SA cohort show significantly higher odds ratios relative to the non-asthma cohort for many comorbidities (Table 1). Apart from chronic kidney disease, hypercholesterolemia, osteoporosis and osteopenia, males with SA have higher odds ratios for all other comorbidities listed in Table 1 relative to non-asthma patients than females with SA. Upon examination of costs for individual comorbidities, males cost more than females for type II diabetes, hypertension, psychiatric disorders, while the opposite was observed for osteoporosis and osteopenia. Significant linear and non-linear increasing relationships were observed across age for costs related to type II diabetes, hypertension, hypercholesterolemia, dyspeptic disorders, cardiovascular disease, osteoporosis and osteopenia. Furthermore cost differentials for age and gender exhibited varying relationships across morbidities.

Conclusions The odds of having many steroid-induced comorbidities are higher among younger persons; differences between genders are also evident. While patients’ with SA cost significantly more than patients without steroid exposure or with mild steroid exposure, the distribution of the cost across age and gender varies across comorbidities.

Abstract P124 Table 1 Summary of odds ratios for comparison of comorbidity risk between severe asthma and rhinitis cohorts

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age-group</th>
<th>Type 2 Diabetes</th>
<th>Obesity</th>
<th>Osteoporosis†</th>
<th>Osteopenia†</th>
<th>Hypertension</th>
<th>Chronic Kidney Disease†</th>
<th>Dyspeptic Disorders</th>
<th>Psychiatric Disorders</th>
<th>Sleep Disorders</th>
<th>Hypercholesterolemia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤45 yr</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>1.0 (0.6–1.6)</td>
<td>1.8 (1–2.4)***</td>
<td>49.2 (11.2–217.7)***</td>
<td>4.5 (2.8–7.3)***</td>
<td>1.9 (1.4–2.6)***</td>
<td>3.9 (2.4–6.6)***</td>
<td>5.5 (4.0–7.6)***</td>
<td>1.6 (1.2–2.3)***</td>
<td>1.2 (0.4–3.4)</td>
<td>2.1 (1.4–3.1)***</td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td>2.7 (1.8–4.1)</td>
<td>2.8 (2.2–3.5)***</td>
<td>4.6 (3.2–6.8)***</td>
<td>4.5 (2.8–7.3)***</td>
<td>1.7 (1.3–2.2)***</td>
<td>1.9 (1.3–2.7)***</td>
<td>7.8 (5.9–10.3)***</td>
<td>2.0 (1.6–2.6)***</td>
<td>3.5 (1.9–6.7)***</td>
<td>1.4 (1.0–1.9)*</td>
</tr>
<tr>
<td></td>
<td>46–60 yr</td>
<td>4.2 (1–18.0)***</td>
<td>3.7 (2.4–5.6)***</td>
<td>18.3 (8.4–52.8)***</td>
<td>50.4 (12.0–210)***</td>
<td>4.1 (1.9–8.9)***</td>
<td>7.7 (3.6–16.8)***</td>
<td>9.4 (5.8–15.2)***</td>
<td>2.6 (1.3–3.9)***</td>
<td>12.9 (1.6–103.3)***</td>
<td>1.4 (1.0–1.9)*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4.0 (2.2–7.2)***</td>
<td>3.3 (2.4–4.6)***</td>
<td>6.2 (3.0–12.6)***</td>
<td>2.7 (1.2–6.3)**</td>
<td>2.4 (1.6–2.6)***</td>
<td>3.2 (1.3–5.9)***</td>
<td>9.8 (6.5–14.7)***</td>
<td>1.8 (1.2–2.5)**</td>
<td>8.1 (2.1–30.3)**</td>
<td>2.2 (1.3–3.8)**</td>
</tr>
<tr>
<td></td>
<td>61–70 yr</td>
<td>1.7 (0.9–3.2)</td>
<td>1.8 (1.3–2.6)***</td>
<td>6.2 (3.0–12.6)***</td>
<td>2.7 (1.2–6.3)***</td>
<td>1.7 (1.2–2.5)**</td>
<td>1.4 (1.0–2.1)*</td>
<td>6.2 (3.9–9.6)***</td>
<td>1.8 (1.2–2.5)**</td>
<td>2.3 (0.7–7.5)</td>
<td>1.7 (1.1–2.6)**</td>
</tr>
<tr>
<td></td>
<td>&gt;70 yr</td>
<td>0.9 (0.5–1.6)</td>
<td>1.8 (1.3–2.6)***</td>
<td>5.2 (4.0–6.9)***</td>
<td>3.1 (1.5–6.6)***</td>
<td>1.2 (0.8–1.7)</td>
<td>1.4 (1.0–2.1)*</td>
<td>4.0 (3.3–4.8)***</td>
<td>1.3 (0.9–2.0)</td>
<td>0.6 (0.2–1.8)</td>
<td>1.2 (0.8–1.8)</td>
</tr>
</tbody>
</table>

†*Age groups ≤45 yr and ≥46–60 yr were combined
††Too few cases of comorbidity for analysis
* P<0.1, ** P<0.05, ***P<0.01

Poster sessions
A PRIMARY CARE AUDIT ON ASTHMA PATIENTS WITH FREQUENT EXACERBATIONS AND THE POTENTIAL IMPACT OF NATIONAL REVIEW OF ASThma DEATHS (NRAD) RECOMMENDATIONS

R. Chaudhari, ¹W. Thomson, ²C. McCallum, ¹H. O’Pray, ³S. Barclay, ¹D. Murray, ¹S. Madhie-Stewart, ²V. Sharma, ¹M. Shepherd, ²W. Lee. ¹Gartnavel General Hospital, Glasgow, UK; ²Contractor Services, NHS Greater Glasgow and Clyde, Glasgow, UK; ³Glasgow Royal Infirmary, Glasgow, UK; ⁴Prescribing and Pharmacy Support Unit, NHS Greater Glasgow and Clyde, Glasgow, UK; ⁵Queen Elizabeth University Hospital, Glasgow, UK

10.1136/thoraxjnl-2016-209333.268

Background One of the key recommendations of NRAD ¹ is that patients who require 2 courses or more of oral corticosteroids (OCS) for asthma in the last 12 months should be referred to a specialist asthma service. This may put undue pressure on secondary care asthma services as the number of such patients is unknown.

Aims To identify asthma patients with recurrent exacerbations who would merit referral to secondary care, and to study the biopsychosocial factors associated with frequent exacerbations.

Methods Data were retrospectively collected on asthma patients aged >18 years from 10 primary care practices in the North Glasgow area over a 12-month period between 2014 and 2015. All prescriptions patients received in primary care were obtained. Only patients who received asthma treatment in the last 12 months were included. Patients were identified as a ‘frequent exacerbator’ if they had received ≥2 courses of OCS for asthma, and a “short-acting beta 2-agonist (SABA) over-user” if they had required >12 SABA inhalers in the last 12 months.

Results Out of 2639 asthma patients studied, 7% were frequent exacerbators, 5% were SABA over-users, 1% were both. Compared with all asthma patients, frequent exacerbators were older (mean age 58 ± 16 vs 48 ± 17) and more likely to be female (68% vs 58%). They had a higher prevalence of cigarette exposure and multiple co-morbidities including COPD, gastro-oesophageal reflux, anxiety, depression, rhinitis and osteoporosis. 41% of frequent exacerbators did not have an asthma review in primary care in the last 12 months and 42% had no previous input from secondary care. The total number of patients who would merit referral to a specialist asthma service from the 10 primary care practices was 78 over a 12-month period.

Conclusions Frequent exacerbators and SABA over-users account for a small proportion of asthma patients attending primary care. The number of new referrals generated by the NRAD recommendation may put additional pressure on secondary care asthma services.

Funder supported by an educational grant from Novartis Pharmaceuticals.

REFERENCE

¹ Levy ML. The national review of asthma deaths: what did we learn and what needs to change? Breathe (Sheff) 2015;11(3):14–24.

INSUFFICIENT ALLERGY DIAGNOSTICS IN SEVERE ASTHMATIC PATIENTS IN GERMANY

J. Schreiber, ¹C. Mallaender. ¹University Hospital, Otto-von-Guericke University, Magdeburg, Germany; ²Novartis Pharma GmbH, Nuernberg, Germany

10.1136/thoraxjnl-2016-209333.269

Introduction Proper evaluation of the allergic sensitizations is inevitable in treating severe asthma. Besides seasonal allergens, perennial aeroallergens have to be considered. However, within the German reimbursement system testing of only 8 allergens per quarter is reimbursed by health insurances, and thus, analyses of relevant allergens beyond the 8 common ones is often not done.

Purpose The aim of this ongoing project is to gain data on sensitizations towards 35 perennial aeroallergens in severe asthmatic patients, in which no allergen could be detected in previous testing and who are thus considered non-atopic.

Methods 35 locally common perennial aeroallergens (mites, fungi, animal epithelia, insects) are tested via Immulite® (specific IgE in blood) in 600 severe asthmatic patients in Germany who had negative results in previous allergen testing by either Skin Prick Test or analyses of specific IgE. Furthermore, total IgE levels are determined and a general anamnesis is documented including historical allergen testing, comorbidities, symptoms, exposure to allergens etc.

Results In an interim analysis, 56.1% of 214 patients demonstrated at least one sensitisation towards a perennial aeroallergen despite they were considered non-atopic before. The most common sensitizations were found towards Rhizopus nigricans (16.8%), Aspergillus fumigatus (15.9%), Cat dander (11.1%), Dermatophagoides farina (10.7%) and Dog dander (9.9%). 84.2% of patients were (partly) uncontrolled according to GINA classification of asthma control and 51.7% had ≥2 exacerbations in the past 12 months. These results indicate a lack in diagnostics of perennial aeroallergens in severe asthmatic patients in Germany. The correct ascertainment of the allergic status is crucial to make optimal treatment decisions for the asthmatic patient.

BENEFITS AND SIDE EFFECTS OF NASAL IRRIGATION IN SEVERE ASTHMA

A Clarke, A H Mansur. Birmingham Regional Severe Asthma Service, Heartlands Hospital, Heart of England NHS Foundation Trust, Birmingham, UK

10.1136/thoraxjnl-2016-209333.270

Introduction and aim Rhinosinus disease is common in asthma and causes nasal congestion, post nasal drip and pain. This can lead to altered breathing patterns, particularly mouth breathing which exposes patients airways to cold dehumidified air and may aggravate their asthma. Nasal irrigation is accepted as an appropriate early intervention for managing allergic rhinitis but may be under-utilised in severe asthma. This study aims to evaluate the effects of nasal irrigation in a severe asthma population.

Method Thirty patients (23 females, mean age 47), with a confirmed diagnosis of severe asthma (22/30 73% atopic) and rhinosinusitis took part in this study, none of the participants had previous nasal irrigation. Patients were taught to irrigate with the netti pot system (0.9% saline), initially 1–2 times each day and to titrate to individual needs. Symptoms were assessed with snott-22 questionnaires before and after three months of treatment, snott scores range from 0–110, a difference of 8.9 points is the minimum change thought to be clinically significant. Data was also collected on ACQ scores, usage, reported benefits and side effects.

Results 26 patients were using nasal irrigation at three month follow-up, mean initial snott scores were 63.2 ± 22.9 compared to 41.7 ± 26.8 post treatment (p = 0.0001). 69% (18/26) patients showed clinically significant decreased nasal symptoms, with a mean improvement of 33.7 points. 19% (5/26) showed no significant change and 12% (3/26) had a clinically significant increase in nasal symptoms. 88% (23/26) patients felt their nasal symptoms had improved, 62% (16/26) felt their chest symptoms had
improved. Mean initial ACQ 3.42 ± 1.39 compared to 2.62 ± 1.58 post treatment (p = 0.01). Usage ranged from BD to 3–5 times per week. 17% (5/30) of patients reported side effects: headache (2) sneezing (1) Nose bleed (1) LBP (1). Three patients stopped treatment due to the side effect.

Conclusion After three months of nasal irrigation 88% of patients reported improved nasal symptoms, 62% reported improved chest symptoms, there were statistically significant improvements in mean snot 22 and ACQ scores. Nasal irrigation is therefore an effective and inexpensive intervention, with few side effects, and should be advocated in severe asthma clinics.
Conclusion In patients attending a severe asthma clinic physiotherapy techniques (ACT and HS-7) were safe and effective. Bronchoscopy had similar requirement for rescue salbutamol nebulisation compared to HS-7, but a higher risk (2%) of severe asthma exacerbation.

REFERENCE

FUNGAL CONTAMINATION OF VALVED HOLDING CHAMBERS (VHCS): POTENTIAL TO PREVENT, AND EFFECT ON DRUG DELIVERY

P129

Introduction and objectives Able Spacerâ–2 VHC (AS2) is one of many accessory devices available to improve pressurised metered dose inhaler (pMDI) drug delivery, but uniquely includes a ~1wt% body polymer silver ion additive (~1%Ag+) to combat microbial growth and reduce static. Drug-specific bacterial growth on VHC polymers1 and the bacterial growth-reducing effects of the Ag+ polymer are known.2 The fungal pathogen Aspergillus fumigatus causes serious pulmonary disease. We assessed the effect of 4%Ag+ on fungal activity and, subsequently, drug delivery characteristics.

Methods Determination of fungal sporidical activity was via modified ISO22196:2011 using flat body polymer discs (n = 3) of AS2 ~1% Ag+ and AS2 4%Ag+, and sterile Control (same polymer minus Ag+, n = 6). 100mL A. fumigatus (5.0 x 10^5 spores/mL distilled water) was pipetted onto disc surfaces. Samples were incubated for 24 h at 35°C/≥95% relative humidity, with silver ions neutralised thereafter. Colony forming units (CFU) were enumerated by spiral dilution and converted to CFU/cm². Aerosol performance of salbutamol (as salbutamol sulphate) pMDI (Ventolinâ EVOHaler, GSK) through AS2 VHC (~1% Ag+ as standard) and a newly-developed AS2 4% Ag+ VHC was assessed through a Next Generation Impactor (NGI) at 30 L/min. pMDIs and NGI were operated, and drug determinations made, using standard procedures.

Results 24 h geometric mean Log10 A. fumigatus CFU/cm² were 4.2 x 10³ (Control), 2.8 x 10³ (~1% Ag+), and 4.5 x 10² (4%Ag+), representing Log10 and% reductions from Control of 0.2 (34%) and 1.0 (89%) for ~1%Ag+ and 4%Ag+. Key salbutamol aerosol performance data were emitted dose (mg) 95.9 ± 11.0 and 94.9 ± 9.1; fine particle fraction (% < 5.0 mm) 54.0 ± 4.3 and 53.6 ± 1.9; and fine particle dose (mg < 5.0 mm) 52.0 ± 8.7 and 50.7 ± 3.8 for AS2 ~1% Ag+ and AS2 4% Ag+ respectively. NGI recovery (Figure 1) profiles were very similar, including the VHC component: 38.9 ± 4.2 (AS2 ~1% Ag+) and 40.2 ± 5.3 (AS2 4% Ag+).

Conclusions Use of 4%Ag+ additive did not affect salbutamol aerosol performance and showed greater effect on A. fumigatus sporid activity in vitro. VHC fungal Candida spp. and nebuliser Aspergillus spp. have been identified. The moist, anti-static setting of the Chamber may support and, of more concern, promote aerosolisation into the lungs of fungal material. Further research and understanding are necessary.

REFERENCE
1 Sanders. PRM 2016;26(16022):16.
P130 PREVALENCE AND CLINICAL OUTCOMES OF FUNGAL SENSITIVE ASTHMA IN A SEVERE ASTHMA POPULATION

N Swaminathan, A Marzur. Birmingham Regional Severe Asthma Service, Birmingham Heartlands Hospital, Birmingham, UK

10.1136/thoraxjnl-2016-209333.273

Introduction It has been proposed that severe asthma patients with fungal sensitisation might endure worse clinical outcomes than non-sensitised patients. However, the extent of fungal sensitisation and its influence on the disease severity remain unconfirmed. This study explores the prevalence of severe asthma with fungal sensitisation (SAFS) and its clinical effect.

Methods Consecutive patients referred to a severe asthma centre has been put through systematic assessment protocol to establish their asthma diagnosis, severity, and clinical outcome measures that includes lung function, biomarkers, exacerbations and hospital admissions frequency. Total and specific serum immunoglobulin E (IgE) and skin prick testing to 27 allergens including 5 fungal allergens were undertaken.

Results A total of 263 patients with a mean age of 45.5 yrs (SD ± 14.6), 72% females, mean age at onset of asthma 21.52 years (range 0.00–69 years), mean pre FEV1% predicted 69.8 (SD ± 24.5) and FEV1/FVC ratio of 66.1 (SD ± 15.3) were considered for the analysis. Allergic characterisation demonstrated atopic status in 182/256 (71.1%), positive sensitisation to alternaria 27/256 (10.5%), aspergillus 57/256 (22.3%), candia 24/256 (9.4%), cladosporium 24/256 (9.4%), penicillium 16/256 (6.2%), meeting SAFS criteria 93/254 (36.4%), and allergic bronchopulmonary aspergillosis (ABPA) 18/247 (7.3%). The SAFS group had higher total IgE than non SAFS group: mean total IgE 974.5 ng/l vs 330.1. However, we observed no statistically different outcomes for the SAFS versus non SAFS groups, ACQ 3.17 vs 3.51, AQLQ 4.0 vs 3.52, FeNO 36.4 ppb vs 32.9, peripheral blood eosinophils (PBE) 385 cells/μl vs 361, annual hospital admissions 1.28 vs 0.97 and annual OCS burst therapy of 5.7 vs 5.9. In contrast the ABPA versus non ABPA cohort had higher PBE 585 cells/μl vs 364, total IgE 2882ng/L vs 326, lower% pre-dFEV1 60.2% vs 71 L, and ever ITU admissions 0.9 vs 0.46.

Conclusion Fungal sensitisation is relatively common in severe asthma but it did not seem to influence overall clinical outcomes. ABPA is less common with worse outcomes.

P131 OUTDOOR FUNGAL SPORE LEVELS, LUNG FUNCTION AND SYMPTOMS IN PATIENTS WITH ASTHMA AND ASPERGILLUS SENSITISATION


10.1136/thoraxjnl-2016-209333.274

Background IgE sensitisation to Aspergillus fumigatus is seen in a significant proportion of patients with refractory asthma. The EVITAT study recently showed that three months’ treatment with voriconazole did not improve asthma-related outcomes in this patient group. It is not known whether daily variations in outdoor fungal spore levels are associated with concomitant fluctuations in symptoms and lung function in patients with Aspergillus-associated asthma.

Methods Participants in the EVITAT study kept daily diaries of peak expiratory flow (PEF) and asthma symptoms during their follow-up period. These diary records were retrospectively analysed together with contemporaneous fungal spore levels measured locally, in those patients (n = 36) who consented to the secondary use of their clinical and research data. Participants also underwent skin-prick tests for Aspergillus, Alternaria, Cladosporium, Penicillium and Botrytis. For each participant, cross-correlation was used to investigate the relationship between PEF and local spore counts of Aspergillus/Penicillium, Alternaria, Cladosporium, Botrytis, Sporobolomyces, Tilletiopsis, and Didymella. Group-level relationships were investigated using linear mixed models for PEF and generalised estimating equations for daily symptom scores, with participants stratified by skin prick test status. The analyses were performed with the exposure and outcome measured on the same day (lag 0), and with the exposure lagged by 1 day with respect to the outcome (lag 1).

Results The analysis cohort comprised 20 men and 16 women with a mean (standard deviation) age of 60 (8) years. No significant or consistent relationships were observed between fungal spore counts and either PEF or self-reported symptom scores, regardless of skin prick test status and lag time between exposure and outcome. In a linear mixed model, the effect size of total fungal spore count on morning PEF was negligible (−0.000011, p = 0.343 for lag 0; −0.000002, p = 0.847 for lag 1).

Conclusion In this retrospective analysis we found no evidence of a significant link between fungal spore counts and either PEF or symptoms in patients with Aspergillus-associated asthma. Further research is required to confirm this result in a prospective study and to identify whether aeroallergen levels relate to other important asthma outcomes such as exacerbations.

P132 FACTORS ASSOCIATED WITH NEAR-FATAL ASTHMA REQUIRING EXTRACORPOREAL MEMBRANE OXYGENATION

S Patel, NM Shah, L Campanota, N Barrett, BD Kent, DJ Jackson. Guy’s and St. Thomas’ NHS Foundation Trust, London, UK

10.1136/thoraxjnl-2016-209333.275

Introduction Until recently the ceiling of management for life-threatening asthma exacerbation involved intubation and mechanical ventilation. In many cases these measures were inadequate given the degree of airflow obstruction. The emergence of extracorporeal membrane oxygenation (ECMO) has offered a management strategy for these otherwise fatal events, however there is a dearth of published data regarding ECMO use in asthma. We sought to investigate factors associated with the requirement for and success of using ECMO in near-fatal asthma.

Methods Patients requiring mechanical ventilation (MV) and/or ECMO for acute asthma at our tertiary centre between 2011–2013 were retrospectively identified from an electronic database.

Results Seventy-five patients were identified. 56/75 (75%) received MV and 19/75 (25%) received ECMO. The proportion of females in the ECMO group was significantly greater than in the MV group (68% vs. 29%, P = 0.002). Median age in the ECMO group was lower (24 years old vs. 41, P = 0.003). There was no statistically significant difference in the smoking history or 30- and 90-day survival between ECMO and MV groups. Bronchoscopy was undertaken in all ECMO and in 28/56 MV patients on admission. Respiratory viruses were identified in significantly more patients requiring ECMO than MV (58% vs. 29%, P = 0.04). The proportion of patients with positive bacterial and fungal cultures was not significantly different between groups. In a subgroup analysis there was no difference in...
duration of ECMO or MV between patients with and without positive virology.

Conclusion In a single regional intensive care unit we demonstrate that requirement for ECMO due to acute asthma is associated with female gender, younger age and positive virology on admission. To our knowledge, this is the first case series analysing factors relating to ECMO use in asthma in the United Kingdom. It highlights the role of respiratory viruses in near-fatal exacerbations and the need for novel anti-viral approaches to reduce morbidity and mortality. Further research is needed in this population to identify whether differences in underlying inflammatory mechanisms exist that may explain the development of such severe events.

**P133 SAFETY AND EFFECTIVENESS OF INFLUENZA VACCINES IN PEOPLE WITH ASTHMA: A SYSTEMATIC REVIEW AND META-ANALYSIS**

1E Vasileiou, 1A Sheikh, 2C Butler, 3K El Farhik, 1Ch Simpson. 1Asthma UK Centre for Applied Research, Uphof University of Population Health Sciences and Informatics, The University of Edinburgh, Edinburgh, UK; 2Nuffield Department of Primary Care Health Sciences, Oxford University, Oxford, UK; 3Institute of Primary Care and Public Health, Cardiff University, Cardiff, UK

10.1136/thoraxjnl-2016-209333.276

**Introduction and objectives** Influenza vaccination is offered annually in the UK to high-risk individuals such as those with asthma as a preventive measure against influenza infection and influenza-related complications. However, the effectiveness and safety of influenza vaccination in people with asthma is not well established.

**Methods** We conducted a systematic review and meta-analysis assessing the overall quality of evidence using the GRADE methodology. Published literature was searched through 13 electronic databases from Jan 1970 to Jan 2016 for clinical trials and epidemiological studies. Unpublished or ongoing literature was searched through references and citations of key publications, and by contacting influenza vaccine manufacturers. The screening for eligible studies, data extraction and quality appraisal was conducted by two reviewers independently. Separate meta-analyses were undertaken for observational and experimental evidence using random-effects models.

**Results** We identified 35 eligible studies, and four contributed to the meta-analyses. Risk of bias was high for one randomised controlled trial (RCT), unclear for 11 RCTs, and low for eight RCTs. The quality of five non-RCTs, four cohorts, and two case-control studies was strong. Moderate quality was found for one non-RCT, and three cohort studies. In people with asthma, pooled vaccine effectiveness (VE) was 45% (OR: 0.55; 95% CI: 0.44 to 0.69; I² = 0%) for laboratory confirmed influenza. Pooled effectiveness of live vaccines was 81% (RR: 0.19; 95% CI: 0.06 to 0.67; I² = 0%) for influenza infection (confirmed by cell culture or rise in antibody titre) and 72% (RR: 0.28; 95%: 0.10 to 0.80; I² = 0%) for influenza-like illness. VE was also observed against asthma attacks. No increased risk of vaccine-induced asthma symptoms and attacks was identified. The quality of the body of evidence was considered very low for all outcomes.

**Conclusions** Evidence on VE in people with asthma against influenza, asthma exacerbations, and other clinical outcomes is limited and of very low quality. Thus, better quality evidence is required, especially in adults with asthma. Vaccination with inactivated or live vaccines was found to be safe and well tolerated in patients with asthma.

**REFERENCE**


**P134 METHACHOLINE CHALLENGE TO DEMONSTRATE THERAPEUTIC EQUIVALENCE OF TERBUTALINE VIA DIFFERENT TURBUHALER DEVICES IN PATIENTS WITH MILD TO MODERATE ASTHMA: APPRAISAL OF A PHASE III, FOUR-WAY CROSSOVER DESIGN**

1L Bjermer, 2G Gauvreau, 3D Postma, 4P O’Byrne, 1M van den Berge, 1L-P Boulet, 1O Beckman, 1T Persson, 1Y Roman, 2M Carlholm, 1K-M Schutze, 1G Eckerwall. 1Skane University Hospital, Lund, Sweden; 2McMaster University, Hamilton, Canada; 3University of Groningen, Groningen, The Netherlands; 4Quebec Heart and Lung Institute, Quebec, Canada; 5AstraZeneca RandD, Gothenburg, Sweden

10.1136/thoraxjnl-2016-209333.277

**Background/objective** To demonstrate therapeutic equivalence of terbutaline via two different Turbuhaler® devices by evaluating its protective effect against methacholine-induced bronchoconstriction in patients with stable asthma.

**Methods** In this double-blind, double-dummy, multicentre, single-dose, 4-way crossover study, patients with stable, mild-to-moderate asthma (FEV1 ≥ 80% predicted normal) were randomised to 0.5 or 1.5 mg terbutaline via either Turbuhaler® M3 or M2 followed by a methacholine challenge test. Primary outcome variable: concentration of methacholine causing a 20% drop in FEV1 (PC20). Patients had to have a PC20 methacholine < 8 mg/mL, reproducible after 2 weeks, and a stable baseline FEV1 at all visits (90–110% of enrolment value).

**Results** 60 patients were randomised to treatment and completed the study. There was a clear dose–response for both devices. The between-devices ratio (M3:M2) was 0.92 (95% CI: 0.75–1.13) for 0.5 mg and 0.88 (95% CI: 0.72–1.08) for 1.5 mg. Both CIs lie inside the interval (0.67–1.50), which was the pre-specified condition for equivalent effect.

**Conclusions** Bronchoprotection with PC20 as the outcome measure in a standardised methacholine challenge model proved to be a useful design to show therapeutic equivalence between devices in patients with mild to moderate asthma. This model provides robust reproducible data, involves smaller patient numbers with fewer dropouts resulting in reduced costs versus a conventional efficacy study.

**Disease Progression and Burden in Obstructive Lung Disease**

**P135 TREATMENT OF LUNG DISEASE IN ALPHA-1 ANTITRYPSIN DEFICIENCY: A SYSTEMATIC REVIEW**

1RG Edgar, 2M Patel, 3S Bayliss, 4E Sapely, 4AM Turner. 1University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK; 2Heart of England NHS Foundation Trust, Birmingham, UK; 3Institute of Applied Health Research, University of Birmingham, Birmingham, UK; 4Institute of Inflammation and Ageing, University of Birmingham, Birmingham, UK

10.1136/thoraxjnl-2016-209333.278

**Introduction** Alpha-1 Antitrypsin Deficiency (AATD) is a rare genetic condition predisposing individuals to COPD. The
majority of treatment for AATD is similar to non-AATD related COPD; intravenous augmentation of Alpha-1 Antitrypsin is a specific treatment but is inequitably used across Europe and not used in the UK. There is a pressing need to systematically investigate efficacy since the publication of a new placebo controlled RCT and to identify patient centred, clinically meaningful outcomes.1

Methods A systematic review was conducted using standard review methodology with meta-analysis and narrative synthesis (registered with PROSPERO-CRD42015019354). Eligible studies were those of any treatment used in severe AATD. RCT’s were the primary focus however case series and uncontrolled studies (n > 10 patients receiving treatment or usual care, with baseline and follow-up data >3 months), were eligible for inclusion to ensure natural history of disease outside RCT’s could be determined.

Results 7296 unique records were reviewed with 51 trials analysed on 5632 participants: 26 AAT-augmentation (3 for meta-analysis); 17 surgical intervention (5 Lung volume reduction (LVR) surgery, 1 Bronchoscopic valve LVR and 11 Lung transplantation); 3 medical interventions and 3 trials completed but not published.

Meta-analysis of AAT-Augmentation demonstrated slower lung CT density decline, difference 0.79 g/l/year (95% CI: 0.29–1.29; p = 0.002), and a small increase in annual exacerbations 0.29/year (95% CI: 0.04–0.54; p = 0.02) compared to placebo (Figure 1).

Survival benefit of transplant was observed in one study (p = 0.006) but not in a second with more stringent matching for groups; however significant improvements in health status, total SGRQ and all domain scores, at one year (p < 0.01) were observed. Mortality post lung transplant was comparable between AATD and non-AATD related COPD cohorts. Surgical lung volume reduction demonstrated inferior outcomes when compared to non-AATD related emphysema.

Conclusion CT density, FEV1, DLCO, health status and exacerbation rates were frequently used as outcomes in AATD related treatment trials. AAT-Augmentation is able to slow the progression of severity of emphysema when measured by CT density change compared to placebo. This systematic review will help assist in the improved monitoring and management of patients with AATD.

REFERENCE

P136 RELATIONSHIP BETWEEN PROGRESSION OF LUNG DISEASE IN ALPHA-1 ANTITRYPSIN DEFICIENCY AND CARDIOVASCULAR RISK

C. Hall, S Samanta, N Vema, B Gooptu, JR Hunt. UCL Respiratory, Royal Free Campus, University College London, London, UK

Introduction Patients with alpha-1 antitrypsin deficiency (AATD) who are homozygous for the mutated Z allele (PiZZ) typically present with emphysema and liver cirrhosis, caused by the uncontrolled action of neutrophil elastase in the lungs and toxic gain-of-function AAT polymer aggregates in the ER of hepatocytes. The link between cardiovascular disease and COPD is widely accepted, but is less well understood in AATD. This study aimed to investigate how markers of lung function severity and the rate of disease progression are associated with cardiovascular risk in a cohort of PiZ patients.

Methods Cardiovascular (CV) risk was determined by the degree of arterial stiffness, measured using aortic pulse wave velocity (aPWV). This was recorded with the Vicorder device which uses the transcutaneous distance between the common carotid and femoral arteries, and the time delay between the feet of the 2 diastolic pulse waveforms to calculate the pulse velocity. Cardiovascular risk was additionally assessed using the QRISK2 algorithm. Pulmonary function was evaluated using FEV1, KCO and RV% TLC, and the degree of AATD disease progression used previous pulmonary function test (PFT) data to determine the rate of lung function decline.

Results We enrolled 48 PiZZ AATD patients (mean (SD) age 52.9 (15.9) years, 19 male) and found significant relationships (denoted by: **p < 0.01 and *p < 0.05) between both aPWV
and QRISK2 and the degree of airflow obstruction (FEV1: \( r = -0.470^{**}, \rho = -0.325^{*} \)), emphysema (KCO: \( r = -0.493^{**}, r = -0.411^{**} \)) and hyperinflation (RV\%TLC: \( r = 0.550^{*}, r = 0.433^{**} \)). Including only patients with \( \geq 3 \) PFT results, we found a significant relationship between emphysema progression and calculated but not measured cardiovascular risk: KCO change vs. QRISK2 \( (r = -0.549, p = 0.015, n = 19). \)

**Conclusions** Reduced lung function was associated with a greater magnitude of measured and calculated cardiac risk in the AATD cohort. However AATD-mediated lung disease progression was not significantly related to measured CV risk – an exception being a significant relationship between the rate of decline of KCO and QRISK2.

**P137 WHY IS ERDOSTEINE RECOMMENDED AS A TREATMENT FOR ACUTE EXACERBATIONS OF CHRONIC BRONCHITIS? A SYSTEMATIC REVIEW OF CLINICAL TRIALS**

1CL Johnson, 2DF Rogers. 1Imperial College London, London, UK; 2National Heart and Lung Institute, Imperial College London, London, UK

10.1136/thoraxjnl-2016-209333.280

**Background** Exacerbations of chronic bronchitis or chronic obstructive pulmonary disease (COPD) are a significant health burden. A substantial component of these exacerbations in many patients is mucus-hypersecretion. Mucolytics, drugs that ‘thin’ mucus, have potential efficacy in these patients.

Currently, erdosteine is the only mucolytic in the British National Formulary (BNF) indicated for “symptomatic treatment of acute exacerbations of chronic bronchitis”, while other BNF mucolytics (carbocisteine, mecysteine and N-acetylcysteine) have had more general or non-respiratory indications, e.g. “reduction in sputum viscosity”. It is theorised that there is clinical evidence that erdosteine is useful in treatment of acute exacerbations of chronic bronchitis, unlike any of the other aforementioned mucolytics.

**Methods** In this narrative systematic review, databases utilised included: Medline, Embase and PubMed. Studies for inclusion had to be Randomised Controlled Trials (RCTs) primarily investigating the effect of erdosteine in exacerbations of chronic bronchitis or COPD. For comparison, RCTs were also included if they investigated carbocisteine, mecysteine and N-acetylcysteine’s effects in exacerbations. A secondary outcome was to investigate the use of these mucolytics in improving COPD signs and symptoms.

Once selected, a two-stage publication elimination process was devised by the author to assess the quality of the trials.

**Results** Very few trials of adequate quality assessed the efficacy of mucolytics in chronic bronchitis or COPD. Of the 5,560 search results, only 62 trials investigated the aforementioned mucolytics use in chronic bronchitis or COPD, 41 were RCTs. Of the 41 RCTs only 13 were found to be of adequate quality; erdosteine (1 RCT), carbocisteine (3 RCTs), mecysteine (0 RCTs) and N-acetylcysteine (9 RCTs).

There was no evidence that erdosteine is useful in treating exacerbations, and very limited, weak evidence for some efficacy in exacerbation prevention. In contrast, carbocisteine showed some strong evidence of efficacy in preventing exacerbations, especially in Asian populations. N-acetylcysteine trial results were variable, and evenly distributed between positive and no effects, with one study showing adverse effects. There were no trials of adequate quality investigating mecysteine.

**Conclusion** There is little evidence that erdosteine is useful in treating chronic bronchitis exacerbations, whereas, overall carbocisteine seems to be more efficacious in exacerbation prevention. 

**P138 AN INNOVATIVE APPROACH TO STUDY DESIGN: USING ELECTRONIC MEDICAL RECORDS TO INFORM THE FEASIBILITY AND DESIGN OF THE NOVELTY STUDY (A NOVEL OBSERVATIONAL LONGITUDINAL STUDY ON PATIENTS WITH ASTHMA AND/OR COPD)**

1HK Reddel, 1M Gerhardsson de Verdier, 1A Agusti, 1R Beasley, 1EH Bel, 1C Janson, 2B Make, 3J Martin, 4P Pavord, 5D Postma, 6D Price, 7C Keen, 1A Garda, 1S Rennard, 2A Sverkus, 1AT Bansal, 1L Brannman, 1N Karlsson, 2J Nuevo, 2F Nyberg, 2S Young, 11Y Vestbo. 1Woolcock Institute of Medical Research, Sydney, Australia; 2AstraZeneca, Madrid, Spain; 3Hospital Clinic University of Barcelona, Barcelona, Spain; 4Medical Research Institute of New Zealand, Wellington, New Zealand; 5Academic Medical Centre, University of Amsterdam, Amsterdam, The Netherlands; 6Uppsala University, Uppsala, Sweden; 7National Jewish Health and University of Colorado, Denver, USA; 8University of Oxford, Oxford, UK; 9University of Groningen, University Medical Centre Groningen, Groningen, The Netherlands; 10Research in Real-Life, Singapore, Singapore; 11Aclareng Ltd, Cambridge, UK; 12The University of Manchester, Manchester, UK

10.1136/thoraxjnl-2016-209333.281

**Introduction** Asthma and COPD have traditionally been viewed as distinct diseases. While they have overlapping biological mechanisms, past studies often focused on specific aspects of each disease based on a single diagnostic label, and many clinical trial populations were defined by strict enrolment criteria with limited generalisability. NOVELTY is a prospective, multinational, observational, longitudinal cohort study aiming to enrol 14,800 patients aged \( \geq 12 \) years with a diagnosis or suspected diagnosis of asthma and/or COPD. In this population, the objectives of NOVELTY are to: (i) describe patient characteristics, treatment patterns and burden of illness over time in clinical practice; and (ii) use biomarkers and clinical parameters to identify phenotypes and endotypes associated with differential outcomes for symptom burden, clinical evolution and healthcare utilisation.

**Aim** This feasibility analysis of electronic medical records (EMRs) aimed to understand the potential study population, assess patient numbers across disease severities and evaluate EMRs as a data source for NOVELTY.

**Methods** EMRs from patients with asthma and/or COPD were identified from national databases covering primary and specialist care in 11 countries (Table). Disease severity was classified using treatment- and/or lung function-based algorithms for asthma and COPD. EMR variable coverage and completeness were assessed for standardised clinical, laboratory and physiological data and patient-reported outcomes (PROs).

**Results** EMRs for 921,888 patients with asthma, 958,945 with COPD and 117,893 with both diagnoses were identified. EMRs routinely documented patient demographics and characteristics, but many disease- and treatment-related data, and PROs/symptoms required for evaluation of disease severity and clinical outcomes were frequently missing (not collected or not documented; Table). Disease severity could not be classified in 561,837 patients (asthma) and 355,743 patients (COPD), representing 22–100% and 7–85% of patients across countries.

**Conclusions** EMR analysis revealed numbers of patients per country potentially eligible for NOVELTY. Many variables required to meet NOVELTY objectives were missing in EMRs (e.g. lung function and PRO/symptoms); therefore, variables in
NOVELTY will primarily be documented in electronic case report forms, not EMRs. The lack of lung function data in many countries suggested divergences in diagnosis of asthma/COPD between clinical guidelines (which include lung function tests) and clinical practice.

Abstract P138 Table 1 Range of proportions of patients with asthma and/or COPD for whom EMRs contained any of selected variables

<table>
<thead>
<tr>
<th>Country</th>
<th>EMR source</th>
<th>Age/sex, %</th>
<th>Height/weight, %</th>
<th>Lung function tests, %</th>
<th>Haematology tests, %</th>
<th>PROs, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>A, GPs (inpatient)</td>
<td>100</td>
<td>21–32</td>
<td>0</td>
<td>31–66</td>
<td>0</td>
</tr>
<tr>
<td>Canada</td>
<td>A</td>
<td>100</td>
<td>34–42</td>
<td>1–10</td>
<td>38–52</td>
<td>0</td>
</tr>
<tr>
<td>China</td>
<td>B (outpatient)</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>2–83</td>
<td>0</td>
</tr>
<tr>
<td>France</td>
<td>A</td>
<td>99–100</td>
<td>13–46</td>
<td>0</td>
<td>7–19</td>
<td>0</td>
</tr>
<tr>
<td>Germany</td>
<td>A</td>
<td>100</td>
<td>18–23</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Italy</td>
<td>A</td>
<td>79–100</td>
<td>18–24</td>
<td>0–4</td>
<td>13–23</td>
<td>0</td>
</tr>
<tr>
<td>Japan</td>
<td>B</td>
<td>100</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Spain</td>
<td>A</td>
<td>100</td>
<td>24–41</td>
<td>0</td>
<td>26–35</td>
<td>0</td>
</tr>
<tr>
<td>Sweden</td>
<td>A</td>
<td>100</td>
<td>34–55</td>
<td>33–56</td>
<td>NA</td>
<td>0</td>
</tr>
<tr>
<td>UK</td>
<td>A (GPs)</td>
<td>100</td>
<td>30–72</td>
<td>0–57</td>
<td>31–59</td>
<td>0</td>
</tr>
<tr>
<td>USA</td>
<td>A, C</td>
<td>100</td>
<td>32–100</td>
<td>0–17</td>
<td>10–70</td>
<td>0</td>
</tr>
</tbody>
</table>

A, physician records; B, hospital records; C, registries; COPD, chronic obstructive pulmonary disease; EMR, electronic medical record; GP, general practitioner; NA, available but not assessed; PROs, patient-reported outcomes.

Please refer to page A271 for declarations of interest in relation to abstract P138.

P139 THE BURDEN OF COPD ACROSS THE EUROPEAN UNION: DEVELOPMENT OF THE EUROPEAN COPD ATLAS

JFM van Boven, 1 J Gaughan, 2 JB Soriano, 3 J Comela de Sousa, 4 N Baxter, 5 MA Rômán-Rodríguez, 5 I Villaró, 5 S Williams, 5 S Fitch, 6 K Kishore, 6 H Chaudhury. 1 European COPD Coalition, Brussels, Belgium; 2 Instituto de Investigación Hospital Universitario de la Princesa (IIP), Universidad Autónoma de Madrid, Madrid, Spain; 3 Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal; ICVS/3B’s – P.1 Government Associate Laboratory, Braga/Guimarães, Portugal; 4 NHS Southwark Clinical Commissioning Group, London, UK; 5 Instituto de Investigación Sanitaria de las Islas Baleares (IdISPa) Balearic Health Service, Palma de Mallorca, Spain; 6 Department of Physiotherapy, Ramon Llull University, Barcelona, Spain; 7 International Primary Care Respiratory Group, Westhill, UK; 8 Fundación Lloret, Madrid, Spain; 9 Health IQ, London, UK

Background Estimating current and future impact of chronic obstructive pulmonary disease (COPD) within the European Union (EU) is essential for targeted and well-informed policy-making, however, current global and regional estimates are contradictory, and comparable standardised data is lacking. Without it the burden felt by individuals and healthcare systems cannot be fully quantified and a collective and coordinated response cannot be achieved to protect economies and communities from further harm.

Aim Our purpose was to
- Collect data to enable a comparative assessment of the COPD burden across EU 28 member states and highlight variation.
- Show the impact of COPD in the workplace, on healthcare utilisation and on quality of life of the EU population.
- Use the data to underpin a simulation model to demonstrate future impact on societies, health inequalities and healthcare utilisation depending on which interventions are selected.

Methods A systematic literature review was performed to identify regional and national data on COPD prevalence, risk factors (e.g., smoking, air pollution), impact and costs across the EU. Workshops with stakeholders from a range of European countries were convened to test the face validity of the data, and to develop policy-level questions from which a simulation model could be developed.

Results Prevalence estimates of COPD varied considerably (1.26% to 13.87%), partly because of different definitions. As smoking rates are less affected by definition differences, these were used in a model that predicts COPD incidence, prevalence and mortality. Correction factors were applied to account for non-smoking related causes and under diagnosis of smoking. Smoking prevalence rates were used to estimate data for equivalent countries for the countries where smoking data were not available. The simulation model is currently in development and first results are expected in Autumn 2016.

Conclusion The European COPD Coalition (ECC) will use the results to facilitate dialogue with EU decision makers (European Commission Council and Parliament) on health policy, outlining the problem and providing evidence to support the call for political actions on COPD. It will also be of significant interest to healthcare professionals, patients, and respiratory organisations with a passion to improve COPD care.

P140 COMORBIDITIES OF SWEDISH PATIENTS DIAGNOSED WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) AND/OR ASTHMA

G Johansson, 1, 2 C Jensen, 1, 2 M Van Der Tol, 1, 2 A Alely, 3 G Bergman, 4 M Uhde, 4 P Sobocki, 2 H Benhaddi, 1 Uppsala University, Uppsala, Sweden; 2 Ieva Pharmaceuticals, (Amsterdam), Amsterdam, The Netherlands; 3 Ieva Pharmaceuticals (France), France; 4 IMS Health, Solna, Sweden

Introduction and objectives Standard of care treatments for asthma and COPD are commonly administered in single-dose or multidose dry powder inhalers. There is a dearth of evidence around the prevalence of comorbidities, especially those that may affect inhaler device handling, among Swedish asthma and COPD patients.

Methods This retrospective study from the Swedish National Health Registries included 495,254 patients receiving inpatient or specialised outpatient care in Sweden between January 1, 2005 and December 31, 2014. Estimates of severity were based on number of asthma/COPD drugs used. Diagnostic codes were used to assess number of patients with a pre-specified comorbidity potentially affecting device handling.

Results Patient characteristics, treatments and comorbidities are summarised in the Table. Comorbidities that may impact inhaler handling were observed in 15.8% (asthma), 50.4% (COPD) and 55.3% (asthma/COPD) patients; incidence was increased with disease severity (patients with severe disease: 26.3%, 52.0%, 55.9%) and advanced age (patients 60–69 years: 33.2%, 45.2%, 50.5%, respectively).

Conclusions Comorbidities potentially affecting device handling were common across all groups, and unexpectedly high among elderly asthma patients. Furthermore, the data indicate that a substantial percentage of patients use two or more separate inhalers. These findings highlight the need for newer, easier to use inhalers, as well as training and monitoring of device use in patients who may have more difficulties using their devices correctly due to comorbidities.
Abstract P140 Table 1

<table>
<thead>
<tr>
<th></th>
<th>Asthma (n = 394,160)</th>
<th>COPD (n = 77,749)</th>
<th>Asthma and COPD (n = 23,345)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, year (SD)</td>
<td>28.9 (24.7)</td>
<td>72.8 (9.8)</td>
<td>71.7 (10.9)</td>
</tr>
<tr>
<td>Male</td>
<td>50.6%</td>
<td>47.5%</td>
<td>48.5%</td>
</tr>
<tr>
<td>Severity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild/moderate/severe</td>
<td>61.4% (34.9%)</td>
<td>32.8% (44.3%)</td>
<td>33.6% (26.4%)</td>
</tr>
<tr>
<td></td>
<td>3.6% (40)</td>
<td>8.8% (52.4%)</td>
<td>7.5% (50.0%)</td>
</tr>
<tr>
<td></td>
<td>16.0% (24.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean Charlson Comorbidity index (SD)</td>
<td>1.3 (1.1)</td>
<td>3.0 (2.2)</td>
<td>2.9 (2.2)</td>
</tr>
<tr>
<td>Treatments (used by &gt;20% patients in any group)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Short-acting beta-agonists</td>
<td>69.8%</td>
<td>45.1%</td>
<td>61.6%</td>
</tr>
<tr>
<td>LABA</td>
<td>8.9%</td>
<td>16.5%</td>
<td>20.2%</td>
</tr>
<tr>
<td>Long-acting muscarinic-antagonist</td>
<td>2.2%</td>
<td>71.6%</td>
<td>50.3%</td>
</tr>
<tr>
<td>ICS</td>
<td>35.3%</td>
<td>16.5%</td>
<td>27.6%</td>
</tr>
<tr>
<td>Fixed ICS/LABA comb.</td>
<td>34.9%</td>
<td>57.5%</td>
<td>68.3%</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>13.8%</td>
<td>33.3%</td>
<td>37.0%</td>
</tr>
<tr>
<td>Oral steroids</td>
<td>20.9%</td>
<td>32.4%</td>
<td>43.1%</td>
</tr>
<tr>
<td>Comorbidities that can affect inhaler handling (observed in &gt;10% patients in any group)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart failure</td>
<td>15.8%</td>
<td>50.4%</td>
<td>55.3%</td>
</tr>
<tr>
<td>Stroke</td>
<td>2.0%</td>
<td>21.8%</td>
<td>22.9%</td>
</tr>
<tr>
<td>Sleep disorders</td>
<td>1.6%</td>
<td>10.8%</td>
<td>9.7%</td>
</tr>
<tr>
<td>Depression or anxiety</td>
<td>3.8%</td>
<td>7.2%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>8.1%</td>
<td>14.4%</td>
<td>17.7%</td>
</tr>
<tr>
<td>Asthma and COPD</td>
<td>1.2%</td>
<td>10.2%</td>
<td></td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease; ICS, inhaled corticosteroids; LABA, long-acting beta-agonists; SD, standard deviation.

Results In this cohort the non-exacerbating phenotype was stable with a total of 69.4% of patients without exacerbations in the 6 months prior to baseline not reporting any exacerbation over the full 2 year follow-up period resulting in an annual exacerbation rate of 0.263 in year 1 and 0.251 in year 2. In contrast, patients with at least one exacerbations in the 6 months prior to baseline showed an annual exacerbation rate of 0.770 in year 1 and 0.633 in year 2. At baseline 44.6% of patients were categorised as GOLD D, one third of these due to their exacerbation history alone. In Year 1 there was a general shift to lower risk categories compared to baseline (GOLD D: 44.6% vs. 31.1%) mainly due to a lower number of exacerbations in Year 1. Overall, categorization then remained relatively stable from Year 1 (GOLD D = 31.1%) to Year 2 (GOLD D = 32.1%).

Conclusions Although, COPD is generally considered to be a progressive disease, this analysis of ‘real life’ data over an observational period of 2 years shows that the ‘non-exacerbating’ phenotype is relatively stable. The data furthermore confirms that exacerbations in the recent history increase the risk of future exacerbations.

P141 2-YEAR FOLLOW-UP OF COPD PATIENTS IN THE NON-INTERVENTIONAL ‘REAL-LIFE’ DACCORD STUDY IN GERMANY

1H Worth, 2R Buhl, 3CP Crie, 4P Kardos, 5C Mailänder, 6N Lossi, 6C Vogelmeier.
2Facharztforum Fürth, Fürth, Germany
3Department of Sleep and Respiratory Medicine, Evangelical Hospital Goettingen-Weendo, Bovenden, Germany; 4Group Practice and Centre for Allergy, Respiratory and Sleep Medicine, Red Cross Maingau Hospital, Frankfurt, Germany; 5Novartis Pharma GmbH, Nürnberg, Germany; 6Department of Medicine, Pulmonary and Critical Care Medicine, University Medical Centre Giessen and Marburg, Philipps-University Marburg, Member of the German Centre for Lung Research (DZL), Marburg, Germany
10.1136/thoraxjnl-2016-209333.284

Introduction Although randomised, controlled trials are important in the development of new pharmacological treatments, they provide limited information on the ‘real life’ management of chronic diseases. Here, we analysed two-year follow-up data from the prospective, non-interventional, observational DACCORD study to evaluate the frequency of exacerbations and the evolution of disease severity using GOLD 2011 categorization.

Methods COPD out-patients were recruited into DACCORD following either a change or initiation of COPD maintenance medication and followed up for 2 years. Data of 3137 patients that completed the 2-year follow-up were analysed; Exacerbation data were collected from the 6 months prior to study entry (baseline), and every 3 months for 2 years after entry; COPD symptoms were evaluated using the COPD Assessment Test (CAT) at baseline as well as the 1 year and 2 year visit.

Results In this cohort the non-exacerbating phenotype was stable with a total of 69.4% of patients without exacerbations in the 6 months prior to baseline not reporting any exacerbation over the full 2 year follow-up period resulting in an annual exacerbation rate of 0.263 in year 1 and 0.251 in year 2. In contrast, patients with at least one exacerbations in the 6 months prior to baseline showed an annual exacerbation rate of 0.770 in year 1 and 0.633 in year 2. At baseline 44.6% of patients were categorised as GOLD D, one third of these due to their exacerbation history alone. In Year 1 there was a general shift to lower risk categories compared to baseline (GOLD D: 44.6% vs. 31.1%) mainly due to a lower number of exacerbations in Year 1. Overall, categorization then remained relatively stable from Year 1 (GOLD D = 31.1%) to Year 2 (GOLD D = 32.1%).

Conclusions Although, COPD is generally considered to be a progressive disease, this analysis of ‘real life’ data over an observational period of 2 years shows that the ‘non-exacerbating’ phenotype is relatively stable. The data furthermore confirms that exacerbations in the recent history increase the risk of future exacerbations.

P142 THE DISTRIBUTION OF BLOOD EOSINOPHIL COUNT IN A COPD CLINICAL TRIALS DATABASE: COMPARING THE UK WITH THE REST OF THE WORLD

1Hilton, 1C Compton, 1D Midwinter, 2JN Barnes. 1GlaxoSmithKline, Brentford, UK; 2William Harvey Institute Barts and the London School of Medicine, UK
10.1136/thoraxjnl-2016-209333.285

Introduction There is accumulating evidence that blood eosinophil count may have predictive value for those individuals with COPD who are more likely to respond to an inhaled corticosteroid in terms of exacerbation reduction and there is evidence that higher blood eosinophil count can also have some predictive value for those at risk of exacerbations. Blood eosinophil counts are known to be raised in a number of conditions including allergies and parasitic or fungal infections. It is therefore possible that the blood eosinophil count would vary between countries and thus influence their predictive value. We have investigated the distribution of blood eosinophil counts in the UK in comparison with blood eosinophil counts worldwide from data in the GSK clinical trials database.

Methods In this post-hoc analysis, the following criteria were used to select studies for consistency with analyses conducted to examine the effects of inhaled corticosteroids on outcomes: global, randomised, double-blind, parallel-group clinical trials in COPD of at least 24 weeks’ duration that included any of fluticasone propionate (FP), fluticasone furoate (FF), salmeterol/FP or FF/vilanterol (VI) as a randomised study drug and a non-steroid-containing arm and for which subjects had a pre-randomisation blood sample taken for eosinophils. Individual subjects’ pre-randomisation eosinophil counts from countries that recruited at least 100 subjects across all trials were pooled to form the global sample (Argentina, Australia, Canada, Chile, Czech Republic, Denmark, Estonia, France, Germany, Greece, Italy, Korea, Lithuania, Mexico, Netherlands, Norway, Peru, Philippines, Poland, Romania, Russia, Slovakia, South Africa, Spain, Sweden, United Kingdom, United States). Individual subjects’ pre-randomisation eosinophil counts for subjects in the UK were pooled to form the UK sample. An empirical cumulative distribution function (CDF) for the UK sample was overlaid on an empirical CDF plot for the global sample.
Results

The blood eosinophil count in COPD patients included in these trials in the UK is very similar to that worldwide (Figure).

Conclusions

This suggests that blood eosinophil count could be used in the UK to help predict response to inhaled corticosteroids in COPD.

REFERENCE


Background and significance

COPD exacerbations are associated with significant morbidity, mortality, and substantial healthcare cost. The eosinophilic phenotype of COPD has been demonstrated to respond better to corticosteroids thus providing better clinical outcomes. This review aims to elucidate further the correlation between blood eosinophilia and outcomes in hospitalised patients with COPD exacerbations.

Methods

We systematically searched published and unpublished literature for potential studies that fulfilled our eligibility criteria. Inclusion criteria include any cohort (prospective or retrospective), case-control or randomised trials that looked into the association of blood eosinophilia and outcomes in hospitalised COPD exacerbation patients. The primary study outcome was length of hospitalisation; other outcomes include readmission and mortality rate within 1 year, in-patient mortality, and need for mechanical ventilation. An extensive eligibility, methodological and risk of bias assessments were performed independently by two authors adhering to the MOOSE and Cochrane standards.

Results

Six studies, with a total of 7293 patients, were included in the review. Five are retrospective cohorts and one is a retrospective analysis of a subgroup of a randomised trial. Patients with blood eosinophilia had significantly shorter hospital stay compared to non-eosinophilic patients (mean difference 0.68 days [95% CI: 1.09, 0.27]). Eosinophilic patients had significantly less frequent readmissions (odds ratio/OR 0.69 [95% CI: 0.55, 0.87]) but there was no statistically significant difference in the 1-year mortality rate (OR 0.88 [95% CI: 0.73, 1.06]). Analysis showed a trend toward lower in-patient mortality among eosinophilic patients, although this difference is not statistically significant (OR 0.53 [95% CI: 0.27, 1.05]). Furthermore, COPD patients with eosinophilia had significantly less need for mechanical ventilation during an exacerbation (OR 0.56 [95% CI: 0.35, 0.89]). Only the primary outcome was significantly heterogenous.

Conclusions

COPD patients with blood eosinophilia had significantly shorter hospital stay, less frequent readmissions, and are less likely to require mechanical ventilation compared to the non-eosinophilic phenotype.
COPD is the 3rd most common cause for hospital admission in the UK. Patients with COPD are often unable to attend specialist clinics, when factors contributing to exacerbations can be treated, due to the unstable nature of the condition and the degree of breathlessness experienced. There is also a high level of polypharmacy in this population. Domiciliary specialist pharmacy intervention may help identify and treat these issues.

Hypothesis
Specialist Domiciliary Pharmacy intervention reduces exacerbation frequency and hospitalisation in patients with Severe COPD

Patients who were referred to a specialist COPD clinic between March 2015 and January 2016 were assessed. Those with polypharmacy and high exacerbation frequency or severe breathlessness (MRC grade 4–5) were identified and offered domiciliary pharmacy review. Patients who consented were visited at home with a comprehensive review of medication, the case was then discussed at an MDT level and therapeutic changes implemented. A comparator group of matched patient were identified and followed up without pharmacy intervention.

Baseline data were collected including demographics, smoking status, FEV1, MRC Grade, hospitalisation rates, exacerbation frequency and current medications. Patient records were then reviewed after a 6 month period to look at impact of intervention on hospitalisation, exacerbation frequency, antibiotic and steroid prescription in the two groups.

Results
A total of 88 patients received intervention and 87 patients were followed up in a comparator group. Patients were matched in terms of sex, BMI, socioeconomic deprivation, smoking status, FEV1, MRC Grade, LTOT use and hospitalisation frequency.

Patients had an average of 3.5 visits with an average of 7.6 interventions per patient, therapeutic changes being the most frequent.

Review after 6 months of intervention demonstrated that the intervention group had a significant reduction in hospitalisation (p < 0.01) and exacerbation frequency (p < 0.01) (Figure 1) along with antibiotic and steroid use in comparison to the comparator group.

This project was a service evaluation rather than a double blinded, randomised control study. The results however suggest that specialist pharmacy intervention in a setting appropriate for a disabled population has a positive impact on exacerbation frequency and hospitalisation.

Abstract P144
Figure 1 Impact of Pharmacy Intervention on Exacerbation Rates and Hospital Admission Rates 6 months prior to and after intervention, compared to comparator group.
**Poster sessions**

**Abstract P145 Table 1** Participants’ characteristics, current treatment attributes and treatment preferences

<table>
<thead>
<tr>
<th>Participant characteristics</th>
<th>Asthma (N = 152)</th>
<th>COPD (N = 150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>48.2 (15.5)</td>
<td>63.7 (8.23)</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>87 (57.2)</td>
<td>66 (44.0)</td>
</tr>
<tr>
<td>Years of having asthma/COPD, mean (SD)</td>
<td>23.4 (14.7)</td>
<td>8.54 (5.35)</td>
</tr>
<tr>
<td>Severity of asthma/COPD, mean score (SD)</td>
<td>18.01 (4.65)</td>
<td>22.8 (8.6)</td>
</tr>
<tr>
<td>Quality of life, mean score (SD)</td>
<td>5.34 (1.17)</td>
<td>55.2 (21.4)</td>
</tr>
<tr>
<td>Participants not paying for their treatment, n (%)</td>
<td>96 (63.2)</td>
<td>141 (94.0)</td>
</tr>
</tbody>
</table>

**Most frequent responses for each attribute of participants’ current treatment, n (%)**

- Proportion of the day that symptoms were well controlled:
  - ‘Most’: 64 (41.1) among Asthma, 62 (41.3) among COPD.
- How many desired physical activities participants could do/day:
  - ‘Most’: 80 (52.6) among Asthma, 73 (48.7) among COPD.
- Sleep disturbance, nights/week participants typically woke up:
  - ‘None’: 66 (43.4) among Asthma, 65 (43.3) among COPD.
- Flare ups/exacerbations of asthma/COPD symptoms/year:
  - ‘Two-three’: 67 (44.1) among Asthma, 46 (30.7) among COPD.
- Times/day participants needed to take maintenance medication:
  - ‘Twice’: 88 (57.9) among Asthma, 89 (59.3) among COPD.
- Ease of use and convenience of inhaler:
  - ‘V. easy’: 115 (75.7) among Asthma, 106 (70.7) among COPD.
- How many desired social activities participants could do/day:
  - ‘All’: 82 (53.9) among Asthma, 53 (35.3) among COPD.

**Ranking of importance of treatment attributes, mean (SD)**

- Proportion of the day that symptoms were well controlled: 3.27 (1.93) among Asthma, 3.11 (1.92) among COPD.
- How many desired physical activities participants could do/day: 3.98 (2.04) among Asthma, 3.82 (1.70) among COPD.
- Sleep disturbance, nights/week participants typically woke up: 4.27 (2.08) among Asthma, 4.53 (2.10) among COPD.
- Flare ups/exacerbations of asthma/COPD symptoms/year: 4.11 (1.90) among Asthma, 3.79 (1.86) among COPD.
- Times/day participants needed to take maintenance medication: 4.51 (2.48) among Asthma, 4.15 (2.53) among COPD.
- Ease of use and convenience of inhaler: 4.69 (2.23) among Asthma, 4.87 (2.16) among COPD.
- How many desired social activities participants could do/day: 5.11 (1.96) among Asthma, 4.59 (1.84) among COPD.
- Cost/month of asthma/COPD medication: 6.06 (2.58) among Asthma, 7.14 (1.78) among COPD.

**Preferences for treatment, OR (95% CI)**

- Not waking up vs waking up 3–4 times/week: 3.02 (2.71–3.37) among Asthma, 2.84 (2.52–3.20) among COPD.
- Costs no more than £10 vs £50/month: 2.90 (2.60–3.24) among Asthma, 3.95 (3.50–4.47) among COPD.
- V. easy and convenient to use vs fairly difficult and inconvenient: 1.91 (1.72–2.12) among Asthma, 1.95 (1.74–2.18) among COPD.
- Experience flare ups/exacerbations no vs two–three times/year: 1.69 (1.52–1.88) among Asthma, 2.43 (2.17–2.73) among COPD.
- Able to do all vs some desired physical activities/day: 1.57 (1.41–1.74) among Asthma, 1.60 (1.44–1.79) among COPD.
- Symptoms are stable and well controlled all vs some of the day: 1.48 (1.34–1.65) among Asthma, 1.64 (1.47–1.84) among COPD.
- Need to take medication once a day vs three times/day: 1.26 (1.13–1.40) among Asthma, 1.39 (1.25–1.56) among COPD.

**REFERENCE**


**P146**

**MORTALITY AND DAY OF ADMISSION FOR ACUTE EXACERBATION OF COPD**

A Duffy, J Steer, SC Bourke, C Echevarria. Northumbria Healthcare NHS Foundation Trust, North Shields, UK

10.1136/thoraxjnl-2016-209333.289

**Background** Excess mortality in patients admitted to hospital at weekends has been reported in many healthcare systems, influencing healthcare policy. The limitations of existing data are well described; there is a need for condition-specific research in well-described populations with adjustment for baseline mortality risk. Acute exacerbations of COPD (AECOPD) are one of the commonest reasons for hospital admission, with high rates of inpatient mortality. We aimed to establish if inpatient mortality is associated with day of admission or death amongst patients admitted with an AECOPD.

**REFERENCE**

EFFECT OF CANNABIS SMOKING ON RESPIRATORY 

MakenseveralCOPDpatientswereidentifiedfrom the DECAF derivation and validation studies.2 All 

patients (n = 2,645) had definite COPD (including spirometric 

confirmation) and the primary reason for admission was 

AECOPD. DECAF indices (dyspnoea, cosinopenia, consolidation, 

acidaemia and atrial fibrillation) and age were collected. 

We captured the number of inpatient deaths per day of admis- 

sion (compared to the total number of admissions on each day) and per day of death (compared to the total number of bed days for each day). Proportions were compared using Fisher’s exact test. The association between period of admission (weekday/weekend) and mortality was assessed in a binary logistic regres- 

sion model, including the DECAF indices and age.

Methods Consecutive admissions from six UK hospitals were 

identified from the DECAF derivation and validation studies.2 All 

patients (n = 2,645) had definite COPD (including spirometric 

confirmation) and the primary reason for admission was 

AECOPD. DECAF indices (dyspnoea, cosinopenia, consolidation, 

acidaemia and atrial fibrillation) and age were collected. 

We captured the number of inpatient deaths per day of admis- 

sion (compared to the total number of admissions on each day) and per day of death (compared to the total number of bed days for each day). Proportions were compared using Fisher’s exact test. The association between period of admission (weekday/weekend) and mortality was assessed in a binary logistic regres- 

sion model, including the DECAF indices and age.

Results Inpatient mortality was 9.3% (63/676) for those admitted on weekends, compared to 8.4% (163/1969) on weekdays (p = 0.47). For day of death, no clear difference in mortality was 

seen between weekdays and weekends although fewer deaths were seen on Fridays. Exacerbation severity was similar between weekday and weekend admissions (median DECAF score 2 vs. 2, p = 0.83). Following adjustment for baseline mortality risk, there was no association between weekend admission and inpatient death; OR 1.11 (0.79 to 1.56), p = 0.55.

**Table 1** Mortality by day of admission and day of death

<table>
<thead>
<tr>
<th>Mortality by day of admission</th>
<th>Mortality by day of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Died/Admissions % Died Days exposed to risk</td>
<td>Died Days exposed to risk</td>
</tr>
<tr>
<td>Mon</td>
<td>30/436</td>
</tr>
<tr>
<td>Tue</td>
<td>33/434</td>
</tr>
<tr>
<td>Wed</td>
<td>23/349</td>
</tr>
<tr>
<td>Thu</td>
<td>39/372</td>
</tr>
<tr>
<td>Fri</td>
<td>32/370</td>
</tr>
<tr>
<td>Sat</td>
<td>26/306</td>
</tr>
<tr>
<td>Sun</td>
<td>37/370</td>
</tr>
<tr>
<td>Total</td>
<td>228/2645</td>
</tr>
</tbody>
</table>

Discussion In a well-described population with an AECOPD, there is no relationship between inpatient mortality and day of admission or day of death, even after adjusting for baseline mortal- 

ity risk.

**REFERENCES**


**REFERENCE**


Asthma Treatments and What Matters to Patients

P148 MAKING SENSE OF PATIENT-REPORTED CURRENTLY TREATED ASTHMA USING ROUTINELY COLLECTED DATA

1 MA Al Sallakh, 1SE Rodgers, 1RA Lyons, 1A Shekh, 1GA Davies. 1Swansea University Medical School, Swansea, UK; 2Usher Institute of Population Health Sciences and Informatics, The University of Edinburgh, Edinburgh, UK

10.1136/thoraxjnl-2016-209333.291

Introduction and objectives Currently treated asthma (CTA) is 

commonly assessed in epidemiological studies and is typically self-reported. We investigated how patient understanding of this label compared with objective measures extracted from routinely 

collected data.

Methods We used the Welsh Health Survey 2014 results for indi- 

viduals aged 16+. Self-reported CTA was measured with the question: “Are you currently being treated for asthma?” We included those who had valid responses, are record-linked to the Secure Anonymised Information Linkage databank, and had complete GP practice registrations between 2009 and 2014. From the GP dataset, we queried their most recent prescriptions, if any, and whether they had ever recorded asthma diagnosis, and cross-tabulated these variables with self-reported CTA. We examined the concordance between self-reported CTA and each of |ever
prescriptions’, ‘ever diagnosis’, and ‘having prescriptions in varying backward intervals from mid-2014’, with the latter repeated by adding ‘ever diagnosis’.

**Results** Of 4,291 eligible people, 10.2% self-reported CTA but, of these, 11.2% had no prescriptions in the past 12 months and 22.4% had no recorded asthma diagnosis ever. Figure 1A shows full intersections between the variables. For concordance between self-reported CTA and each of ‘ever prescriptions’ and ‘ever diagnosis’, Cohen’s kappa was 0.42 and 0.68, respectively. For concordance between self-reported CTA and ‘prescriptions in backward intervals’, kappa was 0.76 for the 12-month interval but peaked to 0.77 at 9-months. After adding ‘ever diagnosis’, the kappa became 0.78 for the 12-month measure (which represents the treated asthma criteria of the Quality of Outcomes Framework, QOF), and peaked to 0.79 at 18-months (Figure 1B).

**Conclusion** In Wales, self-reported currently treated asthma showed good concordance with the QOF treated asthma criteria but a slightly better concordance with ‘any prescriptions in the last 18 months and ever diagnosis’ measured from routine GP data. However, the concordance remains suboptimal, demonstrating that self-reported CTA should be used with caution, and objective measures from routinely collected health data are preferred.

**Introduction** Management plans, while recommended nationally to reduce burden of asthma on individuals and healthcare systems, are poorly and infrequently used (BTS/SIGN 2014). Studies show a mismatch between patients’ expectations and what professionals provide. (Ring et al, 2011).

**Aim** An exploration of health journeys of children with severe and recurrent wheeze: what makes a good management plan?

**Methods** Purposeful sampling techniques were used to recruit patients. A convergent mixed-methods design, comprised of semi-structured interviews and notes review, was used. Data was analysed using inductive thematic analysis and descriptive statistics.

**Results** Eleven children were recruited. Parents are motivated by symptoms and their own perceptions of wheeze to take action. They seek advice from multiple sources according to their own preferences, rather than symptom severity. The median number of admissions to A and E in the last two years was 3, and of GP consultations was 6.5; there was a negative correlation between these.

Barriers to self-management include lack of knowledge, confidence and appropriate resources. Notably, healthcare professionals influenced the ability and willingness to self-manage by either empowering patients or providing paternalistic instruction. There was occasionally poor communication of agreed actions between primary and secondary care, which confused patients. Not all A and E attendances were noted in the GP system, and only one of 5 requests for GP follow-up was carried out. It was noted that patients see A and E as ‘specialist’ and may not follow-up with a ‘general’ physician upon discharge.

Parents and children saw management plans as able to address key barriers. However, no notes in both GP and A and E mentioned providing a written plan.

**Conclusion** Our data suggests the need to ‘nudge’ parents to self-manage before escalating appropriately by modifying existing management plans. Plans should be personalised, for example to target management of key triggers. Crucially, patients and both primary and secondary healthcare professionals must work together to implement mutually acceptable plans.

We are using our data to create a mobile-based application which can be integrated into primary and secondary care, and is responsive to patients’ desires. Preliminary results show this will be well-received, and is perceived to be superior to paper-based plans.
Uncontrolled asthma is a major health problem. Personal perceptions of asthma control often vary between patients and their treating physicians, and both may differ from patient actual control. This can be a major barrier in optimising patient asthma care.

The aim of this cross-sectional survey was to provide UK-specific data on actual and perceived asthma control in a sample of adult (18–75 years) asthma patients attending routine asthma reviews in primary, secondary and tertiary settings. Differences between healthcare professionals’ (HCP) and patients’ perceived assessments of asthma control were evaluated via an online questionnaire and compared to a control – the validated Asthma Control Test (ACT) questionnaire, which was completed by the patient.

Patients with a documented diagnosis of asthma who were taking medication (at least a short acting β-agonist) were enrolled and consented by their HCP within a month of their last clinic appointment. Individuals with a history of an asthma exacerbation within prior 4 weeks; a diagnosis of another respiratory condition; or a smoking history >10 pack years were excluded.

Patients were grouped into BTS/SIGN treatment Steps 1–5.

260 patients were screened. 234 patients were eligible for the study: 33, 52, 50, 49 and 50 patients in Steps 1 to 5, respectively. Women composed 70% (164) of the study population. 47.4% of patients were aged 45–64 years. 164 patients (70%) were classed as non-smokers by HCPs.

The ACT results suggest that asthma was only controlled in 54.7% of patients overall (defined as ACT score ≥20), with levels of uncontrolled asthma highest in Step 4–5 patients. This is in contrast to 84.2% of patients and 73.9% of HCPs who perceived that asthma was controlled.

These data suggest a high level of uncontrolled asthma in UK asthma patients, especially Step 4–5 patients. A significant proportion of both patients and HCPs may have an incorrect perception of asthma control, representing a significant unmet medical need in terms of optimal asthma management.

Overall, correct correlation of ACT score with perception of controlled or uncontrolled asthma only occurred in 67.9% of patients and 68.8% of HCPs. The poorest correlations occurred in Step 4–5 patients.

**Background**

Assessment of adherence to inhaled corticosteroids and long-acting beta-agonist therapy, allows identification of patients classified as having refractory asthma. It is crucial to ensure that adherence is adequately assessed in clinical practice and in the conduct of clinical trials to target the patients who may benefit from expensive potential add-on therapies. We hypothesised that adherence to inhaled corticosteroids and long acting β2-agonists is under-assessed and under-reported in clinical trials of add-on drug treatment interventions in adolescents and adult patients with severe asthma.

**Methods**

A systematic literature search of six major databases was performed to identify randomised controlled trials (RCTs) of asthma drug treatment interventions conducted in severe adolescent and adult asthma patients taking inhaled corticosteroids (ICS) alone or in combination with long-acting beta-agonist therapy (ICS/LABA). Identified studies were reviewed concerning key characteristics of the trial and the intervention; reporting and monitoring of adherence to ICS/LABA and the relationship between measuring adherence and study outcomes was assessed.

This systematic review had been registered on PROSPERO; registration number CRD42015029611.

**Results**

The electronic search retrieved 5696 articles with an additional 19 identified from references. 4008 articles were screened after removal of duplicates of which 72 RCTs were included and underwent data extraction and quality scoring. Of these, only 12 RCTs reported adherence to ICS or ICS/LABA therapy. Measures of adherence used included: self-report, n = 1; self-report and inhaler technique, n = 1; inhaler technique, n = 1; inhaler technique and FeNO, n = 1; dose counting, n = 1; diary, n = 2; prescription records, n = 1; weighing inhaler canister, n = 1; assumption that primary respiratory physician had assessed adherence, n = 1; and method of adherence assessment not reported but measure of adherence included in n = 2 studies. High levels of heterogeneity across studies with...
regard to adherence and exacerbation measurements, designs and analysis precluded a formal meta-analysis. Although effect measures varied, good adherence was associated with fewer severe asthma exacerbations in high-quality studies.

**Conclusion** Good adherence is associated with a lower risk of severe asthma exacerbations. Future studies should use standardised methodology to assess adherence and inhaler technique.

**REFERENCE**


---

**Abstract P154 Table 1** Composite asthma endpoint: Asthma exacerbation (broad) with pneumonia plus asthma worsening

<table>
<thead>
<tr>
<th>MedDRA preferred term</th>
<th>Tiotropium Respimat® 5 µg</th>
<th>Tiotropium Respimat® 2.5 µg</th>
<th>Placebo Respimat®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma exacerbation (broad) + worsening + pneumonia</td>
<td>9 (29.0)</td>
<td>12 (33.3)</td>
<td>19 (55.9)</td>
</tr>
<tr>
<td>Asthma</td>
<td>2 (6.5)</td>
<td>5 (13.9)</td>
<td>10 (29.4)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>2 (6.5)</td>
<td>1 (2.8)</td>
<td>4 (11.8)</td>
</tr>
<tr>
<td>Bronchopneumonia</td>
<td>0</td>
<td>0</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Cough</td>
<td>2 (6.5)</td>
<td>4 (11.1)</td>
<td>3 (8.8)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>1 (3.2)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
<td>1 (2.8)</td>
<td>2 (5.9)</td>
</tr>
<tr>
<td>Viral respiratory tract infection</td>
<td>3 (9.7)</td>
<td>3 (8.3)</td>
<td>4 (11.8)</td>
</tr>
<tr>
<td>Wheezing</td>
<td>0</td>
<td>2 (5.6)</td>
<td>0</td>
</tr>
</tbody>
</table>

Treated set. Percentages calculated using total number of patients per treatment as denominator. AE preferred terms defined by Medical Dictionary for Regulatory Activities version 17.1.
μg (55.6%). Two patients each in the tioR 5 μg (6.5%) and pboR (5.9%) groups were reported with drug-related AEs. Three patients, all in the pboR group, were reported with serious AEs. Asthma exacerbation/worsening was reported by fewer patients in the tioR 5 μg and tioR 2.5 μg groups compared with the pboR group (Table).

Conclusion Once-daily tiotropium Respimat® add-on to maintenance therapy is well tolerated and may reduce exacerbations in pre-school children with symptomatic persistent asthma.

Please refer to page A272 for declarations of interest in relation to abstract P155.

### Abstract P155

#### Summary of adverse events in the VivaTinA-asthma, PensieTinA-asthma and RubaTinA-asthma trials

<table>
<thead>
<tr>
<th>n (%)</th>
<th>Tiotropium Respimat® 5 μg QD</th>
<th>Tiotropium Respimat® 2.5 μg QD</th>
<th>Placebo Respimat® QD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VivaTinA-asthma*, 6–11 years</td>
<td>n = 130</td>
<td>n = 136</td>
<td>n = 134</td>
</tr>
<tr>
<td>Overall AEs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with any AE</td>
<td>56 (43.1)</td>
<td>59 (43.4)</td>
<td>66 (49.3)</td>
</tr>
<tr>
<td>Patients with investigator-defined drug-related AEs</td>
<td>1 (0.8)</td>
<td>0</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>AEs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with AEs leading to discontinuation</td>
<td>2 (1.5)</td>
<td>0</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>Patients with serious AEs</td>
<td>4 (3.1)</td>
<td>2 (1.5)</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td>AEs in &gt;5% pts in any treatment group, by preferred term</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma*</td>
<td>24 (18.5)</td>
<td>20 (14.7)</td>
<td>30 (22.4)</td>
</tr>
<tr>
<td>Decreased peak expiratory flow rate</td>
<td>15 (11.5)</td>
<td>15 (11.0)</td>
<td>20 (14.9)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>6 (4.6)</td>
<td>6 (4.4)</td>
<td>11 (8.2)</td>
</tr>
<tr>
<td>PensieTinA-asthma and RubaTinA-asthma*:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12–17 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall AEs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with any AE</td>
<td>127 (48.1)</td>
<td>121 (48.0)</td>
<td>130 (47.6)</td>
</tr>
<tr>
<td>Patients with investigator-defined drug-related AEs</td>
<td>4 (1.5)</td>
<td>1 (0.4)</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>AEs</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with AEs leading to discontinuation</td>
<td>0</td>
<td>0</td>
<td>3 (1.1)</td>
</tr>
<tr>
<td>Patients with serious AEs</td>
<td>5 (1.9)</td>
<td>3 (1.2)</td>
<td>2 (0.7)</td>
</tr>
<tr>
<td>AEs in &gt;5% pts in any treatment group, by preferred term</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>38 (14.4)</td>
<td>41 (16.3)</td>
<td>46 (16.8)</td>
</tr>
<tr>
<td>Decreased peak expiratory flow rate</td>
<td>11 (4.2)</td>
<td>18 (7.1)</td>
<td>21 (7.7)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>25 (9.5)</td>
<td>19 (7.5)</td>
<td>21 (7.7)</td>
</tr>
<tr>
<td>Viral respiratory tract infection</td>
<td>11 (4.2)</td>
<td>11 (4.4)</td>
<td>14 (5.1)</td>
</tr>
</tbody>
</table>

Please refer to page A272 for declarations of interest in relation to abstract P155.
SEASONAL VARIABILITY OF SEVERE ASTHMA

A168

Chapter 1: Introduction

Chapter 2: Methods

Chapter 3: Results

Chapter 4: Discussion

Chapter 5: Conclusion

References

Poster sessions

Abstract P156 Table 1  Peak FEV1(0–3 h), trough FEV1, FEV1 AUC(0–3 h) and Peak FVC(0–3 h) responses at Week 24 (full analysis set); and overall AEs in treated set

Responses at Week 24

<table>
<thead>
<tr>
<th></th>
<th>Tiotropium</th>
<th>Tiotropium</th>
<th>Tiotropium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Respinat</td>
<td>Respinat</td>
<td>Respinat</td>
</tr>
<tr>
<td>5 µg</td>
<td>n = 135</td>
<td>n = 135</td>
<td>n = 135</td>
</tr>
<tr>
<td>2.5 µg</td>
<td>n = 135</td>
<td>n = 135</td>
<td>n = 135</td>
</tr>
</tbody>
</table>

Adjusted mean difference versus placebo Respinat (% standard error)

<table>
<thead>
<tr>
<th>Background maintenance therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium-dose ICS (200–400 µg budesonide or equivalent) alone or in combination with another controller medication</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Tiotropium</th>
<th>Tiotropium</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Respinat</td>
<td>5 µg</td>
<td>Respinat</td>
</tr>
<tr>
<td>n = 131</td>
<td>n = 135</td>
<td>n = 135</td>
<td>n = 135</td>
</tr>
<tr>
<td>Patients with any AE</td>
<td>89 (67.9)</td>
<td>82 (60.7)</td>
<td>86 (63.7)</td>
</tr>
<tr>
<td>Patients with investigator-defined drug-related AEs</td>
<td>2 (1.5)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients with AEs leading to discontinuation</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Patients with serious AEs</td>
<td>6 (4.6)</td>
<td>1 (0.7)</td>
<td>3 (2.2)</td>
</tr>
</tbody>
</table>

1Full analysis set. Placebo Respinat®, N = 131; Placebo Respinat®, Week 24, n = 126. Mean baseline values (± standard deviation): ICS dose, 310.0 ± 112.0 µg; ACQ-IA total score, 1.87 ± 0.31; FEV1, 1629 ± 393 mL; FVC, 2121 ± 564 mL.

2Add-on to background maintenance therapy.

3Measured 10 minutes before next dose of trial medication.

4ACQ-IA, interviewer-administered Asthma Control Questionnaire

5Treated set. Percentages calculated using total number of patients per treatment group as denominator.

daily tioR add-on therapy, a Phase III trial was carried out in patients aged 6–11 years with moderate symptomatic asthma. Methods This 48-week, Phase III, randomised, double-blind, placebo-controlled, parallel-group study (CanoTinA-asthma®; NCT01634139) was performed in patients aged 6–11 years with moderate symptomatic asthma. Patients received once-daily tioR 5µg (2 puffs, 2.5 µg), tioR 2.5 µg (2 puffs, 1.25 µg) or placebo (pboR; 2 puffs) as add-on to maintenance treatment of at least medium-dose inhaled corticosteroid (ICS) (200–400 µg budesonide or equivalent) alone or in combination with another controller medication. The primary end point was peak FEV1 within 3 hours post-dosing (FEV1(0–3 h)). Secondary end points included trough FEV1 (key end point), FEV1 area under the curve (AUC) (0–3 h), and peak FVC (0–3 h); all measured as response (change from baseline) at Week 24. Adverse events (AEs) were analysed descriptively.

Results Of 403 patients randomised, 401 were treated. Baseline demographics and disease characteristics were balanced between treatment groups. TioR 5 µg and 2.5 µg provided statistically significant improvements in lung function versus pboR at Week 24 (Table) with adjusted mean difference ± standard error peak FEV1 (0–3 h) improvements of 164 ± 31 ml (p < 0.0001) and 170 ± 31 ml (p < 0.0001), respectively. The frequency of patients with AEs was similar across treatment arms, with a low incidence of drug-related and serious AEs (Table); no deaths occurred. The most common AEs were asthma worsening/exacerbation (lower incidence in tioR 5µg and 2.5 µg [34.1% and 36.3%] vs pboR [43.5%]), decreased peak expiratory flow rate (21.5% and 23% vs 20.6%), nasopharyngitis (8.9% and 11.1% vs 9.9%) and respiratory tract infection (9.6% and 8.1% vs 12.2%).

Conclusion In patients aged 6–11 years with moderate symptomatic asthma, once-daily tioR add-on to ICS with or without other maintenance therapy significantly improves lung function compared with pboR. The safety profile of tioR was similar to that of pboR.

REFERENCE


Please refer to page A272 for declarations of interest in relation to abstract P156.

P157

SEASONAL VARIABILITY OF SEVERE ASTHMA EXACERBATIONS AND CLINICAL BENEFIT FROM LEBRIKIZUMAB

DF Choy, TL Staton, JR Arron, J Olsson, CT Holweg, S Grey, A Chai, JG Matthews. Genentech, Inc., South San Francisco, USA

10.1136/thoraxjnl-2016-209333.300

Introduction and objectives Epidemiologic studies have implicated aeroallergens and respiratory infections as triggers underlying seasonal increases in asthma exacerbations in spring and autumn months. These seasonal factors may trigger or amplify airway inflammation in atopic, Type 2 high asthma patients that precipitates acute worsening of symptoms. Biologic therapies targeting Type 2 cytokine pathways have demonstrated efficacy in reducing the rate of severe asthma exacerbations, particularly in patients selected on the basis of Type 2 biomarkers. In children with asthma, increased inhaled corticosteroid or anti-IgE therapy has been effective in reducing seasonal exacerbations in adults with asthma.

Methods We conducted post-hoc analyses of the Phase III LAVOLTA studies (NCT01867125 and NCT01868061) to assess the seasonal dependence of exacerbations and efficacy of lebrikizumab in 2,148 adults with moderate to severe asthma. We employed Poisson regression utilising linear mixed models to estimate the per-month (normalised by hemisphere) annualised exacerbation rate and treatment effect of lebrikizumab in reducing exacerbations (percent rate reduction).

Results Per-month exacerbation rates in placebo treated eosinophil-low (<300/µL) patients were lower and less variable (0.34 to 0.72 per year) than in eosinophil-high (≥300/µL) patients; (0.63/
Abstract P157 Figure 1  Seasonal analysis of exacerbations in subjects defines by baseline blood eosinophil counts. Unadjusted exacerbation rates are plotted as a function month normalised by hemisphere. The month for corresponding hemispheric season are annotated in plot margins. Analyses for subject with baseline blood eosinophils < 300/μL or > 300/μL are plotted on left and right panels respectively.

year in August to 1.43/year in September). The 95% confidence intervals for the per-month lebrikizumab treatment effect overlapped with zero in eosinophil-low patients for all calendar months. The maximum per-month treatment effects for eosinophil-high patients were observed during the autumn and spring months (62.7 [10.1, 84.5]% for September and 65.1 [8.6, 86.7]% for May). The minimum per-month treatment effects were observed in the summer months (11.3 [−148.7, 68.4]% for July and 6.6 [−166.0, 67.2]% for August).

Conclusions  We conclude that seasonal spikes in exacerbations may be primarily dependent on Type 2 inflammatory processes. The molecular pathways underlying asthma exacerbations are heterogeneous and therapeutic strategies targeting Type 2 biology alone may have the greatest efficacy in limiting seasonal spikes in exacerbation rates. Overall, these data highlight that a significant proportion of asthma exacerbations may be independent of seasonal influences and/or Type 2 biology and that increased therapeutic efficacy may require targeting multiple distinct pathways in asthma.

P158 FLUTICASONE FUROATE(FF)/VILANTEROL (VI) ONCE DAILY IMPROVES NIGHT-TIME AWAKENINGS IN ASTHMA

Introduction and objectives FF/VI, the first once daily inhaled corticosteroid/long-acting β2-agonist combination available for the treatment of asthma, has demonstrated a sustained 24 hour improvement in lung function and improvement in symptom-free 24 hour periods.

Methods Post-hoc analyses of diary card data from three Phase III studies were performed to examine whether there was an improvement in night-time awakening during the studies for those patients treated with the addition of vilanterol to fluticasone furoate. The diary card scale used is described below. Changes in night-time awakenings over the duration of the studies were analysed for percentage of patients with ≥50% symptom-free nights, including the time taken for 50% of patients to achieve 7 nights without symptoms.

Night-time Symptom Score:
0 = No symptoms during the night
1 = Symptoms causing me to wake once (or wake early)
2 = Symptoms causing me to wake twice or more (including waking early)
3 = Symptoms causing me to be awake for most of the night
4 = Symptoms so severe that I did not sleep at all
To be counted as symptom-free during the night the patient needed to record a score of 0.

Results The percentage of patients with ≥50% symptom-free nights was generally higher in patients treated with FF/VI compared to either FF or FP alone (Table below). The time (in days) for 50% of patients to achieve 7 nights without symptoms was achieved sooner with patients treated with FF/VI compared to FF alone (Table).

Conclusions In general, night-time awakenings improved over time in asthma patients with FF/VI and improved faster with FF/VI compared with FF or placebo.
A170

The change in Asthma Quality of Life Questionnaire (AQLQ) between baseline and 16 weeks was utilised as the primary outcome measure. The change in a variety of clinical and physiological outcomes at 16 weeks and 52 weeks from baseline between these two groups. Results

The post-hoc meta-analysis included 197 patients from DREAM and MENSA and 251 when including the SIRIUS trial. The mean age was 51.2 and 51.3 years of which 62% and 64% were female, respectively. A 59% (95% CI: 0.31, 0.55; p < 0.001) reduction in clinically significant exacerbations was seen in the meta-analysis of DREAM and MENSA (50% [95% CI: 0.40, 0.64, p < 0.001] sensitivity analysis with SIRIUS). The ACQ score showed an improvement of −0.56 (95% CI: −0.79, −0.33; p < 0.001) and −0.58 (95% CI: −0.79, −0.38; p < 0.001, sensitivity analysis with SIRIUS). The SGRQ was only seen in the meta-analysis of DREAM and MENSA and SIRIUS and showed an improvement in total score of −8.0 (−12.0, −3.9, p < 0.001).

Conclusion Mepolizumab treatment was effective in SMC advice population (adult severe refractory eosinophilic asthma patients with a blood eosinophil count of ≥150 cells/μL at initiation of treatment, and ≥4 exacerbations in the previous year or dependency on mOCS). The use of a post-hoc meta-analysis is a helpful approach to increase our understanding of mepolizumab’s treatment effect in the SMC restricted sub-population.

Funding GSK (NCT010000506, NCT01691521, NCT01691508).

P160 USE OF OMALIZUMAB IN FUNGAL ALLERGIC ASThma

1HV Patel, 2B Kane, 3µ Foden, 4L Holmes, 5GOG Tavemier, 1TB Morris, 2OM Ryan, 2RM Niven. 1University of Manchester, Manchester, UK; 2University Hospital of South Manchester, Manchester, UK

10.1136/thoraxjnl-2016-209333.303

Background The monoclonal anti-IgE agent Omalizumab holds an established place in the management of severe allergic asthma patients (GINA Step 5). Fungal allergic asthma possesses added complexity as fungi are ubiquitous in our environment and are capable of not only triggering asthma, but may grow, colonise and infect host tissue. Current treatment approaches include: Allergen avoidance, mucus reduction, control of bacterial infection, control of inflammation, reducing fungal burden and recently blockade of allergy using Omalizumab.

Aims/purpose Investigate the response to Omalizumab in severe asthma patients who are sensitised to fungal allergens compared to those who are non-fungal allergic. Current literature describes the use of Omalizumab in fungal allergic airways disease, though published data takes the form of case reports/series with limited total population.

Methods Retrospective cohort study of severe asthma patients treated with Omalizumab (n = 168). Patients were grouped into fungal or non-fungal allergy status, followed by a comparison of the change in a variety of clinical and physiological outcomes at 16 weeks and 52 weeks from baseline between these two groups. The change in Asthma Quality of Life Questionnaire (AQLQ) between baseline and 16 weeks was utilised as the primary outcome. Groups will be compared using an unpaired t-test or Chi-
squared test, as appropriate, to test for non-inferiority (threshold –0.25) in the fungal allergic group compared to the non-fungal allergic group.

**Results** The fungal allergic group (n = 76) was found to have a mean AQLQ difference between baseline and 16 weeks of +1.34 (± 1.25). When compared to the non-fungal allergic cohort, the fungal allergic group was found to have a statistically significant mean AQLQ difference between baseline and 16 weeks of −0.41 (95% CI: −0.14 − −0.81). See Figure 1.

**Conclusion** Fungal allergic patients have a less profound AQLQ response to Omalizumab than non-fungal allergic although the benefit is still clinically significant in the majority of cases. The reduced benefit is statistically different in terms of change, though it does not fulfill the a-priori threshold for non-inferiority.

---

**Abstract P161 Table 1** Summary of findings from the treated and untreated populations across European countries

<table>
<thead>
<tr>
<th>Factor</th>
<th>Treated N = 828</th>
<th>Untreated N = 909</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age, years</td>
<td>67</td>
<td>70**</td>
</tr>
<tr>
<td>Male, %</td>
<td>69</td>
<td>64**</td>
</tr>
<tr>
<td>MDT evaluation,%</td>
<td>83</td>
<td>57**</td>
</tr>
<tr>
<td>Lung comorbidities, %</td>
<td>39</td>
<td>51**</td>
</tr>
<tr>
<td>Emphysema</td>
<td>23</td>
<td>33**</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>2</td>
<td>5**</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>22</td>
<td>25</td>
</tr>
<tr>
<td>CV comorbidities, %</td>
<td>39</td>
<td>45</td>
</tr>
<tr>
<td>High risk of coronary artery disease</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Coronary artery disease without history of MI or stroke</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>11</td>
<td>15**</td>
</tr>
<tr>
<td>with history of MI</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Candidate for lung transplantation,%</td>
<td>19</td>
<td>3**</td>
</tr>
<tr>
<td>Confirmed IPF,%</td>
<td>84</td>
<td>51**</td>
</tr>
<tr>
<td>Average time from diagnosis to last consultation, months</td>
<td>15.8</td>
<td>15.9</td>
</tr>
<tr>
<td>Stable IPF, %</td>
<td>31</td>
<td>51**</td>
</tr>
<tr>
<td>Mild IPF (current level), %</td>
<td>18</td>
<td>41**</td>
</tr>
<tr>
<td>Symptomatic at treatment initiation,%</td>
<td>90</td>
<td>70**</td>
</tr>
<tr>
<td>%FVC at last check-up</td>
<td>60.7</td>
<td>64.2</td>
</tr>
<tr>
<td>%DLco at last check-up</td>
<td>47.4</td>
<td>50.6</td>
</tr>
</tbody>
</table>

**Introduction and objectives** Two antifibrotic drugs, pirfenidone and nintedanib, are approved by the FDA and EMA for the treatment of IPF. We investigated treatment patterns of European patients with IPF to understand antifibrotic treatment uptake and identify unmet needs in IPF treatment practice.

**Methods** Between February and March 2016, respiratory physicians from France, Germany, Italy, Spain and the UK participated in an online questionnaire designed to collect information on IPF treatment patterns. Responses were collected from physicians who had consulted with ≥6 (France, Italy, Spain) or ≥10 (Germany, UK) patients with IPF (within 3 months). Patients were categorised as being in the treated population (those who had received approved antifibrotics) or the untreated population (those who had not received approved antifibrotics, but may have received other therapies). Classification of IPF diagnosis (confirmed/suspected) and severity (mild/moderate/severe) for each patient was based on the individual physician’s report.

**Results** Overall, there were 290 respondent physicians reporting on 1838 patients. Of 1783 patients with data, 54% were not treated with an approved antifibrotic. Of patients with a confirmed IPF diagnosis, 41% were not treated. In the 1737 patients analysed, the untreated population was older than the treated population (70 versus 67 years, respectively; p ≤ 0.01) and had less frequent multidisciplinary team (MDT) evaluation (57%) versus 83%, respectively; p ≤ 0.01. At diagnosis, mild, moderate and severe IPF was reported in 43%, 40% and 16% of untreated patients, and 26%, 64% and 10% of treated patients, respectively. Average forced vital capacity (FVC) at diagnosis and last check-up was significantly higher in untreated patients versus treated patients (both p ≤ 0.01; Table); however, fewer untreated patients had an FVC measurement at their most recent check-up.
The advent of novel anti-fibrotic therapies and the introduction of specialist commissioned Interstitial Lung Disease (ILD) centres, has led to an increased workload for Multidisciplinary Team (MDT) meetings. We set out to survey specialist UK centres to gain a better understanding of their organisational processes and associated challenges.

**Methods** Between August and December 2015 we conducted an online survey of all 23 NHS England commissioned ILD centres, plus 5 specialist ILD centres in Scotland, Wales and Northern Island. The survey was sent to the clinical lead of each centre. A total of 20 questions assessed the workforce composition and frequency of meetings. Their workload was also evaluated and we asked them to identify areas that required improvement.

**Results** 26 out of 28 centres responded.

MDTs are coordinated by the ILD lead consultant (57%) or a medical secretary (26%), with only 17% directed by a MDT coordinator.

Peripheral hospitals participate in MDTs in 78% of centres; in person, via video-link or paper referrals; however, the majority of discussed patients are reviewed at the specialist centre.

MDTs are typically held weekly, lasting 1 to 2 hours, with 10 to 20 patients discussed. 26% of MDTs discuss all new referrals, 87% discuss all patients considered for anti-fibrotic therapy, whilst only 22% discuss all patients considered for immunosuppressive therapy (aside from oral steroids).

All respondents agreed that the available MDT time was insufficient. The most common reasons were cited as; lack of dedicated MDT funding (83%), lack of sufficient respiratory radiologist consultant time (78%) and lack of dedicated administrative support (61%).

In 96% of cases there is no local tariff in place to fund MDT discussion and all respondents agreed that a dedicated tariff would improve MDT provision.

92% of centres enrol MDT patients into clinical trials.

**Conclusion** Specialist ILD MDTs are able to concentrate a high level of expertise and allow patients access to vital clinical trials. They are, however, under considerable strain due to lack of funding and administrative support. A dedicated funding stream for this specialist service would be beneficial.
CHANGING PATTERNS OF THE USE OF LUNG BIOPSY IN INTERSTITIAL LUNG DISEASE

L Brockbank, E Hilal, J Holemans, J Greenwood, M Walshaw, K Mohan. Liverpool Heart and Chest Hospital, Liverpool, UK

10.1136/thoraxjnl-2016-209333.307

Introduction Radiological and international guidelines have improved the diagnosis of interstitial lung disease (ILD) subtype in the absence of a surgical lung biopsy (SBx). However, it may still be needed since up to 38% of cases cannot be diagnosed on clinical and radiological grounds alone, and new antifibrotic therapies require more diagnostic certainty for idiopathic pulmonary fibrosis (IPF). We wished to ascertain whether SBx rates and diagnostic outcomes had changed at our regional thoracic centre.

Methods We looked at 104 consecutive patients undergoing SBx between May 2014 to April 2016, and compared their mode of referral and outcome with a previous study (210 cases) in the same centre conducted between 2001 and 2008.

Results There was no evidence of multidisciplinary team (MDT) input prior to SBx in 31 cases (30%), but 18 (17%) were discussed at an ILD MDT and 55 (53%) in local radiology meetings. For SBx outcome see Table. Prior diagnosis was uncertain in 28% of ILD MDT cases and 27% of local radiology meeting cases, whereas SBx confirmed the suspected diagnosis in 22% of ILD MDT cases but only 9% of radiology meeting cases.

Conclusion Overall, there appears to be increase in the ILD cases referred for SBxs. Despite the small proportion of cases discussed at the ILD MDT prior to SBx, there appears to be a trend in the reduction of UIP/NSIP and significant increase in HSP, RBILD and DIP cases. Histological diagnosis remains important in ILD, and the use of other techniques with lower complication rates (e.g. transbronchial cryobiopsy) needs to be established.

REFERENCE

SURGICAL LUNG BIOPSY IN THE DIAGNOSIS OF INTERSTITIAL LUNG DISEASE – WHERE ARE WE NOW?

L Brockbank, E Hilal, L Johns, M Walshaw, K Mohan. Liverpool Heart and Chest Hospital, Liverpool, UK

10.1136/thoraxjnl-2016-209333.308

Introduction With the advent of multidisciplinary team (MDT) working and new therapies in interstitial lung disease (ILD), diagnostic accuracy is increasingly important, and international guidelines1 have reaffirmed the importance of surgical lung biopsy (SBx) where necessary. However, SBx has associated risks: to assess this further we looked at the diagnostic yield and complication rate of SBxs carried out at our regional thoracic centre for patients with ILD.

Methods We looked at all 104 SBxs carried out for ILD over 24 months between 2014–16, collecting data on the nature of the procedure, number of lobes sampled, complications encountered and mortality, and also whether the cases had been discussed at a regional ILD or local radiology MDT meeting prior to SBx.

Results Seventy cases (67%) had been discussed prior to SBx (18 at an ILD MDT). Overall, mean age was 56 years, mean FEV1 79% predicted, FVC 84% predicted, RV 79% predicted, TLC 77% predicted, TLCO 56% predicted, and KCO 77% predicted. All but 3 procedures were carried out by VAT: the median number of lobes sampled was 2 (>1 lobe in 86%), and diagnostic specimens were obtained in 97% (UIP 29%, RB-ILD and DIP 23%, HSP 12%, Sarcoid 10%, NSIP 7%, others 19%). For complications see Table. The mean length of stay was 5.2 days (range 1–44): in-hospital mortality and 30-day mortality were 1% and 3% respectively.
Conclusion Although SBx is here to stay, it has significant morbidity and mortality. Transbronchial cryobiopsy may in the future sit alongside SBx in the diagnostic pathway for ILD, but in addition to offering low morbidity and mortality it must also offer a high diagnostic yield.

Abstract P165 Table 1

<table>
<thead>
<tr>
<th>Major complications</th>
<th>% of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDU/ITU admission</td>
<td>6</td>
</tr>
<tr>
<td>Required reintubation</td>
<td>3</td>
</tr>
<tr>
<td>Required tracheostomy</td>
<td>1</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>3</td>
</tr>
<tr>
<td>Empyema</td>
<td>1</td>
</tr>
<tr>
<td>Ileus</td>
<td>1</td>
</tr>
<tr>
<td>Minor complications</td>
<td>% of cases</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td>6</td>
</tr>
<tr>
<td>Persistent air leak</td>
<td>4</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1</td>
</tr>
<tr>
<td>Lower respiratory tract infection</td>
<td>11</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>1</td>
</tr>
<tr>
<td>Wound infection</td>
<td>2</td>
</tr>
</tbody>
</table>

P166 THE EMERGING ROLE OF AIRWAY CLEARANCE TECHNIQUES IN THE TREATMENT OF INTERSTITIAL LUNG DISEASE

Introduction Patients with interstitial lung disease (ILD) may develop airway abnormalities as part of their underlying condition, in response to fibrotic/tractional dilatation or as a result of repeated bronchiolar infection. While current practice guidelines recommend the provision of pulmonary rehabilitation for ILD patients, no other interventions have been endorsed. We assessed the symptomatic need of patients with ILD for airway clearance techniques (ACT’s) using a visual analogue scale, and whether, in those with fibrotic ILD, the presence of traction bronchiectasis was correlated with the need for ACT’s.

Methods Over a 15-week period, data were prospectively collected on ILD patients who consented for detailed physiotherapy assessment and intervention. Those who reported a sensation of persistent secretion retention, frequent chest infections (>2 in 6 months) or those with pre-existing airway disease had a full clearance assessment. The radiological presence or absence of traction bronchiectasis was noted, as was evidence of other airway pathology such as bronchiolitis.

Results 30 ILD inpatients (16 females) were included in the study (Table 1). The commonest causes for admission were ILD staging (n = 10) and disease deterioration requiring intravenous treatment (n = 14). 27 patients (90%) required physiotherapy input and 11 patients (41%) required ACT’s. 9 patients had positive sputum microbiology; of these, 3 were first isolates. 7 of these 9 patients had traction bronchiectasis on CT acquired within 3 months of assessment. One patient did not undergo CT. The presence of traction bronchiectasis correlated with a higher sputum microbial yield (p < 0.05) but not with a need for ACT (p > 0.05).

Conclusion Airway abnormalities are often not a principal therapeutic focus in ILD but symptoms related to mucostasis, recurrent infection and airflow limitation may be disabling. In this study, the majority of patients with positive microbiology had traction bronchiectasis. Although no firm conclusions can be drawn regarding the role of ACT’s in their management, this intervention improved the yield of specimens for microbial analysis and facilitated pathogen-directed antimicrobial therapy. These findings suggest that a systematic physiotherapy approach including optimisation of airway clearance can benefit patients with parenchymal lung disease.

Abstract P166 Table 1 Patient demographics

<table>
<thead>
<tr>
<th>Total patients, n</th>
<th>30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year), mean (SD)</td>
<td>59.1 (15.7)</td>
</tr>
<tr>
<td>Gender, n females (%)</td>
<td>16 (53)</td>
</tr>
<tr>
<td>Length of stay (days), mean (SD)</td>
<td>11.3 (8.3)</td>
</tr>
<tr>
<td>Patients with traction bronchiectasis, (%)</td>
<td>17 (56.6)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>7</td>
</tr>
<tr>
<td>Idiopathic Pulmonary Fibrosis</td>
<td>5</td>
</tr>
<tr>
<td>Chronic Hypersensitivity Pneumonitis</td>
<td>5</td>
</tr>
<tr>
<td>CTD-ILD</td>
<td>3</td>
</tr>
<tr>
<td>Other*</td>
<td>10</td>
</tr>
</tbody>
</table>

*Other ILD diagnosis or suspected ILD.

P167 DOES ANTIFIBROTIC TREATMENT OUTCOMES DIFFER IN USUAL INTERSTITIAL PNEUMONIA BASED ON HRCT CRITERIA ESTABLISHED BY ATS/ERS/JRS/ALAT IN 2011?

C Ng, J Hornsby, D Anderson. Glasgow Victoria Infirmary, Glasgow, UK

10.1136/thoraxjnl-2016-209333.310

Background Idiopathic pulmonary fibrosis (IPF) is an age-related, progressive and irreversible lung disease.1 The diagnosis of IPF is made using clinical history, pulmonary function testing (PFT), and radiological appearances of Usual Interstitial Pneumonia (UIP) on High Resolution CT (HRCT) Scanning provided other appearances have been excluded. The diagnosis is frequently made at MDT where the images are categorised into Definite UIP, Possible UIP, or Inconsistent with UIP using HRCT criteria.2 In the west of Scotland, patients demonstrating definite or possible UIP patterns on HRCT with a FVC < 80% are considered for antifibrotic therapy. The aim of this study was to assess whether response to antifibrotic therapy in IPF is correlated with the aforementioned categories. The presence of pleural plaques was also considered.

Methods We retrospectively divided 170 patients into three categories: definite UIP pattern, possible UIP pattern, and UIP with pleural plaques. Serial pulmonary function test results were obtained and the change in FVC calculated. Treatment failure was defined as a change in FVC% predicted of >10% per year. The rate of treatment failure, overall mortality, 6-month and 12-month survival was compared between the three groups.
Results 116 patients out of 170 were started on antifibrotic therapy. The average duration of therapy was 256 days. There was a trend towards higher treatment failure in possible (n = 3 of 12 25%) versus definite UIP patterns (n = 6 of 55 11%), this was not statistically significant. Overall mortality rates were similar between possible and definite UIP patterns at 6- and 12-months (Figure 1). 5 patients with UIP and pleural plaques were started on therapy.

Conclusions Mortality at 12 months was similar in possible UIP and UIP groups; there was a trend towards higher levels of treatment failure in patients with possible UIP. A different disease process may exist in some patients with possible UIP which is non-responsive to antifibrotic treatment. Numbers are relatively small and further observation is warranted.

REFERENCES

SAFETY AND TOLERABILITY OF NINTEDANIB IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF): ONE-YEAR DATA FROM POST-MARKETING SURVEILLANCE IN THE UNITED STATES
1T Maher, 1Neth, 1A Allinger, 1M Kaul, 3C Consoscenti, 3D Delberg. 1NIHR Biomedical Research Unit Royal Brompton Hospital and Fibrosis Research Group, National Heart and Lung Institute, Imperial College London, London, UK; 2Pulmonary and Critical Care Medicine, University of Chicago, Chicago, Illinois, USA; 3Boehringer Ingelheim Pharma GmbH and Co. KG, Ingelheim am Rhein, Germany; 4Boehringer Ingelheim Pharmaceuticals, Inc, Ridgefield, Connecticut, USA; 5Western Connecticut Health Network, Danbury Hospital, Danbury, Connecticut, USA

Introduction In the two replicate, 52-week, placebo-controlled IMPULSIS® trials, nintedanib 150 mg twice daily significantly reduced the annual rate of decline in forced vital capacity compared with placebo and had a side-effect profile that was manageable for most patients. After the US approval of nintedanib for the treatment of IPF in October 2014, post-marketing surveillance was initiated to obtain additional information on the safety and tolerability of nintedanib in the real-world clinical setting.

Methods Data were collected from the drug safety database from the time of drug launch (15 October 2014) to 23 October 2015. Data on adverse events in patients treated with nintedanib were collected both via proactive patient communications, as part of a patient support programme, and by the spontaneous reporting system. Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities. Serious adverse events were defined according to International Conference on Harmonisation criteria as adverse events that were fatal or life threatening, required or prolonged hospitalisation, were associated with a congenital anomaly, or resulted in a disability.

Results In the period from drug launch to 23 October 2015, 6,758 patients were treated with nintedanib, with duration of exposure 6 to 390 days (median 113 days). This analysis will present 1-year adverse event data collected both via proactive patient communications, as part of a patient support programme, and by the spontaneous reporting system. Previously reported data collected from drug launch up to 31 May 2015, from 3,838 patients, were consistent with the safety profile described in the product label. In this dataset and as observed in the Phase III trials, the most frequently reported adverse events with nintedanib were gastrointestinal in nature and non-serious in severity.

Conclusion Data from post-marketing surveillance in the US are consistent with the safety profile of nintedanib as described in the label. Treatment with nintedanib in the real-world clinical setting appears to have an acceptable safety and tolerability profile, with no new safety concerns identified.

LONG-TERM SAFETY OF PIRFENIDONE IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS: POOLED ANALYSIS OF 4 CLINICAL TRIALS
1PW Noble, 2C Albera, 3L Lancaster, 4H Hormel, 5U Costabel. 1Cedars-Sinai Medical Centre, Los Angeles, USA; 2University of Turin, Turin, Italy; 3Vanderbilt University Medical Centre, Nashville, USA; 4Genentech Inc, South San Francisco, USA; 5Ruhlandklinik, University of Dussung-Essen, Essen, Germany

Introduction In the two replicate, 52-week, placebo-controlled IMPULSIS® trials, nintedanib 150 mg twice daily significantly reduced the annual rate of decline in forced vital capacity compared with placebo and had a side-effect profile that was manageable for most patients. After the US approval of nintedanib for the treatment of IPF in October 2014, post-marketing surveillance was initiated to obtain additional information on the safety and tolerability of nintedanib in the real-world clinical setting.

Methods Data were collected from the drug safety database from the time of drug launch (15 October 2014) to 23 October 2015. Data on adverse events in patients treated with nintedanib were collected both via proactive patient communications, as part of a patient support programme, and by the spontaneous reporting system. Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities. Serious adverse events were defined according to International Conference on Harmonisation criteria as adverse events that were fatal or life threatening, required or prolonged hospitalisation, were associated with a congenital anomaly, or resulted in a disability.

Results In the period from drug launch to 23 October 2015, 6,758 patients were treated with nintedanib, with duration of exposure 6 to 390 days (median 113 days). This analysis will present 1-year adverse event data collected both via proactive patient communications, as part of a patient support programme, and by the spontaneous reporting system. Previously reported data collected from drug launch up to 31 May 2015, from 3,838 patients, were consistent with the safety profile described in the product label. In this dataset and as observed in the Phase III trials, the most frequently reported adverse events with nintedanib were gastrointestinal in nature and non-serious in severity.

Conclusion Data from post-marketing surveillance in the US are consistent with the safety profile of nintedanib as described in the label. Treatment with nintedanib in the real-world clinical setting appears to have an acceptable safety and tolerability profile, with no new safety concerns identified.
**Introduction** Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive and irreversible disease that requires long-term management. The objective of this study was to assess the long-term safety of pirfenidone from a pooled analysis of 4 clinical studies.

**Methods** All patients who received pirfenidone (2403 mg/d) in the Phase 3 studies (ASCEND/CAPACITY) and/or the long-term extension study (RECAP) were included in this analysis. Safety outcomes were assessed during the period from the first dose until 28 days after the last dose of pirfenidone in either study. Analyses included the final data from the Phase 3 studies and RECAP (data cut, June 30, 2015).

**Results** The pooled population included 1216 patients with a cumulative total exposure of 3366 patient-exposure years. Median pirfenidone exposure was 25.9 months (range, 0–105 months), with a mean dose of 2306 mg/d. 99% of patients reported ≥1 treatment-emergent adverse event (TEAE). 57% of patients reported a serious TEAE (0.51 per patient-exposure year [PPEY]), the most common being IPF (21.5%) and pneumonia (9.3%; Table [PPEY]), the most common being IPF (21.5%) and pneumonia (9.3%; Table [PPEY]). TEAEs led to discontinuation in 45% of patients (0.17 PPEY), the most common being IPF (15.9%), rash (1.6%) and nausea (1.6%). Median survival on treatment (or ≥28 days after discontinuation of pirfenidone) was 82.6 months.

**Conclusions** The safety findings from this pooled analysis are consistent with the known safety profile of pirfenidone and the underlying disease of IPF.

### Abstract P169 Table 1 Summary of TEAEs

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>No. of Patients With an Event</th>
<th>Patient Incidence (n = 1058)</th>
<th>No. of Events</th>
<th>Rate per Patient-Exposure Year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Most Frequent TEAEs (incidence in ≥20% of patients)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>477</td>
<td>39.2%</td>
<td>716</td>
<td>0.213</td>
</tr>
<tr>
<td>Nausea</td>
<td>471</td>
<td>38.7%</td>
<td>789</td>
<td>0.237</td>
</tr>
<tr>
<td>IPF</td>
<td>424</td>
<td>34.9%</td>
<td>669</td>
<td>0.199</td>
</tr>
<tr>
<td>Dizziness</td>
<td>415</td>
<td>34.1%</td>
<td>573</td>
<td>0.170</td>
</tr>
<tr>
<td>Upper RTI</td>
<td>405</td>
<td>33.3%</td>
<td>789</td>
<td>0.234</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>374</td>
<td>30.8%</td>
<td>657</td>
<td>0.195</td>
</tr>
<tr>
<td>Fatigue</td>
<td>359</td>
<td>29.5%</td>
<td>505</td>
<td>0.150</td>
</tr>
<tr>
<td>Rash</td>
<td>331</td>
<td>27.2%</td>
<td>540</td>
<td>0.160</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>325</td>
<td>26.7%</td>
<td>642</td>
<td>0.185</td>
</tr>
<tr>
<td>Headache</td>
<td>281</td>
<td>23.1%</td>
<td>478</td>
<td>0.142</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>280</td>
<td>23.0%</td>
<td>536</td>
<td>0.159</td>
</tr>
<tr>
<td>Dizziness</td>
<td>276</td>
<td>22.7%</td>
<td>409</td>
<td>0.122</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>243</td>
<td>20.0%</td>
<td>306</td>
<td>0.091</td>
</tr>
<tr>
<td><strong>Most Frequent Serious TEAEs (incidence in ≥5% of patients)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IPF</td>
<td>262</td>
<td>21.5%</td>
<td>320</td>
<td>0.095</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>113</td>
<td>9.3%</td>
<td>130</td>
<td>0.039</td>
</tr>
<tr>
<td><strong>TEAEs With Outcome of Death (incidence in ≥1% of patients)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>273</td>
<td>22.5%</td>
<td>273</td>
<td>0.081</td>
</tr>
<tr>
<td>IPF</td>
<td>148</td>
<td>12.2%</td>
<td>148</td>
<td>0.044</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>26</td>
<td>2.1%</td>
<td>26</td>
<td>0.008</td>
</tr>
</tbody>
</table>
| **P170** SINGLE CENTRE EXPERIENCE ON IDIOPATHIC PULMONARY FIBROSIS PATIENT TOLERANCE OF PIRFENIDONE; IMPACT ON NURSE-LED ILD HELPLINE USAGE

A Rathnapala, C Ruggiero, A Fries, LP Ho, RK Hoyles. Oxford Centre for Respiratory Medicine, Oxford, UK

10.1136/thoraxjnl-2016-209333.313

**Introduction** Idiopathic pulmonary fibrosis (IPF) is a progressively scarring lung disease with a poor prognosis. The antifibrotic agent Pirfenidone slows FVC decline and reduces mortality. Side-effect management is critical to help patients remain on treatment.

**Objectives** To examine tolerance to Pirfenidone in our specialist ILD centre: to identify the prevalence, nature and management of adverse effects, and the impact on the ILD nurse-led helpline.

**Methods** In this retrospective study, all patients with an ILD MDT diagnosis (ATS/ERS) of IPF treated with Pirfenidone for >3 months were included. Data was derived from the patient records and nurse-led ILD helpline logs.

**Results** 100 patients were treated with Pirfenidone Feb 2012–July 2016. 16 patients were excluded (<3 months’ treatment (n = 7), death <1 month (n = 2), other (n = 7), 84 remained in the study; Definite: Probable IPF 47:37, male: female 68:16, average age 73.7 (40–88).

72 (85.7%) experienced at least one adverse effect; appetite/weight loss (n = 39, 34.5%), nausea (n = 26, 24%), diarrhoea (n = 17, 15%), fatigue (n = 11, 9.7%), photosensitivity (n = 11, 9.7%), skin rash (n = 9, 8%). No patients required side-effect-related hospital admission.

Management: treatment pause (n = 36, 50%), dose reduction alone (n = 15, 20.8%), initial reduction and subsequent pause (n = 4, 5.6%), n = 17 (23.6%) with mild side-effects were managed with advice alone (dose unchanged).

Of those with dose reductions/pause (n = 55), 21 (38%) were gradually re-escalated to full dose, 1 (2%) continued on reduced dose. Pirfenidone was discontinued and offered symptom-based management in n = 17 (31%), (unable to switch to Nintedanib due to FVC < 50% (7), not preferred (3), bleeding risk (2), other (3)), while n = 16 (29%) were able to switch to Nintedanib.

Impact on the nurse-led helpline was assessed in n = 45 (unselected subset); > 82% used the helpline, often initiated due to side-effects; patients with deteriorating symptoms or end-stage disease engaged most frequently.

**Conclusions** In this real-life study, we found a higher prevalence of side effects than previously described. Nurse-led helpline use was often initiated by side effect concerns, but usage broadened into more holistic support as the nurse patient relationship developed. In response, the Oxford ILD Service has initiated a side-effect management protocol with more cautious (than standard) initial escalation and re-challenging regime.

**P171** HEALTH INEQUALITY EXISTS IN PIRFENIDONE PRESCRIPTION FOR IDIOPATHIC PULMONARY FIBROSIS IN THE ENGLISH MIDLANDS ACCORDING TO PATIENT LOCATION

1 FA Woodhead, 2 S Townsend, 3 D Dasil. 1 Institute for Lung Health, Glenfield Hospital, Leicester, UK; 2 University Hospitals of Coventry and Warwickshire, Coventry, UK

10.1136/thoraxjnl-2016-209333.314
**Background** Pirfenidone is approved in England by NICE for the treatment of Idiopathic Pulmonary Fibrosis (IPF) but its prescription is limited to certain specialised centres. We hypothesised that this may lead to health inequality in the access to the drug per head of population in an area of the Midlands.

**Methods** 2 prescribing centres (PC), and 4 non-prescribing centres (NPC) referring into them were studied. They were the George Eliot Hospital (GEH) in Nuneaton and South Warwick FT (SWFT) in Warwick (both NPC) referring to University Hospitals of Coventry & Warwickshire (UHWC) in Coventry, and Kettering General Hospital (KGH) and Northampton General Hospital (NGH), (both NPCs) referring to Glenfield Hospital, University Hospitals of Leicester (UHL).

The number of patients prescribed pirfenidone up to January 2016 was collected, and corrected per 100,000 head of population according to the patient postcode from 2011 census data. All patients were from the CXLE or NN postcode areas. As data were not normally distributed, analysis was performed with non-parametric statistics using ‘R’, a statistics package. We collected the time and distance of travel to patients’ local hospital, and to their PC.

**Results** There were a total of 64 postcode areas (PCAs) in the region. Travel times to local hospitals (either a PC or NPC according to area) were normally distributed with a median of 19 minutes (range 5–40). Travel time to relevant PC was bimodally distributed, with a median of 26 ½ minutes (range 5–64). This was significantly different (p=1.10^-7). There were no pirfenidone patients in 20 PCAs. Where patients’ local hospital was a NPS there were significantly more pirfenidone-free PCAs (15/32) than where the local hospital was a PC (5/32), p = 0.015. The number of patients prescribed pirfenidone up to January 2016 was collected, and corrected per 100,000 head of population according to the patient postcode from 2011 census data. All patients were from the CXLE or NN postcode areas. As data were not normally distributed, analysis was performed with non-parametric statistics using ‘R’, a statistics package. We collected the time and distance of travel to patients’ local hospital, and to their PC.

**Conclusions** Our data suggest there are significant health inequalities in access to patients affected by ADRs ceased treatment early, suggesting that potential implications for when prescribing Pirfenidone are that we cannot predict those at risk of discontinuation from their demographics. However, a smoking history intriguingly seems to be positively associated with outcome success. Secondly, those that discontinued for ADRs did so much earlier than those that discontinued due to FVC decline or dying on treatment.

Potential implications for when prescribing Pirfenidone are that we cannot predict those at risk of discontinuation from their demographics. However, a smoking history intriguingly seems to be positively associated with outcome success. Secondly, those that discontinued for ADRs did so much earlier than those that discontinued due to FVC decline or dying on treatment.

**Abstract P172 Table 1**

<table>
<thead>
<tr>
<th>Demographic Parameter (mean or number)</th>
<th>Did not stop therapy</th>
<th>Stopped due to Death or FVC Decline</th>
<th>Stopped due to Adverse Drug Reaction</th>
<th>P (ANOVA or X²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at treatment initiation</td>
<td>69.22</td>
<td>68.06</td>
<td>72.04</td>
<td>0.205</td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>20:3</td>
<td>13:3</td>
<td>17:7</td>
<td>0.385</td>
</tr>
<tr>
<td>BMI</td>
<td>24.2</td>
<td>23.2</td>
<td>23.1</td>
<td>0.631</td>
</tr>
<tr>
<td>Smoking Hx (Never: Ex)</td>
<td>6.17</td>
<td>12:4</td>
<td>18.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FVC% predicted</td>
<td>67.39</td>
<td>61.88</td>
<td>66.75</td>
<td>0.127</td>
</tr>
<tr>
<td>FEV1% predicted</td>
<td>69.05</td>
<td>65.25</td>
<td>72.09</td>
<td>0.115</td>
</tr>
</tbody>
</table>

**P173**

**DEMOGRAPHIC FACTORS AND TEMPORAL PATTERNS AFFECTING TREATMENT SUCCESS WITH PIRFENIDONE FOR PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS – A LARGE RETROSPECTIVE REVIEW**

AD Redfern, N Turner, AC Murphy, FA Woodhead. Institute for Lung Health, Glenfield Hospital, Leicester, UK

10.1136/thoraxjnl-2016-209333.315

**Introduction/objectives** Idiopathic Pulmonary Fibrosis is progressive with poor outcomes. Evidence from the CAPACITY and ASCEND trials suggests Pirfenidone slows disease progression (Noble et al, 2011; King et al, 2014). We reviewed all patients with more than a year since initiation to assess the proportion that discontinued Pirfenidone for adverse drug reactions (ADRs) or due to unsuccessful treatment (>10%/year FVC decline or died on therapy), to assess temporal patterns of these stoppages and assess any demographic or disease extent predictors of success (age, sex, BMI, smoking history, %FVC prediction and FEV1).

**Methods** 155 patients have been referred to our consultant pharmacist for Pirfenidone initiation since August 2013, of which 65 started and have more than 1 year of data (i.e., we excluded those starting post July 2015). We reviewed hospital databases and medical notes with subsequent data analysis using appropriate parametric statistical methods.

**Results** 42/65 (64.6%) stopped therapy overall divided between ADRs (24/42, 57.1%), FVC decline >10%/year (11/42, 26.2%), dying on treatment (5/42, 11.9%) and unclear (2/42, 4.8%). Table 1 demonstrates association between demographics and those that discontinued, suggesting there is one subgroup associated with treatment continuation (patient previously smoked P ≤ 0.001). The temporal pattern of stopping treatment for ADRs vs those failing for clinical reasons (death on treatment or FVC decline) demonstrated a median cessation time of 40 days vs 226 respectively.

**Conclusions** Our data suggests two important findings. Firstly, patients’ chances of continuing therapy is intriguingly affected positively by smoking history, causation for which remains unclear. Sex, age, BMI or disease extent does not seem to be associated with outcome success. Secondly, those that discontinued for ADRS did so much earlier than those that discontinued due to FVC decline or dying on treatment.

**P173**

**REDUCTION IN NON-ELECTIVE RESPIRATORY-RELATED HOSPITALIZATIONS IN PATIENTS TREATED WITH PIRFENIDONE: POOLED ANALYSES FROM THREE PHASE 3 TRIALS OF PIRFENIDONE IN IDIOPATHIC PULMONARY FIBROSIS**

1B Ley, 2J Swigris, 3B Day, 4J Stauffer, 5W Chua, 6K Raimundo, 1H Collard. 1University of California–San Francisco, San Francisco, CA, USA; 2National Jewish Health, Denver, CO, USA; 3Genentech, Inc., South San Francisco, CA, USA

10.1136/thoraxjnl-2016-209333.316

**Rationale** Patients with idiopathic pulmonary fibrosis (IPF) are frequently hospitalised for a variety of reasons. Respiratory-related hospitalizations may occur because of acute exacerbations of IPF, respiratory tract infections, respiratory failure and other causes. Regardless of cause, respiratory-related hospitalizations have been linked to poor outcomes in patients with IPF. We
describe the proportion of patients from the three Phase 3 pirfenidone IPF trials with at least one non-elective hospitalisation (all-cause, respiratory-related and non-respiratory-related) over 12 months.

**Methods** In three Phase 3 randomised, placebo-controlled studies of pirfenidone for IPF (CAPACITY I/II and ASCEND), patients were randomised to pirfenidone (2403 mg/day) or placebo. In the two CAPACITY studies, respiratory-related hospitalisations were a pre-specified endpoint. In ASCEND, hospitalisations were reported as adverse events (AEs), and retrospectively categorised as respiratory-related or non-respiratory by case review. The pooled rates of patients experiencing ≥1 non-elective hospitalisations (all-cause, respiratory-related and non-respiratory-related) for pirfenidone and placebo patients over 12 months are summarised. Rate of death post-hospitalisation was also reported.

**Results** A total of 1,247 patients (692 CAPACITY and 555 ASCEND) were included (Table). In pooled analyses, the proportion of patients experiencing ≥1 all-cause hospitalisations over 12 months was no different between pirfenidone and placebo-treated patients. The proportion of patients experiencing ≥1 respiratory-related hospitalizations was 12% in the placebo group vs 7% in the pirfenidone group (odds ratio 0.56; P = 0.004). Deaths after hospitalisation were numerically reduced in the pirfenidone group, most substantially for respiratory-related hospitalizations.

**Conclusion** Patients with IPF frequently require hospitalisation for a variety of reasons. Pirfenidone may reduce the risk of non-elective respiratory-related hospitalisations over 12 months.

## P174

**EFFECT OF CONTINUED TREATMENT WITH PIRFENIDONE FOLLOWING A ≥10% RELATIVE DECLINE IN PERCENT PREDICTED FORCED VITAL CAPACITY (%FVC) IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF)**

AU Wells, UC Albera, UC Costabel, UC Giappole, UN Glasberg, L Lancaster, DJ Lederer, CA Pereira, J Swigris, M Day, W Chou, SD Nathan. Royal Brompton Hospital, London, UK; University of Turin, Turin, Italy; Ruhrlandklinik, Essen, Germany; Alfred Hospital, Melbourne, Australia; University of Miami Miller School of Medicine, Miami, USA; Vanderbilt University Medical Centre, Nashville, USA; Columbia University Medical Centre, New York, USA; Paulista School of Medicine, Federal University of São Paulo, São Paulo, Brazil; National Jewish Health, Denver, USA; Genentech Inc, South San Francisco, USA; Inova Fairfax Hospital, Falls Church, USA

10.1136/thoraxjnl-2016-209333.317

**Background** The variability in disease progression in patients with IPF complicates the assessment of treatment response. Previously a pooled analysis of three Phase 3 trials showed that patients who experienced a ≥10% *absolute* decline in %FVC during the first 6 months of treatment derived a clinical benefit with continued pirfenidone treatment in the subsequent 6 months [Nathan et al. ATS 2015]. To further explore the potential benefit of continued pirfenidone treatment in patients who initially experienced more modest declines, we assessed subsequent outcomes after a ≥10% *relative* decline in %FVC during the first 6 months of treatment.

**Methods** Source data included all patients randomised to receive pirfenidone 2403 mg/d or placebo in the ASCEND or CAPACITY trials (N = 1247). All patients with a ≥10% relative decline in %FVC were selected by the 6-month study visit. The proportion of patients in the pirfenidone and placebo groups who experienced any of the following during the subsequent 6-month interval were compared: (1) ≥10% relative decline in %FVC or death; (2) death; or (3) no further decline in %FVC.

**Results** Of the pooled patients that experienced an initial ≥10% relative decline in %FVC, 80 and 140 patients received pirfenidone and placebo, respectively. In the subsequent 6 months, 17 (21.3%) and 50 (35.7%) patients, respectively, experienced a ≥10% relative decline in %FVC or death. In addition, more patients in the pirfenidone group had no further decline in %FVC and fewer patients died compared with placebo during the subsequent 6-month interval (Table 1).

**Conclusions** In patients who experienced a ≥10% relative decline in %FVC during the first 6 months of treatment, continued treatment with pirfenidone appeared to lower the risk of %FVC decline or death during the subsequent 6 months, similar to previous results observed with a ≥10% absolute %FVC cut-off. Using relative change to calculate a ≥10% initial FVC decline identified more than twice as many patients compared to using absolute change. These findings suggest a potential benefit to continued treatment with pirfenidone despite an initial clinically meaningful decline in FVC ≥10% regardless of calculation method.

## Abstract P174 Table 1

<table>
<thead>
<tr>
<th>Outcome in subsequent 6 months, n (%)</th>
<th>Pirfenidone (N = 80)</th>
<th>Placebo (N = 140)</th>
<th>Difference, %</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥10% relative decline in %FVC or death</td>
<td>17 (21.3)</td>
<td>50 (35.7)</td>
<td>−40.5</td>
<td>0.033</td>
</tr>
<tr>
<td>Death</td>
<td>5 (6.3)</td>
<td>16 (11.4)</td>
<td>−45.3</td>
<td>0.242</td>
</tr>
<tr>
<td>No further decline in %FVC</td>
<td>41 (51.3)</td>
<td>50 (35.7)</td>
<td>43.5</td>
<td>0.033</td>
</tr>
</tbody>
</table>

FVC, forced vital capacity.
**P175 SINGLE CENTRE EXPERIENCE OF THE REAL-LIFE IMPACT OF PIRFENIDONE ON LUNG FUNCTION IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS**

A Rathnapala, A Fries, Y West, LP Ho, RK Hoyles. Oxford Centre for Respiratory Medicine, Oxford, UK

10.1136/thoraxjnl-2016-209333.318

**Introduction** Idiopathic pulmonary fibrosis (IPF) is a progressively destructive lung disease that culminates in respiratory failure and death. Trials have demonstrated that treatment of IPF patients with Pirfenidone reduces %FVC decline, improves progression-free survival and significantly reduces the risk of all-cause mortality at 1 year. Our anecdotal experience is that a small proportion of patients show improvement of %FVC with treatment.

**Objectives** To assess the proportion of patients in an ILD specialist centre that improve, stabilise or decline in their %FVCs on Pirfenidone treatment.

**Methods** In this retrospective study patients with IPF diagnosed according to the ATS/ERS guidelines at the ILD MDT, who were commenced and continued on Pirfenidone for >6 months were included. Data was derived from the clinical records of the Oxford IPF clinic.

**Results** 100 patient records were analysed and 31 were excluded (n = 15 <6 months therapy, n = 5 inadequate data, n = 2 death <1 month, n = 9 other). 58 (84.1%) male, 11 (15.9%) female; 38 (53.1%) had Definite IPF, 31 (44.9%) Probable IPF.

Six months after commencing Pirfenidone (n = 69 patients), 5 (7.25%) experienced significant (>10%) improvement in %FVC, 33 (47.83%) showed stability (−5% to 5% change %FVC), 10 (14.49%) showed significant and 12 (17.39%) showed significant (>10%) decline in %FVC.

After one year of Pirfenidone (n = 44 patients), 3 (6.8%) showed significant and 5 (11.4%) showed marginal improvement, 18 (40.9%) showed stability, 11 (25%) showed mild and 7 (15.9%) showed significant decline of %FVC.

After 2 years of treatment (n = 15 patients), 1 (6.7%) showed significant and 3 (20%) showed mild improvement, 4 (26.7%) showed stability, 3 (20%) showed mild and 4 (26.7%) showed significant decline of the %FVC.

Among 8 patients who had improvement in %FVC at one year, 6 were males, 6 had definite IPF, median age 77 years (68 – 84) and the median FVC was 73.5% predicted (66 – 79).

**Conclusions** Real-life use of Pirfenidone shows clear slowing of decline in the %FVC, whereas a clinically significant subset show improvement in FVC. Potentially the beneficial effect is lost after 22–24 months, although small numbers limit this analysis.

---

**Paediatric Respiratory Disease**

**P176** **DIAGNOSING ASTHMA IN CHILDREN USING SPIROMETRY: EVIDENCE FROM A BIRTH COHORT STUDY**

KCS Murray, PF Foden, LA Lowe, HD Bunting, A Custovic, A Simpson. University of Manchester, Manchester, UK; Imperial College, London, UK

10.1136/thoraxjnl-2016-209333.319

**Background** NICE draft guidance for the diagnosis of childhood asthma proposes algorithms based on four tests of lung function (FEV1/FVC ratio, bronchodilator reversibility [BDR], FeNO, PEFR variability); a minimum of two tests must be positive to make a diagnosis. For FEV1/FVC ratio, the proposed cut-off for a positive test is <70%, or the lower limit of normal (LLN), which is neither defined nor widely available. In this algorithm, spirometry is the first-line investigation, and children with FEV1/ FVC > 70% are not offered BDR. However, the diagnostic test accuracy for FEV1/FVC and BDR is unknown. Within the setting of a population-based birth cohort we investigated the value of FEV1/FVC and BDR in diagnosing asthma.

**Methods** We assessed study participants at clinical follow-up at age 16 years using validated questionnaires and lung function measurement. Spirometry was measured according to ATS/ERS guidelines. Using the Asthma UK reference equations, we calculated LLN for FEV1/FVC. BDR was considered positive if FEV1 increased by >12% following administration of 400 mg of salbutamol. Current asthma was defined as all three of: (1) doctor-diagnosed asthma ever, (2) wheezing in the previous 12 months and (3) current use of asthma treatment. We assigned children negative to all three features as a non-asthmatic control group.

**Results** Spirometry was available for 630 children (325 boys, age range 13.1–16.9 years), of whom 74 (11.7%) had current asthma and 403 were assigned as non-asthmatic controls. FEV1/FVC was significantly lower among asthmatics (84.1% vs. 89.2%, p < 0.001, Figure 1). Ten children (1.6%) had FEV1/FVC<70% (two in asthma group). Discriminative ability of FEV1/FVC < 70% was poor (Receiver operating characteristic curve, AUC = 0.70; sensitivity = 2.7% [2/74], specificity = 98.8% [398/403]). For the calculated FEV1/FVC LLN (74.8% for boys, 78.2% for girls), 28 children (4.4%) had FEV1/FVC<LLN (11 in asthma group). Discriminative ability of FEV1/FVC<LLN was poor (sensitivity 14.9% [11/74]; specificity 97.0% [391/403]). BDR was positive in 54 children (8.7%), of whom 12 had asthma. Discriminative ability of BDR was poor (AUC = 0.64, sensitivity = 16.2% [12/74], specificity = 93.5% [373/399]). Combining these two tests did not result in a better diagnostic accuracy (sensitivity = 2.7%, specificity = 99.0%).

**Conclusions** FEV1/FVC < 70% or < LLN, and BDR > 12% have a poor diagnostic accuracy as tests for childhood asthma.

---

**P177** **HIGH PREVALENCE OF UNRECOGNISED ASTHMA IN CHILDREN WITH SICKLE CELL DISEASE**

MA Akthar, GR Ruiz, SC Chakravorty, CB Bosseley, D Rees, AG Gupta. Kings College Hospital, London, UK

10.1136/thoraxjnl-2016-209333.320

**Background** Sickle Cell Disease (SCD) affects about 1 in 1,900 children born in the UK. Respiratory morbidity affects children as well as adults with SCD and the burden may have been
underestimated in the past. The published literature suggests that asthma, airway hyper-reactivity and sleep disordered breathing (SDB) are common in children with SCD. Furthermore asthma and SDB have been reported to be associated with acute chest syndrome (ACS) and vaso-occlusive crises (VOC). Children with SCD are increasingly referred to our respiratory clinic in a tertiary paediatric centre in the UK. We did an analysis of a sample of these children to gain some preliminary insights into the problem.

Method
A retrospective observational study was carried out using data from children with SCD who had been referred to our tertiary paediatric respiratory clinic between 1st September 2009 and 31st August 2014. Data was collected from electronic patient records and electronic investigation results.

Results
54 patient records were evaluated. The mean age of the children was 11 years and 54% were male. The most common reason for referral was low oxygen saturation on pulse oximetry (23/54).

Surprisingly, asthma and wheeze were uncommon reasons for referrals comprising only 7/54 (Figure 1). However, of all the patients 48% were discovered to have asthma and 52% had SDB. In those patients who underwent lung function testing an abnormal result was reported in 60% (25/42). In addition 71% of children who had a sleep study had an abnormal result (35/49). No association between ACS or VOC events in those patients with asthma or SDB was noted but this could have been due to the small numbers.

Conclusion
In this sample of children with SCD referred mainly because of low oxygen saturation, the high proportion with an abnormal sleep study and SDB might have been expected. However, the relative paucity of reported wheeze and exercise intolerance despite large numbers with abnormal lung physiology suggested that conditions such as asthma may be unrecognised in these patients.
Introduction Despite the common nature of asthma there is no gold standard test for diagnosis. Both under- and over-diagnosis of childhood asthma in primary care have been reported but there is no UK data. Diagnostic algorithms including objective tests have been proposed but not implemented following a recent NICE consultation. Concerns regarding efficacy and additional resources needed in primary care to provide these tests have delayed implementation.

Aims
- Evaluate practice based barriers to spirometry and exhaled nitric oxide (eNO) testing in children aged 5–16 years
- Examine how training impacts on the utilisation of objective tests on asthma diagnosis

Methods Currently 3 GP surgeries of different sizes and demographics participate in this 2-year project.

Initial face-to-face (F2F) meetings and questionnaires are conducted at each practice to identify barriers to implementation. Paediatric spirometry and eNO training is provided to practice staff (F2F theory session plus practical supervision).

All children on the practice asthma register AND those who received asthma medications within the last 12 months (but not on register) are invited for review.

Data collection (medications, exacerbations, asthma diagnosis etc.) and quality of life questionnaires are conducted at baseline and then again at 6 months by post and repeat review of electronic records

Results Recruitment commenced on 01/06/2016.

To date, nursing staff at two practices have received training and 10 children (5–15 years) have been recruited (11 eligible) in the course of 3 asthma review clinics. Spirometry and eNO were successful in 8 of these children.

Practice staff have expressed concerns regarding funding, additional clinic time and staff training as the main barriers against implementation.

Conclusions Our early data suggests that providing spirometry and eNO for children in general practice is achievable with our training package. Both the training package and clinic structure are being refined to improve time and cost-efficiency.

This study (which when complete will contain a health economic analysis) will provide important evidence to inform NHS decision makers and primary care stakeholders on the usefulness of objective testing in children diagnosed and/or under investigation for asthma in general practice.

REFERENCES
IMPACT OF THE LONDON LOW EMISSION ZONE ON CURRENT CHARACTERISTICS, COPING STRATEGIES AND TRANSITION ARRANGEMENTS FOR YOUNG ADULTS

A182 Thorax

Background Low Emission Zones are a novel public health intervention to address the adverse effects of traffic pollution on health. We investigated the association between traffic-derived air pollutants and lung function in 8-9 year old children living in London’s Low Emission Zone.

Methods Sequential yearly cross-sectional study of 2,297 children aged 8-9 years attending east London primary schools between 2009 and 2014, following the introduction of the Low Emission Zone. We examined the relationship between pollutant exposures (NOx, NO2, PM2.5 and PM10) and lung function. We assigned annual exposures by each child’s residential address. In addition, we used spatially resolved estimates of 12-hour, 24-hour, 7-day exposure estimates were employed. We found no evidence of improvements in lung function over the duration of the Low Emission Zone.

Findings We found inverse associations between exposures of PM10 and PM2.5 in the week prior to children’s assessment and lung function. We assigned annual exposures by each child’s residential address. In addition, we used spatially resolved estimates of 12-hour, 24-hour, 7-day and annual exposures prior to each child’s assessment, allowing us to compare the relative effects of very short-, short-, medium- and long-term pollutant exposures. Primary outcome measure was post-bronchodilator FEV1.

Interpretation Exposure of children to traffic pollution in central London is associated with decreased lung function and lung volumes. No detectable health benefit followed the introduction of the Low Emission Zone.

REFERENCE


TRANSITION ARRANGEMENTS FOR YOUNG ADULTS WITH ASTHMA: UK NATIONAL SURVEY

Methods An online survey was sent to 105 trusts with adult asthma services in all parts of the UK to establish their transition arrangements.

Results Of the 43 responding centres (District General Hospital n = 20), only 60% had a designated lead (n = 26) and less than half made any form of specific arrangements for transition (n = 18). University Hospital trusts were more likely to have transitional care arrangements in place (n = 11/22) than District General Hospitals (n = 6/20). In those centres that did run joint clinics (n = 16), in the majority of cases this only involved adult team members attending paediatric clinics (n = 10).

Most centres (n = 25) expected ≤5 patients to transition each year and over 90% (n = 37) did not initiate contact with YA until they were ≥15 yrs old. Only a third of centres delayed transition if YA were not perceived to be ready (n = 15) or remained in full time education (n = 15).

Overall less than a third of respondents (n = 13) were satisfied with their transition arrangements.

Conclusions Our survey reveals for the first time the wide variation in approaches to transition in asthma clinics across the UK. Our data suggests that currently most centres are not committing the recommended resources towards this process, no doubt hampered by part in the relatively small numbers of young adults with asthma transitioning each year.

REFERENCE


TRANSITIONING TO ADULTHOOD OUTCOMES OF YOUNG PEOPLE WITH CYSTIC FIBROSIS TRANSITIONING TO ADULTHOOD

Methods Patients who transferred to the adult service via a transition clinic within the last 5 years underwent an interview with a psychologist using a questionnaire of demographic data, their experience of transition, their concerns and the effect of CF on their lifestyle. They completed the Hospital Anxiety Depression Scale (HADS) and the Ways of Coping Scale. Clinical data, complications and outcomes were noted at transfer and one year later.

Results 45 patients (27 men) participated; mean age at transfer was 17 (range 15–21) years and at interview was 20.7 (17–24) years; 25 (55%) had chronic Pseudomonas infection, 7 (15.5%) were receiving gastrostomy feeding, 9 had diabetes, one had had liver transplantation and one had undergone termination of pregnancy. At the transition clinic 94% attended with a parent but after transfer 33% attended alone and 18% with a partner; 87% felt that the timing of transition was correct and 80% found the transition clinic helpful. Self-reported adherence to treatment declined in 18% and improved in 24%. Life satisfaction was high with 74% reporting that CF had no effect on their social lives, but 52% felt it impacted on work or studies, although 76% were in employment or education. Mean FEV1 remained stable at 76.6% (26.4–119.6)% at transfer and 75.4% (19–111)% one year later, but varied with 15 patients (33%) having a deterioration of >5% and 8 (18%) improving by >5%. Mean BMI changed from 20.8 (16.3–29.7) to 21.2 (17.3–29.2); 11 patients (24%) were not satisfied with their transition arrangements.

Introduction Transition is a process that addresses the medical, psychosocial and vocational needs of young adults, and it is a crucial stage for patients with CF.

Methods Patients who transferred to the adult service via a transition clinic within the last 5 years underwent an interview with a psychologist using a questionnaire of demographic data, their experience of transition, their concerns and the effect of CF on their lifestyle. They completed the Hospital Anxiety Depression Scale (HADS) and the Ways of Coping Scale. Clinical data, complications and outcomes were noted at transfer and one year later.

Results Of the 43 responding centres (District General Hospital n = 20), only 60% had a designated lead (n = 26) and less than half made any form of specific arrangements for transition (n = 18). University Hospital trusts were more likely to have transitional care arrangements in place (n = 11/22) than District General Hospitals (n = 6/20). In those centres that did run joint clinics (n = 16), in the majority of cases this only involved adult team members attending paediatric clinics (n = 10).

Most centres (n = 25) expected ≤5 patients to transition each year and over 90% (n = 37) did not initiate contact with YA until they were ≥15 yrs old. Only a third of centres delayed transition if YA were not perceived to be ready (n = 15) or remained in full time education (n = 15).

Overall less than a third of respondents (n = 13) were satisfied with their transition arrangements.

Conclusions Our survey reveals for the first time the wide variation in approaches to transition in asthma clinics across the UK. Our data suggests that currently most centres are not committing the recommended resources towards this process, no doubt hampered in part by the relatively small numbers of young adults with asthma transitioning each year.

REFERENCE

improved by >1 kg/m², 4 (9%) deteriorated by >1 kg/m². Psychological distress was low with 7 (15.6%) having anxiety and 3 (6.7%) depression; 84.4% used ‘optimistic acceptance’ as their main way of coping, 8.8% used ‘avoidance’ 2.2% ‘distraction’, and 2.2% ‘hopefulness’.

Conclusion Young people with CF still face daunting problems but are functioning well. There is a need for close monitoring during transition to provide treatment and support to those showing clinical deterioration.

REFERENCE

1 Abott J. Disability Rehabilitation 2001; 23:315.

Abstract P183 Table 1

<table>
<thead>
<tr>
<th>Total Cases</th>
<th>Total Controls</th>
<th>Age 6-11 y Case</th>
<th>Age 6-11 y Control</th>
<th>Age 12-17 y Case</th>
<th>Age 12-17 y Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medicaid (CAID), n</td>
<td>1264</td>
<td>3792</td>
<td>642</td>
<td>1926</td>
<td>622</td>
</tr>
<tr>
<td>Proportion with at least 1 IP admission, n (%)</td>
<td>527 (41.2)</td>
<td>107 (2.8)</td>
<td>202 (31.5)</td>
<td>32 (1.7)</td>
<td>319 (51.3)</td>
</tr>
<tr>
<td>Annual IP admissions, mean (SD)</td>
<td>0.87 (1.49)</td>
<td>0.04 (0.25)</td>
<td>0.55 (1.10) *</td>
<td>0.02 (0.17) *</td>
<td>1.20 (1.76)</td>
</tr>
<tr>
<td>LOS per admission, mean (SD), days</td>
<td>10 (9.0)</td>
<td>6.8 (9.3)</td>
<td>9.5 (6.2) b</td>
<td>6.4 (7.7) b</td>
<td>10.5 (10.3) *</td>
</tr>
<tr>
<td>Annual OP office visits, mean (SD)</td>
<td>9.9 (8.0)</td>
<td>3.2 (3.9)</td>
<td>9.6 (7.6)</td>
<td>3.3 (4.1)</td>
<td>10.2 (8.4)</td>
</tr>
<tr>
<td>Annual total prescriptions filled, mean (SD)</td>
<td>67.3 (52.6)</td>
<td>7.2 (13.4)</td>
<td>65.5 (54.0)</td>
<td>6.6 (11.3)</td>
<td>69.1 (51.1)</td>
</tr>
<tr>
<td>Annual unique prescriptions filled, mean (SD)</td>
<td>15.8 (8.5)</td>
<td>3.2 (4.1)</td>
<td>14.5 (7.3)</td>
<td>3.0 (3.8)</td>
<td>17.1 (9.4)</td>
</tr>
<tr>
<td>Commercial (COMM), n</td>
<td>2400</td>
<td>7200</td>
<td>1075</td>
<td>3225</td>
<td>1325</td>
</tr>
<tr>
<td>Proportion with at least 1 IP admission, n (%)</td>
<td>816 (34.0)</td>
<td>107 (1.5)</td>
<td>270 (25.1)</td>
<td>32 (1.0)</td>
<td>546 (41.2)</td>
</tr>
<tr>
<td>Annual IP admissions, mean (SD)</td>
<td>0.64 (1.21)</td>
<td>0.02 (0.20)</td>
<td>0.40 (0.88) *</td>
<td>0.01 (0.10) *</td>
<td>0.85 (1.39)</td>
</tr>
<tr>
<td>LOS per admission, mean (SD), days</td>
<td>8.4 (6.3)</td>
<td>4.5 (5.9)</td>
<td>7.5 (4.8)</td>
<td>3.6 (4.2)</td>
<td>8.8 (6.9)</td>
</tr>
<tr>
<td>Annual OP office visits, mean (SD)</td>
<td>9.9 (6.6)</td>
<td>2.8 (3.5)</td>
<td>9.4 (6.0)</td>
<td>2.7 (2.9)</td>
<td>10.3 (7.0)</td>
</tr>
<tr>
<td>Annual total prescriptions filled, mean (SD)</td>
<td>39.8 (31.4)</td>
<td>3.6 (7.0)</td>
<td>37.5 (29.0)</td>
<td>2.9 (5.6)</td>
<td>41.7 (33.1)</td>
</tr>
<tr>
<td>Annual unique prescriptions filled, mean (SD)</td>
<td>11.6 (7.0)</td>
<td>2.0 (2.8)</td>
<td>10.5 (6.1)</td>
<td>1.7 (2.3)</td>
<td>12.5 (7.5)</td>
</tr>
</tbody>
</table>

*p value <0.001 for all comparisons (case vs control), unless otherwise noted. *p <0.01; *p <0.02. LOS =length of stay.
ventilation inhomogeneity (VI) as assumptions underlying the calculation are invalid; an alternate index that has been suggested is Scond.1

**Aim**
To compare these two methods of CDI assessment in CF children

**Methods**
Children with cystic fibrosis (CF; 67) and healthy controls (61) performed multiple breath washout with sulphur hexafluoride measured using mass spectrometry. Scond was calculated from 1.5 to 6 turnovers and Scond* from breath 2 to 3 turnovers.

**Results**
All measures of VI were significantly higher for CF vs control, mean difference: LCI 4.0, Scond 0.054, Scond* 0.081.

In CF, LCI correlated better with Scond* than Scond (See figure: correlation coefficient LCI vs. Scond* 0.75; LCI vs. Scond 0.42). If children with moderate-severe VI (LCI > 11) were excluded there was an improved correlation for both relationships (correlation coefficient LCI vs. Scond 0.83; LCI vs. Scond* 0.86).

An asymptote for the Scond vs LCI relationship was at Scond 0.07 and Scond* 0.13.

**Conclusion**
Scond* quantifies the mechanism of VI in moderate to severe lung disease, but it may reach asymptote in very severe VI.

**REFERENCE**

---

**P185** SLEEP DISORDERED BREATHING IN CHILDREN WITH SPINA BIFIDA. TIME TO SCREEN?

J Saunders, N Gibson, P Davies. Royal Hospital For Children, Glasgow, UK

**Background**
Spina bifida is associated with sleep disordered breathing (SDB) particularly when associated with Arnold-Chiari malformations. Studies suggest that moderate/severe sleep apnoea is present in up to a third of spina bifida patients (Patel 2015) and yet there are no national guidelines that recommend screening for SDB in children with spina bifida. There is evidence to suggest that many children present late and this can be associated with unnecessary morbidity and even mortality (Kirk 1999).

**Aim**
To assess the prevalence of SDB in children with spina bifida, presenting through clinical presentation alone in the West of Scotland and to explore whether there is a case for screening all children with spina bifida for SDB.

**Method**
The database of the Spina Bifida Association Scotland and clinical records from the regional centre in the Royal Hospital For Children, Glasgow were used to identify all children with spina bifida in the West of Scotland. The level of the spinal lesion, presence of an Arnold-Chiari malformation or ventriculoperitoneal shunt was established, as was the number who had had sleep studies performed and who had required ventilator support.

**Results**
108 children were identified; 44/108 (40%) had an Arnold-Chiari malformation (1 type I, 43 type II); 64/108 had lumbar abnormalities, 14/108 lumbosacral, 4/108 thoracolumbar, 9/108 sacral and 4/108 thoracic. 52/108 had a VP shunt at some point. Only 14 children had presented with clinical symptoms that lead to a sleep study being undertaken (snoring 7, apnoeas 7, cough/wheeze 2, restlessness at night 2, morning headache 2). 5 children had mixed central and obstructive apnoeas, 1 obstructive sleep apnoea, 2 hypoventilation. 8 children went on to require non-invasive mask ventilation of these 7/8 had an Arnold-Chiari malformation (p = 0.005), 7/8 had a previous VP shunt (p = 0.02), 5/8 had lumbar abnormalities and 3/8 thoraco-lumbar.

**Conclusion**
Clinical presentation alone only identifies a small proportion of cases of SDB in children with spina bifida, with a high proportion of these requiring intervention. We remain concerned that there are many children with spina bifida with undiagnosed SDB who may benefit from treatment, particularly those with Arnold-Chiari malformations and therefore that screening is indicated.

**REFERENCE**
1 Saunders, N Gibson, P Davies. Royal Hospital For Children, Glasgow, UK

---

**P186** INCIDENCE AND OUTCOME OF CONGENITAL LUNG AGENESIS IN THE NORTH OF ENGLAND

N Robertson, 1N Miller, 2J Rankin, 3H McKean, 4M Brodie, 4M Thomas. 1James Cook University Hospital, Middlesborough, UK; 2National Congenital Anomaly and Rare Disease Registration Service, Public Health England, Newcastle Upon Tyne, UK; 3Institute of Health and Society, Newcastle University, Newcastle Upon Tyne, UK; 4Great North Children’s Hospital, Newcastle Upon Tyne, UK; 5Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, UK

**Background**
Spina bifida is associated with sleep disordered breathing (SDB) particularly when associated with Arnold-Chiari malformations. Studies suggest that moderate/severe sleep apnoea is present in up to a third of spina bifida patients (Patel 2015) and yet there are no national guidelines that recommend screening for SDB in children with spina bifida. There is evidence to suggest that many children present late and this can be associated with unnecessary morbidity and even mortality (Kirk 1999).

**Aim**
To assess the prevalence of SDB in children with spina bifida, presenting through clinical presentation alone in the West of Scotland and to explore whether there is a case for screening all children with spina bifida for SDB.

**Method**
The database of the Spina Bifida Association Scotland and clinical records from the regional centre in the Royal Hospital For Children, Glasgow were used to identify all children with spina bifida in the West of Scotland. The level of the spinal lesion, presence of an Arnold-Chiari malformation or ventriculoperitoneal shunt was established, as was the number who had had sleep studies performed and who had required ventilator support.

**Results**
108 children were identified; 44/108 (40%) had an Arnold-Chiari malformation (1 type I, 43 type II); 64/108 had lumbar abnormalities, 14/108 lumbosacral, 4/108 thoracolumbar, 9/108 sacral and 4/108 thoracic. 52/108 had a VP shunt at some point. Only 14 children had presented with clinical symptoms that lead to a sleep study being undertaken (snoring 7, apnoeas 7, cough/wheeze 2, restlessness at night 2, morning headache 2). 5 children had mixed central and obstructive apnoeas, 1 obstructive sleep apnoea, 2 hypoventilation. 8 children went on to require non-invasive mask ventilation of these 7/8 had an Arnold-Chiari malformation (p = 0.005), 7/8 had a previous VP shunt (p = 0.02), 5/8 had lumbar abnormalities and 3/8 thoraco-lumbar.

**Conclusion**
Clinical presentation alone only identifies a small proportion of cases of SDB in children with spina bifida, with a high proportion of these requiring intervention. We remain concerned that there are many children with spina bifida with undiagnosed SDB who may benefit from treatment, particularly those with Arnold-Chiari malformations and therefore that screening is indicated.

**REFERENCE**
1 Robertson, N Miller, J Rankin, H McKean, M Brodie, M Thomas. James Cook University Hospital, Middlesborough, UK; National Congenital Anomaly and Rare Disease Registration Service, Public Health England, Newcastle Upon Tyne, UK; Institute of Health and Society, Newcastle University, Newcastle Upon Tyne, UK; Great North Children’s Hospital, Newcastle Upon Tyne, UK; Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, UK
Introduction Congenital lung agenesis is a rare abnormality which has been reported to have an estimated incidence of 1 in 15,000 pregnancies and to carry a poor prognosis, especially when associated with congenital heart anomalies. (1) However, precise incidence data has previously been unavailable and clinical management has improved in recent years with an unknown impact on outcomes.

Methods We used the North of England register of congenital anomalies (NorCAS) cross-referenced with clinical data from our regional paediatric respiratory centre to calculate the first known accurate incidence estimate for this condition. Detailed clinical and outcome data were then collected with informed consent from the families of affected infants.

Results The incidence of lung agenesis was 0.12 per 100,000 live births (95% confidence interval 0.03–0.31). Four cases were identified with a median age at follow-up of 5 years. Lung agenesis was associated with complex congenital heart disease (complete atroventricular septal defect with left atrial isomerism) in one case, and with aortic coarctation and atrial septal defect in another. Both these patients had their heart defects successfully repaired. The third patient had a normal heart but musculoskeletal problems, while lung agenesis was the only anomaly in the fourth patient. All four patients were well and not on home oxygen.

Conclusions We reviewed the course of the four patients with lung agenesis born in the region between 2004 and 2013, and report that medium term outcomes have been good, even when associated with congenital heart disease and other anomalies. This information will provide a useful starting point when counselling parents whose unborn baby has an antenatal diagnosis of lung agenesis. We aim to follow-up these patients to report long-term outcomes as these remain unknown and there is concern about the potential for the development of late onset pulmonary hypertension.1

REFERENCE

From oxygen to the ITU

P187 POTENTIAL IMPACT OF NON-ARTERIAL BLOOD GAS SAMPLING ON CLINICAL PRACTICE

RW Thomas, NP Kelly, RT Abraham, GH Jones. Royal Liverpool University Hospital, Liverpool, UK

10.1136/thoraxjnl-2016-209333.330

Introduction Arterial blood gas (ABG) analysis is commonly used to monitor patients with acute respiratory problems but can be painful and associated with potentially serious side-effects. Recently there has been renewed interest in non-arterial forms of blood gas analysis with a suggestion that such techniques could replace >60% of ABGs.1 It is however difficult to quantify the impact that non-ABG sampling could have as there is little published data on the clinical burden that ABGs represent. We were interested in establishing how many ABGs are routinely done in a real world setting.

Methods We retrospectively analysed acute admissions (all cause) to a ward based level 2 Respiratory Emergency Care Unit (RECU) at a University Teaching Hospital over a 6 month period. Prospectively we analysed visual analogue pain scores (VAS) and complications including attempt rates.

Results Over a 6-month period (Apr-Oct) 57 of 111 patients admitted to the RECU had complete datasets. A total of 432 ABGs were obtained from this cohort giving an average of 7.6 ABGs (range 2 – 22) per patient per admission and on average patients had 2.3 ABGs each day whilst on RECU.

Overall the mean number of attempts per ABG of the prospectively collected cohort (n = 100) was 1.6 (range 1 – 8; 44% physician obtained). Taking this into account a patient could therefore expect to be stabbed 3.7 times every day or 11 times in total during their admission through the RECU. The most commonly documented complication amongst our patients was pain but average pain scores were relatively low in keeping with other published data (median VAS = 3, IQR 5); no serious complications were reported.

Conclusions Our data suggests that patients requiring admission to a level 2 respiratory unit experience a high burden of ABG testing during their stay. Using published literature on the potential impact of Non-ABG sampling our data suggests that >500 ABGs could be avoided each year on our acute respiratory unit alone.

REFERENCE

P188 NASAL HIGH FLOW (NHF) – IS IT APPROPRIATELY PRESCRIBED? A RETROSPECTIVE CASE REVIEW OF 93 ADULT PATIENTS REQUIRING NASAL HIGH FLOW OXYGEN WITHIN A DISTRICT GENERAL HOSPITAL

A Leadbetter, K Heron, J Robinson, R Mason. Royal United Hospitals Bath NHS Foundation Trust, Bath, UK

10.1136/thoraxjnl-2016-209333.331

Background Nasal high flow (NHF) delivers warmed humidified oxygen up to 65L/min and is commonly used in intensive care units (ICU). In a non-critical care setting it can provide a bridge to ICU for hypoxic patients, and symptom palliation for those unsuitable for escalation.

Evidence to support NHF use in a non-critical care setting is limited. We aimed to review patient selection and clinical outcomes for individuals commenced on NHF over two winter periods, in order to highlight prognostic indicators and develop a clinical guideline.

Method We performed a retrospective review of 93 cases managed with NHF September-December in 2014 and 2015 in a medium sized DGH. Patients were included regardless of diagnosis and treatment escalation plan. Data was collected on patient demographics, diagnosis, management and clinical outcome. Results described as %().

Results 93 patients (mean age 71.2 yrs, SD 14.8). Presenting complaint: Pneumonia 57.0% (53), Aspiration pneumonia 4.3% (4), Pulmonary embolism 4.3% (4), Pulmonary oedema 3.2% (3), Interstitial Lung Disease 3.2% (3), other diagnoses 28.0% (26).

Clinical indication: Hypoxia 64.5% (60), hypoxia and work of breathing 14.0% (13), work of breathing alone 7.5% (7) and palliation 14.0% (13).

42 patients (45%) were assessed by ICU, of which 21 patients were deemed appropriate [mean age 65 yrs (40–84)], 62% (13) were intubated. 81% (17) survived to discharge; 5.9% (1) required LTOT. No significant correlation was present between flow rates and mortality (p = 0.7).
72 patients (77.4%) were managed in non-critical care settings (mean age 72.7 yrs (28–99)). 48.6% (35) survived to discharge, 14.3% (5) required LTOT and 5.7% (2) died within 30 days of discharge. Flow rates ranged 20–65 L/min. In non-ICU patients, survival was negatively correlated with increasing flow rates ($r = -0.86$). Patients requiring $\geq 60$ L/min had an 86% mortality rate ($p = 0.0001$).

**Conclusion** Mortality rates were higher in patients managed on NHF in a non-critical care setting. A negative correlation was present between flow rates and survival outside of ICU. This may be explained by an older patient cohort, associated comorbidities and premorbid performance status. However this information could help guide clinical decision making in acutely unwell patients with limited escalation options.

**REFERENCE**

**P190**

**CHARACTERISTICS AND OUTCOME OF PATIENTS WITH ACTIVE TUBERCULOSIS REQUIRING INTENSIVE CARE ADMISSION, 2010–2015**

NM Shah, S Patel, K Myall, H Milburn, RA Breen. Guy’s and St. Thomas’ NHS Foundation Trust, London, UK

**Introduction** Severe tuberculosis (TB) infection requiring admission to the intensive care unit (ICU) has been reported to be associated with a poor prognosis; however, no data on this cohort of patients from the UK is available. We sought to characterise and report the outcome of this patient group, looking to identify prognostic markers of a poor outcome.

**Methods** All patients admitted to the ICU at our London tertiary referral centre between 01/01/10 and 31/12/15 and coded as having TB were identified and cross-referenced against the London TB register.

**Results** 29 patients were identified which represents 4% (29/790) of all TB notified at our centre in the study period. Median age was 41 years (22–86); 72% were male. 69% had pulmonary TB; 24% were HIV-infected, with a median CD4 count on admission of 134/ul. (17–277). 14% were AFB smear-positive; 79% had culture-positive TB and 86% grew fully-sensitive organisms. The most frequent indications for ICU admission were hypoxic respiratory failure (38%), haemodynamic compromise (24%) and hypercapnic respiratory failure (21%). Median A-a gradient was 12.9 kPa, median PaO$_2$/FiO$_2$ ratio was 29.9 kPa. 72% required mechanical ventilation (median ventilation days 8.4). Two patients received extracorporeal membrane oxygenation therapy for severe respiratory failure. Median APACHE II score was 16 and median SOFA score was 4. Median length of stay in ICU was 7 days and in hospital was 24. At 30 days, 35% remained inpatients (of which 14% remained in ICU), 59% had been discharged home and 21% had died.

Table 1 summarises the differences between survivors and those who died.

**Abstract P190 Table 1** Patient characteristics comparing median values in the patients who survived to 30 days, against those who died. Values are displayed as median (range).

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Survived ($n = 23$)</th>
<th>Died ($n = 6$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>41 (22–79)</td>
<td>58 (37–86)</td>
<td></td>
</tr>
<tr>
<td>ICU Length of stay (days)</td>
<td>7 (2–54)</td>
<td>11 (3–64)</td>
</tr>
<tr>
<td>Hospital Length of stay (days)</td>
<td>22 (5–228)</td>
<td>44 (8–66)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>71 (0–103)</td>
<td>104 (58–232)</td>
</tr>
<tr>
<td>White cell count ($x10^9$)</td>
<td>9.1 (3.2–29.9)</td>
<td>11 (3.3–21.3)</td>
</tr>
<tr>
<td>Haemoglobin (g/L)</td>
<td>94 (71–156)</td>
<td>88 (75–111)</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>27 (15–44)</td>
<td>21 (17–27)</td>
</tr>
<tr>
<td>pH (on admission)</td>
<td>7.38 (7.04–7.47)</td>
<td>7.30 (7.14–7.59)</td>
</tr>
<tr>
<td>pO$_2$ (kPa)</td>
<td>10.53 (6.9–40.0)</td>
<td>9.12 (7.0–16.0)</td>
</tr>
<tr>
<td>pCO$_2$ (kPa)</td>
<td>5.92 (3.3–14.6)</td>
<td>9.03 (4.2–21.2)</td>
</tr>
<tr>
<td>PIF ratio</td>
<td>32 (12.2–60.3)</td>
<td>25.2 (12.2–30.3)</td>
</tr>
<tr>
<td>Ventilator days</td>
<td>2 (0–47)</td>
<td>6 (2–56)</td>
</tr>
<tr>
<td>Days on cardiovascular support</td>
<td>0 (0–13)</td>
<td>3 (0–56)</td>
</tr>
<tr>
<td>Days on renal replacement therapy</td>
<td>0 (0–19)</td>
<td>5.5 (0–15)</td>
</tr>
</tbody>
</table>
Conclusion  In our TB population, the requirement for ICU care was infrequent, with respiratory failure being the most common indication. ICU and overall hospital length of stay was prolonged, but with a majority of patients surviving to discharge. Possible markers of a poor outcome include age, and a requirement for cardiovascular/renal support. These markers and TB-related factors now need to be explored in a larger cohort.

Introduction  There is strong emerging evidence on the devastating effect of anthropogenic climate change on lung health. In England, the NHS accounts for 30% of the public sector carbon footprint, with patient travel being accountable for 8% of overall travel (17%). The climate change act (2008) resulted in the government and NHS committing to an 80% reduction in carbon emissions by 2050.

Methods  There are many studies detailed the benefit of telemonitoring in reducing carbon footprint within NHS services. Within the Lancashire and South Cumbria Long Term Ventilation Service (LSCLTVS) we have invested in a ventilator remote monitoring system (EncoreAnywhere™). Over a 3 month time period we analysed the telephone consultations of all 138 patients under the care of the LSCLTVS (80 patients on remote monitoring systems). Patients or carers that called reporting deterioration in a clinical condition that could not be rectified over the telephone were identified. The normal intervention that would follow would be a visit from the GP or community respiratory team, hospital admission, clinic visit or home visit from the ventilation team. A ventilator review was indicated in 29 patients which would normally necessitate either a clinic visit to Royal Preston Hospital or a consultation at home. However as these patients had remote ventilator monitoring we were able to review data and make changes remotely.

Results  In a 3 month time period 29 return journeys were prevented through the use of remote monitoring. This equated to 1029.3 km (623 miles), 249 kg CO2e (0.24 t CO2e)* saved over 28 hours in commuting time and £255 in mileage costs (40 p per mile). It also had a positive impact on patient experience and no hospital admissions or clinic visits were necessary after remote consultation. 62% (n = 18) patients required use of rescue packs including antibiotics and mucolytics as well as remote ventilator changes.

Discussion  The use of remote monitoring within the LSCLTVS has reduced the carbon footprint of the service on average 6.6 kg CO2e per patient. Patients also reported improved satisfaction and compliance.

Introduction and objectives  Respiratory failure is a common clinical problem and a number of treatment options are available. NIV is an established treatment for hypercapnic type two respiratory failure (RF). High Flow Nasal Oxygen (HFNO) is an alternative to standard oxygen or CPAP, and its use in hypoxic patients has been growing.

Methods  A retrospective analysis of data from inpatient type 2 respiratory failure and NIV prior and post BTS Guideline based local protocol implementation was collected. Analysis was done to assess adherence to protocol and compare quality care and outcomes with data prior to implementation. For type 1 respiratory failure a literature review was done, evidence appraised and local guidance and protocol for HFNO developed and a pilot study conducted.

Results  Since introduction of NIV proforma: NIV more frequently initiated in appropriate setting. Compliance with recommended ABG monitoring improved from 85% to 100%. Documentation of escalation plans improved from 50% to 100% (Figure 1).

HFNO was successfully implemented and commenced in our Trust over 10 weeks. All patients on HFNO tolerated therapy. Prevented ITU admission in 80% of cases selected for monitored ward based care of respiratory failure.

Conclusions  In the present study, we showed how to safely implement evidence based local guidance and protocol based care plans for managing type 1 and 2 respiratory failure in a DGH to.
improve quality of care, improve adherence to BTS guidelines, reduce in-hospital mortality and prevent ITU admission.

We believe the guideline and protocol supported the on-call teams to identify and safely manage respiratory failure. We continue to evaluate the service.

P193 EARLY NON-INVASIVE VENTILATION VERSUS STANDARD OXYGEN THERAPY IN IMMUNOCOMPROMISED PATIENTS WITH RESPIRATORY FAILURE: A META-ANALYSIS

RV Villalobos, UK Gopez, K Flores. Department of Medicine, Philippine General Hospital, Manila, Philippines

Background and aims Respiratory failure is common in immunocompromised patients. Intubation and mechanical ventilation (MV) is the mainstay of treatment but is associated with increased risk of pneumonia and other complications. Non-invasive ventilation (NIV) is an alternative to MV in a select group of patients and aims to avoid the complications of MV.

In these patients, we performed a meta-analysis on the effect of early NIV versus conventional oxygen therapy in reducing intubation rates and other important clinical outcomes.

Methods We performed an extensive online and unpublished data search for relevant studies that met the inclusion criteria. We included randomised controlled trials that used early NIV versus conventional oxygen therapy in immunocompromised patients with respiratory failure. Risk of bias and acceptability assessment were independently performed by the authors.

The primary outcome of interest was intubation and MV rate. The secondary outcomes were ICU and all-cause mortality, ICU length of stay and duration of mechanical ventilation.

Results Four studies with a total of 553 patients met the criteria for inclusion and were included in the analysis.

Patients given NIV were 38% less likely to be intubated vs. those given oxygen, RR 0.62 (95% CI: 0.42, 0.93); however, this result is significantly heterogeneous. After sensitivity analysis, results showed 48% less likelihood of intubation and mechanical ventilation in the group treated with NIV, RR 0.52 (95% CI: 0.35, 0.77).

Patients on NIV had 1.18 days less stay in the ICU vs. oxygen group (95% CI: −1.84, −0.5 days). There was no statistically significant decrease in all-cause mortality between the two groups, RR 0.84 (95% CI: 0.63, 1.13), but this effect is heterogenous. After another sensitivity analysis performed specifically for this outcome, results showed a 25% significant reduction in all-cause mortality in patients given NIV vs. oxygen therapy, RR 0.75 (95% CI: 0.58, 0.96).

There is no difference in the duration of mechanical ventilation between groups.

Conclusions In immunocompromised patients with respiratory failure, early NIV reduced intubation rates and decreased all-cause mortality and length of ICU stay compared to standard oxygen therapy.

P194 EARLY WARNING SCORES, TOO IMPRECISE A TOOL IN PATIENTS WITH RESPIRATORY DISEASE?

SF Forster, G Housley, J Hatton, D Shaw. University Of Nottingham, Nottingham, UK; Nottingham University Hospitals Trust, Nottingham, UK

Introduction Guidance from the National Institute of Health and Care Excellence in 2007 has led to the almost universal use of early warning scores (EWS) derived from vital signs observations in hospitals in the UK to highlight patients at risk of deterioration. Lack of high quality prospective studies limits our understanding of the impact of using such monitoring systems on outcomes and working patterns. No EWS has been validated in respiratory patients despite widespread use. Our aim was to examine the ability of both the locally used EWS and National Early Warning Score (NEWS) to predict patient deterioration and associated burden of escalations generated in a respiratory cohort.

Methods Vital signs observations and outcomes for all admissions under the respiratory department at a tertiary referral centre between April 2015 and March 2016 were analysed. Predicted and actual escalation patterns in relation to primary endpoint of mortality were examined comparing NEWS to local EWS. Patients documented as receiving end of life care were removed from analysis.

Results Over 12 months there were 165,184 observations sets during 5293 admissions, with a mean of 38 observations per admission (standard deviation 50). Occurrence of primary endpoint of in-hospital death was 6.74%. 13% of observations triggered clinical escalation to a registered nurse or beyond, with mean of 1075 per month. 112 (31%) patients who died did not trigger escalation on their final set of observations, 1 patient was escalated despite scoring below protocol threshold. Applying NEWS criteria retrospectively predicts 6 patients who died would not be escalated, while generating a mean of 12,409 escalations of vital signs observations per month to registered nurse or beyond, 1,621 in patients who went on to die in hospital.

Abstract P193 Figure 1
Conclusion Our data suggests that neither scoring system provides effective monitoring in patients with respiratory disease, falling short on either sensitivity or specificity for predicting inhospital death. As more data becomes available, modelling may allow more accurate prediction systems to be developed.

REFERENCE


Introduction and objectives An accurate assessment of severity of community acquired pneumonia (CAP) on admission is pivotal in early identification of patients who are critically ill. CURB-65 is recommended by BTS, but is a poor predictor of ICU admissions and often underestimates severity in young patients. We compared this with REA-ICU and SMART-COP in predicting severity and mortality.

Methods The notes of all adult patients admitted with a diagnosis of CAP in June 2016 were reviewed. Inclusion criteria consisted of consolidation on chest radiograph and raised inflammatory markers. Scores were calculated from results obtained within 24 hours of admission. The patients were followed up to ascertain length of stay, complications (effusions, empyema) antibiotic escalation, delivery of non-invasive ventilation (NIV), ICU escalation and death.

Results 43 patients identified with CAP were included in our analysis. 76.7% of patients were ≥65 years old. 24 hours after admission, 39.3% had ward-based ceilings of care in place and 27.9% had no escalation plan documented. 11.6% were still inpatients at the time of analysis. No patients were escalated to ICU.

CURB-65 was 0 to 1 in 23.3%, 2 in 18.6%, and ≥3 in 58.1%. In the low risk group, 50% developed complications, 10% required NIV and there were no inpatient deaths. Amongst the moderate and high risk patients, NIV was administered in 25% and 16% respectively, primarily as the patient’s ceiling of care. Inpatient deaths occurred in 12.5% of moderate risk and 16% of high risk patients.

As shown in Table 1, there was variation in REA-ICU and SMART-COP scores amongst moderate and high risk CURB-65 scores. A high risk CURB-65 score did not correlate with high REA-ICU and SMART-COP scores. We found that higher REA-ICU and SMART-COP scores did not correlate with increased mortality. However, length of stay and antibiotic escalation was increased with higher SMART-COP scores, particularly in those with low CURB-65 scores.

Conclusions CURB-65 score correlates well with mortality, particularly in the elderly group of patients studied. REA-ICU and SMART-COP scores provide useful information regarding the likelihood of complications, antibiotic escalation and length of stay in hospital.
SMART-COP are better at identifying younger, morbidly ill patients with misleadingly low CURB-65 scores requiring early decisions regarding escalation of care.

**P196**

**PREDICTING ESCALATION TO INTENSIVE CARE FOR PATIENTS WITH PNEUMONIA WITH A NEW CLINICAL PREDICTION RULE: SNA³P**

LE Hodgson, BD Dimitrov, C Stubbs, R Venn, LG Forni. University of Southampton, Southampton, UK; Brighton and Sussex Medical School, Brighton, UK; Western Sussex Hospitals NHS FT, Worthing, UK; Royal Surrey County Hospital, Guildford, UK.

Introduction Many clinical prediction rules (CPRs) exist for community-acquired pneumonia (CAP), though few have been investigated to predict escalation to an intensive care unit (ICU). Furthermore, most include components (sometimes subjective) that do not allow the potential for electronic automation in clinical practice.

Methods A historical cohort study was performed at two UK adult acute medical units (2013–15). Inclusion was based on an ICD-10 coded diagnosis of pneumonia. Primary outcome was escalation to ICU. Exclusion criteria was: direct ICU admission from A and E, a stay <1 night, age <18 or ≥80 or frail elderly, neutropenia, HIV, malignancy and palliative care. Predictive performance of CURB-65 was compared to CRB-65, CURB, the National Early Warning Score (NEWS) and a modified SMART-COP (SART-CO, as imaging and ABGs were not available) using receiver operating characteristics (ROC) analysis. Multivariable logistic regression was also performed to investigate additional predictors electronically available at admission (blood and physiological parameters).

Results 1,305 of 24,706 medical admissions were included. 8.3% (n = 109) were escalated to ICU, with significantly increased in-patient mortality (31% vs 6.5%, p < 0.001). 54% of ICU patients had, or developed, AKI vs 11% if not escalated (p < 0.001). To predict escalation, AUCROCs for existing CPRs ranged from 0.54–0.61 (Figure). Using multivariable logistic regression a newly derived CPR – SNA³P - (including 6 components: Sodium, NEWS ≥ 7, Albumin, AST, AKI and Platelets, score range 0–20 points) demonstrated a statistically significant increase in discrimination (AUCROC 0.80, 95% CI: 0.75–0.84).

At a cut-off of 2 points to predict ICU escalation, sensitivity was 92% (95% CI: 85–96%), specificity 48% (45–51), positive predictive value (PPV) 14% (11–16) and negative predictive value 98% (97–99); at 6 points sensitivity was 53% (43–63), specificity 87% (85–89), PPV 27% (21–33) and NPV 95% (94–96).

Conclusion Existing pneumonia CPRs, largely derived to predict mortality, have shortcomings when predicting those who require escalation to ICU. The newly derived rule SNA³P, if externally validated could be incorporated into an electronic clinical decision support system to provide automatic objective assessment and evidence of risk at point-of-care for those who may be considered for escalation.

**P197**

**MEDIUM TERM IMPACTS OF ECMO ON ADULT SURVIVORS**


Abstract P196 Figure 1  AUCROC for escalation to ICU. CURB-65 0.59 (95% CI: 0.52–0.63), CRB-65 0.54 (0.49–0.60), CURB 0.59 (0.54–0.65), NEWS 0.58 (0.53–0.64), SART-CO 0.61 (0.56–0.67), SNAAP 0.80 (0.75–0.84).
Veno-venous Extra-Corporeal Membrane Oxygenation (VV-ECMO) is an established support for severe adult respiratory distress. Previous studies have showed improvement in survival over conventional treatment for ARDS, however little is known about the medium term impact of ECMO on patients, lung physiology and quality of life (QoL). This study investigates these factors in a cohort of patients post-ECMO.

All VV-ECMO survivors at a national cardiothoracic centre were offered follow-up six months post-discharge. Thirty-four patients were followed over a three-year period. We examined lung physiology, six-minute walk distance, chest X-rays and change in BMI. QoL subjective measures included mobility, self-care, psychological state and pain scores.

Mean duration of ECMO support was 14.5 days (± 10.2; range = 3–40 days). Indications were infective (22/34), embolic (4/34), bronchospasm (4/34), trauma (3/34) and drug overdose (1/34). There was insignificant correlation between indication/ECMO duration and lung physiology at six months, with good recovery in all lung physiology parameters (%FEV1 mean = 88.0% ± 16.9; %FVC mean = 93.1% ± 16.2) with the exception of TLCO%predicted (mean = 76.6% ± 16.6). This however didn’t translate into a measureable difference in exercise physiology, with no correlation between six-minute walk distance and ECMO duration (R² = 0.0022, mean = 424 m ± 82.5).

Seventy-nine percent of 29 X-rays assessed were normal. Mean BMI change during ECMO admission was -6.87% ± 11.99 with greater BMI decline alongside longer ECMO support. Interestingly, post-discharge men regained most weight by follow-up whereas females continued to lose (Figure 1).

No significant correlations were seen between ECMO length, indication, and QoL measures. Qualitative analysis suggests worsening anxiety/depression amongst 13 (6 M 7F) patients/family members post-ECMO; four patients giving unprompted mention of flashbacks/nightmares.

ECMO offers undoubted short term improvement in ARDS mortality. In this cohort, recovery of lung physiology, chest radiology and QoL is good. The isolated transfer factor reduction
likely relates to a loss of functioning alveolar units but doesn’t appear to impact exercise physiology or QoL. The main lasting impact appears to be psychological. In the absence of a control group, the impact of critical illness is difficult to separate from that of ECMO, however in this uncontrolled single centre observational study much reassurance can be gained about medium term impact of ECMO.

Service design and delivery

ANCHORING COPD SCREENING TO DRUG SERVICES IN HEROIN AND CRACK SMOKERS TO IMPROVE DIAGNOSIS

COPD is associated with social deprivation which can reinforce health inequality, especially in difficult to access groups. Heroin and crack smoking is associated with early onset severe COPD but this population engages poorly with non-emergency medical services although they engage effectively with specialist drug services. As such, despite an expansion in community spirometry provision, different models of care may be needed to optimise COPD diagnosis and management. In order to access this group Liverpool Clinical Commissioning Group (CCG) funded a COPD screening programme where all current and former heroin and crack smokers using local drug services were offered spirometry at drug key worker appointments where they collected their opioid substitute prescription. If willing they also completed MRC, CAT, a record of cigarette and drug exposure and had oxygen saturations measured. They also provided feedback about the programme.

Eight hundred and seven (807) out of the population of 1100 participated which represents 73% of the client group. Airflow obstruction consistent with COPD was present in 379 (47%) with a further 50 (6%) having reversible airflow obstruction consistent with asthma. Of those with COPD, 154 (41%) had mild, 144 (38%) moderate and 81 (21%) severe or very severe COPD. Mean FEV1 was 2.93L (0.93), mean CAT was 19.5 (10.5) and mean MRC was 2.64 (1.29). Of the 379 with COPD, only a minority (41%) were diagnosed, a third of people were prescribed no inhaler therapy and, when prescribed, treatment was typically sub-optimal. Amongst those with COPD, 337 (90%) were current cigarette smokers while 93 (23%) and 105 (28%) still smoked crack and heroin respectively.

When asked to feedback 96% of respondents were happy with the process and 93% would be willing to attend future COPD appointments at drug centres.

Anchoring spirometry to key worker appointments in heroin and crack smokers was popular amongst service users and a majority completed spirometry. Airway disease was present in a majority with 47% having mostly undiagnosed but symptomatic COPD with significant scope to improve treatment. This model of screening and treatment improved healthcare access and could be used in other hard to reach groups, such as the homeless.
Abstract P199 Figure 1 Flow of patients through our COPD Hyperinflation service in 2015. MDT: multidisciplinary team; EBV: endobronchial valve; LVRS: Lung volume reduction surgery.* Endobronchial coil was offered as part of a clinical trial.

REFERENCE

Abstract P200 Table 1

<table>
<thead>
<tr>
<th>Oct 2014</th>
<th>Oct 2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaler technique checked</td>
<td>24%</td>
</tr>
<tr>
<td>Written Information given</td>
<td>9%</td>
</tr>
<tr>
<td>Rescue Pack Prescribed</td>
<td>27%</td>
</tr>
<tr>
<td>Referred for smoking cessation</td>
<td>59%</td>
</tr>
<tr>
<td>Referred for PR</td>
<td>27%</td>
</tr>
<tr>
<td>Follow up arranged</td>
<td>27%</td>
</tr>
</tbody>
</table>

*significant at P = 0.05 level, paired t test on individual trust data.

REFERENCE

P201 INTEGRATING PATIENT SUPPORT GROUPS INTO RESPIRATORY CARE PATHWAYS

Strategy for change The British Lung Foundation wanted to test if integrating respiratory support groups into the local pathway produced a better understanding of health care services available and lung disease; increased medicine management and compliance; increased patient confidence and development of new skills. Did it also impact on control of health and demand on NHS services including unplanned hospital admissions?

Assessment The aim of this evaluation was two-fold:
1. A process evaluation: to look at the barriers and facilitators to integrating a support group into a respiratory care pathway.
2. An outcome, impact and economic evaluation: to measure impact on both physical and mental wellbeing and the benefits to NHS services, clinicians and commissioners

Methodology We employed validated questionnaires to measure physical, psychological and general wellbeing outcomes in participants. These were disseminated to control and test group at baseline and at 6 monthly intervals. Impact on NHS services was self-reported via telephone interviews with patients.

Effects of changes There was a self-reported 42% reduction in unplanned GP visits and a 57% reduction in unplanned hospital admissions compared to standard support groups.
People living with a lung condition who attended any type of support group had significantly greater quality of life at 6 months compared to control.

Those attending groups maintained quality of life throughout the study whereas quality of life decreased by more than 20% for patients in control group.

Those attending standard groups maintained self-efficacy whereas there was a decrease of 17% for those in control group.

For each pound invested in the integrated support groups there is a return of a minimum £3.43 and a maximum of £9.36.

For each pound invested in the integrated groups, there is a net gain of £8.01 in social return.

Lessons learnt

Integrated respiratory patient support groups is a cost effective programme which has positive outcomes in terms of self-efficacy, health outcomes and wellbeing for attendees, providing cost savings and wider social benefits to local communities.

P202

OPTIMISING SERVICE DELIVERY IN ASTHMA AND COPD: CONSENSUS-DRIVEN RECOMMENDATIONS FOR FUTURE SERVICE DEVELOPMENT

1.1 Ledson, 1.2 Baskaran, 1.3 Dunford, 1.4 Gwynn, 1.5 Khanb, 1.6 Prigmore, 1.7 Scullon, 1.8 Liverpool Heart and Chest Hospital, Liverpool, UK; 1.9 The James O’Jordan Medical Centre, Sutton, UK; 1.10 The Viceroy Surgery, Birmingham, UK; 1.11 Triducive Limited, St Albans, UK; 1.12 NHS London Procurement Partnership, London, UK; 1.13 St Georges Hospital, Tooting, UK; 1.14 Glenfield Hospital, Leicester, UK

Introduction and objectives

Asthma and COPD present a significant resource impact to the NHS. Earlier diagnosis may reduce morbidity and improve quality of life. In the UK, premature mortality from COPD is almost twice the European average and for asthma over 1.5 times the European average. This project sponsored by Teva Respiratory aims to identify differences in perceptions of various stakeholder groups regarding effective outcome improvements in asthma and COPD and make relevant recommendations.

Methods

This group met with the objective of defining consensus statements for the future development of services in asthma and COPD. These statements were tested across a broad respondent sample by questionnaire. A Delphi methodology was used to assess levels of agreement with each statement. Questionnaires were offered to health care professionals across specialties reflecting the roles of this group for completion as paper documents at Teva Respiratory sponsored UK meetings between June 2015 and January 2016.

Results

184 respondents, split across varied professional roles, completed questionnaires. 24 out of 42 statement scores (57%) exceeded the 66% agreement threshold and are thus regarded as supportive of the statements. Some variance was seen in responses between care settings (Figure 1), with primary care respondents commonly indicating lower levels of agreement than their secondary care colleagues (24 out of 42 statements (57%).

Conclusions

Most respondents indicate that it is possible to deliver effective care across all care settings that the patient will encounter. The need for further development of local integrated care approaches is well recognised. Respondents are ambivalent regarding the prioritisation of asthma and COPD, the variance may reflect differences in prioritisation between localities. There is strong agreement that definition of appropriate outcomes will support value-based care models and that interaction between professions is critical to effective integration of care. Respondents agreed there is a sound rationale for the use of branded inhaler therapies in asthma and COPD, which may liberate finite resources for other areas.

Based on this consensus exercise, 10 key recommendations for optimising outcomes in asthma and COPD are offered.

P203

ACUTE ONCOLOGY SERVICES AND THE CHEST PHYSICIAN

J.A Benjamin, K Wingfield, C Garman. Cwm Taf University Health Board, Pontyclun, UK

Background

At our trust (Popn 289400, x2 district general hospitals,) the Acute Oncology Service (AOS) began formally in June 2015. The team consists of 6 members, 3 consultants (1 session per week each; x1 clinical lead at both sites and one clinical lead for metastatic spinal cord compression across both sites,) 2 clinical nurse specialists full time, 1 data coordinator full time. One of the 3 consultants is a chest physician (author.)

- In September 2014 a formal expression of need for AOS development was accepted and supported by Macmillan for a 3 year fixed term project.
There was a well supported process of induction for the nurses and introduction of the service to the Health Board prior to becoming clinically available in September 2016.

Outcomes
- 569 patients have been seen since clinically active (Sept 2015)
- Median reduction in length of hospital stay (LOS) from 11 to 5 days for patients with carcinoma of unknown primary (CUP)
- Median LOS since introduction of service is 5 days for all cancer diagnoses. This equates to a 1 day reduction in LOS.
- Median LOS in preceding years 2011–2015 = 6 days
- The largest number of referrals to the service has been for patients with lung cancer (21%) – see Table

Conclusions/personnel reflections
An effective AOS service improves quantitative outcomes (reduced LOS, efficient processing of CUP patients,) and enhances qualitative outcomes for patients (advocates for CUP patients, better communication*)

The majority of cancers dealt with by the AOS service are lung cancer

The outcomes above are almost exclusively down to the AOS nurses but of all medical and surgical specialties, chest physicians (who deal with lung cancer) are ideally placed as clinical leads for this service due to their cancer experience and established links with radiology, pathology and palliative care (Author’s own opinion.)

For present and future AOS services, this team would recommend that an amenable/enthusiastic chest physician would be a valuable asset to the service

* Patient feedback can be provided on request

---

**P204 QUALITY IMPROVEMENT PROJECT FOR EMERGENCY OXYGEN DELIVERY ON A RESPIRATORY WARD**

KE Hutchinson, S Craik, K Srinivasan, H Moudgil, N Ahmad. Princess Royal Hospital, Telford, UK

10.1136/thoraxjnl-2016-209333.347

**Background** British Thoracic Society (BTS) guidelines state that oxygen should be used to treat hypoxaemia and prescribed to a target saturation range.1 Patients at risk of type 2 respiratory failure should target 88–92%, with the rest 94–98%. In the BTS national audit in 2013, out of 6214 patients, 55% had oxygen prescribed and 52% were prescribed and delivered to within a target saturation range.2

**Methods** We ran a Quality Improvement Project (QIP) involving three PDSA cycles to improve the delivery of oxygen to patients on the Respiratory Ward at the Princess Royal Hospital, Telford.

We set our standards as:
1. 90% of patients receiving oxygen have it prescribed on a drug chart
2. 100% of patients prescribed oxygen have a documented target saturation range
3. 100% of patients have oxygen delivered appropriately to target

The QIP process commenced in Autumn 2015. After the first cycle we used bedside prompt cards and delivered teaching sessions with doctors, nurses and healthcare assistants (HCAs). After the second cycle we appointed a nurse, HCA and two FY1
doctors as ‘O2 Ninjas’. Data were collected at three points after each cycle from drug charts and VitalPaC.

Results

See Table

Abstract P204 Table 1

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients on oxygen</td>
<td>Prescribed</td>
<td>55%</td>
<td>58%</td>
<td>61%</td>
<td>79%</td>
</tr>
<tr>
<td>Prescribed</td>
<td>53%</td>
<td>95%</td>
<td>98%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Prescribed &amp; Targeted</td>
<td>52%</td>
<td>69%</td>
<td>63%</td>
<td>62%</td>
<td>62%</td>
</tr>
</tbody>
</table>

Conclusions

Our QIP shows that education and empowerment of ‘grass root’ healthcare workers can improve oxygen prescription on a Respiratory ward. We suggest this QIP is replicated in other trusts and specialties to improve safe oxygen delivery.

REFERENCES


Introduction

Home oxygen costs the NHS approximately £120 million a year, with £13 million spent on oxygen that is never used.1 Home oxygen teams require integration into the wider respiratory care pathway to ensure appropriate assessment of clinical need and risk, education and follow-up.2 In Derbyshire, prescriptions initiated in the community had appropriate assessments in 90% of cases. In contrast, home oxygen initiated in secondary care at discharge was often prescribed on day of discharge, by junior doctors with no specialist training, without appropriate assessment and education, frequently necessitating early community input. Following two serious incidents post discharge, a study was implemented to evaluate the impact of a different approach to home oxygen prescription following acute hospital stay. The new service included an in-reach oxygen nurse and bespoke risk assessment for hospital discharges.

Methods

A before and after study was performed recording key outcomes, including number of prescriptions, cost, and input required post-discharge. This was carried out over a period of 12 months before and 12 months after implementation of the new service, assessing impact on compliance with guidelines and patient safety.

Results

In the pre-intervention period there were 278 home oxygen prescriptions resulting from the acute care setting, all performed by junior doctors, with 155 urgent (same day) prescriptions totalling £32,815. In the 12 months post-intervention there were 145 home oxygen prescriptions, 88 by in-reach nurses, including 56 urgent orders totalling £11,655. The pre-
vions need for 2 month post discharge visit for assessment and education reduced significantly, with associated dramatic reduction in phone-calls from patients with queries.

Conclusion This study, though limited to single centre, shows significant cost and potential safety benefits. Introducing greater rigour to the in-hospital assessment process was thought to account for the overall fall in oxygen prescription, particularly high-cost urgent orders. With reduction in need for post-discharge intervention also reducing the burden in the community and suggesting greater patient understanding.

REFERENCES
1 Directorate, N.M., COPD Commissioning toolkit. 2012.

Achieving responsible oxygen prescribing to improve value: London care homes

Abstract P206 Table 1 Clinical codes for home oxygen provision for patients in London care homes

<table>
<thead>
<tr>
<th>Clinical code on HOOF</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>COPD</td>
<td>71</td>
</tr>
<tr>
<td>Palliative</td>
<td>55</td>
</tr>
<tr>
<td>Unknown</td>
<td>52</td>
</tr>
<tr>
<td>Paediatric/Neonatal</td>
<td>19</td>
</tr>
<tr>
<td>Neuromuscular disease</td>
<td>11</td>
</tr>
<tr>
<td>Cluster Headache</td>
<td>10</td>
</tr>
<tr>
<td>Primary Pulmonary Hypertension</td>
<td>8</td>
</tr>
<tr>
<td>Other Respiratory</td>
<td>4</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>4</td>
</tr>
<tr>
<td>Obstructive Sleep Apnoea</td>
<td>2</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>2</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>1</td>
</tr>
</tbody>
</table>

Background Around 85,000 patients are currently prescribed home oxygen (HO) in England, costing the NHS > £100 million/yr. There are about 11000 HO users in London costing £12 million/yr. Department of Health data suggest 24%–43% of oxygen prescribed is not used/used inappropriately. The aim of this study was to better understand HO prescriptions/use in London nursing/care homes.

Methods Air Liquide (AL), the London oxygen provider, reviewed their database to identify nursing/residential/care home and hospice residents with an active HO Order Form (HOOF) as of January 2016. Staff education and support was undertaken by the AL respiratory nurse advisor (ALRNA) from Jan–June 2016. Results were reviewed with the London Clinical Oxygen Network.

Results 245 adult patients with a HO prescription were identified across 155 nursing/residential/care homes and hospices in London (mean age 77, range 22–102 years). Table 1 shows the Clinical codes on the HOOFs. The indication for oxygen was unknown in 52 (21%). HO prescription ranged from 0.5–15 LPM; equipment ranged from oxygen concentrators, ambulatory cylinders (89), static cylinders (22), portable oxygen concentrators (5) and liquid oxygen (2). 168 (68%) patients were underusing oxygen while 38 (15%) were overusing, 36 (14%) patients were not using their oxygen at all. Only 90 (36%) patients had a HOOF dating from 2016; 157 (64%) had a HOOF more than a year old. Issues noted included lack of information as to indication for HO and who to contact for guidance, absence of clinical directives from prescribers resulting in ‘PRN’ oxygen use and training needs around storage/use of oxygen equipment.

Conclusion A sizable number of nursing/residential/care home and hospice residents in London are currently prescribed oxygen which is being over/under or inappropriately used without ongoing specialist support/review. For 1 in 5 patients the clinical indication is unknown. New oxygen prescriptions for ‘nursing home’ patients should include guidance on use, staff training and ongoing support. These data exemplify broader issues relating to lack of commissioned HO pathways and the need for commissioned Home Oxygen Review (HOS-R) services across all CCGs to keep patients safe, maximise patient benefit and reduce waste.

Poster sessions

Self-fill oxygen systems – benefits for patients, healthcare providers and the environment

Introduction ‘Non-delivery’ Home oxygen concentrator systems that allow self-filling of ambulatory oxygen (AO) cylinders are emerging. They offer a relatively unlimited supply of AO in suitably assessed people who require Long term oxygen therapy (LTOT) with the proviso that they can use these systems safely and effectively, thus allowing users of LTOT to be self-sufficient and facilitating longer periods of time away from their home.

Methods A national review of the home oxygen service in Scotland was undertaken resulting in consolidation of all home oxygen delivery systems under a single contractor with the transition to this new service delivered over 2013. A health economics analysis was conducted following the transition to compare the differences between the previous conventional AO cylinder home delivery service and the HomeFill (HF) system.

Results Conservative calculations indicate a cost for 3 AO cylinders of about £84 per week, or £4247 per year, compared with a cost for HF of £920 per annum, giving a benefit of around £3344 for each patient. The costs savings related to reduced travel and delivery in 1213 HF users compared to the AO cylinder delivery model is 1.25 million Km’s and the estimated carbon emission (CO2e) reduction for the HF system is 261.29 tonnes of CO2e.

Conclusion Evidence is emerging that ‘Self-fill’/’non-delivery’ oxygen systems can meet the AO needs of many patients using LTOT and can have a positive impact on quality of life; increased time spent away from place of residence and can offer significant financial savings to health care providers. Even with conservative estimates in the health economics analysis, the provision of the HF system to around 1000 patients saves about £1.67 million per year in Scotland. Self-fill oxygen delivery systems have been available in the UK for >5 years and whilst one could argue for a larger randomised controlled trial, the authors would propose...
Background Severe asthma can be due difficult to treat asthma due to poor adherence or due to refractory asthma. Identifying poor adherence can be challenging since the methods of adherence have limitations. We developed a method of assessing adherence using Inhaler compliance assessment (INCA) device, which incorporates both identifying technique errors and time of use of the inhaler. We hypothesised that that feedback on time of use and technique of use to patients, improves adherence, compared to standard education without visual feedback.

Methods This was a 3-month prospective multicentre randomised controlled study, in which patients with severe uncontrolled asthma recruited from specialist asthma clinics were randomised to get feedback on and education using the adherence information downloaded from the INCA device or education alone.

Results At the end of the study period, the mean rate of adherence for month three in the active group (n = 111) was 73% versus 63% in the control group (n = 107), p ≤ 0.01 (95% CI: difference 2.8, 17.6). Only the active group demonstrated significant reductions in the rate of technique errors missed doses, excess-doses with improvement in the habit of use. The mean AQLQ and ACT improved significantly in both groups. At the end of the study period, the mean rate of adherence improved in both groups. Of these, 39 had adherence rates <80%, (mean 52%), while 25 had adherence >80%, indicating refractory asthma.

Conclusion Without changing patients’ therapy, most of the patients’ asthma control improved. Two thirds of those who remained uncontrolled required further adherence counselling. 11% of the total cohort remained unstable despite adequate adherence and hence will require step up therapy. Our study shows that adherence assessment and education using INCA feedback should be considered prior to referring patients for additional therapy.

Introduction and objectives In line with ‘Transforming Your Care’ (restructuring of healthcare provision in Northern Ireland) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) strategy, this project brought specialist trust pharmacist-
absence of a bundle, and completion of its 10 individual elements.

Results In 2015, 125 admissions coded as AECOPD were identified; 93 were bundle-appropriate. 80% of these had a COPD discharge bundle in the electronic record; a significant improvement on the 38% bundle completion in bundle-appropriate patients in 2013 ($p < 0.0001$).

Percentage completion was >90% for seven of the ten elements included in the 2015 e-bundle. Direct comparison of the six points included in both the 2013 paper bundle and the 2015 e-bundle, revealed that more patients were assessed for pulmonary rehabilitation in 2013 (100% vs 92%, $p = 0.0417$); all other elements had no significant change in completion rates.

Conclusions Introduction of an e-bundle and e-prescribing alerts to respiratory support team members more than doubled completion of COPD discharge bundles. This clearly shows the benefit conferred by use of an electronic system for prescribing, referrals and bundle proformas. We advocate the increased use of e-bundles as electronic prescribing and information systems are introduced across trusts.

REFERENCE

Methods Patients registered at general practices within Greater London whose GP practices were part of the CPRD network were identified anonymised by CPRD using a validated codelist and algorithm developed by our team (Quint et al., 2014). GPs were able to verify the suitability of the potential participants identified and post information about the study to them. Patients could register their interest in the study directly with the research team to be enrolled in the study.

Results Feasibility screening by CPRD between January and July 2016 indicated 675 potential study participants at 20 practices and from the CPRD-supplied practice screening lists GPs identified and deemed eligible 462 patients. 462 patients were contacted and the response rate was 136/462 of which 43 (32%) were enrolled and 93 (68%) declined. The main reason for declining was related to the demands that the project entailed of looking after the air monitor and diary for 6 months.

Conclusion Patients with COPD from GP practices within Greater London were successfully screened and recruited through CPRD to participate in research over a 6 month period thus providing access to a milder cohort of research naïve patients who better represent the majority of the COPD population and this method minimised input needed by the GP. This is a novel method of using EHRs to recruit participants for research that is currently underutilised.

### Abstract P212 Table 1 Summary of interventions to increase referral to and uptake of Pulmonary Rehabilitation (PR) programmes for people with Chronic Obstructive Pulmonary Disease (COPD)

<table>
<thead>
<tr>
<th>Authors, Date, Setting</th>
<th>Design</th>
<th>Participants</th>
<th>Intervention</th>
<th>Outcomes</th>
<th>Results/Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angus et al., 2012, UK</td>
<td>Observational/feasibility study covering several aspects of COPD management</td>
<td>293 patients</td>
<td>Computer-guided review by practice nurse</td>
<td>% referred to PR</td>
<td>24% of patients referred</td>
</tr>
<tr>
<td>Foster et al., 2016, UK</td>
<td>Participatory action research with strategies for increasing referrals for PR</td>
<td>22 clinicians</td>
<td>Included in-house education sessions, changes to practice protocols, and ‘pop-ups’ and memory aids (mugs and coasters) to prompt clinician/patient discussions about PR.</td>
<td>Patient survey</td>
<td>Survey reports expectation of increased access to benefits of PR</td>
</tr>
<tr>
<td>Graves et al., 2010, UK</td>
<td>Before/After comparison</td>
<td>126 patients</td>
<td>Group opt-in session prior to individualised assessment and entry to PR</td>
<td>% taking up baseline assessment, % attending and completion of PR</td>
<td>No effect on initial uptake</td>
</tr>
<tr>
<td>Harris et al., 2009, Australia</td>
<td>Controlled Before/After study</td>
<td>249 patients</td>
<td>Patient-held manual of recommended COPD management</td>
<td>% enrolment to PR, other indicators of COPD management</td>
<td>Increased enrolment in PR seen only in most socioeconomically disadvantaged participants (outcome change +12%)</td>
</tr>
<tr>
<td>Hull et al., 2014, UK</td>
<td>Quality improvement with repeated audit cycles</td>
<td>3391 patients on COPD registers across network</td>
<td>Establishment of networks of GP practices with supported case management, education and financial incentives for clinical performance</td>
<td>% PR referrals, other indicators of COPD management</td>
<td>PR referrals rose 25% from 45% to 70%</td>
</tr>
<tr>
<td>Roberts et al., 2015, UK</td>
<td>Pragmatic non-randomised controlled study</td>
<td>1235 patients</td>
<td>Patients provided with individualised COPD care quality “score cards”</td>
<td>% PR referrals</td>
<td>6.1% increase in referrals in intervention group</td>
</tr>
<tr>
<td>Zwar et al., 2012, Australia</td>
<td>Cluster randomised controlled trial with blinded outcome assessment</td>
<td>451 patients</td>
<td>Home visit by nurse with specific COPD training working with GP to implement individualised care plan based on guidelines</td>
<td>% attendance at PR, other indicators of COPD management</td>
<td>21.5% increase in PR attendance (31.1% v 9.6%; OR, 5.16; 95% CI: 2.40-11.10)</td>
</tr>
</tbody>
</table>
Exclusion criteria: individual case studies, conference abstracts and opinion pieces. No date or language restrictions.

Search terms included: ‘pulmonary rehabilitation’ AND ‘referral’ OR ‘uptake’ applied to MEDLINE, EMBASE, CINAHL, PsychINFO, ASSIA, BNI, Web of Science and Cochrane Library from inception to June 2016 supplemented by review of reference lists and citation search. Titles, abstracts and full papers were reviewed independently, quality appraised (using Cochrane Collaboration’s tool for RCTs and ROBINS-I, AMSTAR) and entered into summary tables. The protocol was registered (PROSPERO) and reported according to PRISMA guidelines.

Results We screened 3217 references, from which 7 papers including 6345 patients and 22 clinicians met inclusion criteria. Most studies (n = 5) were UK based.

Designs, interventions and scope of studies were diverse with interventions often part of multifaceted evidence-based management of COPD. Examples included computer-based prompts at practice nurse review, patient information, financial incentives. Most studies (n = 5) reported improvements in referral or uptake of PR (range 0%–25% increase), however most had methodological limitations with risk of bias. Due to heterogeneity, studies were not considered combinable and meta-analysis was inappropriate.

Conclusions There is limited evidence for the efficacy of interventions to increase referral and uptake of PR. Existing studies are diverse and further testing using robust methods in various populations and settings is required to optimise access to PR.

Counter-intuitively, carers reported greater convenience rather than increased burden.

‘Potential Barriers’ were grouped into two sub-constructs: ‘Personal preferences’; and ‘Resistance to change’. Some patients highlighted fear of being alone at night and dislike of strangers visiting their home; nurses cited higher workload and greater responsibility (with experience, viewed positively); whilst operational concerns included keeping medical records in a patient’s home and inability to capture activity within current payment systems.

Conclusions HAH selected by DECAF allows the inclusion of more patients than existing models, and is preferred to inpatient care by most patients and their families. During the trial few barriers to implementation were identified, and were effectively overcome. Hospitals planning to implement HAH selected by DECAF should pre-emptively address these issues.

References

Background Despite endorsement in guidelines, many hospitals do not offer hospital at home (HAH) for COPD exacerbation (AECOPD), partly reflecting the previous lack of a robust prognostic score to guide selection. The DECAF score addresses this concern, and should be routinely scored on admission.1 In a RCT we have shown that HAH selected by DECAF score 0–1 is safe and effective. Up to 50% of admitted patients are suitable. Our population included patients with higher medical dependency than earlier trials and HAH was supported by 24/7 specialist on-call. In an embedded qualitative study, we identified positive drivers for, and potential barriers to, use of HAH to inform service implementation.

Methods Patients, carers, clinicians and managers were purposely selected to ensure diversity. Semi-structured interviews were conducted and Thematic-Construct Analysis employed.2

Results 44 patients (HAH/inpatient care/declined randomisation), 15 carers, 14 consultants, 11 specialist nurses and 4 managers were interviewed. ‘Positive drivers’ were divided into two sub-constructs: ‘Feeling more at ease and comfortable in own home environment’; and ‘Feeling safe, reassured and appreciated through continuity of hospital care’. Positive influences on independence, perceived rate of recovery, sleep quality, mood and contact with friends and family were noted. At 14 days post-presentation, 90% of patients stated they would prefer HAH over inpatient care for subsequent exacerbations of similar severity.

Conclusions There is a significant unmet burden of undiagnosed chronic lung disease, and respiratory symptoms, in our local
CDAT, and a need to improve uptake of smoking cessation services. An economic model of expected gain in life expectancy and Quality Adjusted Life Expectancy (QALYs) from quitting is in development.

**THE INCREMENTAL DISEASE BURDEN ASSOCIATED WITH THE PERSISTENCE OF MORNING, DAYTIME AND NIGHT-TIME SYMPTOMS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS**

1A Munoz, 2J Bailey, 1R Wood, 1A Ribera, 1J Nuñez. 1AstraZeneca, Madrid, Spain; 2Adelphi Real World, Macclesfield, UK

10.1136/thoraxjnl-2016-209333.358

**Introduction**
The current Global Initiative for Chronic Obstructive Lung Disease Strategy makes limited references to the variability of chronic obstructive pulmonary disease (COPD) symptoms according to the time of day patients experience symptoms, on awakening/morning, in the daytime and at night-time; therefore it’s unclear whether specific treatment approaches are needed.

**Aims** To establish the association between time of day of symptoms and the burden experienced by patients; as measured by validated patient-reported outcomes (PROs), healthcare resource utilisation (HRU) and physician-perceived impact of COPD on patients’ lives.

**Methods** Data were taken from four waves (2012–2016) of the Respiratory Disease Specific Programme (DSP); cross-sectional surveys of COPD patients in France, Germany, Italy, Spain, and the UK. Patients were defined as suffering from symptoms on awakening/morning (M), in the daytime (D), at night-time (N) or combinations of these according to physician-reported time of day of symptoms within the last 4 weeks. Kruskal-Wallis tests assessed statistical significance of outcomes across patient groups. Outcomes included HRU in the last 12 months, EQ-5D-3L with visual analogue scale, Jenkins Sleep Evaluation Questionnaire, COPD Assessment Test, activity impairment (measured by the work productivity and activity impairment questionnaire), and physician-reported impact COPD has on the patient’s sleep.

**Results** In total, 8,185 patients receiving treatment were analysed; 25% suffered no symptoms, 16% D only, 17% M/D only, 6% D/N only, 4% M, N or M/N only and 32% M/D/N. Across the four DSP waves, patients suffering any M, D or N symptoms ranged from 46%–64%, 67%–77% and 38%–47%, respectively. All outcomes differed significantly across patient groups (Table 1). In general, M/D/N patients utilised the most healthcare resources, suffered more exacerbations requiring emergency room visits or
hospital admissions, had higher activity impairment and reported worse quality of life and sleep, whilst asymptomatic patients utilised the least resources and reported the best quality of life and sleep. The remaining groups suffered similar levels of burden.

**Conclusions** In this analysis, patients experiencing morning, daytime and night-time symptoms have the worst PROs and more disease burden. Clearer recognition of symptom burden and an individualised treatment approach may be warranted for these patients.

### Abstract P215 Table 1

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>None (n = 2060)</th>
<th>D only (n = 1274)</th>
<th>M/D only (n = 1378)</th>
<th>D/N only (n = 477)</th>
<th>M, N or M/N only (n = 2651)</th>
<th>M/D/N (n = 345)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCP</td>
<td>2.8 (1.9)</td>
<td>3.1 (1.0)</td>
<td>3.0 (1.0)</td>
<td>3.8 (1.2)</td>
<td>3.1 (1.1)</td>
<td>4.4 (4.5)</td>
</tr>
<tr>
<td>Specialist consultations</td>
<td>1.7 (1.8)</td>
<td>2.3 (2.2)</td>
<td>2.4 (2.2)</td>
<td>2.1 (2.0)</td>
<td>1.7 (1.9)</td>
<td>2.8 (2.8)</td>
</tr>
<tr>
<td>ER visits</td>
<td>0.0 (0.3)</td>
<td>0.1 (0.4)</td>
<td>0.2 (0.4)</td>
<td>0.2 (0.2)</td>
<td>0.1 (0.4)</td>
<td>0.3 (0.6)</td>
</tr>
<tr>
<td>Hospital admissions</td>
<td>0.0 (0.2)</td>
<td>0.1 (0.5)</td>
<td>0.2 (0.6)</td>
<td>0.2 (0.5)</td>
<td>0.1 (0.5)</td>
<td>0.5 (1.0)</td>
</tr>
<tr>
<td>% activity impairment</td>
<td>24.6 (20.0)</td>
<td>36.8 (20.1)</td>
<td>41.0 (22.0)</td>
<td>45.0</td>
<td>33.7</td>
<td>56.4 (23.2)</td>
</tr>
<tr>
<td>EQ-SD-3L</td>
<td>0.89 (0.18)</td>
<td>0.85 (0.19)</td>
<td>0.81 (0.22)</td>
<td>0.80</td>
<td>0.86</td>
<td>0.69 (0.28)</td>
</tr>
<tr>
<td>EQ-VAS</td>
<td>72.7 (15.0)</td>
<td>66.7 (14.8)</td>
<td>63.7 (15.0)</td>
<td>62.9</td>
<td>68.6</td>
<td>56.3 (17.6)</td>
</tr>
<tr>
<td>CAT</td>
<td>14.2 (7.4)</td>
<td>18.4 (7.1)</td>
<td>20.2 (6.9)</td>
<td>21.5 (6.1)</td>
<td>18.9 (7.1)</td>
<td>25.7 (6.6)</td>
</tr>
<tr>
<td>JSEQ</td>
<td>2.4 (2.9)</td>
<td>3.6 (3.3)</td>
<td>4.3 (3.9)</td>
<td>5.6 (3.4)</td>
<td>4.4 (3.5)</td>
<td>8.3 (4.8)</td>
</tr>
</tbody>
</table>

Impact on sleep, n (%)

- None | 485 (21.2) | 312 (29.0) | 189 (26.2) | 11 (4.5) | 42 (20.1) | 60 (4.2) |
- Low | 512 (44.5) | 295 (45.7) | 347 (48.1) | 90 (37.0) | 86 (41.1) | 364 (25.2) |
- Medium | 121 (10.5) | 103 (16.0) | 142 (19.7) | 105 | 50 (23.9) | 557 (38.6) |
- High | 30 (2.6) | 33 (5.1) | 39 (5.4) | 36 (14.8) | 22 (10.5) | 367 (25.5) |
- Constant | 3 (0.3) | 2 (0.3) | 4 (0.6) | 1 (0.4) | 9 (4.3) | 94 (6.5) |

PCP = Primary care physician; ER = Emergency Room; M = Morning; D = Daytime; N = Night time; CAT = COPD Assessment Test; JSEQ = Jenkins Sleep Evaluation Questionnaire

**P217** **IMPROVING CARE AND SUPPORT IN ADVANCED COPD – SIX RECOMMENDATIONS FROM THE POPULATION-BASED LIVING WITH BREATHLESSNESS STUDY**

1. **MC Farquhar, 1G Ewing, 2P White, 3M Mahadeva, 1AC Gardener, 1C Moore, 5S Howson, 5S Booth, 5C Saunders, 7Ling, 8University of Cambridge, Cambridge, UK; 2King’s College London, London, UK; 3RAND Europe, Cambridge, UK; 4Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; 5Cambridge and Peterborough Foundation Trust, Cambridge, UK**

**Introduction** Chronic obstructive pulmonary disease (COPD) is a chronic life-limiting condition with high symptom-burden and carer-burden. National guidance on end of life care calls for quality care for patients with any condition, yet we rely on frameworks developed for cancer with its largely predictable trajectory.

**Aim** To develop evidence-based recommendations to inform a new framework to improve care and support of patients living with advanced COPD and their informal carers.

**Methods** The Living with Breathlessness Study was a multiple-component, population-based, mixed-method longitudinal, multi-perspective research project designed to identify new evidence on health and social care needs and preferences of patients with advanced COPD and their carers. It followed more than 500 patients and carers for up to 18-months through interview and survey methods. Qualitative data on barriers and facilitators to meeting needs were collected from clinicians. Programme-wide evidence was synthesised to identify recommendations. Stakeholder views were then collected through a workshop and online survey.

**Results** Six inter-related recommendations emerged, linked by the concept of proactive person-centred care: (1) Stop the
Abstract P216 Table 1 Multivariate analysis of predictive factors significantly associated in univariate analysis with patient or carer PM

<table>
<thead>
<tr>
<th>Patient PM cases (n = 39)</th>
<th>Patient PM non-cases (n = 70)</th>
<th>Odds ratio (95% CI)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carer PM cases, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>17 (15.6)</td>
<td>13 (11.9)</td>
<td>3.667 (0.916–14.600)</td>
</tr>
<tr>
<td>N</td>
<td>22 (20.2)</td>
<td>57 (52.3)</td>
<td>0.728 (0.194–2.740)</td>
</tr>
<tr>
<td>Patient gender, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>24 (22.0)</td>
<td>42 (38.5)</td>
<td>1.313 (1.006–1.713)</td>
</tr>
<tr>
<td>F</td>
<td>15 (13.8)</td>
<td>28 (25.7)</td>
<td>0.392 (0.173–0.889)</td>
</tr>
<tr>
<td>No. of exacerbations at home, median (IQR)</td>
<td>3.5 (2–6)</td>
<td>2 (0–3)</td>
<td>1.227 (0.628–2.398)</td>
</tr>
<tr>
<td>CRQ dyspnoea score, median (IQR)</td>
<td>1.8 (1.6–2.6)</td>
<td>2.8 (1.8–4)</td>
<td>0.392 (0.173–0.889)</td>
</tr>
<tr>
<td>CRQ fatigue score, median (IQR)</td>
<td>2.5 (2–3)</td>
<td>3.75 (3–4.5)</td>
<td>0.392 (0.173–0.889)</td>
</tr>
<tr>
<td>CRQ mastery score, median (IQR)</td>
<td>3.25 (2.25–3.75)</td>
<td>4.75 (4.25–5.5)</td>
<td>0.264 (0.129–0.539)</td>
</tr>
<tr>
<td>No. of patient physical co-morbidities, median (IQR)</td>
<td>4 (3–6)</td>
<td>4 (2–5)</td>
<td>0.832 (0.577–1.201)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient PM cases (n = 30)</th>
<th>Carer PM cases (n = 79)</th>
<th>Odds ratio (95% CI)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carer PM cases, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>17 (15.6)</td>
<td>22 (20.2)</td>
<td>3.869 (1.070–13.990)</td>
</tr>
<tr>
<td>N</td>
<td>13 (11.9)</td>
<td>57 (52.3)</td>
<td>0.728 (0.194–2.740)</td>
</tr>
<tr>
<td>Patient gender, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>2 (1.8)</td>
<td>29 (26.6)</td>
<td>6.180 (1.167–32.712)</td>
</tr>
<tr>
<td>F</td>
<td>28 (25.7)</td>
<td>50 (45.9)</td>
<td>0.859 (0.420–1.755)</td>
</tr>
<tr>
<td>Lives with patient, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Y</td>
<td>24 (22.4)</td>
<td>71 (66.4)</td>
<td>1.883 (0.438–8.100)</td>
</tr>
<tr>
<td>N</td>
<td>6 (5.6)</td>
<td>6 (5.6)</td>
<td>1.247 (0.599–2.609)</td>
</tr>
<tr>
<td>Duration of caring in years, median (IQR)</td>
<td>3.5 (2–12)</td>
<td>7 (4–13)</td>
<td>0.964 (0.903–1.010)</td>
</tr>
<tr>
<td>Hours of caring, median (IQR)</td>
<td>3 (2–3.5)</td>
<td>3 (2–4)</td>
<td>0.859 (0.420–1.755)</td>
</tr>
<tr>
<td>No. of exacerbations at home, median (IQR)</td>
<td>3 (1.5–5.5)</td>
<td>2 (0–3.75)</td>
<td>1.048 (0.880–1.247)</td>
</tr>
<tr>
<td>No. of carer physical co-morbidities, median (IQR)</td>
<td>1 (1–2)</td>
<td>1 (0–2)</td>
<td>1.184 (0.769–1.825)</td>
</tr>
</tbody>
</table>

(a) 1 = <1 h/week, 2 = 1–19 h/week, 3 = 20–49 h/week, 4 = >50 h/week.

Continual focus on the challenge of prognosis and unpredictability of trajectories as barriers to meeting needs, (2) Change targets to incentivise person-centred care within existing services, (3) Enable identification and response to patient support needs (through evidence-based tools and approaches), (4) Identify and support patients’ informal carers (through evidence-based tools and approaches), (5) Identify and respond to psychological morbidity in patients and informal carers identify and respond to psychological morbidity, (6) Change societal attitudes and approaches), (5) Identify and respond to psychological morbidity in patients and informal carers identify and respond to psychological morbidity. Limitations to activities and rescue medication use in the early morning were reported as being the most troublesome and can negatively impact quality of life. This abstract summarises the development and psychometric testing of the Early Morning Symptoms of COPD Instrument (EMSCI) designed to collect data to evaluate COPD patients’ experiences early in the morning.

Methods Following a literature review and clinical expert interviews, four focus groups were conducted to identify initial concepts and develop draft items for the EMSCI. One-on-one cognitive debriefing interviews were conducted with 10 COPD patients to confirm item readability, and comprehensiveness. Data from a clinical trial [AUGMENT] in COPD patients (N = 1663) was used for item analyses to inform item-reduction and scoring; and to evaluate psychometric properties. Test-retest reliability was assessed using intra-class coefficient (ICC). Correlations with baseline assessments including the SGRQ, E-RS, and FEV1 were used to evaluate concurrent validity.

Results Focus group participants (n = 27, mean age = 68.1 y) reported mucus/ phlegm (80%), shortness of breath (52%), coughing (48%), tightness in chest (24%), wheezing (8%) and chest congestion (8%) as the most common early morning symptoms. Limitations to activities and rescue medication use in the early morning were reported by 56% and 24% respectively. Cognitive interviews of early versions of the EMSCI suggested the items were comprehensive, relevant and interpreted as intended. Analyses of EMSCI data collected in the Phase 3 trial confirmed a one-factor structure for the symptom severity items. Reliability was confirmed for the 6-item symptom severity (ICC = 0.84), overall symptom severity (ICC = 0.84), activity limitation ( ICC = 0.85), and rescue medication (ICC = 0.62) scores. Concurrent validity (Table 1) was supported by positive correlations with both the SGRQ and the E-RS scores.
Conclusions The EMSCI is a reliable and valid instrument that was developed based on patients’ experiences to evaluate early morning symptoms and impacts of COPD. It is available to be used for clinical decision making and as a clinical study endpoint for the evaluation of new treatments.

Conclusions This study highlight the importance of context when using the MRC. Grade 1 “strenuous exercise” is unlikely to yield a reliable response from patients diagnosed with COPD. Secondly, if data collection is taking place outside of the home then it is pointless to ask respondents if they are too breathless to leave the house; on the other hand, if studying patients who may require palliative care services, that might well be relevant. For contexts where it would be relevant, we suggest separating Grade 5 components: “leave the house” and “dressing/undressing”.

<table>
<thead>
<tr>
<th>Abstract P218 Table 1</th>
<th>Correlation1 of EMSCI Domain Scores with SGRQ, E-RS Total and FEV1,2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Six-item Symptom Summary Score3</td>
</tr>
<tr>
<td>----------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>SGRQ</td>
<td>0.59***</td>
</tr>
<tr>
<td>total score</td>
<td></td>
</tr>
<tr>
<td>SGRQ</td>
<td>0.67***</td>
</tr>
<tr>
<td>symptoms score</td>
<td></td>
</tr>
<tr>
<td>SGRQ</td>
<td>0.54***</td>
</tr>
<tr>
<td>impacts score</td>
<td></td>
</tr>
<tr>
<td>E-RS total score</td>
<td>0.83***</td>
</tr>
<tr>
<td>FEV1 (trough)2</td>
<td>---0.10</td>
</tr>
</tbody>
</table>

1 Spearman rank order correlation coefficients: ***P<0.0001, **P<0.001, *P<0.05
2 Morning pre-dose value
3 Average score of six symptoms (Cough, Wheezing, Shortness of breath, Tightness in your chest, Chest congestion, Difficulty bringing up phlegm)
4 Single-item measuring overall early morning COPD symptom severity
E-RS = Evaluating Respiratory Symptoms in COPD; FEV1 = forced expiratory volume in 1 second; SGRQ = St. George’s Respiratory Questionnaire

Introduction Inhaler adherence in Chronic Obstructive Pulmonary Disease (COPD) is a crucial component of disease management with studies reporting relationships with both morbidity and mortality. The aim of this study was to identify determinants of inhaler adherence.

Methods Over a 3-year period data was collected on 265 patients with COPD whose inhaler adherence was monitored for one month. Data on personal factors (i.e., cognition, anxiety and depression), disease severity and socioeconomic factors was collected. Inhaler adherence was calculated as a combination of timing of use, interval between doses and technique of use (Actual Adherence).

Results At one month, patients who reported worse breathlessness (5 on the MRC Dyspnoea Scale) had worse Actual Adherence (p = 0.03). Interestingly, patients who had an exacerbation of their COPD within the month after recruitment had significantly lower Actual Adherence than those that didn’t (p = 0.01). In addition, patients with poorer cognition (p = 0.02), poorer cough PEFR (p < 0.01) and more severe COPD (GOLD Stage IV, p = 0.05) had worse Actual Adherence.

Conclusion In the large observational study of severe COPD patients, poor inhaler adherence was associated with worse symptoms, poorer cognition, more severe COPD and more exacerbations. This has significant implications for the long-term

<table>
<thead>
<tr>
<th>Abstract P219 Table 1</th>
<th>Logit (severity) location for each MRC component</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRC Grade</td>
<td>Item</td>
</tr>
<tr>
<td>------------------</td>
<td>------</td>
</tr>
<tr>
<td>2</td>
<td>slight hill</td>
</tr>
<tr>
<td>2</td>
<td>Hurrying on flat</td>
</tr>
<tr>
<td>1</td>
<td>Strenuous exercise</td>
</tr>
<tr>
<td>3</td>
<td>same age</td>
</tr>
<tr>
<td>3</td>
<td>own pace</td>
</tr>
<tr>
<td>4</td>
<td>100 metres</td>
</tr>
<tr>
<td>5</td>
<td>few minutes</td>
</tr>
<tr>
<td>5</td>
<td>dressing</td>
</tr>
<tr>
<td>5</td>
<td>undressing</td>
</tr>
<tr>
<td>5</td>
<td>leave house</td>
</tr>
</tbody>
</table>

1 Sulaiman, B; Cuzhen, IG; Greene, J; Sebeult, D; Seew, F; Rawat, E; MacHale, 1MC Mokoka, 1CN Moran, 1A Sartin-Bhreathnach, 1S Tappuni, 1P MacHale, 1B Deering, 1M Jackson, 1H McCarthy, 1L Mellon, 1F Doyle, 1F Boland, 1RB Reilly, 1RCSI Beaumont Hospital, Dublin, Ireland; 2Trinity College Dublin, Dublin, Ireland

10.1136/thoraxjnl-2016-209333.363

Introduction Inhaler adherence in COPD is a crucial component of disease management with studies reporting relationships with both morbidity and mortality. The aim of this study was to identify determinants of inhaler adherence.

Methods Over a 3-year period data was collected on 265 patients with COPD whose inhaler adherence was monitored for one month. Data on personal factors (i.e., cognition, anxiety and depression), disease severity and socioeconomic factors was collected. Inhaler adherence was calculated as a combination of timing of use, interval between doses and technique of use (Actual Adherence).

Results At one month, patients who reported worse breathlessness (5 on the MRC Dyspnoea Scale) had worse Actual Adherence (p = 0.03). Interestingly, patients who had an exacerbation of their COPD within the month after recruitment had significantly lower Actual Adherence than those that didn’t (p = 0.01). In addition, patients with poorer cognition (p = 0.02), poorer cough PEFR (p < 0.01) and more severe COPD (GOLD Stage IV, p = 0.05) had worse Actual Adherence.

Conclusion In the large observational study of severe COPD patients, poor inhaler adherence was associated with worse symptoms, poorer cognition, more severe COPD and more exacerbations. This has significant implications for the long-term
Poster sessions

P221 COMPARING THE PERCEPTION OF FEEDBACK MECHANISM OF THE BREEZHALER® DEVICE WITH THE ELLIPTA® DEVICE IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD): THE ADVANTAGE STUDY

P Altman, AA Bergna, G Garcia, K Kostikas, T Guerin, AV Pino, J Whiteford. Novartis Pharmaceuticals Corporation, East Hanover, USA; Respiratory Research, CEMER Centro Médico de Enfermedades Respiratorias, Vicente López, Argentina; Pneumology, Cenasma Institute, La Plata, Argentina; Novartis Pharma AG, Basel, Switzerland; Novartis Ireland Limited, Dublin, Ireland; Novartis Argentina S.A., Buenos Aires, Argentina

Background and aims Patient preference and satisfaction with inhalers are important factors that may impact adherence to treatment and hence its outcome.1 The ADVANTAGE study compared the Breezhaler® and the Ellipta® inhalers for patient perception of feedback mechanism and the comfort of the mouth piece, in COPD patients, naïve to dry powder inhaler use.

Methods This open-label cross-over study randomised (1:1) patients (>40 years) with COPD [all severities as per GOLD 2014] and smoking history of > 10 pack-years to use both the Breezhaler® and Ellipta® devices in differing sequences with a separation of ≥ 5 minutes between devices. After inhalation, patients completed a questionnaire2 containing 4 questions that captured patients’ perception of the feedback mechanism (mean of first three questions) and comfort of the mouth piece (fourth question). Questions were answered on a scale of 1 (lower preference) to 5 (higher preference), a Wilcoxon signed rank test was performed to test the difference between devices at a 2-sided 2.5% level of significance for both endpoints. Safety assessments included adverse events, physical examination, vital signs, height and weight.

Results One hundred patients (64 men and 36 women) with a mean (SD) age of 65.2 (9.07) years were randomised to inhale sequentially through both devices. Thirty two patients were current smokers and had a mean (SD) duration of COPD for 6.1 (4.82) years. Overall, patients perceived that the Breezhaler® inhaler offered greater confidence of dose delivery and better comfort of the mouth piece (mean (SD) score 4.3 (0.70) and 4.3 (0.82); respectively) vs. the Ellipta® inhaler [mean (SD) score 3.6 (1.05) and 3.9 (0.84); respectively] (Figure). No safety signals were identified during the study.

Conclusions In this study, COPD patients had greater confidence of receiving full dose with the Breezhaler® device and better comfort with the mouth piece compared with the Ellipta® device.

REFERENCES

P222 INPUT OF A PATIENT ADVISORY GROUP INTO EVALUATING THE BENEFIT: RISK PROFILE OF EXISTING AND POTENTIAL COPD THERAPIES

DR Burrage, M Tumilty, S Ruickbie, EH Baker. St George’s, University of London, London, UK

Introduction People with chronic obstructive pulmonary disease (COPD) have considerable disability and reduced life expectancy, despite current treatments. New medicines are required, but few successfully complete clinical trials and become established in practice. During drug development, understanding the nature and magnitude of benefits relevant to patients and risks they will accept to achieve these is important, particularly where the drug has a narrow therapeutic index. Our aim was to explore patient preferences for potential COPD treatments.

Abstract P221 Figure 1 Mean Scores of the analysis of patients preference of the Breezhaler and the Ellipta devices

* p<.0001
perceptions of the benefit:risk profile of existing and potential COPD therapies.  

Methods Our local respiratory patient advisory group meets every 3 months to provide input into research. A focus group completed a conjoint analysis exercise. Four current (aclidinium, azithromycin, carbocisteine) or potential (drug X) COPD medicines were presented iteratively in pairs (Figure 1), comparing the magnitude of likely benefits (reduced exacerbations, improved overall health) and harms (risk of infection, antibiotic resistance, kidney failure, diabetes). For each pairing, participants indicated which medicine they would choose. Participants also ranked potential benefits (reduced exacerbations, increased survival, increased walking distance) and risks (death, kidney failure, diabetes) of medicines in order of importance and discussed how these should be prioritised.

Results 9 male and 9 female COPD patients (age range 66–86 years, median 77 years, GOLD 1–4) and 2 carers took part. When confronted with two treatment options, participants consistently chose the treatment with a better safety profile, even if this meant less clinical benefit. Being able to walk further was the most important benefit (70% participants), over preventing exacerbations (5%) or increasing life expectancy (5%). Kidney failure was selected as the most concerning potential risk (50% participants) over chance of death (10%). A strong theme emerged that quality of life was more important than life expectancy.

Conclusions Potential users of new treatments can weigh potential benefits and risks and judge their relative importance. This has potential to improve design of clinical trials, patient participation and development of medicines with real relevance to users.

REFERENCE  

Introduction Management guidelines for asthma and COPD guide which inhaled therapies should be prescribed, but not what type of device. There appears to be little evidence in the literature to support if patient involvement influences how concordant patients are with inhaled therapies.

Aims and objectives The aim was for patients to rate inhaler devices and dosing regimens so that discreet choices could be made when adding new drugs and devices to the local joint primary and secondary care prescribing formulary.

Methods 40 patients with asthma (n = 20) or COPD were purposively selected to participate in the study. 30 patients were seen on a one to one basis and ten patients with COPD seen in a patient education group. They were each given devices not normally prescribed in the locality (asthma = 5, COPD = 6). They were given 2 sets of instructions on how to load and use each device, a patient information leaflet (PIL) produced by the manufacturer, and one designed by the local nursing team. Each patient was asked to complete a 5-point questionnaire. Questions included:

- Which device did they prefer the most
- Which device did they least prefer
- Would they like once daily or twice daily maintenance medication
- Would they like all their drugs in one type of device or different devices
- Did they prefer the manufacturers PIL or the locally devised one

Abstract P222 Figure 1  Example of conjoint analysis option comparing person A (taking a prophylactic antibiotic) to person B (taking an inhaled bronchodilator)
Results Preloaded devices were much preferred by both patient groups, although only 2 of the 6 devices needed loading. Once daily dosing regimens were preferred over twice daily dosing (N = 28). Patients comprehensively preferred the local instructions for use compared to the PIL (N = 38). Patients preferred to have the same device for all their inhaled therapies (N = 32).

Conclusions Most new drug delivery systems prescribed to patients are selected by clinicians. This small-scale study highlighted the importance of patient involvement when clinicians prescribe devices and dosing regimens. Manufacturers need to look at simplifying PILs, which may increase patients’ ability to use their device correctly.

P224 TOWARDS PERSON-CENTRED CARE: DEVELOPMENT OF A PATIENT SUPPORT NEEDS TOOL FOR PATIENTS WITH ADVANCED CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN PRIMARY CARE

1AC Gardener, 2GE Wing, 3M Farquhar. 1Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK; 2Centre for Family Research, University of Cambridge, Cambridge, UK

10.1136/thoraxjnl-2016-209333.367

Introduction Patients with advanced COPD have difficulty articulating their support needs to clinicians, undermining person-centred care and support. A new approach, the Support Needs Approach for Patients (SNAP), informed by, and modelled on, the evidence-based Carer Support Needs Assessment Tool (CSNAT), may enable patients to identify and express their support needs and start person-centred conversations with clinicians. SNAP is underpinned by an evidence-based tool (a brief set of questions) to help patients consider and express their support needs. This study aimed to develop the SNAP tool, suitable for use in clinical practice.

Methods Two-stage qualitative study. Stage 1: domains of support need in advanced COPD were identified through a rapid review of the literature, analysis of data from the Living with Breathlessness Study (n = 20 purposively sampled patients with advanced COPD) and patient focus groups. Stage 2: the draft SNAP tool was developed based on the identified domains of support need, then reviewed and refined in stakeholder workshops with patients, carers and clinicians (from primary, secondary and community care, including specialist respiratory care) to ensure acceptability and suitability for clinical practice.

Results A comprehensive range of evidence-based domains of support need were identified in Stage 1 which were then formulated into questions for inclusion on the draft SNAP tool in Stage 2. The draft tool asks patients to consider whether they need more support in relation to 16 broad areas (domains) of support need such as practical help in the home, knowing what to expect in the future, understanding their condition, getting out and about, and support for their carer. Patients, carers and clinical stakeholders from community respiratory care endorsed the content and wording of the draft SNAP tool and the proposed Support Needs Approach for Patients which it underpins (forthcoming workshops with primary and secondary care clinicians will identify their views which will also be reported).

Discussion The SNAP tool has the potential to help patients with advanced COPD identify and express their support needs to
clinicians in order to enable delivery of person-centred care. Future work will test the tool’s validity and feasibility of use in everyday clinical practice.

**Breathlessness**

**P225 TRIGGERS OF VOCAL CORD DYSFUNCTION AND ASTHMA**

1SHK Chua, 1J Haines, 2C Slinger, 3SJ Fowler. 1Manchester Medical School, Manchester, UK; 2Lancashire Teaching Hospitals, Preston, UK

Background Vocal cord dysfunction (VCD) is often initially misdiagnosed as, or may coexist with, asthma. Identifying the differences between the types of triggers for each condition may help differentiate between these two conditions, and could give mechanistic insights.

Aim The aim of this study is to identify and compare patient-reported triggers in VCD and asthma.

Methods This was a two-part study. Part A – A retrospective case note review of the triggers of VCD from endoscopically-confirmed VCD patients was conducted. This information was used to generate a Breathlessness Triggers Survey with triggers recorded under the categories: scents, environmental factors, temperature, emotions, mechanical factors and daily activities. Part B – A prospective study which involved patients with VCD and/or asthma completing the Breathlessness Triggers Survey, rating the likelihood of each item triggering their symptoms using a five-point Likert scale (strongly disagree to strongly agree). Chi-square test was performed to compare responses by cohort.

Results Part A – Data from 202 patients with VCD (73.3% female, mean age 53.1yrs) were included in the retrospective study. The findings were used to create a 23-item Breathlessness Triggers Survey for Part B of the study. Part B – 38 patients with VCD-only (63.2% females, mean age 56.8 yrs), 39 patients with asthma-only (56.4% female, mean age 53.3 yrs) and 12 patients with both VCD and asthma (83.3% female, mean age, 56.8yrs) were recruited. The mean number of patient-reported triggers in the VCD and asthma cohort was 11 and 13 respectively. Mechanical factors such as talking ($p \leq 0.001$), shouting ($p = 0.004$) and swallowing ($p \leq 0.001$) were more common in the VCD cohort, whilst environmental factors such as pollen/flowers ($p = 0.002$) and damp air ($p = 0.039$) were more common in asthma. There were no differences between groups in frequency of reporting scents as triggers (except for vinegar, more common in VCD), temperature, emotions or daily activities.

Conclusion There were notable differences and overlaps between patient-reported triggers of VCD and asthma, which could give clues to diagnosis during clinical assessment. Future work should focus on the mechanisms underlying these findings.

**P226 VOCAL CORD DYSFUNCTION; CLINICAL OUTCOMES OF SPEECH & LANGUAGE THERAPY INTERVENTION**

NPargeter, AH Mansur. Birmingham Heartlands Hospital, Birmingham, United Kingdom

Introduction Vocal cord dysfunction (VCD) is a little-known condition that frequently masquerades as and coexists with asthma resulting in misdiagnosis and mismanagement. Speech & Language Therapy (SLT) is the mainstay of management though treatment efficacy is yet to be proven. We report on VCD patients clinical outcomes prior to and post therapy.

Method All patients referred to a tertiary VCD centre with nasendoscopy-confirmed VCD diagnosis and completed SLT input were considered for this study. Clinical outcomes were recorded on the local VCD registry. Symptoms scores were...
collected pre and post SLT using an in-house designed symptoms-based VCD questionnaire (scale 0–25 with high score indicating poor control). Pre and post therapy frequency of VCD attacks and the annual pre and post therapy hospital admission rates were also collected.

Results Demographics - Two hundred and forty nine patients with nasendoscopy confirmed VCD diagnosis completed SLT. This cohort was comprised of 200/249 (80%) females with a mean age of 45 years (range 14–77), mean BMI 30.9 kg/m², 203 (82%) had associated asthma diagnosis, of which 125 (50%) were on maintenance oral corticosteroids.

Symptom management – Frequency of attacks dropped following SLT with 179 (72%) reporting daily attacks pre-SLT to 25 (10%) noting daily symptoms post-SLT; pre vs. post therapy; mean (± SD) = 16.37 (3.96), 7.75 (4.82) respectively, p < 0.0001. See Figure a.

Hospital admission prevention – significant reduction in hospital admissions was noted in the year post SLT intervention: pre vs. post therapy mean (± SD, range) = 2.44 (4.84, 0–31); 0.31 (1.01, 0–7); p < 0.00001.

Conclusion SLT improves VCD symptoms scores, reduces VCD attacks frequency and hospital admissions. Further work is needed to improve overall VCD recognition and management through development of a national VCD database and regular networking of clinicians working in this area.

REFERENCE

Abstract P227 Table 1

<table>
<thead>
<tr>
<th>VCD Presentation</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden onset attacks</td>
<td>219 (88)</td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>237 (95)</td>
</tr>
<tr>
<td>Difficulty breathing IN</td>
<td>229 (92)</td>
</tr>
<tr>
<td>Tight throat</td>
<td>224 (90)</td>
</tr>
<tr>
<td>Inspiratory wheeze</td>
<td>211 (85)</td>
</tr>
<tr>
<td>Symptoms improve with inhaler</td>
<td>51 (20)</td>
</tr>
<tr>
<td>VCD Triggers</td>
<td>Number (%)</td>
</tr>
<tr>
<td>Inhaler initiants</td>
<td>182 (73)</td>
</tr>
<tr>
<td>Exertion</td>
<td>178 (73)</td>
</tr>
<tr>
<td>Stress</td>
<td>168 (67)</td>
</tr>
<tr>
<td>Coughing</td>
<td>162 (65)</td>
</tr>
<tr>
<td>Reflux</td>
<td>130 (52)</td>
</tr>
<tr>
<td>Treatment</td>
<td>Number (%)</td>
</tr>
<tr>
<td>Inhaled Corticosteroids</td>
<td>224 (90)</td>
</tr>
<tr>
<td>Oral Corticosteroids</td>
<td>125 (50)</td>
</tr>
<tr>
<td>Speech &amp; Language Therapy</td>
<td>249 (100)</td>
</tr>
<tr>
<td>Psychotherapy</td>
<td>76 (31)</td>
</tr>
<tr>
<td>Heliox</td>
<td>11 (4)</td>
</tr>
<tr>
<td>Tracheostomy</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

REFERENCE

P228 IS THE BROMPTON BPAT A USEFUL TOOL TO ASSESS BREATHING PATTERN DISORDER IN ASTHMA?

Introduction Breathing pattern disorder (BPD) is a prevalent cause for persistent dyspnoea in patients with asthma. The diagnosis of BPD is difficult and currently relies exclusively on subjective assessment with no reliable diagnostic tools currently validated to support a clinical assessment.

Aim To determine if the Brompton Breathing Pattern Assessment Tool (BPAT) has value in the assessment of BPD.

Method We audited an objective scoring tool, the BPAT, in patients with asthma and/or unexplained dyspnoea completing a systematic multi-disciplinary assessment. The BPAT (score 0 to 14) evaluates aspects of breathing (including; rate, flow, pattern, rhythm and air hunger). This was compared against BPD diagnosis made by current MDT practise. BPAT measures were also compared with indices of dyspnoea/disease control; e.g. walking test, Dyspnoea 12 (D12), Nijmegen and Asthma Quality of Life Questionnaire (AQLQ).

Results 75 patients; n = 54 females, were divided into 3 groups by diagnosis (asthma, asthma+BPD and BPD alone). BPAT was...
Introduction and objectives Despite multiple trials, there remains a lack of consensus on the optimum management of dysfunctional breathing patients. This service evaluation considers the effectiveness of a novel, multi-factorial intervention, consisting of cardiopulmonary exercise testing (CPET), explanation of physiological findings and breathing retraining, for those suffering from dysfunctional breathing.

Methods Patients who had a history of likely dysfunctional breathing combined with CPET evidence of dysfunctional breathing, hyperventilation or lack of underlying pathology were invited to attend a joint consultation with a respiratory physician and a physiotherapist. To date, fourteen patients have attended initial consultation and six patients have completed full follow up. All patients received chest consultant clinical consultation where their CPET findings were reviewed with them, with particular emphasis on fitness, evidence of underlying disease and breathing pattern. Initial physiotherapist consultation was followed by a bespoke breathing retraining programme. The Nijmegen questionnaire and the self-evaluation of breathing questionnaire formed the main outcome measures. Patients also completed a service satisfaction questionnaire, rating 6 aspects of the service on a scale of 1–5, with 5 being most satisfied. Paired t-tests were used to calculate significance of pre and post values.

Results Fourteen patients have so far been assessed in the initial consultation. Their diagnosis and breathing patterns, demonstrated on CPET, are described in Table 1. Average pre-trial Nijmegen Questionnaire scores demonstrated an improvement post-intervention from the 6 patients who have completed the intervention (26.5 pre to 21.2 post, p = 0.0465). Patients also completed the self-evaluation of breathing questionnaire, before and after the intervention. The average score decreased from 27.2 pre-trial to 15.0 post-trial (p = 0.0098). No changes in functional residual capacity controlled pause (10.0s pre to 11.8s post, p > 0.05) or total lung capacity breath hold (11.8s pre to 21.0s post, p > 0.05) were evident. The average patient satisfaction score was 28.6/30.

Conclusion A novel combined physiological and physiotherapist based intervention may be effective in supporting symptoms in people with dysfunctional breathing.
**Abstract P230 Table 1**

<table>
<thead>
<tr>
<th>Age (gender)</th>
<th>Relevant co-morbidities</th>
<th>CPET findings</th>
<th>Pre-trial questionnaire scores</th>
<th>Post-trial questionnaire scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>17 (F)</td>
<td>Asthma</td>
<td>Pre-test hyperventilation, which resolved on exercise</td>
<td>SEBQ = 5</td>
<td>To be completed</td>
</tr>
<tr>
<td>73 (F)</td>
<td>None</td>
<td>Mixed dysfunctional breathing and hyperventilation</td>
<td>SEBQ = 21</td>
<td>To be completed</td>
</tr>
<tr>
<td>57 (M)</td>
<td>None</td>
<td>Normal</td>
<td>SEBQ = 11</td>
<td>SEBQ = 6</td>
</tr>
<tr>
<td>77 (F)</td>
<td>Asthma</td>
<td>Mixed dysfunctional breathing and hyperventilation</td>
<td>SEBQ = 20</td>
<td>SEBQ = 15</td>
</tr>
<tr>
<td>36 (F)</td>
<td>Fibromyalgia, Anxiety</td>
<td>Pre-test hyperventilation, which partially resolved on exercise</td>
<td>SEBQ = 39</td>
<td>SEBQ = 32</td>
</tr>
<tr>
<td>25 (M)</td>
<td>Asthma</td>
<td>Mixed dysfunctional breathing and hyperventilation</td>
<td>SEBQ = 69</td>
<td>To be completed</td>
</tr>
<tr>
<td>20 (F)</td>
<td>Asthma</td>
<td>Pre-test hyperventilation, which resolved on exercise</td>
<td>SEBQ = 64</td>
<td>To be completed</td>
</tr>
<tr>
<td>59 (F)</td>
<td>None</td>
<td>Mixed dysfunctional breathing and hyperventilation</td>
<td>SEBQ = 21</td>
<td>SEBQ = 9</td>
</tr>
<tr>
<td>75 (F)</td>
<td>Pulmonary embolism, Anxiety</td>
<td>Hyperventilation</td>
<td>SEBQ = 19</td>
<td>SEBQ = 9</td>
</tr>
<tr>
<td>62 (F)</td>
<td>Asthma</td>
<td>Normal</td>
<td>SEBQ = 48</td>
<td>SEBQ = 24</td>
</tr>
<tr>
<td>68 (F)</td>
<td>None</td>
<td>Normal</td>
<td>SEBQ = 31</td>
<td>To be completed</td>
</tr>
<tr>
<td>63 (M)</td>
<td>Pulmonary fibrosis</td>
<td>Hyperventilation</td>
<td>To be completed</td>
<td>To be completed</td>
</tr>
<tr>
<td>26 (F)</td>
<td>Fibromyalgia, Anxiety</td>
<td>Mixed dysfunctional breathing and hyperventilation</td>
<td>To be completed</td>
<td>To be completed</td>
</tr>
<tr>
<td>25 (M)</td>
<td>Respiratory arrest, Anxiety</td>
<td>Mixed dysfunctional breathing and hyperventilation</td>
<td>To be completed</td>
<td>To be completed</td>
</tr>
</tbody>
</table>

Mean [SD]

**REFERENCE**


**P231 BREATHING PATTERN DISORDERS IN A COMPLEX BREATHLESSNESS SERVICE: CLASSIFICATION AND CLINICAL CHARACTERISTICS**

**Background and aim** Many patients presenting to our complex breathlessness service appear to have breathing pattern disorders (BPDs). When suspected clinically, they are referred to a specialist respiratory physiotherapist for assessment and treatment. Here we describe the prevalence of identifiable breathing patterns and their clinical characteristics.

**Methodology** We performed a retrospective review of our clinical database including patients seen for initial physiotherapy assessment between December 2015 and June 2016. Patients underwent a standardised diagnostic assessment (clinical history, physiotherapy assessment, lung function and Nijmegan questionnaire).

**Results** Data from 43 patients with confirmed BPD were included, 77% female, mean age 58 yrs. Relevant respiratory comorbidities included chronic cough (33%), asthma (30%) and vocal cord dysfunction (30%), with no comorbidity in 23%. Other associated conditions included musculoskeletal conditions (47%), chronic pain (44%), obesity (44%), nasal blockage (42%) and anxiety (31%). Four categories of breathing patterns were identified: thoracic dominant (58%), irregular/crescendo (51%), forced abdominal expiration (30%), and thoraco-abdominal asynchrony (2%). More than one BPD was seen in 35% of patients; only forced abdominal expiration and thoracic dominant didn’t co-exist. Conversely all pattern types could be found in isolation, although irregular/crescendo was more likely to co-exist with another pattern type.

**Conclusion** Four separate breathing pattern types were identified, in isolation or in combination. Although anxiety was fairly common, many other associated disease and conditions were seen, especially relating to biomechanical factors. This preliminary data may enable clinicians to identify breathing pattern types, lead to the development of targeted treatment options and promote screening of particular conditions associated with BPD.

**P232 DOES ONE MODEL OF PULMONARY REHABILITATION FIT ALL? A MODIFIED APPROACH TO PULMONARY REHABILITATION**

FM Lang, H Matthews, P Brice. James Paget University Hospital, Great Yarmouth, UK

10.1136/thoraxjnl-2016-209333.375

**Introduction and objectives** Pulmonary Rehabilitation (PR) is defined as a multidisciplinary programme for patients with chronic respiratory impairment that is individually tailored and designed to optimise each patient’s physical and social performance and autonomy (NICE, 2010). Our service was involved in RCP PR Pilot Accreditation Scheme.

Individuals MRC 2–5, functionally limited by breathlessness are referred to PR (BTS, 2013). There is a wide spread of functional disability and breathlessness for these individuals. Does one approach to PR address the needs of all patients within these broad groupings?

**Aims** Modifying PR may improve attendance and completion of full PR for patients MRC5.

**Methods** Following service review, Modified Programme was offered; 2 × Gym Sessions and education. Session one; patients difficulties were discussed. Breathing control techniques, improved posture and lung inflation were demonstrated. Daily home exercises were promoted. Following 2 weeks of homework, the patients were invited to a review. Any improvement in breathlessness and confidence was discussed with the patients offered Full PR where appropriate.
The patient who did not complete full programme continued to attend education. 1 patient attended the first session with no further engagement. 1 patient deferred until June 2016. Qualitative data reports significant benefit.

This modified approach was observed during the RCP site visit. Feedback included the need for feedback to the BTS with regards to greater flexibility with the standards and their future developments as a consequence of observing our modified approach to PR.

What Next? Modification to standard PR offers significant improvement in attendance and completion of PR for patient with significant dyspnoea (MRC5). Could these results be replicated within other PR service?

We continue to offer modified PR and now include MRC4 patients with significant co-morbidities which would otherwise restrict attendance.

REFERENCES

A PILOT DIAGNOSTIC CARDIO-RESPIRATORY BREATHLESSNESS CLINIC: CAN A SYMPTOM-BASED APPROACH ACHIEVE AN EARLIER DIAGNOSIS?


Introduction We aimed to compare the time to diagnosis and treatment between a combined cardio-respiratory diagnostic breathlessness clinic (BC) and usual specialist outpatient care (UC) in patients with chronic breathlessness referred from primary care.

Methods We surveyed patients with undifferentiated chronic breathlessness referred to secondary care outpatient cardiology and respiratory services during March 2015 (UC). Subsequently, we implemented a fortnightly pilot breathlessness clinic (BC) between August 2015 and January 2016 using existing referrals to either cardiology or respiratory specialties. Patients were seen by either a consultant cardiologist or respiratory physician, reviewed by a physiotherapist, and discussed by the MDT at the end of clinic.

The investigations performed in primary care were documented and where needed the following investigations were completed for the BC: haemoglobin, brain natriuretic peptide, spirometry, electrocardiogram, chest radiograph, Nijmegen questionnaire, screening for anxiety and depression symptoms and a physical activity questionnaire. Time to diagnosis, physiotherapy, treatment and discharge were measured and compared with UC. Patients were requested to complete a patient experience questionnaire.

Results Table 1 shows the results of UC compared to the BC. 35% of referrals from primary care reported ≤1 investigation and only 28% had had spirometry performed. The MRC dyspnea scale grade distribution in the BC was MRC1 = 4%, MRC2 = 30%, MRC3 = 37%, MRC4 = 22%, MRC5 = 7%. Co-morbidity was common with over >80% of patients having at least two diagnoses contributing to their breathlessness. Dysfunctional breathing was the commonest primary and secondary diagnosis.

18.5% of patients in the BC could have been diagnosed in primary care. 18.5% were originally referred to the incorrect speciality and in nearly 30% of patients referrals to the other speciality were potentially avoided due to the MDT discussion. Only one third of patients required specialist tests to secure their diagnosis. All patients rated their experience as ‘excellent’.

Conclusions Our pilot diagnostic breathlessness clinic reduced time to diagnosis and treatment, and avoided further between-specialty outpatient appointments. However, our results demonstrate the need for symptom-based breathlessness pathways starting in primary care to utilise simple investigations prior to referral to specialist clinics.

REFERENCE
**Poster sessions**

**Understanding Airways and Blood Vessels in the Lung**

**P234**  **SPUTUM CYTOKINES AND CLINICAL BIOMARKERS IN SEVERE ASTHMA**

R Shrimanker, S Go, S Troublin, L Xue, ID Pavord. Respiratory Medicine Unit, Nuffield Department of Medicine, University of Oxford, Oxford, UK

10.1136/thoraxjnl-2016-209333.377

**Introduction** Emerging treatments for type-2 high asthma such as anti-IL-5 (mepolizumab) and anti-IL-4 and IL-13 (dupilumab) target specific cytokine pathways resulting in type-2 inflammation. Whether patients with type 2 inflammation respond equally to both treatment or have distinct IL-13 and IL-5 profiles is currently unclear. We have tested the hypothesis that these pathways may function independently of each other and that simple biomarkers can help differentiate IL-13 and IL-5 high patients.

**Methods** Patients with well characterised, severe asthma were evaluated with the blood eosinophil count and fractional exhaled nitric oxide (FeNO). Patients also had paired measurements of type-2 cytokines in induced sputum samples. Sputum cytokines were measured using a Luminex assay.

**Results** We found that there was no relationship between the blood eosinophil count and FeNO. There was a positive correlation between FeNO and sputum IL-13 (r = 0.51, p < 0.01) and blood eosinophils and sputum IL-5 (r = 0.47, p < 0.01).

**Conclusions** These findings suggest that readily available, non-invasive biomarkers may be able to differentiate sub-phenotypes in type-2 high asthma. Post-hoc analysis of clinical trial data of anti-IL-5 and anti-IL-4 and IL-13 treatments based on the predominant clinical biomarker would be of interest to see if these predict response to treatment. Simple biomarkers may be of use in deciding which of the emerging biological treatments to use in severe, type-2 high asthma.

**P235**  **EPIGENETIC LANDSCAPE OF THE ASTHMATIC AIRWAYS**

1P McErlane, 1A Kelly, 1J Dhariwal, 1J Watson, 1N Jurdzinski, 1J Smith, 2R Solar, 2MR Edwards, 3A Van Oosterhout, 2J Dhariwal, 1J Watson, 3N Jurdzinski, 3J Smith, 2RS Solar, 2Kings College, London, UK

1Imperial College, London, UK; 2GlaxoSmithKline, Stevenage, UK

10.1136/thoraxjnl-2016-209333.378

The airway epithelium of asthmatics exhibits distinct genomic and phenotypic characteristics. However the mechanisms underlying the establishment and chronicity of these characteristics remains unknown. We investigated if epigenetic changes underpin the genomic characteristics of the asthmatic airways by determining the chromatin landscape of bronchial epithelial cells (BECs) in healthy and asthmatic adults.

We employed ChIP-seq of histone H3 acetylation (H3K27ac) to determine the chromatin landscape in ex vivo cultured BECs from healthy and allergic-asthmatic asthmatics (n = 3 donors each). Regions of differential enrichment were identified (MEDIPS) and associated genes and pathways determined (GREAT). Gene expression profiles were investigated by microarray (Illumina) and differential analysis conducted (Partek Genome Suite). Super enhancers (SEs) were identified (ROSE) and enrichment of transcription factor motifs (MEME) and their tissue distribution (proteinatlas.org) determined.

We identified 33,744 differentially enriched regions (DERs) of H3K27ac between asthma and healthy BECs. DERs were associated with genes (e.g. SERPINB2, TSLP) and pathways (e.g. leukotriene synthesis, antiviral response) previously implicated in asthma and had little overlap with known glucocorticoid receptor binding sites (1.7% of total). DERs occurred up to 100kb from gene promoters and gain or loss of H3K27ac was associated with increased and decreased gene expression in asthmatics respectively. Using a comparative approach, we identified SEs that were common (i.e., present across all donors) and distinct to health and asthma. In addition to established asthma genes (e.g. CLCA1) and transcription factors (e.g. TP63), asthma-SEs encompassed non-coding RNAs (up to 32% of genes) and epithelial-specific transcription factors (e.g. GCM2) previously unreported in asthma.

Our data indicates that asthma influences the chromatin landscape of BECs and suggests the genomic differences observed in the asthmatic airway epithelium are underpinned by established epigenetic mechanisms.

**P236**  **THE ROLE OF HISTONE ARGinine METHYLATION IN GENE EXPRESSION OF AIRWAY SMOOTH MUSCLE CELLS IN ASTHMA**

KA Kaczmarek, RL Clifford, JK Patel, DE Shaw, J Dowden, AJ Knox. University of Nottingham, Nottingham, UK

10.1136/thoraxjnl-2016-209333.379

**Introduction and objectives** Asthma is estimated to affect at least 300 million people globally. About 25% of the patients do not respond to therapy; therefore we need to develop novel treatments. ASM cells have a crucial role in asthma, contributing to airway remodelling, inflammation and airflow obstruction. We have previously shown that epigenetic histone modifications, particularly histone lysine acetylation and methylation regulate the secretion of inflammatory mediators from ASM cells. Here we tested the hypothesis that histone arginine changes are also involved. Protein arginine N-methyltransferases (PRMTs) are the enzymes which catalyse histone arginine methylation (HRme, the addition of a methyl group to arginine residues on the N-terminal tails of histones), and inhibiting them represents a strategy to reduce the secretion of inflammatory mediators from ASM cells.

**Methods** Studies were performed in cultured human ASM cells from asthmatic and non-asthmatic donors at passage 6. PRMT expression in human ASM cells was investigated by qPCR. Protein levels of four PRMTs in human ASM cells were investigated by western blotting. As PRMT1 has previously been suggested to play a role in mouse asthma models, we studied the association of PRMT1 with eotaxin, IL-6, IP-10 and CXCL8 promoters in healthy ASM cells, under basal conditions and following stimulation with TNF-α (1ng/ml), by chromatin immunoprecipitation (ChIP). IgG was used as a negative control, while acetylated histone H4 (AcH4) was used as a positive control.

**Results** We found that ASM cells express the PRMT1, PRMT2, PRMT3, CARM1, PRMT5, PRMT6, PRMT7 and FBX011 mRNA and PRMT1, CARM1, PRMT5, and PRMT6 protein. The analysis showed no difference in the levels of expression between cells isolated from asthmatic and non-asthmatic donors.

**Under basal conditions, PRMT1 was associated with all of the promoters and association increased following 1 hour stimulation with TNF-α.**
Conclusions ASM cells express a number of PRMTs at mRNA and protein levels. PRMT1 associates with a number of chemokine and cytokine promoters after TNF-α stimulation. PRMTs may have an important role in regulating chemokine production from ASM cells in asthma, and are a promising target for future investigations in asthma.

P237 LUNG FUNCTION DECLINE IS ASSOCIATED WITH SERUM PERIOSTIN LEVEL BUT NOT FRACTIONAL EXHALED NITRIC OXIDE OR BLOOD EOSINOPHILS IN SEVERE ASTHMA


10.1136/thoraxjnl-2016-209333.380

Background In the airways, periostin encoded by the POSTN gene is up-regulated by IL13-IL4-TGF-β axis. It is produced by structural cells such as epithelial cells and fibroblasts and inflammatory cells such as eosinophils and macrophages. Consequently it has been linked to airways remodelling, mucus production and subepithelial fibrosis. However, an association between periostin and lung function impairment in severe asthma has not been confirmed.

Methods Unselected patients attending severe asthma centre were clinically characterised using systematic protocol and undergone lung functions, serum periostin, fraction exhaled nitric oxide (FeNO) and peripheral blood eosinophils (PBE) measurement. Correlation analysis and one way analysis of variance were undertaken to explore the relationships.

Results 127 patients consented to the study (mean age 45.5 yrs [range 17–70], 88 [69%] females), 72/103 (69%) were atopic. The mean FEV1 was 2 L, mean%predicted FEV1 68.1, and mean FEV1/FVC ratio was 71.3. The mean inhaled daily corticosteroids dose was 1.65mg/day and 56.3% were on maintenance oral corticosteroids. Periostin measurement was available in 78 patients who had a mean level of 49.5 ng/L (SD ± 18.1). Using 50 ng/L as a cut-off point, 30/78 (36%) patients had high periostin and 48/78 (62%) had low periostin. The mean FEV1 in the periostin high group was 1.69 L Compared to 2.15 L in the low group (p = 0.018) (see Figure). We also observed significant correlation between serum periostin and% predicted FEV1 (r = 0.36, p = 0.0017). In contrast the association analysis between FeNO and PBE with FEV1 were both non-significant (p = 0.8 and p = 0.35 respectively).

Conclusion Raised serum periostin is associated with low lung function in this cohort of severe asthma but not FeNO or BPE. Further research is required to confirm this relation and explore the role of periostin as predictor of decline in lung function and airway remodelling.

P238 INVESTIGATING GENOME WIDE DNA METHYLATION IN AIRWAY SMOOTH MUSCLE CELLS FROM ASTHMATIC AND NON-ASTHMATIC DONORS

1RL Clifford, 1JK Patel, 1DE Shaw, 1AJ Knox, 2MS Kobor. 1Division of Respiratory Medicine and Nottingham Respiratory Research Unit, University of Nottingham, Nottingham, UK; 2Centre for Molecular Medicine and Therapeutics, Child and Family Research Institute, Vancouver, Canada

10.1136/thoraxjnl-2016-209333.381

Rationale Genetic mechanisms fail to fully explain asthma pathogenesis and environmental factors are considered to play an important role. Environmental factors may lead to permanent changes in epigenetic patterns and contribute to asthma. Epigenetics is the study of heritable changes in gene expression that are not due to changes in DNA sequence. DNA methylation is a reversible modification of DNA structure in which a methyl group is added to cytosine residues. Parental smoking affects the methylation of buccal cell DNA from children and children with early onset wheeze have an altered blood DNA methylation profile to healthy individuals. No studies have compared DNA methylation profiles in the disease relevant cell type of airway smooth muscle (ASM) cells.

Methods DNA was isolated from ASM cells at passage 5 and bisulphite treated to convert epigenetic information into sequence-based information. Site specific, quantitative genome wide methylation was determined using the Illumina 450K Infinium Methylation BeadChip array. Hits were validated by Pyrosequencing. RNA was extracted simultaneously for mRNA expression analysis by real time PCR.

Results There were no independent CpG sites associated with asthmatic status of ASM cells following multiple test correction. Without correction over 13000 CpG sites showed a significant difference in methylation (linear modelling, p value >0.05)
between asthmatic and non-asthmatic cells, and a biologically relevant difference in methylation of greater than 10% (β value > 0.1). 10 of these sites were selected as top hits. 7 sites positively validated by pyrosequencing. They were associated with 7 different genes: LGALS3BP, ATP11A, ZNF696, KLF6, TBX1, RUNX3, and SPINT2. Expression of these genes was measured in ASM cells isolated from asthmatic and non-asthmatic donors. LGALS3BP expression was undetectable while ATP11A and ZNF696 displayed no difference in expression between cells from asthmatic and non-asthmatic donors. KLF6 and SPINT2 showed a trend towards increased expression in cells from asthmatic donors while RUNX3 and TBX1 showed a trend towards decreased expression.

Conclusions Differences in CpG methylation exist between ASM isolated from asthmatic and non-asthmatic donors. Future work will focus on identifying differentially methylated regions of DNA and further defining the association to gene and protein expression.

Effects of Tiotropium on Asthma Exacerbations Are Not Explained by Airway Hyperresponsiveness, Exhaled Breath Nitric Oxide or Airway Geometry

S Jabbar, A Manoharan, BJ Lipworth. Scottish Centre for Respiratory Research, Dundee, UK

Background Long acting muscarinic antagonists (LAMA) such as tiotropium (TIO) reduce asthma exacerbations in patients receiving inhaled corticosteroids and long-acting beta-agonists (ICS/LABA). However the mechanism for this protective action of LAMA remains unclear.

Objectives To evaluate the response to indacaterol (IND) either alone in combination with tiotropium (IND/TIO) in addition to ICS on airway hyperresponsiveness (AHR), FeNO and impulse oscillometry (IOS).

Abstract P239 Figure 1

Effects of randomised treatment compared to baseline on mannitol sensitivity and reactivity. Values presented as geometric mean and 95% confidence interval. P value denotes significant difference for randomised treatment compared to baseline. There was also a significant difference between single and chronic dosing for RDR with both treatments.
Methods n = 14 ICS treated asthmatic patients (Mean age 46 years, FEV1 86% predicted, R5 160% predicted, ICS 693ug/day), were randomised in cross-over fashion to receive either IND 150ug alone (ICS/LABA) or in combination with TIO 18ug once daily (ICS/LABA/LAMA) for 4 weeks with 2 week run-in and washout periods. Mannitol sensitivity (PD15) and reactivity (RDR), airway resistance (R5, R5-R20), reactance (AXE) and FeNO were measured at 24 hours after the first and last doses.

Results There were significant improvements in mannitol PD15 and RDR with IND or IND/TIO vs baseline after single but not chronic dosing (Figure). There was also a significant difference in RDR between single and chronic dosing for both treatments. R5, R5-R20 and AXE were significantly improved with both treatments compared to baseline after single and chronic dosing. There were no significant differences between treatments after chronic dosing for either mannitol or IOS. In contrast FeNO was unchanged with either treatment compared to baseline.

Conclusions There were significant improvements in mannitol PD15 and reactivity with either IND or IND/TIO after single but not chronic dosing, while FeNO remained unchanged. Airway resistance and reactance were significantly decreased to the same degree with both treatments after chronic dosing. This in turn suggests that the mechanism by which LAMA reduces exacerbations is unlikely to be related to AHR, FeNO or airway geometry.

Background Omalizumab is an anti-IgE monoclonal antibody therapy used in patients with inadequately controlled persistent allergic IgE mediated asthma who require continuous or frequent treatment with oral corticosteroids. Previous studies have tried to predict a patient’s response to omalizumab based on pre-treatment baseline characteristics. Most recent data has suggested that baseline blood eosinophils, serum periostin or FeNO may be predictive of response to omalizumab in the TH2 phenotype.

Aims This study will attempt to identify a characteristic that may explain why some patients suffering with severe asthma in a single severe asthma centre do not achieve a response when treated with the anti-IgE monoclonal antibody, omalizumab.

Methods The target population was represented by all patients previously treated or undergoing treatment with omalizumab at the Severe Asthma Service at University Hospital South Manchester (n = 185). The study population was those for whom records could be found within the study period (n = 154). Demographic and clinical data was collected retrospectively from patient medical records.

Abstract P240 Figure 1 Comparison of baseline IgE in true nonresponders and true responders
Results 16.2% of patients at UHSM did not show response to omalizumab at 16 weeks. Baseline serum IgE levels in the non-response group were on average 77.28 kU/L lower than those in the response group, statistical analysis of the two groups show that this difference was significant (P = 0.04). Mean eosinophils in the true non-responder group were actually higher than those in the true responder group, however this difference was not statistically significant. No other demographic or disease specific measures predicted a lack of response to omalizumab.

Discussion The results from the study indicate that a lower base-line serum IgE may predict non-response to treatment with omalizumab. The results also show that non-response rates at the NWLC were lower than those demonstrated in clinical trials (INNOVATE), were consistent with other real life studies (PER-SIST/APEX I and APEX II) but markedly lower than those quoted in the eXpeRience registry.

Eosinophil Apoptosis is Negatively Associated with Body Mass Index in Asthma

1Thavakumar, 2AKA Wright, 1MA Ghebe, 1T Thornton, 1CE Brightling. 1Department of Infection, Immunity and Inflammation, University of Leicester, Leicestershire, UK; 2Institute of Lung Health, NHRI Leicester Respiratory Biomedical Unit, University Hospitals of Leicester NHS Trust, Leicester, UK

P241

Background Obese asthmatics are known to have reduced eosinophils in sputum, as well as poor control of asthma symptoms. We have shown that, compared to non-obese patients, there is an elevated number of eosinophils in the airway submucosa of obese asthmatic patients. This study aims to determine whether a differential susceptibility to apoptosis, between obese and non-obese patients, could contribute to these clinical observations.

Method Patients with a clinical diagnosis of asthma were recruited (n = 28) and consented at Glenfield Hospital for blood donation to study eosinophil apoptosis; the patients recruited had varying severities of asthma and BMI. Eosinophils were isolated from whole blood by negative immunomagnetic selection using CD16 microbeads to a purity of mean ± SD 95.7% (± 4). Purified eosinophils (Time 0) were placed into culture in RPMI (1640 + Glutamax-1 supplemented with 10% FBS and 1% penicillin and streptomycin) and harvested at 17 and 21 hours later to measure apoptosis by flow cytometry using Annexin V and Propidium Iodide (Becton Dickinson). Cells were considered apoptotic if they were Annexin V positive/PI negative and reported as a percentage of total eosinophils.

Results At 0 hours, the mean% of annexin V positive cells was 0.47% and there was no significant association with BMI (r = -0.245). At 17 and 21 hours there were 12.68% and 21.0% annexin V positive cells, respectively, and we noted a significant negative Pearson’s correlation between eosinophil apoptosis and BMI at time 17 (r = -0.449; p = 0.028) and time 21 (r = -0.448; p = 0.028). These correlations were independent of lung function, steroid medication and percentage eosinophil purity.

Conclusion Eosinophils from obese asthmatic patients are less susceptible to apoptosis compared to those from non-obese patients. This may contribute to the differential presence of eosinophils in the lamina propria and airway of obese patients compared to non-obese individuals.

P242

The Airway Microbiota in Human Rhinovirus Induced Asthma Exacerbation

EHC Wong, J Dhanival, L Cuthbertson, P James, M Cox, M Moffatt, W Cookson, S Johnston. National Heart and Lung Institute, Imperial College London, London, UK

Background Acute asthma exacerbations (AEs) cause significant morbidity. Up to 60% of AEs may be associated with respiratory viral infections, particularly human rhinoviruses (HRVs). The role of bacteria in AEs is unclear, yet antibiotics are frequently prescribed. Recent studies have demonstrated a greater abundance of potentially pathogenic bacteria (e.g. *Haemophilus* spp.) within the airway microbiota in asthma, whilst a greater abundance of commensals (e.g. *Prevotella* spp.) was observed in health. The aim of this study was to examine the changes within the airway microbiota in asthma in the context of a HRV-induced AE and evaluate if such changes correlate with clinical symptoms and lung function changes.

Methods Eleven moderate asthmatics (BTS step 3–4) and 12 healthy subjects were experimentally infected with HRV-16 and bronchoscopy was performed at baseline, 3 and 8 days following HRV-infection. Subjects completed daily symptom diary and spirometry. DNA was extracted from bronchoalveolar lavage and PCR amplification of the V3-V5 region of bacterial 16S rRNA gene was performed to evaluate microbiota community composition.

Results The microbiota composition did not significantly differ between healthy and asthmatic subjects at baseline, though healthy subjects exhibited significantly greater relative abundance of *Prevotella* spp. following HRV-infection (p < 0.05). At day 3 post-HRV infection, greater *Prevotella* spp. relative abundance was associated with lower symptom scores (R2 = 0.56, p < 0.05). In contrast, at day 8 greater *Neisseria* spp. relative abundance was associated with greater peak flow decline (R2 = 0.41, p < 0.05). Furthermore, HRV-16 viral load exhibited a significant linear relationship with the degree of microbiota community change (as measured by beta-diversity) (R2 = 0.61, p < 0.05).

Conclusion Following HRV infection, greater *Prevotella* spp. relative abundance was associated with less symptoms whilst greater *Neisseria* spp. was associated with greater peak flow decline, suggesting an imbalanced microbiota may exacerbate airway inflammation and ultimately severity of AE. Viral load significantly correlated with degree of microbiota community change, implying HRV infection may directly perturb the airway microbiota. Further studies are needed to confirm these findings and explore the roles of *Prevotella* spp. and *Neisseria* spp. in exacerbating airway inflammation.

References

**Introduction**
Recurrent exacerbations are a characteristic feature of uncontrolled asthma, often due to viral or bacterial infections. We have reported in a retrospective study that immune deficiency is common in asthma and correlates with reduced lung function. We set up a prospective study to determine if this predisposes to a more severe disease.

**Aim**
Our aim is to ascertain if immune deficiency is associated with a more severe disease potentially with radiological changes and clinically with low lung function and frequent exacerbations.

**Methods**
We prospectively collected data from new patients attending the regional asthma and fungal clinics. Demographics, markers of disease severity and specific antibody levels to *Haemophilus influenzae* (HI), and *Streptococcus pneumoniae* (SP), were recorded. Patients with specific antibody deficiency (HI: ≤ 0.15 iu and SP: ≤ 0.35 iu to 6+ of 12 strains tested) received appropriate vaccination(s) in primary care (Pneumovax®).
and Meniotrix®, with repeat samples collected two months later. We also recorded blood and sputum eosinophil counts, radiological findings such as bronchiectasis and bronchial wall thickening, total IgE, smoking status, exacerbations in the last year and ITU admissions.

**Results**

101 patients were followed up (69 asthma, 32 fungal) 67 were male, mean (SD) age 53 (15) years, FEV1 69 (21.9)% predicted, ICS dose 1818 (1244) µg, and BMI 29.9 (8.9) kg/m². Specific antibody levels and responses to vaccination are presented in Figure 1. Immune deficiency at baseline and post vaccination did not correlate with lung function, radiological findings such as bronchial wall thickening or exacerbation frequency.

**Conclusion** Specific antibody deficiency is commonly seen in patients with asthma and fungal disease. Vaccination can provide protection and should be considered in this patient group. We need further analysis with a larger cohort of patients to study the association between antibody deficiency, lung function, radiological changes and disease progression.

---

**P244**

**HAEMOGLOBIN MEDIATED PROLIFERATION AND IL-6 RELEASE IN HUMAN PULMONARY ARTERY ENDOTHELIAL CELLS: A ROLE FOR CD163 AND IMPLICATIONS FOR PULMONARY VASCULAR REMODELLING**

L Ramakrishnan, A Anwar, JS Wort, GJ Quinlan. Vascular Biology Group, NHLI, Imperial College London, London, UK

10.1136/thoraxjnl-2016-209333.387

**Introduction**

Pulmonary arterial hypertension (PAH) is characterised by vascular remodelling of pulmonary arterioles. Disrupted iron homeostasis as well as subclinical haemolysis are implicated in PAH, although exact mechanisms remain unknown. IL-6, a proinflammatory cytokine and regulator of iron homeostasis is elevated in PAH patients and also been implicated in pulmonary vasculopathy. Hb uptake may be facilitated via CD163. These studies may provide novel insights regarding mechanisms for haemoglobin driven proliferative and second messenger responses of relevance to PAH.

**Methods**

Cells were challenged with Hb (10 µM) and/or IL-6 (1–10 ng/mL). Transcriptional regulation was analysed by RT-PCR, protein expression by immunocytochemistry, secretion by ELISA and proliferation by BrdU incorporation.

**Results**

Novel findings demonstrate that Hb and IL-6 individually and in combination increased proliferation of hPAECs (by 32%, 47% and 63% respectively; p < 0.05). CD163, a Hb scavenger receptor, was basally expressed as mRNA and protein (cell surface) on hPAECs and further modulated by Hb or IL-6 exposure. Hb treatment also caused increased transcription (30%; p < 0.05) and release of IL-6 (107%; p < 0.01) from hPAECs.

**Conclusion**

This is the first report of Hb-mediated proliferation, CD163 expression and IL-6 release in hPAECs with potential implications for autocrine and paracrine signalling in pulmonary vasculature. Hb uptake may be facilitated via CD163. These studies may provide novel insights regarding mechanisms for haemoglobin driven proliferative and second messenger responses of relevance to PAH.

**Abstract P244 Figure 1** IL-6 release after 24h

---

**P245**

**WHOLE BLOOD LEVELS OF MICRORNAs-34A PREDICT SURVIVAL AND REGULATE GENES ASSOCIATED WITH PULMONARY ARTERIAL HYPERTENSION**

J Lin, J Inemonger, J Pickworth, A Rothman, H Casbolt, N Arnold, C Elliot, R Condiffe, D Kiely, A Lawrie. University of Sheffield, Sheffield, UK

10.1136/thoraxjnl-2016-209333.388

**Introduction**

Despite advanced therapies for pulmonary arterial hypertension (PAH), the hyperproliferative pulmonary vasculopathy persists. Circulatory microRNAs (miR) offer considerable promise as both a prognostic biomarker, and to identify molecular mechanisms underlying PAH. Previous study from our lab identified whole blood miR-34a as downregulated in patients with PAH.

**Objectives**

To validate changes in whole blood miR-34a levels in patients with PAH and relate them to disease severity and survival, and determine the phenotypic effect on pulmonary artery smooth muscle cells (PASMC).

**Methods**

Whole blood RNA was isolated from 27 treatment-naive patients with PAH, 12 age-matched healthy volunteers (HV) and experimental models of PAH (Monocrotaline-MCT, Sugen5416/hypoxia-SuHx and controls, n = 5/group). Whole blood miR-34a-5p and −3p levels were measured by qPCR. The phenotypic effect of miR-34a-5p and −3p levels was assessed on PASMC in-vitro. Differences between groups were determined by Student’s t-test or ANOVA-Tukey.

**Results**

Whole blood miR-34a-5p was reduced in patients with PAH (p < 0.0001) and experimental models of PAH (MCT p < 0.05, SuHx p < 0.001). Receiver operating characteristic curve identified that miR-34a-5p levels discriminates patients with PAH from HV (AUC = 0.86, p = 0.001). MiR-34a-5p levels were significantly lower in patients with severe PAH, as defined by a cardiac index of <2 vs >2.5 l/min/m² (p < 0.05) and NT-proBNP > 300 vs <300 ng/l (p < 0.001) and predict survival at 5 years. MiR-34a-5p levels were negatively correlated with pulmonary vascular resistance (r = −0.4, p < 0.05) and pulmonary arterial wedge pressure (r = −0.4, p < 0.05). Preliminary data showed that whole blood miR-34a-5p was reduced in patients with PAH (p = 0.0267) and experimental models of PAH (MCT p < 0.01, SuHx p < 0.01); and delineates patients with PAH from HV (AUC = 0.925, P = 0.01). Transfection of PDGF-stimulated PASMC with miR-34a-5p or −3p inhibitor...
promote PASMC proliferation (p < 0.001). In contrast, miR-34a-5p and −3p mimic suppress PASMC proliferation (p < 0.05 and p < 0.001 respectively). Additionally, transfection with miR-34a-3p increases caspase-3/7 activities in PASMC (p < 0.0001).

Conclusions Reduced miR-34a-5p levels associate with increased disease severity and poor prognosis in PAH. MiR-34a-5p and −3p levels regulate PASMC proliferative-phenotype in response to PDGF. This research identifies miR-34a-5p and −3p as potential biomarkers, subsequent network analysis may identify novel disease mechanisms. Further experiments in preclinical models are currently underway.

Methods Research ethics committee approval was obtained for the use of human tissue for this study. Patients undergoing lung resection were consented for their resected lung tissue to be included in the study. Patients under the age of 18 and who cannot give informed consent were excluded from the study and twelve patients were enrolled in this study.

Pulmonary arteries were dissected from disease free areas of lung resection and 35 PA rings of internal diameter 2–4 mm and 2 mm long were prepared. PA rings were mounted in a multiwire myograph system containing Krebs-Henseleit solution (aerated with 21% O2:5% CO2 at 37°C) for measuring changes in isometric tension. A basal tension of 1.61 g was applied and the rings left to equilibrate for 60 min. After equilibration rings were pre-constricted to 11.21 μM PGF2α (EC80) then concentration response curves were constructed to Sildenafil, SNP, ANP and BNP by cumulative addition to the myograph chambers. The integrity of the endothelium was confirmed with 1 μM Acetylcholine and smooth muscle viability was confirmed by exposure to potassium chloride.

Results ANP was the most potent and effective vasodilator whereas BNP had little effect. SNP was marginally less potent and effective than ANP and the maximum effect of sildenafil was about 50% that of ANP. The EC50 for ANP, BNP, Sildenafil and SNP were 1.105 nM, 28.78 nM, 1.06 μM and 22.6 nM respectively.

Conclusion This study demonstrated the differential effect of commonly used agonists on pulmonary vascular reactivity and this is the first comparison of these agents in human pulmonary arterial tissue. These effects may need to be considered in the clinical setting.
Respiratory Physiology

P247 SPECIFICITY OF DYSPNOEA RELIEF WITH INHALED FUROSEMIDE
10.1136/thoraxjnl-2016-209333.390

Introduction Dyspnoea is prevalent and reduces quality of life in patients with chronic disease. Inhaled furosemide offers a potential complementary novel treatment for these patients. The mechanism of action is unclear but current theory suggests sensitisation of slowly adapting pulmonary stretch receptors (saPSR) altering neural feedback that informs the brain of the level of breathing. Clinical dyspnoea comprises several components including air hunger (AH; an uncomfortable urge to breathe) and a sense of breathing work/effort (WE) which are thought to arise from different neural pathways. We therefore hypothesised that inhaled furosemide would relieve AH but not WE.

Methods A double-blind, placebo-controlled trial was conducted on healthy volunteers (n = 16; 9 males). Test sessions involved 3 inhalations of furosemide (40 mg) or saline (4 ml) separated by 30–60 mins. Order of inhalations was furosemide-saline-furosemide in half the subjects and saline-furosemide-saline in the other half. Before and after each inhalation, AH was induced with hypercapnia (mean ± SD PCO2 = 49.8 ± 3.7 mmHg) and constrained ventilation (mean ± SD 9.2 ± 1.5 l/min) on one test-day while WE was induced with targeted ventilation (mean ± SD 16.6 ± 3.1 l/min) and external resistive load (20cmH2O/L/s) on the other test-day. During saline inhalations 1.5 mg furosemide in 15ml saline was infused to match the expected systemic absorption of furosemide from the lungs over 15 mins of inhalation. Corresponding infusions of saline during furosemide inhalations maintained blinding from noticeable diuresis. Subjects rated AH or WE every 20s on a visual analogue scale (VAS). Hypercapnia (AH) or targeted ventilation (WE) were imposed for 4 mins and the ratings in the last minute were analysed using Linear Mixed Model procedure (SAS 9.4).

Results The final model produced a main effect of mist (furosemide or saline; p = 0.016), time (pre or post inhalation; p = 0.047) and a significant condition (AH or WE) * mist interaction (p = 0.004). Mean ± SE AH was significantly lowered by inhaled furosemide relative to inhaled saline (-9.7 ± 2.1 mmVAS; p = 0.0015) but mean ± SE WE was not (+ 1.6 mm ± 2.4; p = 0.903).

Conclusion Inhaled Furosemide is effective at relieving AH, but not WE. This is consistent with a mechanism involving modulation of parenchymal lung mechanoreceptor activity leading to dyspnoea relief that specifically applies to the AH component. The treatment may therefore benefit patients with the most unpleasant form of dyspnoea.

P248 PATIENT ELIGIBILITY FOR ANTI-FIBROTIC THERAPY IN IDIOPATHIC PULMONARY FIBROSIS CAN BE ALTERED BY USE OF DIFFERENT SETS OF REFERENCE VALUES FOR CALCULATION OF FVC PERCENT PREDICTED
K Ward, L Spurr, NR Goldman, GA Margaritopoulos, M Kokasi, E Renzoni, F Chua, TM Maher, S Ward, AL Wells. Intestinal Lung Disease Unit, Department of Respiratory Medicine, Royal Brompton Hospital, London, UK
10.1136/thoraxjnl-2016-209333.391

Introduction Antifibrotic drugs for idiopathic pulmonary fibrosis (IPF) patients in England and Scotland are only available to those with FVC percent predicted (FVC%pred) less than or equal to 80%. The prescribing guidance does not state which reference values should be used.

Aims To find out if the use of different sets of reference values affects the numbers of patients with FVC%pred greater than and less than 80%.

To find out which reference equations were in use at UK centres prescribing antifibrotics for IPF in April 2016.

Methods We searched databases for patients diagnosed with IPF at our interstitial lung disease (ILD) unit from 1/1/2010 to 31/12/2015. We calculated FVC%pred using three different sets of reference values (ECSC, GLI or NHANES). The chief respiratory physiologist in each ILD centre in England was contacted and asked which reference values they used to calculate FVC%pred. In Scotland, four hospitals with an ILD MDT were contacted and asked the same. McNemar tests were used to compare the proportion of patients eligible for antifibrotic prescription when FVC%pred was calculated by ECSC or either NHANES or GLI.

Results See Table 1. We identified 671 unique patients: after exclusions, 528 had complete data.

There was a higher proportion of patients calculated to have an FVC%pred > 80% (ineligible for antifibrotics) using ECSC than GLI: Chi-square 22.0, 1df; P<0.0001. The difference in proportions was greater when ECSC was compared to NHANES: Chi square 33.03, 1df, P<0.0001. Of 30 patients with ECSC FVC%pred 80–85%, 27 (90%) had their FVC%pred fall to <80% when recalculated with NHANES.

18 of 20 ILD centres in England were using ECSC to calculate FVC%pred; others used GLI (n = 1) and Falaschetti (n = 1). All four Scottish centres were using ECSC.

Discussion Many patients with ECSC FVC%pred too high for antifibrotics fall into the eligible range when NHANES, the set of reference values used in the ASCEND pirfenidone trial, or GLI, as recommended by the UK Association for Respiratory Technology and Physiology(ARTP) are used.

Conclusions We urge physicians and physiologists to ensure that reference values used to calculate FVC%pred are cited in lung

Abstract P247 Figure 1 Means±SE changes in VAS ratings before and after inhaled furosemide relative to the change before and after inhaled saline for experimentally induced air hunger (AH) and experimentally induced breathing work/effort (WE) in 16 healthy individuals.
function reports. Those choosing reference values must be aware of implications for patients.

P249 COMPARISON OF PHYSIOLOGICAL VERSUS MATHEMATICAL METHODS FOR QUALITY CONTROL IN MBW NORMALISED PHASE III ANALYSIS

1M Arigliani, 2N Verger, 3E Raywood, 4J Duncan, 5A Bush, 6P Aurora on behalf of the London Cystic Fibrosis Collaboration. 1Department of Clinical and Experimental Medical Sciences, Unit of Paediatrics, University Hospital of Udine, Udine, Italy; 2Université Pierre et Marie Curie, Paris, France; 3Respiratory, Critical Care and Anaesthesia Section, IIIP, UCL Institute of Child Health, London, UK; 4The National Heart and Lung Institute, Imperial College, London, UK; 5Department of Respiratory Medicine, Great Ormond Street Hospital for Children, London, UK

10.1136/thoraxjnl-2016-209333.392

Background Breathing pattern cannot be controlled in small children, so multiple breath washout SnIII analysis has to exclude inadequate volume breaths.

Aim To compare an existing mathematical breath exclusion algorithm with a physiological method.

Methods School age children with CF (30) and controls (30) performed SF6MBW with mass spectrometer, with uncontrolled tidal breathing. Two different breath exclusion methods were compared, with exclusion based on:

1) Expired tidal volume (VT) deviating by >25% of the median VT
2) VT <3 Langley dead space volume or 90% bigger than the median VT

Runs with >33% excluded breaths were removed. Volume corrected Scond was calculated from subjects with 3 valid runs.

Results Far fewer subjects were excluded by the physiological Langley method, than by the mathematical method (Table). The mean and SD for Scond was identical by both methods, implying that the mathematical algorithm excludes valid data.

Conclusion A physiological approach to data cleaning prior to SnIII analysis allows retention of data that would be inappropriately excluded mathematically.

REFERENCES

P250 REAL FLIGHT SPO2 COMPARES WITH HYPOXIC CHALLENGE TESTING IN ADULTS WITH CYSTIC FIBROSIS

R Peat, J Furlong, E Spencer, D Russell, M Ledson, M Walshaw. Liverpool Heart and Chest Hospital, Liverpool, UK

10.1136/thoraxjnl-2016-209333.393

Introduction Limited data are available comparing air travel with the hypoxic challenge test (HCT) in adults with cystic fibrosis (CF). The aim of this study was to assess the predictive capability the HCT to in-flight hypoxaemia in adult passengers with CF.

Methods Fifteen subjects (three male) volunteered for this study. Lung function measurements (FEV1) were performed pre and post flight. Oxygen saturation measured by pulse oximetry (SpO2) and symptoms were recorded in-flight on both outward and inward flights. The HCT was performed post flight and the in-flight oxygenation response was compared to the HCT and lung function results.
RESULTS

All subjects flew without the use of oxygen, and no adverse events were recorded in-flight. Air travel caused significant desaturation ($p < 0.001$) (mean pre-flight $SpO_2$ 95 ± 1%; mean in-flight $SpO_2$ 90 ± 3%). The HCT caused mean desaturation ($p < 0.001$) that was comparable to that of air travel (90 ± 3%). The pre-flight FEV1 and in-flight $SpO_2$ showed weak correlation ($r = 0.41, p = 0.125$). The HCT $SpO_2$ showed strong correlation with in-flight $SpO_2$ ($r = 0.74, p < 0.001$). The HCT showed the strongest correlation with the lower $SpO_2$ value measured from both outward and inward flights ($r = 0.92, p < 0.001$).

Conclusions

Significant in-flight desaturation can be expected in passengers with CF. The HCT results compare favourably with air travel data and may be considered the best widely available laboratory test to predict in-flight hypoxaemia in adults with CF.

REFERENCES


Abstract P251 Table 1

<table>
<thead>
<tr>
<th></th>
<th>FeNO +ve (≥16 mI/ml)</th>
<th>FeNO –ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC20 +ve (≥16 mI/ml)</td>
<td>6</td>
<td>32</td>
</tr>
<tr>
<td>PC20 –ve (&gt;16 mI/ml)</td>
<td>17</td>
<td>90</td>
</tr>
<tr>
<td>Pearson Chi-Square</td>
<td>0.000, DF = 1, $p = \text{Value} = 0.989$</td>
<td></td>
</tr>
</tbody>
</table>

P252

ACCURATE MEASUREMENT OF LUNG FUNCTION IN THE WORKPLACE AND POTENTIAL EFFECTS OF UNDERESTIMATION

Introduction

Accurate workplace spirometry measurement is key to giving workers the best clinical assessment of their respiratory health. We were interested in the underestimation of spirometry that occurs if best practice is not adhered to and the significance of this on assessment of health at work.

Methods

667 stone, brick and foundry workers (with varying spirometry experience), carried out lung function testing as part of a larger cross sectional workplace study. Each performed a minimum of 3 forced expirations. Testing continued until each worker had met the ATS/ERS guidance. The final FEV1 and FVC recorded was the maximum value attained from 3 technically acceptable blows, and that the two highest FEV1 and FVC values were within 150 ml. Using the final FEV1 and FVC for each worker, it was then possible to calculate the underestimate of both measures, had only the first blow, or the maximum of the first two blows, been used for interpretation.

Results

613 of the 669 (91.6%) attained the ATS/ERS criteria based on FEV1. Analysis of the first actual blow, regardless of technical quality, showed an FEV1 mean underestimate of 250 mls (median = 80 mls, IQR = 210 mls). If only the first technically acceptable blow had been carried out, the FEV1 would have been underestimated by a mean of 114 mls (60 mls, 150 mls). If only two technically acceptable blows had been carried out, and the maximum of these used, the FEV1 would have been underestimated by a mean of 36 mls (0 mls, 50 mls). Similarly, the FVC would have been underestimated by a mean of 131 mls (75 mls, 180 mls) if only the first technically acceptable blow had been used for interpretation. If only two technically acceptable blows were carried out, the FVC would have been underestimated by a mean of 43 mls (0 mls, 50 mls).

Conclusion

Non adherence to ATS/ERS lung function testing guidance at work can cause the FEV1 and FVC to be underestimated by clinically significant amounts.

Abstract P252 Table 1

<table>
<thead>
<tr>
<th></th>
<th>FeNO +ve</th>
<th>FeNO –ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC20 +ve (≥16 mI/ml)</td>
<td>6</td>
<td>32</td>
</tr>
<tr>
<td>PC20 –ve (&gt;16 mI/ml)</td>
<td>17</td>
<td>90</td>
</tr>
<tr>
<td>Pearson Chi-Square</td>
<td>0.000, DF = 1, $p = \text{Value} = 0.989$</td>
<td></td>
</tr>
</tbody>
</table>

P253

COULD APPLICATION OF SIMPLE DIAGNOSTIC ALGORITHM AIM ONWARD REFERRAL FOR OPTIMISATION OF PRE-EXISTING CONDITIONS IN PATIENTS BEING CONSIDERED FOR MAJOR SURGERY?

Introduction

Cardiopulmonary exercise testing (CPET) is used to identify physiological limitation to exercise and aid diagnosis of cardiorespiratory, psychological and muscle disorders. It is also frequently used to stratify operative risk thereby aiding decision making in patients considered for major surgical procedures.
The evidence for risk stratification is based on the oxygen consumption at anaerobic threshold (VO2 AT) along with metabolic equivalence. Attention is therefore generally paid to the numerical value of these measures rather than full interpretation of the data. Further interpretation may allow further diagnosis and optimisation of pre-existing conditions.

**Methods** We retrospectively applied a simple diagnostic algorithm (Figure 1) to CPETs undertaken by patients considered for major surgery in the Victoria Infirmary, Glasgow between 2014–2016.

**Results** The records of 39 patients who had a pre-operative CPET testing were analysed: 22 male, 17 female, age range 43–88, median 73. A total of 26 patients were classified as high risk, 23 achieved an AT <11 mls/kg/min and 3 with a metabolic equivalent <4.0mlsO2/kg/min. Both parameters were low in 13 patients. Ten patients had their procedures cancelled due to this. Eleven high risk patients had a normal VO2 max.

Upon applying the diagnostic algorithm; 15 patients were deconditioned, 6 had cardiovascular limitation, 3 had respiratory limitation and 15 were normal.

In the ‘high risk’ population: 2 patients had respiratory limitation with pre-existing respiratory conditions and were cancelled. Six patients had cardiovascular limitation with 3 patients having pre-existing cardiac diagnosis, 3 were cancelled. Seven of the patients were ‘deconditioned’; 5 were cancelled as a result.

**Conclusion** This algorithm suggests that 8 patients were considered high risk as a result of cardiorespiratory disease and a further 7 as a result of deconditioning. Appropriate specialty review and intervention or an exercise prescription pre-operatively might allow patients to improve their operative risk and therefore to proceed to major surgery.

**REFERENCES**
Poster sessions

P255 Reproducibility of Lung Clearance Index (LCI) in Clinically Stable Adults with Mild Cystic Fibrosis (CF)

1AR Horsley, 1A Shawcross, 2M Oladapo, 3A Maina, 5C Cunningham, 4AM Jones, 1J Smith, 6F Gilchrist. 1University of Manchester, Manchester, UK; 2Royal Manchester Children’s Hospital, Manchester, UK; 3Royal Hospital for Sick Children, Edinburgh, UK; 4Manchester Adult Cystic Fibrosis Centre, Manchester, UK; 5Royal Stoke University Hospital, Stoke, UK

Background In order for lung clearance index (LCI) to be a clinically useful measurement, a better understanding is required of short-term variability. LCI-SEARCH is a longitudinal study in children and adults with CF, with LCI measured at each clinical review using a portable closed-circuit wash-in system (www.lci-search.com). Here we report initial LCI repeatability from the adult cohort.

Methods LCI measurements were performed in triplicate using a closed-circuit wash-in method (Horsley et al. ERJ open). The most recent paired LCI measurements were included providing they were within 6 months of each other, the patient was deemed clinically stable by a physician and the patient scored <2 on a 4-point respiratory symptom score. Repeatability was assessed by Bland-Altman analysis.

Results Of 40 CF adults, paired data were available on 21 (7 subjects had completed only 1 assessment, 1 withdrawn, 11 clinically unstable). These 21 subjects (14 male) completed a median of 5 LCI measurements each (range 2–11), a median of 84 (range 42–189) days apart. Mean age was 28 yrs, mean FEV1 82% predicted, 11 pancreatic sufficient, 11 had never had pseudomonas infection.

Mean (SD) LCI at visit 1 was 8.68 (2.96) vs 8.73 (2.81) at visit 2 (p = ns). Median coefficient of variation for LCI was 3.9% (visit 1) and 4.2% (visit 2). Mean change in LCI between visits was 0.05 (1% of baseline LCI). 95% limits of agreement (LOA) were –1.1 (–13.7)% to 1.0 (11.6)% of baseline LCI. In this very mild cohort, 7 patients had normal LCI (<7); exclusion of these did not substantially alter LOA (–13.9 to 13.1%). There was greater variability in FRC: mean bias –1.5% of baseline (LOA 30 to –33%).

Conclusions Even in this very mild cohort of CF adults, patients are frequently unwell or more symptomatic at routine review. Within-visit repeatability was good, and similar to previous reports. When clinically stable, LCI variability over a period of up to 6 months was approximately ±10%. Addition of more adult as well as paediatric data to this assessment will widen the applicability of these confidence intervals.

P256 Respiratory Muscle Strength Measurements in Primary School Children

NTS Gharbawi, EA Gaillard, M Viskaduraki, CS Beardsmore. University of Leicester, Leicester, UK

Background Previous tests of respiratory muscle strength have rarely included measurements of inspiratory pressure. As part of a study looking at ethnic differences in respiratory muscle strength, we have measured maximum inspiratory and expiratory pressures in primary school children.

Aim We sought to determine the success rate and within-test repeatability of respiratory muscle strength measurements.

Methods We measured spirometry, height and weight and respiratory muscle strength by measuring maximal inspiratory and expiratory pressure (MIP and MEP) using Carefusision Vynus in children aged 5–11 yr. Children breathed through a mouthpiece and pneumotachograph attached to a shutter, while wearing a noseclip. After a period of tidal breathing the child breathed in to total lung capacity and then tried to exhale forcibly against the shutter. We measured maximal (peak) expiratory pressure (MEP).

For measurements of MIP the child exhaled towards residual volume before making an inspiratory effort against the occlusion. Manoeuvres were excluded if the peak pressures were less than 3.50 kPa. We reported the largest pressures recorded, provided that the second-best was no more than 20% below the best. We calculated the percent difference between best and 2nd best manoeuvres and compared mean percentage differences in MIP and MEP.

Results Two hundred and thirty-one children were studied. We obtained MIP on 199 and MEP on 216, and paired data for MIP and MEP on 165 (87 boys and 78 girls). Overall, MIP was higher than MEP (mean (SD) MIP = 7.26 (1.92) kPa, MEP = 6.64 (1.76) kPa, p = 0.002). However, MEP tended to be bigger than MIP when the values were smaller (in the younger, smaller children) (Figure). There was no significant difference between% difference MIP and% difference MEP (mean (SD) 5.50 ± 4.29 and 4.68 ± 3.96 kPa respectively, p = 0.07).

Conclusion The success rates of MIP and MEP measurements were 94% and 86% respectively, suggesting that MIP was easier for the children to perform. The success rate for paired measurements was 71%. The repeatability of inspiratory and expiratory pressures was not different. We speculate that the change with age between which measurement was greatest (MIP or MEP) may reflect dysanaptic muscle development.
UNDERSTANDING THE EFFECTS ON LUNG FUNCTION OF CHEST BINDER USE IN THE TRANSGENDER POPULATION

1RJM Cumming, 2K Sylvester, 2J Fuld. 3University of Cambridge, Cambridge, UK; 4Addenbrookes Hospital, Cambridge, UK

10.1136/thoraxjnl-2016-209333.400

Introduction Chest binders are garments used for compression of breast tissue by transgender individuals. Deleterious consequences of binder reported include shortness of breath with associated reduced exercise tolerance and speech difficulties; some have suggested lung function is monitored in users of chest binders. We conducted a study to investigate any respiratory deficits caused by chest binders as currently used in the transgender population.

Methods We recruited 20 participants from the transgender community. All were assigned female at birth. Ages ranged from 19–47 with median age 22; 4 were current smokers and 4 had mild to moderate asthma. All were habitual users of chest binders. Participants underwent spirometry testing and measures of chest circumference and posture with and without their own binder. The order of testing with or without the binder was random. Ethics approval was granted by the University of Cambridge.

Results Table 1 shows abnormal baseline lung function. The median FEV1/FVC is abnormally high but not acutely influenced by the binder. The standard residual of all forced spirometric values was significantly (p < 0.001) below predicted values (based on sex assigned at birth); peak expiratory flow (PEF) values were also lower than predicted. There was a significant reduction in expiratory vital capacities, both SVC and FVC (p < 0.01) when the binder was on but no other significant acute change. On average chest circumference was reduced by the binder. There was no average change in thoracic kyphosis due to high variability.

Conclusions Transgender individuals using chest binders have abnormal lung function. The acute effect of wearing the binder appears to be an overall volume reduction with little other change. Abnormal lung function in the population may indicate a chronic effect of binder usage or generally poor respiratory health. However, due to the small size and timeframe of the study no control population was tested and thus a systematic error cannot be ruled out.

INFORMATION LUNG FUNCTION TESTING: A NEW APPROACH USING A RAPID, PORTABLE SYSTEM FOR MEASURING LUNG CLEARANCE INDEX (LCI) IN HEALTH AND DISEASE

1A Shawcross, 1CS Murray, 2J Kirkby, 3J Miles, 4K Pike, 5S Ree, 6P Aurora, 7A Horsley. 1University of Manchester, Centre for Respiratory Medicine and Allergy, Manchester, UK; 2Respiratory, Critical Care and Anaesthesia Section, Institute of Child Health, UCL, London, UK; 3Lung Function Unit, Great Ormond Street Hospital for Children, London, UK

10.1136/thoraxjnl-2016-209333.401

Introduction Lung clearance index (LCI) is a sensitive measure of lung disease in infants, with potential applications in clinical practice and research. However, measuring LCI in infants is technically challenging and there is no simple method of assessing LCI outside of specialist research laboratories in this population.

We have previously described an alternative method of measuring LCI, in which expired gas is collected and analysed to derive functional residual capacity (FRC) and LCI without directly measuring flow. This eliminates one of the major technical challenges, whilst also reducing the system’s dead space. This method is highly accurate in vitro, with a mean accuracy of FRC measurement to within 1%, down to FRC of 100ml. The method does not require large external gas tanks, and washout is performed breathing room air, making the system fully portable.

Aim To assess the performance of this method in vivo.

Method Healthy controls and infants with CF are currently being recruited to undergo LCI measurement using this method. Practical applicability of the system is determined by the number of successful tests and within-subject repeatability, defined as coefficient of variation (CV%) of same-visit repeats. Comparison will be made with LCI measurements obtained using a respiratory mass spectrometer, currently considered the gold standard for infant LCI measurement.

| Abstract P257 Table 1 Median spirometry values acquired with the binder off vs. on. A reduction in vital capacity is seen with the binder on. |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
|                | FVC (litres)    | FEV1 (litres)   | FEV1/FVC (%)    | PEF (C0)       | SVC (litres)    | Median (SR)    |
| Off            | On              | Off            | Off            | On              | Off            | Off            |
| Median         | 4.35            | 4.29           | 3.46           | 3.53            | 0.82           | 0.82           |
| Median (% Pred.)| 87.7            | 87.0           | 87.0           | 87.0            | 87.0           | 87.0           |
| p value        | 0.0062          | 0.0701         | 0.3603         | 0.2349          | 0.0008         | 0.0008         |

REFERENCE

Results To date, 10 healthy controls (mean age 53 weeks) and 2 infants with CF (mean age 55 weeks) have successfully undergone LCI measurement using this method. Mean LCI in controls was 6.62 (range 5.79–7.91). Mean within-subject CV% was 5.9%. Mean LCI in infants with CF was 7.63 (CV 5%).

Conclusion Preliminary data suggest this is a feasible and reproducible method of performing LCI in infants. Results in both infants with CF and controls fall within ranges predicted by the respiratory mass spectrometer and within accuracy limits set by international guidelines. This could provide a more accessible alternative to current technologies, enabling this test to be offered in more centres.

REFERENCES

COST ANALYSIS OF IMPLEMENTING A PE PATHWAY INCORPORATING 3-LEVEL WELLS SCORING, PERC RULES AND AGE-ADJUSTED D-DIMERS
A Mahmood, C Durrans, S Naik, M Anwar. Princess Alexandra Hospital, Harlow, UK
10.1136/thoraxjnl-2016-209333.402

Background Acute pulmonary embolism (PE) is a common presentation. Currently NICE recommends 2-level Well scoring, which may over-investigate patients leading to unnecessary anti-coagulation and contrast-related risks and significant financial costs. We investigated whether further risk stratification using a combination of 3-level Wells scoring, PERC rules and age-adjusted D-dimers could minimise costs and enhance patient safety.

Methods Retrospective analysis of patients who underwent CTPA and had complete data between September 2014 and August 2015 was carried out. Wells scores, PERC scores and age-adjusted D-dimers were calculated and compared against CTPA findings.

Results Out of 1174 patients who underwent CTPA, 1158 had complete data set. Application of PERC rules to low-risk patients (Wells score 0–1; n = 311, 27%) would have avoided 64 CTPAs, but missed 3 PEs, with a 95% sensitivity (95% CI: 0.85–0.97), 24% specificity (95% CI: 0.19–0.30), and avoided 56 D-dimers.

For intermediate-risk patients (Wells score 2–7), age-adjusted D-dimers would have avoided 265 CTPAs but missed 32 PEs, with an 81% sensitivity (95% CI: 0.74–0.86), 50% specificity (95% CI: 0.45–0.55). High-risk patients should proceed directly to CTPA.

The combination of 3-level Wells scoring, PERC rules, and age-adjusted D-dimers would have avoided 450 CTPAs (39%) but missed 39 PEs (8%), with an estimated financial saving of at least £255,150 (local CTPA tariff £567). Non-age adjusted D-dimers would have reduced this avoiding 132 CTPAs (11%), and missing only 7 PEs (5%). Further saving would have resulted from avoiding D-dimer testing in low risk PERC negative patients, and high risk patients.

Conclusion The use of a PE algorithm incorporating multiple clinical assessment tools results in a pathway which can help rationalise the number of CTPAs performed and D-dimers requested, without significantly increasing the proportion of missed PEs.

REFERENCES

Pneumonia and Bronchiectasis: Why Fore and Where to

P260 THE UTILITY OF ATYPICAL PNEUMONIA SCREENING IN COMMUNITY ACQUIRED PNEUMONIA: THE LEICESTER EXPERIENCE
JA Bennett, S Robinson, R Rupesinge, J Skeemer, D Jenkins, G Woltmann. Glenfield Hospital, Leicester, UK
10.1136/thoraxjnl-2016-209333.403

Introduction Microbiological testing for atypical pathogens in patients attending hospital with community acquired pneumonia (CAP) is recommended for moderate or severe disease (NICE CG191 2014) or for patients failing to respond to treatment. Although it is unclear whether testing improves outcome even in severe disease, many patients have such tests performed regardless of severity. Having revised our pathways for assessment, treatment and documentation of patients with community acquired pneumonia we hypothesised that testing for atypical organisms has no impact on treatment decisions for these patients.

Method We retrospectively identified all patients with a diagnosis of CAP who had investigations for atypical microbiology, September 2013 to May 2014, via our pneumonia database. We assessed CURB-65 score, atypical microbiology results and laboratory costings. The notes for all patients with positive atypical microbiological results were reviewed.

Results 343 patients were identified for whom 329 were analysed.

329 patients generated 991 samples in total (825 serum, 165 urine antigen, 1 urine virology) at a laboratory cost of £5,594.29.

Five samples were positive, one for urine legionella antigen. Greater than 50% of serological samples had no second (paired) sample sent.

There was no correlation between CURB-65 scores and requesting of atypical microbiology requesting.

One patient with positive legionella antigen had prolongation of treatment from 5 days to 14 days.

No other patients had treatment changes as a consequence of atypical microbiological testing.

Conclusion Atypical microbiological testing, in hospital, for CAP patients is commonly performed at significant cost with minimal clinical utility. We recommend that non-selective serological sampling is abandoned. The impact of legionella urinary antigen testing on outcome in moderate and severe cases requires a prospective study.
Streptococcus pneumoniae (pneumococcus) is a major cause of morbidity and mortality worldwide. To date 93 capsular serotypes of pneumococcus have been described, but many of these are rarely found in disease. Currently vaccines are targeted at between 7 and 23 of the most common circulating serotypes. However, with the uptake of any pneumococcal serotype based vaccine the risk of serotype-replacement and an increase in disease caused by non-vaccine serotypes remains. This highlights the importance of determination of the serotype responsible for the infection.

The diagnosis and subsequent serotype surveillance of pneumococcal infection relies heavily on culture techniques which are known to be insensitive, particularly in cases of non-invasive disease. There are, therefore, potentially many pneumococcal infections from which a culture is never obtained. In the many cases of pneumococcal disease from which a culture is obtained, but does not give serotype information. There are, therefore, many pneumococcal infections that are currently being incompletely diagnosed.

Previously described serotype-specific urine assays covering mainly conjugate vaccine serotypes, give no very little information about circulating non-vaccine serotypes and are currently only available in one or two specialist laboratories.

Our laboratory has just completed initial development of an extended range antigen capture Luminex based assay to detect S. pneumoniae serotype specific antigen in urine samples using highly purified human, full length monoclonal antibodies. The assay covers 24 different serotypes/groups plus C-polysaccharide, including all the currently available conjugate vaccine and 23-valent polysaccharide vaccine types plus some cross-reactive serotypes.

We have validated the assay for sensitivity, specificity and reproducibility using spiked urine samples and a panel of BinaxNOW tested clinical urine specimens, some of which were from patients from whom a pneumococcal isolate was also cultured. The results for the validation will be presented.

This assay can be extended to testing other clinical samples such as cerebrospinal and pleural fluids and with development has the potential to greatly improve serotype-specific surveillance in the many cases of pneumococcal disease from which a culture is never obtained.

### Abstract P260 Table 1

<table>
<thead>
<tr>
<th>Score</th>
<th>Not detected</th>
<th>Detected</th>
<th>No result or comment</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>CURB 0</td>
<td>65</td>
<td>5</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>CURB 1</td>
<td>57</td>
<td>5</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>CURB 2</td>
<td>72</td>
<td>13</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>CURB 3</td>
<td>62</td>
<td>12</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>CURB 4</td>
<td>14</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>CURB 5</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Not recorded</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not in database</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOTAL</td>
<td>592</td>
<td>87</td>
<td>32</td>
<td>3</td>
</tr>
</tbody>
</table>

*Eletu, Sheppard, Thomas, Smith, Lit, Fry. Respiratory and Vaccine Preventable Bacterial Reference Unit, London, UK; Department of Biology, University of Washington, Seattle, USA; Oklahoma Medical Research Foundation, Oklahoma City, USA.

10.1136/thoraxjnl-2016-209333.404

**P261 DEVELOPMENT OF AN EXTENDED SPECIFICITY MULTIPLEX IMMUNOASSAY USING HUMAN MONOCLONAL ANTIBODIES FOR DETECTION OF STREPTOCOCCUS PNEUMONIAE SEROTYPE-SPECIFIC ANTIGEN IN URINE**

Streptococcus pneumoniae (pneumococcus) is a major cause of morbidity and mortality worldwide. To date 93 capsular serotypes of pneumococcus have been described, but many of these are rarely found in disease. Currently vaccines are targeted at between 7 and 23 of the most common circulating serotypes. However, with the uptake of any pneumococcal serotype based vaccine the risk of serotype-replacement and an increase in disease caused by non-vaccine serotypes remains. This highlights the importance of determination of the serotype responsible for the infection.

The diagnosis and subsequent serotype surveillance of pneumococcal infection relies heavily on culture techniques which are known to be insensitive, particularly in cases of non-invasive disease. There are, therefore, potentially many pneumococcal disease cases where an isolate for serotyping is never obtained. In the many cases of pneumococcal disease from which a culture is obtained, but does not give serotype information. There are, therefore, many pneumococcal infections that are currently being incompletely diagnosed.

Previously described serotype-specific urine assays covering mainly conjugate vaccine serotypes, give no very little information about circulating non-vaccine serotypes and are currently only available in one or two specialist laboratories.

Our laboratory has just completed initial development of an extended range antigen capture Luminex based assay to detect S. pneumoniae serotype specific antigen in urine samples using highly purified human, full length monoclonal antibodies. The assay covers 24 different serotypes/groups plus C-polysaccharide, including all the currently available conjugate vaccine and 23-valent polysaccharide vaccine types plus some cross-reactive serotypes.

We have validated the assay for sensitivity, specificity and reproducibility using spiked urine samples and a panel of BinaxNOW tested clinical urine specimens, some of which were from patients from whom a pneumococcal isolate was also cultured. The results for the validation will be presented.

This assay can be extended to testing other clinical samples such as cerebrospinal and pleural fluids and with development has the potential to greatly improve serotype-specific surveillance in the many cases of pneumococcal disease from which a culture is never obtained.
Community acquired pneumonia (CAP) is a leading cause of admission and mortality. CURB-65 is the traditional risk stratification score. This can under predict severity in the young and does not predict requirement for higher level care. Combining CURB-65 with lactate can improve this.\textsuperscript{1} We reviewed CAP admissions over one month to determine if lactate improved risk stratification.

CAP patients were identified via coding. Authors reviewed admission chest radiographs and reports to confirm CAP. CURB-65 score was calculated from the electronic patient record (EPR), and electronic discharge letters. Lactate values were identified from Emergency Department documents scanned into EPR.

Accuracy of coding and mortality in a wrongly coded group was a secondary measurement. A LAC–CURB score of low, medium or high was allocated.

138 episodes of CAP were coded. 89 were confirmed CAP. Mean age was 71.2 yrs (21–98). CURB-65 score was available in 87. 45 scored CURB-65 0–1 with 2 deaths (4.4%). 24 were CURB-65 2, with 8 deaths (33.3%) and 6 of 18 CURB-65 3–5 patients died (33.3%).

A lactate value was available in 52. 16 had a low LAC-CURB score with 0 deaths and 1 ICU admission. 23 had a medium score, with 3 deaths (13%) and 2 ICU admissions. 13 had a high LAC-CURB score, with 4 deaths (31%) and 1 ICU admission. In 4 patients it was the lactate value that increased the risk category from a medium CURB-65 score to a High LAC-CURB score. All 4 were admitted to ICU, with 2 deaths. Length of stay did not alter significantly with CURB-65 or LAC-CURB, but increased with severity. Diagnoses were available in 45 of the 49 patients coded incorrectly as CAP with a 17.78% mortality rate, identical to the CAP group.

Mortality was higher for medium and high CURB-65 patients, but a difference between them was only seen when the LAC-CURB score was applied. A high lactate identified patients in the medium CURB-65 group who died or required higher level care. Patients wrongly coded as CAP also have a high mortality.

\textbf{REFERENCE}

\textsuperscript{1} Chen YX. Thorax 2015;70(5).

\textbf{P264 PREDICTING MORTALITY IN HOSPITAL ACQUIRED PNEUMONIA: A MULTIVARIATE ANALYSIS}

CB Morris, SV Valapraya, AM McCance, AM Turner, DS Dosanjh. Heart of England NHS Foundation Trust, Birmingham, UK; University of Birmingham, Birmingham, UK

Background Hospital Acquired Pneumonia (HAP) is defined as lung infection in a non-intubated patient with new infiltrates on chest X-ray, >48 hours after hospital admission. Prediction scores exist for Community Acquired Pneumonia (CAP); no such scores exist in HAP. We aimed to identify features which are predictive of mortality in HAP.

Methods All cases coded as HAP in Heart of England Foundation NHS trust in 2013 trust were identified (293 cases). For each of these cases the chest X-ray (including radiologists report) was reviewed; if X-ray did not show infiltrates consistent with pneumonia, cases were excluded leaving 153 cases for whom case notes were reviewed. Cases were excluded if diagnosis of HAP...
was made <48 hours after admission leaving 136 cases. Data was collected regarding demographics, co-morbidities, investigations, observations, mortality during admission and within 12 months.

Univariate analysis was conducted to identify features associated with mortality. Multivariate analysis was completed using identified associated features.

Results
Sixty-four cases (47.0%) died during admission; and a further 32 within 12 months (70.5%).

Demographics: Mean age was 81.6 years (range 52–98); mean number of co-morbidities was 5 (range 0–11). Mean haemoglobin was 110.9 g/dL. The mean white cell count (WCC) was 13.68 × 10⁹/L (range 1.87–51.7 × 10⁹/L). Mean urea was 10.5 mmol/L (range 1.9–6.1 mmol/L).

Univariate analysis: Table 1 shows the results of the univariate analysis.

Multivariate analysis: Only combination of raised urea and raised or low WCC were significantly associated with mortality (p = 0.024). Adding features of age, observations and co-morbidities did not improve prediction of mortality.

Conclusion
Prediction of mortality in HAP is more complex than in CAP. On multivariate analysis, raised urea and raised or low WCC were predictive of mortality. Other features including age, number of comorbidities and observations at the time of diagnosis were not associated with mortality. This perhaps reflects our elderly cohort, with the majority having multiple co-morbidities, with very small numbers aged <65 years or with few co-morbidities. Further work with a larger dataset is ongoing.

**Abstract P265 Table 1**

<table>
<thead>
<tr>
<th>Feature and cut-off used</th>
<th>P-value</th>
<th>Odds Ratio and 95% Confidence Interval</th>
<th>P-value</th>
<th>Odds Ratio and 95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 65</td>
<td>0.376</td>
<td>1.51 [0.422-5.437]</td>
<td>0.295</td>
<td>1.707 [0.489-5.924]</td>
</tr>
<tr>
<td>&gt;5 co-morbidities</td>
<td>0.610</td>
<td>0.821 [0.396-1.699]</td>
<td>0.081</td>
<td>0.457 [0.185-1.107]</td>
</tr>
<tr>
<td>Haemoglobin &lt;120g/L</td>
<td>0.226</td>
<td>1.40 [0.689-2.847]</td>
<td>0.181</td>
<td>1.541 [0.713-3.330]</td>
</tr>
<tr>
<td>Urea &gt;7.8 mmol</td>
<td>0.095</td>
<td>2.663 [1.312-5.40]</td>
<td>&lt;0.001</td>
<td>3.412 [1.63-7.17]</td>
</tr>
<tr>
<td>White Cell Count (WCC) &gt;12 × 10⁹/L or &lt;4 × 10⁹/L</td>
<td>0.082</td>
<td>1.72 [0.870-3.401]</td>
<td>&lt;0.039</td>
<td>2.034 [1.37-3.067]</td>
</tr>
<tr>
<td>New confusion</td>
<td>0.821</td>
<td>0.882 [0.325-2.391]</td>
<td>0.030**</td>
<td>0.347 [0.117-1.00]</td>
</tr>
<tr>
<td>Respiratory rate &gt;20 breaths per minute</td>
<td>0.541</td>
<td>1.027 [0.510-2.067]</td>
<td>0.441</td>
<td>1.138 [0.542-2.389]</td>
</tr>
<tr>
<td>Pulse &gt;90 beats per minute</td>
<td>0.044**</td>
<td>1.921 [0.969-3.801]</td>
<td>0.030**</td>
<td>2.332 [1.029-4.420]</td>
</tr>
<tr>
<td>Systolic BP &lt;100 mmHg</td>
<td>0.439</td>
<td>1.226 [0.455-3.209]</td>
<td>0.595</td>
<td>1.026 [0.358-2.94]</td>
</tr>
<tr>
<td>Diastolic BP &lt;60 mmHg</td>
<td>0.415</td>
<td>0.844 [0.383-1.863]</td>
<td>0.439</td>
<td>0.862 [0.380-1.96]</td>
</tr>
</tbody>
</table>

**Represents significance at p <0.05. Fishers exact test on 2 × 2 table, using R statistical package. OR = Odds Ratio CI = 95% confidence interval**
Background Pneumonia is a leading cause of hospital admission. With mortality exceeding 18% (BTS CAP Audit 2013) the search for strategies to reduce this continues. Statins are receiving increasing attention for a potential role in improving survival from acute bacterial infections. MHRA guidance recommends that statins should be paused during treatment with a macrolide due to risk of myopathy and rhabdomyolysis.

We undertook a retrospective study to determine the frequency of concurrent statin and macrolide administration in patients diagnosed with pneumonia and whether concurrent use of a statin and macrolide antibiotic to treat pneumonia improved survival compared to stopping statin treatment, and whether concurrent use was safe and tolerable.

165 patient episodes were identified by searching for patients who were coded as having pneumonia and were prescribed a statin and macrolide. Data was collected on statin, dose, severity of pneumonia including intensive care admission, comorbidities, survival, renal and liver function.

Results 62% of the cohort continued a statin throughout pneumonia treatment. In the continued statin group survival to hospital discharge was 79% versus 64% in the group in whom the statin was paused (p = 0.034).

Severity of pneumonia (CURB score) was similar for both groups. Statin users were less likely to be admitted to intensive care (28% vs 46%, p = 0.0219). Charlson comorbidity index score was similar for the statin (6.4, IQR = 5–8) and non-statin (6.1, IQR = 5–8) groups.

There was no increased risk of acute liver, kidney injury or myopathy in the continued statin group.

Conclusion Continued statin use during treatment for pneumonia with a macrolide antibiotic is safe and may improve survival compared to stopping statin use. Current guidance on concurrent use of statins and macrolides should be reviewed.

P266 OUTCOMES FROM THE INTRODUCTION OF FUNGAL BIOMARKERS TO THE NEUTROPENIC FEVER PATHWAY IN A TERTIARY HAEMATOLOGY DEPARTMENT

R Swayne, D Enoch, S Aliyu, C Crawley, P Krishnamurthy, J Craig, G Follows, B Uttenthal, J Babar, CR Sander. Cambridge University NHS Foundation Trust, Cambridge, UK

Background Invasive fungal disease (IFD) frequently occurs in febrile neutropenic haemato-oncology patients (NHP). Until 2012 no biomarkers were available for the diagnosis of IFD in our Trust. The neutropenic fever pathway was modified to include serial serum Aspergillus galactomannan (GM), serum Aspergillus PCR (APCR) from national reference laboratory and Bronchoalveolar lavage (RAL) GM and APCR.

We compared 299 NHP who were investigated with the original pathway between October 2009 and April 2012 with 307 NHP investigated with the novel pathway between April 2013 and 2015. Primary end point was non-inferiority of novel pathway in terms of 12 month mortality. Secondary outcomes were 30 day mortality, length of treatment, length of stay and confidence of diagnosis based on EORTC/MSG criteria and concordance of the different biomarkers.

Abstract P266 Figure 1 Increased confidence in diagnosis of IFD according to EORTC/MSG criteria with novel pathway
Method Prospective patients (2013–15 cohort) were identified from ward lists. Retrospective patients (2009–12 cohort) were identified from haemato-onyology patients who had had blood cultures and were co-incidentally found to be neutropenic. Medical notes, drug charts, discharge letters and microbiology results were reviewed.

Results The 2 cohorts were well matched in terms of haemat-oncology diagnosis. The 2009/12 cohort included 561 episodes, with 333 CT chests and 62 bronchoscopies compared to 508 episodes, 288 CT chests and 86 bronchoscopies in 2013/15 group. 12 month mortality was 42% in 2009/12 versus 34% in 2013/15 cohort. 30 day mortality was 11% for both cohorts. There was no significant difference in length of antifungal treatments, although 24% switched to voriconazole following positive biomarkers.

Concordance between serum and BAL GM was 14.8% and APCR was 6.3%. Concordance between serum GM and APCR was 7% and between BAL GM and PCR was 41%.

Confidence in diagnosis of IFD increased with the novel pathway See Figure 1.

Conclusion The introduction of a novel NF pathway was found to be non-inferior in terms of 12 month and 30 day mortality. Although there was increased confidence in the diagnosis of IFD, this did not translate to reduced antifungal treatment, although it did influence switching to voriconazole and secondary chemoprophylaxis. Negative serum GM and PCR did not rule out the diagnosis of IFD and BAL biomarkers were more sensitive than serum ones.

REFERENCE

P267 DLCO PREDICTS DISEASE SEVERITY AND MORTALITY IN BRONCHIECTASIS
MJ McDonnell, M O’Mahony, D Breen, JJ Gilmartin, A O’Regan, RM Rutherford. Galway University Hospitals, Galway, Ireland
10.1136/thoraxjnl-2016-209333.410

Background Few studies have assessed the role of lung diffusing capacity (DLCO%) in bronchiectasis. We sought to examine the relationship between DLCO% and clinical and radiological variables in a well-defined population of bronchiectasis patients to determine its potential prognostic significance and compare with FEV1%.

Methods Of 312 consecutive bronchiectasis patients attending our institution over a 3-year period, 204 patients were suitable for study inclusion. Exclusion criteria consisted of patients with cystic fibrosis or traction bronchiectasis, patients with missing data and patients with absent radiological evidence of bronchiectasis on independent expert thoracic radiologist review. Univariate analyses was performed using Pearson’s correlation. Backwards stepwise logistic regression analysis was subsequently performed to determine independent associations of DLCO% and FEV1%.

Results DLCO% strongly correlated with all measured lung function parameters FEV1%, FVC%, FEF 25–75% and FEV1/FVC ratio (all p < 0.001). Negative correlations were noted with age at diagnosis (p = 0.047), body mass index (p < 0.001) and number of comorbidities (p = 0.002). Significant symptom associations included SOB (p = 0.001) and fatigue (p < 0.001).

Reduced DLCO% was associated with higher MRCD scores (p < 0.001), higher number of hospitalisations on follow up (p = 0.015), higher BSI scores (p < 0.001) and increased mortality (p = 0.028). No correlations were noted with gender, smoking history, aetiology or bacterial colonisation of any form. Reduced DLCO% was associated with increased number of lobes (p = 0.004), and higher total Reiff and modified Bhalla HRCT scores (p = 0.001 and p < 0.001 respectively). The modified Bhalla was excluded from stepwise regression as unavailable in most clinical settings. Backwards elimination showed DLCO% to be significant in predicting BSI (p < 0.001), number of lobes (0.017) and mortality (p = 0.028). Comparatively, backwards stepwise regression of FEV1% showed significance in predicting BSI (p < 0.001), number of hospitalisations on follow up (p = 0.008), and mortality (p = 0.024). Separate regression models of DLCO% and FEV1% using modified Bhalla components as cofactors showed DLCO% to be associated with disease extent (p = 0.002), bronchial wall thickness (p < 0.001), bronchial wall dilatation (p < 0.001) and reduced parenchymal attenuation (p = 0.015); FEV1% was associated with bronchial wall dilatation only (p < 0.001).

Conclusion DLCO% predicts radiological disease, disease severity and mortality in bronchiectasis, independently of aetiology, and may identify patients with advanced disease who could benefit from intensive management.

P268 IS BRONCHIECTASIS SEVERITY INFLUENCED BY AETIOLOGY OR CO-MORBID AIRWAYS DISEASE?
TM Quinn, AT Hill. Royal Infirmary and University of Edinburgh, Edinburgh, UK
10.1136/thoraxjnl-2016-209333.411

Background There is increased interest whether aetiology and co-morbid airways disease influence bronchiectasis disease severity.

Methods We conducted a retrospective study of 400 patients attending a specialist bronchiectasis clinic in NHS Lothian, Edinburgh, UK between May 2013 and September 2014 and using multivariable models we identified independent risk factors that influenced bronchiectasis disease severity using the Bronchiectasis Severity Index. We adjusted for age, sex, smoking history, aetiology and presence of co-morbid airways disease (asthma and COPD).

Results 400 patients were included in this study. The mean age was 66.0 (13.9) years. 253 (63.2%) were female. The majority (77%) had idiopathic (53%) or post infective bronchiectasis (24%). Other aetiologies were: allergic bronchopulmonary aspergillosis 8%; immune/auto-immune 6%; interstitial lung disease 3%; ciliary defects 3%; and inflammatory bowel disease 3%. Co-existing airways disease was common but not the predominant diagnosis (36% had asthma and 19% COPD).

Independent risk factors for severe bronchiectasis (BSI ≥ 9) were age 70–79 (OR 6.3, p = 0.003), age 80 and above (OR 7.3, p = 0.003) and smoking (OR 1.02, p = 0.002). It was not influenced by presence of airways disease or aetiology.

Conclusion In conclusion, neither aetiology nor presence of airways disease was independent risk factors for severe bronchiectasis severity. Age was the strongest independent predictor for severe bronchiectasis severity.
Background *Pseudomonas aeruginosa* is an opportunistic pathogen that chronically colonises the lungs of bronchiectasis patients and is associated with a decline in lung function. Epidemic strains of *P. aeruginosa* including Liverpool, Manchester and Midlands-1, have been described in cystic fibrosis (CF) patients and have been associated with increased morbidity and mortality, but have not previously been described in bronchiectasis patients. This study aimed to establish if there was cross transmission of *P. aeruginosa* amongst bronchiectasis patients and if epidemic strains were present.

Material/methods During the period February 2013 to May 2014 *P. aeruginosa* isolates from sputum samples from bronchiectasis patients were collected. The samples were taken in both primary and secondary care. All isolates were epidemiologically typed using multiple-locus variable number tandem repeat (VNTR) typing. For 20 patients multiple isolates from the same sample were analysed and for 14 patients multiple samples were analysed. A strain-specific PCR to identify the Midlands-1 and Liverpool epidemic *P. aeruginosa* strains was used on a sub-set of isolates that had VNTR profiles related to known Liverpool and Midland-1 epidemic strains.

Results VNTR profiles were obtained for a total of 144 isolates from 84 patients. A total of 126 unique VNTR profiles were observed. Typing of multiple isolates from the same sample and the same patient revealed multiple types, with STRD > 3 in 10/20 isolates from the same sample and 14/15 of multiple samples from the same patient. A total of 3 patients were chronically infected with epidemic strains, one with Midlands-1 and two with Liverpool. All of these patients had had long stays on the cystic fibrosis ward where patients with the epidemic strains are nursed.

Conclusions Cross transmission of the *P. aeruginosa* epidemic strains from the CF population to the bronchiectasis patients occurred on several occasions. However, there is no evidence of cross transmission of non-epidemic strains amongst the bronchiectasis population. This study provides evidence for segregating bronchiectasis and cystic fibrosis patients to prevent acquisition of epidemic strains. Prospective data is required to see if patients develop *Pseudomonas aeruginosa* infection if seen in non-segregated clinic spaces.

**Abstract P270 Figure 1** Kaplan-Meier plot illustrating the survival of bronchiectasis patients, with S. maltophilia infection resolved (grey) and unresolved (black) subgroups. There is a statistically significant difference between the plots (log rank test; *p* < 0.001).
characteristics and outcomes of this patient group. Bronchiectasis patients with S. maltophilia were identified from microbiology records and demographic data was recorded from electronic patient information. Comparisons were made to a previously prospectively collected dataset of bronchiectasis patients without S. maltophilia growth.

There were 174 patients with S. maltophilia and bronchiectasis. Intravenous and oral antibiotics were taken by 38.7% and 48.1% of the cohort respectively in the 2 months prior to the first S. maltophilia culture. Patients were followed up for a median of 6 (2–11) years and the mortality was 28.7%. Infection resolved (3 negative sputa) in 119/174 patients with recurrence of infection in 32/119. Specific treatment for the S. maltophilia was given in 91/174 patients, however treatment did not significantly affect resolution. Failure of resolution was however significantly associated with mortality (p < 0.001) (Figure 1). In the year prior to S. maltophilia culture, 12.7% grew non-tuberculosis mycobacterium (NTM). In comparison with a separate bronchiectasis cohort, those with S. maltophilia had a lower FEV1 (59.2% vs 68.4%) and there was more immunodeficiency as the underlying aetiology (10.3% vs 2.38%). Persistent S. maltophilia has a poor outcome in bronchiectasis. It may act as a marker of disease severity and the requirement for antibiotics, and acquisition frequently follows antibiotic use. It was also associated with the isolation of NTM. The resolution of infection is common but is not related to treatment directed against the organism, however persistent infection is associated with increased mortality.
Clinical Characterisation of Idiopathic Pulmonary Fibrosis

Introduction and objectives The last comprehensive survey of UK respiratory disease epidemiology was the British Thoracic Society’s 2006 Burden of Lung Disease report. We performed an analysis covering 2004–2012. Findings pertaining to IPF are presented here.

Methods Prevalence and incidence rates were estimated from a primary care database (the Health Intelligence Network) representing ~5 per cent of the population, using a broad range of primary care codes considered to encompass the IPF definition. Mortality figures were derived from official government statistics. For international mortality comparisons and numbers of hospital admissions/inpatient bed-days we used WHO data.

Results An estimated 32,500 people in the UK live with IPF, a prevalence rate of about 50/100,000. This is more than double the previous estimate of 15/100,000. There are around 6,000 new cases diagnosed/year, greater than previous estimates of around 5,000. Overall, 5,300 people/year die from IPF, slightly more than the previous commonly accepted estimate of 5,000. There are nearly 9,000 admissions/year for IPF, accounting for around 1.3% of all admissions due to lung disease and 1.4% of all hospital bed days, despite IPF affecting less than 0.25% of people who have had a lung disease diagnosis. IPF is 50% more common in men, and killed 60% more men than women from 2008–2012. In this period, 13,974 men and 8,624 women died from IPF, broadly in line with previous estimates. Incidence increases with age, around 85% of diagnoses being made in people aged over 70. Prevalence is highest in Northern Ireland, north-west England, Scotland and Wales. IPF is least common in London. Incidence is not influenced by measures of deprivation.

Conclusions Although rare, IPF is considerably more common than previously recognised and represents a small but significant burden on NHS hospital services.

Introduction and objectives Idiopathic Pulmonary Fibrosis (IPF) is strongly associated with advanced age. Our aim is to identify if the baseline characteristics of patients aged >80 who are excluded from pharmaceutical trials differ compared to patients aged <80 years.

Methods Consecutively diagnosed IPF patients ≥80 (n = 61) and <80 (n = 320) presenting to the ILD Unit of the Royal Brompton Hospital from 1/1/2010 to 31/12/2013 were included in this analysis. Data regarding age, smoking status, pulmonary function tests including (FEV1, FVC, DLco and Kco) were extracted from medical records. All cases were discussed by an ILD multi-disciplinary panel for the purpose of assigning a consensus diagnosis.

Results The baseline characteristics of both study groups are summarised in Table 1. Patients were also grouped by smoking status; the smoking history of 10 patients in the <80 groups was unavailable.

We divided both groups to smokers and non-smokers. FEV1 and FVC did not differ between non-smokers from both study groups whereas were both significantly lower in the smokers aged <80 years than in smokers aged >80 years (74.44 ± 18.24 versus 86.34 ± 12.67 p = 0.0005 for FEV1 and 72.96 ± 20.77 versus 88.34 ± 13.68 p = 0.0001 for FVC). DLco and Kco did not differ between smokers and non-smokers.

Conclusion Patients with IPF aged ≥80 years present with higher spirometric values than those < 80 in particular when a history of smoking is taken into consideration. Mean FVC did not differ between the non-smoking cohorts in each age-separated group while baseline DLco and Kco were not different between the two study groups regardless of smoking status. The higher FVC in smokers with IPF aged >80 compared to younger smokers could be due to the concomitant presence of radiologically evident emphysema. This finding has clinical implications with respect to eligibility for NICE-approved anti-fibrotic treatment. Analysis of the extent of emphysema in these patients and further studies of a higher number of patients is underway.
COGNITIVE FUNCTION IN IDIOPATHIC PULMONARY FIBROSIS

1C Sharp, 1HI Adamali, 1AB Millar, 1JN Dodd, 1Academic Respiratory Group, University of Bristol, Bristol, UK; 2Bristol Interstitial Lung Disease (BILD) Service, North Bristol NHS Trust, Bristol, UK

10.1136/thoraxjnl-2016-209333.417

Introduction

Patients with Chronic Obstructive Pulmonary Disease (COPD) are known to have cognitive dysfunction and share many co-morbidities with those with Idiopathic Pulmonary Fibrosis (IPF). This led us to hypothesise that patients with IPF may also have cognitive dysfunction. To investigate this, we conducted a prospective, observational study examining cognitive function in IPF patients with normal oxygen saturations, comparing them to COPD and smoking controls.

Methods

Patients with IPF and oxygen saturations >88% in room air were recruited from outpatient clinics. Exclusion criteria were dementia, neurological disease and illiteracy. Data from the NOVASC study were used for the COPD and control arms.

Pulmonary physiology results and demographic data, including educational and smoking status were collected. Patients completed the Montreal Cognitive Assessment (MoCA) and Hospital Anxiety and Depression Scale (HADS).

Group differences were assessed using unpaired t-test, analysis of variance and χ² test. Multivariable linear regression models were constructed to establish which variables contributed to observed variability in MoCA results.

Results

30 patients with IPF were recruited and were compared to 31 patients with COPD and 26 smoking controls. Results are shown in Table 1. MoCA scores were lower in both IPF and COPD groups and a greater proportion of IPF patients had scores in the “mild cognitive dysfunction” range of 18–25 (46.7%, compared to COPD 32.3%, control 11.5%, p = 0.018).

We also compared the IPF cohort to normative data in a population aged 70–79. The mean MoCA in this population was 27.5 (SD = 5.56, n = 53). The IPF patients had a significantly lower MoCA score (p = 0.035).

A multivariable linear regression model including diagnosis, age, education and FVC predicted 18.8% of the variance in MoCA (F (4,79) = 4.57, p = 0.002). Age was the only significant variable.

Conclusions

46.7% of non-hypoxaemic patients with ILD demonstrate at least mild cognitive dysfunction, some of this can be explained by the effect of age, but compared to published age adjusted normative data, there remains a significant reduction in cognitive function in IPF. This cognitive dysfunction has implications for decision making around treatments in IPF which may have significant side-effects.

Abstract P274 Table 1 Demographic and physiology results

<table>
<thead>
<tr>
<th>Variable</th>
<th>IPF (n = 30)</th>
<th>COPD (n = 31)</th>
<th>P (t-test)² between IPF/COPD</th>
<th>Control (n = 26)</th>
<th>P (t-test)² between IPF/Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (% male)</td>
<td>67%</td>
<td>52%</td>
<td>0.232</td>
<td>54%</td>
<td>0.327</td>
</tr>
<tr>
<td>Age</td>
<td>75.6 (5.8)</td>
<td>66.6 (7.1)</td>
<td>&lt;0.001</td>
<td>62.9 (9.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>25.4 (3.6)</td>
<td>28.4 (5.2)</td>
<td>0.011</td>
<td>27.4 (5.3)</td>
<td>0.111</td>
</tr>
<tr>
<td>Pack years smoking</td>
<td>15.1 (18.9)</td>
<td>41.6 (22.8)</td>
<td>&lt;0.001</td>
<td>29.2 (16.1)</td>
<td>0.005</td>
</tr>
<tr>
<td>&lt;12 years full-time education</td>
<td>33.3%</td>
<td>77.4%</td>
<td>0.001</td>
<td>80.8%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MoCA</td>
<td>25.2 (2.6)</td>
<td>25.5 (2.8)</td>
<td>0.649</td>
<td>27.2 (2.2)</td>
<td>0.005</td>
</tr>
<tr>
<td>HADS</td>
<td>7.6 (5.0)</td>
<td>9.5 (5.4)</td>
<td>0.150</td>
<td>6.6 (4.8)</td>
<td>0.457</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>89.6 (18.4)</td>
<td>57.1 (18.7)</td>
<td>&lt;0.001</td>
<td>99.6 (19.2)</td>
<td>0.052</td>
</tr>
<tr>
<td>FVC (%)</td>
<td>88.1 (24.4)</td>
<td>86.7 (20.5)</td>
<td>0.805</td>
<td>110.3 (19.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Ratio</td>
<td>0.8 (0.07)</td>
<td>0.54 (0.13)</td>
<td>&lt;0.001</td>
<td>0.69 (0.28)</td>
<td>0.036</td>
</tr>
<tr>
<td>DLCO (%)</td>
<td>51.7 (15.1)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>So2 (%)</td>
<td>94.7 (1.9)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

IPF – Idiopathic Pulmonary Fibrosis, COPD – Chronic Obstructive Pulmonary Disease, BMI – Body Mass Index, MoCA – Montreal Cognitive Assessment, HADS – Hospital Anxiety and Depression Scale, FEV1 – forced expiratory volume in 1 second, FVC – forced vital capacity, DLCO – diffusing capacity for carbon monoxide, So2 – Oxygen saturations
results were compared against one another using a paired t-test. Total of 46 sets of data collected.

**Results**

Patients felt they were given more information about their diagnosis (mean 5.15 – >9.08, p value < 0.0001), prognosis (mean 4.76 – >9.04, p value < 0.0001) and treatment options (mean 4.63 – >9.28, p value < 0.0001). Patients felt they had more control over their disease (mean 3.67 – >6.66, p value < 0.001) and more confidence they were being managed correctly (mean 4.39 – >8.52, p value < 0.001). Patients felt more satisfied with their care after being seen at an ILD specialist clinic (mean 6.04 – >9.44, p value < 0.0001). More patients strongly agreed information given met their expectations (7/45 – >36/45) and was delivered in a way that was clear and easy to understand (11/45 – >36/45). 87% (40/46) of patients strongly agreed there is more benefit in being seen at a specialist centre.

**Conclusion**

Evidence supports the utilisation of specialist centres to manage patients with ILD. Results show there is a significant improvement in patient understanding, experiences and satisfaction.

**P276 DEVELOPMENT OF PATIENT REPORTED EXPERIENCE MEASURE (PREM) FOR IDIOPATHIC PULMONARY FIBROSIS (IPF)**

1AM Russell, 2Sonecha, 3A Datta, 4H Hewitt, 2A Howell, 2A Elliott, 3M Wickremasinghe. 1National Heart and Lung Institute, London, UK; 3Roche Products Limited, Welwyn Garden City, UK; 4Northwick Park Hospital, London, UK; 2Imperial College NHS Healthcare Trust, London, UK

**Background**

Research into patient experiences of living with IPF has increased. A key challenge is how to use this data intelligently to enable commissioners and providers to improve the quality of services delivered to this group of patients. This project aims to develop an IPF-PREM informed by patients’ perceptions of their healthcare experiences. The IPF-PREM is underpinned by the NHS Patient Experience Framework (NPEF); 1 National Institute for Health and Care Excellence (NICE) Quality Standards (QS15 and 79) and aligned to national initiatives integrating Patient Reported Outcome Measures (PROMs) and PREMs into NHS care.

**Abstract P276 Table 1**

<table>
<thead>
<tr>
<th>NPEF domain</th>
<th>Focus group themes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respect for patient-centred values</td>
<td>Recalibrating quality of life and wanting feedback on PROMs data; impact of breathlessness on independence; the need to talk and the need not to talk to be respected</td>
</tr>
<tr>
<td>Coordination and integration of care</td>
<td>Challenges of managing other health issues and lack of social/fiscal support – administrative processes often a barrier</td>
</tr>
<tr>
<td>Information, communication and education</td>
<td>The need to talk to others affected with IPF; more information at the beginning; to understand choices in healthcare; information customised to specific needs</td>
</tr>
<tr>
<td>Physical comfort</td>
<td>Impact on activities of daily life and how to physically manage these – support with transitions to oxygen therapy; need for effective symptom relief</td>
</tr>
<tr>
<td>Emotional support</td>
<td>Better access to psychological/counselling services for self and caregivers; Value having telephone support; healthcare professionals responding promptly to requests for advice. Wanting and not wanting to know prognosis</td>
</tr>
<tr>
<td>Involvement of family and friends</td>
<td>Family may have different information needs – respecting patient’s wishes – support for wives; husband’s; partners often lacking – guilt associated with burden of caring</td>
</tr>
<tr>
<td>Transition and continuity</td>
<td>Do not want to be abandoned at end of life – feel better supported by clinicians known at diagnosis. Value copies of correspondence. Value having a key contact – particularly specialist nurse</td>
</tr>
<tr>
<td>Access to care</td>
<td>Having a progressive condition makes waiting to be seen by a specialist centre or for transplant assessment stressful. Travel presents challenges: dichotomy of wanting care close to home but with specialist input; too many health care appointments</td>
</tr>
</tbody>
</table>

**Methods**

A scoping exercise was undertaken with patients diagnosed with IPF on their journey through the healthcare system covering eight areas corresponding to the NPEF. 3 Twenty patients representing all stages of the disease trajectory participated in one of three focus groups. Transcripts underwent content and thematic analysis. Patient preferences were also sought on questionnaire design.

**Results**

A number of key themes emerged. See Table 1. Of particular importance were issues concerning access: to specialist centres, medication and primary care services; consistency of care to prevent confusion; coordination of care especially for patients with multi-morbidities and getting the right information at the right time in the right way. Information enabling practical self-management was highly valued. Overarching was the need for continuity of care close to home. Participants valued having a nurse to co-ordinate care and to talk to at all stages of the care pathway. The response categories patients were keen to avoid were visual images such as smiley faces.

**Conclusions**

The IPF-PREM will provide a valuable quality indicator for IPF service delivery at all stages of the disease trajectory complementing IPF PROMs. Implementation of the PREM will enable commissioners and providers to improve the quality of the services and the patient experience of care delivered across the wider inter-disciplinary team.

**REFERENCE**

1 DH 2011 NHS Patient Experience Framework.
SB time is not confounded by this limitation and may be a more reliable measurement of activity in patients with severe exercise limitation such as IPF.

Methods

Thirty-nine IPF patients wore a GENEActiv actiwatch continually for 7 days. Participants underwent measurement of forced vital capacity (FVC), diffusion capacity of carbon monoxide (DLCO), 6 minute walk distance (6MWD).

Results

Valid data was downloaded from 35 of the 39 participants (89.7%). Mean acceleration intensity recorded in the most active 5 hours of each day (M5; in milli-g) were 43.8 milli-g and time spent in SB was 551.7 minutes per day, higher than estimates of time in SB in similar age demographics in previous studies. Daily SB time correlated moderately with M5 values (pearson correlation $R^2 = 0.366$, p = 0.030). Only M5 values predicted time in SB. No variability in SB time was seen by day of the week.

There was a trend towards higher one and two year mortality with greater periods of time in SB.

Conclusions

Wrist-worn accelerometers reliably collected data and were well tolerated. IPF patients spent long periods of time in sedentary behaviours. Of the standard clinical measures used, 6MWD predicted daily activity but not SB time; no clinical measures predicted SB time. Increased time in SB with light activity may be a more achievable goal than increasing moderate or vigorous activity levels in IPF patients and improve outcomes.

DOES THE SIX-MINUTE WALK TEST PREDICT SURVIVAL AT ONE YEAR AND IN THE LONGER TERM IN PATIENTS IDIOPATHIC PULMONARY FIBROSIS (IPF)?

1J Herridge, 2K Yull, 1AH Kendrick. 1University Hospitals and University of West of England, Bristol, UK; 2University of West of England, Bristol, UK

Over 4000 new cases of IPF are diagnosed each year with a poor prognosis and median survival time of 3 to 5 years. Assessments of exercise performance using the 6-minute walk test (6MWT) have been shown to be useful in predicting survival in a variety of pulmonary conditions.

Aim

We wished to determine if indices of the six-minute walk test could predict survival in patients with IPF at one year and long-term survival.

Methods

We undertook a retrospective data analysis of patients with a confirmed diagnosis of IPF over the last 4 years. Data was obtained on 86 patients, who were divided into Group 1 – survivors ($n = 56$) and Group 2 – non-survivors ($n = 30$).

Indices obtained from the 6MWT included $\text{SpO}_2$, min, median $\text{SpO}_2$ rest, BORG scores, HR,rest and HR,max and distance walked. Spirometry, static lung volumes, and date of death were also recorded. Data are presented as median (IQR) in the format (Group 1 vs Group 2). Kaplan-Meier analysis was used to compared various indices and between groups.

Results

There was no significant differences between the two groups for FEV$_1$ (2.0 (0.58) vs 2.01 (0.55)), FVC (2.83 (1.16) vs 2.52 (0.88)) or TLC (4.19 (1.58) vs 4.09 (1.62)). From the 6 MWT, $\text{SpO}_2$,rest was not significantly different (95 (2) vs 94 (5.5)), nor were HRrest, HRmax or BORG scores.

There was a significant difference for $\text{SpO}_2$, min (90 (8) vs 84 (13); p < 0.01) and distance walked (380 (140) vs 340 (180); p < 0.05). Kaplan-Meier analysis was used to assess outcomes for distance walked of < or >250 m and 350 m and $\text{SpO}_2$, min < or >85% and 88%.
Abstract P278 Figure 1  Kaplan-Meier survival curve for SpO2 min <88% (red line) and >88% (blue line). The green dashed line plotted shows survival of 365 days of 90%. The blue and red dotted lines are the 95% confidence interval for survival.

For an SpO2 min cut-off of 85%, survival was 791 (<85%) and 1181 (>85%) days (p < 0.05; hazard ratio 3.356). With a cut-off of 88%, survival was 757 (<88%) and 1272 (>88%) days (p = 0.0012; hazard ratio 3.161). Survival at one year as 84% (<88%) and 91% (>88%) (Figure).

Distance walked was not significantly different at cut-offs of 250 m or 350 m.

Conclusions From this retrospective analysis, these results suggest that a cut-off for SpO2 min of 88% may be a useful predictor of survival at one year and in the longer term. Distance walked appears to contribute little to prediction of survival.

Abstract P279 Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Change from baseline</th>
<th>P value</th>
<th>Change from baseline</th>
<th>P value</th>
<th>Between group changes</th>
</tr>
</thead>
<tbody>
<tr>
<td>6MWT-D (m)</td>
<td>57.50 [11.25, 120]</td>
<td>0.027*</td>
<td>60 [30, 98.5]</td>
<td>0.027*</td>
<td>0.9</td>
</tr>
<tr>
<td>Borg-D</td>
<td>-1.00 [-1.20, 0.00]</td>
<td>0.059</td>
<td>-1.50 [-1.20, 0.00]</td>
<td>0.015*</td>
<td>0.9</td>
</tr>
<tr>
<td>(D-12)-D</td>
<td>-1.00 [-1.20, 0.00]</td>
<td>0.462</td>
<td>-1.50 [-1.20, 0.00]</td>
<td>0.026*</td>
<td>0.282</td>
</tr>
<tr>
<td>MIP-D (cmH2O)</td>
<td>15.00 [11, 25.50]</td>
<td>0.072*</td>
<td>3.50 [-2.50, 11.50]</td>
<td>0.207</td>
<td>0.043*</td>
</tr>
<tr>
<td>Sniff-D (cmH2O)</td>
<td>15.00 [5.50, 26.00]</td>
<td>0.025*</td>
<td>4.40 [-3.25, 11.25]</td>
<td>0.027*</td>
<td>0.142</td>
</tr>
<tr>
<td>CAT-D</td>
<td>-0.50 [-4.75, 1.50]</td>
<td>0.248</td>
<td>-1.50 [-4.25, 2.50]</td>
<td>0.500</td>
<td>0.9</td>
</tr>
<tr>
<td>(SGQ-D)-D</td>
<td>-10.61 [-14.5, -5.05]</td>
<td>0.025*</td>
<td>-8.8 [-21.2, -2.9]</td>
<td>0.075</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Introduction The 2013 ATS/ERS guidelines on Pulmonary Rehabilitation suggest that IMT confers significant improvements in various outcomes in chronic obstructive pulmonary disease (COPD). IMT may play a role in dyspnoea and exercise tolerance in patients with ILD; Feasibility of delivering an outpatient IMT programme for ILD is yet to be determined.

Aim The aim of this pilot-feasibility study was to assess the acceptability and practicality of delivering an outpatient IMT programme in patients with ILD.

Methods Randomised trial recruited 17 patients with ILD from St George’s Hospital chest clinic, London. Inclusion criteria were: ILD patients on stable medical treatment, with breathlessness MRC >3. 9 patients (intervention group); median (IQR) DLco predicted 44 [28, 45]% underwent H-IMT; exercised at 60% of sustained maximal inspiratory pressure (SMIP); 8 patients (control group) median (IQR) DLco 39.5 [24, 60]% underwent low intensity IMT (S-IMT); exercised at 15% of SMIP. Data collection included pre-post IMT in the following outcomes: six minute walk test (6MWT), quality of life (SGRQ-I), dyspnoea: (Borg and Dyspnoea-12), maximal inspiratory pressure (MIP) and sniff nasal inspiratory pressure (Sniff-P).

Results 76 patients were screened; 26 meet the criteria to participate. 19 (75%) consented to partake in the study. Completion rates for HIIMT was 89% (8/9), and 75% (6/8) for LIMT. HI-IMT-G exhibited significantly higher MIP compared to LI-IMT-G (p = 0.043); There were no significant between-group differences in the other parameters. Within group analysis demonstrated that: HI-IMT improved significantly on 6MWT, MIP, Sniff-P and SGRQ-I. LI-IMT, improved significantly on 6MWT, Borg and D-12 (Table 1).

Conclusions HI-IMT was well accepted and accepted by ILD patients, and it demonstrated improvements in measured outcomes; IMT requires close monitoring and input to enhance motivation; this type of training can only fit small groups of patients and the extra cost should be considered. IMT may be an alternative option to exercise training for ILD patients to ameliorate dyspnoea and combat exercise deconditioning; larger studies are required to explore effectiveness and cost effectiveness of IMT in ILD.

Abstract P278

FEASIBILITY OF AN 8-WEEK OUT-PATIENT INSPIRATORY MUSCLE TRAINING (IMT) PROGRAMME IN PATIENTS WITH INTERSTITIAL LUNG DISEASE (ILD)

1M Koulopoulou, 2S Greenwood, 2C Reilly, 3F Chua. 1Kingston University and St George’s University of London, London, UK; 2King’s College Hospital, London, UK; 3Royal Brompton Hospital, London, UK

10.1136/thoraxjnl-2016-209333.422

Abstract P279

P280 PULMONARY REHABILITATION (PR) FOR INTERSTITIAL LUNG DISEASE (ILD). DO PATIENTS’ PERCEPTIONS MATCH FUNCTIONAL OUTCOMES?

L Stanley, C Cobbett, E Morris, D Gibson, SV Fletcher. University Hospital Southampton NHS Foundation Trust, Southampton, UK

10.1136/thoraxjnl-2016-209333.423

Introduction ILD refers to a group of fibrotic lung conditions that differ in terms of treatment, prognosis and association. The NICE quality statement (2013) supports PR for patients with IPF, the most common form of ILD. There is no clear guidance for delivery of PR to ILD patients, so current practice is to extrapolate from the benefits of PR in COPD (Spruit et al., 2013), despite the differing pathophysiology.

Aim The focus of the study was to observe the patients’ perceptions of a modified ILD PR programme against functional and health related quantitative measures.
Introduction

Asbestosis is commonly considered to be associated with slowly progressive pulmonary fibrosis. However, there is limited recent data to support this opinion. We set out to analyse the change in pulmonary function test (PFT) over time in a cohort of outpatients with asbestosis.

Methods

Patients were recruited to the program either by self-referral or by ILD clinicians. Seven participants were recruited. The 6-week PR program consisted of 60 minutes exercise and 30 minutes education with the emphasis on strength training over endurance. Focus group interviews were used to collect qualitative data and analysed using an inductive approach utilising thematic analysis as a method.

Results

7 patients completed the programme (5M:2F, mean age 73.4). Initial qualitative analysis demonstrates psychological benefit from the sharing of disease experiences, prioritising exercise as a means of management, empowerment and understanding. 6MWT and Kings Brief ILD questionnaire showed no significant change pre and post PR, see Table 1. These quantitative results do not reflect patient perceptions of improved functional status.

Conclusion

Patients perceptions were positive regarding the content and impact it had on their education needs concerning their disease. The predominant perceived benefit was that of the comradery found in sharing experiences with other ILD patients. No firm conclusions can be drawn from this study regarding the effectiveness of PR for patients with ILD due to small numbers. It is unclear whether the tools used to assess functional and health measures are suitable to detect changes in outcomes post PR or whether the effects of an ILD PR programme are predominantly that of disease management and education, explaining the disparity observed between quantitative and qualitative outcomes. Further appropriately powered controlled studies could examine the impact of PR and in particular that of PR education specifically for ILD patients, as supported by Holland et al. (2015).

Abstract P280 Table 1

<table>
<thead>
<tr>
<th>Distance</th>
<th>PFT Mean differences pre and post scores for 6MWD and Kings ILD questionnaire</th>
</tr>
</thead>
<tbody>
<tr>
<td>12m</td>
<td>6MWD 12m +0.5, Kings ILD Questionnaire</td>
</tr>
<tr>
<td></td>
<td>Psychological Activities</td>
</tr>
<tr>
<td></td>
<td>Psychological Symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P281

ANNUAL CHANGE IN PULMONARY FUNCTION IN ASBESTOSIS

S Clarke, J Hoyle. North Manchester General Hospital, Manchester, UK

10.1136/thoraxjnl-2016-209333.424

Introduction

Asbestos is commonly considered to be associated with slowly progressive pulmonary fibrosis. However, there is limited recent data to support this opinion. We set out to analyse the change in pulmonary function test (PFT) over time in a cohort of outpatients with asbestosis.

Methods

Patients were identified retrospectively from a pool of clinic patients who had consented to participate in research. The diagnosis of asbestosis had been made on CT findings, history of asbestos exposure, exclusion of other causes of interstitial lung disease and agreement at occupational MDT. The PFT data from tests closest to the time of initial diagnosis were compared to the most recent PFT results. Parameters assessed were FEV1, FVC, VC, TLC and KCO. The values were expressed as percentage predicted to ensure adjustment for age, weight etc. Annual change was calculated by dividing the total change by the number of years elapsed between PFT. Smoking status was also documented.

Results

57 patients were identified with a diagnosis of asbestosis. 9 had only had 1 set of PFT (awaiting follow-up) and hence were excluded leaving 48 patients. The mean time difference between PFT was 3.0 years (range 0.2–6.1 years). In 21 cases TLC had not been measured in one or both PFT and in 10 KCO had not been measured.

Conclusions

As expected baseline FEV1 decreased with increased smoking exposure. The other parameters at baseline were lower in those with the highest smoking exposure with the exception of TLC which was more varied. The greatest rate of change was seen in KCO% predicted, consistent with previous research. Unexpectedly the groups demonstrating the maximal decline in KCO were those with a low (<20 pack year) smoking history (7.2% annual decline) followed by lifelong non-smokers (3.9% annual decline). Those with the heaviest smoking history showed a lower rate of decline in all parameters compared to both non-smokers and the population as a whole. KCO and TLC were not performed in those with the most severe disease due to breathlessness, thus these results are likely to be an under-estimate of lung function changes.
Conclusions Using ECCS, 50% of patients met the NICE criteria for anti-fibrotic treatment. When NHANES III and GLI are used, patient eligibility for treatment increases to 61% and 59% respectively. Interestingly both the NHANES and GLI equations decrease the % predicted, and those patients that are just above the 80% cut off when ECCS is used become eligible for treatment. These data question, the use of predictive FVC cut-offs in prescribing anti-fibrotic treatments in a progressive lung disease without providing a national reference standard, especially when the particular prediction equation used could significantly impact on patients’ eligibility for treatment.
Conclusion Structural changes from TBX may cause stenting of the airways from fibrotic tissue, holding them open during forced expiration. Our volume corrected PEF/FVC predicts reduced TLC and RV percent predicted, indicating reduced lung volumes and lung stiffness in patients with restrictive lung disease. The evidence of TBX on CT imaging suggests the hypothesis that airways are held open during forced expiration, allowing increased efficiency of lung emptying in patients with a PEF/FVC >2.0. The magnitude of the ratio did not correlate with TBX severity but further work to determine a cut off ratio to predict future fibrosis is required. This index may be of use indicate a value beyond which TBX is likely to be present.

REFERENCE

Abstract P283 Table 1 Patient demographics and PEF/FVC correlation results

<table>
<thead>
<tr>
<th>Demographics</th>
<th>PEF/FVC</th>
<th>PEF/FVC</th>
<th>Dependant</th>
<th>Independent</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 119</td>
<td>(mean ± SD)</td>
<td>(mean ± SD)</td>
<td>R</td>
<td>R²</td>
</tr>
<tr>
<td>&lt; 10</td>
<td>2.96</td>
<td>136.15</td>
<td>PEF/FVC</td>
<td>−0.792</td>
</tr>
<tr>
<td>&gt; 10</td>
<td>2.68</td>
<td>130.50</td>
<td>TLC (%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease Category</th>
<th>PEF/FVC</th>
<th>PEF/FVC</th>
<th>Dependant</th>
<th>Independent</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILD</td>
<td>1.13</td>
<td>59.90</td>
<td>PEF/FVC</td>
<td>−0.759</td>
</tr>
<tr>
<td>Obstructive</td>
<td>0.30</td>
<td>(9.41)</td>
<td>RV (%)</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>1.96</td>
<td>91.20</td>
<td>VA (%)</td>
<td>−0.665</td>
</tr>
</tbody>
</table>

*Patient demographics and PEF/FVC correlation results

P284 IDENTIFYING PATIENTS AT RISK OF ACUTE EXACERBATION OF IPF USING THE CPI SCORE

Introduction Disease course in IPF is punctuated by acute exacerbations, often termed acute exacerbations of IPF (AEIPF) and portends to a mortality of 80% within 3 months. The cause of AEIPF is poorly understood; and there is currently no effective treatment. There is an urgent need to understand the causes and to characterise the parameters that identify patients at risk of AEIPF. Because lung function (DLCO and FVC) and CT imaging are the most accessible (potential) methods for identification of patients at risk of AEIPF, we question if these could be used to identify patient at risk of AEIPF. We explored the utility of the CPI (composite physiological index) for this purpose.

Methods Patients with IPF diagnosed by clinico-pathological-radiological criteria, according to the 2011 ATS/ERS/JRS/ALAT guidelines, with definite or probable diagnosis of IPF were recruited over a one year period, and divided into stable (n = 12) and AEIPF (n = 8) groups. AEIPF was defined as: 1) deterioration in dyspnoea over 30 days or less 2) new airspace infiltrates on HRCT (with or without evidence of infection) 3) exclusion of pulmonary emboli and heart failure. Lung function (FVC and DLCO) and CPI at 12 months before recruitment and rate of change of FVC within these 12 months were determined.

Results and Discussion Patients with AE-IPF had a significantly higher CPI; (mean ± SD) – 62 ± 13 vs stable 45 ± 7; p = 0.001. In contrast, there was no significant difference in FVC levels between the two groups – 61 ± 4% predicted in AE-IPF group vs 72 ± 3% in stable; p = 0.07. CPI but not FVC or DLCO was worse 12 months prior to recruitment in the AEIPF group. Rate of loss in FVC in the year before AEIPF was not significantly different from those with stable disease.

Conclusions Early findings suggest that in contrast to DLCO and FVC, high CPI is associated with occurrence of AEIPF within a year. Rate of FVC loss did not correlate with AEIPF in this small study. CPI could be a more sensitive predictor for AEIPF than FVC and DLCO but larger numbers and a prospective study will be required to test this concept.

REFERENCE
1 Wells AU. AJRCCM 2003.

Drugs and Devices in COPD


Introduction The prospective, non-interventional DACCORD study collects data from a representative cohort of COPD outpatients across Germany who either initiated or changed COPD maintenance medication prior to entry. Initially, DACCORD consisted of two treatment groups (Glycopyrronium-based therapy vs. any other COPD maintenance medication with the exception of Glycopyrronium). Following the approval of LABA/LAMA fixed-dose combinations (FDC) in 2013, DACCORD was extended to follow an additional cohort of patients receiving any LABA/LAMA FDC over a period of 2 years.

Methods 5223 patients with complete baseline data (3815 LAMA/LABA FDC vs. 1408 standard treatment group) were analysed here. Baseline exacerbations were evaluated 6 months prior to study entry and were annualised for GOLD 2011 categorization; COPD symptoms were evaluated using the COPD Assessment Test (CAT) and the mMRC questionnaire. Prior and concomitant COPD medication were captured and analysed by substance class.

Results Baseline characteristics are summarised in Table 1. Based on FEVI assessment, approx. 75% of patients suffered from moderate to severe COPD. Less than a quarter of patients reported a history of exacerbations and only 6.7% experienced ≥2 exacerbations in the 6 months prior to study.
Poster sessions

Abstract P285 Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th>LABA/LAMA-FDC-based treatment (N = 3815)</th>
<th>Standard therapy without LABA/LAMA FDC (N = 1408)</th>
<th>Total Population (N = 5223)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>59.4</td>
<td>57.3</td>
</tr>
<tr>
<td>Height (cm), mean</td>
<td>170.4</td>
<td>170.0</td>
</tr>
<tr>
<td>Weight (kg), mean</td>
<td>80.3</td>
<td>80.6</td>
</tr>
<tr>
<td>BMI (kg/m²), mean</td>
<td>27.6</td>
<td>27.8</td>
</tr>
<tr>
<td>Age (years), mean</td>
<td>66.6</td>
<td>66.6</td>
</tr>
<tr>
<td>Age groups, &lt; 65</td>
<td>42.7%</td>
<td>42.8%</td>
</tr>
<tr>
<td>65–75</td>
<td>35.8%</td>
<td>33.6%</td>
</tr>
<tr>
<td>&gt;75</td>
<td>21.5%</td>
<td>23.7%</td>
</tr>
<tr>
<td>FEV₁ predicted (litr), mean</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAT total score, mean</td>
<td>18.9</td>
<td>18.6</td>
</tr>
<tr>
<td>mMRC total score, mean</td>
<td>1.7</td>
<td>1.7</td>
</tr>
<tr>
<td>Airflow limitation according to GOLD 2011, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>19.1</td>
<td>23.4</td>
</tr>
<tr>
<td>Moderate</td>
<td>51.7</td>
<td>50.9</td>
</tr>
<tr>
<td>Severe</td>
<td>25.2</td>
<td>22.7</td>
</tr>
<tr>
<td>Very severe</td>
<td>4.0</td>
<td>3.1</td>
</tr>
<tr>
<td>COPD severity according to GOLD 2011, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GOLD A</td>
<td>9.3</td>
<td>10.1</td>
</tr>
<tr>
<td>GOLD B</td>
<td>45.2</td>
<td>47.6</td>
</tr>
<tr>
<td>GOLD C</td>
<td>3.4</td>
<td>2.8</td>
</tr>
<tr>
<td>GOLD D</td>
<td>42.2</td>
<td>39.6</td>
</tr>
</tbody>
</table>

Abstract P286

COST-CONSEQUENCE OF FLUTICASONE FUROATE/ VILANTEROL 100/25MCG FOR THE MANAGEMENT OF COPD IN THE SPANISH NHS: AN ANALYSIS BASED ON THE COPD SALFORD LUNG STUDY

A Huerta, J Boucot, MT Driessen. GlaxoSmithKline, Brentford, UK
10.1136/thoraxjnl-2016-209333.429

Introduction

The Salford Lung Study (SLS) is an open label prospective randomised controlled effectiveness trial. The study was conducted in the UK between 2012 and 2015 in a population intended to be representative of everyday clinical practice and was intended to provide relevant evidence to support healthcare decisions in the management of Chronic Obstructive Pulmonary Disease (COPD) for clinicians, providers and policy makers. SLS investigated the effectiveness and safety of initiating treatment with fluticasone furoate/vilanterol (FF/VI) 100/25 mcg compared with continuing with usual COPD maintenance treatment (usual care). Compared with usual care, FF/VI statistically significantly reduced the annual rate of moderate and severe exacerbations by 8.41% (NNT = 7) in the intention to treat (ITT) population (>1 exacerbation in the previous 3 y; n = 2799) and in patients with >1 exacerbation in the previous 1 y; n = 2269). The objective of the present analysis is to estimate the economic impact of these results when applied to a Spanish setting.

Methods

An Excel based 1-year cost-consequence model was developed based on SLS results and from the Spanish National Health System (NHS) perspective. Mean annual rates of moderate/severe exacerbations were directly obtained from SLS (1.50 FF/VI and 1.64 usual care; ITT population). Serious adverse events were excluded from the analysis. Patients included in the analysis were diagnosed COPD patients >40 years old, being treated with a maintenance treatment and having a history of exacerbations (N = 232,730, estimated from Spanish prevalence data). Costs were estimated from Spanish public sources and encompassed annual retail drug costs (FF/VI: 627.26 €, usual care: 782.24 €) and COPD exacerbation management costs (344€: moderate event; 903 €: severe event). It was assumed that within one year the use of FF/VI would increase from 3% to 10%.

Results

Substituting usual care with FF/VI is likely to be associated with reduced COPD medication and exacerbation management costs. Total annual savings of 3,236,647 € were obtained for this population.

Conclusion

The decreased rate of exacerbations with FF/VI compared with usual care observed in SLS trial could be transferable, translating into potential healthcare savings for the Spanish NHS. SLS results may support informed healthcare decisions across different settings.

Abstract P287

PATIENT PREFERENCE FOR INHALATION DEVICES IN COPD: A COMPARISON OF THE BREEZHALER AND RESPIMAT DEVICES

1P O’Hagan, J Deede, V Boom, M Gasser, S Walda. Healthcare Consultancy, Maidenhead, UK; 2Novartis Pharma AG, Basel, Switzerland; 3Novartis Healthcare, Hyderabad, India; 4GfK Switzerland AG, Basel, Switzerland
10.1136/thoraxjnl-2016-209333.430

Background and aims

Difficulties and errors in the use of maintenance inhalation devices in COPD are common and can result in loss of control and an increased risk of exacerbations, hospitalisation and death. In this research, participants handled the

REFERENCE

Breezhaler® (BH) device (Novartis) and the Respimat® (RM) device (Boehringer Ingelheim) assessing each against a number of handling-related device attributes and against each other, to reveal their preferred device.

**Method**

240 maintenance device-naive respondents across Australia, Brazil, Germany, and Japan handled each device in a randomised order. Prior to handling the devices, participants ranked 22 handling-related device attributes according to their perception of importance for use. Participants familiarised themselves with the correct handling procedure for each device by consulting relevant 'Instructions for Use' and short training videos.

After device-handling, participants indicated their level of agreement with pre-defined handling attributes on a 7-point scale from 'I do not agree at all' to 'I completely agree'. In addition and after having handled both devices, participants expressed their preferred device.

**Abstract P287 Figure 1  Assessment of the devices against 22 devices handling-related attributes**

*The Top 2 box score encompasses participants who had a high level of agreement, that is, they either ‘fully agreed’ (=7) or ‘agreed’ (=6).*
Results Participants perceived BH to be superior to RM on 20 of 22 and similar on 2 of 22 handling-related device attributes (Figure 1). Participants found BH more intuitive to use (69:31), easier to use (60:40) and offering higher confidence that the full dose has been taken (58:42). Finally, there was a preference for BH over RM (56:44).

Conclusions The consistently higher preference for BH regarding device handling-related attributes and its position as the preferred device suggest that it offers an opportunity for improved compliance and therefore improved control of COPD.

Abstract P288 Table 1 Comparison of PIF rates (L/min) by COPD severity (per protocol set)

<table>
<thead>
<tr>
<th>Inhalation device</th>
<th>n</th>
<th>PIF rate, Mean (SE)</th>
<th>Comparison</th>
<th>Mean difference</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderate COPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breezhaler®</td>
<td>45</td>
<td>108.3 (3.81)</td>
<td>Breezhaler® vs. Elipta®</td>
<td>28.9</td>
<td>(23.68, 34.16)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezhaler® vs. HandiHaler®</td>
<td>57.5</td>
<td>(51.64, 63.36)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Elipta®</td>
<td>41</td>
<td>80.4 (2.64)</td>
<td>Elipta® vs. HandiHaler®</td>
<td>29.4</td>
<td>(25.62, 33.15)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HandiHaler®</td>
<td>45</td>
<td>50.8 (1.78)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe COPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breezhaler®</td>
<td>38</td>
<td>108.8 (3.67)</td>
<td>Breezhaler® vs. Elipta®</td>
<td>26.2</td>
<td>(19.73, 32.62)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezhaler® vs. HandiHaler®</td>
<td>51.3</td>
<td>(42.60, 60.31)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Elipta®</td>
<td>37</td>
<td>82.1 (4.03)</td>
<td>Elipta® vs. HandiHaler®</td>
<td>24.5</td>
<td>(16.99, 32.08)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HandiHaler®</td>
<td>38</td>
<td>57.5 (4.66)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very severe COPD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breezhaler®</td>
<td>10</td>
<td>99.2 (4.29)</td>
<td>Breezhaler® vs. Elipta®</td>
<td>28.1</td>
<td>(23.94, 32.32)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Breezhaler® vs. HandiHaler®</td>
<td>47.9</td>
<td>(32.75, 63.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Elipta®</td>
<td>10</td>
<td>71.0 (4.20)</td>
<td>Elipta® vs. HandiHaler®</td>
<td>19.8</td>
<td>(6.36, 33.18)</td>
<td>0.0087</td>
</tr>
<tr>
<td>HandiHaler®</td>
<td>10</td>
<td>51.3 (3.98)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Poor quality (flat line) inhalation profiles with erroneous PIF values were not considered in the analysis.

CI, confidence interval; COPD, chronic obstructive pulmonary disorder; PIF, peak inspiratory flow; SE, standard error

Background and aim Chronic and progressive nature of COPD necessitates the patients to regularly self-administer inhaled medication. Inhalation effort required and flow rates achieved through DPIs, are some of the important considerations while selecting...
dry power inhalers (DPIs). Here, we present the comparison of the peak inspiratory flow (PIF) rates achieved by COPD patients, with varying degrees of airflow limitation, through three types of DPIs (Breezhaler®, Ellipta® and HandiHaler®). We also assessed the effect of severity of airflow limitation on PIF rates.

Methods This randomised, open-label, multicentre and cross-over study recruited patients with moderate-to-severe airflow limitation (GOLD 2014) aged ≥40 years with a smoking history of ≥10 pack years. No active drug or placebo was administered during the study. After training the patients on correct use, inhalation flow profiles of patients were recorded using pressure tapped inhalers attached to a pressure transducer. For each patient, the inhalation profile with the highest PIF rate, out of three replicate inhalations per device, was selected for analysis. The primary analysis was based on the per-protocol set comprising 93 patients who completed all three inhalations per device. A paired t-test was performed to compare PIF means between each combination of devices.

Results In total, 97 COPD patients were randomised, of whom 96 completed the study and 93 patients (per-protocol set) were included in the analysis. The highest mean PIF rate (L/min ± SE) was observed with the Breezhaler® (107.5 ± 2.4), followed by the Ellipta® (80.0 ± 2.2) and the HandiHaler® (53.6 ± 2.1), in all patients (patients with moderate-to-severe airflow limitation). The mean PIF rate (L/min) achieved via the Breezhaler® was higher vs the Ellipta® (mean difference Δ = 27.7; p < 0.0001) and also vs the HandiHaler® (Δ = 53.9; p < 0.0001). Also, when assessed by severity of airflow limitation, the Breezhaler® device exhibited significantly higher PIF rate vs the Ellipta® and vs the HandiHaler® (Table).

Conclusions COPD patients with varying degree of airflow limitation (moderate-to-severe COPD) achieved the highest PIF rates via the Breezhaler® compared with the Ellipta® or the HandiHaler® inhaler.

P289 DRUG PRODUCT PERFORMANCE THROUGH INHALER LIFE USING A LAMA/LABA COMBINATION IN A DRY POWDER INHALER
J Plugge, U Basaldella, B Fyrns, T Pieper. Sofotec GmbH, Bad Homburg, Germany
10.1136/thoraxjnl-2016-209333.432

Introduction Studies to test the delivered dose uniformity (DDU) and fine particle dose (FPD) delivery over inhaler life were performed with aclidinium bromide 400 μg/formoterol fumarate dihydrate 12 μg inhalation powder in the Genuair™ inhaler.

Methods Developmental batches representative for commercial production were used. Samples were tested before and after cleaning of the mouthpiece with a dry tissue, after dosing at various orientations (+45°−45°) to the horizontal axis of the inhaler, or before and after dropping the inhaler in different orientations from a 1 m height. Test parameters included delivered dose uniformity (DDU) and fine particle dose (FPD).

Results All results for the LAMA (aclidinium bromide) and LABA (formoterol fumarate dihydrate) active ingredients were within the expected ranges and well inside the acceptance criteria applied during development (Figure 1). For aclidinium bromide, DDU mean values between 388 and 424 μg (specification range 320–480 μg), and single values between 343 and 464 μg (not specified) were observed. Mean FPD was tested within 156 and 175 μg (specification range 120–200 μg), and FPD single values between 136 and 198 μg (not specified). Results for the LABA active ingredient, formoterol fumarate dihydrate, were between 11.7 and 12.8 μg for DDU mean values (specification range 9.6–14.4 μg) and between 9.6 and 13.8 μg for DDU single values (not specified). Mean FPD was observed within 3.1 and 3.5 μg (specification range 2.2–4.5 μg), and FPD single values between 2.6 and 4.0 μg (not specified).

Conclusions The studies show that stable pharmaceutical quality can be guaranteed even if the device is used in different positions to the one explained in the patient information leaflet, after cleaning the mouthpiece, or after dropping the device in different orientations.

"Registered trademark of AstraZeneca group of companies; for use within the USA as Pressair® and Genuair™ within all other licensed territories.

P290 DRUG PRODUCT PERFORMANCE AFTER SIMULATED PATIENT HANDLING OF AN INHALATION POWDER USING A LAMA/LABA COMBINATION IN A DRY POWDER INHALER
J Plugge, U Basaldella, B Fyrns, T Pieper. Sofotec GmbH, Bad Homburg, Germany
10.1136/thoraxjnl-2016-209333.433

Introduction Three studies simulating various patient handling effects were performed with aclidinium bromide 400 μg/formoterol fumarate dihydrate 12 μg inhalation powder in the Genuair™ inhaler.

Methods Developmental batches representative for commercial production were used. Samples were tested before and after cleaning of the mouthpiece with a dry tissue, after dosing at various orientations (+45°−45°) to the horizontal axis of the inhaler, or before and after dropping the inhaler in different orientations from a 1 m height. Test parameters included delivered dose uniformity (DDU) and fine particle dose (FPD).

Results All results for the LAMA (aclidinium bromide) and LABA (formoterol fumarate dihydrate) active ingredients were within the expected ranges and well inside the acceptance criteria applied during development (Figure 1). For aclidinium bromide, DDU mean values between 388 and 424 μg (specification range 320–480 μg), and single values between 343 and 464 μg (not specified) were observed. Mean FPD was tested within 156 and 175 μg (specification range 120–200 μg), and FPD single values between 136 and 198 μg (not specified). Results for the LABA active ingredient, formoterol fumarate dihydrate, were between 11.7 and 12.8 μg for DDU mean values (specification range 9.6–14.4 μg) and between 9.6 and 13.8 μg for DDU single values (not specified). Mean FPD was observed within 3.1 and 3.5 μg (specification range 2.2–4.5 μg), and FPD single values between 2.6 and 4.0 μg (not specified).

Conclusions The studies show that stable pharmaceutical quality can be guaranteed even if the device is used in different positions to the one explained in the patient information leaflet, after cleaning the mouthpiece, or after dropping the device in different orientations.

"Registered trademark of AstraZeneca group of companies; for use within the USA as Pressair® and Genuair™ within all other licensed territories.
Delivered dose uniformity (DDU) and fine particle dose (FPD) for formoterol fumarate dehydrate (upper), and corresponding mass balances for formoterol fumarate dehydrate and aclidinium bromide (lower) [RH: relative humidity]

Abstract P289 Figure 1
Three stability studies simulating patient use were performed on aclidinium bromide 400 μg/formoterol fumarate dihydrate 12 μg inhalation powder in the Genuair™ inhaler.

Samples of a development batch representative for commercial production were tested after corresponding pre-storage for 12, 22, and 35 months over an in-use period of 10 weeks, at climatic zone II and IVb conditions.
Abstract P291 Figure 1  Delivered dose (DD) and fine particle dose (FPD) over in-use period of aclidinium bromide and formoterol fumarate dehydrate in µg (RH: relative humidity)
At day 0 and appropriate time intervals until the final dose was dispensed and the lock-out mechanism of the inhaler was activated, the following parameters were assessed: water content, degradation products, content per cartridge, delivered dose (DD), fine particle dose (FPD) and microbial growth. All results, notably DD and FPD (Figure 1), were within the expected range and well inside the specifications applied during development. More precisely, the mean results of DD for aclidinium bromide were between 370 μg and 451 μg (specification 320–480 μg) and for FPD between 139 μg and 182 μg (specification ≥80μg), while the mean values of DD for formoterol fumarate dihydrate were between 10.1 μg and 13.1 μg (specification 9.6–14.4 μg) and for FPD between 2.5 μg and 3.7 μg (specification ≥1.8 μg).

The studies show that stable pharmaceutical quality can be guaranteed under in-use conditions for a period longer than the allowed 60 days after unpacking the drug product pre-stored even up to the end of shelf life.

*Registered trademark of AstraZeneca group of companies; for use within the USA as Pressair® and Genuair™ within all other licensed territories.

**P292**

PILOT STUDY TO ASSESS BRONCHODILATOR RESPONSE DURING AN ACUTE EXACERBATION OF COPD USING A VIBRATING MESH NEBULISER VERSUS JET NEBULISER FOR BRONCHODILATOR DELIVERY

B Cushen, A Alsaid, A Abdulkareem, RIW Costello. RCSI Beaumont Hospital, Dublin, Ireland

10.1136/thoraxjnl-2016-209333.435

Introduction Recovery from COPD exacerbation is associated with increases in respiratory lung volume. Accelerating these changes through improved bronchodilator delivery could hasten recovery.

Hypothesis Vibrating mesh nebuliser (Aerogen® Ultra) results in greater change in lung physiology compared to standard volume jet nebuliser.

Methods Patients with an exacerbation of COPD were randomised to receive combined salbutamol 2.5 mg/iptropium bromide 0.5mg via vibrating mesh (Active group) or standard hospital jet nebuliser (Control) on one occasion between day 2–7 of hospitalisation.Spirometry, body plethysmography and impulse oscilometry were performed pre-bronchodilator and at 1 hour post. Borg breathlessness score was measured.

Results Thirty-one patients have been recruited to date, 16 to the active group and 15 control group. Mean FEV1 was 48 ± 18% predicted. Baseline demographics were comparable between groups. Both groups had significant improvements in FEV1 and Inspiratory Capacity post-bronchodilator, with greater increases in FVC in the active group (0.40 ± 0.39 L vs 0.19 ± 0.19 L, p = 0.06). Significant changes in operating lung volumes and airway impedance were seen in both groups. There was no significant difference in Borg score.

Conclusion Bronchodilator administration, during a COPD exacerbation, results in significant improvements in spirometry, lung volume and airway impedance. Drug delivery by vibrating mesh nebuliser results in greater absolute increases in FVC. Further studies will assess whether this translates into accelerated exacerbation recovery.
clinically significant events in patients with GOLD stage B COPD.

Methods A total of 5162 patients were randomised to O 5 μg, T 2.5 μg, T 5 μg, T/O 2.5/5 μg or T/O 5/5 μg (delivered via Respimat® inhaler) in two 52-week, parallel-group, double-blind studies (NCT01431274; NCT01431287). In this post hoc analysis of the combined TONADO® data, clinical deterioration was defined according to a composite end point: time to first decrease in trough forced expiratory volume in 1 second (FEV1) from baseline of ≥100 mL; increase in St George’s Respiratory Questionnaire (SGRQ) total score from baseline of ≥4 units; severe (hospitalised) exacerbation; or death. Only patients classified as GOLD stage B were included. Data are presented for comparisons of the licensed doses of T 5 μg and T/O 5/5 μg.

Results 306 and 310 patients were included in this analysis in the T5 μg and T/O 5/5 μg treatment groups, respectively. Time to clinical deterioration was significantly longer with T/O 5/5 μg than T 5 μg (25th percentile 128 versus 85 days; HR 0.650; 95% CI: 0.524, 0.805; p < 0.0001) (Figure). Times to trough FEV1 decline and SGRQ increase were significantly longer with T/O 5/5 μg than T 5 μg (226 versus 91 days and 369 versus 175 days, respectively). 25th percentiles for time to severe exacerbation and time to death were not estimable due to low event rates.

Conclusions In the TONADO® studies, T/O increased time to clinical deterioration compared to T alone in patients with GOLD stage B disease. This suggests that, in this patient population, T/O is more effective than T in preventing these significant events. Further studies are warranted to prospectively study this effect.

Funding Boehringer Ingelheim.

Please refer to page A272 for declarations of interest in relation to abstract P294.

EFFICACY AND SAFETY OF TIOTROPIUM/LODATEROL IN PATIENTS WITH COPD BY ATS CATEGORY

Rationale The once-daily combination of tiotropium (T), a long-acting muscarinic antagonist, and olodaterol (O), a long-acting β2-agonist, has demonstrated efficacy and safety in chronic obstructive pulmonary disease (COPD).1 Recently, it has been demonstrated that patients with milder disease (GOLD 2) have better bronchodilator responses compared to those with more severe disease. This post hoc analysis investigated whether the response to T/O and to T alone is influenced by forced expiratory volume in 1 second (FEV1) American Thoracic Society (ATS) category (mild, moderate or severe).
EFFECT OF TIOTROPIUM/OLODATEROL THERAPY ON COPD EXACERBATIONS IN THE TONADO® STUDIES

E Derom, 1MF ležar, 2L Grönke, 2F Vož, 4R Buhl. 1Ghent University Hospital, Ghent, Belgium; 2University Clinic of Respiratory and Allergic Diseases, Goležnik, Slovenia; 3Boehringer Ingelheim Pharma GmbH and Co. KG, Ingelheim, Germany; 4Pulmonary Department, Mainz University Hospital, Mainz, Germany

Abstract P296 Table 1 Treatment comparisons of time to first COPD exacerbation and first moderate/severe COPD exacerbation

<table>
<thead>
<tr>
<th>Treatment comparison, µg</th>
<th>Time to first COPD exacerbation</th>
<th>Time to first moderate/severe COPD exacerbation</th>
<th>Time to first severe COPD exacerbation</th>
</tr>
</thead>
<tbody>
<tr>
<td>T/O 5/5 –</td>
<td>0.938</td>
<td>0.931</td>
<td>1.279</td>
</tr>
<tr>
<td>T 5</td>
<td>(0.801, 1.099)</td>
<td>(0.791, 1.095)</td>
<td>(0.874, 1.871)</td>
</tr>
<tr>
<td>T/O 5/5 –</td>
<td>0.897</td>
<td>0.901</td>
<td>1.105</td>
</tr>
<tr>
<td>T 2.5</td>
<td>(0.767, 1.049)</td>
<td>(0.767, 1.059)</td>
<td>(0.766, 1.593)</td>
</tr>
<tr>
<td>T/O 2.5/5 –</td>
<td>0.819</td>
<td>0.822</td>
<td>0.817</td>
</tr>
<tr>
<td>T 2.5</td>
<td>(0.698, 0.960)*</td>
<td>(0.697, 0.969)*</td>
<td>(0.551, 1.210)</td>
</tr>
<tr>
<td>T/O 2.5/5 –</td>
<td>0.857</td>
<td>0.850</td>
<td>0.948</td>
</tr>
<tr>
<td>T 5</td>
<td>(0.730, 1.007)</td>
<td>(0.720, 1.003)</td>
<td>(0.632, 1.424)</td>
</tr>
<tr>
<td>T/O 5/5 –</td>
<td>1.095</td>
<td>1.096</td>
<td>1.352</td>
</tr>
<tr>
<td>T 2.5</td>
<td>(0.931, 1.288)</td>
<td>(0.927, 1.295)</td>
<td>(0.922, 1.983)</td>
</tr>
</tbody>
</table>

REFERENCE

Please refer to page A273 for declarations of interest in relation to abstract P296.
the TONADO® studies did not show a significant difference in the hazard ratios for time to exacerbation end points. These findings are partially attributable to a higher number of severe exacerbations with T/O 5/5 mg in TONADO®. TONADO® was not designed for formal comparison of exacerbations with T/O versus T; however, a study powered to assess this is ongoing.

**Funding** Boehringer Ingelheim.

Please refer to page A273 for declarations of interest in relation to abstract P296.

**P297** LUNG-FUNCTION PROFILE BEFORE AND AFTER THE FIRST MODERATE TO SEVERE EXACERBATION DURING THE WISDOM STUDY

E Wouters, H Magnussen, R Rodriguez-Roisin, K Tetzlaff, S Bell, A Calverley.

1 Department of Respiratory Medicine, University of Maastricht, Maastricht, the Netherlands; 2 Pulmonary Research Institute at Lung Clinic Grosshansdorf, Airway Research Centre North, German Centre for Lung Research, Grosshansdorf, Germany; 3 Servei de Pneumologia, Hospital Clinic IDIBAPS-CIBERES, Universitat de Barcelona, Barcelona, Spain; 4 Boehringer Ingelheim Pharma GmbH and Co. KG, Ingelheim, Germany; 5 Department of Biometry and Data Management, Boehringer Ingelheim, Bracknell, UK; 6 Institute of Ageing and Chronic Disease, Aintree University Hospital, Liverpool, UK

10.1136/thoraxjnl-2016-209333.440

**Rationale**

The WISDOM study (NCT00975195) showed no increased risk of exacerbation when inhaled corticosteroid (ICS) was withdrawn stepwise in patients with severe COPD on LAMA + LABA maintenance therapy versus continued LAMA + LABA + ICS.1 Daily home spirometry measured the time course of lung-function changes throughout the study. The aim of this post hoc analysis was to address the lung-function profile leading up to, during and following the first moderate-to-severe exacerbation.

**Methods**

WISDOM was a multinational, randomised, double-blind study.1 Patients with severe to very severe COPD entered a 6-week run-in with LAMA + LABA + ICS (tiotropium 18 μg once daily; salmeterol 50 μg twice daily; fluticasone propionate 500 μg twice daily), and were randomised to continue LAMA + LABA + ICS or salmeterol/tiotropium for 52 weeks while discontinuing ICS in a stepwise manner over 12 weeks. On-treatment daily forced expiratory volume in 1 second (FEV1) change from baseline was calculated before and after the first moderate-to-severe exacerbation. In this post hoc analysis, we included patients who experienced a moderate-to-severe exacerbation after the ICS-withdrawal visit, did not have an exacerbation in the 8 weeks before or after the exacerbation, and had daily home-measured FEV1 data available for every week analysed.

**Results**

Of 2488 patients, 262 experienced a moderate-to-severe exacerbation after the ICS-withdrawal visit and had lung-function data for every week. For all patients combined (ICS and ICS withdrawal), change in FEV1 remained relatively stable 56–14 days before the first moderate-to-severe exacerbation (mean FEV1 change from baseline values: –0.04 to –0.07 L) (Figure).

There was a decline in lung function starting 2–3 weeks before exacerbation (FEV1 change value of –0.12 L from baseline), followed by a moderate improvement over ~14 days. Post-exacerbation lung function did not reach pre-exacerbation levels.

**Conclusions**

Lung function was relatively stable in both treatment groups. Home spirometry measurements showed a marked decline in FEV1 prior to moderate-to-severe exacerbation with improvements seen post-exacerbation, although not to pre-exacerbation levels. These findings support the usefulness of home
spirometry to predict exacerbations and to indicate subsequent worsening of lung function resulting from a previous COPD exacerbation.

**Funding** Boehringer Ingelheim.

Please refer to page A273 for declarations of interest in relation to abstract P297.

**REFERENCE**


---

**P298**

**TIOTROPIUM/OLONADEROL THERAPY PROVIDES SYMPTOMATIC BENEFITS IRRESPECTIVE OF PRIOR MAINTENANCE TREATMENT: POST HOC ANALYSES OF THE OTEMTO® STUDIES**

Rationale The combination of tiotropium (T), a long-acting muscarinic antagonist (LAMA), plus olodaterol (O), a long-acting β2-agonist (LABA), is approved for once-daily maintenance treatment of COPD. The randomised, double-blind, Phase IIIb OTEMTO® 1 and 2 studies (NCT01431274; NCT01431287) showed improvements in quality of life and lung function after 12 weeks’ treatment with T/O compared to T alone or placebo in patients with moderate to severe COPD. This post hoc analysis investigated whether previous maintenance treatment with a long-acting bronchodilator or inhaled corticosteroid (ICS) influenced symptomatic benefits of T/O.

Methods Patients aged ≥40 years received T/O 2.5/5 μg, T/O 5/5 μg, T 5 μg or placebo once daily for 12 weeks via Respimat® inhaler. St George’s Respiratory Questionnaire (SGRQ) total score was a primary end point, alongside lung function (FEV1 area under the curve from 0–3 hours and trough FEV1 responses). Secondary end points included Mahler Transition Dyspnoea Index (TDI) focal score. Salbutamol/albuterol was provided as rescue medication and use was recorded in an e-diary. We report comparisons between T/O 5/5 μg, T 5 μg and placebo.

Results Of the 1621 patients evaluated, 943 had received prior maintenance treatment (66.7% LABA; 59.4% LAMA; 64.5% ICS) and 678 had not. Similar improvements in mean SGRQ total score were observed with T/O compared to T and placebo, respectively, in patients receiving prior maintenance treatment (−2.02 and −4.59 units) and those without (−2.20 and −4.78 units) (Table). TDI focal scores improved with T/O compared to T and placebo, respectively, in patients receiving prior maintenance treatment (0.60 and 1.87 units) and those without (0.60 and 1.33 units) (Table). Patients with and without prior maintenance treatment demonstrated similar improvements in daytime and night-time rescue medication use and lung-function improvements with T/O compared to T and placebo.

Conclusions T/O provides symptomatic benefits as demonstrated by improvements in SGRQ score, TDI focal score and decreased rescue medication use compared to placebo and T, independent of previous maintenance treatment. These findings suggest T/O is beneficial over monotherapy when used as first COPD maintenance treatment.

**Funding** Boehringer Ingelheim.

Please refer to page A273 for declarations of interest in relation to abstract P298.

**Abstract P298 Table 1**

<table>
<thead>
<tr>
<th>Treatment comparison</th>
<th>Prior maintenance treatment</th>
<th>No prior maintenance treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>SGRQ total score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T/O 5/5 μg – placebo</td>
<td>−4.59 (−10.23, 1.06)</td>
<td>−4.78* (−6.93, −2.63)</td>
</tr>
<tr>
<td>T/O 5/5 μg – T</td>
<td>−2.02 (−5.42, 1.37)</td>
<td>−2.20* (−4.34, −0.07)</td>
</tr>
<tr>
<td>Mahler TDI focal score</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T/O 5/5 μg – placebo</td>
<td>1.87** (1.36, 2.39)</td>
<td>1.33** (0.76, 1.90)</td>
</tr>
<tr>
<td>T/O 5/5 μg – T</td>
<td>0.60* (0.09, 1.10)</td>
<td>0.60* (0.04, 1.17)</td>
</tr>
</tbody>
</table>

Adjusted mean (95% confidence interval) **p<0.001, *p<0.05

---

**P299**

**EFFECTS OF SYMPTOM SEVERITY AT BASELINE ON LUNG-FUNCTION AND SGRQ RESPONSES IN THE OTEMTO® STUDIES**

Rationale In the randomised, double-blind, Phase IIIb OTEMTO® 1 and 2 studies (NCT01431274; NCT01431287), the combination of tiotropium (T), a long-acting muscarinic antagonist, plus olodaterol (O), a long-acting β2-agonist, showed meaningful improvements in quality of life (St George’s Respiratory Questionnaire [SGRQ]) and lung function in patients with moderate to severe COPD after 12 weeks’ treatment compared to T alone or placebo. This post hoc analysis investigated whether symptomatic status at inclusion, as measured by the modified Medical Research Council (mMRC) dyspnoea scale and the Base-line Dyspnoea Index (BDI), influenced lung-function and SGRQ responses.

Methods Patients aged ≥40 years received T/O 2.5/5 μg, T/O 5/5 μg, T 5 μg or placebo once daily for 12 weeks via Respimat® inhaler. SGRQ total score and lung function (FEV1 area under the curve from 0–3 hours [AUC0–3] and trough FEV1 responses) were primary end points. Patients completed the mMRC and BDI scales at baseline. We report comparisons between T/O 5/5 μg, T 5 μg and placebo.

Conclusions The combination of tiotropium (T), a long-acting muscarinic antagonist (LAMA), plus olodaterol (O), a long-acting β2-agonist (LABA), is approved for once-daily maintenance treatment of COPD. The randomised, double-blind, Phase IIIb OTEMTO® 1 and 2 studies (NCT01431274; NCT01431287) showed improvements in quality of life and lung function after 12 weeks’ treatment with T/O compared to T alone or placebo in patients with moderate to severe COPD. This post hoc analysis investigated whether previous maintenance treatment with a long-acting bronchodilator or inhaled corticosteroid (ICS) influenced symptomatic benefits of T/O.

**Funding** Boehringer Ingelheim.

Please refer to page A273 for declarations of interest in relation to abstract P298.
**Results** 1621 patients were evaluated: 736 patients (45%) had mMRC scores <2, 883 patients (54%) ≥2 (scored from grade 0–5, lower is better); 418 patients (26%) had BDI scores <6, 1201 patients (74%) ≥6 (scored from 0–12, higher is better). Patients were distributed evenly across treatment arms with respect to mMRC and BDI scores, and baseline characteristics were consistent across treatment arms. Improvements in FEV1 AUC0–3 and trough FEV1 were observed with T/O compared to T and placebo in patients with mMRC score <2 and ≥2, as well as in patients with BDI score ≥6 and <6 (Table). All BDI and mMRC groups demonstrated improvements in SGRQ with T/O compared to placebo above the minimal clinically important difference.

**Conclusions** There was a trend towards better lung-function improvement with T/O versus T or placebo in less symptomatic patients assessed by baseline BDI. More severe dyspnoea by mMRC category was associated with improved SGRQ with T/O versus T or placebo, but did not affect lung-function improvement. Overall, T/O provided lung-function and quality of life benefits regardless of symptomatic status prior to treatment.

**Funding** Boehringer Ingelheim.

Please refer to page A274 for declarations of interest in relation to abstract P299.
Attitudes and Barriers to Healthcare

DEVELOPMENT OF A ‘STOP-GO’ SCREENING TOOL FOR STREAMLINING ASSESSMENT OF COMMON COMORBIDITIES IN COPD PATIENTS

SL Kennie, HK Lamplough, EH Baker, S McIvor. St George’s University of London, London, UK

Introduction and objectives People with COPD admitted to hospital with exacerbations have multiple co-morbidities, impacting on survival, re-hospitalisation and health status. Although commonly described, there is no consensus coordinating management of COPD and co-morbidities in time- and resource-limited healthcare. We developed a pragmatic ‘stop-go’ pre-screening tool to streamline co-morbidity assessment and determined its efficacy in predicting co-morbid diagnoses made ad-hoc in COPD patients in the year following hospitalisation.

Methods Criteria were developed from NICE guidelines for twelve common COPD co-morbidities (Table). These indicated whether each condition was either not present or already diagnosed and treated (STOP – no further action required) or whether it could be present but undetected or could not be assessed (GO – further action required).

Electronic records (all patients) and hospital notes (84 patients) were reviewed for COPD patients admitted with exacerbations 1/9/2014–31/12/14 who survived for the subsequent year. The ‘stop-go’ screening tool was completed from admission data. Ad-hoc identification of new co-morbidities, defined by physician-diagnosis or commencement of new medication, was noted over 1 year follow up.

Results 120 patients (53% male, 47% female; age 73 ± 10 years) were included. The “stop-go” screening tool identified 7 ± 2 co-morbidities per patient requiring no action and 5 ± 2 co-morbidities (could be present, 2 ± 1; ‘unable to assess’ 3 ± 3) where further action was required. Information from patient records was generally insufficient to screen for anxiety and depression and lacking for around one quarter of patients for atrial fibrillation, diabetes mellitus and cognitive impairment.

During 1 year follow-up, patients developed 0.6 ± 0.9 (range 0–3) new diagnoses from the co-morbidities list. The ‘stop-go’ tool was most effective at predicting ad-hoc diagnosis of hypertension, heart failure and osteoporosis (table) and less effective at predicting atrial fibrillation and ischaemic heart disease.

Conclusions The ‘stop-go’ pre-screening tool has potential to cut down the number of co-morbidities that need to be assessed in time-limited consultations. This could be improved by inclusion of anxiety and depression scoring, routine ECG and HbA1c. It shows early promise in predicting ad-hoc diagnoses, but now needs to be tested prospectively towards improving systematic and cohesive care provision.

REFERENCE


Abstract M1 Table 1 Identification of co-morbidities requiring further assessment using the ‘stop-go’ tool and relationship between screen results and actual co-morbidities identified by ad hoc healthcare contact over 1 year

<table>
<thead>
<tr>
<th></th>
<th>STOP</th>
<th>GO</th>
<th>New diagnoses at 1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Screen negative</td>
<td>Screen positive</td>
<td>Data not available</td>
</tr>
<tr>
<td>STOP</td>
<td>Prior diagnosis</td>
<td>Data not available</td>
<td>n (%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>20</td>
<td>62</td>
<td>23</td>
</tr>
<tr>
<td>(BP &lt;130/90)</td>
<td>(17)</td>
<td>(52)</td>
<td>(19)</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>71</td>
<td>21</td>
<td>1</td>
</tr>
<tr>
<td>Sinus rhythm on ECG</td>
<td>(59)</td>
<td>(18)</td>
<td>(1)</td>
</tr>
<tr>
<td>Ischaemic heart disease</td>
<td>44</td>
<td>50</td>
<td>6</td>
</tr>
<tr>
<td>(No CVS symptoms)</td>
<td>(37)</td>
<td>(42)</td>
<td>(5)</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>39</td>
<td>29</td>
<td>33</td>
</tr>
<tr>
<td>BNP &lt;100 pg/ml</td>
<td>(33)</td>
<td>(24)</td>
<td>(28)</td>
</tr>
<tr>
<td>Dyslipidaemia</td>
<td>11</td>
<td>64</td>
<td>27</td>
</tr>
<tr>
<td>QRISK2 score &lt;10%</td>
<td>(9)</td>
<td>(53)</td>
<td>(23)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>60</td>
<td>22</td>
<td>9</td>
</tr>
<tr>
<td>(HbA1c &lt;42 mmol/mol)</td>
<td>(50)</td>
<td>(18)</td>
<td>(8)</td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>(HADS-D &lt;10)</td>
<td>(1)</td>
<td>(17)</td>
<td>(0)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>1</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>(HADS-A &lt;10)</td>
<td>(1)</td>
<td>(5)</td>
<td>(0)</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>73</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>(AMTS ≥7)</td>
<td>(61)</td>
<td>(6)</td>
<td>(5)</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>9</td>
<td>18</td>
<td>82</td>
</tr>
<tr>
<td>(No history of fragility or no oral corticosteroids for ≥3 months)</td>
<td>(8)</td>
<td>(15)</td>
<td>(68)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>99</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>(eGFR ≥60ml/min/1.73m² at discharge)</td>
<td>(83)</td>
<td>(3)</td>
<td>(14)</td>
</tr>
<tr>
<td>Anemia</td>
<td>88</td>
<td>3</td>
<td>28</td>
</tr>
<tr>
<td>(Hb &gt;120 g/L at discharge)</td>
<td>(73)</td>
<td>(3)</td>
<td>(23)</td>
</tr>
</tbody>
</table>

AMTS (Abbreviated Mental Test Score), BNP (B-type Natriuretic Peptide), CVS (Cardiovascular system), eGFR (Estimated Glomerular Filtration Rate), HADS-A/D (Hospital Anxiety and Depression Scale), Hb (Haemoglobin), HbA1c, (Glycated Haemoglobin), # (fracture).

Thorax 2016;X(Suppl X):A1–A285
DO PATIENTS AND INFORMAL CARERS AGREE ON SYMPTOM BURDEN IN ADVANCED COPD?

EZ Mi, EZ Mi, S Mendonca, AC Gardener, MC Farquhar. School of Clinical Medicine, University of Cambridge, Cambridge, UK; Department of Public Health and Primary Care, University of Cambridge, Institute of Public Health, Cambridge, UK

Introduction

Informal carers are a valuable source of information on patients’ symptom experiences for clinicians, and carer assessment determines decisions regarding symptom management by carers themselves. However, previous studies have reported that proxies overestimate symptom burden, particularly subjective psychological and emotional symptoms, but proxy studies in COPD are few. We sought to assess congruency between patient and carer assessment of symptom burden, and to identify factors associated with incongruence.

Methods

Well-characterised patients with advanced COPD and their carers (n = 117 patient-carer dyads) independently rated patients’ breathlessness, fatigue, constipation, diarrhoea, anxiety and depression on a 4-point scale, and average breathlessness in prior 24 hours using a Numerical Rating Scale (NRS). McNe mar’s and Wilcoxon signed rank test were performed to identify differences between patients and carers in proportions reporting presence and reporting of severity of symptoms respectively. Intraclass correlation (ICC) was used to assess agreement on symptom scores in dyads.

Results

Patient mean age was 71.4 (SD 8.7) and 62% were male; carer mean age was 64.2 (SD 14.5) and 27% were male. 87% of patients lived with their carer and 84% of carers were spouses. There were no significant differences between patients and carers in total proportions reporting presence or assessment of severity, of any symptom. ICCs (Table 1) showed patient-carer agreement was only fair to moderate. Higher agreement was found for physical symptoms (constipation, diarrhoea) than psychological (anxiety, depression) or those with emotional valence (breathlessness, fatigue). Carers more frequently underestimated than overestimated symptoms, with the exception of physical symptoms.

Conclusions

Patient-carer agreement on symptom burden was generally low, and differed depending on symptom type. Poorer agreement for emotional symptoms and symptom underestimation by carers in this prospective population-based study may reflect patient concealment within dyads or the differences of a cohort recruited through primary care, compared to previous proxy studies in secondary care. These findings may also be due to longer disease trajectories in COPD, compared to previous studies in cancer, leading to carer compassion-fatigue or response-shift. Our findings have implications for the interpretation of proxy data in COPD, and suggest the need for carer education and support in symptom assessment.

<table>
<thead>
<tr>
<th>Abstract M2 Table 1</th>
<th>Intraclass correlation coefficients for patient-carer dyads of symptom scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>106</td>
</tr>
<tr>
<td>Fatigue</td>
<td>105</td>
</tr>
<tr>
<td>Constipation</td>
<td>91</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>93</td>
</tr>
<tr>
<td>Anxiety</td>
<td>96</td>
</tr>
<tr>
<td>Depression</td>
<td>100</td>
</tr>
<tr>
<td>Average breathlessness in prior 24 hours (NRS)</td>
<td>100</td>
</tr>
</tbody>
</table>

(a) Different numbers of pairs for each symptom as not all symptoms assessments were completed by both patient and carer in each pair. (b) Two-way mixed effect model; absolute agreement definition; single measure ICC. (c) <0.20 as poor agreement; 0.20–0.39 as fair agreement; 0.40–0.59 as moderate agreement; 0.60–0.79 as substantial agreement; and 0.80–1.0 as excellent agreement.

ATTITUDES AND BARRIERS TO RESPONSIBLE EMERGENCY OXYGEN PRESCRIBING AMONG HEALTHCARE PROFESSIONALS

T Sanctuary, M Johnson, V Lord, I Patel, King’s College Hospital, London, UK

Abstract M3 Figure 1

Ability to identify groups at risk of hypercapnic respiratory failure by attitude to O2 prescribing.

A258 Thorax 2016;X(Suppl X):A1–A285
Introduction The 2015 BTS Emergency Oxygen Audit showed that 4/10 patients on oxygen did not have a valid prescription, 1/3 patients received inappropriate levels of oxygen and almost 1/10 patients were at risk of iatrogenic hypercapnia. Over half of hospitals didn’t provide adequate training in oxygen provision and monitoring. Despite significant efforts to improve practice at King’s College Hospital, the audit revealed a drop in appropriate prescribing. We conducted a staff survey of attitudes to and knowledge around oxygen prescribing to better understand the barriers.

Methods Hospital based healthcare professionals completed a survey of attitudes to oxygen prescribing as well as a knowledge quiz using Survey Monkey®.

Results There were 113 respondents. 67% were doctors (13% Foundation Year; 44% ST1-8; 38% Consultants). 29% were nurses, (76% Band 5/6). Most worked in acute specialties (28% A&E, 15% anaesthetics, 14% ICU, 13% acute medicine). Only 66% of respondents believed that oxygen should be prescribed on a drug chart. Among doctors, support for oxygen prescribing was high, especially in acute medicine (93%) and A&E (86%). It was lower amongst ICU doctors (50%). Amongst nurses, support was 41%. Nurses working in medical specialties largely agreed with oxygen prescribing (80%). Those working in A&E and ICU did not (33% and 22% respectively).

Perceived barriers to prescribing were lack of time, lack of awareness/habit, difficulty accessing computers and a perception that the oxygen prescription would not allow for changes in a patient’s condition. Those who believed oxygen did not need to be prescribed felt concerned that prescribing could delay emergency treatment. In the quiz, this group was less able to identify patients at risk of hypercapnic respiratory failure (see figure 1).

Conclusion Oxygen prescribing is still seen by many as a cause of possible delays in emergency treatment. Education of clinical staff, particularly nurses, around risks as well as benefits of emergency oxygen therapy is still needed. Emergency oxygen prescription needs to be as flexible as possible so that prescribing is seen as a means to deliver right care and reduce these risks particularly for those patients at risk of hypercapnic respiratory failure.

M4 LATE ASTHMATIC RESPONSE TO EPOXY RESINS: A CASE REPORT

1E Solano, 2B Fitzgerald, 3J Cannon, 2P Cullinan, 2J Feary, 2Ramon y Cajal. University Hospital, Madrid, Spain; 2Royal Brompton and Harefield NHS Foundation Trust, London, UK

10.1136/thoraxjnl-2016-209333.446

Introduction Epoxy resins (ER) systems are used extensively in industry in adhesives, reinforced plastics and surface coatings. ER are converted to the final product by mixing with a “hardener” or curing agent to form a polymer. This process releases fumes which can be respiratory sensitisers and a cause of occupational asthma (OA).

Method A non-atopic, non-smoker, 41 year old was referred with a six-month history of new onset asthma and 10 month history of nasal congestion and sneezing. His wheeze and dyspnoea occurred in the evenings and improved on holidays. He worked as a materials technician developing bonding agents and had started to use a new ER system one year previously. OA to the ER system was suspected and an in-patient specific inhalational challenge (SIC) performed. On day 1, a pre-treatment solution and a solvent (negative controls) were brushed on to a hard surface for 30 minutes. On day 2, the challenge was repeated using the same methods but with the addition of the ER system used at work. Histamine responsiveness 24 hours post challenge, FEV1 and symptoms were all monitored. At baseline FEV1 was 4.3L and bronchial response to histamine was normal (PC 20 16mg/ml). Blinding was not possible due to the patient’s intimate knowledge of the products.

Results Exposure to the control agents induced no symptoms and no change in FEV1 or histamine responsiveness. Six hours after the active challenge FEV1 fell by 16% and the patient reported chest tightness and wheeze. 22 h post-challenge FEV1 reached a
nadir of 2.0 L (52% fall) and bronchodilator therapy was administered (Figure). Histamine responsiveness 24 h post challenge increased with a PC 20 of 3.3 mg/ml. The active challenge was not repeated.

Conclusion We demonstrated an isolated sustained late asthmatic reaction to the ER system confirming OA. The likely sensitiser was cyclohexylamine (an aliphatic amine hardener) which had a high "Chemical Asthma Hazard Assessment Score" of 0.9283. To ensure patient safety, it is important to be aware of this pattern of response (which is typical of low molecular weight agents). It also explains why the patient did not closely link his symptoms with work. The exact immunological mechanisms are not currently known.

**Abstract M5 Table 1**

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Satisfaction with information about medicines Scale (SIMS) – likelihood to be satisfied with preventer inhaler medication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male (n = 26)</td>
<td>No significant difference between genders found</td>
</tr>
<tr>
<td>White Caucasian (n = 46)</td>
<td>Satisfied (P &lt; 0.01)</td>
</tr>
<tr>
<td>Asian (n = 21)</td>
<td>Not satisfied (P &lt; 0.01)</td>
</tr>
<tr>
<td>Black Afro-Caribbean (n = 6)</td>
<td>No significant correlation between satisfaction and adherence found</td>
</tr>
<tr>
<td>European (n = 2)</td>
<td>Increased salbutamol use when not satisfied (P &lt; 0.05)</td>
</tr>
<tr>
<td>≥80% Adherence to inhaled corticosteroids (ICS) as per GP refill information</td>
<td>Increased rate of exacerbations when not satisfied (P &lt; 0.05)</td>
</tr>
</tbody>
</table>

**M5** THE CORRELATION BETWEEN SATISFACTION WITH INFORMATION ABOUT MEDICINES AND CLINICAL OUTCOMES IN AN ETHNICALLY DIVERSE DIFFICULT ASTHMA COHORT

H Dihue, H Khachi. Bart’s Health NHS Trust, London, UK

Introduction It is thought that a common cause of poor asthma control is lack of information about medication and their use. This study aims to investigate the influence of satisfaction with information about medicines and its associated clinical outcomes in patients in a difficult asthma cohort.

Methodology Ethics approval was granted. All patients attending a difficult asthma clinic in a large tertiary centre were invited to participate. The Satisfaction with Information about Medicines Scale (SIMS) questionnaire was used. This validated 17 item questionnaire, explores various aspects of medication information with preventer inhalers and the associated patient satisfaction with this. Demographic and adherence information from the GP were also collected. SPSS version 22.0 was used to analyse the data.

Results The table shows that patients from non-Caucasian backgrounds had statistically significantly lower reported satisfaction with information about medicines. There was also a statistically significant correlation between low satisfaction with information and increased salbutamol use and rates of asthma exacerbations.

Discussion This study shows the importance of ethnicity to the level of satisfaction with information about medicines. Language barriers, lack of understanding or health beliefs could be contributing factors. Our study found no statistical significance found between GP prescription refill rates (adherence) and associated exacerbations and salbutamol use. However, it is worth noting that our study did not investigate whether patients who picked up their preventer inhalers were indeed using them as intended by their clinician, nor did it assess inhaler technique.

Conclusion We have shown that using a validated questionnaire can help identify patients who are at risk of having a lower satisfaction with their medicines and in turn a greater likelihood of having poorer clinical outcomes. Eliciting satisfaction with information about medication can help tailor interventions to support clinical outcomes in patients from ethnic minorities.

**REFERENCE**


**M6** IMPROVING FOLLOW-UP IN PATIENTS ATTENDING AND DISCHARGED FROM ACCIDENT AND EMERGENCY WITH ASTHMA EXACERBATIONS

WJ Newman, O Lamont. Forth Valley Health Board, Larbert, UK

Introduction The Respiratory and Accident and Emergency (A&E) departments in Forth Valley audited asthma care in the emergency department over the past years. Shortcomings in a number of areas have been identified and quality improvement measures undertaken.

One area was the failure to organise follow-up for patients following attendance at A&E, (24% in 2009, 47% in 2012). As a result a new system was introduced.

Methods Forth Valley Health Board serves a population of 310,000 and has one acute hospital with 860 beds. The Respiratory Service comprises of 6 Consultants and 5.5 Respiratory Nurses. There are specialist asthma clinics run by the physicians/nurses. Patients with an asthma exacerbation discharged from the A&E department are identified by interrogating the A&E patient nurses. There are specialist asthma clinics run by the physicians/nurses. Patients with an asthma exacerbation discharged from the A&E department are identified by interrogating the A&E patient management system daily and clinical and contact details obtained. The Respiratory nurses contact any patient to obtain further information (standardised questionnaire) and make a management plan with the patient. Their case is then discussed with the on-call Respiratory physician and further recommendations instituted.

Results 88 cases (27 (30%) male, 61 (70%) female) were identified as having attended with an exacerbation of their asthma and discharged from A&E during 2015. Median age 36 (range 17–78), 46 (58%) presented at weekends or outwith working hours (0800–1800), 70 (80%) were discharged home with oral steroids.

Of the 88 patients one had no telephone/one lived outside the UK. 26 (30%) patients did not reply and the GP practice was
DESIGNING AROUND PLACEBO INHALER DEVICE

CONCERN AND IMPROVING ASTHMA HEALTHCARE

PROFESSIONAL PATIENT TRAINING

M7

MJ Sanders, R Bruin. Clement Clarke International Ltd, Harlow, UK

10.1136/thoraxjnl-2016-209333.449

Introduction Effective asthma control with drug therapy delivered via pressurised metered dose inhalers (pMDIs) is critically dependent on good inhaler technique. Healthcare professionals (HCPs) dedicate significant time and resources to patient education and review sessions, which tend to focus on the co-ordination of pMDI actuation with the slow inspiratory breath. Tools exist to facilitate this experience: dummy pMDIs, add-on devices which whistle at the ideal inspiratory flow rate and the highly valued but difficult-to-obtain placebo pMDIs. The latter currently offer the closest real-life training experience but are hampered by the multiple-use concerns of cross-infection (or confident decontamination), HCP-only demonstration, and unnecessary exposure to fluorocarbon propellants. The alternative of training with the active pMDI raises the issues of overdosing and drug wastage.

Methods Our self-imposed project brief was to design an improved low-cost solution to the placebo/dummy pMDI training conundrum which included patient participation as an absolute, the ability of the HCP to visually assess technique, avoidance of contamination, and compatibility with different actuator formats; and specifically excluded, for example, validation and implementation of new decontamination techniques.

Results The solution is an add-on device, confirmed to fit all UK active and placebo pMDIs. The device (Figure 1, Flo-Check®) is inserted into the pMDI actuator mouthpiece orifice and completely occludes the aerosol path. The lip-guard feature prevents mouth-contact contamination of the actuator and, when the patient inhales, inspiratory air is drawn in via side vents engineered to mimic the general resistance of a pMDI. The solution is confirmed to fit all UK active and placebo pMDIs. The device (Figure 1, Flo-Check®) is inserted into the pMDI actuator mouthpiece orifice and completely occludes the aerosol path. The lip-guard feature prevents mouth-contact contamination of the actuator and, when the patient inhales, inspiratory air is drawn in via side vents engineered to mimic the general resistance of a pMDI. The alternative of training with the active pMDI raises the issues of overdosing and drug wastage.

Conclusions A survey of manufacturer-supplied respiratory support devices in relation to all UK inhaled products (London Medicines Evaluation Network, 2013) revealed an almost universal lack of product specific devices with the exception of the Accuhaler™ (Glaxo Group Limited) and Symbicort® (AstraZeneca AB) training whistles; neither of which addresses the issues raised above. Several specific placebo pMDIs are available but the pharmaceutical industry is cognizant of fluorocarbon use justification, the danger of misinterpretation as an active product, and manufacturing a low volume high unit-cost product. It is hoped that developments such as the Flo-Check address some of the issues: for manufacturer, patient and HCP.

Abstract M7 Figure 1 Flo-Check device

M8

ASTHMA MANAGEMENT IN AN INNER-CITY TEACHING HOSPITAL EMERGENCY DEPARTMENT: REAL-LIFE AFTER NATIONAL REVIEW OF ASTHMA DEATHS (NRAD)


10.1136/thoraxjnl-2016-209333.450

Background The National Review of Asthma Deaths (NRAD) made multiple recommendations in the form of quality indicators linked to improving care of asthma patients in light of a review of all asthma deaths. We undertook an audit to establish the degree to which a busy Emergency Department in inner London adheres to these.

Method Patients admitted in the month of June 2015 with an asthma related admission were identified via the coding department. This list was reviewed to include those patients confirmed to have an acute asthma admission and seen and discharged directly from the ED department (including the short stay ED ward). The electronic records of those included were reviewed using a data collection form relating to the NRAD quality indicators.

Results A total of 42 patients were included. Our findings included the following: 83% had mild or moderate severity, the remainder having acute-severe. Almost one third of patients did not have their peak flow documented on arrival, 76% did not have their usual best or predicted best documented and 66% did not have a discharge peak flow documented. There was no documentation if any patient had been provided with a personal asthma action plan (PAAP). Checking of inhaler technique was adhered to these.

Discussion Simple measurements and interventions were omitted in a significant number of patients, highlighting the need for improvement. Some of these were straightforward such as more meticulous recording of peak flow. Others may have reflected lack of competency in the healthcare professional e.g. inhaler

Thorax 2016;Suppl X:A1–A285 A261
technique training and PAAP. The development of an asthma care pathway that captures the essence of the NRAD quality indicators, together with staff training, is urgently required to ensure that EDs lead the way in reducing the morbidity and mortality associated with acute asthma presentations.

**Funding** Sponsorship for the audit was provided by Novartis.

**REFERENCE**

---

**M9 A HIGH PREVALENCE OF OBSTRUCTIVE SLEEP APNOEA (OSA) IN THE SEVERE/DIFFICULT TO TREAT ASTHMA (SDTA) POPULATION**

1SE Davies, 2N Cachada, 1A Turner, 2S Wharton, 1A Mansur. 2Birmingham Regional Severe Asthma Service, Heartlands Hospital, Birmingham, UK; 1Respiratory Department, Heartlands Hospital, Birmingham, UK

10.1136/thoraxjnl-2016-209333.451

**Introduction** An association between OSA and asthma has been demonstrated. The exact prevalence in the SDTA population is unknown.

**Aim** To determine the prevalence and predictors of OSA in the SDTA population.

**Methods** All patients who attended a severe asthma regional centre between January 2013 and August 2016 with confirmed SDTA were asked to participate. All patients without a pre-existing OSA diagnosis had an overnight limited-channel sleep study. Patients underwent bioelectrical impedance measurements and completed the Epworth Sleepiness Score (ESS).

**Results** 72 patients consented and were included in the analysis. 69.4% (n = 50) had OSA. 33.3% (n = 24) had a pre-existing diagnosis of OSA and 79% (n = 19) of this group were receiving Continuous Positive Airway Pressure (CPAP). 36% (n = 26) had a new diagnosis of OSA. 31% (n = 22) had OSA excluded with a negative sleep study. Mild OSA (Apnoea Hypopnoea Index (AHI) ≥5–14.9) = 31.9% (n = 23), moderate OSA (AHI ≥15–29.9) = 16.7% (n = 12), severe OSA (AHI ≥30) = 4.2% (n = 3), AHI was unknown for 16.6% (n = 12) with pre-existing OSA receiving CPAP from a specialist centre.

The mean age was 47.7 years (18–73) and 72.2% (n = 52) were female. Mean Body Mass Index (BMI) was 32 (18.6–32.3) and body fat percentage (38.7 ± 12.37 vs 28.3 ± 14.03 fat%, p = 0.003) compared to the no-OSA group. The OSA group had a significantly higher incidence of hypercholesterolaemia compared to the no-OSA group (32.6% vs 8%, p = 0.0239). There was a higher incidence of diabetes (18.6% vs 8%, p = 0.0932), hypertension (27.9% vs 16%, p = 0.1643) and gastro-oesophageal reflux (60.5% vs 54.2%, p = 0.6189) in the OSA group. Blood eosinophil levels were significantly lower in the OSA group compared with the no-OSA group (0.23 ± 0.18 vs 0.39 ± 0.29 x10^9/L, p = 0.004).

**Conclusion** A significant prevalence of OSA was noted in this SDTA population. BMI, percentage body fat and hypercholesterolaemia were the strongest predictors of OSA. Patients with OSA had significantly lower blood eosinophil levels when compared to the no-OSA group. Alternatives to eosinophilic inflammation as a driver for severe/difficult to treat asthma should always be considered.

---

**Symptom Assessment and Investigation of Lung Disease**

**M10 LIVING WITH RELAPSING POLYCHONDRIITIS; A PATIENT AND CARER ENGAGEMENT EXPLORATION**

1J Haines, 2J Hull, 3T Clark, 4R Niven. 1North West Lung Centre, University Hospital of South Manchester, Manchester, UK; 2Department of Respiratory Medicine, Royal Brompton Hospital, London, UK; 3Relapsing Polychondritis Support Group, National, UK

10.1136/thoraxjnl-2016-209333.452

**Introduction** Relapsing polychondritis (RP) is a poorly understood rare condition in which recurrent bouts of inflammation affect the cartilage of the ears, nose, larynx and tracheobronchial tree. Prospective research is extremely limited and true prevalence data unknown. There are no identified optimal diagnostic pathways and treatment is not standardised. Seeking patient experience and opinion is invaluable to support and inform clinical and research strategies. We report the first known public involvement data relating to living with RP.

**Method** The RP patient support group hosted a patient engagement event to provide a reciprocal education environment for healthcare professionals, sufferers and their carers. A one-hour patient and carer focus group, aiming to identify key issues

---

**Abstract M10 Table 1** Priority resource allocation for addressing themed issues of living with RP

<table>
<thead>
<tr>
<th>RP Suffer (n = 13)</th>
<th>Resource coins assigned</th>
<th>% resource (priority rank)</th>
<th>RP Carer (n = 9)</th>
<th>Resource coins assigned</th>
<th>% resource (priority rank)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group defined theme</td>
<td>Resource coins assigned (n = 52)</td>
<td>% resource (priority rank)</td>
<td>Group defined theme</td>
<td>Resource coins assigned (n = 36)</td>
<td>% resource (priority rank)</td>
</tr>
<tr>
<td>Lack of understanding of health care providers</td>
<td>15</td>
<td>29 (1)</td>
<td>Lack of understanding of health care providers</td>
<td>7</td>
<td>19 (2)</td>
</tr>
<tr>
<td>Loss of identity</td>
<td>10</td>
<td>19 (2)</td>
<td>Restrictions on planning ahead</td>
<td>7</td>
<td>15 (2)</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>8</td>
<td>15 (3)</td>
<td>Impact on relationships</td>
<td>4</td>
<td>11 (4)</td>
</tr>
<tr>
<td>Pain</td>
<td>7</td>
<td>13 (4)</td>
<td>Financial worry</td>
<td>2</td>
<td>6 (5)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>5</td>
<td>10 (5)</td>
<td>Frustration</td>
<td>1</td>
<td>3 (6)</td>
</tr>
<tr>
<td>General side effects</td>
<td>3</td>
<td>6 (6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Restrictions on planning ahead</td>
<td>2</td>
<td>4 (7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Impact on relationships</td>
<td>2</td>
<td>4 (7)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
M11

THE IMPACT OF RESPIRATORY SPEECH AND LANGUAGE THERAPY ON PATIENTS’ COUGH RELATED SYMPTOMS

1J Haines, 2C Singer, 3N Vyas, 5S Chua, 4SI Fowler. 1North West Lung Centre, University Hospital of South Manchester, Manchester, UK; 2Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK; 3University of Manchester Medical School, Manchester, UK

Introduction Unexplained chronic cough may persist despite systematic evaluation and medical treatment of relevant comorbidities. Currently there are no effective, acceptable anti-tussive agents for the treatment of such patients and significant physical, social and psychological morbidity is described. The role of non-pharmacological treatment approaches and specifically speech and language therapy have been reported to be effective.

In our specialist tertiary airways service, all patients with unexplained chronic cough greater than 8 weeks in duration, remaining unexplained after investigation and supervised therapeutic trials, are referred for respiratory speech and language therapy (rSLT).

Aims To determine the effect of rSLT on the Leicester Cough Questionnaire (LCQ) and establish specifically whether the impact occurs across each of the described domains: physical, psychological and social.

Methods We included retrospective data from all patients with unexplained chronic cough who completed rSLT between January and June 2016, and who had LCQ data available before and after treatment.

Results Sixteen full data sets [69% female; median (range) age 58 (35–73) years] were available for analysis; rSLT median = 4, (range = 3–6) sessions. There was overall improvement in LCQ from median (range) 13.0 (7.0–18.0) pre to 17.4 (8.0–21.0) post rSLT [minimal important difference (MID) 1.3; Wilcoxon’s signed rank p < 0.001]. Each domain improved post rSLT: physical from 4.7 (3.0–7.0) pre to 6.0 (2.0–7.0) post (MID 0.2; p = 0.004); psychological: from 4.0 (1.0–6.0) to 6.1 (3.0–7.0) (MID 0.8; p = 0.001); and social from 4.0 (2.0–7.0) to 5.7 (3.0–7.0) post (MID 0.2, p = 0.001). Individual answers to 10 of the 19 LCQ questions showed statistically significant improvements.

Conclusion These preliminary data indicate that rSLT improves cough related symptoms similarly across all domains. Further investigation is needed to inform which aspects of patients’ cough related symptoms do/do not improve with therapy to guide treatment refinement. Specifically, closer investigation of response to individual LCQ questions may lead to improvements in therapeutic strategies.
THE USE OF ONLINE HEALTH FORUMS BY CHRONIC COUGH SUFFERERS

A. Sinha, A.M. Wilson, T. Porter. University of East Anglia, Norwich, UK
10.1136/thoraxjnl-2016-209333.455

Introduction Chronic cough represents a significant health problem, affecting 10–20% of the population, for which effective medical support is often unavailable. In such circumstances, and having exhausted medical options, patients may turn to online health forums to exchange support and seek information. We aimed to determine how patients use health forums and in turn, how medical professionals might utilise them in clinical practice.

Methods Three prominent open health forums were searched for threads related to cough, and screened against inclusion criteria adapted from the BTS guidance on cough. Included threads were transcribed verbatim into QSR NVivo, and subjected to qualitative thematic analysis. Findings were validated through the use of multiple reviewers.

Results 96 threads were reviewed, with contributions from 223 forum users. Three predominant themes emerged: the impact of chronic cough, treatment suggestions, and supportive posts. Regarding the impact of chronic cough, users highlighted the physical and psychological sequelae from prolonged cough, and the limitations imposed upon daily activities. Users suggested both prescribed treatments and alternative remedies, with many offering potential diagnoses to query with medical professionals. Supportive posts involved various strategies designed to show sympathy and empathy with others.

Conclusions Chronic cough patients use health forums to exchange information, advice and support. Health forums are a potential tool for clinicians wishing to access this population to provide medical care and promote patient education. We propose further research into these opportunities.

REFERENCES

A MULTI-SITE ONLINE CROSS-SECTIONAL SURVEY ASSESSING INFLUENZA VACCINATION UPTAKE AMONG LONDON MEDICAL STUDENTS AND MODIFIABLE FACTORS INFLUENCING THIS

10.1136/thoraxjnl-2016-209333.456

Introduction and objectives Around 1 in 5 healthcare workers (HCWs) may become infected during the influenza (flu) season. Currently, HCWs are not encouraged to vaccinate, as they are not classed as a priority group. However, HCWs with direct clinical roles were vaccinated, with lower than expected uptake (28–59%), raising questions about the effectiveness of educational interventions. Furthermore, vaccinating HCWs could, in turn, affect the vaccination uptake of those more vulnerable. We aimed to identify factors that influence vaccination uptake and assess the potential impact of future interventions among HCWs.

Methods A cross-sectional survey was conducted at four London medical schools, between October 2015 and March 2016. Demographic and self-reported factors were collected, and vaccination uptake was compared. Logistic regression was used to conduct multivariate analysis.

Results 734 students were recruited, with a response rate of 85%. 52% of respondents were male, and 64% were aged 20–24 years. 57% of respondents reported receiving the flu vaccine, however, only 36% of students who received the vaccine had received it between October and December 2015, with 95% confidence intervals of 83–96%. Factors associated with vaccination uptake included: self-perceived risk of contracting the flu (odds ratio [OR] 3.19, 95% CI 1.97–5.08), risk of infecting others (OR 3.05, 95% CI 1.69–5.46), and the perception that flu is preventable (OR 2.63, 95% CI 1.73–4.00). Factors that were not associated with vaccination uptake included: gender, ethnicity, socio-economic status, and known vaccination status.

Conclusion Students at London medical schools are increasingly likely to receive the vaccine, particularly if they believe flu is preventable, and feel at risk from contracting the disease or infecting others. Interventions that target these beliefs in future may improve vaccination uptake among HCWs.
### Abstract M14 Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>Number of students*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccinated</td>
<td>132 (44%)</td>
</tr>
<tr>
<td>Not vaccinated</td>
<td>170 (56%)</td>
</tr>
<tr>
<td><strong>Clinical years</strong></td>
<td></td>
</tr>
<tr>
<td>MBBS5</td>
<td>123 (41%)</td>
</tr>
<tr>
<td>MBBS4</td>
<td>88 (29%)</td>
</tr>
<tr>
<td>MBBS5</td>
<td>91 (30%)</td>
</tr>
<tr>
<td><strong>Positive vaccine uptake across clinical years</strong></td>
<td></td>
</tr>
<tr>
<td>MBBS5</td>
<td>51 (41%)</td>
</tr>
<tr>
<td>MBBS4</td>
<td>32 (36%)</td>
</tr>
<tr>
<td>MBBS5</td>
<td>49 (54%)</td>
</tr>
<tr>
<td><strong>Teaching hospital</strong></td>
<td></td>
</tr>
<tr>
<td>King’s College Hospital</td>
<td>121 (40%)</td>
</tr>
<tr>
<td>Guy’s and St Thomas’ Hospitals</td>
<td>116 (38%)</td>
</tr>
<tr>
<td>University Hospital Lewisham</td>
<td>54 (18%)</td>
</tr>
<tr>
<td>Not Applicable</td>
<td>11 (4%)</td>
</tr>
<tr>
<td><strong>Positive vaccine uptake across teaching hospitals</strong></td>
<td></td>
</tr>
<tr>
<td>King’s College Hospital</td>
<td>44 (36%)</td>
</tr>
<tr>
<td>Guy’s and St Thomas’ Hospitals</td>
<td>60 (32%)</td>
</tr>
<tr>
<td>University Hospital Lewisham</td>
<td>22 (41%)</td>
</tr>
<tr>
<td>Not Applicable</td>
<td>6 (55%)</td>
</tr>
<tr>
<td><strong>Hours of patient contact per week</strong></td>
<td></td>
</tr>
<tr>
<td>1 to 5</td>
<td>21 (7%)</td>
</tr>
<tr>
<td>6 to 10</td>
<td>71 (23%)</td>
</tr>
<tr>
<td>11 to 15</td>
<td>79 (26%)</td>
</tr>
<tr>
<td>16 to 20</td>
<td>59 (20%)</td>
</tr>
<tr>
<td>Over 20</td>
<td>72 (24%)</td>
</tr>
<tr>
<td><strong>Positive vaccine uptake across hours of patient contact</strong></td>
<td></td>
</tr>
<tr>
<td>1 to 5</td>
<td>7 (33%)</td>
</tr>
<tr>
<td>6 to 10</td>
<td>25 (35%)</td>
</tr>
<tr>
<td>11 to 15</td>
<td>35 (44%)</td>
</tr>
<tr>
<td>16 to 20</td>
<td>24 (41%)</td>
</tr>
<tr>
<td>Over 20</td>
<td>41 (57%)</td>
</tr>
<tr>
<td><strong>Was the vaccine offered to those who were not vaccinated?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>62 (36%)</td>
</tr>
<tr>
<td>No</td>
<td>108 (64%)</td>
</tr>
<tr>
<td><strong>Did students receive information about the vaccine?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>151 (50%)</td>
</tr>
<tr>
<td>No</td>
<td>151 (50%)</td>
</tr>
<tr>
<td><strong>Who provided the information?</strong></td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>7 (5%)</td>
</tr>
<tr>
<td>Hospital Trust</td>
<td>111 (73%)</td>
</tr>
<tr>
<td>General Practitioner</td>
<td>13 (9%)</td>
</tr>
<tr>
<td>Other</td>
<td>20 (13%)</td>
</tr>
<tr>
<td>Provided with information and vaccinated</td>
<td>102 (68%)</td>
</tr>
<tr>
<td>Not provided with information and vaccinated</td>
<td>30 (20%)</td>
</tr>
<tr>
<td><strong>Did students think they should get vaccinated?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>247 (82%)</td>
</tr>
<tr>
<td>No</td>
<td>55 (18%)</td>
</tr>
<tr>
<td><strong>Of those who thought they should get vaccinated</strong></td>
<td></td>
</tr>
<tr>
<td>Were actually vaccinated</td>
<td>121 (51%)</td>
</tr>
<tr>
<td>Were not vaccinated and not offered the vaccine</td>
<td>79 (33%)</td>
</tr>
<tr>
<td>Were not vaccinated and not provided with information</td>
<td>84 (70%)</td>
</tr>
<tr>
<td><strong>Did students know how to access the vaccine?</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>217 (72%)</td>
</tr>
<tr>
<td>No</td>
<td>85 (28%)</td>
</tr>
</tbody>
</table>

*The survey was disseminated to 1037 students. 302 students completed the survey.

average rates seen in London. Like any HCW, medical students should be actively encouraged to get vaccinated. Our aim was to assess levels of flu vaccine uptake among London medical students and investigate the negative influences affecting uptake that could be addressed at an institutional level.

**Methods** A cross-sectional online survey, developed by a focus group of respiratory consultants and medical students, was disseminated to London medical students at King’s College Hospital, Guy’s and St Thomas’ Hospitals and University Hospital Lewisham. Data was collected and analysed using SurveyMonkey Inc.

**Results** 302 medical students completed the survey (Table 1). There was a good representation of students across different sites and clinical years. Overall, 44% students reported receiving the flu vaccine. Uptake varied between teaching sites and clinical years. 82% of students felt they should get vaccinated with 51% of those doing so.

64% of those who were not vaccinated said they were not offered it, of whom 73% felt vaccination was appropriate. 50% of all students said they were not provided with any information about the vaccine. 68% of those who were provided with information were vaccinated whereas 20% of those who were not provided with information were vaccinated.

**Conclusions** Vaccination rates among London medical students are lower than for most HCWs. There appears to be a discrepancy between willingness to get vaccinated and actual uptake rates. This may be due to a lack of information and encouragement rather than a lack of access, as 72% of all students were aware of how to access the vaccine. Teaching hospitals and the University should address this by introducing flu vaccination awareness into the curriculum and consider adding it to mandated occupation health assessments.

---

**M15 EVALUATION OF A NOVEL INTERVENTION FOR PATIENTS WITH BRONCHIECTASIS: THE BRONCHIECTASIS INFORMATION AND EDUCATION FEASIBILITY (BRIEF) STUDY**

1KLM Hester, 1J Newton, 1T Rapley, 2A De Soyza. 1Newcastle University, Newcastle upon Tyne, UK; 2Adult Bronchiectasis Service, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK.

10.1136/thoraxjnl-2016-209333.457

**Introduction** There is currently limited information about bronchiectasis available to patients. We co-developed a novel patient and carer information resource, based on needs identified in previous work.1 The resource was evaluated in the BRIEF study with the following objectives:-

1. To establish the feasibility of carrying out a multi-centre randomised controlled trial (RCT) to determine effect on understanding, self-management and health outcomes.
2. To evaluate and refine the intervention.

**Methods** This was a feasibility study with a single-centre RCT design, comparing use of the resource to usual care in bronchiectasis.2

Adults with bronchiectasis were recruited from respiratory clinics in the North of England. Those randomised to the intervention received the information resource (website www.bronchiectasis.me and booklet). Outcome measures (resource satisfaction, bronchiectasis knowledge, quality of life, unscheduled healthcare visits, exacerbation frequency, and lung function)
CONSTRUCT VALIDITY OF THE NEEDS ASSESSMENT TOOL PROGRESSIVE DISEASES FOR INTERSTITIAL LUNG DISEASE (NAT: PD-ILD) PATIENTS

1C Reigada, 2C Fairhurst, 3J Yorke, 4J Ross, 5Boland, 6S Hart, 7D Currow, 8G Grande, 9S Bajwa, 10A Wells, 11U Maedoe, 12M Bland, 13M Johnson. 1Hull York Medical School, Hull, UK; 2University of York, York, UK; 3University of Manchester, Manchester, UK; 4Royal Brompton and Harefield NHS Foundation Trust, London, UK; 5Hull and East Yorkshire Hospitals NHS Foundation Trust, Hull, UK; 6Funders University, Australia; 7Cicely Saunders Institute, London, UK.

10.1136/thoraxjnl-2016-209333.458

Background People with ILD, currently have less access to SPC and there is no validated needs assessment tool (NAT). We adapted the NAT:PD-cancer for use in ILD and conducted psychometric testing. 

Aim To test the construct validity of NAT:PD-ILD.

Methods ILD clinicians in four hospitals were trained to use the NAT:PD-ILD. After a consultation, the clinician completed the NAT:PD-ILD, patients completed the St. George’s Respiratory Questionnaire (SGRQ-I) and carers completed the Carer Strain Index (CSI) and Carer Support Needs Assessment Tool (CSNAT).

Kendall’s Tau-b correlation coefficient (and associated p-value) was calculated to determine the correlation between the NAT: PD-ILD items relating to patient wellbeing, and a total score for a subset of SGRQ-I questions identified a priori as measuring similar constructs. The prevalence and bias adjusted kappa (PABAK), Cohen’s kappa and percentage of agreement were used to assess whether responses were similar between the NAT: PD-ILD items relating to the ability and wellbeing of the carer and appropriate CSI and CSNAT items which were considered to measure similar concerns/support needs.

Results A total of 68 patients were recruited. The average age of participating patients was 66 years (range 34 to 87) and 62% were male. Forty-five (66%) patients had a carer of whom 27 completed the CSI (mean 4.4, SD 3.0, median 4, range 0–11) and 29 completed at least one item of the CSNAT.

Items 2, 3, 5 and 6 of the NAT: PD-ILD statistically significantly positively correlated with their comparator SGRQ-I scores (ρ range 0.24 to 0.36, p < 0.05). PABAK values comparing the NAT: PD-ILD items with appropriate CSI and CSNAT items show most items have PABAK positive values (range from 0.04 to 0.57, with a minimum of 52% agreement). However, NAT:PD-ILD items 11 and 13 have negative PABAK values (Inter-personal relationships and Grief topics – Psychosocial Dimension).

Conclusion The NAT: PD-ILD has adequate construct validity for most domains. However, agreement is poor for physical symptoms and spiritual concerns. This may indicate that clinicians identify concerns with symptoms less well unless they are severe.

LIMITED VALUE OF BASELINE CHEST RADIOGRAPHY IN ADULTS WITH NON-TUBERCULOUS MYCOBACTERIA

1ME Murphy, 2NM Shah, 3B Bharucha, 4C Cash, 5R Cleverley, 6M Copley, 7S Hopkins, 8MC Lipman. 1University College London, London, UK; 2Kings College London, London, UK; 3Royal Free London NHS Foundation Trust, London, UK.

10.1136/thoraxjnl-2016-209333.459

Chest radiographic changes are associated with mycobacterial burden, treatment response and outcome in patients with tuberculosis. There is a paucity of similar data for non-tuberculous mycobacteria (NTM). We describe the chest radiology (CXR) findings in a cohort of adults without cystic fibrosis.

Methods Patients with NTM isolated from respiratory specimens between 2010–2013 at our centre were reviewed. Chest X-rays (CXR) nearest the date of positive NTM culture were read independently by two consultant Radiologists for 5 categories of abnormality (nodules, cavities, bronchiectasis, bronchial wall thickness [BWT] and consolidation) in each of 6 zones. A consensus result was agreed where discrepant. CXR results were recorded as “normal” or “abnormal” overall and for each category per zone. The total number of zones affected in all categories was summed to provide a measure of radiological extent of disease (with a maximum score of 30), e.g. a patient with cavitation in 2 zones and bronchiectasis in 3 would score 5/30. Results...
were compared to clinical and microbiological data (including time-to-positivity in liquid culture, TTP).

**Results**

Of 79 patients, 44/79 (56%) were male, median age 63 years [IQR 53;75]. CXR was performed median 5-days [IQR 2;28] from sample collection. Inter-rater CXR agreement was 92%, kappa 0.57 [95% CI: 0.52–0.63]. 58/79 (75%) of subjects had an abnormal CXR [Table 1]: half had nodules and BWT, with 41%, 23% and 20% bronchiectasis, consolidation and cavities respectively. Using symptoms present in >1/3 patients, only sputum and difficulty breathing were significantly associated with CXR score (p = 0.04; p = 0.01). *M.avium* and *M.intracellulare* were the most common NTM isolated [Table 1]. The highest abnormal median score for CXR was for *M.xenopi* (6/30) followed by *M.perigrinum* (5/30), and *M.abscessus* (4/30). For *M.kansasii* there was significant correlation between CXR score and TTP (r = 0.82 ; p = 0.01) with cavitation being associated with a significantly lower TTP (4.5 vs 17.5 days; p = 0.03). CXR score did not predict whether or not a patient started treatment (OR 1.07; p = 0.40).

**Conclusion**

CXR abnormalities were present in 75% of patients in whom NTM was isolated. Unlike *M.tuberculosis*, the extent of radiographic changes correlated poorly with clinical symptoms or mycobacterial burden. Better simple, repeatable measures of NTM disease severity are required.

**Abstract M17 Table 1** Numbers of non-tuberculosis mycobacteria (NTM) isolates with numbers and proportions of abnormal chest-x-rays (CXR), median CXR scores, median time to culture positivity (TTP) and whether treated (Rx)

<table>
<thead>
<tr>
<th>NTM</th>
<th>N (%)</th>
<th>Abnormal CXR N (%)</th>
<th>Median CXR score</th>
<th>Median TTP (days)</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>M.avium</em></td>
<td>24 (30)</td>
<td>20 (25)</td>
<td>3.5</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td><em>M.intracellulare</em></td>
<td>13 (16)</td>
<td>12 (15)</td>
<td>5</td>
<td>13.5</td>
<td>2</td>
</tr>
<tr>
<td><em>M.fortuitum</em></td>
<td>12 (15)</td>
<td>7 (9)</td>
<td>4</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td><em>M.kansasii</em></td>
<td>8 (10)</td>
<td>4 (5)</td>
<td>5</td>
<td>6.5</td>
<td>0</td>
</tr>
<tr>
<td><em>M.chelonae</em></td>
<td>5 (6)</td>
<td>3 (4)</td>
<td>3</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td><em>M.perigrinum</em></td>
<td>4 (5)</td>
<td>4 (5)</td>
<td>5</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td><em>M.gordonae</em></td>
<td>4 (5)</td>
<td>0 (0)</td>
<td>0</td>
<td>29</td>
<td>0</td>
</tr>
<tr>
<td><em>M.xenopi</em></td>
<td>3 (4)</td>
<td>3 (4)</td>
<td>6</td>
<td>24</td>
<td>1</td>
</tr>
<tr>
<td><em>M.mucogencum</em></td>
<td>2 (3)</td>
<td>2 (3)</td>
<td>2</td>
<td>12.5</td>
<td>0</td>
</tr>
<tr>
<td><em>M.abscessus</em></td>
<td>2 (3)</td>
<td>1 (1)</td>
<td>4.5</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td><em>M.polstrit</em></td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>0</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td><em>M.vulnieri</em></td>
<td>1 (1)</td>
<td>1 (1)</td>
<td>4</td>
<td>–</td>
<td>1</td>
</tr>
</tbody>
</table>

**M18**

**ENHANCED TRAINING FOR MEDICAL REGISTRARS LEARNING CHEST DRAINS AND THORACOCENTESIS. UNDERSTANDING TOTAL COMPETENCY LEVEL IN THE WORK FORCE**

AL Chapman, M Gingell, E Clissold. Waitemata District Heath Board, Auckland, New Zealand

10.1136/thoraxjnl-2016-209333.460

Performing a chest drain procedure with a safe technique is a core skill for a medical registrar and arguably the highest risk procedure they are expected to perform at junior level.

The competency level of a cohort of registrars who typically rotate every six months is often not known. Little regard is given to this when drawing up on call rotas and training needs are often missed. In this initiative we aimed to address these failings.

**Methods**

By way of induction for the general medical registrars beginning a six month post in our hospitals we arranged a short verbal introduction to the group about local processes of how chest procedures within our hospital are performed eg. location of equipment in centralised packs, standardised equipment lists, check lists and use of bedside US and patient information/consent.

Over the first two weeks of the run we arranged “one on one” teaching with a Consultant chest physician who taught each registrar according to their needs on realistic mannequins. Three techniques taught: thoracocentesis with an 8 F drainage pack; a small bore 12 F seldinger drain and a surgical 28 F drain drain according to need. Teaching of 32 registrars was completed within a two week time frame in the space of four PA/clinic sessions. Competency was judged at the end of the session and electronic DOPS and feedback from the registrars was obtained. We encouraged further discussion with educational supervisors with regard to ongoing training requirements for individuals.
Results and evaluation  Attendance was 31/32. 59% had 12 months or less experience as a registrar. 66% were able to perform thoracocentesis and 63% seldinger drain independently. Most others were competent enough to perform with a colleague supervising. Additionally 38% and 25% of registrars were deemed to be able to teach other thoracocentesis and seldinger drains respectively.

Learning feedback was extremely positive and self-rated confidence and safety improved from 5–7.6 and 5.2 to 7.7 out of 10 respectively. Responses highly valued the fact this was delivered by a Consultant and identified a need for further bedside chest US training.

Background and objectives Barking, Havering and Redbridge University Trust (BHRUT) serves a population of 750,000 patients with a large burden of pleural disease. Patients admitted and requiring pleural drainage usually results in a long length of stay of around 7–10 days. Outpatient ambulatory management of undiagnosed and known malignant pleural effusions is increasing nationally in the UK through development of pleural clinics. Previous reports have demonstrated these to be financially efficacious and avoid hospitalisation. We sought to demonstrate that they are also well received and favoured by patients.

Methods In December 2015, an outpatient weekly pleural aspiration service was established receiving referrals directly from respiratory outpatients, A&E and acute medicine. We prospectively audited patients attending this service between December 2015 and June 2016. Patients were asked to complete an in-depth questionnaire to assess their experience on the day, any procedure discomfort and attitudes toward such an outpatient service.

Results 81 patients attended our service over this period. Median age was 74 (range 30–92), 40% female. 58 patients returned a completed questionnaire. 86% of patients were seen within a week of referral with the rest waiting less than 2 weeks. The majority (74%, n = 43) of patients did not notice any deterioration in their symptoms during this wait. Median pain score was 3 (range 1–10), 78% (n = 45) of patients felt they could continue with their normal activities post procedure. Only 2 patients would have preferred to undergo the procedure as an inpatient citing frailty as the reason. 98% (n = 57) of patients felt that an outpatient pleural service was a good idea. 78% (n = 45) rated the service as excellent, 17% (n = 10) as ‘above average’ and only 5% (n = 3) as ‘average.’

Conclusions Outpatient management of pleural effusions is favoured by patients with most rating our service as excellent. Patients are seen promptly with the majority reporting no deterioration in their symptoms during the wait. The procedure is well tolerated and allows patients to continue with their normal daily activities. In addition to important financial benefits of reducing hospital bed-days in patients with pleural effusions, our newly established service has been shown to be beneficial in promoting a positive patient experience.
included if both CT and ultrasound scans had been performed ≤10 days apart with no intervening pleural procedure. Consultant radiologists reported effusions on CT as small, moderate or large. Thoracic ultrasound scans were performed by the pleural team (level 1 Royal College of Radiologists practitioners). The height of the effusion (in rib spaces) and maximal medial depth (in cm) were recorded. Small, moderate and large effusions by ultrasound were defined as ≤1, 2–3 and ≥4 rib spaces respectively. CT and ultrasound categories were compared using the Stuart-Maxwell Test.

Results In 51 patients the median age was 70 (interquartile range [IQR] 59–80) years and 26 (51%) were male. Right effusions were dominant in 29 (56%), and 48 (94%) had a CT chest or CT pulmonary angiograms. CT scan reported size was available in 37 (72%) cases, and of these, 6 (16%), 11 (30%) and 20 (54%) were defined as small, medium and large respectively. For small, moderate and large effusions by ultrasound, the median height in rib spaces was 1.5 (IQR 1–2), 3 (IQR 2–3) and 3.5 (IQR 2.75–4) respectively. Height in rib spaces (r = 0.537, p < 0.001) and depth of effusion (r = 0.365, p = 0.02) correlated with CT reported size. However overall classification of ultrasound size was not associated with CT size (p = 0.04). In 15 (40%) effusions, the size classification differed.

Conclusions Our findings indicate that pleural effusions size determined by CT and ultrasound differed. Revised simple methodology to estimate effusion size should be sought, and may help to refine patient pathways of care.
Declarations of interest

$S4$ EFFECT OF 8 AND 12 WEEKS’ ONCE-DAILY Tiotropium AND OLODATEROL, ALONE AND COMBINED WITH EXERCISE TRAINING, ON EXERCISE ENDURANCE DURING WALKING IN PATIENTS WITH COPD

T Troosters has received grants from Innovative Medicines Initiative Joint Undertaking and speaker fees from Boehringer Ingelheim and GlaxoSmithKline.

J Bourbeau has received grants from the Canadian Institute of Health Research R&D collaborative programme (AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Merck, Nycomed, Novartis), Canadian Respiratory Research Network, Respiratory Health Network of the FRQS and Research Institute of the MUHC, and an educational grant from GlaxoSmithKline.

F Malais has received grants from Boehringer Ingelheim, GlaxoSmithKline, AstraZeneca, Nycomed and Pfizer, personal fees from Boehringer Ingelheim, GlaxoSmithKline and Novartis, and other financial support from GlaxoSmithKline.

N Leidy is employed by Evidera, a health-care research firm that provides consulting and other research services to pharmaceutical and other organisations including the study sponsor.

D Erzen, D De Sousa, L Korducki and A Hamilton are employees of Boehringer Ingelheim Pharma GmbH & Co. KG.

KL Lavoie reports personal fees from Boehringer Ingelheim for personnel training as well as a grant from AbbVie and personal fees from Bayer, Janssen, Novartis, AbbVie, Mundipharma and Almirall.

W Janssens has no conflict of interest to report.

$S109$ TARGETING THE PROSTACYCLIN PATHWAY IN THE TREATMENT OF CONNECTIVE TISSUE DISEASE ASSOCIATED PULMONARY ARTERIAL HYPERTENSION (PAH): INSIGHTS FROM THE RANDOMISED CONTROLLED GRIPHON TRIAL WITH SELEXIPAG

The GRIPHON study was sponsored by Actelion Pharmaceuticals Ltd.

G Coghlan: Consulting fees: Actelion Pharmaceuticals Ltd, Bayer HealthCare, GlaxoSmithKline, GenenTech, United Therapeutics. Speaker’s honoraria and research grants: Actelion Pharmaceuticals Ltd, GlaxoSmithKline, Bayer HealthCare, United Therapeutics.

S Gaine: Consulting fees/honoraria: Actelion Pharmaceuticals Ltd, Bayer HealthCare, GlaxoSmithKline, United Therapeutics, Novartis, Pfizer. Steering Committee membership: Actelion Pharmaceuticals Ltd, GlaxoSmithKline, United Therapeutics, Novartis.


N Galí: Consulting fees/honoraria: Actelion Pharmaceuticals Ltd, Bayer HealthCare, GlaxoSmithKline, Pfizer. Steering Committee membership: Actelion Pharmaceuticals Ltd.


MM Hooper: Consulting fees/honoraria: Actelion Pharmaceuticals Ltd, Bayer HealthCare, GlaxoSmithKline, Pfizer, Gilead Sciences. Steering Committee membership: Actelion Pharmaceuticals Ltd.

I Lang: Consulting fees/honoraria: Actelion Pharmaceuticals Ltd, Bayer HealthCare, GlaxoSmithKline, Novartis Corporation, United Therapeutics. Steering Committee membership: Actelion Pharmaceuticals Ltd.


$S112$ LONG-TERM SAFETY AND EFFICACY OF IVACAFTOR IN PEDIATRIC PATIENTS AGED 2-5 YEARS WITH CYSTIC FIBROSIS AND A CFTR GATING MUTATION

JC Davies has served on advisory boards, undertaken educational activities, and served as national/site principal investigator for trials, for which her institution has received funding from Vertex Pharmaceuticals Incorporated.

S Robertson is an employee of Vertex Pharmaceuticals Incorporated and may own stock or stock options in that company.

J Cooke is an employee of Vertex Pharmaceuticals Incorporated and may own stock or stock options in that company.

M Higgins is an employee of Vertex Pharmaceuticals Incorporated and may own stock or stock options in that company.

M Rosenfeld: has served as a national and site investigator for trials and as a consultant, for which her institution received funding from Vertex Pharmaceuticals Incorporated.
GT Ferguson, during the conduct of the study, reports grants, personal fees and non-financial support from Boehringer Ingelheim and, outside the submitted work, grants, personal fees and non-financial support from Boehringer Ingelheim, personal fees from GlaxoSmithKline, grants and personal fees from Novartis, AstraZeneca, Pearl Therapeutics and Sunovion, and grants from Forest.

R Abrahams reports grants and personal fees from Boehringer Ingelheim during the conduct of the study and, outside of this work, grants and personal fees from GlaxoSmithKline and grants from AstraZeneca and Pearl Therapeutics.

L Bjerner reports no conflicts of interest.

L Grönlund and F Voß are employees of Boehringer Ingelheim Pharma GmbH & Co. KG.

D Singh reports other financial activities from Boehringer Ingelheim during the conduct of the study and, outside of the submitted work, grants and personal fees from Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Glenmark, Johnson & Johnson, Merck, NAPP, Novartis, Pfizer, Takeda, Teva, Theravance and Verona, and personal fees from Genentech and SkyePharma.

The NOVELTY study is supported by AstraZeneca.

M Gerhardsson de Verdier, C Keen, A Garde, S Rennard, A Sveréus, L Brannman, N Karlson, J Nuevo, F Nyberg and S Young are employees of AstraZeneca.

HK Reddel has participated in advisory boards for AstraZeneca, GlaxoSmithKline and Novartis, a data safety monitoring board for AstraZeneca, GlaxoSmithKline, Merck and Novartis, has provided independent educational presentations for AstraZeneca, GlaxoSmithKline, Boehringer Ingelheim, Mundipharma and Teva, and has received independent research funding from AstraZeneca and GlaxoSmithKline.

R Beasley has received research funding from AstraZeneca, Genentech, Cephalon, GlaxoSmithKline, Novartis and Sanofi, and has received payments for lectures and/or participation in advisory boards from AstraZeneca, GlaxoSmithKline and Novartis.

E Helsel has received research grants from Roche, AstraZeneca, GlaxoSmithKline, and honoraria for research consulting from AstraZeneca, GlaxoSmithKline, Novartis, and Sanofi/Regeneron.

C Janson has no disclosures to declare.

B Make has received honoraria for participation in NOVELTY planning meeting, and has received grant funding, participated in advisory boards and provided non-branded talk for AstraZeneca.

He has received honoraria for participation in medical advisory boards for Aerocrine, Boehringer-Ingelheim, CSL Bering, GlaxoSmithKline, Forest, Novartis, Spiration, Theravance, and Sunovion. He has participated in research studies funded by Boehringer-Ingelheim, GlaxoSmithKline, Pfizer, Forest, Sunovion.

RJ Martin has received consulting fees from AstraZeneca, Teva, Genentech, Boehringer Ingelheim, and PMD. His institution has received grants from NHLBI (AsthmaNet) and MedImmune. He has also received travel/accommodation/meeting expenses from the Respiratory Effectiveness Group.

J Pavord has received speaker’s honoraria for speaking at sponsored meetings from Astra Zeneca, Boehringer Ingelheim, Aerocrine, Almirall, Novartis, and GSK and a payment for organising an educational event from AZ. He has received honoraria for attending advisory panels with Almirall, Genentech, Regeneron, Astra Zeneca, Boehringer Ingelheim, GSK, MSD, Schering-Plough, Novartis, Dey, Napp and RespiVert. He has received sponsorship to attend international scientific meetings from Boehringer Ingelheim, GSK, Astra Zeneca and Napp.

D Price has board membership with Aerocrine, Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, Meda, Mundipharma, Napp, Novartis, and Teva Pharmaceuticals; consultancy with Almirall, Amgen, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Meda, Mundipharma, Napp, Novartis, Pfizer, and Teva Pharmaceuticals; grants and unrestricted funding for investigator-initiated studies (conducted through Research in Real-Life Ltd and Observational and Pragmatic Research Institute Pte Ltd) from UK National Health Service, British Lung Foundation, Aerocrine, AKL Ltd, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Eli Lilly, GlaxoSmithKline, Meda, Merck, Mundipharma, Napp, Novartis, Orion, Pfizer, Respiratory Effectiveness Group, Takeda, Teva Pharmaceuticals, and Zentiva; payments for lectures/speaking from Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, Cipla, GlaxoSmithKline, Kyorin, Meda, Merck, Mundipharma, Novartis, Pfizer, Skypharma, Takeda, and Teva Pharmaceuticals; payment for manuscript preparation from Mundipharma and Teva Pharmaceuticals; patents (planned, pending or issued) from AKL Ltd; payment for the development of educational materials from GlaxoSmithKline and Novartis; stock/stock options from AKL Ltd which produces phytopharmaceuticals; owns 80% of Research in Real Life Ltd, 75% of the social enterprise Optimum Patient Care Ltd and 75% of Observational and Pragmatic Research Institute Pte Ltd; received payment for travel/accommodations/meeting expenses from Aerocrine, Boehringer Ingelheim, Mundipharma, Napp, Novartis, and Teva Pharmaceuticals; funding for patient enrolment or completion of research from Almirall, Chiesi, Teva Pharmaceuticals, and Zentiva; and peer reviewer for grant committees of the Medical Research Council (2014), Efficacy and Mechanism Evaluation programme (2012), HTA (2014).

AT Bansal is a paid consultant of AstraZeneca, GlaxoSmithKline, iVivo and Roche.

J Vestbo has received honoraria from AstraZeneca, Boehringer-Ingelheim, Chiesi, GlaxoSmithKline and Novartis for advising and presenting.
Declarations of interest

P154 SAFETY OF TIOTROPium IN PRE-SCHOOL CHILDREN WITH SYMPTOMATIC PERSISTent ASThma

10.1136/thoraxjnl-2016-209333.469

H Bisgaard has been a consultant for AstraZeneca, Boehringer Ingelheim and Chiesi;
M Vandewalker has received research grants and personal fees from Boehringer Ingelheim;
L Graham made no relevant disclosures;
P Moroni-Zentgraf is an employee of Boehringer Ingelheim;
M Engel is an employee of Boehringer Ingelheim;
G El Azzi is an employee of Boehringer Ingelheim;
SD Vulcu is an employee of Boehringer Ingelheim;
H Finnigan is an employee of Boehringer Ingelheim;
EJLE Vrijelandt has received personal fees from Boehringer Ingelheim

P155 SAFETY OF TIOTROPium RESPIMAT® ADD-ON THERAPY IN PATIENTS AGED 6–17 YEARS WITH SYMPTOMATIC ASThma

10.1136/thoraxjnl-2016-209333.470

C Vogelberg has participated in an advisory board for Boehringer Ingelheim;
SJ Szefler has received personal fees from Aerocrine, Boehringer Ingelheim, Daiichi Sankyo, Genentech, GlaxoSmithKline, Merck, Novartis, and Roche, and research grants from GlaxoSmithKline;
E Hamelmann has received research grants and other fees from Boehringer Ingelheim and non-financial support from Boehringer Ingelheim;
A Boner has nothing to disclose;
P Moroni-Zentgraf is an employee of Boehringer Ingelheim;
M Engel is an employee of Boehringer Ingelheim;
G El Azzi is an employee of Boehringer Ingelheim;
SD Vulcu is an employee of Boehringer Ingelheim;
H Finnigan is an employee of Boehringer Ingelheim;
M Vandewalker has received research grants and personal fees from Boehringer Ingelheim.

P156 EFFICACY, SAFETY AND TOLERABILITY OF ONCE-DAILY TIOTROPium RESPIMAT® ADD-ON THERAPy IN CHILDREN WITH MODerate SYMPTOMATIC ASThma

10.1136/thoraxjnl-2016-209333.471

O Schmidt has received research grants from Boehringer Ingelheim;
E Hamelmann has received research grants and other fees from Boehringer Ingelheim and non-financial support from Boehringer Ingelheim;
C Vogelberg has participated in an advisory board for Boehringer Ingelheim;
I Laki has nothing to disclose;
G El Azzi is an employee of Boehringer Ingelheim;
M Engel is an employee of Boehringer Ingelheim;
P Moroni-Zentgraf is an employee of Boehringer Ingelheim;
H Finnigan is an employee of Boehringer Ingelheim;
M Vandewalker has received research grants and personal fees from Boehringer Ingelheim.

P183 BURDEN OF ILLNESS IN SCHOOL-AGED PATIENTS WITH CYSTIC FIBROSIS (CF) IN THE UNITED STATES

10.1136/thoraxjnl-2016-209333.472

J Rubin: is an employee of Vertex Pharmaceuticals Incorporated and may own stock or stock options in that company.
M Bonafede: is employed by Truven Health Analytics which received funding from Vertex Pharmaceuticals Incorporated.
S Sikirica: is an employee of Vertex Pharmaceuticals Incorporated and may own stock or stock options in that company.
B Limone: is employed by Truven Health Analytics which received funding from Vertex Pharmaceuticals Incorporated.
N Adolph: is employed by Truven Health Analytics which received funding from Vertex Pharmaceuticals Incorporated.
M Konstan: received consultant fees and his institution has received financial support from Vertex Pharmaceuticals Incorporated for study participation.

P294 BENEFITS OF TIOTROPium/OLODATEROL OVER TIOTROPium AT DELAYING CLINICALLY SIGNIFICANT EVENTS IN PATIENTS WITH COPD CLASSIFIED AS GOLD B

10.1136/thoraxjnl-2016-209333.473

R Buhl reports financial support to his institution from Boehringer Ingelheim during the conduct of the study and, outside of the submitted work, financial support from Boehringer Ingelheim, AstraZeneca, Chiesi, Novartis, Teva, Roche and GlaxoSmithKline for attendance at advisory boards and speaking activities, and research support to his institution from Boehringer Ingelheim, GlaxoSmithKline, Novartis and Roche.
L McGarvey reports personal fees from Applied Clinical Intelligence during the conduct of the study, and grants from Asthma UK, NI Chest Heart & Stroke, NC3Rs, British Heart Foundation and Chiesi, and other from Boehringer Ingelheim, GlaxoSmithKline, Chiesi, Almirall and NAPP outside the submitted work.
S Korn has received grants and personal fees from AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, Novartis and Takeda, grants from Teva and MedImmune, and personal fees from Almirall and Grifols.
GT Ferguson, during the conduct of the study, reports grants, personal fees and non-financial support from Boehringer Ingelheim and, outside the submitted work, grants, personal fees and non-financial support from Boehringer Ingelheim, personal fees from GlaxoSmithKline, grants and personal fees from Novartis, AstraZeneca, Pearl Therapeutics and Sunovion, and grants from Forest.
L Grönke, C Hallmann and F Voß are employees of Boehringer Ingelheim Pharma GmbH & Co. KG.
Declarations of interest

P299 EFFECTS OF SYMPTOM SEVERITY AT BASELINE ON LUNG-FUNCTION AND SGRQ RESPONSES IN THE OTEMTO® STUDIES

FJ Martinez reports financial support from AstraZeneca, Afferent, Boehringer Ingelheim, ConCert, Genentech, GlaxoSmithKline, Kadmon, Mero, Pearl, Unity, Novartis, Takeda, Sunovion, Theravance and Veracyte for attendance at advisory boards, research support for steering committees from Afferent, Bayer, GlaxoSmithKline and Takeda, personal fees from UpToDate for a COPD CME programme, and financial support from Biogen and GlaxoSmithKline for participation in data safety monitoring boards.

R Abrahams reports grants and personal fees from Boehringer Ingelheim during the conduct of the study and, outside of this work, grants and personal fees from GlaxoSmithKline and grants from AstraZeneca and Pearl Therapeutics.

GT Ferguson, during the conduct of the study, reports grants, personal fees and non-financial support from Boehringer Ingelheim and, outside the submitted work, grants, personal fees and non-financial support from Boehringer Ingelheim, personal fees from GlaxoSmithKline, grants and personal fees from Novartis, AstraZeneca, Pearl Therapeutics and Sunovion, and grants from Forest.

L Bjørner reports no conflicts of interest.

L Grönke and F Voß are employees of Boehringer Ingelheim Pharma GmbH & Co. KG.

D Singh reports other financial activities from Boehringer Ingelheim during the conduct of the study and, outside of the submitted work, grants and personal fees from Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Glenmark, Johnson & Johnson, Merck, NAPP, Novartis, Pfizer, Takeda, Teva, Theravance and Verona, and personal fees from Genentech and SkyPharma.
The number next to the author indicates the page number, not the abstract number.

Aalamian-Mattheis M, A22
Abbara A, A51, A143
Abdelaziz MM, A190
Abdulkareem A, A251
Abi Musa Asa`ari AKA, A268
Abid G, A140, A141
Abraham RT, A185
Abrahams R, A113, A255
Abubakar I, A50
Abunga Y, A144
Abunga YO, A146
Achaiah A, A26
Adamali HI, A13, A237
Adams K, A36, A38
Adamson V, A39
Addeo A, A89
Adeniji K, A33
Adizie JB, A24, A96
Adlakha A, A1
Adolph N, A183
Agalioti T, A7
Agbetile J, A154
Agostini P, A36, A38
Agrawal S, A73
Agustí A, A157
Ahern N, A51
Ahmad N, A195
Ahmed A, A77
Ahmed L, A84, A86
Ahmed M, A83
Ahmed N, A41
Ahmed R, A109
Akers S, A174
Akram N, A28
Akram R, A109
Akthar M, A179
Al-Ameri A, A76
Al-Shelkify B, A18
Albera C, A57, A175, A178
Albers FC, A5, A170
Aldik MG, A93, A268
Aldridge KA, A10
Ali A, A241
Ali FR, A261
Ali H, A91
Ali NJ, A91, A122
Aliyu S, A232
Aliyu SA, A104
Allen D, A5
Allen G, A3
Allen J, A76
Allen M, A121
Allen MB, A224
Allinger A, A175
Allinson JP, A1
Allison DJ, A101
Allisp L, A91
Almond MH, A142
Alola JF, A60
Alsaid A, A251
Altmann P, A206, A246
Alton E, A44
Alton EFW, A44
Alvi A, A109
Anderson A, A182
Anderson D, A161, A174, A224
Anderson K, A121
Anderson R, A29
Andreassen A, A80
Anwar M, A22
Atkinson PJ, A124
Atkinson RD, A220
Anwar M, A97, A228
Arbene G, A33, A68
Archibald J, A251
Archer FA, A187
Arntz RJ, A103
Arden MA, A20
Arent M, A251
Ariely R, A158
Arigiani M, A183, A223
Aris E, A23
Armstrong J, A98, A99
Armstrong-James DAJ, A1
Ameli K, A19
Arnold DT, A54
Arnold N, A49, A220
Arnold ND, A50
Aron JR, A168
Arshad A, A74
Arumugam J, A73
Arvanitis R, A138
Ashcroft H, A34
Asher A, A96
Ashford-Turner V, A76
Ashston D, A62
Ashworth A, A141
Askew K, A182
Aslani M, A8
Atkins CP, A238
Aurora P, A183, A223, A227
Austin A, A268
Avery G, A104
Axmann J, A171
Azzopardi G, A104
Babar J, A192, A232
Babawale L, A100
Babu S, A33
Bacon J, A193
Badenes Bonet D, A236
Baldacheil M, A28, A40, A61
Baggotte C, A13
Bailley J, A202
Bain A, A121
Bajaj MK, A105
Bajjwah S, A266
Baker A, A224
Baker A, A107
Baker EH, A9, A105, A206, A257
Baker L, A146
Baker-Wilding R, A201
Baksi S, A131
Balata H, A37
Baldwin DR, A77
Bales E, A97, A98
Ball D, A121
Baluwala A, A120
Bamford J, A182
Bancroft H, A39
Banerji D, A116
Bansal AT, A157
Bapuam A, A95
Barber CM, A70, A224
Barclay ST, A151
Barker CI, A9
Baflow M, A105
Barnayehvar B, A235
Barnes N, A159, A169
Barnfather S, A114
Barr H, A133
Barratt B, A199
Barrett A, A6
Barrett D, A133
Barrett N, A154
Barrick TR, A105
Barry LB, A150
Bart PI, A135
Basaldella U, A247
Basist A, A145
Baskaran L, A194
Basewide H, A229
Batcher M, A238
Baxter N, A158
Bayliss S, A155
Beadle J, A174
Beardsley B, A44
Beardmore CR, A181
Beardmore CS, A126
Beasley R, A157
Beck S, A144
Beckett P, A35, A139
Beckman O, A155
Bedi P, A62
Beer S, A40
Beivers S, A199
Bel EH, A157
Belchamber KB, A72
Belchamber KBR, A2
Belcher J, A39
Belgravec D, A148
Bell S, A254
Bellamy M, A39
Belton M, A146
Benamore R, A30, A103, A243
Benhaddi H, A158
Benjamin JA, A194
Benlahrech A, A30
Bennett JA, A228
Bennett M, A237
Bennett R, A221
Berge M van den, A155
Bergman G, A158
Bergman P, A60
Bergna MA, A206
Beynon W, A29
Bhagani S, A50
Bharucha T, A266
Bhavsar PK, A9
Bhowmik A, A83
Bibby AC, A69
Bikarna S, A55, A140, A268
Bilanda R, A119
Billings C, A66, A98
Billings CG, A99
Bird J, A28
Birling SS, A13, A17, A263

Thorax 2016;X(Suppl X):A1–A285

Author index
<table>
<thead>
<tr>
<th>Author</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisgaard H</td>
<td>A166</td>
</tr>
<tr>
<td>Bishay E</td>
<td>A36, A38, A39, A88</td>
</tr>
<tr>
<td>Bishop P</td>
<td>A37</td>
</tr>
<tr>
<td>Bjerner L</td>
<td>A113, A155, A255</td>
</tr>
<tr>
<td>Black E</td>
<td>A224</td>
</tr>
<tr>
<td>Black S</td>
<td>A229</td>
</tr>
<tr>
<td>Blackwood B</td>
<td>A10</td>
</tr>
<tr>
<td>Blakey J</td>
<td>A5</td>
</tr>
<tr>
<td>Blakey S</td>
<td>A125</td>
</tr>
<tr>
<td>Bland M</td>
<td>A266</td>
</tr>
<tr>
<td>Blaxill P</td>
<td>A76</td>
</tr>
<tr>
<td>Bleda M</td>
<td>A63</td>
</tr>
<tr>
<td>Bilardo K</td>
<td>A30</td>
</tr>
<tr>
<td>Bloch SAA</td>
<td>A125</td>
</tr>
<tr>
<td>Blyth KG</td>
<td>A86, A129</td>
</tr>
<tr>
<td>Boer W De</td>
<td>A103</td>
</tr>
<tr>
<td>Boggaard H</td>
<td>A63</td>
</tr>
<tr>
<td>Boland F</td>
<td>A165, A205</td>
</tr>
<tr>
<td>Boland J</td>
<td>A266</td>
</tr>
<tr>
<td>Bonafede M</td>
<td>A183</td>
</tr>
<tr>
<td>Bonella F</td>
<td>A58, A171</td>
</tr>
<tr>
<td>Boner A</td>
<td>A167</td>
</tr>
<tr>
<td>Boomi V</td>
<td>A244</td>
</tr>
<tr>
<td>Booth HL</td>
<td>A45</td>
</tr>
<tr>
<td>Booth S</td>
<td>A203</td>
</tr>
<tr>
<td>Boother E</td>
<td>A101</td>
</tr>
<tr>
<td>Botton R</td>
<td>A37, A76, A141</td>
</tr>
<tr>
<td>Borg E</td>
<td>A6</td>
</tr>
<tr>
<td>Borthwick L</td>
<td>A80</td>
</tr>
<tr>
<td>Bossley C</td>
<td>A179</td>
</tr>
<tr>
<td>Bothamley GH</td>
<td>A263</td>
</tr>
<tr>
<td>Bott J</td>
<td>A193</td>
</tr>
<tr>
<td>Boucot II</td>
<td>A114, A244</td>
</tr>
<tr>
<td>Boukerroui D</td>
<td>A94</td>
</tr>
<tr>
<td>Boulet L-P</td>
<td>A155</td>
</tr>
<tr>
<td>Bourne E</td>
<td>A6</td>
</tr>
<tr>
<td>Bourne SC</td>
<td>A69, A162, A201</td>
</tr>
<tr>
<td>Bourke SC</td>
<td>A69, A162, A201</td>
</tr>
<tr>
<td>Bourke S</td>
<td>A68</td>
</tr>
<tr>
<td>Bourne E</td>
<td>A263</td>
</tr>
<tr>
<td>Bourne M</td>
<td>A154</td>
</tr>
<tr>
<td>Bourne SC</td>
<td>A23</td>
</tr>
<tr>
<td>Boven JFM van</td>
<td>A158</td>
</tr>
<tr>
<td>Boyle M</td>
<td>A134</td>
</tr>
<tr>
<td>Bradbury L</td>
<td>A20, A134</td>
</tr>
<tr>
<td>Bradding PH</td>
<td>A166</td>
</tr>
<tr>
<td>Bradley B</td>
<td>A146</td>
</tr>
<tr>
<td>Bradley JM</td>
<td>A10, A20, A134</td>
</tr>
<tr>
<td>Bradshaw L</td>
<td>A161</td>
</tr>
<tr>
<td>Bradshaw LM</td>
<td>A224</td>
</tr>
<tr>
<td>Brady J</td>
<td>A3</td>
</tr>
<tr>
<td>Breithwaite A</td>
<td>A49</td>
</tr>
<tr>
<td>Breithwaite AT</td>
<td>A50</td>
</tr>
<tr>
<td>Brand Ol</td>
<td>A31, A32</td>
</tr>
<tr>
<td>Branneman L</td>
<td>A157</td>
</tr>
<tr>
<td>Breen D</td>
<td>A233</td>
</tr>
<tr>
<td>Breen RA</td>
<td>A186</td>
</tr>
<tr>
<td>Brew J</td>
<td>A17</td>
</tr>
<tr>
<td>Brewster D</td>
<td>A78</td>
</tr>
<tr>
<td>Brije P</td>
<td>A212</td>
</tr>
<tr>
<td>Briggs A</td>
<td>A76</td>
</tr>
<tr>
<td>Briggs J</td>
<td>A242</td>
</tr>
<tr>
<td>Brightling CE</td>
<td>A28, A218</td>
</tr>
<tr>
<td>Brij S</td>
<td>A73</td>
</tr>
<tr>
<td>Brij SQ</td>
<td>A130, A144, A146</td>
</tr>
<tr>
<td>Brimicombe J</td>
<td>A200</td>
</tr>
<tr>
<td>Brockbank L</td>
<td>A85, A173</td>
</tr>
<tr>
<td>Brockelsby C</td>
<td>A83, A90</td>
</tr>
<tr>
<td>Brodie M</td>
<td>A43, A68, A184</td>
</tr>
<tr>
<td>Brotto A</td>
<td>A71</td>
</tr>
<tr>
<td>Brown A</td>
<td>A35</td>
</tr>
<tr>
<td>Brown KK</td>
<td>A59</td>
</tr>
<tr>
<td>Brown KP</td>
<td>A2</td>
</tr>
<tr>
<td>Brown T</td>
<td>A33</td>
</tr>
<tr>
<td>Brownlow S</td>
<td>A101</td>
</tr>
<tr>
<td>Brin R</td>
<td>A153, A261</td>
</tr>
<tr>
<td>Bryant JM</td>
<td>A2</td>
</tr>
<tr>
<td>Bucciarelli-Ducci C</td>
<td>A107</td>
</tr>
<tr>
<td>Buell K</td>
<td>A51, A143</td>
</tr>
<tr>
<td>Buhl R</td>
<td>A159, A243, A251, A253</td>
</tr>
<tr>
<td>Burden T</td>
<td>A126</td>
</tr>
<tr>
<td>Burge P</td>
<td>A203</td>
</tr>
<tr>
<td>Burge PS</td>
<td>A149</td>
</tr>
<tr>
<td>Burgess H</td>
<td>A25</td>
</tr>
<tr>
<td>Burhan H</td>
<td>A5, A182, A192</td>
</tr>
<tr>
<td>Burke S</td>
<td>A77</td>
</tr>
<tr>
<td>Burke-Gaffney A</td>
<td>A9</td>
</tr>
<tr>
<td>Burman MGK</td>
<td>A147</td>
</tr>
<tr>
<td>Burnage DR</td>
<td>A206</td>
</tr>
<tr>
<td>Burton R</td>
<td>A127</td>
</tr>
<tr>
<td>Bush A</td>
<td>A44, A183, A223</td>
</tr>
<tr>
<td>Bushell V</td>
<td>A143</td>
</tr>
<tr>
<td>Butera P</td>
<td>A17</td>
</tr>
<tr>
<td>Butler C</td>
<td>A130, A155, A222</td>
</tr>
<tr>
<td>Buxton M</td>
<td>A197</td>
</tr>
<tr>
<td>Buyinkhsihie B</td>
<td>A67</td>
</tr>
<tr>
<td>Byrne T</td>
<td>A192</td>
</tr>
<tr>
<td>Cachada N</td>
<td>A262</td>
</tr>
<tr>
<td>Cade N</td>
<td>A15</td>
</tr>
<tr>
<td>Cajal Ramon y</td>
<td>A259</td>
</tr>
<tr>
<td>Callister M</td>
<td>A76, A78</td>
</tr>
<tr>
<td>Callister MEI</td>
<td>A38</td>
</tr>
<tr>
<td>Calverley P</td>
<td>A68</td>
</tr>
<tr>
<td>Calverley PM A</td>
<td>A254</td>
</tr>
<tr>
<td>Calvert LD</td>
<td>A130</td>
</tr>
<tr>
<td>Camara M</td>
<td>A133</td>
</tr>
<tr>
<td>Camargo CA</td>
<td>A60</td>
</tr>
<tr>
<td>Camiru N</td>
<td>A148, A149</td>
</tr>
<tr>
<td>Camporota L</td>
<td>A154</td>
</tr>
<tr>
<td>Caninau C</td>
<td>A35</td>
</tr>
<tr>
<td>Cane JL</td>
<td>A61</td>
</tr>
<tr>
<td>Canizales J</td>
<td>A69</td>
</tr>
<tr>
<td>Cannon J</td>
<td>A259</td>
</tr>
<tr>
<td>Cannon JE</td>
<td>A80, A97, A98</td>
</tr>
<tr>
<td>Capener D</td>
<td>A106</td>
</tr>
<tr>
<td>Capocci S</td>
<td>A50</td>
</tr>
<tr>
<td>Capps J</td>
<td>A131</td>
</tr>
<tr>
<td>Cargt O</td>
<td>A3</td>
</tr>
<tr>
<td>Carlholm M</td>
<td>A155</td>
</tr>
<tr>
<td>Carlin C</td>
<td>A35</td>
</tr>
<tr>
<td>Carmellet P</td>
<td>A48</td>
</tr>
<tr>
<td>Can motivated #</td>
<td>A22</td>
</tr>
<tr>
<td>Carroll B</td>
<td>A6</td>
</tr>
<tr>
<td>Carroll WD</td>
<td>A131</td>
</tr>
<tr>
<td>Caruso P</td>
<td>A48</td>
</tr>
<tr>
<td>Casbolt H</td>
<td>A220</td>
</tr>
<tr>
<td>Casbolt HL</td>
<td>A50</td>
</tr>
<tr>
<td>Cash C</td>
<td>A266</td>
</tr>
<tr>
<td>Caskey S</td>
<td>A134</td>
</tr>
<tr>
<td>Castellani W</td>
<td>A22</td>
</tr>
<tr>
<td>Cates CJ</td>
<td>A6</td>
</tr>
<tr>
<td>Cauthart F</td>
<td>A135</td>
</tr>
<tr>
<td>Cawthorne C</td>
<td>A103</td>
</tr>
<tr>
<td>Cecconi M</td>
<td>A9</td>
</tr>
<tr>
<td>Chadhuri N</td>
<td>A237</td>
</tr>
<tr>
<td>Chadwick HK</td>
<td>A136</td>
</tr>
<tr>
<td>Chai A</td>
<td>A168</td>
</tr>
<tr>
<td>Chakrabarti B</td>
<td>A15, A34</td>
</tr>
<tr>
<td>Chakraborty B</td>
<td>A124</td>
</tr>
<tr>
<td>Chakravorty S</td>
<td>A179</td>
</tr>
<tr>
<td>Chalmers J</td>
<td>A143</td>
</tr>
<tr>
<td>Chambers RC</td>
<td>A31</td>
</tr>
<tr>
<td>Chan WY</td>
<td>A127</td>
</tr>
<tr>
<td>Channick R</td>
<td>A65</td>
</tr>
<tr>
<td>Chapman AL</td>
<td>A267</td>
</tr>
<tr>
<td>Charalampopoulos A</td>
<td>A98</td>
</tr>
<tr>
<td>Charif R</td>
<td>A51</td>
</tr>
<tr>
<td>Charles P</td>
<td>A54</td>
</tr>
<tr>
<td>Chatunvedi A</td>
<td>A87</td>
</tr>
<tr>
<td>Chatzidakos L</td>
<td>A199</td>
</tr>
<tr>
<td>Chatzimavroudi-Gorgiadou V</td>
<td>A110</td>
</tr>
<tr>
<td>Chaudhry M</td>
<td>A221</td>
</tr>
<tr>
<td>Chaudhuri R</td>
<td>A151</td>
</tr>
<tr>
<td>Chaudhury H</td>
<td>A158</td>
</tr>
<tr>
<td>Chauhan A</td>
<td>A33</td>
</tr>
<tr>
<td>Chen T</td>
<td>A3, A16</td>
</tr>
<tr>
<td>Chew J</td>
<td>A192</td>
</tr>
<tr>
<td>Chlilwes ER</td>
<td>A27, A61</td>
</tr>
<tr>
<td>Chin K</td>
<td>A65</td>
</tr>
<tr>
<td>Chinyanganya N</td>
<td>A76</td>
</tr>
<tr>
<td>Chiu G</td>
<td>A165</td>
</tr>
<tr>
<td>Cho PSP</td>
<td>A122</td>
</tr>
<tr>
<td>Chong DLW</td>
<td>A30</td>
</tr>
<tr>
<td>Chou W</td>
<td>A57, A177, A178</td>
</tr>
<tr>
<td>Chowdhury P</td>
<td>A142</td>
</tr>
<tr>
<td>Choy DF</td>
<td>A168</td>
</tr>
<tr>
<td>Christodoulides M</td>
<td>A42</td>
</tr>
<tr>
<td>Chua F</td>
<td>A174, A222, A236, A240</td>
</tr>
<tr>
<td>Chua S</td>
<td>A263</td>
</tr>
<tr>
<td>Chua SHK</td>
<td>A209</td>
</tr>
<tr>
<td>Church AC</td>
<td>A65</td>
</tr>
<tr>
<td>Clark A</td>
<td>A127</td>
</tr>
<tr>
<td>Clark T</td>
<td>A262</td>
</tr>
<tr>
<td>Clarke A</td>
<td>A151</td>
</tr>
<tr>
<td>Clarke S</td>
<td>A241</td>
</tr>
<tr>
<td>Clarke SC</td>
<td>A23</td>
</tr>
<tr>
<td>Clemens A</td>
<td>A22</td>
</tr>
<tr>
<td>Cleverley JR</td>
<td>A266</td>
</tr>
<tr>
<td>Cliff J</td>
<td>A241</td>
</tr>
<tr>
<td>Cliff II</td>
<td>A224</td>
</tr>
<tr>
<td>Clifford D</td>
<td>A198</td>
</tr>
<tr>
<td>Clifford RL</td>
<td>A79, A214, A215</td>
</tr>
<tr>
<td>Clissold E</td>
<td>A267</td>
</tr>
<tr>
<td>Coates MS</td>
<td>A44</td>
</tr>
<tr>
<td>Cobbett C</td>
<td>A240</td>
</tr>
<tr>
<td>Coding A</td>
<td>A70, A224</td>
</tr>
<tr>
<td>Coghlan G</td>
<td>A63, A65</td>
</tr>
<tr>
<td>Colclough R</td>
<td>A198</td>
</tr>
<tr>
<td>Cole CC</td>
<td>A28</td>
</tr>
<tr>
<td>Cole JE</td>
<td>A50</td>
</tr>
<tr>
<td>Cole R</td>
<td>A201</td>
</tr>
<tr>
<td>Cole SL</td>
<td>A45, A103</td>
</tr>
<tr>
<td>Collard H</td>
<td>A177</td>
</tr>
<tr>
<td>Collett A</td>
<td>A84</td>
</tr>
<tr>
<td>Collier T</td>
<td>A18</td>
</tr>
<tr>
<td>Collin SM</td>
<td>A51, A143</td>
</tr>
<tr>
<td>Collins A</td>
<td>A108</td>
</tr>
<tr>
<td>Compton C</td>
<td>A159</td>
</tr>
<tr>
<td>Cordifflke AM</td>
<td>A27</td>
</tr>
<tr>
<td>Cordifflke R</td>
<td>A66, A220</td>
</tr>
<tr>
<td>Cordifflke RA</td>
<td>A98</td>
</tr>
<tr>
<td>Congleton J</td>
<td>A193</td>
</tr>
<tr>
<td>Connaire S</td>
<td>A229</td>
</tr>
<tr>
<td>Connell D</td>
<td>A143</td>
</tr>
<tr>
<td>Conoscenti CS</td>
<td>A175</td>
</tr>
<tr>
<td>Conway S</td>
<td>A147</td>
</tr>
</tbody>
</table>
Author index

Fadleen A, A137
Feary J, A69, A71, A259
Feldman C, A29
Feller-Kopman D, A86
Ferguson GT, A113, A251, A255
Ferguson TEG, A79
Ferreira D, A108
Field J, A138
Finn D, A47
Finn J, A138
Finisguerra V, A61
Finney LJ, A2
Finnigan H, A166, A167
Fishbane N, A79
Fisher AJ, A79, A80
Fishwick D, A224
Fitch S, A158
Fitzgerald B, A69, A71, A259
Fitzgerald C, A69
Fitzgerald M, A47
Flaherty KR, A59
Fleischer M, A253
Fletcher A, A97, A98
Fletcher SV, A240
Fletcher L, A188
Flick S, A198
Flood J, A20
Floyd P, A37, A141, A170, A179
Fogar A, A133
Fogar AW, A13
Fogel R, A116
Follows G, A232
Fonseka D De, A53, A54, A89
Forbes S, A61
Ford A, A17
Forman S, A224
Forni LG, A190
Forrester D, A133
Forster S, A188, A196
Forth R, A169
Forty EJ, A30
Foster SJ, A61
Fowler S, A5, A32
Fowler SJ, A4, A209, A212, A219, A263
Fowles H, A19
Fowles J, A190
Fowles N, A53, A54, A89
Frances Mair F, A78
Franks K, A38
Fraser E, A30, A243
Fraser SD, A46
Fredrickson J, A12
Free RC, A112
Friel A, A198
Fries A, A60, A176, A179
Fry N, A62, A229
Fucile S, A116
Fulford J, A200, A227
Fulford JP, A211
Furlong J, A192, A223
Fyfe MY, A247
Gaga M, A22
Gaillard B, A181
Gaillard E, A181
Gaillard EA, A42, A226
Gaine S, A65
Gait C, A5
Gal M, A43
Galiè N, A65
Ganaie B, A87
Ganguli A, A108
Garman D, A60, A67
Gao F, A11
Garate E De, A107
Garcia Gil E, A204
Garcia GR, A206
Gardener AC, A203, A208, A258
Gardner A, A157
Gardner M, A197
Garfield BE, A64
Garman C, A104
Garthwaite H, A172
Garthwaite HS, A104
Gatifis S, A138
Geir J, A66
Geisler J, A66
Gerhardsson de Verdier M, A157
Gerovasili V, A23
Gharbawi NTS, A226
Ghebre MA, A218
Ghosh D, A120
Gibbons N, A184
Gilchrist F, A226
Gilchrist FJ, A131
Gill DE, A63
Giles I, A45
Gilliespie SHT, A52, A147
Gillmister Jr, A233
Gingell M, A267
Gippanou I, A7
Glasspoole I, A57, A178
Glassberg MK, A57, A178
Gleeson FV, A94, A109
Gn YM, A34
Go S, A214
Goffe K, A130
Golddan N, A125
Goldman NR, A222
Gompelmann D, A23
Gompertz S, A198
Gomem S, A154
Goodall EC, A60
Gooding MJ, A94
Goodfellow J, A89
Goodman S, A100
Gooptu B, A156
Gopez UK, A188
Gordon S, A108
Gossain S, A234
Gowers KHC, A7
Goyal P, A246
Grönke L, A113, A251, A252, A253, A255
Gracie K, A76, A78
Graf S, A63
Graham L, A186
Grande G, A266
Grannon V, A131
Grant C, A60
Gray J, A69
Green B, A26
Green DC, A149
Green RH, A166
Greenberg L, A60
Green E, A205
Greening N, A107
Greening NJ, A73, A112
Greenwood H, A11
Greenwood J, A173
Greenwood S, A240
Greulich T, A22
Grey S, A168
Griffiths AP, A6
Griffiths CJ, A60, A182
Grigg J, A182
Grillo L, A210
Grogono DM, A2
Grogono JC, A222
Grote L, A14
Groves AM, A104
Gruubinska FS, A231
Gruddy-Jones K, A20
Grundy S, A138
Guerin T, A206, A246
Gunerson H, A128
Günsøy NB, A5, A170
Gupta A, A73, A179
Gupta U, A268
Gupta V, A117
Gwynn S, A194
Haasstrup M, A197
Habgood A, A31
Hackett TL, A79
Hackshaw A, A76
Hadinsopola C, A14, A63, A80
Hainemel M, A63
Haines J, A209, A262, A263
Haldar P, A112
Hales P, A229
Halhead R, A34
Hall C, A156
Hall IP, A105
Hall J, A146
Hall M, A198
Halliday N, A133
Hallifax R, A54
Hallifax RJ, A83, A84, A109
Hallmann C, A251
Hameed AG, A61
Hamelmann E, A167
Hamilton A, A21
Hamilton FW, A54
Hamilton N, A98
Hammerton C, A106
Hancock J, A95
Hansel T, A51, A143
Harden S, A139
Hardinge M, A121
Hardman E, A51
Hardy K, A234
Hardy R, A1
Hareendran A, A204
Hargadon B, A154
Haris M, A55, A87, A140, A141, A268
Harlow L, A97, A98
Harries C, A64, A99
Harris SR, A2
Hart N, A3, A16, A68, A126
Hart S, A103, A266
Hart SP, A46, A104, A211
Hartley T, A69
Hartmann CEA, A5, A170
Harvey-Dunston T, A166
Hashmi M, A199
Hastings R, A93
Hata A, A48
Hatton J, A188
Haworth CS, A2
Hawramy B, A76
Hawrylowicz CM, A148
Haywood B, A105
Healey A, A201
Heaney LG, A4
Heaney LH, A150
Hedner J, A14
Helm E, A103
Hendry J, A128
Hepple M, A224
Heron K, A185
Herre J, A192
Hertington KJ, A4
Heussel CP, A23
Hewitt R, A238
Hewitt S, A166
Hex N, A197
Hickes W, A94
Hicks AP, A33
Higgins M, A67
Higgins P, A224
Hilal E, A173
Hill AT, A62, A233
Hill E, A2
Hills S, A116
Hilton E, A159, A161
Hince K, A32
Hindle M, A93
Hirani N, A12
Ho LP, A30, A45, A60, A103, A176, A179, A243
Ho TR, A148
Hobkins S, A111
Hodgson LE, A190
Hodgson SA, A129
Hoenderdos K, A27
Hooper MM, A65
Holden KA, A42
Holemans J, A173
Holme J, A87
HOLMES LI, A170, A217
Holmes M, A198
Holmes P, A117
Holmes V, A45, A104
Holt K, A17
Holweg CTJ, A168
Hooper RL, A60
Hopkins S, A266
Hopkinson K, A49
Hornel P, A175
Horsely J, A174, A224
Horsley AR, A227
Horsley AR, A226
Horst C, A77
Houghton C, A90
Housley G, A174, A188
How N, A97
Howe FA, A105
Howell I, A238
Howells P, A11
Howells PA, A10
Howson S, A203
Hoyle J, A241
Hoyles R, A238
Hoyles RK, A60, A176, A179
Hubbard R, A20, A35, A139, A236
Hubbard RB, A13
Hudson N, A182
Huerta A, A244
Hutton A, A128, A129
Hughes C, A198
Hughes DA, A26
Hughes J, A124, A131
Hughes JMB, A101
Hughes P, A68
Hull J, A71, A210, A262
Hulter H, A175
Hunt N, A128
Hurst V, A161
Hurdtman J, A66, A98
Hurst JR, A68, A116, A156
Hurst L, A48
Hurst R, A211
Hussain A, A221
Hussain I, A141
Hussain N, A66
Hutchinson KE, A195
Hynds RE, A7
Ibrahim J, A140, A141
Ibrahim W, A144
Ignacio T, A114
Ihtesham M, A145
Iles R, A102, A103
Ind P, A74, A163
Isqbal M, A268
Iremonger J, A49, A50, A220
Issa B, A18
Ito K, A44
Izadi H, A222
Jabbal S, A216
Jack R, A139
Jackson DJ, A154
Jackson DP, A213
Jackson JE, A101, A102
Jackson M, A205
Jackson MW, A46
Jackson NE, A264
James B, A107
James BD, A112
James GD, A115
James H, A182
James P, A218
Jamson SL, A120
James S, A7, A76
James SM, A6, A77
Jansen C, A158
Janson C, A157
Jansens W, A21, A60
Jarrold J, A20, A236
Janis D, A71
Janis H, A51, A142
Javid A, A145
Jayadev A, A125
Jawad M, A74
Jayasekara G, A65
Jenkins G, A80
Jenkins D, A228
Jenkins DP, A97, A98
Jenkins G, A13, A31, A32
Jensen M, A6
Jiwa K, A80
Jiwa KJ, A28
Johansson G, A158
Johar A, A123
Johns CS, A106
Johns L, A173
Johns RH, A268
Johnson CL, A157
Johnson JA, A3
Johnson M, A40, A111, A258, A266
Johnson MA, A50
Johnson MK, A65
Johnson RS, A61
Johnson SR, A13
Johnson V, A92
Johnston A, A9
Johnston SA, A218
Johnstone E, A126
Jolley CJ, A15, A201
Jolliffe DA, A60
Jones A, A25, A135, A136
Jones AM, A133, A135, A226
Jones AP, A238
Jones C, A198
Jones D, A32
Jones GH, A182, A185
Jones M, A12, A37, A69
Jones P, A39, A107
Jones PJ, A205
Jones PW, A105
Jones R, A116
Jones RB, A135
Jones RL, A199
Jorup C, A115
Josephs L, A40, A111
Josh J, A251
Jouneua S, A171
Jurdzinski N, A214
Kaczmarek KA, A214
Kadiri T, A94
Kadiri S, A39
Kardos P, A139
Kaeber R, A268
Kalayo O, A148
Kalkat M, A36, A38, A39, A88, A235
Kalomenidis I, A7
Kalomenidis I, A7
Kamalanathan M, A84, A146
Kanda N, A30
Kane B, A5, A170
Kanelakis N, A7, A54
Kanelakis NL, A7
Kangombe A, A192
Kardos P, A243
Kafsson N, A157
Kaul M, A175
Kaye PM, A46
Keenan M, A164
Keen C, A157
Author index

Keenan E, A89
Kel C, A234
Kelleher M, A201
Kelly A, A214
Kelly F, A182
Kelly NP, A185
Kemp P, A64
Kemp SV, A91
Kendrick AH, A239
Kendrick D, A78
Kendrick YK, A45, A103
Kennedy M, A76, A78
Kennedy MPT, A38
Kennie SL, A257
Kent BD, A14, A154
Kent W, A90
Kerr A, A39
Kerr R, A164
Kessler B, A54
Khachi H, A260
Khakwani A, A35, A139
Khali A, A103
Khali S, A131
Kambh M, A194
Khan A, A145
Khan FA, A56
Khan M, A205
Khan NA, A145
Khan RA, A145
Khan S, A55, A140, A141, A268
Khatri S, A213
Khawaja A, A30
Khawaja AA, A45
Khetarpal A, A121
Kiely D, A63, A220
Kiely DG, A66, A98, A106
Kibourn T, A17
Killane I, A198
Kim VL, A23
Kimbrell HK, A187
Kingsnorth A, A107
Kipper K, A9
Kirkhässler K, A58
Kirkby J, A227
Kishore K, A158
Kitt M, A17
Klaiber R, A164
Knight J, A44
Knox A, A133
Kobor MS, A79, A215
Kocjan G, A76
Koeogluer H, A58
Kokosi M, A222, A236
Kolk M, A58
Kolluri K, A6
Kon OM, A51, A142, A143
Konstan M, A183
Kontogianni K, A23
Korducki L, A21
Korn S, A251
Koschel D, A58
Kostikas K, A22, A116, A206, A246
Kotecha J, A127
Kotidis K, A221
Kouloupoulos M, A240
Krasnodynembkaya A, A46
Kreuter M, A58
Krishke B, A197
Krishnamurthy P, A232
Kronsten V, A229
Krysiak P, A37
Kuh D, A1
Kuhn L, A200
Kumar M, A13
Kunst H, A147
Kyriacou T, A131
Laaksi I, A60
Lakl I, A167
Lalvani A, A142, A143
Lamont O, A260
Lamplough HK, A257
Lancaster L, A57, A175, A178
Lane S, A22
Lane SJ, A198
Lang FM, A212
Lang I, A65
Laresgoiti U, A3
Lau S, A80
Lavender P, A214
Lavoie JR, A48
Lavoie KL, A21
Law H, A141
Lawrie A, A49, A50, A61, A63, A220
Lawton CL, A136
Layton M, A101
Lee A, A140, A141
Leadbetter A, A185
Leather D, A161
Leav B, A80
Lechuga-Ballesteros D, A251
Lederer DJ, A57, A178
Ledson M, A128, A129, A194, A223
Ledson MJ, A131, A138
Lee CJW, A182
Lee KK, A122
Lee M, A237
Lee T, A182
Lee WT, A151
Lee YGG, A86
Leidy N, A21
Lenhard B, A1
Leonard C, A237
Lewis A, A61
Lewis K, A68, A72
Lewis I, A70, A224
Ley B, A177
Leykathallah Khan S, A87
Li G, A251
Li W, A27
Lilis I, A7
Lim R, A80
Lim WS, A62
Limone B, A183
Lin J, A220
Ling T, A203
Linne-Geyer S, A249
Lipman MCI, A50, A266
Lipworth BI, A216
Litt D, A62, A229
Little S, A197
Littleford R, A78
Livingston R, A210
Lo DKH, A181
Lock C, A197
Lodge KM, A27
Loebinger MR, A25, A234
Loke YK, A4
Long L, A48
Lonsdale DO, A9
Lord RW, A135
Lord V, A258
Losni N, A159, A243
Lostanlen V, A140, A141
Loubani M, A221
Lourenco S, A6
Lowe LA, A179
Lowrey G, A196
Lowrie R, A161
Lugg S, A11
Lugg SJ, A36, A38, A72, A198
Lunnis KL, A38
Lund-Palau H, A44
Luo Y, A3, A16
Lyons RA, A163

MacBride-Stewart S, A151
Macduff A, A96
MacHale E, A198, A205
MacHale P, A205
Mack P, A251
Mackenzie A, A65
MacLay J, A86
Macleod U, A266
Maddekar H, A55, A140, A141, A268
Maddock N, A131
Magillanes J, A113, A160
Magee N, A76
Magkouta S, A7
Magnussen H, A254
Mahadeva R, A192, A203
Mahendra S, A142
Maher T, A12, A175, A236
Maher TM, A31, A58, A171, A222, A236
Mahida RY, A8
Mahmood A, A140, A141, A228
Mahomed Z, A51, A143
Mailänder C, A159
Mailaender C, A243
Mailaender CM, A151
Mailra A, A226
Majd S, A166
Mak V, A118, A197
Make B, A157, A204
Malfattano A, A26
Maltotra P, A128
Mallia P, A2
Maltaias F, A21, A251, A252
Malter E, A49
Mamo J, A144
Manalain K, A143
Manasek-Holland S, A60
Mangera Z, A261
Maniatis L, A7
Mann EH, A148
Manoharan A, A216
Mansfield MW, A136
Mansur A, A154, A262
Mansur AH, A151, A209, A210, A215
Manton C, A154
Manzoor S, A234
Mapsoudou U, A55
Maquere CM, A187
Maraziotis A, A7
Marchbank A, A93
Marciniak S, A48
Marciniak SJ, A44, A49
Margaritopoulos GA, A222, A236
Author index

Norton-Wangford R, A74
Noth I, A175
Novacic K, A109
Novell M, A76
Nuevo J, A157, A202
Nunez X, A22
Nunn AJ, A52, A147
Nurmatov U, A6
Nyangoma S, A132
Nyberg F, A157
O’Byrne P, A155
O’Doughue M, A142
O’Driscoll BR, A186
O’Driscoll R, A5
O’Hagan P, A244
O’Kane C, A29, A46
O’Kane CM, A24, A47
O’Leary RO, A187
O’Mahony M, A233
O’Neill B, A10, A20
O’Neill C, A150
O’Neill K, A134
O’Pray H, A151
O’Regan A, A233
O’Reilly JF, A15
O’Reilly L, A102
O’Shea K, A215
O’Shea OM, A20
Oakes A, A124
Obaray S, A261
Obita GP, A211
Oelbaum B, A192
Oelberg D, A175
Oey I, A119
Oglesby S, A145
Oladapo M, A226
Oldfield IB, A9
Olsson J, A168
Onofri A, A33
Oosterhout A Van, A214
Ordway D, A2
Orme M, A107
Orriston ML, A48
Oscoft N, A68, A229
Osman W, A55
Ostridge KK, A23
Osvald N, A39
Osvald WK, A88
Oswhiga J, A108
Packer G, A198
Pagaria M, A24
Palmer EL, A16
Panzone L, A109
Pandy T, A166
Pang L, A31, A32
Pankin GA, A264
Paramasivam E, A76
Parfitt L, A64
Parfrey H, A14, A44
Farqeret N, A209, A210
Park J, A242
Park JES, A229
Parkes ED, A149
Parksill J, A2
Parmar J, A81, A137, A190, A192
Parmar S, A111
Parrott H, A135
Parry S, A117
Parvu O, A109
Passcual CC, A54
Paschley C, A154
Pasini A, A31, A32
Patalano F, A22
Patel AS, A264
Patel BR, A182
Patel HV, A170, A217
Patel I, A197, A258
Patel IS, A264
Patel J, A11
Patel JK, A214, A215
Patel M, A155
Patel N, A39
Patel S, A154, A186
Patel T, A100, A102
Paton JY, A68
Patout M, A33
Pattani H, A126
Patterson CP, A150
Patterson KD, A131
Pavard I, A7, A40, A157
Pavard ID, A214
Peacock A, A63
Peacock AI, A65
Peake M, A76
Peake MD, A140
Pearson JS, A135
Pear J, A192, A223, A225
Peckham D, A136
Peel AM, A4
Pemberton K, A115
Pengo M, A3, A33
Pengo MF, A16
Pepe M, A7
Pepeke Zaba J, A80
Pepeke-Zaiba J, A63, A97, A98
Pepperell J, A68
Pereira A, A26
Pereira CA, A57, A178
Perez-Iraketa C, A48
Pericleous C, A45
Pericleous P, A119
Persehelis JS, A142
Perks J, A100
Perrott S, A192
Perry M, A73
Persson T, A155
Petherick E, A107
Pfeffer PE, A148
Philips BJ, A9
Phillips DI, A42
Philpot S, A26
Pickup L, A124
Pickup LC, A94
Pickworth J, A49, A220
Pickworth JA, A50
Pieper T, A247, A249
Pitchig E, A234
Pike K, A227
Pino AV, A206, A246
Pinho R, A85
Pitcher A, A147
Pizzichini E, A252
Plewa B, A139
Plugge J, A247
Pointon K, A13
Polkey MI, A3, A16, A64, A68
Porter J, A172
Porter JC, A50, A45, A104, A172
Porter T, A264
Postma D, A155, A157
Potter J, A147
Power U, A41
Prasad A, A137
Prathibha B, A189
Preiss R, A65
Preston JA, A61
Price D, A157
Price DP, A150
Price L, A64
Piggmore S, A194
Proklou A, A226
Prudon B, A124
Psallidas I, A7, A54, A83, A84, A109
Pullinger R, A40
Puthran P, A93
Qadi S, A221
Qasim M, A24
Quaseral SR, A98
Quails S, A77
Quinlan GJ, A220
Quinn TM, A233
Quint JK, A41, A199
Quint M, A33
Quon B, A133
Rabe KF, A251
Rafferty G, A3
Rafferty GF, A16
Raghulu G, A59
Rahman N, A7
Rahman NM, A7, A54, A83, A84, A86, A94, A109
Raimundu K, A177
Rainey A, A122
Rajabzadeh-Hehejeh V, A132
Rajaram S, A66
Rajasekar P, A79
Rajesh P, A39, A88
Rajesh PB, A36, A38
Rajhan A, A122
Raju VM, A268
Ramakrishnan L, A220
Ramjug S, A66
Rammohan K, A37
Rand ID Du, A187
Rankin J, A184
Rapcan V, A198
Rapley T, A265
Rasiah MG, A9
Rass D, A44
Rathnapala A, A60, A176, A179
Ratnakumar R, A109
Ratneswaran C, A3, A16
Rawat F, A265
Rawlings EL, A3
Ray AM, A145
Raywood E, A183, A223
Read N, A146
Rebeiro C, A30
Reddel HK, A157
Reddy RV, A56, A126
Redfearn AD, A177
Reed K, A3
Reed KL, A16
Rees D, A179
Rees JR, A60
Rees S, A227
Rehal S, A68
<table>
<thead>
<tr>
<th>Author</th>
<th>Starting Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reid D</td>
<td>A95</td>
</tr>
<tr>
<td>Reigada C</td>
<td>A266</td>
</tr>
<tr>
<td>Reihill JA</td>
<td>A133</td>
</tr>
<tr>
<td>Reilly C</td>
<td>A240</td>
</tr>
<tr>
<td>Reilly RB</td>
<td>A198, A205</td>
</tr>
<tr>
<td>Reinhart JA</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Renwick S</td>
<td>A192</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rendall JC</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Renzi E</td>
<td>A58, A222</td>
</tr>
<tr>
<td>Renzi EA</td>
<td>A236</td>
</tr>
<tr>
<td>Rendall J</td>
<td>A134</td>
</tr>
<tr>
<td>Rennard S</td>
<td>A157</td>
</tr>
</tbody>
</table>
Author index

Snell N, A20, A236
Sobocinski P, A158
Solamalai A, A50
Solano E, A259
Soriano JB, A158
Southgate L, A63
Southwood M, A47, A48
Spencer DA, A43, A68
Spencer E, A223
Spencer K, A38
Spencer L, A265
Spence J, A126
Spencer MC, A73, A112
Sperrin M, A148
Spilling CA, A105
Spiro S, A76
Spiteri M, A241
Spiteri MA, A39
Springett JT, A100
Sproule M, A78
Spurr L, A222
Sridhar S, A143
Sridharan K, A76
Srikanthan K, A92, A93
St Noble V, A243
Stacey RM, A212
Stadon L, A53
Stahl K, A249
Stait G, A26
Staley KG, A42
Standing JF, A9
Stanley L, A240
Stansfield R, A59
Staples KJ, A23, A42
Stathopoulos GT, A7
Staton TL, A168
Staubert J, A57, A177
Staveacre L, A125
Stear J, A69, A162
Stein I, A3, A15, A26
Staines R, A23, A42
Stathopoulouos GT, A7
Staton TL, A168
Stauffer J, A57, A177
Staveacrai L, A125
Stevens KJ, A126
Steen H, A137
Steiner M, A107
Steiner MC, A73, A112, A213
Stelmach I, A60
Stewart C, A86
Stewart DJ, A48
Stewart GA, A12
Steyn R, A39, A88, A140
Steyn RS, A36, A38
Stimson RH, A61
Stibbice V, A30
Stockley R, A111
Stone H, A241
Sorayette DM, A27
Strom M, A12
Strachan D, A20, A236
Strading J, A68
Strading JR, A123
Strang J, A201
Strange J, A136
Stratton G, A165
Strongman H, A12
Stubs C, A190
Stygall C, A124
Succhini L, A7
Sukumarab, A92
 Sulaiman I, A165, A198, A205
 Sulaneky K, A190
 Sullivan A, A235
 Sullivan F, A78
 Sullivan J, A215
 Sullivan JAL, A51, A143
 Sullivan R, A127
 Sultanah M, A199
 Sumner J, A70
 Sumner JE, A224
 Sun D, A3
 Svendsater H, A161
 Sveres A, A157
 Svermova T, A9
 Swaison J, A262
 Swaminathan N, A154
 Swanev R, A232
 Sweeney JS, A150
 Swietlik EM, A80, A97, A98
 Swift A, A98
 Swift AJ, A66, A106
 Swigis JJ, A57, A177, A178
 Syed AE, A109
 Syed I, A109
 Sylvester K, A14, A227
 Szefler SJ, A167
 Szmack P, A225
 Taboada D, A80, A97, A98
 Talwar A, A54, A83, A84, A94, A109
 Tan J, A80
 Tang J, A4
 Tanner K, A95
 Tansley J, A122
 Tappuni S, A205
 Tavani G, A32, A219
 Tavernier G, A32, A219
 Tavernier GOG, A170
 Taylor C, A187
 Taylor J, A39
 Taylor M, A77
 Taylor P, A87
 Taylor T, A78, A198
 Teixeira VH, A6
 Tencioni S, A119
 Tennyson C, A37
 Tetlow SJ, A126
 Tetzlaff K, A254
 Tey CL, A189
 Thackray-Nocera S, A19
 Thakrar R, A7, A77
 Theron AJ, A29
 Theron AS, A54
 Thicke D, A11, A231
 Thicke DR, A5, A10, A72
 Thomas A, A121
 Thomas DM, A40
 Thomas E, A229
 Thomas M, A111, A184
 Thomas MF, A43, A68
 Thomas RW, A185
 Thomas S, A181
 Thompson AAR, A50, A61
 Thompson JA, A103
 Thompson N, A13
 Thompson R, A98
 Thompson JP, A61
 Thomson NC, A151
 Thornton T, A218
 Thorpe G, A39
 Thorpe J, A105
 Thulborn BS, A214
 Thulborn SJ, A28
 Tiberi S, A147
 Tighe HC, A100
 Tilbrook SD, A122
 Timoney M, A138
 Tintinger GR, A29
 Todd SJ, A210
 Toms N, A73, A107, A112
 Toshner MR, A80
 Toshner T, A98
 Tourish R, A35
 Townsend S, A176
 Trafalga R, A128
 Trafalga RM, A129
 Trampisch M, A58
 Tran CT, A153
 Tran I, A12
 Tregidgino L, A61
 Trembatth R, A63
 Trethewey R, A107
 Treweek S, A78
 Tillok Kumar G, A60
 Troosters T, A20, A21
 Tsiligianni I, A116
 Trin S, A86
 Tuck AC, A23
 Tucker O, A10
 Turnity M, A206
 Turnball MM, A134
 Turnbull A, A44
 Turnbull CD, A121, A123
 Turner A, A262
 Turner AM, A155, A230
 Turner I, A181
 Turner N, A177
 Turner RD, A263
 Turner SW, A41
 Tweed CD, A52, A147
 Twiddy M, A120
 Udheid M, A158
 Ullah I, A145
 Ullah U, A145
 Urstead M, A242
 Urashima M, A6, A60
 Usher A, A111
 Ustasbasi C, A32
 Utenthal B, A232
 Vagheia D, A147
 Valapraya S, A230
 Valenzanov K, A190
 Valero-Sanchez I, A73, A213
 Vally Y, A56, A126
 Van Manen A, A96
 Van-Wersch A, A69, A201
 Vancfier C, A171
 Vandewalker M, A166, A167
 Vang K, A251
Author index

Vartsaba N, A38
Vasileiou E, A155
Vedhara K, A78
Venn R, A190
Verger N, A183, A223
Verma D, A2
Verma N, A156
Vernon S, A139
Vestbo J, A110, A157, A205
Villar O, A158
Villalobos RE, A113, A160
Villalobos RV, A188
Virgilio E, A39
Viskaduraki M, A226
Vogelberg C, A167
Vogelmeier C, A22, A159, A243
Vonk Noordegraaf A, A63
Vreka M, A7
Vrijlandt EJLE, A166
Vulcu SD, A166
Vulysteke A, A190
Vyas A, A5, A34, A187, A212, A263
Wahida R, A97
Walda S, A244
Walker B, A15, A79
Walker PP, A192
Walker S, A53
Wallace F, A141
Waller D, A119
Waller J, A77
Wallington JC, A42
Walmsley SR, A27, A61
Walsh G, A41
Walshaw M, A92, A93, A129, A173
Walshaw MJ, A128, A131, A223, A225
Walters GI, A149
Walton R, A182, A213
Ward CW, A28
Ward J, A200
Ward K, A222
Ward S, A222
Ward-Booth ES, A68
Wardlaw AJ, A154
Warren N, A224
Watson J, A214
Watson JP, A145
Webb J, A39
Wedzicha WA, A68
Wedlbach JA, A1, A2
Webbe L, A246
Wells A, A90, A266
Wells AU, A178, A222, A236
Wellwood I, A200
Werpauchowska AW, A187
Wertheim D, A8
West A, A86
West D, A35
West S, A16, A121
West SD, A124
West T, A179
Wetering G van de, A114
Weycker D, A58
Wharton J, A63
Wharton S, A262
White L, A215
White P, A203
White VLC, A147
Whiteford J, A206
Whitehall DT, A91
Whitehouse JL, A234
Whorwell PJ, A135
Whyte MKB, A61
Widremasangihe M, A143, A238
Wiggins RE, A70, A224
Wiggins E, A73
Wijesinghe M, A186
Wild J, A98
Wild JM, A106
Wilkins M, A63
Wilkinson T, A111
Wilkinson TM, A23
Wilkinson TMa, A40, A42
Willems JMY, A94
Williams A, A3, A16
Williams C, A35
Williams J, A73
Williams L, A61
Williams N, A40, A111
Williams NP, A23
Williams P, A133
Williams S, A158, A197
Williams SP, A27
Wills G, A52, A147
Willson J, A61
Wilson A, A107, A127, A181
Wilson AM, A4, A165, A238, A264
Wilson R, A25, A102, A103, A234
Winfield CF, A211
Wingfield K, A194
Winn C, A165
Wollerton R, A89
Woltmann G, A112, A228
Wood EHC, A218
Wood K, A44
Wood H, A182
Wood N, A139
Wood R, A202
Wood S, A187
Woodcock HV, A31
Woodhead FA, A176, A177
Woolcock SC, A89
Woolhouse I, A35, A139
Wootton SA, A23
Wort A5, A43
Wort JS, A220
Wort SJ, A63, A64
Worth H, A159, A243
Wouters E, A254
Wright A, A108
Wright AKA, A218
Wright M, A199
Wrightson J, A84
Wrightson JM, A83, A109
Wyts W, A58
Xiao S, A16
Xue L, A214
Yates L, A169
Yavuz S, A148
Yorke J, A89, A205, A266
Young CA, A34
Young R, A192
Young S, A157
Yuill K, A239
Yung H, A81
Zaat S, A189
Zaidi S, A108, A219
Zaiser E, A204
Zalewska KI, A80
Zawia A, A49
Zazara D, A7
ACKNOWLEDGEMENTS

The BTS Science and Research Committee organised the programme of the Winter Meeting 2016:

Professor Gisli Jenkins (Chair)  Dr Neil Greening  Dr Elizabeth Sapey
Dr Ian Balfour-Lynn  Dr Ricardo Jose  Dr Aran Singanayagam
Professor Alison Condliffe  Professor Nick Maskell  Dr Duncan Wilson
Dr Benedict Creagh-Brown  Dr Justin Pepperell  Dr Hannah Wilson
Professor Jane Davies  Dr Jennifer Quint  Dr Hannah Woodcock
Professor Louise Donnelly  Dr Robert Rintoul  

The Society’s Specialist Advisory Groups also provided suggestions for symposia content.

Topic Leaders, who organised the symposia, were:

Professor Alison Condliffe  Professor Nick Maskell  Dr Chris Scotton
Professor Jane Davies  Dr Justin Pepperell  Dr Aran Singanayagam
Professor Louise Donnelly  Dr Jennifer Quint  Dr Amanda Tatler
Dr Neil Greening  Dr Robert Rintoul  Dr Hannah Woodcock
Professor Gisli Jenkins  Dr Elizabeth Sapey  Dr Duncan Wilson

The BTS/BALR/BLF Early Career Investigators and Medical Student Award abstracts were judged by:

Dr James Chalmers  Professor Louise Donnelly  Professor Gisli Jenkins

The refereeing of the abstracts was performed by:

Professor Ian Adcock  Dr Matthew Callister  Dr Stephen Holmes
Dr Sanjay Agrawal  Dr George Chalmers  Dr Luke Howard
Dr Mohamed Al-Aloul  Dr James Chalmers  Dr Rachel Hoyles
Dr Martin Allen  Professor Rachel Chambers  Professor Richard Hubbard
Professor Eric Alton  Dr Brian Choo-Kang  Ms Claire Hurlin
Mr Joseph Annandale  Dr Robina Coker  Dr John Hurst
Dr George Antunes  Professor Alison Condliffe  Dr Philip Ind
Dr Mona Bafadhel  Professor Paul Corris  Professor Sam Janes
Dr Sabrina Bajwah  Dr Benedict Creagh-Brown  Professor Gisli Jenkins
Professor David Baldwin  Professor Donna Davies  Dr Christopher Johnson
Dr Ian Balfour-Lynn  Dr Michael Davies  Dr Jack Kastelik
Dr Christopher Barber  Dr Owen Dempsey  Professor Onn Min Kon
Mr Sion Barnard  Professor Stuart Elborn  Dr Allan Lawrie
Dr Caroline Beardsmore  Dr Mark Elliott  Dr Seamus Linnane
Dr Andrew Bentley  Dr Matthew Evison  Dr Marc Lipman
Dr Matthew Berry  Professor Andrew Fisher  Dr Michael Loebinger
Dr Jayesh Bhatt  Professor David Fishwick  Dr James Lordan
Dr Charlotte Bolton  Dr Andrew Fogarty  Dr Toby Maher
Professor Graham Bothamley  Dr Jonathan Fuld  Dr Vincent Mak
Dr Stephen Bourke  Dr Neil Greening  Dr William Man
Professor Chris Brightling  Professor Mark Griffiths  Dr Karen Heslop-Marshall
Professor John Britton  Dr Justine Hadcroft  Professor Nick Maskell
Professor Jeremy Brown  Dr Simon Hart  Dr Robin McAnulty
Professor Andrew Bush  Professor Adam Hill  Professor Danny McAuley
Dr Robert Buttery  Dr Edwin Hiscocks  Dr Frank McCaughan
I would like to record my sincere thanks to BTS staff for all their support and expert help in organising this Meeting, and in particular to Cathryn Stokes, Joan Thompson, Sally Welham, Sheila Edwards, Bernice Bruce-Vanderpuije, Kerry Reid and Luke Wilson.

I am also grateful to all listed above and to our session chairs and invited speakers. Special thanks to Professor Alison Condliffe, Dr Justin Pepperell, Dr Jennifer Quint, Dr Robert Rintoul, Dr Elizabeth Sapey and Dr Louise Fleming for their help and guidance in producing the final programme.

Professor Gisli Jenkins, Chair, BTS Science and Research Committee
ACKNOWLEDGEMENTS

The British Thoracic Society gratefully acknowledges the support of the following exhibitors:

Adherium Ltd  
Aerogen  
Airsonett AB  
Alere  
Ambu  
Aquilant Endoscopy  
AstraZeneca  
Baywater Healthcare  
Boehringer Ingelheim Ltd  
Boston Scientific Corporation  
CareFusion  
Chiesi Limited  
Clement Clarke International  
General Medicine Group  
GlaxoSmithKline  
Insmed  
Medela Healthcare  
Mylan  
Napp Pharmaceuticals Ltd  
Novartis Pharmaceuticals UK Ltd  
Olympus  
PARI Medical Ltd  
Pfizer UK  
PneumRx Ltd  
Pulmonx  
Rocket Medical  
Sandoz Ltd  
Teva Respiratory  
Trudell Medical International  
Unisoft  
Ventmed  
Vertex  
Vitalograph Ltd  
Wisepress Medical Bookshop
Aims and Scope: Thorax aims to cover all areas of respiratory medicine from paediatric to adults through publishing original papers, systematic reviews and meta-analyses, trial protocols, state of the art reviews, invited editorials, case-based discussions and images. The priorities are originality, rigour and excellence.

Subscription Information

Thorax is published monthly (subscribers receive all supplements)

Institutional Rates 2016

Print
£176; US$1397; €967

Online
Site licences are priced on FTE basis and allow access by the whole institution. Details available online at http://journals.bmj.com/site/subscribe or contact Subscription (see above right).

Personal Rates 2016

Print (includes online access at no additional cost)
£301; US$587, €407

Online only
£164; US$320, €222

ISSN 0040-6376 (print)
ISSN 1468-3296 (online)

Contact Details

Editorial Office
Thorax, BMA House, Tavistock Square, London WC1H 9JR, UK
T: +44 (0)20 7383 6373
E: thorax@bmj.com
Twitter: @ThoraxBMJ

British Thoracic Society
17 Doughty Street, London WC1N 2PL, UK
T: +44 (0)20 7831 8778
E: bts@brit-thoracic.org.uk
W: https://www.brit-thoracic.org.uk/

Permissions
W: http://www.bmj.com/company/products-services/rights-and-licensing/permissions/

Supplement Enquiries
T: +44 (0)20 7383 6057
E: support@bmj.com

Display Advertising Sales
Sophie Fitzsimmons (Sales Manager)
T: +44 (0)20 7383 6783
E: sfitzsimmons@bmj.com

Online Sales Advertising
Marc Clifford (Sales Manager)
T: +44 (0)20 7383 6161
E: mclifford@bmj.com
W: http://www.bmj.com/company/raise-visibility-and-reach/

Display & Online Advertising Sales (USA)
Jim Cunningham
T: +1 201 767 4170
E: jcummingham@cunnasso.com

Author Reprints
Reprints Administrator
T: +44 (0)20 7383 6305
E: admin.reprints@bmj.com

Commercial Reprints (except USA & Canada)
Nadia Gurney-Randall
T: +44 (0)120 8445 5825
M: +44 (0)7866 262344
E: ngurneyrandall@bmj.com

Commercial Reprints (USA & Canada)
Ray Thibodeau
T: +1 267 895 1758
M: +1 215 933 8484
E: ray.thibodeau@contentednet.com

Production Editor
Emma Chan
E: production.thorax@bmj.com

Subscription Information

Thorax is published monthly (subscribers receive all supplements)

Institutional Rates 2016

Print
£176; US$1397; €967

Online
Site licences are priced on FTE basis and allow access by the whole institution. Details available online at http://journals.bmj.com/site/subscribe or contact Subscription (see above right).

Personal Rates 2016

Print (includes online access at no additional cost)
£301; US$587, €407

Online only
£164; US$320, €222

ISSN 0040-6376 (print)
ISSN 1468-3296 (online)

Contact Details

Editorial Office
Thorax, BMA House, Tavistock Square, London WC1H 9JR, UK
T: +44 (0)20 7383 6373
E: thorax@bmj.com
Twitter: @ThoraxBMJ

British Thoracic Society
17 Doughty Street, London WC1N 2PL, UK
T: +44 (0)20 7831 8778
E: bts@brit-thoracic.org.uk
W: https://www.brit-thoracic.org.uk/

Permissions
W: http://www.bmj.com/company/products-services/rights-and-licensing/permissions/

Supplement Enquiries
T: +44 (0)20 7383 6057
E: support@bmj.com

Display Advertising Sales
Sophie Fitzsimmons (Sales Manager)
T: +44 (0)20 7383 6783
E: sfitzsimmons@bmj.com

Online Sales Advertising
Marc Clifford (Sales Manager)
T: +44 (0)20 7383 6161
E: mclifford@bmj.com
W: http://www.bmj.com/company/raise-visibility-and-reach/

Display & Online Advertising Sales (USA)
Jim Cunningham
T: +1 201 767 4170
E: jcummingham@cunnasso.com

Author Reprints
Reprints Administrator
T: +44 (0)20 7383 6305
E: admin.reprints@bmj.com

Commercial Reprints (except USA & Canada)
Nadia Gurney-Randall
T: +44 (0)120 8445 5825
M: +44 (0)7866 262344
E: ngurneyrandall@bmj.com

Commercial Reprints (USA & Canada)
Ray Thibodeau
T: +1 267 895 1758
M: +1 215 933 8484
E: ray.thibodeau@contentednet.com

Production Editor
Emma Chan
E: production.thorax@bmj.com
TWO STRENGTHS. ONE PRICE.

Enabling appropriate prescribing at no extra cost.

Fostair 100/6 and 200/6:
2 devices, 2 strengths, 1 price £29.32.