British Thoracic Society
Winter Meeting 2015

The Queen Elizabeth II Centre
Broad Sanctuary
Westminster
London SW1P 3EE

2 to 4 December 2015

Programme and Abstracts
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.

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2 to 4 December 2015
Programme and Abstracts

Approved by the Federation of the Royal Colleges of Physicians of the UK for 18 category 1 (external) credits.
Code: 99652
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.
Full café facilities will be open in the Pickwick on the 1st floor from 8.00am to 4.00pm on Wednesday 2 and Thursday 3 December and from 8.00am to 2.30pm on Friday 4 December. Snack bars, serving hot and cold drinks, sandwiches and confectionery only, will be open at the same times in the Whittle & Fleming on the 3rd floor.
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<td>Authors present</td>
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<td>10.00am – 11.00am</td>
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<td></td>
<td>Non-IPF ILDs: diagnosis and management</td>
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<td>New markers of lung physiology</td>
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<td>Diagnosis and management of paediatric lung disease</td>
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<td>Sleep apnoea and hypoventilation: screening and treating high risk populations</td>
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<td>10.30am – 12.30pm</td>
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<td>TIME to change: management of pleural disease</td>
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<td>SAG Open meeting</td>
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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 bars in the Whittle & Fleming (3rd floor).
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<td>Symposium</td>
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<td>3.00pm – 4.30pm</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming and Britten/3&lt;sup&gt;rd&lt;/sup&gt; and Cambridge/5&lt;sup&gt;th&lt;/sup&gt; (3.15pm – 3.30pm only)</td>
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<td>The BTS President’s Address/Moran Campbell Lecture</td>
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<td>BTS Annual General Meeting</td>
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<td>Whittle &amp; Fleming/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<tr>
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<td>Pulmonary rehabilitation and physical activity Whittle &amp; Fleming/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<td>Asthma treatment Whittle &amp; Fleming/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<td>Lung cancer management Whittle &amp; Fleming/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<td>Managing pleural disease Whittle &amp; Fleming/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<td>Home non-invasive ventilation Whittle &amp; Fleming/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<td>Moore/4th</td>
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<tr>
<td>3.00pm – 4.00pm</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming, Britten/3rd</td>
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<tr>
<td>3.15pm – 4.15pm</td>
<td>SAG Open meeting</td>
<td>Victoria/2nd</td>
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<tr>
<td>3.15pm – 4.15pm</td>
<td>SAG Open meeting</td>
<td>Albert/2nd</td>
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<tr>
<td>3.15pm – 4.45pm</td>
<td>Poster discussion P133-P144</td>
<td>Rutherford/4th</td>
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<tr>
<td>3.30pm – 5.30pm</td>
<td>Poster discussion P145-P160</td>
<td>Westminster/4th</td>
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<tr>
<td>3.30pm – 5.30pm</td>
<td>Poster discussion P161-P176</td>
<td>Abbey/4th</td>
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<tr>
<td>3.45pm – 5.15pm</td>
<td>Symposium</td>
<td>Churchill/Ground</td>
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<tr>
<td>3.45pm – 5.15pm</td>
<td>Spoken session S82-S86</td>
<td>St James/4th</td>
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<tr>
<td>3.45pm – 5.20pm</td>
<td>Poster discussion P177-P189</td>
<td>Windsor/5th</td>
</tr>
<tr>
<td>4.00pm – 5.20pm</td>
<td>Poster discussion P190-P200</td>
<td>Mountbatten/6th</td>
</tr>
<tr>
<td>4.00pm – 5.30pm</td>
<td>Spoken session S87-S91</td>
<td>Moore/4th</td>
</tr>
<tr>
<td>5.30pm – 7.15pm</td>
<td>The President’s Reception – All welcome!</td>
<td>Britten/3rd</td>
</tr>
</tbody>
</table>

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

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# Daily Programme

## Friday 4 December 2015

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
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<tbody>
<tr>
<td><strong>8.00am – 9.00am</strong></td>
<td><strong>COFFEE/TEA</strong></td>
<td>Whittle &amp; Fleming/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<tr>
<td><strong>8.45am – 2.00pm</strong></td>
<td><strong>Poster viewing</strong></td>
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<tr>
<td>Authors present</td>
<td>P201-P214 Double pneumonia and other</td>
<td>Whittle &amp; Fleming/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<tr>
<td>10.00am – 11.00am</td>
<td>P215-P227 Epidemiology in lung disease</td>
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<td>P228-P235 Improving patient care in cystic</td>
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<td>P236-P243 Clinical studies in cough</td>
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<td>P244-P250 Asthma quality improvement</td>
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<td>P251-P264 Improving outcomes in TB</td>
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<td></td>
<td>P265-P273 Diagnosis and management of</td>
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<td></td>
<td>pulmonary arterial hypertension</td>
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<td>P274-P281 Treatment options in cystic</td>
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<td>P282-P291 Investigating lung disease: novel</td>
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<td></td>
<td>techniques and old interventions</td>
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<tr>
<td><strong>8.45am – 2.30pm</strong></td>
<td><strong>Moderated poster viewing</strong></td>
<td>Cambridge/5&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td><strong>8.00am – 8.30am</strong></td>
<td><strong>BTS Journal Club</strong></td>
<td>Albert/2&lt;sup&gt;nd&lt;/sup&gt;</td>
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<tr>
<td><strong>8.30am – 10.00am</strong></td>
<td><strong>Symposium</strong></td>
<td>Churchill/Ground</td>
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<td><strong>8.30am – 10.00am</strong></td>
<td><strong>Symposium</strong></td>
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<td><strong>8.30am – 10.15am</strong></td>
<td><strong>Spoken session</strong></td>
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<td></td>
<td>S92-S97 Mechanisms of airway</td>
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<td></td>
<td>inflammation and remodelling</td>
<td>Moore/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td><strong>8.30am – 10.30am</strong></td>
<td><strong>Symposium</strong></td>
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<td><strong>8.45am – 10.00am</strong></td>
<td><strong>Spoken session</strong></td>
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<td></td>
<td>S98-S101 The next steps of pulmonary</td>
<td>St James/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<td></td>
<td>rehabilitation</td>
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<td><strong>8.45am – 10.00am</strong></td>
<td><strong>Spoken session</strong></td>
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<td></td>
<td>S102-S105 Lung cancer biology and biomarkers</td>
<td>Abbey/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td><strong>9.00am – 10.00am</strong></td>
<td><strong>SAG Open meeting</strong></td>
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<td></td>
<td>Asthma SAG</td>
<td>Victoria/2&lt;sup&gt;nd&lt;/sup&gt;</td>
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<tr>
<td><strong>10.00am – 11.00am</strong></td>
<td><strong>COFFEE/TEA</strong></td>
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<tr>
<td><strong>10.15am – 12.00pm</strong></td>
<td><strong>Spoken session</strong></td>
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<tr>
<td></td>
<td>S106-S111 Nintedanib or pirfenidone?</td>
<td>St James/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td><strong>10.15am – 12.15pm</strong></td>
<td><strong>Symposium</strong></td>
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<tr>
<td></td>
<td>Sensational developments in lung disease</td>
<td>Churchill/Ground</td>
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<tr>
<td><strong>10.30am – 11.30am</strong></td>
<td><strong>SAG Open meeting</strong></td>
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<td></td>
<td>COPD SAG</td>
<td>Albert/2&lt;sup&gt;nd&lt;/sup&gt;</td>
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<tr>
<td><strong>10.30am – 11.30am</strong></td>
<td><strong>Open meeting</strong></td>
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<tr>
<td></td>
<td>BTS/SIGN Asthma Guideline update</td>
<td>Windsor/5&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
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<tbody>
<tr>
<td>10.30am – 11.45am</td>
<td>Spoken session</td>
<td>S112-S115</td>
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<tr>
<td>10.30am – 12.00pm</td>
<td>Spoken session</td>
<td>S116-S120</td>
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<tr>
<td>10.45am – 12.45pm</td>
<td>Symposium</td>
<td>Occupational lung disease: the general chest clinic and beyond</td>
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<tr>
<td>12.00pm – 2.00pm</td>
<td>LUNCH</td>
<td>Dancing only</td>
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<tr>
<td>12.30pm – 1.30pm</td>
<td>SAG Open meeting</td>
<td>Cystic Fibrosis SAG</td>
</tr>
<tr>
<td>1.00pm – 2.00pm</td>
<td>SAG Open meeting</td>
<td>Occupational and Environmental Lung Disease SAG</td>
</tr>
<tr>
<td>1.30pm – 3.00pm</td>
<td>Spoken session</td>
<td>COPD weighs heavy on the heart</td>
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<tr>
<td>1.30pm – 3.15pm</td>
<td>Spoken session</td>
<td>Basic mechanisms of airways disease</td>
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<tr>
<td>1.30pm – 3.15pm</td>
<td>Poster discussion</td>
<td>Double pneumonia and other infections</td>
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<tr>
<td>1.30pm – 3.30pm</td>
<td>Symposium</td>
<td>Interventional bronchoscopy for benign disease</td>
</tr>
<tr>
<td>1.45pm – 3.25pm</td>
<td>Poster discussion</td>
<td>Epidemiology in lung disease</td>
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<tr>
<td>1.45pm – 3.45pm</td>
<td>Symposium</td>
<td>Pulmonary embolism: from acute to chronic</td>
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<tr>
<td>2.00pm – 3.00pm</td>
<td>Poster discussion</td>
<td>Improving patient care in cystic fibrosis</td>
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<tr>
<td>2.00pm – 3.00pm</td>
<td>Poster discussion</td>
<td>Clinical studies in cough</td>
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<tr>
<td>2.00pm – 3.00pm</td>
<td>Poster discussion</td>
<td>Asthma quality improvement</td>
</tr>
<tr>
<td>2.00pm – 3.00pm</td>
<td>Moderated poster discussion</td>
<td>Education and training; from simulation to social media</td>
</tr>
<tr>
<td>3.10pm – 4.50pm</td>
<td>Poster discussion</td>
<td>Improving outcomes in TB</td>
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<tr>
<td>3.30pm – 4.30pm</td>
<td>Poster discussion</td>
<td>Treatment options in cystic fibrosis</td>
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<tr>
<td>3.30pm – 4.40pm</td>
<td>Poster discussion</td>
<td>Diagnosis and management of pulmonary arterial hypertension</td>
</tr>
<tr>
<td>3.30pm – 4.45pm</td>
<td>Poster discussion</td>
<td>Investigating lung disease: novel techniques and old interventions</td>
</tr>
<tr>
<td>3.00pm – 4.45pm</td>
<td>COFFEE/TEA</td>
<td>Britten/3rd</td>
</tr>
</tbody>
</table>

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ADDITIONAL SESSIONS

The programme will also include open meetings of the BTS Specialist Advisory Groups (SAGs). Further details may be found in the leaflets in the conference bags.

WEDNESDAY 2 DECEMBER 2015

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.30am – 10.30am</td>
<td>Pulmonary Rehabilitation Advisory Group</td>
<td>Moore/4th floor</td>
</tr>
<tr>
<td>11.00am – 12.00am</td>
<td>Lung Infection SAG</td>
<td>Victoria/2nd floor</td>
</tr>
<tr>
<td>11.00am – 12.00am</td>
<td>Tuberculosis SAG</td>
<td>Rutherford/4th floor</td>
</tr>
<tr>
<td>11.30am – 12.30pm</td>
<td>Interstitial and Rare Lung Disease SAG</td>
<td>Albert/2nd floor</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>Nurse Advisory Group</td>
<td>Victoria/2nd floor</td>
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<tr>
<td>12.30pm – 1.30pm</td>
<td>Tobacco SAG</td>
<td>Rutherford/4th floor</td>
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<tr>
<td>12.45pm – 1.45pm</td>
<td>Critical Care SAG</td>
<td>Albert/2nd floor</td>
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<tr>
<td>3.15pm – 3.35pm</td>
<td>Clinical Data SAG</td>
<td>Victoria/2nd floor</td>
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THURSDAY 3 DECEMBER 2015

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
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<tbody>
<tr>
<td>9.00am – 10.00am</td>
<td>Interventional Procedures SAG</td>
<td>Victoria/2nd floor</td>
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<tr>
<td>9.00am – 10.00am</td>
<td>Sleep Apnoea SAG</td>
<td>Rutherford/4th floor</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>Lung Cancer and Mesothelioma SAG</td>
<td>Victoria/2nd floor</td>
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<tr>
<td>12.30pm – 1.30pm</td>
<td>Pulmonary Vascular Disease SAG</td>
<td>Albert/2nd floor</td>
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<tr>
<td>3.15pm – 4.15pm</td>
<td>Specialist Trainees Advisory Group</td>
<td>Victoria/2nd floor</td>
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<tr>
<td>3.15pm – 4.15pm</td>
<td>Lung Physiology SAG</td>
<td>Albert/2nd floor</td>
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FRIDAY 4 DECEMBER 2015

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
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<tbody>
<tr>
<td>9.00am – 10.00am</td>
<td>Asthma SAG</td>
<td>Victoria/2nd floor</td>
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<tr>
<td>10.30am – 11.30am</td>
<td>COPD SAG</td>
<td>Albert/2nd floor</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>Cystic Fibrosis SAG</td>
<td>Victoria/2nd floor</td>
</tr>
<tr>
<td>1.00pm – 2.00pm</td>
<td>Occupational and Environmental Lung Disease SAG</td>
<td>Albert/2nd floor</td>
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</tbody>
</table>

BTS MEDAL AND AWARD PRESENTATIONS

Wednesday 2 December 2015 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/BLF/BALR Early Career Investigator Awards and the Medical Student Awards just before the BTS President’s Address/Moran Campbell Lecture from Professor Mike Morgan. Please come along to this session to congratulate the winners.

THE BTS PRESIDENT’S RECEPTION

Thursday 3 December 2015, 5.30pm to 7.15pm in the Britten, 3rd floor

All participants are warmly invited to join us on this social occasion.
Charity and non-commercial stands

**Britten, 3rd floor**

69  Action for Pulmonary Fibrosis
57 & 58  American Thoracic Society
65  Association for Respiratory Technology and Physiology (ARTP)
64  Association of Chartered Physiotherapists in Respiratory Care (ACPRC)
63  Association of Respiratory Nurse Specialists (ARNS)
70  BHD Foundation (a subsidiary of the Myrolytis Trust)
55  BMJ Group
61  British Association for Lung Research (BALR)
66  British Lung Foundation
51  British Thoracic Society
62  BTS Nurse Advisory Group
52  BTS Stop Smoking Champions
60  Education for Health
71  European Respiratory Society
53  National COPD Audit Programme, led by the Royal College of Physicians
54  National Lung Cancer Audit, led by the Royal College of Physicians
68  National Paediatric Respiratory & Allergy Nurses Group
59  Primary Care Respiratory Society UK
67  PCD Family Support Group
50  Respiratory Futures

Exhibitors and stand numbers

**Whittle & Fleming, 3rd floor**

31 & 32  Actavis
15  Aquilant Endoscopy
4  AstraZeneca Ltd
21, 22, 27 & 28  Bayer
1  Boehringer Ingelheim
36  Boston Scientific
3  Chiesi Ltd
17  Clement Clarke International
9, 10, 11, 12 & 13  GlaxoSmithKline
14  Medela
18  Medtronic
2  my mhealth
6  Napp Respiratory
5  Novartis
7 & 8  Olympus
30  Pfizer
35  PneumRx Ltd
16  Pulmonx
19 & 20  Rocket Medical
34  Slater & Gordon
23, 24, 25 & 26  Teva UK Ltd
33  Vertex Pharmaceuticals (Europe) Ltd
29  Vitalograph

**Britten, 3rd floor**

48  Bioxydyn
45  CareFusion
40  COSMED
39  Hill-Rom Ltd
37  Michael W Halsall Solicitors Ltd
47  Mylan
41  Nutricia Advanced Medical Nutrition
44  Sandoz
49  Wisepress Medical Bookshop
Wednesday 2 December 2015

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-P14
Idiopathic pulmonary fibrosis boldly goes where no disease has gone before
Discussion of abstracts will take place from 12.45pm to 2.30pm in the Moore, 4th floor

P15-P27
Clinical studies of advanced COPD
Discussion of abstracts will take place from 1.15pm to 2.50pm in the Abbey, 4th floor

P28-P36
Non-IPF ILDs: diagnosis and management
Discussion of abstracts will take place from 2.00pm to 3.10pm in the Albert, 2nd floor

P37-P51
Acute exacerbations of COPD and acute NIV
Discussion of abstracts will take place from 2.00pm to 3.55pm in the Albert, 2nd floor

P52-P65
Occupational lung disease
Discussion of abstracts will take place from 2.30pm to 4.15pm in the St James, 4th floor

P66-P78
Asthma phenotyping and biomarkers
Discussion of abstracts will take place from 2.40pm to 4.15pm in the Moore, 4th floor

P79-P86
New markers of lung physiology
Discussion of abstracts will take place from 3.00pm to 4.00pm in the Albert, 2nd floor

P87-P100
Diagnosis and management of paediatric lung disease
Discussion of abstracts will take place from 3.30pm to 5.15pm in the Mountbatten, 5th floor

SCIENTIFIC PROGRAMME

8.45am – 4.00pm
Cambridge, 5th floor
MODERATED POSTER VIEWING

M1-M13
Difficult symptom control and breathlessness
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

SLEEP
Professor John Stradling (Oxford)

8.30am – 10.15am
Churchill, Ground Floor

SYMPOSIUM

MESOTHELIOMA – POTENTIAL NEW TREATMENT OPTIONS AND ONGOING CONTROVERSIES
Chaired by: Professor Nick Maskell (Bristol) and Dr Robert Rintoul (Cambridge)

8.30am
The role of prophylactic radiotherapy to large incision sites in cases of mesothelioma: results from the SMART trial
Dr Amelia Clive (Bristol)

8.55am
The now and next in systemic therapy for mesothelioma
Dr Peter Szlosarek (London)

9.20am
Pro-con debate: The role of surgery in the management of mesothelioma
Pro: Mr David Waller (Leicester)
Con: Professor Gary Lee (Perth)

This symposium will provide an update for respiratory physicians, allied health care professionals and researchers on:

a) current understanding of the role of prophylactic radiotherapy in large incision sites in cases of mesothelioma – the primary results from the SMART trial
b) evidence base for thoracic surgery in mesothelioma
c) novel oncological treatments for mesothelioma, including checkpoint inhibitors
**SCIENTIFIC PROGRAMME**

**SPOKEN SESSION: S1 – S6**

Cutting edge pulmonary hypertension

*Chaired by: Professor Andrew Peacock (Glasgow) and Dr Joanna Pepke-Zaba (Cambridge)*

**8.35am S1***

Does paradoxical emboli of particulate matter through pulmonary arteriovenous malformations precipitate migraines?

T Patel, A Elphick, J E Jackson, CL Shovlin

**8.50am S2**

Vascular quiescence factor BMP9 is regulated by inflammation and neutrophil activation

W Li, L Long, K Hoenderdos, PD Upton, X Yang, AM Condliffe, ER Chilvers, NW Morrell

**9.05am S3**

Reduced BMPR2 expression potentiates a pulmonary artery smooth muscle cell specific IL-1ß response

J Pickworth, S Shay, S Gladson, J Iremonger, AMK Rothman, S Francis, J West, L A Lawrie

**9.20am S4**

Pulmonary artery pressure and exercise tolerance in patients with pulmonary arteriovenous malformations

T Hall, H Tighe, K Hornby, M Park, V Santhirapala, K Murphy, J E Jackson, L Howard, CL Shovlin

**9.35am S5**

Idiopathic pulmonary arterial hypertension demonstrates a peripheral blood signature of dysregulated immunity

K Zalewska, E Groves, H Baxendale, M Southwood, J Pepke Zaba, N Morrell, M Toshner

**9.50am S6**

The profiles of JMJD3, UTX and H3K27me3 expression in pulmonary vasculature in rat MCT model of PAH and human iPAH: implications for pulmonary arterial hypertension

D Shao, BE Garfield, A Crosby, P Young, F Perros, M Humbert, IM Adcock, N Morrell, SJ Wort

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**Wednesday 2 December 2015**

*S1 – BTS Medical Student Award Highly Commended*

**8.30am – 10.15am**

St James, 4th Floor

**SPOKEN SESSION: S7 – S12**

Phenotyping and treating severe asthma

*Chaired by: Dr Elizabeth Gamble (Bristol) and Dr Robert Niven (Manchester)*

**8.35am S7**

Airway pathological phenotypes and their clinical utility in adult asthma

S Siddiqui, A Shikotra, M Richardson, E Doran, D Choy, M Shelley, B Hargadon, J Arron, C Brightling, L Heaney, A Wardlaw, P Bradding

**8.50am S8**

A nationwide real-life study: exploring the difficulties of confirming the asthma diagnosis in patients with severe asthma

A von Bülow, V Backer, U Bodtger, NU Soes Petersen, T Skjold, K Dahl Assing, C Porsbjerg

**9.05am S9**

Equivalence of fluticasone propionate/salmeterol delivered via AirFluSal® Forspiro® and Seretide® Accuhaler® in adolescent and adult asthma

P Kuna, I Gath, U Thyroff-Friesinger, S Jones

**9.20am S10**

The impact of omalizumab on lung function and quality of life in patients with severe allergic asthma in UK clinical practice: a multi-centre prospective observational study – APEX II

R Niven, R Kurukulaaratchy, L Heaney

**9.35am S11**

Audit of the safety of bronchial thermoplasty using a national register and Hospital Episode Statistics

J Burn, AJ Sims, K Keltie, H Patrick, SWelham, RM Niven, LG Heaney
Wednesday 2 December 2015

9.50am  **S12**
Efficacy of bronchial thermoplasty in clinical practice using the British Thoracic Society UK Difficult Asthma Registry and Hospital Episode Statistics
J Burn, AJ Sims, K Keltie, H Patrick, S Welham, RM Niven, LG Heaney

8.30am – 10.30am
Westminster, 4th Floor
**JOINT BTS/BALR SYMPOSIUM (part 1)**
**EPIGENETICS AND LUNG DISEASE**
Chaired by: Dr Mark Perry (London) and Dr Andrew Williams (London)

8.30am  Epigenetics and lung disease
Dr Ivana Verona Yang (Denver)

9.10am  Targeting BET proteins; the development of novel epigenetic tools
Professor Panagis Filippakopoulos (Oxford)

9.50am  The role of MicroRNAs in COPD
Dr Guy Brusselle (Gent, Belgium)

**Learning objectives:**
a) to understand the different classes of epigenetic regulation (ie DNA methylation, histone modification and ncRNA regulations)
b) to understand the role of epigenetics in asthma, COPD and lung cancer
c) to understand the difficulty of targeting these mechanisms in a clinical setting

8.45am – 10.15am
Mountbatten, 6th Floor
**SYMPOSIUM**
**NEW DIRECTIONS IN TB DIAGNOSTICS AND THERAPY**
Chaired by: Dr Martin Dedicoat (Birmingham) and Professor Onn Min Kon (London)

8.45am  Current clinical diagnosis and measures of treatment response in TB
Dr Marc Lipman (London)

9.05am  S14*
Cumulative genetic risk of asthma severity in children and young people
VL Collis, JO Cunningham, S Dumble, R Tavendale, SJH Vijverberg, AH Maitland-van der Zee, HE Smith, SW Turner, CNA Palmer, S Mukhopadhyay

9.05am  S15
Measuring bronchodilator response by interrupter technique to predict response to inhaled steroid therapy in wheezy preschool children
R Willson, C Olden, L Symes, N Beydon, E Lombardi, D Wertheim, P Seddon

9.45am  How should we use the GeneXpert/rapid diagnostic tools in clinical practice?
Dr Catharina Boehme (FIND)

**Learning objectives:**
a) to identify key aspects of clinical diagnosis of tuberculosis and established evidence-based measures of assessing response to treatment
b) to understand the role and use of transcriptomics in the diagnosis and management of tuberculosis
c) to understand the role of the GeneXpert test as a rapid diagnostic tool for drug-sensitive tuberculosis and multi-drug resistant tuberculosis

8.45am – 10.30am
Abbey, 4th Floor
**SPOKEN SESSION: S13 – S18**
**Paediatrics: early life influences on lung health**
Chaired by: Professor Jane Davies (London) and Professor John Henderson (Bristol)

8.50am  S13
Early persistent childhood wheeze is a risk for more troublesome young adult asthma
C Hodgekiss, SH Arshad, RJ Kurukulaaratchy

9.05am  S14*
Cumulative genetic risk of asthma severity in children and young people
VL Collis, JO Cunningham, S Dumble, R Tavendale, SJH Vijverberg, AH Maitland-van der Zee, HE Smith, SW Turner, CNA Palmer, S Mukhopadhyay

9.20am  S15
Measuring bronchodilator response by interrupter technique to predict response to inhaled steroid therapy in wheezy preschool children
R Willson, C Olden, L Symes, N Beydon, E Lombardi, D Wertheim, P Seddon
### Wednesday 2 December 2015

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<tr>
<th>Time</th>
<th>Session</th>
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<tr>
<td>11.30am</td>
<td>Progress in treating the basic gene defect</td>
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<td><em>Professor Eric Alton (London)</em></td>
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<td><strong>Learning objectives:</strong></td>
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<td></td>
<td>a) identify risk factors for the development of bronchiectasis in cystic fibrosis</td>
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<td>b) recognize the science behind the evidence-based guidelines for cross-infection policy and surveillance for <em>M. abscessus</em> in cystic fibrosis</td>
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<td>c) understand the new developments in cystic fibrosis targeted gene therapy</td>
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<td>11.30am – 12.15pm</td>
<td><strong>SPOKEN SESSION: S25 – S30</strong> Sleep apnoea and hypoventilation: screening and treating high risk populations</td>
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<td><em>Chaired by:</em> Dr Justin Pepperell (Taunton) and Dr Sophie West (Newcastle upon Tyne)*</td>
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<td>10.35am</td>
<td>Establishing a normal range in driving simulator performance using standard deviation of lane position (SDLP) in an advanced PC-based driving simulator (MiniUoLDS)</td>
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<td>A Dwarakanath, D Ghosh, SL Baxter, PD Baxter, MW Elliott</td>
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<td>10.50am</td>
<td>Is the “time spent with saturations below 90%” on sleep study helpful in identifying obesity hypoventilation syndrome in the sleep clinic?</td>
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<td>GM Probert, B Prudon, SD West</td>
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<td>11.05am</td>
<td>Predictive performance of STOPBANG questionnaire for diagnosis of sleep apnoea in a cardiac surgical cohort</td>
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<td>M Mason, J Hernández-Sánchez, D Horton, A Clutterbuck-James, I Smith</td>
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<tr>
<td>11.20am</td>
<td>Effect of sleep apnoea on post-operative outcomes in cardiac surgery</td>
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<td>M Mason, J Hernández-Sánchez, D Horton, A Clutterbuck-James, I Smith</td>
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11.35am  S29
Predictors of continuous positive airways pressure usage at six months in minimally symptomatic patients. Further data from the MOSAIC trial
CD Turnbull, DJ Bratton, SE Craig, M Kohler, JR Stradling

11.50am  S30
Nutrition and exercise rehabilitation in obesity hypoventilation syndrome (NERO): a pilot randomised controlled trial
S Mandal, ES Suh, R Harding, A Vaughan-France, M Ramsay, B Connolly, D Bear, H McLaughlin, S Greenwood, M Polkey, M Elliott, A Douiri, J Moxham, N Hart

10.30am – 12.30pm
Churchill, Ground Floor
SYMPOSIUM
FIFTY YEARS OF COPD: WHERE NEXT ON ASSESSMENT AND TREATMENT?
Chaired by: Dr Charlotte Bolton (Nottingham) and Dr Neil Greening (Leicester)

10.30am  Functional outcomes of the patient
Dr Samantha Kon (London)

11.00am  Co-morbidities in COPD
Dr Frits Franssen (Maastricht)

11.30am  Targeting exacerbations
Dr Mona Bafadhel (Oxford)

12.00pm  The future of COPD treatment: the next 50 years
Professor Shawn Aaron (Ottawa)

2015 marks 50 years since the term COPD was first used. This session aims to look at the current thinking in assessing the patient with COPD and direction of treatments that may shape the next few years. This session will move beyond the measures of lung function and consider exertional dyspnoea and exercise, the role of multi-morbidity, exacerbations and acute events, and what the future holds for the management of COPD.

10.45am – 12.30pm
Windsor, 5th Floor
SPOKEN SESSION: S19 – S24
TIME to change: management of pleural disease
Chaired by: Dr Amelia Clive (Bristol) and Professor Gary Lee (Perth)

10.50am  S19
Interventions for the management of malignant pleural effusions
AO Clive, HE Jones, R Bhatnagar, NJ Preston, NA Maskell

11.05am  S20
Primary result of the 1st therapeutic interventions in malignant effusion (TIME1) Trial: A 2 x 2 factorial, randomised trial of chest tube size and analgesic strategy for pleurodesis in malignant pleural effusion

11.20am  S21
Early contrast enhancement: a perfusion-based magnetic resonance imaging biomarker of pleural malignancy
S Tsim, CA Humphreys, DB Stobo, GW Cowell, R Woodward, JE Foster, C Dick, KG Blyth

11.35am  S22
VATS for primary spontaneous pneumothorax – a cohort study of 1415 patients
G Cardillo, OJ Bintcliffe, F Carleo, NA Maskell
SCIENTIFIC PROGRAMME

11.50am  S23
Ambulatory percutaneous lung biopsy with early discharge and Heimlich valve management of iatrogenic pneumothorax – a new model for the UK
RR Abdullah, AN Tavare, DD Creer, S Khan, R Vancheeswaran, SS Hare

12.05pm  S24
Lung parenchymal assessment in primary and secondary pneumothorax – a case-control study
OJ Bintcliffe, AJ Edey, IS Negus, NA Maskell

11.00am – 12.00pm  Victoria, 2nd Floor
SAG OPEN MEETING
BTS Lung Infection Specialist Advisory Group

11.00am – 12.00pm  Rutherford, 4th Floor
SAG OPEN MEETING
BTS Tuberculosis Specialist Advisory Group

11.00am – 1.00pm  Westminster, 4th Floor
JOINT BTS/BALR SYMPOSIUM (part 2)
EPIGENETICS AND LUNG DISEASE
Chaired by: Dr Andrew Durham (London) and Professor Mark Lindsay (Bath)

11.00am
The epigenetic regulation of remodelling and fibrosis
Professor David Schwartz (Colorado)

11.40am
DNA methylation and asthma
Dr Paul Lavender (London)

12.20pm
Epigenetics in lung cancer
Dr Triantafillos Liloglou (Liverpool)

Learning objectives:
a) to understand the different classes of epigenetic regulation (ie DNA methylation, histone modification and ncRNA regulations)
b) to understand the role of epigenetics in lung disease, including fibrosis and asthma
c) to understand the role of epigenetics in lung cancer

11.30am – 12.30pm  Albert, 2nd Floor
SAG OPEN MEETING
BTS Interstitial and Rare Lung Disease Specialist Advisory Group

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
OPEN MEETING
BTS Nurse Advisory Group

12.30pm – 1.30pm  Rutherford, 4th Floor
SAG OPEN MEETING
BTS Tobacco Specialist Advisory Group

12.45pm – 1.30pm  Churchill, Ground Floor
THE SNELL MEMORIAL LECTURE
BCG – old story with new twists
Professor Paul Fine (London)
Introduced by: Professor Ann Millar (Bristol)

12.45pm – 1.45pm  Albert, 2nd Floor
SAG OPEN MEETING
BTS Critical Care Specialist Advisory Group

12.45pm – 2.15pm  St James, 4th Floor
SPOKEN SESSION: S31 – S35
Interventional progress
Chaired by: Dr Mohammed Munavvar (Preston) and Dr Mark Slade (Cheltenham)

12.50pm  S31
Safety and yield of physician led ultrasound guided transthoracic lung/pleural biopsies
R Reddy, M Naeem, GTsaknis

Wednesday 2 December 2015
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1.05pm  S32
Virtual bronchoscopic navigation followed by radial EBUS to biopsy peripheral pulmonary lesions: a pilot study
N Denny, J Mills, L Brown, SJ Fowler, M Munavvar

1.20pm  S33
Performance of EBUS-TBNA in the pathological subtyping and molecular testing of non-small cell lung cancer (NSCLC) in a UK thoracic oncology centre
H Al-Najjar, M Evison, J Martin, P Barber, P Crobbie, R Booton

1.35pm  S34
Do bronchial washings improve the diagnostic sensitivity for lung cancer when endobronchial tumour is seen?
A Dewar, S Bartlett, R Breen

1.50pm  S35
Methylene blue staining differentiates non-small cell lung cancer tissue
P Riddell, EL Molloy, S Finnegan, EP Judge, KC Redmond, N Mulligan, M Maguire, S O’Dea, JJ Egan

12.45pm – 2.30pm
Moore, 4th Floor
POSTER DISCUSSION: P1 – P14
Idiopathic pulmonary fibrosis boldly goes where no disease has gone before
Chaired by: Dr Nik Hirani (Edinburgh) and Professor Monica Spiteri (Stoke-on-Trent)

P1 Preliminary results for association of survival time in idiopathic pulmonary fibrosis cases with the 11p15.5 region
RJ Allen, MD Tobin, LV Wain, R Braybrooke, G Jenkins

P2 Platelet reactivity as a potential biomarker in idiopathic pulmonary fibrosis
MG Crooks, C Wright, S Fraser, AH Morice, SP Hart

Scientific Programme

P3 Pilot study to test the feasibility of a psychological support workshop for patients newly diagnosed with idiopathic pulmonary fibrosis (IPF) and their families
J Cove, AM Russell, J Wright, C Hogben, M Kokosi, V Mak, F Chua, A Wells, AM Doyle, E Renzoni

P4 Patient and carer co-investigators: shared experiences of a research steering group from the idiopathic pulmonary fibrosis patient reported outcome measure (IPF-PROM) study
AM Russell, AM Doyle, D Ross, C Burdett, J Gane, S Fleming, Z Aden, TM Maher, P Cullinan

P5 Quality of life and functional outcomes in post-transplant IPF patients aged over 70
P Riddell, S Winward, K Redmond, JJ Egan

P6 Early clinical experience with nintedanib – a two centre review
E Nuttall, M Crooks, S Gudur, C Leonard, C Major, S Hart, N Chaudhuri

P7 Interim analysis of nintedanib in an open-label extension of the INPULSIS® trials (INPULSIS®-ON)
B Crestani, T Ogura, K Pelling, C Coeck, M Quaresma, M Kreuter, M Kaye

P8 Pooled analysis of data from the TOMORROW and INPULSIS® trials of nintedanib in IPF
L Richeldi, KK Brown, V Cottin, M Selman, T Kimura, S Stowasser

P9 Nintedanib for the treatment of idiopathic pulmonary fibrosis – initial clinical experience in a UK cohort

P10 Effect of pirfenidone on gas transfer in patients with idiopathic pulmonary fibrosis
PM George, L Richardson, EA Renzoni, M Kokosi, TM Maher, AU Wells, F Chua

P11 Pirfenidone treatment is only available in the UK for a minority of patients with usual interstitial pneumonitis
G Burge, D Petkova, S Ghani, J Reynolds, M Djearman, E Hoey, S Hussain, PS Burge
SCIENTIFIC PROGRAMME

P12  Pirfenidone post-authorisation safety registry (PASSPORT) – update and concomitant use of N-acetylcysteine and/or corticosteroids
T Maher, V Cottin, A Azuma, L Groves, P Hormel, M Sköld, S Tomassetti, D Koschel

P13  Safety of pirfenidone in patients with idiopathic pulmonary fibrosis (IPF): integrated analysis of cumulative data from 5 clinical trials
PW Noble, C Albera, WZ Bradford, U Costabel, I Glaspole, MK Glassberg, DJ Lederer, Z Lin, SD Nathan, CA Pereira, JJ Swigris, D Valeyre, L Lancaster

P14  Pirfenidone is efficacious in patients with idiopathic pulmonary fibrosis (IPF) with more preserved lung function
PW Noble, WZ Bradford, U Costabel, I Glaspole, MK Glassberg, E Gorina, D Kardatzke, L Lancaster, DJ Lederer, SD Nathan, C Pereira, D Spirig, JJ Swigris, D Valeyre, C Albera

Wednesday 2 December 2015

P19  Predictors of COPD mortality, 2 year follow-up data from the ARCADE study
NS Gale, A Albarrati, MM Munnery, R Tal Singer, JR Cockcroft, DJ Shale

P20  A database approach to DOSE score calculation as a tool to identify ‘at risk’ chronic obstructive pulmonary disease patients through clinical records
LA Rigge, M Johnson, D Culliford, N Williams, L Josephs, M Thomas, T Wilkinson

P21  The applicability of current cardiovascular risk scores and cardiovascular surrogates in chronic obstructive pulmonary disease: a case-control study
IS Stone, MJ Khanji, W-Y James, A Balawon, R Boubertakh, L John, NC Barnes, SE Petersen

P22  Distribution and prediction of 10-years risk for coronary heart disease in COPD
A Albarrati, NS Gale, M Munnery, JR Cockcroft, DJ Shale

P23  Q/A method – a novel way of assessing pulmonary artery stiffness in COPD using cardiac MRI
S Saikia, NS Gale, JCL Rodrigues, RG Wise, C Bucciarelli-Ducci, JR Cockcroft, DJ Shale

P24  Underuse of beta-blockers in patients with heart failure and COPD
D Skinner, B Lipworth, G Devereux, V Thomas, J Ling, J Martin, V Carter, D Price

P25  Standards of end-of-life care in patients with non-malignant respiratory disease
H Brothers, A Gleeson, J Kilbane, M Scott, J Evans, E Powell, S Margetts

P26  Measuring the value of a consultant-led community respiratory (CORE) multidisciplinary team (MDT) in a deprived inner city area: achieving parity in respiratory care for housebound sick patients
M Heightman, D Dullaghan, A Rafferty, E Jones, H Townes, L Gardiner, J Dzingai, C Nimoh-Bing, H Broomfield, G Fabris, R Dharmagunawardena, L Restrick, M Stern

1.15pm – 2.50pm
Abbey, 4th Floor
POSTER DISCUSSION: P15 – P27
Clinical studies of advanced COPD
Chaired by: Dr Lisa Davies (Liverpool) and Dr Alice Turner (Birmingham)

P15  Regional cerebral atrophy and cognitive function in chronic obstructive pulmonary disease
CCS Savage, CP Pennington, PWJ Jones, JWD Dodd

P16  Prospective risk of osteoporotic fracture in patients with advanced COPD
A Gupta, NJ Greening, RA Evans, N Toms, A Samuels, MC Steiner

P17  Respiratory impact of diabetes mellitus in people without a primary diagnosis of chronic lung disease
S Ruickbie, A Prasad, PW Jones, EH Baker

P18  The effects of acute and repeated bouts of unilateral neuromuscular electrical stimulation on quadriceps muscle inflammation in COPD
A Gray, L Latimer, A Parmar, P Bradding, NJ Greening, MC Steiner
Wednesday 2 December 2015

P27 Patients with advanced COPD have unmet care and support needs across clinical settings: how can we identify needs to enable patient-centred care?
MC Farquhar, AC Gardener, C Moore, H Holt Butcher, G Ewing, P White, S Booth, S Howson, R Mahadeva

1.30pm – 3.10pm Cambridge, 5th Floor
MODERATED POSTER DISCUSSION: M1 – M13
Difficult symptom control and breathlessness
Chaired by: Dr Sara Booth (Cambridge) and Mrs Geraldine Burge (Birmingham)

M1 An audit of electronic oxygen prescribing and oxygen saturation readings showing a high prevalence of risk factors for hypercapnia and a high incidence of iatrogenic hyperoxaemia
P Whittemore, BR O’Driscoll

M2 Using a transportable oxygen concentrator (TPOC) to facilitate prompt and safe hospital discharge
F Hamilton, G Luxford, J Bott

M3 Anxiety and depression in patients with breathing pattern disorders or chronic respiratory disease
SD Naylor, J Haines, A Vyas, SJ Fowler

M4 Association of descriptors of breathlessness with diagnosis, self-reported severity of breathlessness and self-reported distress due to breathlessness in patients with advanced chronic obstructive pulmonary disease or cancer
S Chowienczyk, S Javadzadeh, S Booth, M Farquhar

M5 Comparison of respiratory health-related quality of life in patients with intractable breathlessness due to advanced cancer or advanced COPD
S Javadzadeh, S Chowienczyk, S Booth, M Farquhar

M6 Can clinical psychology input improve care quality and reduce admissions among patients with respiratory disease?
G Thew, J MacCallam, J Robinson, P Salkovskis, J Suntharalingam

SCIENTIFIC PROGRAMME

M7 Leading for improvement – an essential ingredient in quality patient care: a respiratory experience
S Kumar, M Gittus, A Cracknell, SDW Miller

M8 Prevalence of respiratory disease in severe morbid obesity
SIW Lipworth, T Thevanathan, SW Copack, J Emmanuel

M9 Lung health of opiate users (LHO): a pilot study to assess the respiratory health of opiate misusers attending a community substance misuse clinic
A Pitt, C Mitchell, B Colwell, I Appelqvist, F Ashby, C Lloyd, S Gilbody, R Lawson

M10 The development of a vocal cord dysfunction laryngoscopic appearance scale
J Haines, A Vyas, C Slinger, L Howell, SJ Fowler

M11 A preliminary biopsychosocial model of vocal cord dysfunction (VCD)
CC Maskell, N Pargeter, J Fellows, A Mansur, R Howard

M12 The utilisation of Heliox21 in a tertiary vocal cord dysfunction service
J Haines, A Vyas, C Slinger, SJ Fowler

M13 Clinical characteristics and management of patients presenting to the “Airways Clinic”: a specialised tertiary multi-disciplinary respiratory service
J Haines, A Vyas, C Slinger, N Cheyne, SJ Fowler

1.45pm – 3.15pm Mountbatten, 6th Floor
JOINT BTS/BPRS SYMPOSIUM
INFECTION IN CHRONIC SUPPURATIVE AIRWAYS DISEASES
Chaired by: Professor Jane Davies (London) and Dr Jeremy Webb (Southampton)

1.45pm Understanding and treating bacterial biofilms
Dr Jeremy Webb (Southampton)

2.15pm Battle of the bugs: how Pseudomonas destroys its enemies
Dr Lhousseine Touqui (Paris)
2.45pm  Fungal infections in chronic lung disease  
Professor Malcolm Richardson  
(Manchester)

Learning objectives: to understand the mechanisms underlying the chronic survival of organisms in the airway, mechanisms of evading host defence and of out-competing co-infecting pathogens; to appreciate some of the new advances in treatment, including non-antibiotic approaches; to become aware of gaps in our collective knowledge and which areas require further investigation.

2.00pm – 3.10pm  
Albert, 2nd Floor  
POSTER DISCUSSION: P28 – P36  
Non-IPF ILDs: diagnosis and management  
Chaired by: Dr Simon Hart (Hull) and Dr Elizabeth Renzoni (London)

P28 Real world MDT diagnosis of idiopathic pulmonary fibrosis  
M Hanley, C Leonard, N Chaudhuri

P29 Bristol interstitial lung disease (BILD) service experience: BILDing on the MDT  

P30 Efficacy of pulsed cyclophosphamide and methyl-prednisolone therapy in patients with progressive interstitial lung disease  
P Dutta, P Avery, L Mansell, B Griffiths, I Forrest, A John Simpson

P31 A retrospective analysis of interstitial lung disease screening in a regional centre for patients with scleroderma  
L Chenciner, F Pearce, PC Lanyon, SR Johnson

P32 Role of non acid and proximal reflux in scleroderma-associated interstitial lung disease  

P33 Rituximab as rescue therapy in advanced progressive systemic sclerosis associated interstitial lung disease  
M Kokosi, P Saunders, K Karagiannis, F Chua, TM Maher, EA Renzoni, AU Wells

Wednesday 2 December 2015

P34 Sarcoïdosis and co-existent aspergillus lung disease  
S Gudur, E Nuttall, C Harris, N Chaudhuri, C Leonard, E Muldoon

P35 Identifying novel predictors of outcome in sarcoidosis  
P Minnis, M Poland, G Nolan, SC Donnelly

P36 Ethnic differences in composite physiologic index (CPI) in pulmonary sarcoidosis: a 10-year experience in a specialist sarcoidosis clinic  
TT Tully, JG Galloway, JL Lally, ES Silber, PB Brex, SV Walsh, GL Larkin, JB Barker, SB Birring

2.00pm – 3.30pm  
Churchill, Ground Floor  
SYMPOSIUM  
RESPIRATORY VIRAL INFECTIONS: LEARNING FROM THE PAST, TREATING THE PRESENT, PREDICTING THE FUTURE  
Chaired by: Dr Anthony De Soyza (Newcastle upon Tyne) and Dr Tom Wilkinson (Southampton)

2.00pm  Learning from pandemic influenza 1918 to 2009  
Professor John Oxford (London)

2.30pm  The current burden of respiratory viral infection  
Dr Tristan Clarke (Southampton)

3.00pm  Predicting the future  
Dr Nicola Lewis (Cambridge)

This symposium focuses on the importance to global health of respiratory viral infections and particularly influenza. The first talk, given by the globally renowned expert Professor John Oxford, will explain how studies of the 1918 pandemic have informed our understanding of how pandemics develop and the measures required to prevent them developing. The second speaker, Dr Clarke an infectious disease expert, will review the evidence highlighting the current clinical burden of respiratory viral infections, new techniques for rapid diagnosis and their utility in clinical decision making in the NHS. Finally, looking forward, Dr Nicola Lewis from the Centre of Pathogen Evolution in Cambridge, will discuss emerging future pathogen associated risks and the science of prediction in this field.
Wednesday 2 December 2015

2.00pm – 3.30pm
Westminster, 4th Floor

SYMPOSIUM

BTS/BLF/BALR Early Career Investigators Symposium

Chaired by: Professor Edwin Chilvers (Cambridge) and Professor Moira Whyte (Edinburgh)

Judged by: Professor Sam Janes (London), Dr Gisli Jenkins (Nottingham), Professor Terry Tetley (London) and Professor Ann Millar (Bristol)

T1 Fluticasone propionate alters the resident airway microbiota and impairs anti-viral and anti-bacterial immune responses in the airways
A Singanayagam, N Glanville, R Pearson, P James, L Cuthbertson, M Cox, M Moffatt, W Cookson, N Bartlett, S Johnston

T2 Vitamin D supplementation reduces perioperative systemic and alveolar inflammation in patients undergoing oesophagectomy: results of the VINDALOO trial
RCA Dancer, D Parekh, A Scott, GD Perkins, DR Thickett

T3 Mitochondrial transfer is an important mechanism by which mesenchymal stromal cells (MSC) facilitate macrophage phagocytosis in the in vitro and in vivo models of acute respiratory distress syndrome (ARDS)
MV Jackson, TJ Morrison, CM O’Kane, DF McAuley, AD Krasnodembskaya

T4 Optically detectable antimicrobial peptides enable the immediate detection of bacteria and fungi in the lung
AR Akram, N Avlonitis, M Vendrell, S Chankeshwara, N McDonald, T Aslam, E Scholefield, T Walsh, C Haslett, M Bradley, K Dhaliwal

T5 MicroRNA-140-5p regulates disease phenotype in experimental pulmonary arterial hypertension via SMURF1
AMK Rothman, ND Arnold, JA Pickworth, J Iremonger, L Ciucian, R Allen, S Guth-Gundel, M Southwood, NW Morrell, SE Francis, DJ Rowlands, A Lawrie

2.00pm – 3.30pm
Rutherford, 4th Floor

SPOKEN SESSION: S36 – S40

Management of TB

Chaired by: Professor Onn Min Kon (London) and Professor Peter Ormerod (Blackburn)

2.05pm S36 Weekly audiograms pre-emptively identify amikacin related ototoxicity in MDR-TB
A Abbara, S Lang, OM Kon, SM Collin, D Pan, T Hansel, R Ravindran, R Holder, L John, RN Davidson

2.20pm S37 The response of objectively-measured cough to treatment in tuberculosis: an exploratory study
RD Turner, SS Birring, GH Bothamley

2.35pm S38 Predictive accuracy and clinical impact of Xpert MTB/RIF for the diagnosis of sputum smear-negative pulmonary tuberculosis using bronchoalveolar lavage fluid
W Ho, DW Connell, A Singanayagam, A Singanayagam, H Donaldson, OM Kon

2.50pm S39 Preliminary results of a latent tuberculosis screening and treatment project and the role of TB services in secondary care
MGK Burman, G Ahmed, JL Potter, VLC White, N Jayasekera, H Kunst

3.05pm S40 Optimisation of a human BCG challenge model
MEM Wilkie, A Minhinnick, S Harris, J Peter, L Stockdale, ZR Manjaly-Thomas, S Vermaak, I Satti, P Moss, H McShane
**SCIENTIFIC PROGRAMME**

2.00pm – 3.55pm  
Windsor, 5th Floor  

**POSTER DISCUSSION: P37 – P51**  
Acute exacerbations of COPD and acute NIV  
Chaired by: Dr James Calvert (Bristol) and Dr Rama Vancheeswaran (London)

**P37** Frailty and its relationship to mortality in patients receiving acute non-invasive ventilation (NIV) for respiratory failure in a district general hospital  
M Hatton, D Daley, L Hughes, BC Creagh-Brown

**P38** Improved mortality and outcomes for patients requiring non-invasive ventilation managed in a dedicated hyper acute medical unit  
T Buttle, H Chreif, H Woods, S Lohani

**P39** Non invasive pH with transcutaneous PCO2 monitoring as an alternative to arterial line sampling: a new patient friendly approach to monitoring acute NIV  
I Adejumo, J Khan, M Sovani

**P40** Should provision of acute inpatient non invasive ventilation in a district general hospital be exclusively a respiratory consultant-led service?  
C Baker, L Santharam, LA Hems, M Pagaria

**P41** Outcomes of patients transferred to respiratory care unit (RCU) on tracheotomy ventilation: a 4 year experience  
S Nisar, A Baluwala, MW Elliott, D Ghosh

**P42** Factors affecting the duration of acute non invasive ventilation required in patients with acute hypercapnic respiratory failure  
A Bishop, N Sayeed, A Oakes, B Beauchamp, B Chakraborty, R Mukherjee

**P43** How appropriately is NIV used as a ceiling of treatment?  
S Woolf, J Jitan, J Robinson, J Suntharalingam

**P44** Chronic obstructive pulmonary disease exacerbation and respiratory acidosis: patient outcomes at 6 months  
S Jackson, TM McKeever, G Hearson, G Housley, C Reynolds, W Kinnear, TW Harrison, AM Kelly, DE Shaw

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| **P45** Practical use of the DECAF score: can we improve outcomes in acute exacerbation of COPD admissions?  
L Collier, T David, C Craig, R Yadavilli |
| **P46** Frequency of COPD exacerbations in the German DACCORD Registry  
P Kardos, R Buhl, C-P Criée, C Vogelmeier, C Mailaender, H Worth |
| **P47** Recording of hospitalisations for acute exacerbations of COPD in UK electronic healthcare records databases  
KJ Rothnie, H Mullerova, JR Hurst, L Smeeth, J Chandan, K Davis, S Thomas, JK Quint |
| **P48** Identifying exacerbations using symptoms: reading between the lines  
CG Johnson, REK Russell, M Bafadhel |
| **P49** Higher service use amongst patients with advanced COPD and psychological co-morbidities: associations with quality of life, co-morbidities and exacerbations  
AC Gardener, M Farquhar, H Holt Butcher, C Moore, G Ewing, P White, S Howson, R Mahadeva, S Booth, P Burge, S Mendonca |
| **P50** Predicting readmission following exacerbation of COPD using a non-contact sensor – a proof of concept study  
P Minnis, R O’Meara, H Kane, A Zaffaroni, F O’Dea, J Britton, B Caulfield, SC Donnelly |
| **P51** Advancing quality (AQ) reducing variation and improving quality and outcomes for patients with chronic obstructive pulmonary disease (COPD) in the North West of England  
J Roberts, D Szwandt, S Hammond |

2.30pm – 4.15pm  
St James, 4th Floor  

**POSTER DISCUSSION: P52 – P65**

**Occupational lung disease**  
Chaired by: Dr Michael Greenstone (Hull) and Dr Jennifer Hoyle (Manchester)

**P52** Epidemiology of occupational extrinsic allergic alveolitis reported to SWORD 1996-2014  
CM Barber, M Carder, R Agius
P53 Determination of specific IgE antibodies to mouse proteins in laboratory animal workers
J Canizales, J Welch, B Fitzgerald, Z Lightfoot, W Banya, J Feary, P Cullinan, M Jones

P54 Respiratory symptoms, lung function and quality of life in British foundry workers
RE Wiggans, L Lewis, J Sumner, E Robinson, L Bradshaw, A Codling, D Fishwick, CM Barber

P55 The occupations associated with COPD risk in the large population-based UK Biobank cohort study
S De Matteis, D Jarvis, S Hutchings, A Darnton, L Rushton, P Cullinan

P56 Cross-sectional study of prevalence of sensitisation to mouse allergens in laboratory animal workers: the SPIRAL (safe practice in reducing allergy in laboratories) study
JR Feary, B Fitzgerald, Z Lightfoot, W Banya, M Jones, P Cullinan

P57 Immune mechanisms in pigeon fancier’s lung
S Hasan, S Bourke, N Kakkar, A Heaps, C McSharry, S Todryk

P58 Carry out of animal allergens from animal facility on skin of laboratory animal workers
H Campbell, J Canizales, S Semple, J Feary, P Cullinan, M Jones

P59 To determine Mus m 1 personal exposure in laboratory animal workers in facilities where mice are housed in open cages and individually ventilated cages
J Canizales, M Jones, S Semple, J Feary, P Cullinan

P60 Uptake and quality of health surveillance for occupational asthma in the UK
D Fishwick, D Sen, P Barker, A Codling, D Fox, S Naylor

P61 Respiratory ill health in the silica exposed brick manufacturing sector
D Fishwick, J Sumner, CM Barber, E Robinson, A Codling, L Lewis, C Young, N Warren

P62 A comparison of the relative effects of exposure on FEV1 and FVC in occupational COPD
JG Macfarlane, SC Stenton
**Scientific Programme**

### P71
The relationship between the Leicester cough questionnaire, eosinophilic airway inflammation and asthma patient related outcome measures in severe asthma
S Siddiqui, R Free, P Bradding, L McGarvey

### P72
T2 biomarkers relate to exacerbations and control in refractory asthma
S Srivastava, A Sahal, A Mansur

### P73
A pilot study to investigate the use of serum inhaled corticosteroid concentration as a potential marker of treatment adherence in severe asthma
KE George, BG Keevil, G Tavernier, K Hince, DM Ryan, SJ Fowler, RM Niven

### P74
Prevalence of specific antibody deficiency in severe asthma
SZ Zaidi, GT Tavernier, DR Ryan, RMN Niven, SJF Fowler

### P75
Cluster classification as a predictor of adverse radiological outcomes in allergic fungal airways disease (AFAD)
K Woolnough, C Newby, M Richardson, AJ Wardlaw

### P76
Psychogenic voice disorder mimicking treatment-refractory respiratory disease
J Selby, G Sandhu, G Scadding, A Menzies-Gow, JH Hull

### P77
Hypoxic challenge testing for fitness to fly in severe asthma
CM Orton, PM George, S Ward, A Menzies-Gow, JH Hull

### P78
Study of mortality in severe and difficult to treat asthma
J Sullivan, K O'Shea, A Mansur

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**Wednesday 2 December 2015**

### P80
Extrapolating lung clearance index (LCI) from shortened measurements
K Tanou, S Irving, F Ahmad, L Fleming, M Rosenthal, A Bush

### P81
Feasibility of measuring lung clearance index (LCI) in a clinic setting in preschool children with a range of airway diseases
B Downing, S Irving, Y Bingham, L Fleming, A Bush, S Saglani

### P82
Lung clearance index (LCI) and genotype-phenotype correlations in primary ciliary dyskinesia (PCD)
S Irving, M Dixon, S Ollosson, C Hogg, A Shoemark, A Bush

### P83
Remote pulmonary function testing — computer gaming in the respiratory world
C Sharp, V Soleimani, S Hannuna, M Camplani, D Damen, J Viner, M Mirmehdi, J Dodd

### P84
The InspiWave™ trial on adult healthy volunteers — insights gleaned from postural studies
CZ Zhang, PP Phan, DG Geer, CH Hahn, AF Farmery

### P85
A composite index of saturation and distance walked during a 6-minute walk test (6MWT): a retrospective methodological comparison
R Brown, AH Kendrick

### P86
Spirometric values of Greek healthy people and comparison with ECSC values in COPD people
NT Tatsis, SK Kakavas, EB Balis, NK Koulouris, KH Hadjistavrou, GT Tatsis

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### 3.00pm – 4.00pm

**Abbey, 4th Floor**

**Poster Discussion: P79 – P86**

**New markers of lung physiology**

*Chaired by: Dr Caroline Beardsmore (Leicester) and Dr Karl Sylvester (Cambridge)*

**P79**
Comparison of CF and non CF LCI results using the Exhalyzer D and InnocorTM devices
KJ Bayfield, C Saunders, EWFV Alton, JC Davies

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### 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)**

### 3.15pm – 3.35pm

**Victoria, 2nd Floor**

**SAG OPEN MEETING**

**BTS Clinical Data Specialist Advisory Group**
Wednesday 2 December 2015

3.30pm – 5.15pm
Mountbatten, 6th Floor

POSTER DISCUSSION: P87 – P100

Diagnosis and management of paediatric lung disease

Chaired by: Dr Sejal Saglani (London) and Dr Stephen Turner (Aberdeen)

P87  Repeat survey of vitamin K prescribing patterns and bone health surveillance in UK paediatric CF centres
MR Nortier, DS Urquhart

P88  The evaluation of Exophiala in paediatric cystic fibrosis
LB Patel, J Panickar, A Shawcross, S Wilkinson

P89  Does the Department of Health’s paediatric community assessment tool predict severe bronchiolitis in infants on admission?
LS Shorthouse, MGS Semple

P90  Towards a protocol for the management of very severe chronic lung disease
M Hurley, R Khetan, J Bhatt

P91  Post-infective obliterative bronchiolitis acquired beyond the first 3 years of life
S Sonmez-Ajtai, S Moss

P92  Real-time online analysis of volatile organic compounds in the exhaled breath of preschool children
KA Holden, SF Hussain, D Roland, TJ Coats, EA Gaillard

P93  The practicalities of using allergen-impermeable bed covers in children with mite allergic asthma
H Sumner, H Begum, A Simpson, A Custovic, CS Murray

P94  Effect of hydroxyurea on nocturnal and awake oxygen saturation in children with sickle cell disease
L van Geyzel, B Singh, M Akthar, G Ruiz, B Inusa, D Rees, A Gupta

P95  Growth and nutrition in ataxia telangiectasia
EL Stewart, A Tooke, S Pasalodos, M Suri, A Bush, J Bhatt

P96  Interstitial lung disease caused by STING-associated vasculopathy with onset in infancy (SAVI)
EJ Pellowe, SLN Clarke, TN Hilliard, AV Ramanan

P97  Uptake of the emergency salbutamol inhaler in North East England secondary schools following amendment of the Human Medicines Regulations
W Funston, SJ Howard

P98  The relationship between invasive and non-invasive measures of inflammation in children with severe therapy-resistant asthma
SM McKeon, SS Saglani, AB Bush, LF Fleming

P99  Colonisation with filamentous fungi and acute exacerbations in children with asthma
KG Staley, CH Pasley, J Satchwell, AJ Wardlaw, EA Gaillard

P100 Improving paediatrics’ pressurized metered dose inhaler technique and asthma control: inhaler verbal counselling vs. Trainhaler
WG Ammari, NK Al-Hyari, N Obeidat, MKhater, A Sabouba, M Sanders

4.15pm – 4.40pm
Churchill, Ground Floor

AWARD PRESENTATIONS

Presentation of the BTS Medal, BTS Award for Meritorious Service, BTS/BLF/BALR 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/
MORAN CAMPBELL LECTURE

“From pain to gain”
Professor Mike Morgan (Leicester)
Introduced by: Professor Ann Millar (Bristol)

5.30pm – 6.00pm
Churchill, Ground Floor

BRITISH THORACIC SOCIETY ANNUAL GENERAL MEETING

(BTS members only)
SCIENTIFIC PROGRAMME
Thursday 3 December 2015

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-P107
Best of science advances
Discussion of abstracts will take place from 2.00pm to 3.00pm in the Albert, 2nd floor
P108-P118
Sleep services: current delivery and future directions
Discussion of abstracts will take place from 2.00pm to 3.25pm in the Windsor, 5th floor
P119-P132
Phenotypes and response to treatment in COPD
Discussion of abstracts will take place from 2.00pm to 3.45pm in the Moore, 4th floor
P133-P144
Pulmonary rehabilitation and physical activity
Discussion of abstracts will take place from 3.15pm to 4.45pm in the Rutherford, 4th floor
P145-P160
Asthma treatment
Discussion of abstracts will take place from 3.30pm to 5.30pm in the Westminster, 4th floor
P161-P176
Lung cancer management
Discussion of abstracts will take place from 3.30pm to 5.30pm in the Abbey, 4th floor
P177-P189
Managing pleural disease
Discussion of abstracts will take place from 3.45pm to 5.20pm in the Windsor, 5th floor
P190-P200
Home non-invasive ventilation
Discussion of abstracts will take place from 4.00pm to 5.20pm in the Mountbatten, 6th floor

Thursday 3 December 2015

8.45am – 4.00pm
Cambridge, 5th Floor
MODERATED POSTER VIEWING
M14-M24
Improving quality of care in COPD
Discussion of abstracts will take place from 2.00pm to 3.15pm in the Cambridge, 5th floor

8.00am – 8.30am
Albert, 2nd Floor
BTS JOURNAL CLUB
ASTHMA
Professor Liam Heaney (Belfast)

8.30am – 10.00am
Churchill, Ground Floor
SYMPOSIUM
JOINT BTS/BTOG SYMPOSIUM
LUNG CANCER HORIZONS: NOT SO FAR AWAY
Chaired by: Dr Anna Rich (Nottingham) and Dr Robert Rintoul (Cambridge)

8.30am
The CRUK Stratified Medicine Programme/MATRIX trial
Dr Sanjay Popat (London)

9.00am
Immunotherapy: a new paradigm for lung cancer?
Professor Ross Camidge (Denver)

9.30am
CT screening: where we are, new data and what we should be doing
Professor Harry de Koning (Rotterdam)

This year’s BTS/BTOG joint symposia brings you the near future in lung cancer care. From this session you will gain knowledge of the CRUK next generation sequencing platform and how patients’ mutational profile will direct treatment strategy. Our US speaker will outline where he predicts lung cancer therapies will be in five years time, with a particular insight into the novel immune therapies everyone is talking about, and finally the lead of the NELSON CT Screening Trial will tell us whether we will be CT screening in the UK in 2016!
Thursday 3 December 2015

8.30am – 10.00am
Mountbatten, 6th Floor

JOINT BTS/BPRS SYMPOSIUM
GLOBAL THREATS IN PAEDIATRIC LUNG DISEASE

Chaired by: Dr Ian Balfour-Lynn (London) and
Dr Hui-Leng Tan (London)

8.30am HIV/TB co-infection in childhood
Dr Steven Welch (Birmingham)

9.00am Reducing children’s exposure to tobacco smoke: what works, what doesn’t and where do we go next?
Dr Premila Webster (Oxford)

9.30am The obesity epidemic and its impact on children’s respiratory health
Dr Hui Leng Tan (London)

Learning objectives: to understand the clinical problems posed by co-infection with TB in HIV positive children; to appreciate the magnitude of the second-hand smoke problem and what strategies are being considered to overcome it; to improve awareness of the impact of obesity on lung health, how it is monitored and what works in terms of treatments.

8.30am – 10.15am
Westminster, 4th Floor

SPOKEN SESSION: S41 – S46

IPF diagnosis and prognosis and biomarkers

Chaired by: Dr Gisli Jenkins (Nottingham) and
Dr Hannah Woodcock (London)

8.35am S41
Interstitial lung disease MDT presentations post VATS lung biopsy changes the original histological diagnosis in 30%

8.50am S42
Transbronchial cryobiopsies in the diagnosis of interstitial lung diseases – first UK experience
TA Mikolasch, E Borg, R Thakrar, V Holmes, HL Booth, JC Porter, N Navani

8.30am – 10.15am
Abbey, 4th Floor

SPOKEN SESSION: S47 – S52

The breath of life: respiratory physiology

Chaired by: Professor Mary Morrell (London) and
Dr Kyle Pattinson (Oxford)

8.35am S47
Neural respiratory drive responses to increases in continuous positive airway pressure in healthy subjects
ES Suh, S Mandal, MC Ramsay, G Rafferty, J Moxham, N Hart

8.50am S48
Continuous positive airway pressure titration in awake obese subjects with obstructive sleep apnoea and its impact on neural respiratory drive and breathlessness
S Xiao, J Bastianpillai, C Ratneswaran, M Pengo, YM Luo, CJ Jolley, J Moxham, J Steier

SCIENTIFIC PROGRAMME

9.05am S43
JP Hutchinson, TM McKeever, AW Fogarty, RB Hubbard

9.20am S44
Prognostic scoring systems for idiopathic pulmonary fibrosis: comparison of the composite physiologic index (CPI) and the GAP score
K Relf, K Sylvester, M Toshner, H Parfrey

9.35am S45
MUC5B genotype does not influence cough severity in IPF
P Saunders, CJ Stock, PL Molyneaux, M Kokosi, S Kingston, MG Belvisi, AU Wells, EA Renzoni, TM Maher

9.50am S46
An RCT of 28 day treatment with Fostair® pMDI 200/12 BD on platelet biomarkers in patients with idiopathic pulmonary fibrosis
CE Wright, K Arnell, S Fraser, M Crookes, Y Hayman, S Hart, S Thackray-Nocera, AH Morice
SCIENTIFIC PROGRAMME

9.05am  S49
Ventilatory irregularity quantified by approximate entropy identifies disordered breathing in patients with unexplained dyspnoea
T Bansal, GS Haji, HB Rossiter, MI Polkey, JH Hull

9.20am  S50
Understanding heroin overdose: a study of the acute respiratory depressant effects of injected pharmaceutical heroin
CJ Jolley, J Bell, GF Rafferty, J Moxham, J Strang

9.35am  S51
Arterial oxygen content reflects haemoglobin more than oxygenation indices in 440 patients with pulmonary arteriovenous malformations
CL Shovlin, B Chamali, V Santhirapala, L Williams, JE Jackson, H Tighe

9.50am  S52
The effect of age on arterial oxygen content in patients with pulmonary arteriovenous malformations (PAVMs)
AF Rizvi, L Babawale, JMB Hughes, JE Jackson, CL Shovlin

8.30am – 10.30am
Windsor, 5th Floor
SYMPOSIUM
PROTEASE MEDIATED TISSUE REMODELLING IN CHRONIC LUNG DISEASES
Chaired by: Professor Louise Donnelly (London) and Professor Terry Tetley (London)

8.30am  S53
Neutrophils in COPD and alpha-1-antitrypsin deficiency
Dr Elizabeth Sapey (Birmingham)

9.00am  S54
Novel mechanisms in protease mediated lung damage
Professor Simon Johnson (Nottingham)

Thursday 3 December 2015

9.30am  S50
Matrix metalloproteinases in tuberculosis
Professor Jon Friedland (London)

10.00am  S51
Pro-fibrotic activities of MMPs in IPF and ALI
Dr Caroline Owen (Harvard)

Tissue remodelling and damage occurs in all chronic lung diseases and is the cause of respiratory disability for patients. This session will provide four state of the art translational research talks in the areas of neutrophil derived proteases in chronic obstructive pulmonary disease and alpha-1-antitrypsin deficiency, novel mechanisms of proteolysis in common and rare lung diseases and how proteases affect both tissue damage, tissue destruction and fibrosis in tuberculosis, IPF and acute lung injury.

8.45am – 10.00am
St James, 4th Floor
SPOKEN SESSION: S53 – S56
Advances in cystic fibrosis
Chaired by: Dr Helen Rodgers (Edinburgh) and Dr Joanna Whitehouse (Birmingham)

8.50am  S53
Outcomes following bronchial artery embolisation for haemoptysis in adults with cystic fibrosis
WG Flight, PJ Barry, RJ Bright-Thomas, S Butterfield, R Ashleigh, AM Jones

9.05am  S54
Cognitive function in adults with and without cystic fibrosis related diabetes (CFRD) attending a large UK cystic fibrosis unit
HK Chadwick, AM Morton, A Driffill, A Wood, L Gillgrass, L Dye, CL Lawton, MW Mansfield, DG Peckham

9.20am  S55
Towards the clinical application of anti-pseudomonal bacteriophage: activity is retained following nebulisation with a range of commercially available nebuliser systems
R Pabary, A Alegro, EWF Alton, D Bilton, S Morales, F Smrekar, JC Davies
Thursday 3 December 2015

9.35am S56
Moving lentiviral-based gene therapy into a first-in-man CF trial

8.45am – 10.15am
Moore, 4th Floor
SPOKEN SESSION: S57 – S61
Clinical studies in COPD
Chaired by: Professor Shawn Aaron (Ottawa) and Professor Wisia Wedzicha (London)

8.50am S57
Short-term clinically important deterioration predicts long-term clinical outcome in COPD patients: a post-hoc analysis of the TORCH trial
I Naya, L Tombs, P Jones

9.05am S58
The PEARL score predicts 90 day readmission or death following hospitalisation for an exacerbation of COPD

9.20am S59
Using venous blood gas analysis in the management of COPD exacerbations: a prospective cohort study
DE Shaw, AM Kelly, G Housley, G Hearson, C Reynolds, TW Harrison, TM McKeever

9.35am S60
Efficacy and safety of aclidinium/formoterol fixed-dose combination in patients with COPD, stratified by ICS use
D Singh, A D’Urzo, E Garcia Gil

9.50am S61
Analysis of the efficacy and safety of the combination of tiotropium + olodaterol in patients with COPD by previous usage of inhaled corticosteroids
S Korn, R Buhl, L Grönke, L Korducki, VC Amato, GT Ferguson, R Abrahams

9.00am – 10.00am
Victoria, 2nd Floor
SAG OPEN MEETING
BTS Interventional Procedures Specialist Advisory Group

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

10.15am – 12.00pm
St James, 4th Floor
SPOKEN SESSION: S62 – S67
Mechanisms of lung injury and fibrosis remodelling on the fly
Chaired by: Professor Rachel Chambers (London) and Professor Danny McAuley (Belfast)

10.20am S62
Using drosophila melanogaster to study pathogenic mutants of surfactant protein C
E Malzer, SJ Marciniak

10.35am S63
Human mesenchymal stromal cell (hMSC) regulation of human macrophages in vitro models of the acute respiratory distress syndrome (ARDS)
T Morrison, M Jackson, A Kissenpfennig, C O’Kane, D McAuley, A Krasnodembskaya
10.50am  S64
Alveolar epithelial type II cell expression of VEGF-A\textsuperscript{a} is critical for development of idiopathic pulmonary fibrosis (IPF): an anti-fibrotic role for VEGF-A\textsuperscript{b} anti-angiogenic isoforms?
SL Barratt, T Blythe, C Jarrett, K Ourradi, GI Welsh, C Scotton, DO Bates, AB Millar

11.05am  S65
The role of Src kinase in inspiratory resistive breathing-induced pulmonary inflammation
D Toumpanakis, P Zacharatos, T Michailidou, G Tsoukalas, T Vassilakopoulos

11.20am  S66
Caffeine inhibits TGF\beta activation by epithelial cells, interrupts fibroblast responses to TGF\beta, and reduces pulmonary fibrosis in ex vivo precision-cut lung slices
AL Tatler, J Barnes, A Habgood, A Goodwin, R McNulty, RG Jenkins

11.35am  S67
Vitamin D deficiency drives pulmonary inflammation in a human model of the acute respiratory distress syndrome induced by inhaled lipopolysaccharide in healthy volunteers
M Fitzgerald, M Shyamsundar, JJ McNamee, DR Thickett, CM O’Kane, DF McAuley

10.15am – 12.15pm
Mountbatten, 6th Floor
SYMPOSIUM
COPD MAP – COLLABORATIVE RESEARCH PROVIDING INSIGHTS INTO COPD
Chaired by: Professor Chris Brightling (Leicester) and Dr Alasdair Gaw (InnovateUK)

10.15am  Understanding COPD: phenotypes to endotypes
Professor Dave Singh (Manchester)

Thursday 3 December 2015

10.45am  Bacterial colonisation in COPD: impact and mechanisms
Professor Louise Donnelly (London)

11.15am  Oxidative stress in COPD: a consequence of mitochondrial dysfunction?
Professor Ian Adcock (London)

11.45am  Skeletal muscle dysfunction in COPD
Professor Michael Polkey (London)

Learning objectives:

a) to understand the complexity of COPD and how phenotyping the heterogeneity provides insights into mechanisms and endotypes
b) to provide insights into the mechanisms of bacterial colonisation in COPD
c) to describe the role of mitochondrial dysfunction in promoting oxidative stress in COPD
d) to describe the mechanisms of skeletal muscle dysfunction and comparisons of exercise tests in COPD

10.30am – 12.15pm
Churchill, Ground Floor
PLENARY SCIENTIFIC SYMPOSIUM
Chaired by: Professor Andrew Fisher (Newcastle upon Tyne) and Professor Sam Janes (London)

10.30am  Making measurements in muscles – the new era of translational physiology
Dr Nicholas Hart (London)

10.55am  Neuropulmonology: insights from studying cough
Professor Jacky Smith (Manchester)

11.20am  Neutrophilic inflammation in bronchiectasis
Dr James Chalmers (Dundee)

11.45am  Epigenetics and asthma
Dr Pandurangan Vijayanand (Southampton and La Jolla, USA)

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.

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 3 December 2015
12.15pm – 1.15pm
Victoria, 2nd Floor
SAG OPEN MEETING
BTS Lung Cancer and Mesothelioma Specialist Advisory Group

12.15pm – 1.45pm
Rutherford, 4th Floor
OPEN SESSION
UKRRC – Getting your respiratory research funded: what's out there and how to access it
Chaired by: Professor Maria Belvisi (London)

This session, organised by the UK Respiratory Research Collaborative (UKRRC), will comprise short presentations from the major funders of respiratory research in the UK, including Ian Jarrold, BLF, Dr David King, NIHR, Dr Stephen Meader, MRC, Dr Samantha Walker, Asthma UK and a representative from Wellcome. The presentations will be followed by an interactive Q&A session. Come and hear all about the opportunities on offer, meet potential collaborators and learn how to maximise chances of success in applying.

12.30pm – 1.15pm
Churchill, Ground Floor
THE BTS LECTURE
Addressing COPD complexity
Dr Alvar Agusti (Barcelona)
Introduced by: Professor Mike Morgan (Leicester)

12.30pm – 1.30pm
Albert, 2nd Floor
SAG OPEN MEETING
BTS Pulmonary Vascular Disease Specialist Advisory Group

1.45pm – 3.00pm
Victoria, 2nd Floor
SPOKEN SESSION: S68 – S71
Lung infection and primary ciliary dyskinesia
Chaired by: Dr Ricardo Jose (London) and Dr Jane Lucas (Southampton)

SCIENTIFIC PROGRAMME

1.50pm  S68
A longitudinal study characterising a large adult primary ciliary dyskinesia cohort
A Shah, A Shoemark, SJ Macneill, B Bhaludin, A Rogers, D Bilton, DM Hansell, R Wilson, MR Loebinger

2.05pm  S69
Development of an in vitro assay to detect chemically-induced changes in ciliary beat frequency
A Turnbull, A Shoemark, H Lund-Palau, A Bush, E Alton, J Davies

2.20pm  S70
Experimental human pneumococcal colonisation is an asymptomatic event in healthy adults
A Trimble, AM Collins, CA Hancock, SB Gordon, DM Ferreira, AD Wright

2.35pm  S71
Anti-microbial immune responses in obstructive lung diseases
F Jaat, S Hasan, C Lanyon, A De Soyza, S Todryk

1.45pm – 3.15pm
Abbey, 4th Floor
SYMPOSIUM
CLINICAL AUDIT AND QUALITY IMPROVEMENT
Chaired by: Dr James Calvert (Bristol)

1.45pm  Introduction
Dr J Calvert (Bristol)

1.50pm  National COPD Audit Programme
- The pulmonary rehabilitation audit
Professor Michael Steiner (Leicester)
- Update on the primary and secondary care audit work streams
Dr Noel Baxter (London) and the COPD Audit Team

2.35pm  BTS National Community Acquired Pneumonia Audit 2014/15
Dr Wei Shen Lim (Nottingham)

2.50pm  BTS Lung Disease Registry Programme
Professor Monica Spiteri (Stoke-on-Trent)
SCIENTIFIC PROGRAMME

3.10pm  Concluding comments
Dr J Calvert (Bristol)

The objective of this session is to provide an update on the latest information from the National COPD Audit Programme, and an overview of the Society’s Audit and Quality Improvement activities, including results from the 2014/15 BTS Community Acquired Pneumonia audit, and the BTS Lung Disease Registry.

1.45pm – 3.15pm
St James, 4th Floor
SPOKEN SESSION: S72 – S76
Improving lung cancer outcomes
Chaired by: Dr Neal Navani (London) and Dr Helen Powell (Nottingham)

1.50pm  S72
Improving lung cancer survival in England evidenced through multiple data sources
P Beckett, I Woolhouse, S Walters, S Benitez-Majano, P Muller, D West, S McPhail, J Broggio, MD Peake

2.05pm  S73
Healthcare costs associated with lung cancer diagnosed at emergency hospitalisation
MPT Kennedy, PS Hall, MEJ Callister

2.20pm  S74
Assessing the diagnostic accuracy of the British Thoracic Society algorithm for investigation of solid pulmonary nodules
A Al-Ameri, P Malhotra, H Thygesen, S Vaidyanathan, S Karthik, A Scarsbrook, M Callister

2.35pm  S75
A clinical model to estimate the probability of pulmonary nodule malignancy in a population of oncology follow-up patients
A Talwar, LC Pickup, JMY Willaime, M Gooding, T Kadir, NM Rahman, F Gleeson

Thursday 3 December 2015

2.50pm  S76
“Straight to CT” in primary care – improving the lung cancer patient journey
A Nanapragasam, N Maddock, A McIver, C Smyth, MJ Walshaw

1.45pm – 3.15pm
Westminster, 4th Floor
SPOKEN SESSION: S77 – S81
The smoking gun
Chaired by: Professor John Britton (Nottingham) and Dr Keir Lewis (Swansea)

1.50pm  S77
Processing of cigarette graphic health warning labels decrease with prolonged exposure
C Ratneswaran, B Chisnall, MY Li, S Tan, A Devanand, J Steier

2.05pm  S78
Electronic cigarette advertising impacts adversely on smoking behavior within a London student cohort: a cross-sectional survey
C Ratneswaran, R Judge, M Colquhoun, J Steier, TK Khong

2.20pm  S79
The electronic case-based discussion; a novel teaching method applied to smoking cessation
AJK Wilkinson

2.35pm  S80
Game on? The gamification of mHealth apps in the context of smoking cessation
M Ahmed, Y Sherwani, M Muntasir, A El-Hilly, S Iqbal, S Siddiqui, Z Al-Fagih, O Usmani, A Eisingerich

2.50pm  S81
Feasibility and uptake of enhanced smoking cessation services within ambulatory HIV care
C Kyriacou, N Stewart, A Melville, J Brown, K Edwards, R Lloyd, M Johnson, J Flint, A Rodger, M Lipman
Thursday 3 December 2015

2.00pm – 3.00pm
Albert, 2nd Floor
POSTER DISCUSSION: P101 – P107

Best of science advances
Chaired by: Dr Mark Griffiths (London) and Dr Amanda Tatler (Nottingham)

P101 Peripheral blood type 2 innate lymphoid cell count in patients with severe eosinophilic asthma
B Hilvering, S Go, L Stoeger, K Borg, C Connelly, S Thulborn, S Pahlke, ID Pavord, L Xue

P102 Development of a novel assay for the detection of active neutrophil elastase in patients with chronic obstructive pulmonary disease
KL Moffitt, SL Martin, J Chalmers, B Walker

P103 Inhibition of asthma-related immunological responses by cultured epithelial cell lines
W Sargent, L Stoeger, I Pavord, TJ Powell

P104 Structural and cellular relationships in the peripheral lung: combining micro-CT and immunohistochemistry
JJ Ramsden, JL Norman, PM Lackie, JA Warner

P105 Identification of large alveolar macrophages and pulmonary intra-vascular macrophages in COPD patients
AK Ravi, J Plumb, S Mason, G Booth, J Vestbo, SD Singh

P106 Tissue factor pathway inhibitor (TFPI) is cleaved by multiple proteases in COPD lungs to affect circulating TFPI levels
B Mallia-Milanes, H Bailey, G Meakin, A Sheehan, A Knox, C Bolton, S Johnson

P107 Functional significance of the nitric oxide-asymmetric dimethylarginine-dimethylarginine dimethylaminohydrolase (NO-ADMA-DDAH) axis in TGF-β mediated epithelial-mesenchymal transition
HK Lota, JM Leiper

2.00pm – 3.00pm
Rutherford, 4th Floor
OPEN SESSION

British Lung Foundation research highlights
Chaired by Dr Noel Snell (Director of Research, BLF)

2.00pm
Hypoxia upregulates neutrophil degranulation with increased potential for tissue injury
Professor Alison Condliffe (Sheffield)

2.20pm
Increasing radiotherapy responsiveness of mesothelioma by activating tumour specific cell death
Dr Saurabh Dayal (Glasgow)

2.40pm
Preclinical evaluation of FK228 (Romidepsin) as a potential therapy for idiopathic pulmonary fibrosis (IPF)
Professor Donna Davies (Southampton)

2.00pm – 3.15pm
Cambridge, 5th Floor
MODERATED POSTER DISCUSSION: M14 – M24

Improving quality of care in COPD
Chaired by: Dr Katrina Curtis (London) and Dr Sarah Foster (Taunton)

M14 Surgical interventions for emphysema: the experience of a community based COPD service
AB Hardy, S Cowdell, P Griffiths

M15 Use of e-cigarettes in patients accessing secondary care in Croydon
R Siva

M16 Are we shouting loud enough? A comparison of primary versus secondary care spirometry
EJA Harris, S Grant, SYarde, GO’Connell-Ramsay, S Sturney, JSuntharalingam

M17 Improve accuracy of chronic obstructive pulmonary disease (COPD) diagnosis by offering quality assured spirometry
A Gulati, C Crocker, J Barrett, T Win

M18 Knowledge and attitudes of secondary care staff toward giving advice on smoking, weight management, alcohol and physical activity
SMendes, BMenezes, BMallia, HAbusriwil
**SCIENTIFIC PROGRAMME**

**M19** The cost of high dose corticosteroid prescribing in London – how much is too much?
V Mach, G D’Ancona, R Rampersad, J Khambh

**M20** A five-year analysis of an integrated COPD service in Hackney, London – is this the right direction?
A Garner, M Hodson, G Ketsetzis, A Bhowmik

**M21** Comparison of the effect of a ventilation multidisciplinary meeting on utilisation of critical care resources
A Bishopp, N Santana-Vaz, B Beauchamp, B Chakraborty, G Raghuraman, R Mukherjee

**M22** Does a nurse-led non invasive ventilation (NIV) service improve patient outcomes?
H Mainman, S Chambers, H J Curtis

**M23** The use of wearables for COPD patients: a qualitative study
S Nabhani, R Siva, R Kayyali, C Yagambrun, P Robinson, M Spruit, A Vaes, J Wacker, L Caldani, R Mulkherjee

**M24** Prevalence of anxiety and patient characteristics from a randomised controlled trial (RCT) to identify if cognitive behavioural therapy (CBT) by respiratory nurses reduces anxiety in COPD
K Heslop-Marshall, C Baker, D Carrick-Sen, SC Stenton, J Newton, GP Burns, A De Soya

2.00pm – 3.25pm
Windsor, 5th Floor

**POSTER DISCUSSION: P108 – P118**

**Sleep services: current delivery and future directions**
Chaired by: Dr Grace Robinson (Reading) and Dr Joerg Steier (London)

**P108** Quality of life, diet and exercise measurements in obese individuals with and without ventilatory failure
CD Turnbull, AR Manuel, L Pirkis, JR Stradling

**P109** Predicting difficult mechanical ventilation in obese patients undergoing laparoscopic surgery: an observational study
D Hallsworth, R Wingate, A Klucniks, A Manuel

**P110** A review of persistent hypercapnia and subsequent referral for obese patients admitted into an intensive care unit
K Manalan, K Sanderson, T Akhtar, N Hart, P Murphy

**P111** Respiratory flow limitation in the absence of obstructive sleep apnoea responds to CPAP therapy
B Chakrabarti, S Emegbo, S Craig, J Heseltine, T Wright, N Duffy, JF O’Reilly

**P112** CPAP role on the perioperative outcomes of patients with obstructive sleep apnoea
VM Macavei, D King, J Sumpter, M Berger, OE Mohr, J Mitic, TC O’Saughnessy

**P113** Clinical use of adaptive servo-ventilation across the UK: results of a postal survey
CJ Murphy, D Gosh, S West

**P114** Can a dedicated ‘fast track’ sleep service successfully establish vocational drivers on CPAP within four weeks of referral?
BAM Downie, G Olds, M Tomlinson, SD West

**P115** Outcomes of sleep studies and targeted therapies in patients with myotonic dystrophy: a cohort study
SD West, KN Anderson, J Hughes, A Atalaia, SV Baudouin, H Lochmuller

**P116** Impact of bariatric surgery on OSAS: a 4-year experience
V Palissery, S Kumar, D Ghosh, M O’Kane, MW Elliott

**P117** Comparison of the effects of continuous positive airway pressure and mandibular advancement devices on subjective daytime sleepiness in patients with obstructive sleep apnoea: a network meta-analysis
DJ Bratton, T Gaisl, C Schlazer, M Kohler
Thursday 3 December 2015

**P118** Factors affecting concordance with continuous positive airway pressure (CPAP) in obstructive sleep apnoea syndrome (OSAS)
N Shilliday, A Bishop, B Chakraborty, M Daniels, R Mukherjee

2.00pm – 3.30pm
Churchill, Ground Floor
SYMPOSIUM
HIGHLIGHTS FROM THORAX
Chaired by: Dr Nicholas Hart (London), Dr Gisli Jenkins (Nottingham) and Professor Alan Smyth (Nottingham)

2.00pm Sphingosine 1-phosphate lyase is an endogenous suppressor of pulmonary fibrosis. Role of S1P signaling and autophagy
Professor Viswanathan Natarajan (Chicago)

2.30pm Achieving high treatment success for MDR-TB in Africa: initiation and scale-up of MDR-TB care in Ethiopia, an observational cohort study
Dr Anne Goldfeld (Boston)

3.00pm Neural respiratory drive predicts clinical deterioration and safe discharge in exacerbations of COPD
Dr Eui-Sik Suh (Dartford)

3.15pm Gait speed and readmission following hospitalisation for acute exacerbations of COPD: a prospective study
Dr Samantha Kon (Harefield)

2.00pm – 3.45pm
Mountbatten, 6th Floor
SYMPOSIUM
COMBATING EOSINOPHILIC INFLAMMATION IN ASTHMA
Chaired by: Professor Douglas Robinson (London) and Dr Duncan Wilson (Birmingham)

2.00pm How eosinophils cause exacerbations of asthma
Professor Andrew Wardlaw (Leicester)

2.30pm From biomarkers to stratified therapy
Dr Joseph Arron (San Francisco)

SCIENTIFIC PROGRAMME

3.00pm Allergen immunotherapy for asthma
Dr Victoria Cardona (Barcelona)

After the asthma symposium, attendees will understand the role that eosinophils play in the pathogenesis of exacerbations and will be aware of the spectrum of potential therapeutic targets that are being explored in order to reduce the eosinophilic inflammation that underlies symptoms including IgE, cytokines (IL-4, IL-5 and IL-13), chemokines and host response to allergen.

2.00pm – 3.45pm
Moore, 4th Floor
POSTER DISCUSSION: P119 – P132
Phenotypes and response to treatment in COPD
Chaired by: Dr Charlotte Bolton (Nottingham) and Dr John Hurst (London)

**P119** Characterising non-eosinophilic COPD
K Hambleton, REK Russell, CE Brightling, M Bafadhel

**P120** Real life distribution of COPD severity in the German DACCORD registry: lung function is the main driver of classification in GOLD group C and D
H Worth, R Buhl, C-P Criée, P Kardos, C Mailaender, CF Vogelmeier

**P121** Characteristics of COPD patients with and without maintenance treatment at baseline, by GOLD stage: TONADO
S Korn, R Abrahams, L Grönke, L Korducki, VC Amatto, R Buhl

**P122** Combination therapy with inhaled salmeterol plus fluticasone propionate is more effective than salmeterol alone in reducing the risk of clinically important deterioration in COPD: a post-hoc analysis of the TORCH trial
I Naya, L Tombs, P Jones

**P123** Inhaled corticosteroid plus long-acting β2-agonist therapy is overused in the treatment of patients with chronic obstructive pulmonary disease: post hoc analyses of two 1-year studies
H Watz, GT Ferguson, L Grönke, F Voß, R Abrahams, R Buhl
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<tr>
<th>Paper Number</th>
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<tr>
<td>P124</td>
<td>A randomised, parallel-group study to evaluate the effect of umeclidinium added to inhaled corticosteroid/long-acting beta-agonist combination therapy in subjects with chronic obstructive pulmonary disease</td>
<td>AR Sousa, JH Riley, A Church, CQ Zhu, YS Punekar, WA Fahy</td>
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<td>P125</td>
<td>Tiotropium plus olodaterol combination therapy provides lung-function benefits when compared to tiotropium alone, irrespective of prior treatment with a long-acting bronchodilator: post hoc analyses of two 1-year studies</td>
<td>R Buhl, R Abrahams, L Grönke, L Korducki, M Fiežar, GT Ferguson</td>
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<td>P126</td>
<td>Efficacy of aclidinium bromide compared with tiotropium and placebo in symptomatic patients with moderate to severe chronic obstructive pulmonary disease (COPD): post-hoc analysis of a Phase IIIb study</td>
<td>J Beier, Robert Mroz, F Chuecos, E Garcia Gil</td>
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<td>P127</td>
<td>Superiority of glycopyrronium versus tiotropium in early onset of bronchodilation in patients with moderate to severe COPD – the FAST study</td>
<td>H Watz, C Mailaender, A-M Kirsten</td>
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<td>P128</td>
<td>Pooled safety analysis of adjudicated serious adverse events with the combination of tiotropium + olodaterol</td>
<td>R Buhl, K Tetzlaff, L Korducki, C Vogelmeier, L McGarvey</td>
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<td>P129</td>
<td>What is the patient’s preference: tiotropium monotherapy or fixed-dose indacaterol/glycopyrronium combination therapy? – the FAVOR study</td>
<td>P Kardos, I Hagedorn</td>
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<td>P130</td>
<td>Effectiveness and safety of initiating treatment with fluticasone/salmeterol via MDI versus DPI in COPD</td>
<td>R Jones, J Martin, V Thomas, D Skinner, J Marshall, D Price</td>
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<td>P131</td>
<td>Efficacy of tiotropium and olodaterol combination in patients with COPD on β-blockers</td>
<td>E Derom, S Korn, A Hamilton, VC Amatto, Y Zhao, F Maltais</td>
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<td>P132</td>
<td>Health care utilization and costs among COPD patients newly prescribed maintenance therapy in the United Kingdom (UK)</td>
<td>Y Punekar, SH Landis, K Bonar, H Le</td>
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**Thursday 3 December 2015**

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**3.00pm – 4.30pm**

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

**3.15pm – 4.15pm**

**Victoria, 2nd Floor**

**OPEN MEETING**

**BTS Specialist Trainees Advisory Group**

**3.15pm – 4.15pm**

**Albert, 2nd Floor**

**SAG OPEN MEETING**

**BTS Lung Physiology Specialist Advisory Group**

**3.15pm – 4.45pm**

**Rutherford, 4th Floor**

**POSTER DISCUSSION: P133 – P144**

**Pulmonary rehabilitation and physical activity**

*Chaired by: Miss Julia Bott (London) and Dr Sarah Elkin (London)*

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<tr>
<td>P133</td>
<td>A multidisciplinary patient education programme significantly improves asthma control and quality of life in patients with severe asthma</td>
<td>RD Daly, LJ Holmes, H Scanlon, D Ryan, RM Niven</td>
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<td>P134</td>
<td>Exercise responses to one-legged cycling in patients with idiopathic pulmonary fibrosis</td>
<td>TS Reilly, SM Majd, B Popat, NJ Greening, TE Dolmage, SA Agrawal, FA Woodhead, RA Evans</td>
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**Thursday 3 December 2015**

**P135** Physical activity profile of patients with COPD during an exercise class: what are patients actually doing early in the rehabilitation course?
T Maheswaran, L Houchen-Wolloff, SJ Singh

**P136** Do structured exercise classes for inpatients with COPD increase community pulmonary rehabilitation (PR) referral and completion rates?
TC Avent, RC Colclough, RG Edgar, C Owen, KH Swindells, S Gompertz

**P137** ‘I really live for coming here’. The effect of a long-term singing group on control of breathlessness, social empowerment and psychological wellbeing of patients with respiratory disease: a qualitative study
R Thomas, H Williams, M Stern

**P138** Early vs delayed rehabilitation: a randomised controlled trial
O Revitt, S Ward, MD Morgan, SJ Singh

**P139** Investigating the profile of physical activity in COPD patients 7 days post discharge from a respiratory-related admission. Does brief advice have an effect?
P Kanabar, V Warrington, L Houchen-Wolloff, S Singh

**P140** Effects of indacaterol/glycopyrronium on lung function and physical activity in patients with moderate to severe COPD
H Watz, C Mailaender, A-M Kirsten

**P141** An evaluation of the acceptability of supervised ward-based exercise for patients admitted to hospital for acute exacerbation of COPD
L Hogg, S Madden-Scott, J Turnbull, L Osman

**P142** Reduced all cause healthcare utilisation after breathing retraining for dysfunctional breathing
FC Thomson, DJ Ford

**P143** Associations between quadriceps isokinetic endurance and exercise test parameters in COPD patients
TJ Hargreaves, JP Fuld, KP Sylvester

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**SCIENTIFIC PROGRAMME**

**P144** A comparison of shuttle walking test endpoints in exercise studies in patients with COPD
S Singh, F Maltais, L Tombs, WA Fahy, M Vahdati-Bolouri, JH Riley

*3.30pm – 5.30pm Westminster, 4th Floor*

**POSTER DISCUSSION: P145 – P160**

**Asthma treatment**

*Chair by: Dr Tracy Bradshaw (Edinburgh) and Professor Ian Pavord (Oxford)*

**P145** Using fractional exhaled nitric oxide (FeNO) suppression and inhaled compliance assessment (INCA) to identify and manage non-adherence in difficult asthmatics
LG Heaney, KJ Hetherington

**P146** Prescribing respiratory medicines without making a diagnosis of asthma in UK primary care
S Clayton, V Carter, W Lenney, D Price, I Small, J Smith

**P147** Evidence of prescribing errors in primary asthma care
C Lewis, E Humphreys, V Carter, A Chisholm, D Price, S Walker

**P148** Once-daily tiotropium Respimat® add-on to at least ICS maintenance therapy reduces exacerbation risk in patients with uncontrolled symptomatic asthma
D Halpin, ED Bateman, P Paggiaro, ER Bleecker, M Engel, P Moroni-Zentgraf, H Schmidt, HAM Kerstjens

**P149** Once-daily tiotropium Respimat® add-on to at least ICS in adult patients with symptomatic asthma: pooled safety analysis
D Dusser, R Buhl, M Castro, HAM Kerstjens, P Paggiaro, M Engel, P Moroni-Zentgraf, A Unseld, ED Bateman

**P150** Once-daily tiotropium Respimat® reduces risk of severe asthma exacerbation and asthma worsening in symptomatic asthma, independent of allergic and inflammatory status
R Dahl, T Casale, M Vandewalker, H Schmidt, M Engel, P Moroni-Zentgraf, HAM Kerstjens
P151 Tiotropium Respimat® add-on therapy reduces exacerbation risk in patients with moderate or severe symptomatic asthma, independent of TH2 status
T Casale, R Dahl, JC Virchow, M Engel, P Moroni-Zentgraf, R Lühmann, HAM Kerstjens

P152 Fluticasone furoate (FF)/Vilanterol (VI) once daily reduces asthma symptoms both day and night
DA Leather, R Forth, L Yates, LA Jacques

P153 Fluticasone propionate/formoterol pressurised metered-dose inhaler ‘2-3-4’ training paradigm aids correct inhaler technique
D Bell, L Mansfield, M Lomax, S Dissanayake

P154 Evaluation of inhaler technique mastery for Budesonide Formoterol Spiromax® compared with Symbicort Turbohaler® in adult patients with asthma: primary results from the easy low instruction over time [ELIOT] study
H Chrystyn, R Dekhuijzen, C Rand, S Bosnic-Anticevich, N Roche, F Lavorini, V Thomas, J Steele, P Raju, D Freeman, I Small, J Canvin, D Price

P155 Fluticasone furoate (FF)/Vilanterol (VI) once daily reduces rescue medication use both day and night
LA Jacques, R Forth, L Yates, DA Leather

P156 Overuse of inhaled corticosteroids in asthma patients with concurrent exercise-induced laryngeal obstruction
CP Porsbjerg, AS Sverrild, EW Walsted, KM Mirza

P157 Individual patterns of inhaler use and health outcomes in adolescents with asthma
S Howard, M Patel, AR Lang, C Youle, H Vyas, D Shaw, S Sharples

P158 The cost of steroid induced morbidity among severe asthma patients in the UK
L Barry, J Sweeney, C O’Neill, C Patterson, D Price, L Heaney

P159 The use of omalizumab in severe asthma is associated with a decline in blood eosinophils
LJ Holmes, G Tavernier, S Fowler, K Hince, RM Niven

P160 Bone protection in oral corticosteroid dependant asthmatics
HH Hashim, PL Molyneux, S Regan, JH Hull, A Menzies-Gow

3.30pm – 5.30pm
Abbey, 4th Floor
POSTER DISCUSSION: P161 – P176
Lung cancer management
Chaired by: Dr Frank McCaughan (Cambridge) and Dr Anna Rich (Nottingham)

P161 How has the surgical treatment of lung cancer in the UK evolved over the last two decades? An illustrative surgeon’s experience
R Bilancia, A Paik, A Sharkey, D Waller

P162 CT follow up after surgery for lung cancer – should the availability of radio-surgery prompt a change in screening protocol to detect early intracerebral recurrence?
S Roberts, L Jones, C Exley

P163 Outcomes from a novel nurse led telephone clinic post thoracic surgery
A Hyde, A Moore, J Love, S Berwick, RA Thomas

P164 Smoking at the time of curative-intent lung cancer surgery increases perioperative complications: is there a role for electronic cigarettes?
ST Lugg, T Tikka, PJ Agostini, A Kerr, J Webb, K Adamas, E Bishay, RS Steyn, MS Kalkat, PB Rajesh, DR Thickett, B Naidu

P165 Results of the Northumbria direct access CXR project
M Weatherhead

P166 The frequency of chest radiographs prior to the onset of lung cancer symptoms
MPT Kennedy, O Walkowiak, MEJ Callister

P167 A ‘virtual’ lung nodule clinic: a novel approach to improve efficiency and accuracy of indeterminate lung nodule surveillance
J Thomas, S Grundy

P168 The ‘real world’ impact of the new BTS Lung Nodule Surveillance Guidelines
J Thomas, S Grundy
Thursday 3 December 2015

P169  FDG PET-CT scans – who best uses this expensive resource?
N Nwosu, M Ledson, Mj Walshaw

P170  Outcomes following pursuit of a tissue diagnosis in elderly patients with suspected lung cancer
S Crawley, J Butler, G Lumsden, N O’Rourke, S Sheridan, M Sproule, C Carlin

P171  A local cancer network root cause audit of 62-day lung cancer pathway breaches
O Eneje, N Kumar, D Powrie, B Yung, M Lawson

P172  Training nurses in sampling and acquisition of specimen during EBUS guided transbronchial needle aspiration
V Johnson, W Stables, S Binu, C Smyth, M Walshaw, K Mohan

P173  The investigation of patients referred with haemoptysis via the two week wait system in Southmead Hospital, Bristol, UK
J Harper, J Curran, M Plummeridge

P174  CATCH – a year in profile and further reductions in 2WW referrals
VTY Ng, A Walsham, A Sharman, SCO Taggart

P175  Use of a virtual clinic to improve the lung cancer patient journey
A Nanapragasam, N Maddock, A McIver, C Smyth, Mj Walshaw

P176  Epidermal growth factor receptor (EGFR) mutation testing and treatment choice in advanced non-small cell lung cancer (NSCLC): UK findings from a global survey
J Spicer, B Tischer, M Peters

3.45pm – 5.15pm
Churchill, Ground Floor
SYMPOSIUM
WHAT’S NEW IN RARE LUNG DISEASES?
Chaired by: Dr Rachel Hoyles (Oxford) and Professor Simon Johnson (Nottingham)

3.45pm  Eosinophilic lung diseases: new phenotypes
Professor Jean-Francois Cordier (Lyon)

SCIENTIFIC PROGRAMME

4.15pm  Expanding spectrum of cystic lung disease
Dr Frank McCormack (Cincinnati)

4.45pm  Alveolar proteinosis
Dr Bruce Trapnell (Cincinnati)

This session will provide an update on the ever expanding range of rare lung disease phenotypes. Three international experts will discuss the new understanding of rare eosinophilic lung disease phenotypes, the expanding spectrum of cystic lung diseases and their differential diagnosis. Finally, new understanding on the mechanisms of alveolar proteinosis and disease related biomarkers. The session will therefore provide an update on the recognition and assessment of rare lung diseases for the clinician.

3.45pm – 5.15pm
St James, 4th Floor
SPOKEN SESSION: S82 – S86
Lung infection mechanisms
Chaired by: Dr James Chalmers (Dundee) and Dr David Smith (Bristol)

3.50pm  S82  ‘The kiss of death’ – calcineurin inhibitors prevent actin-dependent lateral transfer of aspergillus fumigatus in necroptotic human macrophages
A Shah, S Kannambath, S Herbst, A Rogers, M Carby, A Reed, S Mostowy, S Shaunak, D Armstrong-James

4.05pm  S83  Calcineurin inhibition impairs phenotypic maturation of dendritic cells in an in vitro model of invasive aspergillosis in lung transplant recipients
AG Adlakha, DPH Armstrong-James, B Lenhard

4.20pm  S84  Sputum neutrophils but not Interleukin-8 (IL-8) or Interleukin 17 (IL-17) correlate with the Bronchiectasis Severity Index (BSI)
S Koustas, A Peel, J Scott, J Davison, K Jiwa, S Carnell, Aj Simpson, A De Soyza
SCIENTIFIC PROGRAMME

4.35pm  S85
Pneumolysin triggers the production of platelet-activating factor by human neutrophils in vitro
R Anderson, JG Nel, AJ Theron, TJ Mitchell, C Feldman

4.50pm  S86
The anti-inflammatory effects of pneumolysin
JN Periselneris, T James, M Noursadeghi, JS Brown

3.45pm – 5.20pm
Windsor, 5th Floor
POSTER DISCUSSION: P177 – P189
Managing pleural disease
Chaired by: Dr Ingrid Du Rand-Darwood (Hereford) and Dr Najib Rahman (Oxford)

P177 Cost effectiveness of ambulatory management of spontaneous pneumothorax
C Pillay, B Shah, M Naeem, R Reddy

P178 Ambulatory care of primary spontaneous pneumothorax with a Pneumostat device – cost effective and safe
M Samuel, P Sivakumar, A West

P179 The effectiveness of chemical pleurodesis agents in spontaneous pneumothorax: a systematic review
RJ Hallifax, A Yousuf, JP Corcoran, I Psallidas, NM Rahman

P180 5 year retrospective evaluation of indwelling pleural catheter safety in patients undergoing chemotherapy
C Chan Wah Hak, P Sivakumar, L Ahmed

P181 Indwelling pleural catheters for malignant pleural effusions – do septations change outcomes?
E Nuttall, H Balata, M Al-Aloul, M Evison, J Holme

P182 Prophylactic doxycycline following indwelling pleural catheter insertion for malignant pleural effusions
E Nuttall, H Balata, M Al-Aloul, M Evison, J Holme

P183 Mesothelioma in rural Scotland: a review of 5 years of experience
JMF Thomas, SR Thomas

Thursday 3 December 2015

P184 Modified WHO safety checklist for pleural interventions – preventing system errors
N Hutchinson, K Marshall, H Espley, AA Ionescu

P185 Evaluation of the LENT prognostic score in a large tertiary pleural service
H Balata, N Anwar, P Foden, M Al Aloul, J Holme, M Evison

P186 Chest drain care bundle improves chest drain insertion in district general hospital
H Steer, J Hutton, S Graham, R Jones

P187 The difficulty in implementing a safety checklist for pleural procedures
HJG Meredith, C-L Te, S Sivanantham, G Boehmer

P188 Survey of use of safety checklists and standardisation of practice in thoracoscopy centres in the UK
T Duncan, S Clarke, J Hoyle

P189 Development of patient-centred outcomes for a pleural disease service
VM Smith, E Rowlandson, F Early

4.00pm – 5.20pm
Mountbatten, 6th Floor
POSTER DISCUSSION: P190 – P200
Home non-invasive ventilation
Chaired by: Dr Sonya Craig (Liverpool) and Dr Patrick Murphy (London)

P190 Development of a respiratory question set for remote monitoring in motor neurone disease (MND)
HJ Ashcroft, H Ando, B Chakrabarti, R Halhead, P Levene, RM Angus

P191 Survival in patients with chronic type 2 respiratory failure: a comparison of obesity hypoventilation syndrome, COPD and overlap syndrome
A Jothieswaran, M Mascareno, S Bokhari, N Chaudhry, TW Felton, AM Bentley

P192 Clinical effectiveness of non-invasive ventilation in patients with motor neuron disease
D Freeman, A Jothieswaran, M Mascareno, N Chaudhry, S Bokhari, TW Felton, AM Bentley
Thursday 3 December 2015

P193 How safe is domiciliary change of tracheostomy tube in ventilator dependent patients?  
J M Palmer

P194 Inpatient adjustment of sub-optimal home mechanical ventilation (HMV) – an effective use of resources?  
F Frost, B Al-Hakim, S Wordingham-Baker, V Ford, H Ashcroft, K Ward, R Parker, B Chakrabarti, R Angus, N Duffy

P195 Demographics and outcomes of NIV in MND: a frontline perspective  
K Ward, V Ford, H Ashcroft, S Wordingham-Baker, B Chakrabarti, N Duffy, R Angus, R Parker

P196 A local domiciliary non-invasive ventilation (NIV) service reduces length of hospital stay for patients unable to wean from NIV  
A Lane, S Harlow, P Murray

P197 Efficacy of a local domiciliary non-invasive ventilation (NIV) service for motor neurone disease (MND): patient survival, safety and satisfaction  
A Lane, J Tollit, R Lewis, P Murray

P198 Managing ventilatory failure in patients on LTOT: a case series of outcomes using NIV  
K Hambleton, J Turner-Wilson, J Riley, J Young, N Gabriel, A Nickol, M Bafadhel, M Hardinge

P199 Does average volume assured pressure support (AVAPS) ventilation improve safety in motor neurone disease?  
TS Buttle, S Nathoo, J Kindred, S Banerjee

P200 Domiciliary nocturnal NIV in COPD – still controversial?  
J Barnacle, CME Longley, V Padmanaban, S Elkin, SAA Bloch

4.00pm – 5.30pm  
Moore, 4th Floor  
SPOKEN SESSION: S87 – S91  
New developments in cough  
Chaired by: Dr Lorcan McGarvey (Belfast) and Professor Jacky Smith (Manchester)

4.05pm S87  
Are oral steroids effective in treating the symptoms of acute lower respiratory tract infection in non-asthmatic adults? The oral steroids for acute cough (OSAC) placebo-controlled randomised trial  
AD Hay, HE Downing, ST Brookes, G Young, A Harnden, SP Hollinghurst, D Kendrick, P Little, MT May, MV Moore, E Orton, K Wang, MJ Thompson

4.20pm S88  
The viral mimic polyinosinic:polycytidylic acid (Poly I:C) induces TRPA1 channel hyper-responsiveness in an adult human stem cell-derived sensory neuronal model  
R Clarke, K Monaghan, I About, I El Karim, JG McGeown, SL Cosby, TM Curtis, FT Lundy, L McGarvey

4.35pm S89  
Hypersensitivity to adenosine triphosphate in chronic cough patients  
HE Fowles, AH Morice

4.50pm S90  
‘Chronic cough, cause unknown’: a qualitative study of patient perspectives of idiopathic cough  
K Hulme, S Dogan, SM Parker, V Deary

5.05pm S91  
A randomised, double-blind, placebo-controlled crossover study to assess the efficacy of a single dose of 100 mg of VFP700 by inhalation in reducing the frequency and severity of cough in adult patients with idiopathic pulmonary fibrosis  
I Satia, H Badri, N Chaudhuri, G Brown, K Abbott-Banner, J A Smith

5.30pm – 7.15pm  
Britten, 3rd Floor  
THE PRESIDENT’S RECEPTION – All welcome!
SCIENTIFIC PROGRAMME

Friday 4 December 2015

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

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

P201-P214
Double pneumonia and other infections
Discussion of abstracts will take place from 1.30pm to 3.15pm in the St James, 4th floor

P215-P227
Epidemiology in lung disease
Discussion of abstracts will take place from 1.45pm to 3.25pm in the Moore, 4th floor

P228-P235
Improving patient care in cystic fibrosis
Discussion of abstracts will take place from 2.00pm to 3.00pm in the Westminster, 4th floor

P236-P243
Clinical studies in cough
Discussion of abstracts will take place from 2.00pm to 3.00pm in the Rutherford, 4th floor

P244-P250
Asthma quality improvement
Discussion of abstracts will take place from 2.00pm to 3.00pm in the Albert, 2nd floor

P251-P264
Improving outcomes in TB
Discussion of abstracts will take place from 3.10pm to 4.50pm in the Windsor, 5th floor

P265-P273
Diagnosis and management of pulmonary arterial hypertension
Discussion of abstracts will take place from 3.30pm to 4.40pm in the St James, 4th floor

P274-P281
Treatment options in cystic fibrosis
Discussion of abstracts will take place from 3.30pm to 4.30pm in the Moore, 4th floor

Friday 4 December 2015

P282-P291
Investigating lung disease: novel techniques and old interventions
Discussion of abstracts will take place from 3.30pm to 4.45pm in the Abbey, 4th floor

8.45am – 4.00pm
Cambridge, 5th Floor
MODERATED POSTER VIEWING
M25-M32
Education and training: from simulation to social media
Discussion of abstracts will take place from 2.00pm to 3.00pm in the Cambridge, 5th floor

8.00am – 8.30am
Albert, 2nd Floor
BTS JOURNAL CLUB

CT SCREENING
Professor David Baldwin (Nottingham)

8.30am – 10.00am
Churchill, Ground Floor
SYMPOSIUM
ANTIBIOTIC RESISTANCE
Chaired by: Dr Jo Fothergill (Liverpool) and Professor Helen McShane (Oxford)

8.30am
The epidemiology of antimicrobial resistance in respiratory infections
Professor David Livermore (Norwich)

9.00am
Molecular diagnosis of bacteria and resistance
Professor Stuart Elborn (Belfast)

9.30am
An international perspective on antibiotic practice and resistance
Dr Grant Warterer (Perth)

After this session participants will have an overview of the epidemiology of resistance in important respiratory pathogens including Streptococcus pneumoniae. Participants will learn about new methods of diagnosing infections and identifying resistant pathogens using modern molecular techniques. Finally, they will gain an understanding of the microbiological and cultural factors that drive variation in antibiotic practices and guidelines across the world.
Friday 4 December 2015

8.30am – 10.00am
Windsor, 5th Floor

SYMPOSIUM
BREATHING LIFE INTO MND: ELECTRICITY, AIR AND CARE
Chaired by: Dr Michael Davies (Cambridge) and Professor Anita Simonds (London)

8.30am  Diaphragm pacing in MND
Dr Christopher McDermott (Sheffield)

9.00am  A service fit for treatment: NIV
Dr Ian Smith (Cambridge)

9.30am  Adding life to time: ethical decision-making
Professor Christina Faull (Leicester)

Learning objectives:
a) to provide a cutting edge review of the latest developments in respiratory care for patients with MND
b) to understand the possible role of diaphragm pacing in patients with MND, via the presentation of the results of a major UK study
c) to understand how the evolution of NIV services for patients with MND has led to improved patient outcomes
d) to reflect on the benefit of early collaborative working with palliative care teams to optimise outcome

8.30am – 10.15am
Moore, 4th Floor

SPOKEN SESSION: S92 – S97
Mechanisms of airway inflammation and remodelling
Chaired by: Professor Alan Knox (Nottingham) and Dr Elizabeth Sapey (Birmingham)

8.35am  S92
Matrix metalloproteinase-1 activation by mast cell tryptase causes airway remodelling and is associated with bronchial hyper-responsiveness in patients with asthma
S Naveed, D Clements, D Jackson, D Shaw, S Johnston, SR Johnson

8.50am  S93
Pulmonary matrix metalloproteinases and small airways disease in COPD – the origins of airflow obstruction?
K Ostridge, N Williams, V Kim, M Bennett, S Harden, L Welch, S Bourne, N Coombs, P Elkington, K Staples, T Wilkinson

SCIENTIFIC PROGRAMME

9.05am  S94
The role of oxidative stress and antioxidants in severe asthma; a case control study
A Bishop, R Sathyamurthy, AH Mansur

9.20am  S95
Peripheral blood CRTH2 positive cell count in patients with severe eosinophilic asthma
B Hilvering, L Stoeger, S Go, C Connelly, K Borg, S Thulborn, S Pahlke, ID Pavord, L Xue

9.35am  S96
Free-living haemophilus influenzae is associated with increased pulmonary inflammation
S Thulborn, JL Cane, A Ceroni, CE Brightling, M Bafadhel

9.50am  S97
Severity of lung but not liver disease impacts cardiovascular risk in alpha-1 antitrypsin deficiency
S Samanta, AD Saleh, B Gooptu, A Marshall, D Thorburn, DA Lomas, JR Hurst

8.30am – 10.30am
Mountbatten, 6th Floor

SYMPOSIUM
ILD: WHAT’S ON THE HORIZON?
Chaired by: Professor Ann Millar (Bristol) and Dr Joanna Porter (London)

8.30am  New biomarkers for IPF
Dr Toby Maher (London)

8.55am  LPA in IPF
Dr Andrew Tager (Harvard)

9.20am  Nintedanib and Pirfenidone – which one or both?
Dr Helen Parfrey (Cambridge)

9.45am  Pro-con debate: Lung transplant for IPF patients – patients over 65 should be referred for assessment at diagnosis
Pro: Professor Jim Egan (Dublin)
Con: Professor Andrew Fisher (Newcastle upon Tyne)
**SCIENTIFIC PROGRAMME**

This session will provide an update on the rapidly developing field of idiopathic pulmonary fibrosis. The rationale and patient choice for prescribing new anti-fibrotic therapies will be discussed in the light of recent clinical studies. New biomarkers predicting patients at risk of rapid progression have been identified and will be discussed, and the expanding indications for pulmonary transplantation will be debated by two leading UK transplant physicians. Finally, Andrew Tager from Harvard will discuss his work examining how lysophosphatidic acid and the sphingosine 1 phosphate pathway direct the fibrotic response to lung injury.

8.45am – 10.00am
St James, 4th Floor
**SPOKEN SESSION: S98 – S101**
The next steps of pulmonary rehabilitation
Chaired by: Dr Neil Greening (Leicester) and Professor Sally Singh (Leicester)

8.50am  **S98**
Effectiveness of home maintenance tele-rehabilitation on COPD exacerbations
G Kaltsakas, Al Papaioannou, M Vasilopoulou, S Spetsioti, SA Gennimata, AF Palamidas, N Chynkiamis, E Kortianou, T Vasilogiannakopoulou, IVogiatzis, NG Koulouris

9.05am  **S99**
Pulmonary rehabilitation in interstitial lung disease – a prospective, observational study
C Sharp, M McCabe, MJ Hussain, H Adamali, DL Smith, A Edwards, AB Millar

9.20am  **S100**
Is it feasible to assess dynamic hyperinflation during an incremental treadmill test in patients with severe asthma?
S Majd, TE Dolmage, RH Green, P Bradding, SJ Singh, RA Evans

9.35am  **S101**
Do those patients with a chronic respiratory disease that walk at a faster walking speed improve more post pulmonary rehabilitation?
EJL Chaplin, S Lohar, SJ Singh, SJ Singh

**Friday 4 December 2015**

8.45am – 10.00am
Abbey, 4th Floor
**SPOKEN SESSION: S102 – S105**
Lung cancer biology and biomarkers
Chaired by: Dr Richard Booton (Manchester) and Professor Tariq Sethi (London)

8.50am  **S102**
SOX2 initiates carcinogenesis in a novel organotypic model of bronchial dysplasia
LD Correia, H Farah, DM Rasul, RC Rintoul, T Sethi, TD Littlewood, GI Evan, F McCaughan

9.05am  **S103**
Synthesis of gold-based nanomedicines to treat non-small cell lung cancer
AM Cryer, P Ruenraroengsak, TD Tetley, AJ Thorley

9.20am  **S104**
Factors affecting sensitising EGFR mutation rate and cell type in stage IIIB/IV lung cancer
MPT Kennedy, JA Quinn, AR Biswas, A Rothwell, A Scally, L Cheyne, MEJ Callister

9.35am  **S105**
Microdroplet digital PCR for the longitudinal monitoring of circulating tumour DNA biomarkers in unselected patients with advanced lung cancer
E Karampini, A Muhith, H Farah, J King, P Cane, J Spicer, F McCaughan

9.00am – 10.00am
Victoria, 2nd Floor
**SAG OPEN MEETING**
BTS Asthma Specialist Advisory Group

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

10.15am – 12.00pm
St James, 4th Floor
**SPOKEN SESSION: S106 – S111**
Nintedanib or pirfenidone?
Chaired by: Dr Toby Maher (London) and Professor Luca Richeldi (Southampton)
Friday 4 December 2015

10.20am  S106
Consistent effect of nintedanib on decline in FVC in patients across subgroups based on HRCT diagnostic criteria: results from the INPULSIS® trials in IPF

10.35am  S107
Disease progression modelling in idiopathic pulmonary fibrosis: a prediction of time to disease progression and life expectancy with pirfenidone
M Fisher, T Maher, C Hill, J Marshall

10.50am  S108
Effect of baseline FVC on decline in lung function with nintedanib in patients with IPF: results from the INPULSIS® trials
M Kolb, T Kimura, S Stowasser, C Hallmann, L Richeldi

11.05am  S109
Effect of continued treatment with pirfenidone following a clinically meaningful decline in percent predicted forced vital capacity in patients with idiopathic pulmonary fibrosis (IPF)
PW Noble, C Albera, WZ Bradford, U Costabel, I Glaspole, MK Glassberg, L Lancaster, DJ Lederer, Z Lin, CA Pereira, JJ Swigris, D Valeyre, SD Nathan

11.20am  S110
Efficacy and safety of nintedanib in patients with IPF beyond week 52: data from the Phase II TOMORROW trial
L Richeldi, U Costabel, M Selman, Z Xu, T Kimura, S Stowasser, C Hallmann

11.35am  S111
Does rate of decline in lung function predict response to pirfenidone therapy in patients with idiopathic pulmonary fibrosis?
JA Eaden, C Barber, SM Bianchi

SCIENTIFIC PROGRAMME

10.15am – 12.15pm
Churchill, Ground Floor

SYMPOSIUM
SENSATIONAL DEVELOPMENTS IN LUNG DISEASE
Chaired by: Professor Maria Belvisi (London) and Professor Alyn Morice (Hull)

10.15am  The role of airway nerves in lung disease: the big picture
Professor Pierangelo Geppetti (Florence)

10.45am  TRP channels: role in chronic cough
Dr Mark Birrell (London)

11.15am  What have clinical challenge tests told us about airway hypersensitivity?
Dr Shoaib Faruqi (Hull)

11.45am  Targeting airway nerves to treat cough, wheeze and dyspnoea
Dr Surinder Birring (London)

This session will: describe how sensory neurons in the airways link with the nervous system to relay airway sensation; identify the specific neuronal receptors that are important in human airways and how these can be modelled in animals; recognise how perturbations of these pathways contribute to common airway symptoms such as cough, wheeze, and breathlessness, and give examples of novel drugs that are being developed to treat patients; explain the various clinical challenge tests that have been developed to test airway sensitivity and how these can be applied in different clinical settings.

10.30am – 11.30am
Albert, 2nd Floor

SAG OPEN MEETING
BTS COPD Specialist Advisory Group

10.30am – 11.30am
Windsor/5th Floor

OPEN MEETING
BTS/SIGN Asthma Guideline update
Chaired by: Dr James Paton (Glasgow) and Dr John White (York)

New and revised recommendations from updated sections of the guideline will be presented, including Dr Hilary Pinnock (Edinburgh) speaking on diagnosis and Dr Anne Boyter (Strathclyde) on pharmacological management.
SCIENTIFIC PROGRAMME

10.30am – 11.45am
Westminster, 4th Floor
SPOKEN SESSION: S112 – S115
Pseudomonas: digging for gold or search and destroy?
Chaired by: Dr Kathryn Bateman (Bristol) and Dr Adam Hill (Edinburgh)

10.35am  S112
Variability in susceptibility to antibiotics and bacteriophages between individual colonies of Pseudomonas aeruginosa from cystic fibrosis sputum samples: implications for future clinical trial design
V Khoo, R Pabary, H Lund Palau, A Turnbull, N Madden, S Schelenz, A Jones, S Morales, EWFW Alton, JC Davies

10.50am  S113
An epidemiological review of strains of Pseudomonas aeruginosa in a non-cystic fibrosis bronchiectasis cohort
P Mitchelmore, A Brown, C Sheldon, C Scotton, M Bull, E Mahenthiralingam, N Withers

11.05am  S114
Feasibility study for a randomized controlled trial of Pseudomonas aeruginosa eradication treatment in patients with bronchiectasis
HR Abo-Leyah, A Smith, M Clark, J Hill, TC Fardon, JD Chalmers

11.20am  S115
Efficacy of Pseudomonas aeruginosa eradication regimens in non-CF bronchiectasis
E Vallieres, K Tunelty, MM Tunney, R Hannah, O Hewitt, JS Elborn, DG Downey

Friday 4 December 2015

10.35am  S116
GDF-15, the miR-542 cluster and miR-422a are associated with muscle wasting in intensive care unit acquired paresis
RG Paul, MI Polkey, PR Kemp, MJD Griffiths

10.30am – 12.00pm
Abbey, 4th Floor
SPOKEN SESSION: S116 – S120
Best of basic science advances
Chaired by: Professor Louise Donnelly (London) and Dr Sarah Walmsley (Edinburgh)

10.35am  S116
GDF-15, the miR-542 cluster and miR-422a are associated with muscle wasting in intensive care unit acquired paresis
RG Paul, MI Polkey, PR Kemp, MJD Griffiths

10.50am  S117
rSIVF/HN-mediated gene therapy enables lungs to produce therapeutically relevant levels of FVIII
KMP Pytel, MPS Paul-Smith, JM McIntosh, MC Chan, CM Meng, IP Pringle, LD Davis, MI Inoue, MH Hasegawa, SC Hyde, DR Gill, AC Nathwani, EWFW Alton, UG Griesenbach

11.05am  S118
Circadian glucose patterns in adult cardiothoracic transplant recipients
A Nixon, S Manduell, B Issa, M Al-Aloul

11.20am  S119
MicroRNA-200b represses TGF-β1 induced EMT in BEAS-2B and primary bronchial epithelial cells
S Ladak, C Ward, S Ali

11.35am  S120
Serum MicroRNA profiles in IPF patients – biomarkers or potential therapeutic targets?
P Minnis, R Kane, R Lumsden, S Whitty, SC Donnelly, MP Keane

10.45am – 12.45pm
Mountbatten, 6th Floor
SYMPOSIUM

OCCUPATIONAL LUNG DISEASE: THE GENERAL CHEST CLINIC AND BEYOND
Chaired by: Dr Peter Reid (Edinburgh) and Dr Joanna Szram (London)

10.45am  S116
Occupational lung disease in the 21st Century: space as the final frontier
Dr Kim Prisk (San Diego)
Friday 4 December 2015

11.15am Specific inhalation challenge testing for occupational asthma: what’s the evidence, what lies ahead?
Professor Paul Cullinan (London)

11.45am Causes and consequences of occupational HP: evidence for diagnostic patterns and approaches
Dr Richard Barraclough (Manchester)

12.15pm Asbestos exposure and IPF
Dr Christopher Barber (Sheffield)

This symposium will provide an update for respiratory physicians, allied health care professionals and researchers on:
a) current understanding of the occupational and environmental aetiologies, diagnostic approaches and subsequent management of HP
b) evidence base for specific inhalation challenges in occupational asthma
c) contemporary particle research related to extreme 21st Century occupations
d) management issues in cases of asbestosis compared to UIP

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

12.30pm – 1.30pm
Victoria, 2nd Floor
SAG OPEN MEETING
BTS Cystic Fibrosis Specialist Advisory Group

1.00pm – 2.00pm
Albert, 2nd Floor
SAG OPEN MEETING
BTS Occupational and Environmental Lung Disease Specialist Advisory Group

1.30pm – 3.00pm
Windsor, 5th Floor
SPOKEN SESSION: S121 – S125
COPD weighs heavy on the heart
Chaired by: Dr Jennifer Quint (London) and Dr Eui-Sik Suh (Dartford)
SCIENTIFIC PROGRAMME

1.30pm  S126
Measuring ER protein mobility during ER fragmentation in alpha-1-antitrypsin deficiency
JA Dickens, A Ordonez, JE Chambers, DA Lomas, SJ Marciniak

1.50pm  S127
Gene therapy for alpha-1-antitrypsin deficiency using a pseudotyped lentivirus vector
MC Paul-Smith, JF Gelinas, K Pytel, M Chan, C Meng, L Cammack, L Cameron, C Moran, I Pringle, L Davies, M Inoue, M Hasegawa, SC Hyde, DR Gill, EWF Alton, U Griesenbach

2.05pm  S128
Soluble ADAM33 causes airway remodelling to promote allergic airway inflammation
ER Davies, JA Whitsett, DE Davies, HM Haitchi

2.20pm  S129
A two species proteomics approach to determine MMP-12 substrates in COPD
B Mallia-Milanes, A Dufour, H Bailey, G Meakin, A Leme, C Bolton, S Shapiro, C Overall, S Johnson

2.35pm  S130
Axl receptor tyrosine kinase on airway macrophages has a key role in lung immune homeostasis
N Denny, AM Grabiec, G Tavernier, S Holden, H Francis, D Ryan, R Niven, SJ Fowler, A Simpson, T Hussell

2.50pm  S131
Deficiency mutations of alpha-1-antitrypsin differentially affect folding, function and polymerisation
I Haq, JA Irving, AD Saleh, L Dron, GL Regan-Mochrie, N Motamed-Shad, JR Hurst, DA Lomas, B Gooptu

Friday 4 December 2015

1.30pm – 3.15pm
St James, 4th Floor
POSTER DISCUSSION: P201 – P214

Double pneumonia and other infections
Chaired by: Dr Siobhan Carr (London) and Dr Jimstan Periselneris (London)

P201 Living your life with bronchiectasis: an exploration of patients and carers information needs informing development of a novel information resource
KLM Hester, J Newton, A De Soyza, T Rapley

P202 Assessment of bronchiectasis scoring systems: a long term cohort study
HC Ellis, S Cowman, M Fernandes, R Wilson, MR Loebinger

P203 A description of immunological and specific antibody profile in a cohort of non-CF bronchiectasis patients
GM Miller – WITHDRAWN

P204 Risk factors for requiring intravenous antibiotic therapy delivered in hospital for exacerbations of bronchiectasis
P Palani Velu, P Bedi, K Turnbull, AT Hill

P205 Admission trends and outcomes of individuals with bronchiectasis admitted to adult general critical care units in England, Wales and Northern Ireland
V Navaratnam, C Muirhead, RB Hubbard, A De Soyza

P206 Experience of establishing funding for a home IV service for bronchiectasis
A Booth, A McCleary, RA Thomas

P207 Thoracic involvement in IgG4-related disease
RM Anstey, JP Corcoran, EL Culver, A Talwar, RJ Hallifax, I Psallidas, TN Cargill, CD Manganis, E Barnes, NM Rahman

P208 Prevention of ventilator-associated pneumonia with chest physiotherapy: a meta-analysis
GF Javelosa, RK De Borja, M Lagmay, K Villareal
Friday 4 December 2015

P209 The burden of hospital acquired pneumonia: a cohort study
V Navaratnam, E O’Dowd, H Staniforth, L Haynes, J Lacey, A Gummow, RB Hubbard, T Bewick

P210 Community acquired pneumonia – severity and mortality
K Tariq, P McDermott, S Sunny, H Burhan, J Hadcroft

P211 Impact of door-to-radiograph time on pneumonia management
JM Dudziak, KL Scott, A Ashton, R Varia

P212 Microbiological sampling in community-acquired pneumonia: do we follow the guidelines and does it help our patients?
S Sunny, P McDermott, K Tariq, J Hadcroft, J Folb

P213 CXR follow-up after community acquired pneumonia (CAP): outcomes of adherence to guidelines
P Eaton, HJ Curtis

P214 Arrhythmias in pneumonia: a review of incidence, outcomes and management
DR Cox

1.30pm – 3.30pm
Mountbatten, 6th Floor
SYMPOSIUM
INTERVENTIONAL BRONCHOSCOPY FOR BENIGN DISEASE
Chaired by: Dr Neal Navani (London) and Dr Pasupathy Sivasothy (Cambridge)

1.30pm Debate: Bronchoscopic lung volume reduction is the future
Pro: Dr Nick Hopkinson (London)
Con: Professor Walter Weder (Zurich)

2.30pm Bronchial thermoplasty for severe asthma – is it safe and will it work?
Dr Pallav Shah (London)

3.00pm Should we be using cryobiopsy in the diagnosis of interstitial lung disease?
Dr Jurgen Hetzel (Tubingen)

SCIENTIFIC PROGRAMME

Learning points: this symposium will address topical issues in interventional bronchoscopy for benign lung disease. By the end of this session delegates will have: new insights into the best approach to lung volume reduction therapy; discovered whether bronchial thermoplasty is going to be safe and effective; learnt whether cryobiopsy will improve the diagnosis of interstitial lung disease.

1.45pm – 3.25pm
Moore, 4th Floor
POSTER DISCUSSION: P215 – P227
Epidemiology in lung disease
Chaired by: Professor Richard Hubbard (Nottingham) and Dr Bipen Patel (Exeter)

P215 The epidemiology of pneumothorax in England (1968-2011)
RJ Hallifax, R Goldacre, NM Rahman, M Goldacre

P216 Duration of total and exclusive breastfeeding, timing of solid food introduction and risk of allergic diseases: a systematic review and meta-analysis
V Garcia-Larsen, D Ierodiakonou, J Leonardi-Bee, T Reeves, J Chivinge, Z Robinson, K Jarrold, N Geoghegan, E Andreou, N Tagiyeva-Milne, U Nurmatov, S Cunha, RJ Boyle

P217 Chronic mucus hypersecretion may represent a biomarker of airways disease activity rather than simply a phenotype: a longitudinal study of a nationally representative British birth cohort
JP Allinson, R Hardy, GC Donaldson, SO Shaheen, D Kuh, JA Wedzicha

P218 The epidemiological, healthcare and societal burden and costs of asthma in the UK and member nations: analyses of national databases
M Mukherjee, A Stoddart, R Gupta, B Nwaru, M Heaven, A Farr, D Fitzsimmons, A Bandyopadhyay, C Aftab, C Simpson, R Lyons, C Fischbacher, C Dibben, M Shields, C Phillips, D Strachan, G Davies, B McKinstry, A Sheikh

P219 Potential impact of air pollution coverage in the media on respiratory disease admissions
PS Tang, D Shaw, G Smith, J Goulding
**SCIENTIFIC PROGRAMME**

| P220 | Using funnel plots to make meaningful centre comparisons  
| L Pierotti, MA Mohammed, M Wildman,  
| D Bilton, J Boote, SB Carr, K Collins,  
| P Cullinan, C Elston, S Harrison, P Norman,  
| SJ MacNeill |

| P221 | Evaluation of exacerbation frequency and re-hospitalization, and risk for subsequent exacerbations in asthma patients in a UK primary care setting  
| RY Suruki, JB Daugherty, N Boudiaf,  
| FC Albers |

| P222 | Rates of hospitalisation after diagnosis of lung cancer: a linked audit and Hospital Episode Statistics study  
| A Khakwani, RB Hubbard, LJ Tata |

| P223 | Validity and interpretation of spirometry for patients in primary care  
| KJ Rothnie, H Mullerova, H Goss, J Chandan,  
| JK Quint |

| P224 | The association between degree of airflow limitation and degree of coronary artery atheroma is not attributable to smoking history  
| S Ruickbie, A Prasad, PW Jones, EH Baker |

| P225 | Identifying asthma patients in Wales using latent class analysis of routine data  
| MAI Sallakh, SE Rodgers, RA Lyons,  
| A Sheikh, GA Davies |

| P226 | Impaired respiratory health status in the UK HIV infected population despite the use of antiretroviral therapy  
| JP Brown, J McGowan, S Capocci, C Smith,  
| D Ivens, F Lampe, M Johnson, L Sathaia,  
| AK Rodger, M Lipman |

| P227 | Lung cancer diagnosis at emergency admission – how does Dorset compare?  
| C Bradley, E Harvey, N Ranaweera |

| 1.45pm – 3.45pm | Churchill, Ground Floor  
| SYMPOSIUM  
| PULMONARY EMBOLISM: FROM ACUTE TO CHRONIC  
| Chaired by: Dr Charlie Elliot (Sheffield) and  
| Dr John Wort (London) |

**Friday 4 December 2015**

| 1.45pm | Treatment of acute PE  
| Dr Trevor Baglin (Cambridge) |

| 2.15pm | A new approach to the pathobiology of chronic thromboembolic pulmonary hypertension  
| Dr Joanna Pepke-Zaba (Cambridge) |

| 2.45pm | Balloon pulmonary angioplasty versus pulmonary endarterectomy: a debate  
| Dr Irene Lang (Vienna) and  
| Mr David Jenkins (Cambridge) |

**Learning objectives:**

*a) to understand the latest European guidelines on the diagnosis and management of acute pulmonary embolism  
b) the latest information on the pathogenesis of chronic thromboembolic pulmonary hypertension (CTEPH)  
c) a debate on the relative merits of pulmonary endarterectomy (PEA) and balloon pulmonary angioplasty (BPA) for the treatment of CTEPH*

| 2.00pm – 3.00pm | Westminster, 4th Floor  
| POSTER DISCUSSION: P228 – P235  
| Improving patient care in cystic fibrosis  
| Chaired by: Dr Caroline Elston (London) and  
| Dr Martin Walshaw (Liverpool) |

| P228 | Impact of social media on adult CF centres across the UK  
| G Fitch, C Etherington, P Whitaker,  
| D Peckham |

| P229 | Use of inhaled antibiotics in CF Burkholderia spp chronic infection  
| JE Marlow, K Delisle, S Ajab, M Ledson,  
| J Greenwood, M Walshaw |

| P230 | Investigating the role of chest physiotherapy in the collection of sputum samples from individuals with cystic fibrosis (CF)  
| R Dacie, R Howlin, M Carroll, G Connett |

| P231 | A prospective cohort study of integrated palliative care of cystic fibrosis (CF)  
| SJ Bourke, R Mackley, Z Booth, S Doe,  
| A Anderson, S Rice, AD Gascoigne,  
| R Quibell |

| P232 | Too sweet for too long?  
| S Ali, R Khetan, P Sachdev, J Bhatt |
Friday 4 December 2015

P233  Cough swabs should not be used to exclude non-tuberculous mycobacterial (NTM) infection in adults with cystic fibrosis
C Brown, J Choyce, N Rodgers, R Rashid, JL Whitehouse, EG Smith, EF Nash

P234  Prevalence of non-pulmonary complications following lung transplantation in adult patients with cystic fibrosis (CF)
S Kumar, C Etherington, P Whitaker, D Peckham

P235  Temoctilin for Burkholderia infection in cystic fibrosis – adding to treatment options?
S Ajab, J Marlow, K Delisle, M Walshaw, M Ledson

2.00pm – 3.00pm
Rutherford, 4th Floor
POSTER DISCUSSION: P236 – P243

Clinical studies in cough
Chaired by: Dr Surinder Birring (London) and Dr Robert Buttery (Cambridge)

P236  Psychological profile of individuals presenting with chronic cough
K Hulme, S Dogan, V Deary, SM Parker

P237  Cough frequency in acute stroke
ST Kulnik, SS Birring, GF Rafferty, J Moxham, L Kalra

P238  A randomised, double-blind (sponsor-unblind), placebo controlled, cross-over study to investigate the efficacy, effect on cough reflex sensitivity, safety, tolerability and pharmacokinetics of inhaled GSK2339345 in patients with chronic idiopathic cough using an aqueous droplet inhaler

P239  Low prevalence of extra-thoracic airway hyper-responsiveness in UK patients with chronic refractory cough
A Menon, J Hull, KF Chung, O Usmani, S Ward

P240  Validation of the Leicester cough questionnaire in pulmonary tuberculosis
RD Turner, GH Bothamley, SS Birring

P241  The feasibility and validity of objective cough monitoring in children using an adult cough detection system
D Deblej Elghamoudi, H Sumner, K McGuiness, J Smith, CS Murray

P242  The order effect of experimental oesophageal acidification on cough reflex sensitivity in chronic cough patients and healthy volunteers
D Valdramidou, H Sumner, E Hilton, S Whiteside, J A Smith

P243  Assessing the effect of pH on citric acid cough challenges in chronic cough patients and healthy volunteers
ZR Rai, HF Fowles, JH Howard, AM Morice

2.00pm – 3.00pm
Albert, 2nd Floor
POSTER DISCUSSION: P244 – P250

Asthma quality improvement
Chaired by: Professor Stephen Scott (Chester) and Dr John White (York)

P244  The impact of “seven day working” on respiratory inpatient activity at St Helens and Knowsley NHS trust: “The slow drift model”
S Twite, P Stockton, V Sreeguru Lakshman, P Malhotra, S Alapati, S Koduri, J Naveed, J Howard

P245  “… No cleaning, no stairs, no sex… everything just stops”: understanding living with severe asthma to inform effective self-management
LD Apps, S Hewitt, R Green, P Bradding, A Murphy, N Martin, SJ Singh, SJ Singh, N Hudson, R Evans

P246  Should we telephone missed asthma appointments? A follow-up evaluation of four years of practice
Y Narang, B McDonough, M Ahmad, S Mault, C Dillon, H Burhan, NER Beveridge

P247  The prevalence of asthma and level of treatment in current or former heroin smokers
BH Vlies, N Lewis-Burke, L Davies, PP Walker
SCIENTIFIC PROGRAMME

Friday 4 December 2015

M31  Introduction of EBUS into a respiratory department – a reflection on experience required
     AL Chapman, M Cornere

M32  Design and development of a new pMDI training aid
     MJ Sanders, R Bruin, C Tran

2.00pm – 3.00pm
Cambridge, 5th Floor
M25 – M32
MODERATED POSTER DISCUSSION:
Education and training: from simulation to social media
Chair by: Dr Sega Pathmanathan (Hull) and Dr Georgia Tunnicliffe (Frimley)

M25  Oxygen: too much of a good thing? Can simulation improve education?
     JL Parkin, E Lloyd

M26  Tweeting is teaching – #RespEd: free, open-access Twitter educational resource
     for trainees and specialists in respiratory medicine
     RW Lee, LJ Smith, T Hillman

M27  Wheezes, coughs and splutters: how do paediatric trainees manage them?
     M Ramphul, LJ Thanikkel, R Ross Russell

M28  Respiratory clinicians’ experiences of end-of-life care in idiopathic pulmonary fibrosis
     B Turnpenny, K Shepherd, Z Borrill

M29  Trying to cause less pain for our patients!
     Using local anaesthesia for arterial blood gas sampling
     N Maningo, S Chaudhry, A Parwaiz, B Suwal, RA Evans, RH Green, I Valero-Sanchez

M30  Respiratory skills course for post-graduate medical trainees; inspiring future respiratory trainees
     R Young, T McLellan, C Walters

3.10pm – 4.50pm
Windsor, 5th Floor
POSTER DISCUSSION: P251 – P264
Improving outcomes in TB
Chair by: Dr Marc Lipman (London) and Dr Michael Loebinger (London)

P251  Tuberculosis in older versus younger adult patients: a retrospective comparison of patient characteristics and treatment outcomes at a major UK referral centre
     A Abbara, KG Buell, JAL Sullivan, SM Collin, OM Kon, T Hansel, L John, RN Davidson

P252  A retrospective evaluation of the diagnostic utility of adenosine deaminase in pleural tuberculosis in a low-prevalence area
     L Marples, P Sivakumar, R Breen, L Ahmed

P253  Isoniazid and multi-drug resistant Mycobacterium tuberculosis: the East London experience
     H Liddicoat, S Mohd-Afzal, J Potter, V White, N Jayasekera, M Darmalingam, H Kunst

P254  Utilizing community empowerment and biometrics to improve tuberculosis treatment outcomes in Delhi’s slum population: the Op ASHA model
     DP Pan, EL Lee, LL Lock, RB Batra, IA Abubakar, SB Batra, ML Lipman

P255  Utility of a screening protocol incorporating an interferon-gamma release assay (IGRA) on detection and decision to treat latent tuberculosis infection (LTBI) prior to anti-TNF therapy
     E Zatyka, A Nundoll, RAM Breen, N Price

P256  Clinical sequelae of tuberculosis in children attending a single UK centre: an 11 year retrospective study
     S Bhownik, S Nicol, C Bell, C Murray, F Child
Friday 4 December 2015

P257 Modern day scrofulous swellings: breast tuberculosis in East London
BJ Butler, A Khanam, VLC White, N Jayasekera, JL Potter, H Kunst

P258 Multi-drug resistant tuberculosis monitoring guidance: are we following the national guidelines?
S Parmar, R Singal, H Khachi

P259 Central nervous system tuberculosis: diagnostic difficulties
L Macpherson, R Cuthbert, J Potter, V White, N Jayasera, H Kunst

P260 Potential impact of the 2015 NICE Consultation Guideline for Tuberculosis on the number of children assessed and treated for TB infection and disease in the UK
L Turnbull, C Bell, F Child

P261 Chemoprophylaxis for LTBI following mass screening in the workplace: unexpected outcomes in the over 35s
Y Abunga, M Day, J Williams, JP Mamo, SO Brij

P262 Skeletal tuberculosis – a retrospective review at two inner city UK hospitals
GC Hagan, J Piper, H Bagnall, I Ahmed, N Nathani

P263 Does age influence the diagnostic pathway in patients with TB lymphadenitis?
K Dave, A Saigal, F Ullah, F Miah

P264 A multi-centre review of the management of pulmonary non-tuberculous mycobacterial (NTM) infection in HIV-negative subjects
TM Rawson, A Abbara, K Kranzer, A Ritchie, J Milburn, T Brown, D Adeboyeju, J Buckley, RN Davidson, M Berry, OM Kon, L John

3.30pm – 4.30pm
Moore, 4th Floor
POSTER DISCUSSION: P274 – P281
Treatment options in cystic fibrosis
Chaired by: Dr Daniel Peckham (Leeds) and Dr Rebecca Thomas (York)

P274 Moving from rescue to prevention: real world evidence of reduction in IV antibiotic requirement following improvement in adherence to maintenance nebulised treatment in an adult cystic fibrosis centre
ZH Hoo, R Curley, C Carolan, C Hinchliffe, M Hutchings, MJ Campbell, MJ Wildman

P275 Prevalence and strain typing results of gram-negative emerging bacterial pathogens in patients attending a large UK adult CF centre
HD Green, R Bright-Thomas, D Kenna, AM Jones

P276 The prevalence of ticarcillin hyper-susceptible Pseudomonas aeruginosa isolates from non cystic fibrosis bronchiectasis patients compared to patients with cystic fibrosis and controls
IT Hettiarchchi, T O’Sullivan, M Wootton, J Duckers, R Dhillon

P277 Physiological response to exercise in an adult cystic fibrosis population: investigating the relationship between HRR at anaerobic threshold and FEV1% predicted
G Comber

P278 Is there a role for telemedicine in cystic fibrosis? A systematic review
R Curley, ZH Hoo, R Archer, MJ Wildman

P279 The female disadvantage in UK CF Registry data 2008-2013
S Hippolyte, R Keogh, S MacNeill, N Simmonds, U Griesenbach

P280 A single centre experience of spontaneous clearance of Mycobacterium abscessus in cystic fibrosis patients
HD Green, PJ Barry, R Bright-Thomas, AM Brennan, AK Webb, R Lord, A Horsley, AM Jones

P281 The effectiveness of acupuncture in managing symptoms in CF adults
EF Nash, H Bradley, E Chapman, R Rashid, JL Whitehouse
POSTER DISCUSSION: P265 – P273

Diagnosis and management of pulmonary arterial hypertension
Chairied by: Professor Nicholas Morrell (Cambridge) and Dr Claire Shovlin (London)

P265 The clinical utility of biomarkers associated with inflammation and endothelial dysfunction in CTEPH
C Hadinnapola, M Southwood, J Hernandez-Sanchez, K Sheares, S Preston, D Jenkins, N Morrell, M Toshner, J Pepke-Zaba

P266 Do endothelin-1 and inflammation play a role in airway obstruction in pulmonary arterial hypertension associated with congenital heart disease?
AT Low, SJ George, AB Millar, RMR Tulloh

P267 The effects of Apelin on serum NT-proBNP levels in pulmonary hypertension patients versus controls
GS Reid, KS Wilson, K Suveizdyte, L Brash, AJ Peacock, DJ Welsh

P268 The role of growth and differentiation factor 15 in smooth muscle cell proliferation in pulmonary hypertension
B Garfield, D Shao, A Crosby, P Yang, N Morrell, M Polkey, P Kemp, SJ Wort

P269 Perioperative outcomes in patients with pulmonary hypertension undergoing non-cardiac non-obstetric surgery in a designated UK pulmonary hypertension centre

P270 Identifying the optimal D-dimer cut off value for ruling out PEs in an ambulatory care setting
FA Khan, K Ryanna, E Bailie, Y Vali

P271 Using age-adjusted D-dimers for ruling out PEs in an ambulatory care setting
FA Khan, K Ryanna, E Bailie, Y Vali

POSTER DISCUSSION: P282 – P291

Investigating lung disease: novel techniques and old interventions
Chairied by: Dr Georgina Hands (Barnstaple) and Dr Rebecca Mason (Bath)

P282 The design and validation of a novel semiautomatic lung navigation platform
KA Khan, P Nardelli, J Alex, C O’Shea, P Cantillon-Murphy, MP Kennedy

P283 Hyperpolarised gas MRI – a pathway to clinical diagnostic imaging

P284 V/Q scanning using oxygen-enhanced magnetic resonance imaging
JL Ulloa, AR Morgan, T Lacey, C Roberts, GJM Parker

P285 Helium magnetic resonance imaging identifies regional ventilation, perfusion and microstructure abnormalities in a case of “horse-shoe” lung
SZ Zaidi, JM Wild, AS Swift, HM Marshall, NW Weateherley, FCH Horn, RMN Niven, DR Ryan
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**P286** Correlations of functional multi-nuclear MR imaging indices with pulmonary function tests in the assessment of idiopathic pulmonary fibrosis
ND Weatherley, NJ Stewart, H Marshall, G Collier, K Hart, F Horn, G Norquay, MK Whyte, S Bianchi, JM Wild

**P287** Offline fractional exhaled nitric oxide and breath frequency
C Howard, V MacBean, A Lunt, A Greenough

**P288** Prevalence of non-pulmonary embolism diagnoses on CT pulmonary angiography. One year experience in a district general hospital
S Barnes, C Ingham, A Pryce, R Russell

**P289** Isolated mediastinal and/or hilar lymphadenopathy: what can EBUS-TBNA add?
V Connor, V Tippet, T Kennedy, B Challoner

**P290** Do lung function indices correlate with risk of pneumothorax following CT-guided biopsy?
P Griffiths, J Heaton, S Claxton, D Hughes

**P291** Relationship of in vitro particle size to in vivo lung deposition and exhaled fraction
G Poli, B Lipworth

3.00pm – 4.45pm
COFFEE/TEA will be served in the Britten, 3rd floor
SPEAKERS’ BIOGRAPHICAL DETAILS

Dr Shawn Aaron is a Professor in the Department of Medicine, the University of Ottawa and a Senior Scientist at the Ottawa Hospital Research Institute. Dr Aaron’s research focus is in clinical and epidemiologic studies, with a specific interest in the critical assessment of interventions designed to improve diagnosis and treatment of asthma, COPD and cystic fibrosis.

Professor Ian Adcock has a long term interest in the regulation of inflammation in COPD and severe asthma by oxidative stress and epigenetic mechanisms. He has published over 300 papers in these areas. He is a PI in the MRC-ABPI COPDMAP project, the IMI U-BIOPRED project and the MRC-Asthma UK mechanisms of asthma centre.

Professor Alvar Agustí, MD, PhD, FRCP, FERS is currently Director of the Thorax Institute at the Hospital Clinic in Barcelona (www.hospitalclinic.org) and Professor of Medicine at the University of Barcelona. His main research interest includes translational research in COPD. He has published more than 400 papers in peer-reviewed journals and has over 40 contributions to books. He is an Honorary Fellow of the Royal College of Physicians of Edinburgh (UK) and a Fellow of the ERS (FERS).

Professor Eric Alton is Professor of Gene Therapy and Respiratory Medicine at Imperial College, London. He co-ordinates 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.

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.

Dr Mona Bafadhel graduated from the University of Birmingham and undertook her junior medical training firstly in Birmingham and then at the Royal Brompton Hospital, London. Her continual interests in respiratory medicine led her to undergo her specialist training in the Oxford deanery. A period of research training was spent in Leicester where she gained a PhD studying chronic obstructive pulmonary disease and identifying sub-groups which respond to therapy differently. In Oxford her research and clinical interests include using diagnostic applications and phenotyping to improve the management of patients with airways disease, in particular chronic obstructive pulmonary disease.

Dr Trevor Baglin is Consultant Haematologist to Cambridge University Hospitals. His main expertise is in thrombosis and haemostasis and in particular venous thrombosis and antithrombotic therapy. He has been Chair of the Haemostasis and Thrombosis Task Force for the British Society for Haematology and the Anticoagulant Committee of the International Society for Thrombosis and Haemostasis.

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 130 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.

Dr Ian Balfour-Lynn is a Consultant, Co-Director of Children’s Services and Director of Paediatric Cystic Fibrosis at the Royal Brompton Hospital, London. He specialises in all aspects of paediatric respiratory medicine including both tertiary and secondary care. He is Chair of the Cystic Fibrosis CRG, and Chair of the Cystic Fibrosis Group (Paediatric assembly) of the European Respiratory Society.

Dr Chris Barber is a Respiratory Consultant with a clinical and research interest in occupational lung disease. His work is split between clinical sessions in Sheffield and research at the Centre for Workplace Health in Buxton. He is a member of the Group of Occupational Respiratory Disease Specialists
**SPEAKERS’ BIOGRAPHICAL DETAILS**

(GORDS), and the BTS Occupational and Environmental Lung Disease Specialist Advisory Group. Dr Barber has previously published research in the area of UK asbestos usage and IPF.

**Professor Maria Belvisi** is Head of the Respiratory Pharmacology Group at the National Heart and Lung Institute, Imperial College, London. She was awarded a BSc in pharmacology by King’s College London, and a PhD by the National Heart and Lung Institute in 1990. Professor Belvisi is an internationally recognized expert in the respiratory field with both academic and industrial experience. Her research is focused on the cellular and molecular mechanisms of asthma, COPD and chronic cough, and developing therapies for these diseases. Her research is translational and takes data generated in vitro through to in vivo models and clinical studies with collaborators. Together with Professor Peter Barnes at NHLI she was involved in generating key data sets during the development of tiotropium bromide (Spiriva) a long acting muscarinic receptor antagonist used as a bronchodilator for the treatment of chronic obstructive pulmonary disease. Professor Belvisi also worked for a period at Rhone-Poulenc Rorer/Aventis Pharma, leading a team in the company’s respiratory research therapeutic area. During this time she was involved in the development of Ciclesonide (Alvesco) an inhaled corticosteroid for asthma with an improved therapeutic ratio. Professor Belvisi has an extensive publication record in peer review journals and serves on the editorial board of several publications including the American J Respiratory and Critical Care Medicine. She has also received several prizes and awards, including the Women in Inflammation Science (2009), awarded by the World Inflammation Society, and the AstraZeneca Women in Pharmacology Prize (2011). She was elected a fellow of the British Pharmacological Society in 2005 and European Respiratory Society in 2014. In 2010 she formed, together with Dr Mark Birrell, IR Pharma a preclinical respiratory drug discovery organisation which is part of the Imperial Innovations portfolio of companies http://www.irpharma.co.uk/

**Dr Mark Birrell** leads the Respiratory Pharmacology Group with Professor Maria Belvisi at the National Heart and Lung Institute, Imperial College, London. The group focuses on studying the pathophysiology of respiratory diseases (eg asthma, COPD) and the interaction between sensory nerves and inflammation in the control of respiratory symptoms. He is an internationally recognised expert in the respiratory field and has a substantial publication record.

**Dr Charlotte Bolton** is Clinical Associate Professor in Respiratory Medicine at the University of Nottingham. Alongside her clinical COPD service, the focus of her research has been on the extrapulmonary manifestations of chronic respiratory disease – predominantly COPD and also pulmonary rehabilitation. In addition, she is interested in the long term respiratory sequelae of being born preterm. She is one of the clinical leads of the East Midlands Respiratory Programme.

**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.

**Dr Guy Brusselle** MD, PhD, studied Medicine at the University of Ghent and qualified as a Specialist in Internal Medicine and Respiratory Diseases. He completed his PhD thesis (promotor Prof Dr R Pauwels) on “Investigation into the functional role of cytokines in allergen-induced airway changes.” Since 2002 he has been a Pulmonary Physician at Ghent University Hospital; since 2005, Head of the Laboratory for Translational Research of Obstructive Pulmonary Diseases, Ghent University; and since 2008, Professor of Medicine at Ghent University. In 1996, Dr Brusselle was awarded the Boehringer Ingelheim prize for Pneumology, granted by the Belgian Society of Pneumology; in 2007, the Astra Zeneca Foundation Asthma and COPD Award, granted by the Belgian Fund for Scientific Research; and in 2010, the ERS COPD Research Award, granted by the European Respiratory Society. He has published more than 170 A1 papers, and is Editor of The Lancet Respiratory Medicine and Editor of American Journal of Respiratory and Critical Care Medicine.

**Dr Victòria Cardona** MD, PhD, specialised in Allergy (1994-7) at the Hospital Universitari Vall d’Hebron, Universitat Autònoma Barcelona, where she is currently responsible for the Allergy Section, Department of Internal Medicine. Her main research interests are: anaphylaxis, mediators, co-factors, immunotherapy and patient reported outcomes, having published more than 50 papers (Hirsh index 17). She has been EAACI Vice-president Communications/ Membership (2009-2013), and is Managing Editor of Clinical and Translational Allergy.
SPEAKERS’ BIOGRAPHICAL DETAILS

Dr James Chalmers is a Wellcome Trust Postdoctoral Fellow, 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, 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 Edwin R Chilvers PhD, FMedSci, is Professor of Respiratory Medicine at the University of Cambridge and Honorary Consultant Physician at Addenbrooke’s Hospital, CUHNHSFT and Papworth Hospital NHSFT. His research interests include understanding the molecular basis of neutrophil priming, activation and apoptosis, in particular; the role of the phosphoinositide 3-kinases and the use of radiolabelled autologous granulocytes to define neutrophil kinetics in vivo.

Dr Tristan Clark is an Associate Professor and Consultant in Infectious Diseases at the University of Southampton. His research interests include the clinical evaluation of pandemic influenza vaccines, respiratory virus antiviral agents and point-of-care diagnostics for infection in acute respiratory illness.

Dr Amelia Clive is a Senior Respiratory Registrar in the Severn Deanery, having qualified from University College Medical School in 2004. She has recently completed a PhD at the University of Bristol in malignant pleural disease, during which time she co-ordinated the SMART Trial, a multi-centre RCT evaluating the role of prophylactic radiotherapy in mesothelioma. She maintains a clinical and research interest in thoracic ultrasound and the management of pleural disease.

Professor Henricus J de Koning is Professor of Public Health and Screening Evaluation in the Department of Public Health of the Erasmus Medical Center in Rotterdam. Born in the Netherlands, Professor Henricus (Harry) J de Koning worked as a Researcher and an Assistant Professor in the Department of Public Health of the Erasmus University in Rotterdam from 1987 to 1999. He became an Associate Professor in 1999 and in 2008 he was appointed Professor of Public Health and Screening Evaluation in the same department in Rotterdam. He was also Senior Associate, Department of Health Policy and Management at the Johns Hopkins Bloomberg School of Public Health from 2011 to 2012. Since 2011 he has been a Member of the Medical Advisory Board of the Royal Netherlands Academy of Arts and Sciences (KNAW). His major scientific contributions are in the areas of:
- designing, running and evaluating large-scale multidisciplinary population-based randomized controlled screening trials to establish the efficacy of screening;
- evaluating active international screening programmes and tests to establish effectiveness;
- guiding public health policies using predictions of favorable and unfavorable effects and the cost of screening, based on micro-simulation modelling of the natural history of disease, and cost-effectiveness and cost-utility analyses.

See also: http://www.erasmusmc.nl/mgz/organisation/people/h-de-koning/http://survey.erasmusmc.nl/pwp/hdekoning

Dr Anthony De Soyza is an academic clinician with interests in COPD and bronchiectasis and works at the Freeman Hospital Newcastle. He runs a clinical research programme in these, particularly on host-pathogen interaction and the systemic consequences of pulmonary inflammation aspects. He is lead applicant for the MRC funded Bronch-UK Network and he is a member of the EU EMBARC Network in Bronchiectasis. He is Vice-Chair of the EU Network in Cystic Fibrosis Pathogens COST BM1003. He is also medical lead for the Sir William Leech Clinical Trials Centre based at the Freeman Hospital and is actively involved in clinical trials development in the UK. He was previously Deputy Chair of the National Comprehensive Local Research Network and is Associate Director for Industry Studies in his LRN area. He is incredibly well supported by an enthusiastic patient cohort and colleagues for which he is very grateful.

Dr Martin Dedicoat is an Infectious Disease Consultant at the Heart of England Foundation Trust (HEFT), Birmingham. He is the Clinical Lead for Tuberculosis at HEFT and Clinical Lead for Birmingham and Solihull. Dr Dedicoat’s main interests are in the epidemiology of tuberculosis in urban areas.

Professor Louise Donnelly is a Professor of Respiratory Cell Biology, in the Section of Airway Disease at the National Heart and Lung Institute,
SPEAKERS’ BIOGRAPHICAL DETAILS

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.

Dr Andrew Durham is a Research Fellow in the Airway Disease Section of the National Heart and Lung Institute (NHLI) at Imperial College London. His research is focused on identifying the molecular and epigenetic mechanisms which drive remodelling in chronic lung diseases including asthma and chronic obstructive pulmonary disease (COPD).

Professor Jim Egan MB, MD, FRCP, FRCPed, FRCPath, FJFICMI is a Consultant Respiratory Physician, having graduated from University College Galway, Ireland and trained in pulmonary medicine at Wythenshawe Hospital Manchester. He is currently Medical Director, Irish National Lung Transplant Programme, Mater Misericordiae University Hospital, Dublin and Clinical Director, Heart Lung Unit, Mater Misericordiae University Hospital. Professor Egan is Director of Organ Donation and Transplant Ireland and chair of the National Transplant Advisory Group. He is a former member of Irish Business and Employers Confederation (IBEC), and the Medical Technology Clinical Trials Task Force Committee 2007. He is a spokesman for the Irish Medical Devices Association Clinical Trials Task Force June 2006. Professor Egan is co-chair of the joint American and European Thoracic Societies committee for the development of guidelines for the management of idiopathic pulmonary fibrosis May 2008-2010, and an invited member of the joint American and European Thoracic Societies committee for the classification of idiopathic pneumonias 2009-2010.

Dr Christina Faull is a clinician, educator and researcher. Her two books (Handbook of Palliative Care and Palliative Care) were both awarded the BMA medical book of the year. Her recent research has explored the experiences of professionals and family in withdrawing ventilation at the request of a patient with MND.

Professor Panagis Filippakopoulos, PhD is Associate Professor in Structural Biology at NDM, Oxford and Principal Investigator, SGC/LICR, Wellcome Trust Career Development Fellow. Professor Filippakopoulos’ research focuses on structural comparisons of protein families, the discovery of shared and distinct mechanisms determining substrate recognition and regulation, as well as the design of inhibitors that modulate epigenetic signaling, aiming to target cancer.

Professor Paul Fine is Professor of Communicable Disease Epidemiology at the London School of Hygiene and Tropical Medicine. He trained originally in veterinary medicine in the USA before joining the LSHTM in 1976. He directed a large epidemiological research programme (the “Karonga Prevention Study”) in Malawi from 1978-2006, and has a longstanding interest in vaccines and vaccine schedules.

Professor Andrew Fisher is Professor of Respiratory Transplant Medicine, Newcastle University. He graduated from Nottingham University in 1993, received research training as an MRC training fellow and graduated PhD in 2001 from Newcastle University. He was subsequently awarded a GlaxoSmithKline Senior Clinical Fellowship in 2004 and was appointed Professor of Respiratory Transplant Medicine in 2009. He works in the Institute of Cellular Medicine at Newcastle University and is an Honorary Consultant Respiratory and Transplant Physician at Freeman Hospital, Newcastle Upon Tyne. He is the Academic Director of the Institute of Transplantation in Newcastle and Associate Dean for clinical academic training in the Faculty of Medical Sciences. Professor Fisher’s research interests focus on mechanisms of acute and chronic injury to the transplanted lung and clinical studies on increasing the supply of suitable donor organs for lung transplantation.

He is a past Chair of the British Thoracic Society Science and Research Committee 2009-2012, currently sits on the Board of Directors of the International Society of Heart and Lung Transplantation (ISHLT) and is Programme Chair for the 2016 ISHLT Annual Scientific Meeting.

Professor Andres Floto is Professor of Respiratory Biology and a Wellcome Trust Senior Investigator at the University of Cambridge, and Research Director of the Cambridge Centre for Lung Infection at Papworth Hospital Cambridge. His research is focused on understanding the molecular and genetic determinants regulating host immunity during bacterial infections.
**SPEAKERS’ BIOGRAPHICAL DETAILS**

**Dr Frits Franssen** is a Respiratory Physician and the medical coordinator for chronic respiratory diseases at CIRO, a centre of expertise for chronic organ failure in Horn, the Netherlands. He is also a Respiratory Consultant at the Department of Respiratory Medicine at Maastricht University Medical Centre in Maastricht. His primary research interest is COPD as a systemic disease with a particular focus on co-morbidities and extra-pulmonary features of the disease.

**Professor Jon S Friedland FRCP, FMedSci** is Hammersmith Campus Director and Head of Infectious Diseases and Immunity at Imperial College London, and Honorary Consultant in Infectious Diseases at Imperial College Healthcare NHS Trust. His main research interest is the role of innate immunity and in particular, matrix metalloproteinases in the host response to tuberculosis.

**Dr Nicholas Hart** MB BS BSc PhD MRCP FFICM is the Clinical and Academic Director of the Lane Fox Respiratory Unit at St Thomas’ Hospital, Honorary Reader in Respiratory and Critical Care Medicine at Kings College London, Directorate Research and Development Lead at Guy’s and St Thomas’ NHS Foundation Trust and Joint Editor-in-Chief for Thorax. The Lane Fox Respiratory Unit is a national weaning, rehabilitation and complex home ventilation unit specialising in provision of long-term ventilatory support. Since 2007, he has established the Lane Fox Clinical Respiratory Physiology Research Centre and developed a programme of translational physiological research focused on (1) mechanism of skeletal muscle wasting in non-neuromuscular conditions (2) rehabilitation strategies to improve outcome in patients with chronic respiratory disease and post critical illness (3) advanced physiological monitoring in acute illness to prevent inpatient deterioration and readmission and (4) clinical trials to improve outcome in chronic respiratory failure.

**Dr Nicholas Hopkinson** MA PhD FRCP is a Reader in Respiratory Medicine and Honorary Consultant Physician at The National Heart and Lung Institute of Imperial College and the Royal Brompton Hospital where he runs the Advanced COPD service. His research focuses on addressing exercise and activity limitation in COPD in areas including pulmonary physiology and lung volume reduction, skeletal muscle impairment and pulmonary rehabilitation. He chairs the British Thoracic Society COPD Specialist Advisory Group and is also active in tobacco control advocacy. Follow @COPDdoc

**Dr Rachel Hoyles** leads the Oxford ILD Service. She has a clinical and academic interest in connective tissue disease-associated ILD, having completed a PhD investigating the role of alveolar epithelial cell injury in scleroderma-associated lung fibrosis, both in clinical cohort and in animal models with genetic perturbations of the TGFβ axis. She has published one of few multi-centre RCTs in scleroderma-associated pulmonary fibrosis, and is local PI for several multinational IPF pharmaceutical trials, and a multicentre vasculitis study. She has active research interests in SSc-ILD biomarkers, myositis-ILD immunology, acute exacerbations of ILD and imaging modalities in ILD.

**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 Chair of the BTS Winter Meeting 2013-2015.

**Mr David Jenkins** is a Consultant Cardiothoracic Surgeon at Papworth Hospital, Cambridge, UK. Specialist experience includes surgical treatment of pulmonary hypertension, intra-thoracic transplantation, and mechanical circulatory support including extracorporeal membrane oxygenation. In 2004, he became lead surgeon for the UK National Pulmonary Endarterectomy (PEA) Program, and is an executive board member of the International CTEPH Association.

**Professor Simon Johnson** is Professor of Respiratory Medicine and Director of the National Centre for Lymphangioleiomyomatosis (LAM) at the University of Nottingham. His research group work on matrix metalloproteinase mediated remodelling in
chronic respiratory diseases and a bench to bedside programme of LAM research.

**Professor Onn Min Kon** is a Respiratory Physician at St Mary’s Hospital and Head of Service for TB at Imperial College London Healthcare NHS Trust. He is also an Adjunct Professor and Reader at the National Heart and Lung Institute, Imperial College London. He is a member of the UK National MDRTB advisory service and Chair of the British Thoracic Society Specialist Advisory Committee on TB. He is a member of the National TB Oversight Group and the Joint Tuberculosis Committee. His research interests include the clinical and immune diagnosis of tuberculosis and the delivery of care and management of the disease. Professor Kon also organises the London Advanced TB course.

**Dr Samantha Kon** is a Clinical Research Fellow at the Royal Brompton and Harefield NHS Foundation Trust and Chest Physician at Hillingdon Hospital. Her main research interests are evaluating functional outcome measures and health related quality of life in COPD.

**Dr Paul Lavender** completed his PhD at St Bartholomew’s Hospital Medical College. This was followed by Post-Doctoral studies under Jacques Drouin at the IRCM in Montreal and Tony Kouzarides at the Gurdon Institute in Cambridge. He is a Senior Lecturer at King’s College London and his major areas of study are epigenetics and regulation of gene expression.

**Professor Gary Lee** is a Professor at 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.

**Dr Nicola S Lewis** BSc BVetMed PhD MRCVS is a Senior Research Associate at the Centre for Pathogen Evolution and WHO Collaborating Centre for Modelling, Evolution and Control of Emerging infectious Diseases, Department of Zoology, University of Cambridge. Dr Lewis’s research focuses on how pathogens evolve, particularly in animal hosts. Also a qualified vet, she has strong links with Central Asia studying emerging avian viruses from wildlife and leads a new global initiative funded by the US NIAID to establish the risk of emergent swine influenza A viruses to human health. She is a member of several expert panels of the World Organisation for Animal Health, including those involved in vaccine strain selection for non-human influenza viruses.

**Professor Mark Lindsay** is based within the Department of Pharmacy and Pharmacology at the University of Bath. His research has focused upon understanding the role of microRNAs and long non-coding RNAs in the regulation of the immune response and during the development of respiratory diseases including asthma, COPD and lung cancer.

**Dr Marc Lipman** is Senior Lecturer in Respiratory and HIV Medicine at the Royal Free London NHS Foundation Trust and University College London. He is a member of the NICE TB Clinical Guideline Development Group and the National TB Drug Resistance Clinical Advisory Service. His research focuses on tuberculosis, respiratory infection and HIV.

**Professor David Livermore** gained his BSc in 1978 and PhD in 1983. He worked at the London Hospital Medical College, then at Public Health England and its predecessor organisations, becoming Director of its Antibiotic Laboratory in 1998 and remaining until October 2011 when he became Professor of Medical Microbiology at the University of East Anglia. He has a long research and publication track record on the evolution and epidemiology of antibiotic resistance.

**Dr Toby Maher** is an NIHR Clinician Scientist and Consultant Physician at the Royal Brompton Hospital, London. He is an Honorary Senior Lecturer at the National Heart and Lung Institute, Imperial College, London where he leads the Fibrosis Research Group. 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. Dr Maher has authored over 100 papers and chapters on idiopathic pulmonary fibrosis, sarcoidosis and other ILDs.

**Professor Nick Maskell** is Professor of Respiratory Medicine, University of Bristol and Honorary Consultant, North Bristol NHS Trust. He undertook his DM thesis on pleural diseases in Oxford prior to...
SPEAKERS’ BIOGRAPHICAL DETAILS

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 UoB. He is the PI for a number of mesothelioma and pleural RCT research studies. He chaired the last BTS pleural disease guideline group, and is co-chair of the 2015 BTS mesothelioma guideline group.

Dr Christopher McDermott is a Reader in Neurology and Consultant Neurologist at the University of Sheffield. He studied for his medical degree at the University in Leeds, graduating in 1994. He then continued in general medical and specialist neurology training in Leeds before taking up a clinical research training fellowship at the University of Newcastle upon Tyne. He moved to the University of Sheffield with Professor Dame Pamela Shaw in 2000 to undertake his Wellcome Trust Research Training PhD Fellowship and to complete his Specialist Training in Neurology to become a Consultant Neurologist in 2006. Dr McDermott is now a Reader in Neurology at SITraN and a Consultant Neurologist at the Sheffield Teaching Hospitals Foundation NHS Trust, regularly undertaking specialist clinics in Sheffield and Barnsley.

The main drive of Dr McDermott’s research programme is developing the evidence base for delivering supportive and symptomatic care for patients living with motor neuron disease. He is also interested in studying mechanisms of neurodegeneration, in order to develop treatments for patients with motor neuron disease and hereditary spastic paraplegia.

He is the course leader of the Clinical Neurology MSc at the University of Sheffield and takes an active role in teaching and mentoring undergraduate and postgraduate students. He has received funding for his research from the MND Association, NIHR, Spastic Paraplegia Foundation amongst others.

Professor Helen McShane has extensive experience in TB immunology and vaccinology. She is currently Professor of Vaccinology at Oxford University, Wellcome Senior Clinical Research Fellow, Honorary Consultant Physician in HIV Medicine and an Academic Foundation Programme Lead. She also chairs the Tuberculosis Vaccine Initiative Advisory Committee. Helen has led the TB vaccine research group at Oxford University for 14 years and notably headed the development of MVA85A; one of the most clinically advanced new TB vaccine candidates and the first to enter human efficacy testing.

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 the current President of the BTS.

Professor Mike Morgan is the National Clinical Director for Respiratory Services in England. He is a Consultant Respiratory Physician at the Department of Respiratory Medicine, Allergy and Thoracic Surgery at the University Hospitals of Leicester NHS Trust at Glenfield Hospital and Honorary Professor at the University of Leicester. He is also a Vice President of the British Lung Foundation, the editor of Chronic Respiratory Disease and previously, Chairman of the Asthma UK research committee. He has recently demitted as Chairman of the Executive of the British Thoracic Society and is now President-Elect of the Society.

Professor Alyn H Morice is Professor 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 he was appointed to the Foundation Chair in Respiratory Medicine in Hull University, now part of the 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.
SPEAKERS’ BIOGRAPHICAL DETAILS

Dr Neal Navani MA MSc PhD FRCP qualified in Medicine from Cambridge and UCL in 2000 with distinction and several University prizes. He trained in Respiratory Medicine at the Brompton and Hammersmith Hospitals before winning a Medical Research Council Fellowship in 2008 and completing his PhD at UCL in 2011. He has also completed an MSc in Clinical Trials at the London School of Hygiene and Tropical Medicine. Dr Navani was appointed as a Consultant in Thoracic Medicine at University College London Hospital in 2011.

Dr Navani is clinical lead for lung cancer and bronchoscopy services at UCLH. He is a member of the British Thoracic Society guideline development group for bronchoscopy and is on the interventional procedures specialist advisory group. He is a member of the National Cancer Research Institute lung cancer clinical studies group and chairs the Screening and Early Disease subgroup. Dr Navani holds an honorary contract with the MRC Clinical Trials Unit at UCL and has authored over 40 peer-reviewed publications. He is the co-author of a textbook on respiratory disorders and the lung cancer chapter in the Oxford Textbook of Medicine. Dr Navani also sits on the lung cancer board of London Cancer as research lead and is a peer reviewer for many journals including BMJ, ARCCM and Thorax. @LungConsultant

Dr Caroline A Owen, MD, PhD works in the Division of Pulmonary and Critical Care Medicine at Brigham and Women’s Hospital, Harvard Medical School. Her group is investigating the activities of matrix metalloproteinases (MMPs) and proteinases with a disintegrin and a metalloproteinase domain (ADAMs) in acute and chronic lung diseases. They study mice genetically deficient in MMPs and ADAMs in murine models of acute lung injury, pulmonary fibrosis, COPD, asthma, and pulmonary infections.

Dr Helen Parfrey is a Consultant Respiratory Physician at Papworth Hospital and clinical lead for the Cambridge Interstitial Lung Disease Service. She has clinical and translational research interests in the role of innate immunity in pulmonary fibrosis and the genetics of familial and idiopathic pulmonary fibrosis.

Dr Sanjay Popat is Consultant Thoracic Medical Oncologist at the Royal Marsden Hospital. He Chairs the British Thoracic Oncology Group (BTOG), and the Advanced Diseases Sub-group of the NCRI Lung Cancer Clinical Studies Group, and is co-director for Cancer in the London South NIHR Clinical Research Network. He is active in the EORTC Lung Group, the European Thoracic Oncology Platform (ETOP), and the International Thymic Malignancy Interest Group (ITMIG).

Dr Joanna Porter runs the Interstitial Lung Disease service at UCLH, is Medical Director of the UCL partners ILD Consortium and runs the Leukocyte Trafficking Laboratory at UCL. She has a clinical research interest in novel imaging techniques, biomarkers and therapies in ILD particularly in the context of drug-toxicity and autoimmune rheumatic disease.

Professor Kim Prisk is a Professor of Medicine and Radiology at the University of California, San Diego. He has managed pulmonary experiments on the Space Shuttle, and International Space Station, and currently develops quantitative functional MRI techniques to study gas exchange and its determinants in the human lung.

Dr Peter Reid is a Consultant Respiratory Physician in the Western General Hospital, Edinburgh with a clinical interest in occupational and environmental lung disease.

Dr Anna Rich is a Respiratory Consultant in Nottingham. She completed an MD in lung cancer epidemiology in 2010. Her thesis was based on validating the National Lung Cancer Audit database, and evaluating the inequality in lung cancer outcomes across England. She is currently co-chair of an ERS taskforce looking at data collection in thoracic oncology across Europe.

Professor Malcolm Richardson PhD, FRSB, FISSE, FRCPath is Director of the Mycology Reference Centre Manchester and Professor of Medical Mycology, University of Manchester. His research over 42 years has focused on the diagnosis of systemic fungal infections and the mycobiome of indoor environments. He has published extensively and has an h-index of 46. In May 2015 Professor Richardson took up the position of President of the International Society for Human and Animal Mycology.

Dr Robert Rintoul is a Consultant Respiratory Physician in Thoracic Oncology at Papworth Hospital, Cambridge and an Honorary Visiting Senior Fellow in the University of Cambridge. He undertook clinical training in Edinburgh and London and performed his PhD in cancer cell biology at the University of
Edinburgh. Currently he is lead clinician for cancer at Papworth Hospital and Director of the Papworth Hospital Clinical Trials Unit. Part-funded by the NIHR Cambridge Biomedical Research Centre, the Cambridge Cancer Centre and the Clinical Research Network Eastern, the focus of his work is around clinical trials and translational research in mesothelioma and the early detection of lung cancer. He is Principal Investigator for several clinical trials and Chief Investigator of MesobanK UK. He is the sub-specialty research lead for lung cancer for the East of England Strategic Clinical Network and a member of the BTS Science and Research Committee and NHS England Lung Cancer Clinical Reference Group.

Professor Douglas Robinson is Lead Consultant for Asthma at UCLH NHS Foundation Trust, and recently set up an adult severe asthma service at the Trust. He was previously Professor of Respiratory Medicine at Imperial College London. He has a research background in the immunology of asthma, in particular type 2 inflammation, and in clinical characterisation and assessment of severe asthma.

Dr Elizabeth Sapey qualified as a physician from the Royal London Medical School, UK. She gained her PhD studying neutrophil inflammation in age and 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.

Professor David Schwartz is a Professor of Medicine and Immunology, and is serving as the Robert Schrier Chair of the Department of Medicine at the University of Colorado. The Schwartz lab has provided new insights into the genetics, epigenetics, and genomics of interstitial lung disease, asthma, and innate immunity.

Professor Anita Simonds is a Consultant in Respiratory and Sleep Medicine at the Royal Brompton and Harefield NHS Foundation Trust. She has a clinical and research interest in sleep disordered breathing and ventilatory support, and manages 1800 adults and children on long term ventilation, and 7000 on CPAP. She is chief editor of European Respiratory Journal Open Research, and the new ERS Handbook of Non-Invasive Ventilation.

Professor Dave Singh is Professor of Respiratory Pharmacology at the University of Manchester in the UK. He graduated from Cambridge University and went on to train in medicine and clinical pharmacology in Manchester, which included working in industry on early phase clinical trials. Professor Singh’s research interests are in the pharmacotherapy of asthma and COPD, with studies spanning from basic pharmacology of anti-inflammatory drugs to clinical trials. He has acted as principal investigator on numerous clinical trials of novel therapies in asthma and COPD, and has over 130 publications in peer reviewed journals. He is a member of the GOLD Science Committee.

Professor Peter Sly is Director, Department of Children’s Health and Environment, Director, WHO Collaborating Centre for Children’s Health and Environment, Deputy Director Queensland Children’s Medical Research Institute, NHMRC Senior Principal Research Fellow and Paediatric Respiratory Physician Children’s Health, Queensland, Brisbane. Professor Sly is an acknowledged pioneer in understanding the early origins of lung disease and the long-term implications for lung health. He has discovered major risk factors for the development of asthma and for the onset of cystic fibrosis lung disease, leading to a number of testable hypotheses to prevent or delay the onset of lung disease, which are currently being trialled internationally. He has been instrumental in developing methods for measuring lung function in infants and preschool-aged children which enable for the first time the study of antenatal versus postnatal environmental influences on lung growth and development.
SPEAKERS’ BIOGRAPHICAL DETAILS

Dr Ian Smith is the Director of the RSSC at Papworth, the UK’s first internationally accredited sleep centre. He co-founded the regional MND care network and continues to work clinically and through research to improve its services. Under his directorship R&D at Papworth recently achieved NIHR CTU status. He is the current Chair of the BTS Specialist Advisory Group for Sleep Apnoea.

Professor Jacky Smith runs a multi-disciplinary research team who focus on understanding and treating cough through interventional studies of novel therapies and translation of findings in animal models through to human disease. She also leads a specialist cough service seeing patients with refractory chronic cough from around the North West.

Dr Kevin Southern was appointed Senior Lecturer and Honorary Consultant at the University of Liverpool in January 2000. Since his appointment he has been based at Alder Hey Children’s Hospital in the Institute of Child Health. As Deputy Head of the Department of Women’s and Children’s Health, he has responsibility for the academic team working in the Institute. He is Clinical Lead for the regional CF team and his research has focused on improving the lives of children with CF. He had an important role in establishing the national UK newborn screening programme for CF and is lead of the European Neonatal Screening Working Group. He has been responsible for numerous papers on this topic, improving the experience for families and supporting implementation across Europe and beyond. He is now a Board Member of the European CF Society.

Professor John Stradling 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. He has published over 180 original publications in peer reviewed journals, recently receiving the William C Dement Award from the AASM, an honorary doctorate from Grenoble University, and the BTS Medal.

Dr Hui-Leng Tan is a Consultant in Paediatric Respiratory and Sleep Medicine at the Royal Brompton Hospital and Honorary Senior Lecturer, Imperial College, London. Her current areas of interest include inflammation in children with obstructive sleep apnoea and non-invasive ventilation in children with neuromuscular disease. She did her MD research and paediatric respiratory training at the Royal Brompton and Great Ormond Street Hospitals. She was awarded an ERS fellowship to pursue paediatric sleep research at the University of Chicago.

Dr Lhoussine Touqui is a Research Director in the Department of Infection and Epidemiology, Pasteur Institute, Paris and also the leader of the research team “Animal models of lung infections and inflammatory diseases” in this department. He has a strong expertise in the field of airways inflammation and is an internationally recognized expert on phospholipase A2 (PLA2) and phospholipid metabolism. The main focus of his research is the investigation of the roles of toll like receptors (TLRs) and PLA2 in lung inflammatory diseases. He has developed various cell and animal models to examine these roles with a particular focus on cystic fibrosis (CF). He is also involved in clinical collaborations to study the implications of these factors in human lung inflammatory diseases such as adult respiratory distress syndrome, CF and (more recently) chronic obstructive pulmonary disease. The work of his laboratory focuses on the role of bacterial lung...
infections in the pathogenesis of these pulmonary diseases and how antimicrobial strategies (including antimicrobial peptides such PLA2, LL-37 and collaborative studies on bacteriophages) control bacterial infections. Dr Touqui has authored over 90 articles and chapters on PLA2, ARDS, CF and lung bacterial infections.

**Mr David Waller** graduated from Nottingham in 1985. He has been a Consultant Thoracic Surgeon at Glenfield Hospital, Leicester since 1997 and an Honorary Senior Lecturer at Leicester University. He has been a member of the NCRI Lung CSG, founder member of BTOG and author of over 40 papers on mesothelioma surgery.

**Dr Grant Waterer** is a Respiratory Physician at Royal Perth Hospital and is a Professor of Medicine at the University of Western Australia and Professor of Medicine at Northwestern University, Chicago. He is currently the Chair of the American Thoracic Society and Infectious Diseases Society of America Community Acquired Pneumonia Guidelines and a panel member of the ATS/IDSA HAP/VAP guidelines. He has over 140 peer reviewed publication, more than 60 invited international presentations and is on the Editorial Board of eight journals, including the American Journal of Respiratory and Critical Care Medicine, Chest and the European Respiratory Journal.

**Dr Jeremy Webb** is Associate Professor in Microbiology in the Centre for Biological Sciences, Faculty of Natural and Environmental Sciences at the University of Southampton. His research focuses on the molecular, ecological and evolutionary bases for microbial biofilm development and has led to a number of translational outcomes in the area of biofilm control. He has received a series of fellowship awards from the Leverhulme Trust, the Australian Research Council, and a BBSRC David Phillips award for his research in this area, including the discovery that biofilm disaggregation can be modulated by nitric oxide. This technology is now being exploited for therapeutic applications within cystic fibrosis. [http://www.southampton.ac.uk/biosci/about/staff/jswebb.page](http://www.southampton.ac.uk/biosci/about/staff/jswebb.page) Theme lead, IfLS Biofilms and Microbial Communities Group [http://www.southampton.ac.uk/ifls/research/ifls/biofilms.page](http://www.southampton.ac.uk/ifls/research/ifls/biofilms.page)

**Professor Moira Whyte** is Professor of Respiratory Medicine at the University of Edinburgh and Director of the MRC/University of Edinburgh Centre for Inflammation Research ([www.cir.ed.ac.uk/investigator/Professor-Moira-Whyte](http://www.cir.ed.ac.uk/investigator/Professor-Moira-Whyte)). She is Registrar of the Academy of Medical Sciences and Chair of the MRC Clinical Training and Careers Panel. Her research group have interests in basic mechanisms of innate immunity and she has clinical interests in chronic obstructive pulmonary diseases (COPD) and interstitial lung diseases.

**Dr Tom Wilkinson** is Associate 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 focuses on understanding the mechanisms which contribute to the vulnerability to and impact of respiratory infections in patients with chronic lung disease. His group uses cohort studies and experimental approaches to discovery to enable development of novel approaches to vaccination and targeted anti-viral therapy. Dr Wilkinson leads a long term collaborative programme of research with the GSK vaccines division based in Rixensart, Belgium and is a member of the British Thoracic Society Scientific and Home Oxygen Guidelines committees.

**Dr Andrew Williams** PhD is a Senior Research Associate within the Centre for Inflammation and Tissue Repair, Division of Medicine at University College London. He works within a broad range of disciplines including immunology, inflammation, infectious disease, cell biology and epigenetics, with a focus on understanding the mechanisms of ARDS and inflammatory lung disease.

**Dr Ivana Yang** is an Associate Professor of Medicine and Epidemiology at the University of Colorado Anschutz Medical Campus and National Jewish Health, Denver. She has a broad background in genomics, genetics, and bioinformatics. Her current research focus is epigenetic regulation of transcriptional profiles in lung disease, specifically pulmonary fibrosis, asthma, and granulomatous lung diseases.
EXHIBITORS’ INFORMATION

Actavis
Stand numbers 31 & 32
Our Mission
We develop and manufacture pharmaceuticals of the highest quality. We meet current and future customer needs through smart investments in R&D. We deliver best-in-class service and superior value. We celebrate the many cultures of our global team. We enhance the communities in which we live and work.
Website: www.actavis.com

Action for Pulmonary Fibrosis
Stand number 69
Action for Pulmonary Fibrosis was set up in 2013 by patients, family members and medical professionals, all with a personal connection to IPF. Our vision is a world in which everyone affected by pulmonary fibrosis has a better future. We are working towards recognising our vision by raising awareness, supporting patients, educating where we find knowledge of the disease is poor, and by raising research funds. In the past year we have set up six new patient support groups, funded IPF-specific palliative care rooms, supported nurse training and surveyed 300+ patients about their treatment and care. We welcome requests from professionals with ideas and projects that will help us achieve our vision.
Tel: 07554 803 293
Website: www.actionpulmonaryfibrosis.org
Social media: Twitter @ActionPFcharity and www.facebook.com/actionpulmonaryfibrosis.org

American Thoracic Society
Stand numbers 57 & 58
With a mission of improving respiratory health worldwide, the American Thoracic Society offers educational opportunities to medical professionals through high-impact journals, international conference sessions and online programmes, and clinical guidelines and statements; many of these offer ABIM and ABP MOC, CME and nursing contact hours. The Society also provides research support, advocacy programmes and patient education. ATS activities advance research, education, global health, patient health and clinical services.
Website: www.thoracic.org

Aquilant Endoscopy
Stand number 15
Aquilant Endoscopy (formerly known as Imotech Medical) has been providing first class endoscopy equipment and services to the NHS since 1997. The company is proud to be the UK’s sole distributor of Fujifilm endoscopy products. Enormous investment by Fujifilm Japan since the 1990s has seen Fujifilm products remain consistently at the cutting edge of endoscope technology. The introduction of the world’s first honeycomb Super CCD instruments in 2004 has been followed up with continual improvements, and the latest range of endoscopes offer unparalleled true high definition image quality. Aquilant Endoscopy combines friendly, efficient and flexible customer support with the technical excellence of the high definition Fujifilm product to deliver an unrivalled service in the field of endoscopy. Testimony to our quality and success are longstanding client relationships with over 130 major UK hospitals. Aquilant Endoscopy strives to constantly develop successful strategic partnerships over the long term, which are mutually beneficial to customers and principle suppliers in order to build lifetime loyalty and secure the best outcomes for patients.
The business has very solid foundations and superb backing from its membership of UDG Healthcare plc (formerly United Drug), with annual revenues in excess of €2 billion. UDG Healthcare plc employs over 6,000 people in the UK, Ireland, Western Europe and North America.
Website: www.aquilantendoscopy.com

Association for Respiratory Technology and Physiology (ARTP)
Stand number 65
ARTP is the sole professional organisation in the UK for practitioners working in respiratory and sleep physiology and will be celebrating its 40th anniversary in 2016. ARTP provides nationally, professionally recognised qualifications in lung function testing/spirometry. An important function of 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 co-ordinates spirometry training centres throughout the UK and also writes/publishes 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 (APRC)  
Stand number 64
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

Association of Respiratory Nurse Specialists (ARNS)  
Stand number 63
ARNS was created in 1997 by respiratory nurses, for respiratory nurses, and is still the only nursing-led membership organisation within the UK respiratory specialty field. Today, our organisation benefits from the participation of more than 1,300 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: 0774 011 7902
Email: info@arns.co.uk
Website: www.arns.co.uk
Social media: Twitter: @ARNs_UK You can also find us on Facebook

AstraZeneca Ltd  
Stand number 4
AstraZeneca is a global, innovation-driven biopharmaceutical business that focuses on the discovery, development and commercialisation of prescription medicines, primarily for the treatment of cardiovascular, metabolic, respiratory, inflammation, autoimmune, oncology, infection and neuroscience diseases. AstraZeneca operates in over 100 countries and its innovative medicines are used by millions of patients worldwide.
Tel: 01582 836 000
Website: www.astrazeneca.com

Bayer: Science For A Better Life  
Stand numbers 21, 22, 27 & 28
Bayer is a global enterprise with core competencies in the fields of health care, nutrition and high-tech materials. The company's products and services are designed to benefit people and improve their quality of life. At the same time Bayer creates value through innovation, growth and high earning power. The Group is committed to the principles of sustainable development and to its role as a socially and ethically responsible corporate citizen. Economy, ecology and social responsibility are corporate policy objectives of equal rank.
Tel: 01635 563 000
Email: communicationsukireland@bayer.com
Website: www.bayer.co.uk

The BHD Foundation  
Stand number 70
The BHD Foundation (www.BHDSyndrome.org) promotes research into the inherited condition Birt-Hogg-Dubé Syndrome (BHD). BHD is associated with benign pneumothoraces, skin growths and renal cell carcinoma. BHD is relatively unknown among medical professionals including pulmonologists and radiologists and is therefore believed to be under-diagnosed. The BHD Foundation aims to raise the profile of BHD Syndrome to increase early diagnoses and enable life-saving monitoring for tumour growth.
Tel: 020 7193 8921
Email: contact@bhdsyndrome.org
Website: www.bhdsyndrome.org

Bioxydyn  
Stand number 48
Bioxydyn is a medical imaging software and services provider, delivering high value quantitative imaging solutions. Our Pulmolux tools enable researchers to investigate lung structure and function without ionising radiation, breath-holds or expensive additional equipment. Our unique algorithms and advanced technologies provide high value quantitative readouts from conventional MRI and deliver richer information for clinical research and drug trials.
Email: info@bioxydyn.com
Website: www.bioxydyn.com; www.pulmolux.com

Boehringer Ingelheim  
Stand number 1
The Boehringer Ingelheim group is one of the world's 20 leading pharmaceutical companies. Headquartered in Ingelheim, Germany, Boehringer Ingelheim operates globally with 142 affiliates and a total of more than 47,400 employees. The focus of the family-owned company, founded in 1885, is researching, developing, manufacturing and marketing new medications of high therapeutic value for human and veterinary medicine.
Tel: 01344 424 600
Website: www.boehringer-ingelheim.co.uk
EXHIBITORS’ INFORMATION

**Boston Scientific**  Stand number 36

Boston Scientific (NYSE: BSX) is a worldwide developer, manufacturer and marketer of medical devices with investment in R&D of $861 million and approximately 23,000 employees worldwide. Boston Scientific aims to transform lives through innovative medical solutions that improve the health of patients around the world, as a global medical technology leader for more than 30 years, we advance science for life by providing a broad range of high performance solutions that address unmet patient needs and reduce the cost of healthcare.

For enquiries relating to Bronchial Thermoplasty please contact Angela Smith.

Tel: 07468 708 039

Email: angela.smith@bsci.com

Website: www.btforasthma.com

**British Association for Lung Research**  Stand number 61

The BALR has provided a focus for exchange of ideas between all respiratory researchers, basic scientists and clinicians alike. Fostering collaboration and furthering fundamental pulmonary research for over twenty years, thus fulfilling the initial focus of the Society to promote respiratory research throughout the UK.

Our aims:

- promote and encourage studies in the field of experimental research, related to the elucidation of normal lung function and the mechanisms of lung disease;
- promote interchange of ideas between workers in this field, with organisation of regular scientific meetings;
- encourage exchange of materials and techniques between laboratories, for their mutual assistance and as a means of standardisation in appropriate areas of research.

The BALR has an annual summer meeting and a joint meeting with the BTS in the form of the BALR symposium at the BTS Winter Meeting each year. More information is available on the website.

Website: www.balr.co.uk

**The British Lung Foundation**  Stand number 66

The British Lung Foundation is the only UK charity fighting to help the 1 in 5 people in the UK affected by lung disease, by researching new treatments, campaigning for better awareness and services, and providing support and advice for patients, carers and family members. For help and support, call the BLF Helpline on 03000 030 555. To donate £5 to help the BLF fight lung disease, please text LUNGS to 70500.

Website: www.blf.org.uk

Social media: Follow us on Twitter at http://twitter.com/lunguk or join us on Facebook at http://www.facebook.com/britishlungfoundation

**British Thoracic Society Nurse Advisory Group**  Stand number 62

The British Thoracic Society Nurse Advisory Group (BTS NAG) provides nursing expertise to the British Thoracic Society, with the majority of the BTS Specialist Advisory Groups benefiting from nursing representation guaranteeing that the ‘nursing voice’ is heard!

We are currently conducting a study (led by Sam Prigmore, PI) to develop a set of indicators to measure the added value that respiratory nursing brings to patient care. We are also in the early development stages of a project to develop respiratory nursing competency statements. We are very keen to ensure that the needs of current and future nurse members are met, so would be very pleased to see you at the Meeting. We will be based at stand number 62 in the Britten.

Website: www.brit-thoracic.org.uk

**British Thoracic Society Stop Smoking Champions**  Stand number 52

The BTS Stop Smoking Champions project was launched as part of the Case for Change in 2011 – a campaign for every hospital in the country to have a Stop Smoking Service to TREAT sick smokers. Smoking cessation services within secondary care remain under-funded, under-prioritised and still not deemed a core part of TREATMENT strategy for smoking-related illness. Dedicated, comprehensive and sustainable stop smoking services are necessary for hospitals.

For more information about the Stop Smoking Champions work we will be based at the BTS stands in the Britten.

Email: stopsmokingchampions@brit-thoracic.org.uk

Website: www.brit-thoracic.org.uk/clinical-information/smoking-cessation/

**CareFusion**  Stand number 45

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-customersupport@carefusion.com
Website: www.carefusion.co.uk/medical-products/interventional-specialties/

**Chiesi Limited**

Chiesi Limited is a research focused, international company, developing innovative pharmaceutical solutions which aim to relieve symptoms and improve the quality of human life. Chiesi is established in the areas of respiratory, cardiovascular and musculoskeletal medicine, with a research pipeline focused in the treatment of respiratory diseases.

This Meeting has been supported by Chiesi through the purchase of exhibition trade space.

Tel: 0161 488 5555
Email: info@chiesi.uk.com
Website: www.chiesi.uk.com

**Clement Clarke International**

Respiratory specialists, Clement Clarke International have a series of device innovations to showcase at the BTS Meeting. Among them; New DispozABLE Spacer, the paper cup spacer for emergency SABA delivery, new training tools aimed at standardising pMDI technique training based on existing Flo-Tone device now with improved features.

Tel: 01279 414 969
Websites: www.clement-clarke.com; www.peakflow.com

**COSMED**

COSMED is a world-renowned manufacturer of cardiopulmonary diagnostics equipment since 1980. Its extensive product range includes:

- **Portable Spirometry**: effective, simple lung screening in any environment with a complete selection of light-weight spirometers (desktop, hand-held and PC-based USB)
- **Pulmonary Function Equipment**: innovative modularity and networking available with COSMED PFT lab for truly customized solutions (spirometry, body box, DLCO, respiratory mechanics and more)

COSMED products fully comply with ATS/ERS guidelines and are powered by the new diagnostic software OMNIA.

Tel: +39 06 931 5492
Email: info@cosmed.com
Website: www.cosmed.com

**Education for Health**

Education for Health is the UK’s leading education charity for health professionals working with patients with long term conditions and our education has been shown to measurably improve services and health outcomes. We find ourselves being asked to set the standard for effective education and asked to partner with health organisations across the globe to pioneer best practice learning experiences to materially and substantially benefit patient care. We would welcome any opportunity to share this unique information, knowledge and expertise. Our educational programmes are run throughout the UK and internationally and are accredited by the Open University.

Tel: 01926 493 313
Email: g.schofield@educationforhealth.org
Website: www.educationforhealth.org

**European Respiratory Society**

The European Respiratory Society (ERS) is an international organisation that brings together physicians, healthcare professionals, scientists and other experts working in respiratory medicine. ERS is one of the leading medical organisations in the respiratory field, with a growing membership representing over 140 countries worldwide.

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Website: www.ersnet.org

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GSK is a UK-based science-led global healthcare company that makes innovative medicines, vaccines and consumer health products, used by millions of
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Email: csUK@covidien.com
Website: www.medtronic.com

Michael W Halsall Solicitors Ltd Stand number 37

The Occupational Disease team at Michael W Halsall Solicitors Ltd have the knowledge, experience and resources to provide its clients with the best possible service and advice in connection with asbestos-related and other pulmonary diseases arising from occupational exposure. We care passionately about our clients and are conscious of the devastating impact an occupational disease can have upon the individual and their family. We can assist clients with a claim for damages and put them in contact with relevant support organisations.

Tel: 01942 402 402
Email: emma.downie@halsalls.com
Website: www.halsalls.com

my mhealth Stand number 2

my mhealth are healthcare professionals and IT experts working together to develop, trial and bring to market mobile solutions for patients and clinicians. Our speciality is the development of platforms for patients suffering with long-term conditions that are fully language and region translatable for the emerging global mhealth revolution.

Our mobile applications customise to the individual, enabling the delivery of stratified medicine with licensed pharmaceuticals, and the reporting of population based analytics.

In order to set the standard for the mhealth market, we have a development pipeline that matches regulatory approval and testing with the same rigour as new pharmaceuticals.
Mylan

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In the UK, Mylan has the 3rd largest portfolio of generic and branded generic drugs, offering an extensive range of dosage forms and delivery systems, including oral solid dosages, transdermal patches, inhalers, injectables, topicals, soft gel capsules, nasal sprays, solutions, suspensions and ophthalmic products.

Respiratory is one of the key focus and growth drivers for Mylan. The Mylan Global Respiratory Group – Inhalation Manufacturing Centre (MGRG-IMC) based in Sandwich, UK, and its people provide broad technical capability across all aspects of pharmaceutical formulation and process development of inhalation products for Mylan. We have recently launched the first generic brand of leading LABA/ICS combination in the UK and have a robust pipeline in development.

Tel: 02380 970 217
Email: mycopd@mymhealth.com
Websites: www.mymhealth.com; www.mycopd.mymhealth.com; www.mypulmonary.rehab

Napp Respiratory

Napp Respiratory is a division of Napp Pharmaceuticals Limited, a successful and growing UK healthcare company with a strong track record in delivering medicines for long-term conditions. We provide high-quality asthma medicines to the NHS that meet genuine needs, make a positive difference to patients and are appropriate for today's cost-constrained healthcare environment. We support delivery of real-world evidence and education to help healthcare professionals provide better asthma care. Our collaborative approach enables us to create long-lasting partnerships with NHS organisations to improve asthma outcomes.

Tel: 01223 424 444
Email: enquiries@napp.co.uk
Website: www.napp.co.uk

National Chronic Obstructive Pulmonary Disease (COPD) Audit Programme, led by the Royal College of Physicians

Stand number 53

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. It provides physicians within the United Kingdom and overseas with education, training and support throughout their careers. As an independent body representing over 30,000 fellows and members worldwide, it advises and works with government, the public, patients and other professions to improve health and healthcare.

Through an extensive partnership approach, the Chronic Obstructive Pulmonary Disease (COPD) audit programme brings together primary care, secondary care, pulmonary rehabilitation and patient experience. This national audit programme comprises comprehensive multidisciplinary, collaborative working and 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), to develop and deliver this ambitious national audit programme. The programme is commissioned by the Healthcare Quality Improvement Partnership as part of the National Clinical Audit Programme (NCA).

For further information contact: Emma Skipper, Programme Manager, or Juliana Holzhauer-Barrie, Programme Coordinator.

Tel: 020 3075 1502
Email: copd@rcplondon.ac.uk
Website: www.rcplondon.ac.uk/COPD
Social media: Twitter: #COPDaudit, #COPDwhocares, #COPDwhocaresmatters

National Lung Cancer Audit (NLCA), led by the Royal College of Physicians

Stand number 54

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. It provides physicians within the UK and overseas with education, training and support throughout their careers. As an independent body representing over 30,000 fellows and members worldwide, it advises and works with government, the
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public, patients and other professions to improve health and healthcare.
The National Lung Cancer Audit (NLCA) is commissioned by the Healthcare Quality Improvement Partnership as part of the National Clinical Audit Programme.
The NLCA is a highly regarded and successful audit that has been driving change in care for people with lung cancer since 2004. The NLCA has achieved outstanding levels of NHS participation, with data being used to support local service improvement and contribute to national and international policy and quality initiatives. NLCA data have been used to underpin NICE guidelines, to inform research protocols and to guide national service developments. The RCP has recently been awarded the contract for the NLCA, and it aims to deliver a new audit that builds on the success of the previous audit while incorporating key advances in the field of lung cancer diagnosis and treatment.
The RCP works closely with a range of key stakeholders to develop and deliver the national audit, including the National Cancer Registration Service, the University of Nottingham, the Society for Cardiothoracic Surgery, the Roy Castle Lung Cancer Foundation, the National Lung Cancer Forum for Nurses and the Welsh Lung Cancer Specialist Advisory Group.
For further information, please contact Rosie Dickinson, NLCA project manager.
Tel: 020 3075 1739
Email: NLCA@rcplondon.ac.uk
Website: www.rcplondon.ac.uk/resources/national-lung-cancer-audit

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**The PCD Family Support Group**

Stand number 67

The PCD Family Support Group is a registered charity who:

- Provide support to patients with Primary Ciliary Dyskinesia (PCD) and parents of children with the condition
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Stand number 30

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**PneumRx Ltd a BTG International Group Company**

Stand number 35

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South Africa, Canada and Australia. It is approved for investigational use only in the USA.

Tel: +31 73 303 0599
Email: Info-EU@pneumrx.com
Website: www.pneumrx.com

**Primary Care Respiratory Society UK (PCRS-UK) and npj Primary Care Respiratory Medicine**

Stand number 59

The Primary Care Respiratory Society UK is the UK-wide professional society dedicated to meeting the vision of “optimal respiratory health for all”. Through its open access resources and membership scheme, PCRS-UK offers a wealth of practical and easy to use resources to help primary care deliver high value patient centred respiratory care.

Online-only and open access, npj Primary Care Respiratory Medicine is the only fully-indexed scientific journal devoted to the management of respiratory diseases in primary care.

Tel: 01675 477 600
Emails: info@pcrs-uk.org; npjpcrm@nature.com
Websites: www.pcrs-uk.org; www.nature.com/npjpcrm

**Pulmonx**

Stand number 16

Pulmonx strives to be the cornerstone of interventional pulmonology by focusing on developing life-changing, cost-effective technologies that improve the lives of patients suffering from lung disease worldwide. Pulmonx has developed the Endobronchial Valve (EBV) Therapy, a non-surgical approach to treating late stage emphysema that is designed to reduce the volume of the diseased region of the lung by blocking airflow. The therapy incorporates a diagnostic technology called the Chartis Pulmonary Assessment System that is designed to optimize patient selection and targeting, enhancing clinical outcomes.

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**Respiratory Futures**

Stand number 50

Seed-funded by BTS and NHS England, and chaired by Professor Mike Morgan, www.respiratoryfutures.org.uk supports improved early diagnosis and prevention, promotes guidance on best-practice for long-term conditions and reflects issues of importance to the wider healthcare community.

Its light-touch editorial policy balances third party resources with original webinars and feature interviews from across the UK health community.
Respiratory Futures encourages radical approaches to delivering care that can impact positively and significantly on patient outcomes, serving as a central forum for the diverse range of professionals working to improve the nation’s respiratory health.

Email: aileen.muir@brit-thoracic.org.uk
Website: www.respiratoryfutures.org.uk

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Website: www.sandoz.com

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Slater and Gordon specialise in providing expert legal advice to people who have been exposed to asbestos dust and go on to develop mesothelioma and lung cancer.
Our Chest and Asbestos Disease Group was formed by bringing together leading law firms including John Pickering and Partners, Pannone and Fentons who, during their many years’ experience, have been involved in some of the most important and ground-breaking cases.
Please come and speak to us at the conference if you would like further information about how we can assist your patients.

Tel: 0161 383 3527 or 0800 884 0275
Website: www.slatergordon.co.uk/personal-injury/asbestos/

Teva UK Limited Stand numbers 23, 24, 25 & 26
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We supply medicines to pharmacies and hospitals, from painkillers to antibiotics, and cholesterol reducers to lifesaving injectable medicines to fight cancer. Our specialities are generic medicines, which are usually medicines whose patents have expired; and respiratory medicines, especially inhalers to relieve the symptoms of asthma.
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Vertex work with leading researchers, institutions and companies. Together we deploy emerging technologies in new areas to advance science and accelerate the discovery, development and commercialisation of critical medicines.
Vertex has been involved in cystic fibrosis (CF) research since 1998 and we are committed to continuing our research and development efforts to help more people with CF.
Tel: 01923 437 672
Email: Vertexmedicalinfo@vrtx.com

Vitalograph Stand number 29
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**FLUTICASONE PROPIONATE ALTERS THE RESIDENT AIRWAY MICROBIOTA AND IMPAIRS ANTI-VIRAL AND ANTI-BACTERIAL IMMUNE RESPONSES IN THE AIRWAYS**

A Singanayagam, N Glanville, R Pearson, P James, I Cuthbertson, M Cox, M Moffatt, W Cokson, N Bartlett, S Johnston. Imperial College, London, UK

10.1136/thoraxjnl-2015-207770.1

**Background** Inhaled corticosteroids are the cornerstone of therapy in asthma and COPD but cause only modest reduction in exacerbations and are associated with increased pneumonia frequency. This has raised concern about potential detrimental effects on host-defence against respiratory pathogens. The aim of this study was to evaluate the effects of fluticasone propionate on airway anti-viral and anti-bacterial host-defence.

**Methods** C57BL/6 mice were intranasally treated with fluticasone propionate (1 mg/kg) or vehicle control. 16S Quantitative PCR was used to evaluate total bacterial loads and pyrosequencing was used to evaluate microbiota community composition in lung tissue. Using mouse models of infection with rhinovirus 1B and S. pneumoniae D39, effects of fluticasone administration on anti-viral and anti-bacterial immune responses, airway inflammation and pathogen control were evaluated.

**Results** Mice treated with fluticasone had increased lung bacterial loads compared to vehicle-treated controls at 8 h post administration (p < 0.05). Evaluation of community composition revealed that fluticasone treatment was associated with significant increases in *Stenotrophomonas* genera (p < 0.05). In a mouse model of *S. pneumoniae* infection, fluticasone administration suppressed anti-bacterial responses including expression of cytokines IL-6 and TNF-α (4 h post-infection; p < 0.001) and airway neutrophil recruitment (8 h post-infection; p < 0.001) and was also associated with increased lung bacterial loads measured by quantitative culture (8 h post-infection; p < 0.001). In a mouse model of rhinovirus infection, fluticasone suppressed innate anti-viral responses including BAL protein levels of interferon-β and -3.2/3 (day 1 post-infection; p < 0.001). Virus clearance was impaired by fluticasone with increased viral RNA copies observed in lung tissue (day 1&2 post-infection; p < 0.001). The late expression of rhinovirus-induced airway mucins MUC5AC and MUC5B BAL proteins was increased by fluticasone (p < 0.01 and p < 0.05 respectively at day 7). Administration of recombinant interferon-β in combination with fluticasone and rhinovirus led to upregulation of interferon-stimulated genes and improved virus clearance, thereby demonstrating that adverse effects of fluticasone on RV clearance are causally related to interferon suppression. Recombinant IFN-β did not alter the increased mucins observed with fluticasone treatment.

**Conclusion** Fluticasone alters the airway microbiota and impairs airway anti-viral and anti-bacterial host-defence in mice. Human studies are required to confirm the relevance of these effects in the context of inflammatory airway diseases.
Background ARDS remains a major cause of respiratory failure in critically ill patients with no specific therapy. MSC based cell therapy is a promising candidate and is being used in clinical trials for ARDS. However, the mechanisms of MSC effect in lung injury are not very well understood. Islam et al., 2012 showed mitochondrial transfer from MSC to alveolar epithelial cells was protective in the mouse model of LPS induced pneumonia. Pathophysiology of ARDS is underpinned by dysregulated inflammation and pulmonary macrophages are key cellular mediators of the lung immune response. This study was undertaken to test if MSC could transfer their mitochondria to macrophages and to investigate the effects of MSC mitochondria transfer on macrophage function in the in vivo and in vitro models of ARDS.

Methods In vivo studies were performed using a mouse model of *E.coli* pneumonia induced ARDS. C56BL/6 mice were infected with *E.coli*, human bone marrow-derived MSC or PBS instilled intra-nasally 4 h after infection. For in vitro studies primary human monocyte-derived macrophages (MDM) were infected with *E.coli* and co-cultured with MSC in contact. MSC mitochondria were pre-stained with MitoTracker Red and MDM stained for CD45 expression. Double positive cells were visualised with confocal microscopy and quantified using flow cytometry. Phagocytosis was assessed using fluorescent *E.coli* bioparticles by flow cytometry.

Results When co-cultured with MSC >90% of MDMs acquired MitoRed fluorescence, indicating mitochondrial transfer from BM-MSC. Confocal imaging revealed presence of Mito-Red positive tunnelling nanotubes (TNTs) formed by MSC. In vivo >78% of CD11chi/F4-positive alveolar macrophages retained MSC mitochondria at 24 hr post infection. Alveolar macrophages that had acquired MSC mitochondria had a significantly higher phagocytic index compared to those without. This was assessed by an increase in Mean fluorescence Intensity (MFI). Some of the materials employed in this work were provided by the Texaz A&M Health Science Centre College of Medicine Institute for Regenerative Medicine at Scott and White through a grant from NCRR of the NIH, Grant #P40RR017447.

Conclusions Our findings suggest that anti-microbial activity of macrophages is enhanced at least partially by transfer of BM-MSC mitochondria through TNTs, representing an important mechanism of MSC effect in ARDS. Supported by: MRC MR/L017229/1.

REFERENCE

T4

**OPTICALLY DETECTABLE ANTIMICROBIAL PEPTIDES ENABLE THE IMMEDIATE DETECTION OF BACTERIA AND FUNGI IN THE LUNG**

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10.1136/thoraxjnl-2015-207770.4

Introduction The immediate detection of pathogens in the lungs of patients with unexplained pulmonary opacities in the intensive care unit would represent a significant advance in their management. An optical imaging strategy, including the endobronchial administration of bacterial specific Smartprobes, would confer a number of advantages over conventional techniques such as bronchoalveolar lavage, principally real-time detection to immediately inform antimicrobial therapy. The aims of this study were to fluorescently label and iteratively develop anti-microbial peptides to image bacteria in situ in the lung using fibered confocal fluorescence microscopy (FCFM).

Methods Antimicrobial peptides (AMP) have been synthesised on a dendrimeric scaffold (AMP-1) and conjugated to an environmentally sensitive fluorophore called NBD, following the continuous development a linear counterpart. A further construct consists of an AMP with gram-selectivity conjugated to the endobronchial administration of bacterial specific Smartprobes.

Conclusions Our findings suggest that anti-microbial activity of macrophages is enhanced at least partially by transfer of
allow distal alveolar imaging at micron resolution in an ex vivo ovine model of bacterial infection.

**Results** AMP-1 demonstrates bacterial binding affinity in a concentration-dependent manner and labels a diverse panel of bacteria, including a panel consisting of >70% of ventilator-associated pneumonia causing organisms and the pathogenic fungi Aspergillus fumigatus. AMP-1 demonstrates significantly higher fluorescence over isomolar linear equivalents for E. coli, K. pneumoniae, P. aeruginosa, MSSA, A. baumannii and S. pneumoniae (all p < 0.01), is selective for bacteria over mammalian cells and has improved chemical stability over the linear equivalent when incubated with bronchoaveolar lavage from patients with acute respiratory distress syndrome. Furthermore, AMP-1 can label E. coli, K. pneumoniae, P. aeruginosa and MSSA in situ in an ex vivo ovine model when instilled endobronchially and imaged with PCFM (pin vitro and remains selective for gram-negative bacteria over mammalian cells. In the ex-vivo model AMP-2 selectively labels the gram-negative bacterial segments (P. aeruginosa, K. pneumoniae and E. coli) over the gram-positive (MSSA, MRSA and S. pneumoniae) or control pulmonary segments (all p < 0.05).

**Conclusions** A Smartprobe/FCFM strategy to immediately detect bacteria with gram selectivity in size relevant pre-clinical models is described, and are undergoing first-in-man translation.

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**T5 MICRONNA-140–5P REGULATES DISEASE PHENOTYPE IN EXPERIMENTAL PULMONARY ARTERIAL HYPERTENSION VIA SMURF1**

1AMK Rothman, 1ND Arnold, 1IA Pidsworth, 1Tiemonger, 2Cixian, 3R Allen, 3G Guth-Gundel, 1M Southwood, 3NW Morrell, 5DF Francis, 1DU Rowlands, 1A Lawrie, 1University of Sheffield, Sheffield, UK; 2Novartis Institutes for Biomedical Research, Basel, Switzerland; 3University of Cambridge, Cambridge, UK; 4University of Cambridge, Cambridge, UK

**Introduction and objectives** Clinical therapies for the treatment of pulmonary arterial hypertension (PAH) target vasoconstriction. However, the proliferative pulmonary vascular remodelling that drives disease persists contributing to significant patient morbidity and mortality. MicroRNA (miR) are short non-coding RNA that mediate post-transcriptional regulation of mRNA targets. We hypothesise that dysregulation of miR leads to depression of cellular targets central to disease pathogenesis. We sought to identify dysregulated circulating miR in patients with PAH, determine their phenotypic effect using in vitro and in vivo models and identify key mechanistic regulators that may represent novel therapeutic targets.

**Methods** Two patient cohorts were used to identify and validate differential expression of miR in whole blood by microarray and single assay qPCR. Binding site and network analysis was used to identify key miR targets. Effect of miR on identified targets and disease phenotype was determined in pulmonary artery smooth muscle cells (PASMC) and in the monocrotaline (MCT) and Sugen5416 plus Hypoxia (SuHx) models of PAH.

**Results** Expression of miR-140–5P was reduced in whole blood samples from patients with PAH and experimental models of PAH. Network and pathway analysis identified key regulators of TGFβ and PDGF signalling as miR-140–5P targets. Transfection with miR-140–5P inhibitor resulted in increased proliferation and migration of PASMC and de-repression of key targets. Nebulised delivery of miR-140–5P mimic prevented the development of PAH in the MCT rat model and attenuated progression of established PAH in MCT and SuHx rat models. In experimental models levels of SMURF1 protein correlated inversely with miR-140–5P. Direct regulation of SMURF1 by miR-140–5P was demonstrated in vitro by 3′UTR luciferase activity. Both miR-140–5P mimic and SMURF1 siRNA increased BMP response element activity identifying SMURF1 as a key negative regulator of BMP signalling in PASMC. Genetic ablation of SMURF1 in C57BL6 mice conferred allele dependent protection from SuHx induced PAH. Finally, whole blood mRNA and pulmonary vascular immunoreactivity of SMURF1 was increased in patients with PAH.

**Conclusions** These studies suggest that miR-140–5P and SMURF1 are key regulators of BMP signalling and disease pathology in PAH and highlight SMURF1 as a potential novel therapeutic target.

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**T6 MET TARGETED THERAPY IN LUNG ADENOCARCINOMA: DOES ‘RESISTANT’ EGFR MAKE A MET-RESPONSIVE DIMER?**

1RW Lee, 1E Ortiz-Zapater, 2G Weitsman, 1G Fujihara, 1W Owen, 2T Ng, 3G Santis. 2Division of Asthma, Allergy and Lung Biology, Guy’s Hospital, King’s Health Partners, London, UK; 3Richard Dimbleby Department of Cancer Research, Randall Division of Cell and Molecular Biophysics, King’s College London, London, UK; 4Department of Imaging Chemistry and Biology Division of Imaging Sciences and Biomedical Engineering School of Medicine, King’s College London, London, UK

**Introduction** Lung cancer has extremely poor survival with few effective treatments. Activating EGFR mutations (e.g. L858R), select for impressive EGFR tyrosine kinase inhibitor (TKI) responses but most develop resistance e.g. T790M mutations or MET amplification, which is thought to mediate EGFR-HER3 kinase switching. Preclinical studies suggest EGFR-MET TKI synergy and whilst phase III trials have failed, optimism remains for biomarker driven therapy.

**Hypothesis** EGFR-MET dimerisation determines MET TKI response.

**Objectives**
1. Explore MET TKI responsiveness in EGFR mutant lung adenocarcinoma.
2. Develop an EGFR-MET FLIM assay indicative of MET TKI responsiveness.


Cells and xenografts (gavage) were challenged with exquisitely selective MET TKI, SGX523. Response was assessed by BrdU proliferation assays in vitro alongside random migration assays mimicking tumour cell motility. Xenograft tumours (FFPE) were stained for Ki67/phosphohistoneH3 (proliferation) and Masson’s trichrome/anti-sma (Collagen/stroma).

EGFR-MET interaction was assessed by co-immunoprecipitation and Forster resonance energy transfer (FRET) FLIM to quantify EGFR-MET dimers after SGX523 treatment.

**Results** SGX523 treatment significantly reduced H1975 xenograft tumour growth/weight. Proliferation was suppressed in vitro (BrdU %) and in vivo (phosphohistone-H3). Conversely in H1975 L858R, SGX523 reduced stroma (Masson’s trichrome) and migration. EGFR-MET dimers were more common in H1975 than H1975 L858R/WT. This was associated with a
mesenchymal, migratory phenotype in the H1975 cells whilst H1975 L858R were more proliferative.

SGX523 reduced EGFR-MET dimerization (FRET %) in H1975 cells/FFPE xenograft tumours but induced dimer formation in H1975 L858R. H1975 WT showed little response to MET inhibition and low EGFR-MET FRET. In treated mice, FRET correlated with Ki67.

Conclusions
1. MET therapy was most effective in H1975 suggesting greater MET dependence with EGFR L858R/T790M.
2. EGFR L858R-T790M interacted most with Untreated MET.
3. MET inhibition reduced EGFR-MET dimerization in H1975 but increased H1975-L858R FRET.
4. EGFR-MET FRET assays can be applied to ‘FFPE’ processed lung cancer tissue from murine xenografts.

![FRET(%): EGFR-MET Murine Xenograft](image)
Cutting edge pulmonary hypertension

**S1** DOES PARADOXICAL EMBOLI OF PARTICULATE MATTER THROUGH PULMONARY ARTERIOVENOUS MALFORMATIONS PRECIPITATE MIGRAINES?

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10.1136/thoraxjnl-2015-207770.7

Introduction and objectives Pulmonary arteriovenous malformations (PAVMs) are an example of a right-to-left shunt resulting in deoxygenated, unfiltered venous blood bypassing the pulmonary capillaries to re-enter the systemic arterial circulation. Patients with PAVMs are known to have an increased incidence of migraines, reducing following PAVM treatment by embolisation. This study aimed to examine if paradoxical embolism of particulate matter through PAVMs may precipitate migraines.

Methods A structured survey was designed for online completion by people with hereditary haemorrhagic telangiectasia (HHT), the most common cause of PAVMs. Question logic directed participants through a series of unbiased questions that asked about HHT features including presence of PAVMs; variables in relation to migraines; and whether participants had undergone imaging tests. Stratified by whether contrast had been given, participants reporting migraines were asked whether any difference in migraines had been noted following scans, by ticking that “migraines were no different really”; “seemed a bit better”; “seemed a bit worse”; “seemed to bring on a migraine”; “seemed to stop a migraine”. Participants were recruited from 26/07/2013- 21/04/2015, yielding 702 consented responses. Data were downloaded to an Excel spreadsheet for participant stratifications, and statistical analyses using GraphPad Prism 6.0 and STATA 13.1 (Statacorp LP).

Results Overall, 557 participants had HHT, of whom 180 (32.3%) reported features consistent with migraines. HHT participants with migraines more commonly reported PAVMs than those without migraines (62.8% vs 38.5%, p < 0.00001). For computerised tomography (CT) scans, images “with injection of contrast” were associated with a higher proportion of participants reporting worsening migraines than “without injection of contrast” CT scans (11.7% vs 3.4%, p = 0.0065). This association strengthened following paired analysis of participants who had undergone both methods (13.6% vs 3.2%, p = 0.0032). In multiple regression analyses, there was no additional contribution from other participant demographics such as alcohol consumption or smoking habit. Analysis of magnetic resonance imaging (MRI), contrast echocardiography and ultrasound data is ongoing.

Conclusion This study strongly indicates that an association between injecting contrast media and the worsening of migraines, in participants with right-to-left shunts due to PAVMs, exists. Further research is required to establish the exact mechanism responsible for this phenomenon.

*S1* BTS Medical Student Award Highly Commended.

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**S2** VASCULAR QUIESCENCE FACTOR BMP9 IS REGULATED BY INFLAMMATION AND NEUTROPHIL ACTIVATION

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10.1136/thoraxjnl-2015-207770.8

Introduction Endothelial bone morphogenetic protein type II receptor (BMPR-II)-mediated signalling is essential for protecting vascular endothelium. Loss of BMPR-II predisposes human pulmonary artery endothelial cell (hPAEC) monolayers to apoptosis and increased permeability. In *in vivo*, reduced BMPR-II function promotes endothelial permeability and the development of pulmonary arterial hypertension (PAH). Importantly, BMP9, the only confirmed active circulating BMP, signals preferentially via BMPR-II and induces BMPR-II expression to maintain endothelial integrity and homeostasis. It was recently shown that administration of recombinant BMP9 prevented LPS-induced lung vascular leakage *in vivo* and reversed established PAH in three rodent models.1 However, it is not known how circulating BMP9 is regulated during LPS-induced inflammation and in PAH.

Objective To investigate whether BMP9 is regulated by inflammatory stimuli *in vivo* and *in vitro*.

Results Intraperitoneal LPS challenge in mice led to a significant increase in circulating neutrophil elastase levels with a reciprocal reduction in BMP9 levels (both measured by ELISA) within 24 h. Since this reduction in BMP9 might be due to reduced BMP9 synthesis in the liver or cleavage of BMP9 by neutrophil-derived proteases, we quantified BMP9 synthesis in the liver after LPS challenge, as well as changes in alpha-1 antitrypsin, the major elastase inhibitor in man. Synthesis of BMP9 fell sharply 3 h after LPS-challenge but recovered completely by 18 h. No increase in the synthesis or levels of circulating active alpha-1 antitrypsin was observed. Supernatants from purified human peripheral blood neutrophils activated in *vitro* degraded recombinant BMP9. Inhibition studies confirmed that the BMP9-cleavage activity released by activated neutrophils was largely attributable to neutrophil elastase.

Conclusions and discussions Synthesis of the endothelial protective factor BMP9 is actively regulated by inflammation, and BMP9 is subject to neutrophil elastase-mediated cleavage. Since inflammation has been shown to be a second hit in the pathogenesis of PAH, this study could provide a potential link between inflammation and reduced endothelial BMPR-II signalling.

REFERENCE


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**S3** REDUCED BMPR2 EXPRESSION POTENTIATES A PULMONARY ARTERY SMOOTH MUSCLE CELL SPECIFIC IL-1ß RESPONSE

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10.1136/thoraxjnl-2015-207770.9

Introduction and objectives Bone morphogenetic protein receptor type 2 (BMPR2) mutations are found in heritable and idiopathic pulmonary arterial hypertension however penetrance is incomplete implying necessity for a ‘second hit’. IL-1ß and IL-6 are increased in PAH patients and animal models and are
thought to have a role in disease. We aimed to determine pulmonary specific interplay between BMPR2 and IL-1β signalling through assessing IL-1β responsiveness of pulmonary artery and aortic smooth muscle cells (Ao/PA SMC) and determine the effects of reduced BMPR2.

**Methods** Microarray analysis of PASMC and AoSMC mRNA was performed using microarray on mRNA isolated from cells cultured in SMGM-2 (Lonza) +/- functional BMPR2 (by use of siRNA) and stimulation with 10 ng/ml IL-1β for 6 h. Subsequent bioinformatics was performed using R. Findings were validated using quantitative PCR and western blots. Furthermore R899X+/- BMPR2 transgenic mice were fed western diet for six weeks and injected daily with IL-1β then assessed for inflammatory activation and PAH phenotype (catherter/echo). mRNA and protein changes were measured by TaqMan PCR, western blotting and serum ELISA. Immuno-staining of paraffin embedded lung sections assessed pulmonary vascular remodelling.

**Results** Array data shows reduced inflammatory activation in response to IL-1β in PASMC compared with AoSMCs, analysis of cells lacking functional BMPR2 identified an exaggerated inflammatory response to IL-1β in PASMC lacking BMPR2 (siRNA). Significant up-regulation of IL-6, IL-1α and adhesion molecules (>2-fold) shown by array analysis was validated by qPCR. In the absence of BMPR2 a 1.5 fold increase in proliferation was observed in response to IL-1β compared to PASMC with functional BMPR2. Mice treated with IL-1β show higher white blood cell counts (1.7-fold), and protein levels of OPG and IL-6 (serum) matching in vitro data.

**Conclusion** IL-1β induces a pulmonary specific transcriptome altered by suppression of BMPR2 signalling indicating cross-talk between the pathways. In the presence of BMPR2, PASMCs show limited response to IL-1β however reducing BMPR2 exacerbated this response increasing the likelihood of a PAH phenotype in PASMCs. This highlights a mechanism that increased IL-1β may provide “second hit” to reduced BMPR2 to stimulate development of PAH.

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**S4** PULMONARY ARTERY PRESSURE AND EXERCISE TOLERANCE IN PATIENTS WITH PULMONARY ARTERIOVENOUS MALFORMATIONS

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10.1136/thoraxjnl-2015-207770.10

**Introduction and objectives** Pulmonary arteriovenous malformations (PAVMs) provide direct communications between pulmonary arteries and pulmonary veins, bypassing the pulmonary capillary bed. Greater improvements in exercise capacity following embolization therapy have been reported by PAVM patients with raised pulmonary artery pressures (PAPs). The objective of this study was to test the hypothesis that lower PAPs are associated with greater exercise capacity in hypoxaemic PAVM patients.

**Methods** Patients attending our tertiary care institution were recruited at the time of PAVM assessment or embolization. Pulmonary artery pressure measurements were obtained by right-heart catheterisation immediately prior to contrast injection and embolization. For both patients and healthy controls, incremental cardiopulmonary exercise tests were performed seated on an adjustable cycle ergometer (MasterScreen CPX; Via Sprint).

**Results** A total of 19 patients and 26 controls were recruited for the study. Significantly lower arterial oxygen saturations (median 91% vs. 98%, p < 0.0001) and end-tidal PCO2 levels were demonstrated in patients alongside significantly raised V[dot]O2/V[dot]CO2 slopes (32.2 vs. 24.1 L/min/L/min, p = 0.0003). The regression models that best described peak oxygen uptake (V[dot]O2) as a percent of predicted values, were similar between PAVM patients and controls. Surprisingly, despite the differences in SaO2 between PAVM and control subjects, the addition of SaO2 to the final models did not improve the significance of the final model nor did it raise the adjusted-r² value. For the PAVM subgroup, the median mean PAP was 14.5 mmHg, (IQR 12.5–16.0; range 6–22). Univariate and multiple regression analyses demonstrated no significant relationships between systolic, diastolic or mean PAPs, and peak exercise parameters.

**Conclusions** This study has demonstrated in a population of PAVM patients with hypoxaemia and PAPs essentially within the normal range, that PAP does not have a major influence on peak exercise capacity.
and complement deposition was not significantly different between disease and control in precapillary lung vessels.

Conclusions There is evidence of immune dysfunction in IPAH, notably consistent with previous reports in autoimmunity. Dysregulated immunity is emerging as a potentially important factor in IPAH pathogenesis.

REFERENCES

Abstract S5 Figure 1  IPAH patients demonstrated significantly increased populations of T follicular helper (Tfh) cells and PD1+CD4+ T-cells compared to healthy controls

Abstract S6 Figure 1  Increase expression of JMJD3 and decrease of H3K27me3 in remodelled PA in the lung from MCT rat

Introduction and objectives There is increasing interest in the role of epigenetic gene regulation in the pathogenesis of...
Phenotyping and treating severe asthma

S7 AIRWAY PATHOLOGICAL PHENOTYPES AND THEIR CLINICAL UTILITY IN ADULT ASTHMA

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Background Airway remodelling and cellular inflammation are well recognised pathological features of asthma. However the relationship between asthma phenotype, treatment intensity and pathobiology is poorly understood.

Objectives We performed a study of common pathological features in adult asthmatic bronchial biopsies to identify (i) whether discrete ‘pathological phenotypes/subtypes’ exist and (ii) their clinical utility.

Methods 202 patients (142 asthma and 60 healthy volunteers) were recruited. Patients underwent bronchoscopy and endobronchial biopsy. Bronchial biopsies were evaluated for eleven common features of asthma pathology. Standard biostatistical analyses including a range of cluster analyses and machine learning were applied to pathological features alone to evaluate our objectives.

Results Three distinct immunopathological clusters were identified and characterised by distinct biopsy features of cellular inflammation and remodelling. Specifically, i) late onset severe eosinophilic asthma [cluster 1] with evidence of reticular basement membrane thickening, increased epithelial area and vascular remodelling, ii) milder late onset asthma [cluster 2] with few features of remodelling and iii), an early onset atopic eosinophilic asthma [cluster 3] with features of Th2 high asthma, increased airway smooth muscle (ASM) mass, increased mast cells within the ASM and a mixed granulocytic submucosal inflammation. Pre bronchodilator FEV1 and decline (in a subset) differed across the clusters. Pathological features did not add value to the clinical prediction of asthma.

Conclusion We identified three novel pathological clusters of asthma with differing features of airway remodelling, cellular inflammation and airway function. Asthma may be characterised by variable pathological phenotypes warranting further evaluation in larger population studies.

S8 A NATIONWIDE REAL-LIFE STUDY: EXPLORING THE DIFFICULTIES OF CONFIRMING THE ASTHMA DIAGNOSIS IN PATIENTS WITH SEVERE ASTHMA

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Introduction Many conditions may mimic severe asthma. Therefore, patients with asthma who receive high dose asthma therapy are recommended to undergo systematic evaluation in order to objectively confirm the diagnosis of asthma.

Aims and objectives To evaluate to which extent patients treated by respiratory specialists for severe asthma had the diagnosis of asthma verified by the demonstration of variable airflow obstruction.

Methods A retrospective cross-sectional study was performed in 2013. Patient record forms of all patients (18–65 years) newly referred to one of five respiratory outpatient clinics in Denmark in the period of 2009–2010 with a diagnose of asthma (ICD-10: D45-D459) were screened after a two-year observation period for having severe asthma. Patients were included in the study, if they had a doctors diagnosis of asthma and received inhaled corticosteroids equivalent to ≥1600 μg budesonide and a second controller (long acting beta-2-agonist, theophylline or leukotriene-antagonist) for a minimum of twelve months or were treated with oral prednisolone (minimum six months). Diagnostic tests for asthma were registered: Day-to-day PEF monitoring, reversibility test (short-acting beta-2-agonist or prednisolone) and bronchial challenge test (methacholine, mannitol, exercise test, eucapnic voluntary hyperpnoea test).

Results A total of 1417 newly referred subjects were screened, of whom 98 patients fulfilled the above criteria of having severe asthma. Overall, 84% were assessed with at least one diagnostic test; Reversibility test 63%, PEF monitoring 57% and bronchial challenge test 21%.

In total, 50% of the study population had at least one positive diagnostic test; 37% had a positive reversibility test, 17% had significant peak flow variation and 12% had a positive bronchial challenge test. Among those having negative reversibility test or negative peak flow measurements with FEV1≥70%, only 30% had a bronchial challenge test performed.

Conclusion Among patients managed for severe asthma in five specialist hospital clinics in Denmark, only half had the asthma diagnosis confirmed objectively. This indicates a substantial room for improvement in order to ensure that patients receiving high dose asthma therapy truly have asthma.
EQUIVALENCE OF FLUTICASONE PROPIONATE/SALMETEROL DELIVERED VIA AIRFLUSAL® FORSPIRO® AND SERETIDE® ACCUHALER® IN ADOLESCENT AND ADULT ASTHMA

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Introduction and objectives Guideline-defined asthma control may be achieved and maintained in the majority of patients by treatment with a combination of a corticosteroid and a long-acting \( \beta_2 \)-agonist. AirFluSal\textsuperscript{®} Forspiro\textsuperscript{®}, a multi-dose dry powder inhaler (mDPI), provides this proven combination of inhaled corticosteroid fluticasone propionate (FP) and a long-acting inhaled \( \beta_2 \)-agonist salmeterol (Sal). This study compared the efficacy of AirFluSal\textsuperscript{®} Forspiro\textsuperscript{®} with Seretide\textsuperscript{®} Accuhaler\textsuperscript{®} in adolescent and adult patients with moderate-to-severe persistent asthma.

Methods This study, conducted in 279 patients (12–65 years) with GINA guideline-defined moderate-to-severe persistent asthma, was undertaken as a double-blind, double-dummy, parallel-group, multicentre trial. Patients were randomised to 12 weeks treatment with AirFluSal\textsuperscript{®} Forspiro\textsuperscript{®} 500 \( \mu \text{g} \)/50 \( \mu \text{g} \), or Seretide\textsuperscript{®} Accuhaler\textsuperscript{®} 500 \( \mu \text{g} \)/50 \( \mu \text{g} \). Primary efficacy measures were the change from baseline of the forced expiratory volume in 1 s (FEV\textsubscript{1}) to show non-inferiority of AirFluSal\textsuperscript{®} Forspiro\textsuperscript{®} to Seretide\textsuperscript{®} Accuhaler\textsuperscript{®} (non-inferiority margin \( \Delta = -0.200 \text{ L} \)) and the area under the FEV\textsubscript{1} curve at study termination (AUC\textsubscript{0–12}). Secondary endpoints included mean changes in FEV\textsubscript{1}, FEV\textsubscript{1}/FVC\textsuperscript{50} predicted, morning peak expiratory flow (PEF) and global evaluation of efficacy. Safety was assessed and patient preference for each device was rated using a visual analogue scale (VAS).

Results Assessment of the effect of treatment on the absolute change in FEV\textsubscript{1} from baseline to study termination demonstrated non-inferiority between AirFluSal\textsuperscript{®} Forspiro\textsuperscript{®} and Seretide\textsuperscript{®} Accuhaler\textsuperscript{®} (difference in least squares mean [95% CI] = -0.032 L [-0.121;0.057]). Assessment of AUC\textsubscript{0–12} at study termination demonstrated equivalence between devices. All secondary efficacy measures demonstrated comparable results for both inhalers, with no significant differences observed. The use of rescue medication and the average asthma symptom scores decreased from baseline in a similar manner for both devices. Overall safety profiles were equivalent. Patient ratings for each device were 81.97 ± 13.89 mm VAS for AirFluSal\textsuperscript{®} Forspiro\textsuperscript{®} and 79.67 ± 16.48 mm VAS for Seretide\textsuperscript{®} Accuhaler\textsuperscript{®} (data includes 276 patients randomised at baseline to use the devices at a dose of 100 \( \mu \text{g} \)/50 \( \mu \text{g} \)).

Conclusions AirFluSal\textsuperscript{®} Forspiro\textsuperscript{®} shows therapeutic equivalence to Seretide\textsuperscript{®} Accuhaler\textsuperscript{®}, providing a proven combination treatment in an intuitive, easy-to-use device.

THE IMPACT OF OMALIZUMAB ON LUNG FUNCTION AND QUALITY OF LIFE IN PATIENTS WITH SEVERE ALLERGIC ASTHMA IN UK CLINICAL PRACTICE: A MULTI-CENTRE PROSPECTIVE OBSERVATIONAL STUDY – APEX II

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10.1136/thoraxjnl-2015-207770.16

Background A previous retrospective UK study (APEX I) demonstrated omalizumab significantly reduced oral corticosteroid (OCS) use, exacerbations, lung function and quality of life (QoL) in severe allergic asthma (SAA) patients.

Aim This multi-centre observational study was conducted to confirm the observed retrospective findings prospectively.

Methods Retrospective data were collected 12 months prior to and prospective data were collected 12 months following omalizumab initiation in SAA patients ≥16 years. The primary endpoint was the mean daily oral corticosteroid (OCS) dosage. Secondary endpoints included changes in lung function, ACT and AQLQ scores and missed days in education/work and
AUDIT OF THE SAFETY OF BRONCHIAL THERMOPLASTY USING A NATIONAL REGISTER AND HOSPITAL EPISODE STATISTICS

Results 258 patients were enrolled from 22 UK centres (January 2012–February 2015); mean age 44.7 years (±SD 14.2), 65% females, mean asthma duration 25.1 years (±SD 15.1). For the ITT population (n = 235), 82.4% of patients were classified as responders. At 12 months, daily OCS dose significantly decreased by 16% from 10.3 mg/day (±7.1) to 8.7 mg/day (±8.6) (n = 211, p < 0.001) and 61.6% of patients stopped OCS or reduced OCS dose by ≥8.6% (n = 211, p < 0.001). For the ITT population (n = 235), 82.4% of patients were classified as females, mean asthma duration 25.1 years (±SD 15.1) for the 12 months post compared to pre-omalizumab initiation (p < 0.001 n = 118). Comparing the 12 months periods prior to and following initiation of omalizumab, the mean ACT score improved from 9.8 (±4.3) to 14.4 (±5.7) (n = 162, p < 0.001) and the mean AQLQ score improved from 3.2 (±2.0) to 4.4 (±1.5) (n = 161, p < 0.001). There was a significant decrease in missed days from work/education following omalizumab initiation (12 months pre-omalizumab: 14.65 days; 12 months post-omalizumab 6.22 days with p < 0.01; n = 63). For 93 patients unemployed/not in education at the study start, 72 were unemployed/not in education at study end.

Conclusions The data prospectively confirm that omalizumab is associated with significant reduction in OCS use, lung function, ACT score improved from 9.8 (±4.3) to 14.4 (±5.7) (n = 162, p < 0.001) and the mean AQLQ score improved from 3.2 (±2.0) to 4.4 (±1.5) (n = 161, p < 0.001). There was a significant decrease in missed days from work/education following omalizumab initiation (12 months pre-omalizumab: 14.65 days; 12 months post-omalizumab 6.22 days with p < 0.01; n = 63). For 93 patients unemployed/not in education at the study start, 72 were unemployed/not in education at study end.

Introduction and objectives NICE Guidance for bronchial thermoplasty (BT) recommends the collection of long term safety evidence. In this study we assess patient characteristics and safety outcomes using the British Thoracic Society (BTS) UK Difficult Asthma Registry (DAR) and the Hospital Episodes Statistics (HES) database.

Methods BT patient records were extracted from DAR. HES was searched for episodes from 1st April 2011 to 31st January 2015 with OPCS-4 code combinations known to be used for BT; for these patients, inpatient and A&E episodes were extracted in a second search from 1st April 2010 to 31st January 2015.

DAR and HES were reviewed for complications, post-procedure stay, 30-day readmissions and A&E attendances. Using anonymised matching, records from both sources were used to calculate combined safety outcomes. As BT is usually delivered in three treatments, first, second and third BT procedures were analysed separately.

Results Details of 215 BT procedures (83 patients) were extracted from DAR and 203 procedure episodes (85 patients) were extracted from HES, of which 152 procedures (59 patients) matched. In comparison with three clinical trials (AIR, AIR2 and RISA), patients receiving BT in routine clinical practice were on average older, had worse baseline FEV₁ (except for RISA trial) and had lower AQLQ scores (Table 1).

There were no significant differences in outcomes between first, second and third BT procedures; hence rates for all three procedures were combined for the matched cohort (Table 1). In the matched cohort, 27% (41/152) of procedures were associated with a complication, readmission or A&E attendance. This is higher than reported hospitalisation rates for the AIR2 8.4% (16/190) and AIR trials 7.3% (4/55), and comparable with the RISA trial, 26.7% (4/15).

Conclusion We present the safety of BT in routine clinical practice using combined information from a clinical register with good coverage and routine administrative data. It is likely that the clinical practice has been to treat patients with severity levels of asthma comparable to that seen in the RISA trial (high severity), compared to those used in the pivotal trial AIR2 or AIR studies, (moderate to severe), nevertheless these findings warrant further study.
Efficacy of bronchial thermoplasty in clinical practice using the British Thoracic Society UK difficult asthma registry and hospital episode statistics

Introduction and objectives NICE Guidance encourages further research on the efficacy of bronchial thermoplasty (BT). This study used data from the British Thoracic Society (BTS) UK Difficult Asthma Registry (DAR) and the Hospital Episodes Statistics (HES) database to assess aspects of efficacy and compares these with previous trials.

Methods Lung function (FEV1), quality of life (AQLQ), rescue steroid use, healthcare visits and days lost from work/school were compared at BT baseline and 12 month follow-up in patients for whom DAR data were available. In calculating annualised figures, baseline data were assumed to represent 12 months pre-BT, and 12 month follow-up data were scaled according to the time period that the follow-up represented.

Significance testing for differences in FEV1 and AQLQ used a paired t-test. Differences in event counts were tested using non-parametric bootstrap hypothesis tests.

HES was searched for BT episodes from 1st April 2011 to 31st January 2015. An anonymised matching technique was used to link patients in HES and DAR, and for those whom sufficient time had elapsed since BT, HES A&E attendances were compared in the 12 months pre-BT and the 12 months starting from 30 days post-BT (to exclude any transient increases).

Results 31 patients had 12 month follow-ups in DAR, enabling comparison with BT baseline where data were available. All outcomes from DAR showed improvement at 12 month follow-up compared to BT baseline (Table 1). The mean improvement in AQLQ score (0.92) was smaller than that reported in AIR2 compared to BT baseline where data were available. All outcomes from DAR showed improvement at 12 month follow-up compared to BT baseline (Table 1).

Abstract S12 Table 1 Summary of efficacy outcomes

<table>
<thead>
<tr>
<th></th>
<th>BT baseline</th>
<th>12 month follow-up</th>
<th>n</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (DAR)</td>
<td>71.62 ± 19.95</td>
<td>79.14 ± 23.18</td>
<td>21</td>
<td>p = 0.051</td>
</tr>
<tr>
<td>AQLQ (DAR)</td>
<td>3.88 ± 1.15</td>
<td>4.80 ± 1.24</td>
<td>13</td>
<td>p = 0.002</td>
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<tr>
<td>Rescue steroid courses (annualised, DAR)</td>
<td>3.0 [0.0–10.0]</td>
<td>1.99 [0.0–14.04]</td>
<td>22</td>
<td>p = 0.236</td>
</tr>
<tr>
<td>Unscheduled healthcare visits (annualised, DAR)</td>
<td>4.0 [0.0–15.0]</td>
<td>2.65 [0.0–8.94]</td>
<td>20</td>
<td>p = 0.039</td>
</tr>
<tr>
<td>Hospital admissions (annualised, DAR)</td>
<td>2.0 [0.0–6.0]</td>
<td>0.0 [0.0–11.23]</td>
<td>23</td>
<td>p = 0.277</td>
</tr>
<tr>
<td>Days lost from work/school (annualised, DAR)</td>
<td>0.0 [0.0–35.0]</td>
<td>0.0 [0.0–0.0]</td>
<td>11</td>
<td>p = 0.013</td>
</tr>
<tr>
<td>A&amp;E (all causes) attendances (annualised, HES)</td>
<td>2 [1–10]</td>
<td>2.5 [1–4]</td>
<td>12</td>
<td>p = 0.159</td>
</tr>
</tbody>
</table>

Values reported as mean ± SD or median [min–max]; p < 0.05 for statistical significance

Paediatrics: early life influences on lung health

Early persistent childhood wheeze is a risk for more troublesome young adult asthma

Background Until recently being a wheezy infant was not felt to confer significant respiratory health risks in later life. Using the Isle of Wight Birth Cohort (IOWBC) we assessed the association of persistent childhood wheeze with young adult lung function, wheezing status/morbidity, allergic comorbidity and smoking.

Methods The Isle of Wight Birth Cohort (n = 1,456) was reviewed at 1, 2, 4, 10 and 18-years with recording of current wheeze at each visit. At 10-years, 4 separate childhood wheeze phenotypes were defined. Those who wheezed in the first 4-years of life and at 10-years were labelled Persistent-Wheeazers (PW). The outcome of PW was then assessed at 18-years to determine the effects of early life persistent wheeze on adult lung health.

Results Wheezing occurred in 57.7% PW at 18-years. Asthma prevalence in PW fell from 76.0% to 58.2% over adolescence and PW comprised 38% of currently diagnosed asthma at 18-years. PW had significantly impaired lung function at 18-years compared to Non-Wheeazers (NW) who never wheezed in the 1st decade of life. This included impaired FEV1, FEV1/FVC ratio and FEF25–75 along with significantly elevated bronchodilator response (BDR), bronchial hyperresponsiveness (BHR), exhaled Nitric Oxide (FeNO) plus significantly reduced gain in FEF25–75 over adolescence (Table 1).
Compared to NW at 18-years, PW were significantly more likely to have atopy, eczema, and rhinitis (Table 1). Of concern, prevalence of current smoking (44.4%) at 18-years was significantly greater in PW than NW as was passive smoke exposure through the life course (Table 1).

Discussion Our findings highlight young adult respiratory consequences of PW. While there was some outgrowth of disease over adolescence a considerable proportion of PW showed significant airways disease at 18-years. We previously showed that PW already have impaired lung function by 10-years and these further findings suggest that phenomenon tracks through adolescence with possible additional effects on small airways growth. The longer term consequences of that finding allied to the high smoking prevalence in this phenotype merit attention.

Abstract S14 Table 1 Cumulative effect of number of risk variants CHI3L1 rs4950928, MMP9 rs17576, MMP9 rs6073983, MMP12 rs652438 on asthma exacerbations

<table>
<thead>
<tr>
<th>Combined analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of risk variants</td>
</tr>
<tr>
<td>0 (n = 41)</td>
</tr>
<tr>
<td>Hospital admission</td>
</tr>
<tr>
<td>OR</td>
</tr>
<tr>
<td>Oral steroid intake</td>
</tr>
<tr>
<td>OR</td>
</tr>
</tbody>
</table>

Count (%), odds ratio (95% confidence intervals), p values calculated by binary logistic regression adjusted for age, sex and study membership.

Introduction and objectives Single nucleotide polymorphisms (SNPs) in Chitinase 3-like-1 (CHI3L1), Matrix Metalloproteinase 9 (MMP9) and Matrix Metalloproteinase 12 (MMP12) act on the biological process of airway remodelling that is linked to asthma exacerbations. The cumulative presence of these SNPs could help identify patients at increased risk of asthma exacerbations. The aim of this study is to assess whether these genetic variants increase the risk of asthma exacerbations in children and young adults and exert a cumulative effect on this risk.

Methods Gene-environmental interactions were investigated in three observational asthma cohorts (BREATHE, PAGES, PACTMAN), across three European countries (England, Scotland and the Netherlands), and a pooled dataset including, in total 2,701 patients with asthma, aged between 3 and 22 years (recruited between 2003 and 2011). Participants were genotyped for four biologically related SNPs in three genes (CHI3L1, MMP9 and MMP12).

Results In single SNP analysis all four investigated SNPs were associated with markers of asthma severity. In the BREATHE study the four investigated SNPs showed a cumulative association with exacerbations involving the use of a course of oral steroids, asthma-related absence from school/college/work, overall asthma exacerbations (OR for overall exacerbations with four risk variants compared to zero risk variants = 3.14, p < 0.001) and asthma treatment step (p value for trend = 0.036). Furthermore, a combined meta-regression analysis of the four investigated SNPs in the pooled dataset (n = 2701) replicated this cumulative association with exacerbations requiring hospital admission (OR per genotypic step 1.18; p = 0.046) and...
Managing recurrent wheeze in preschool children is problematic, with conflicting evidence on the effectiveness of asthma therapy. One reason is the heterogeneous nature of preschool wheeze: distinguishing “transient viral wheeze” from asthma at presentation is currently impossible. Bronchodilator response (BDR) measured by interrupter resistance (Rint) is greater in preschool children with diagnosed asthma than in healthy controls, but the usefulness of Rint in clinical practice has not been studied. We aimed to assess whether measuring BDR using Rint can predict clinical response to inhaled corticosteroids (ICS).

We studied children aged 2 years to 6 years from seven children at two recruiting centres (the Royal Alexandra Children’s Hospital, Brighton, UK; Hôpital Armand Trousseau, Paris, France). We included children who had not performed baseline Rint before age 4 years (cohort 1) or who had performed baseline Rint before age 4 years (cohort 2). All children had asthma, were monitored for 2 years, and had RRR of 2.9 and 3.1 respectively for EVW at follow-up compared with MTW at baseline. Among children with wheeze at baseline, 58–76% with EVW and 46–67% with MTW were in remission 2 years later (cohort 1) and 14–20% and 4–11% (cohort 2).

MTW had greater reported symptom-severity at all time-points compared with EVW.

When adjusted for symptom-severity, children with EVW at baseline had relative risk ratios (RRR) of 2.9–7.4 and 4.1–15.5 (cohorts 1 and 2 respectively) for EVW and RRR 1.7–2.9 and 1.6–4.0 for MTW at follow-up. Children with MTW at baseline had RRR of 3.1–6.2 in cohort 1 and 3.6–15.6 in cohort 2 for MTW and 1.1–2.7 and 1.4–7.0 respectively for EVW at follow-up.

Conclusions When adjusted for symptom-severity, wheezing phenotypes based on reported triggers remained stable between 2–6 years of age. Symptom-severity may be a more important determinant than triggers of future wheeze classification in young children.
weight, height, ethnicity) and spirometry nearest to 6 years of age because repeatable measurements in a clinical context are feasible at this age. The primary outcome was FEV1% predicted (%p) (GLI reference equation [http://www.lungfunction.org/]) and VS at annual assessment. Between 1–5 scans were performed prior to the age 6 year spirometry, and were independently reported as normal or abnormal (at least one abnormal VS). Statistical analysis was performed using Student t test. P < 0.05 was considered significant.

Results 143/217 children (72 females, 71 males) had data on VS and spirometry available; mean age at first spirometry was 6.36 (range 5.0–7.6). The remaining 73 were excluded due to late diagnosis, moving away before the first reliable spirometry, or first being seen later than the window for ventilation scans (1–5 years). Children with ≥1 abnormal VS had a statistically significant reduction in lung function (mean FEV1% p 83.4%) when compared with children with normal ventilation scans (mean FEV1% p%89.6), P = 0.03 (Figure 1).

Abstract S17 Figure 1 Dot plot showing%p comparison between those with normal and abnormal scans. The black horizontal lines are the group means.

Conclusion Although abnormal VS predict abnormal first spirometry, the overlap between the two groups means that VS are not a useful clinical tool to delineate a high risk group.

Introduction and objectives Ivacaftor, a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator, has demonstrated improved outcomes in patients aged ≥6 years with cystic fibrosis (CF) and a CFTR gating mutation. The phase 3, open-label, 24-week KIWI study assessed safety and pharmacokinetics of ivacaftor (50- or 75-mg granules twice daily [bid]) for weight.

Methods Patients who completed KIWI could enrol in KLIMB (an 84-week, open-label extension study). Dosing was the same as in KIWI for patients aged <6 years; for patients aged ≥6 years, dosing was 150-mg tablets bid.

Results KIWI enrolled 34 patients (mean age, 3.2 years); 33 enrolled in KLIMB. Cough was the most common AE in both KIWI (56%) and KLIMB (64%). Over the total 72-week treatment period, 8 patients had ALT or AST elevations of >8× the upper limit of normal (ULN), 6 of whom had liver function tests (LFTs) >2× ULN at pretreatment baseline. Six of the 8 patients with LFTs >8× ULN had drug interruption; study drug was subsequently resumed. In total, 3 patients permanently discontinued study drug (elevated LFTs, n = 2; needle phobia, n = 1). Improvements in sweat chloride, faecal elastase-1, and immunoreactive trypsinogen were maintained over 72 weeks. Overall improvements from baseline in other exploratory outcome measures were also observed (Table 1).

Conclusions A favourable overall safety profile was demonstrated with ivacaftor during extended follow-up in preschool patients with CF. Reported adverse events were consistent with the known safety profile of ivacaftor; additional monitoring of liver function may be required in this age group, particularly in patients with a history of elevated LFTs. Improvements in markers of pancreatic function and sweat chloride were sustained over the extended follow-up.

Abstract S18 Table 1 Summary of exploratory efficacy outcome measures

<table>
<thead>
<tr>
<th></th>
<th>KIWI (Wk 24)</th>
<th>KLIMB (Wk 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absolute change from KIWI baseline, mean (SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweat chloride, mmol/L</td>
<td>-46.9 (26.2) P &lt; 0.0001</td>
<td>-45.4 (31.3) P &lt; 0.0001</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>1.4 (0.6) P &lt; 0.0001</td>
<td>3.2 (1.1) P &lt; 0.0001</td>
</tr>
<tr>
<td>Weight-for-age z-score</td>
<td>0.2 (0.3) P &lt; 0.0001</td>
<td>0.1 (0.5) P = 0.3</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>0.3 (0.5) P = 0.002</td>
<td>-0.2 (0.7) P = 0.2</td>
</tr>
<tr>
<td>BMI-for-age z-score</td>
<td>0.4 (0.4) P &lt; 0.0001</td>
<td>0.1 (0.5) = 0.5</td>
</tr>
<tr>
<td>Stature, cm</td>
<td>3.3 (1.2) P &lt; 0.0001</td>
<td>10.2 (1.8) P &lt; 0.0001</td>
</tr>
<tr>
<td>Stature-for-age z-score</td>
<td>-0.01 (0.3) P = 0.8</td>
<td>0.1 (0.3) P = 0.01</td>
</tr>
<tr>
<td>Fecal elastase-1, µg/g</td>
<td>99.8 (38.4)</td>
<td>101.9 (152.3)</td>
</tr>
<tr>
<td>Immunoreactive trypsinogen, ng/mL</td>
<td>20.7 (24.0)</td>
<td>-18.9 (28.0)</td>
</tr>
</tbody>
</table>

P values for both KIWI and KLIMB assessed for absolute change from KIWI baseline.

1 Significance was not assessed for these changes.
TIME to change: management of pleural disease

S19 INTERVENTIONS FOR THE MANAGEMENT OF MALIGNANT PLEURAL EFFUSIONS

Aims Malignant pleural effusion (MPE) is a common clinical problem and a number of treatment options are available to manage these patients.

We undertook a systematic review of the literature and meta-analysis in order to ascertain the optimal management strategy for adults with symptomatic MPE.

Methods We searched CENTRAL, MEDLINE, EMBASE, CINAHL; SCI-EXPANDED and SSCI (ISI Web of Science) databases to May 2015. We included randomised controlled trials of intrapleural interventions for adults with symptomatic MPE. Two review authors independently extracted the data and assessed the studies’ risk of bias.

The primary outcome measure was pleurodesis failure rate. Secondary outcome measures were adverse effects and complications, patient reported control of breathlessness, quality of life, cost, mortality, duration of inpatient stay and patient acceptability.

We performed network meta-analysis with random effects to analyse the primary outcome data and those secondary outcomes with enough data. If this was not possible, we reported the results by narrative synthesis.

Results Of the 1888 records identified, 62 randomised trials, including a total of 3428 patients, were eligible for inclusion. All studies were at high risk of bias for at least one domain and the majority were unblinded.

Network meta-analysis evaluating the rate of pleurodesis failure suggested Talc Poudrage to be the most effective method (estimated rank 1 [95% CI 1, 4]). The estimated ranks of the other evaluated methods are shown in the Figure. The estimates were imprecise as evidenced by the wide credible intervals. Both statistical and clinical heterogeneity was high.

Abstract S19 Figure 1 Estimated ranks (95% Cr-I) for each of the pleurodesis methods from the main network meta-analysis.

The secondary outcomes were inconsistently reported. Network meta-analysis was only performed for pain, fever and mortality and minimal evidence was obtained suggesting differences between treatments for these outcomes. Indwelling pleural catheters were examined in two RCTs, both reporting improved breathlessness when compared to Talc Slurry pleurodesis, despite lower pleurodesis success rates.

Conclusions Based on the available evidence, Talc Poudrage may be the optimal method for obtaining a pleurodesis in MPE. However, there is minimal evidence to suggest large differences between the next most effective methods. Global experience of these agents and their adverse events must also be considered when selecting a sclerosant.

S20 PRIMARY RESULT OF THE 1ST THERAPEUTIC INTERVENTIONS IN MALIGNANT EFFUSION (TIME1) TRIAL: A 2 × 2 FACTORIAL, RANDOMISED TRIAL OF CHEST TUBE SIZE AND ANALGESIC STRATEGY FOR PLEURODESIS IN MALIGNANT PLEURAL EFFUSION

Background Optimal management of pleurodesis for malignant pleural effusion (MPE) has not been defined either in terms of optimal analgesia or chest tube size. Non-steroidal anti-inflammatory drugs (NSAID) are highly effective analgesics, but are avoided in pleurodesis as they may reduce pleurodesis efficacy. Smaller (<14 French) chest tubes may be less painful compared to larger chest tubes, but their efficacy in MPE pleurodesis has not been proven. This study investigated chest tube size (large versus small) and analgesia (NSAID versus opiate) in this setting.

Methods A 2 × 2 factorial, phase 3 randomised controlled trial in 320 patients with MPE undergoing pleurodesis. Patients were randomised to opiate/NSAID and 24 French drain/12 French drain. Co-primary outcomes were; pain while tube in situ, measured on 100 mm visual analogue scale (VAS) over 5 days (superiority comparison) and pleurodesis efficacy at 3 months (non-inferiority comparison, margin of non-inferiority 15%). Secondary outcomes included use of rescue analgesia, pleurodesis success to 6 months, adverse events and mortality.

Results 320 patients were randomised (63% male, mean age 71.8 years), with similar baseline characteristics. Mean VAS scores in opiate and NSAID groups were similar (adjusted mean difference, -1.5 mm (95% confidence interval [CI], -5.0 to 2.0; p = 0.40). Patients receiving NSAID required more rescue analgesia (38% vs. 26%). Pleurodesis failure occurred in 33/144 (23%) NSAID patients compared with 30/150 (20%) of participants receiving opiate, meeting criteria (15%) for non-inferiority (difference 3%; (90% CI -3% to 10%)). Smaller chest tubes
were modestly less painful than larger tubes (adjusted mean difference, -6.0 mm (95% CI, -11.7 to -0.2; p = 0.04)) and were associated with a higher pleurodesis failure rate which failed to meet non-inferiority criteria (pleurodesis failure 15/50 (30%) and 12/50 (24%) respectively, difference 6% (90% CI, -9% to 20%)). Adverse events did not differ between analgesic groups, but complications during insertion occurred more commonly with smaller drains (adjusted odds ratio, 1.91; 95% CI 0.71 to 5.13, p = 0.20).

Conclusion NSAID and opiate analgesia were not significantly different in treatment of post-pleurodesis pain and neither was associated with impaired efficacy of pleurodesis. Smaller chest tubes were associated with less pain, but may be associated with reduced pleurodesis success compared with larger tubes. These results challenge current guidelines for pleurodesis of MPE, which advocate avoidance of NSAID and use of small chest tubes.

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**Introduction and objectives** Radiological detection of pleural malignancy (PM) remains challenging. In early-stage Malignant Pleural Mesothelioma (MPM) a pleural effusion may be the only significant abnormality, indistinguishable from benign asbestos-related pleural effusion (BAPE). PM is associated with neovascularisation. We report the diagnostic performance of a novel perfusion-based Magnetic Resonance Imaging (MRI) biomarker of PM – Early Contrast Enhancement (ECE).

**Methods** 24 patients with suspected PM were recruited prospectively. All underwent contrast-enhanced Computed Tomography (CT) scanning, 3T Pleural MRI and Thoracoscopy.

18/24 had complete MRI examinations: T1-weighted 3D-spoiled-gradient-echo sequences acquired at baseline, 40 s, 80 s and 4.5, 9 and 13.5 min after intravenous Gadobutrol contrast. Mean signal intensity (SI) of representative parietal pleura was derived from 15 regions of interest placed by two respiratory physicians. ECE was defined objectively by an early peak in mean SI (≤4.5 min) on the resulting SI/time curve (Figure 1). Morphology suggestive of PM on CT and MRI was recorded by two thoracic radiologists. Diagnostic performance and inter-observer agreement for ECE, MRI and CT morphology were compared. All analyses were blinded.

Pleural SI data were correlated against Microvessel Density (MVD) measured in paraffin-embedded pleural biopsies stained with CD34 and Factor VIII immunostains.

**Results** Mean patient age was 73 (SD 8) years. 18/24 were asbestos-exposed and 12/18 had pleural thickening ≤5 mm. ECE was present in 10/11 patients with PM (MPM (n = 10); lung cancer (n = 1)). The false negative case had MPM. ECE was absent in 6/7 patients with benign pleural disease (BAPE (n = 4); fibrothorax (n = 2), TB (n = 1)). The false positive case had TB.

Overall diagnostic accuracy of ECE, MRI and CT morphology: sensitivity 91%, 91%, 98%; specificity 86%, 71%, 50%; negative predictive value 86%, 83%, 80%; positive predictive value 91%, 83%, 69% respectively. Inter-observer agreement was 0.766 for ECE, 0.727 for MRI and 0.753 for CT.

Figure 1 shows the relationship between MVD and Pleural SI.

**Conclusions** ECE appears an accurate and reproducible, perfusion-based, objective biomarker of PM, out-performing subjectively-defined CT and MR morphology. ECE assessment can be performed in patients with minimal pleural thickening, suggesting potential utility as a biomarker of early-stage MPM or low-volume metastatic PM.

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**VATS FOR PRIMARY SPONTANEOUS PNEUMOTHORAX – A COHORT STUDY OF 1415 PATIENTS**

**Background** Video-assisted thoracic surgery (VATS) is an increasingly common treatment for recurrent or persistent primary spontaneous pneumothorax (PSP). Surgery usually involves a diffuse treatment of the pleura and possible targeted surgical techniques on areas of bullos disease. There is no robust evidence to guide the use of specific surgical techniques. The purpose of this large observational cohort study was to examine the recurrence rates associated with VATS and identify predictors of outcome.
Methods Patients undergoing VATS for PSP at Carlo Forlanini hospital in Rome between January 2000 and December 2012 were prospectively collected. All patients underwent talc poudrage. Targeted surgical techniques were selected based on the presence of air leak and Vanderschueren stage. Patients had regular clinical and radiological follow-up for a minimum of 2 years. Surgical details, demographics and smoking histories were collected at baseline and data on duration of hospital stay, complications and recurrence rates were collated.

Results 1415 patients underwent VATS for PSP during the trial period. The majority of patients were male (76.2%). Median age was 25.3 years (IQR 21.0–29.4). The majority of patients underwent surgery due to recurrent pneumothorax (92.2%). Median length of stay was 5 days (IQR 5–6). 47 patients had incomplete follow up in December 2014 and so complete recurrence data is available for 1368 patients.

Abstract S22 Figure 1

VATS had a low complication rate of 2%, the majority of which was prolonged air leak (1.7%). Recurrent pneumothorax occurred in 26 patients (1.9%) over a median follow up of 8.5 years. Recurrence rates were significantly higher in current smokers at the time of surgery (24/573–4.2%) than in non-smokers (2/796–0.25%) p < 0.001. Bullae suturing (3.9%) and ligation (15%) were associated with statistically significant higher rates of recurrence compared with poudrage alone when controlled for smoking status and Vanderschueren stage.

Conclusions The marked difference in recurrence rates between smokers and non-smokers suggests that this factor is of key importance in predicting recurrence risk after VATS. This study demonstrates a low incidence of recurrence for patients undergoing VATS for PSP. Bullae ligation and bullae suturing appear to be associated with a higher risk of recurrence.

S23 AMBULATORY PERCUTANEOUS LUNG BIOPSY WITH EARLY DISCHARGE AND HEIMLICH VALVE MANAGEMENT OF IATROGENIC PNEUMOTHORAX – A NEW MODEL FOR THE UK

RR Abdullah, AN Tavare, DD Creer, S Khan, R Vancheeswaran, SS Hare. Barnet General Hospital, Royal Free London NHS Foundation Trust, London, UK

Aim To determine if an early discharge radiology-led percutaneous lung biopsy (PLB) service, incorporating ambulatory outpatient small calibre Heimlich valve chest drain (HVCD) to treat pneumothorax, is potentially safe and advantageous to the NHS.

Methods A prospective study of 489 consecutive outpatient image-guided PLBs, performed between March 2011–March 2015, was conducted. Patients were discharged at 30 min if no pneumothorax was present; repeat 60-minute CXR was performed if a small asymptomatic pneumothorax was noted. If stable, patients were discharged. In enlarging or symptomatic pneumothorax, patients were discharged with HVCD in situ and followed up for drain removal. Data on complications was concurrently collected, including pneumothorax rates, numbers of patients requiring HVCD and failed early discharge. A retrospective blinded pulmonary function test (PFT) analysis was also performed at the end of the study period.

Results 489 PLBs were performed with diagnostic accuracy of 97.8%. 402 (82.2%) patients were discharged at 30 min, all without further incident. 87 patients developed pneumothorax (17.8%). 35 patients with a small stable, asymptomatic pneumothorax were discharged at 60 min without complication. 52 patients required HVCD, with 5/52 proceeding to PLB with drain in-situ: 38/52 (73.1%) had drain removal at 24 h and 14/52 (26.9%) at 48 h, with none requiring HVCD greater than 48 h. 4/489 patients were admitted, for social issues.

A blinded retrospective review of PFT data, available in 212/489 patients, revealed 28 with FEV1 <1l. 22/28 (78.6%) were discharged at 30 min without incident; 6/28 patients (21.4%) developed post–PLB pneumothorax with three (10.7%) requiring outpatient HVCD, for 24 h duration.

Conclusion This prospective study of 489 consecutive outpatient PLBs, novel in the NHS setting, provides evidence for a paradigm shift in current UK lung biopsy practice: (i) early discharge PLB, facilitated by use of ambulatory HVCD, is safe and expeditious, thereby enabling more prompt lung cancer diagnosis; and (ii) use of outpatient HVCD is clinically and economically beneficial, saving precious hospital beds whilst also facilitating lung biopsy in severely emphysematous patients with negligible morbidity.

S24 LUNG PARENCHYMAL ASSESSMENT IN PRIMARY AND SECONDARY PNEUMOTHORAX - A CASE-CONTROL STUDY

OJ Bintcliffe, AJ Edey, IS Negus, NA Mackell. University of Bristol, Bristol, UK; North Bristol NHS Trust, Bristol, UK; University Hospitals Bristol NHS Foundation Trust, Bristol, UK

Aim To determine if an early discharge radiology-led percutaneous lung biopsy (PLB) service, incorporating ambulatory outpatient small calibre Heimlich valve chest drain (HVCD) to treat pneumothorax, is potentially safe and advantageous to the NHS.

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Conclusion This prospective study of 489 consecutive outpatient PLBs, novel in the NHS setting, provides evidence for a paradigm shift in current UK lung biopsy practice: (i) early discharge PLB, facilitated by use of ambulatory HVCD, is safe and expeditious, thereby enabling more prompt lung cancer diagnosis; and (ii) use of outpatient HVCD is clinically and economically beneficial, saving precious hospital beds whilst also facilitating lung biopsy in severely emphysematous patients with negligible morbidity.
Introduction Primary pneumothorax has been defined as occurring in patients with no known lung disease but the assumption that the underlying lung is normal is increasingly contentious. The purpose of this case-control study is to evaluate lung structure and quantify the extent of any emphysema in patients with primary and secondary spontaneous pneumothorax compared with a control group without pneumothorax and to assess the influence of smoking on this process.

Methods 20 patients with primary pneumothorax (PSP), 20 patients with secondary pneumothorax (SSP) and 40 control patients with computed tomography scans suitable for quantitative analysis were evaluated. Demographics and smoking histories were collated. Quantitative evaluation of low attenuation areas of the lung was performed using semi-automated software. The percentage of segmented lung below the low attenuation threshold value of -950 Hounsfield units was calculated, based on a previously validated threshold. The extent of emphysema-like destruction was also assessed visually by an experienced consultant chest radiologist.

Results The extent of emphysema and percentage low attenuation area was greater in PSP patients compared with controls matched for age and smoking history (Median 0.25 vs 0.00, p = 0.019) and was also higher in SSP compared with PSP patients (16.15 vs 0.25, p < 0.001). PSP patients who smoked had significantly greater low attenuation area than PSP non-smokers (0.7 vs 0.1, p = 0.034). No such difference was detected between smokers and non-smokers within the control group (0.0 vs 0.05, p = 0.798).

Conclusions The majority of patients with PSP had quantifiable evidence of parenchymal destruction and emphysema. The presented data is supportive of the hypothesis that there is likely to be a spectrum of lung damage ranging from ‘normal patients’ through to patients with SSP, and rather than a clear distinction between PSP and SSP these conditions exist on a continuum.

REFERENCE

Sleep apnoea and hypoventilation: screening and treating high risk populations

ESTABLISHING A NORMAL RANGE IN DRIVING SIMULATOR PERFORMANCE USING STANDARD DEVIATION OF LANE POSITION (SDLP) IN AN ADVANCED PC-BASED DRIVING SIMULATOR (MINIUOLDS)

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Introduction Some patients with OSAS are at higher risk of being involved in road traffic accidents. No objective tests have been shown to predict reliably whether an individual is safe to drive or not and there is significant variation in the advice given by the clinicians. Using a continuously measured variable (SDLP) on an advanced PC-based driving simulator the at risk patients can be identified with a high degree of accuracy. We have now compared driving performance based on SDLP in controls and untreated OSAS patients and have established a normal range.

Methods 129 untreated male OSAS patients (Age 53 +/-12, ESS 14 +/-5, ODI 41 +/-26, BMI 36 +/-8,) and 79 male controls (Age 56 +/-15, ESS 4 +/-3, BMI 28 +/-8) were recruited in the study. All performed a simulator run after initial acclimatisation. The simulator run consisted of eight epochs and on average needed 7 min to complete one epoch driving at 70 miles per hour. The simulator layout was designed in line with the UK highways agency road standards. The mean SDLP in epoch-3 (SDLP3) was compared between the two groups using unpaired T-test. The SDLP3 in the patient group was evaluated and this was compared with the mean and 95th centile values of SDLP 3 among the controls.
Results There was a significant difference in SDLP3 between OSAS patients and controls (0.44 vs 0.39, P = 0.03), 10% of patients had worse SDLP3 than the 95th centile among controls (Figure 1).

Conclusions Worse SDLP is a marker of poor driving performance and this is significantly worse in untreated OSAS patients as compared to controls. The choice of 95% is arbitrary but is consistent with the approach taken to establish a normal range. Establishing where a patient lies in comparison to controls may be useful in advising patients whether they are at increased risk of an accident due to OSAS. Defining a normal range based on continuously measured variable in MiniUoLDS holds promise be useful in advising patients whether they are at increased risk of an accident due to OSAS. Defining a normal range based on continuously measured variable in MiniUoLDS holds promise of an accident due to OSAS. Defining a normal range based on continuously measured variable in MiniUoLDS holds promise.

Abstract S26 Table 1 Patient numbers for those with and without OHS, showing time spent with saturations less than 90%

<table>
<thead>
<tr>
<th>OHS (on biochemistry)</th>
<th>Satuations ≤90%</th>
<th>≤30% of night</th>
<th>Saturations ≤90%</th>
<th>≤30% of night</th>
</tr>
</thead>
<tbody>
<tr>
<td>No OHS</td>
<td>32</td>
<td>TRUE POSITIVE</td>
<td>22</td>
<td>FALSE NEGATIVE</td>
</tr>
<tr>
<td>Saturations ≤90%</td>
<td>72</td>
<td>FALSE POSITIVE</td>
<td>64</td>
<td>TRUE NEGATIVE</td>
</tr>
</tbody>
</table>

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S27 PREDICTIVE PERFORMANCE OF STOPBANG QUESTIONNAIRE FOR DIAGNOSIS OF SLEEP APNOEA IN A CARDIAC SURGICAL COHORT

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10.1136/thoraxjnl-2015-207770.33

Introduction and objectives Questionnaires to assess the risk of obstructive sleep apnoea (OSA) prior to surgery could reduce the need for screening sleep studies. STOPBANG questionnaire is user friendly and was previously validated in a general surgical population. A high risk of OSA has been defined as a score of ≥3 and low risk as a score 0–2. We aimed to validate the STOPBANG against nocturnal oximetry in a population undergoing major cardiac surgery and assessed its prognostic value for post-operative outcomes.

Methods Patients were screened for high risk of OSA with the STOPBANG questionnaire. The presence of sleep apnoea (SA), prior to surgery, was assessed with overnight oximetry. SA was defined as mild with a 4% oxygen desaturation index (ODI) of 5–14/hr, moderate with ODI of 15–29/hr and severe ODI ≥30/hr. Predictive performance of STOPBANG against nocturnal oximetry was assessed for diagnosis of mild and moderate SA by assessing the area under curve receiver operating characteristic (AUC-ROC) and sensitivity and specificity were calculated. A multiple-logistic regression model was used to assess association of STOPBANG and post-operative outcomes.

Results The AUC-ROC for mild SA was low 0.57 (95% CI = 0.47–0.67). Good performance was observed for moderate SA with AUC-ROC 0.82 (95% CI = 0.69–0.95) (Figure 1) but specificity of STOPBANG at the conventional cut of value of ≥3 for moderate SA was very low at 5% whilst sensitivity was 100%. The best predictive STOPBANG cut-off value for moderate SA was ≥6 with sensitivity and specificity of 75% and 77% respectively. Assessing predictive value for severe SA was not possible due to the lack of severe SA cases in our cohort. STOPBANG was not found to be an independent predictor of worse post-operative outcomes.
Abstract S27 Figure 1 ROC curves for STOPBANG to predict ODI ≥ 5 and ODI ≥ 15

Conclusion Predictive performance of STOPBANG in our patient cohort at the conventional cut off value was poor. The probable explanation is that the cardiac surgical population is preselected as male, older and most suffer with hypertension. Thus the majority will score as high risk for OSA. STOPBANG had no prognostic value on worse postoperative outcomes in our study, which again contrasts with the findings in general surgical cohorts.

S28 EFFECT OF SLEEP APNOEA ON POST-OPERATIVE OUTCOMES IN CARDIAC SURGERY

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10.1136/thoraxjnl-2015-207770.34

Introduction and objectives Obstructive sleep apnoea (OSA) is common and can be associated with adverse health outcomes. There are conflicting data for the impact of undiagnosed OSA on the outcome of surgical procedures but at least some results suggest an association with worse outcomes. EuroSCORE risk model was developed to calculate the risk of mortality after cardiac surgery. We evaluated the prevalence and impact of undiagnosed sleep apnoea (SA) on postoperative outcomes in cardiac surgery.

Methods Patients undergoing coronary artery bypass grafting with or without cardiac valve surgery were screened for the presence of SA, prior to surgery, with the STOPBANG questionnaire and overnight oximetry. SA was defined as a 4% oxygen desaturation index (ODI) of ≥ 5/hr. A Weibull model was used to analyse lengths of stay (LoS) in intensive care unit (ICU). Complications in ICU were dichotomised and analysed with binary logistic regressions. Parsimonious models were obtained using a combination of step-wise regression and manually removing predictors that did not reach the 5% significance level.

Results 122 subjects were included in final analysis of which 57 (47%) had a new diagnosis of SA. Of those, 45 (79%) had mild SA and 12 (21%) had moderate/severe SA. There was no simple relationship between OSA as measured by ODI and LoS in ICU. The most significant predictor for ICU LoS was developing complications at ICU (p < 0.001). The independent predictors associated with increasing likelihood of developing major organ complications following cardiac surgery were EuroSCORE, ODI and intravenous opioid analgesia (IOA). When patients with mild and moderate SA received IOA, predicted probability of complications rose 2.4 and 1.4 times respectively (Figure 1).

Abstract S28 Figure 1 Predicted probabilities and 95% CI of suffering a complication at ICU as ODI increases for individuals with average EuroSCORE (5) and with or without IOA

Conclusion We found a high prevalence of undiagnosed sleep apnoea in our cohort. EuroSCORE, SA and the administration of intravenous morphine were found to be independent risk factors for developing post-operative complications. This risk has increased when patients with SA received intravenous morphine.

S29 PREDICTORS OF CONTINUOUS POSITIVE AIRWAYS PRESSURE USAGE AT SIX MONTHS IN MINIMALLY SYMPTOMATIC PATIENTS. FURTHER DATA FROM THE Mosaic Trial

1CD Turnbull, 2DJ Bratton, 3SE Craig, 2M Kohler, 1JR Stradling. 1Oxford Centre for Respiratory Medicine and NIHR Oxford Biomedical Research Centre, Oxford, UK; 2University Hospital Zurich, Zurich, Switzerland; 3Aintree Chest Centre, Liverpool, UK

10.1136/thoraxjnl-2015-207770.35

Introduction Severity of OSA and early patterns of CPAP usage have previously been shown to determine subsequent long term CPAP use in patients with symptomatic moderate-to-severe disease. We wished to see if different factors influenced compliance in minimally symptomatic patients.

Methods Patients were randomised to 6-months of CPAP or standard care if they had an ODI of > 7.5 h due to OSA on a baseline sleep study, but had insufficient daytime OSA symptoms to mandate CPAP. Baseline characteristics (Table 1), medical history, ESS, SAQLI and SF-36 were recorded. Repeat overnight pulse oximetry was performed after entry for uniformity of trial ODI across recruiting centres.
CPAP usage data were downloaded at the 2–4 week assessment, and at the 6 month assessment. Those who withdrew were assumed to have 0:00 h/n usage.

Correlations were calculated between CPAP usage at the 6 month assessment and both the baseline characteristics and to the 2–4 week CPAP usage data.

**Abstract**

Table 1: Baseline characteristics from all 195 patients randomised to CPAP with 6 month follow-up data

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean (SD); Median (IQR) or Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean; SD)</td>
<td>57.9 (7.2); 45–75</td>
</tr>
<tr>
<td>Gender (number male;%)</td>
<td>153 (78.5%); -</td>
</tr>
<tr>
<td>Ethnicity (number white;%)</td>
<td>188 (96.4%); -</td>
</tr>
<tr>
<td>BMI (mean kg/m²; SD)</td>
<td>32.2 (5.6); 21.6–51.6</td>
</tr>
<tr>
<td>Smoking status (number;%)</td>
<td>17 (8.7%); -</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>102 (52.3%); -</td>
</tr>
<tr>
<td>Never smoker</td>
<td>76 (39%); -</td>
</tr>
<tr>
<td>Reported snoring (number yes;%)</td>
<td>190 (97.4%); -</td>
</tr>
<tr>
<td>Reported apnoeas (number yes;%)</td>
<td>142 (72.8%); -</td>
</tr>
<tr>
<td>Reported choking (number yes;%)</td>
<td>66 (33.8%); -</td>
</tr>
<tr>
<td>Reported nocturia (number yes;%)</td>
<td>114 (58.5%); -</td>
</tr>
<tr>
<td>Oxygen desaturation index (ODI, median; IQR)</td>
<td>10.2 (4.7, 17.5); 0.5–58.0</td>
</tr>
<tr>
<td>Epworth Sleepiness Score (ESS, mean; SD)</td>
<td>7.9 (4.4); -18</td>
</tr>
<tr>
<td>Short sleep apnoea quality of life index (SAQLI, mean; SD)</td>
<td>4.9 (1.1); 2.3–6.9</td>
</tr>
<tr>
<td>SF-36 Physical Summary (mean; SD)</td>
<td>42.0 (12.3); 9.4–61.3</td>
</tr>
<tr>
<td>SF-36 Mental Summary (mean; SD)</td>
<td>48.1 (10.3); 19.9–61.7</td>
</tr>
</tbody>
</table>

**Results**

Median CPAP usage at 2–4 week follow-up was low at 2:49 h/n (n = 174, IQR 0–44, 5:13). Median usage at 6 month follow-up was 2:17 h/n (n = 195, IQR 0:08, 4:54).

At 6 months males had significantly greater mean usage at 2:56 h/n compared to 1:47 h/n in females (95% confidence intervals of the difference, -1.49 to -0.09 h/n, p = 0.02). There were no other significant predictors of 6 month usage (age, BMI, ODI, ESS, sleep symptoms, smoking status, ethnicity, SAQLI, SF-36).

Average usage of CPAP at 2–4 week assessment was moderately correlated with the average usage at the 6 month assessment (r = 0.76, p < 0.001).

**Conclusions**

Male gender predicted greater CPAP usage at 6 months, but no other baseline characteristics were predictive of CPAP usage in these minimally symptomatic patients with generally mild OSA. 2–4 week CPAP usage was predictive of 6 month usage, but by no means could all patients’ usage be predicted at such an early stage. Thus in clinical practice, trials of CPAP are necessary in patients with minimally symptomatic OSA but it may be necessary for patients to try CPAP for longer than 1 month to determine those benefitting from treatment in the long term.

**References**

1. Thorax 2010;65:829–32
2. Thorax 2012;67:1090-66

**S30 NUTRITION AND EXERCISE REHABILITATION IN OBESITY HYPOVENTILATION SYNDROME (NERO): A PILOT RANDOMISED CONTROLLED TRIAL**


**Introduction**

We have previously shown that treatment of obesity hypoventilation syndrome (OHS) with non-invasive ventilation (NIV) results in weight reduction and an increase in physical activity (Murphy et al., 2012). We therefore hypothesised that a multi-modal rehabilitation programme, in addition to NIV, would lead to enhanced weight loss.

**Method**

We conducted a randomised controlled trial of NIV alone vs. NIV and a personalised rehabilitation programme in patients with OHS. Subjects in the intervention group received a bespoke diet and exercise regime, from a dietician and physiotherapist. All patients, in both groups, were reviewed monthly for 3 months. Anthropometrics, exercise capacity and health related quality of life (HRQL) were measured at baseline and at 3 months. The primary outcome measure at 3 months was weight loss. Secondary outcomes included: body mass index (BMI), neck circumference (NC), waist circumference (WC), hip circumference (HC) blood pressure (BP), rectus femoris cross-sectional area (RFCSA) and quadriceps maximal voluntary contraction (QVCMC), 6 min walk distance (6MWD) and HRQL measures.

**Results**

37 subjects were randomised with data from 30 patients analysed at 3 months (15 in each group). There were no differences between the groups in all parameters measured at baseline. The intervention group showed greater weight loss than the control group (-11.9 ± 6.7 vs. -2.4 ± 6.2 kg; p < 0.0001). There were also differences in NC, WC and HC (all p < 0.001, Table 1) with an improvement in BP observed in the intervention group (Table 1). In addition, there was an increase in weight corrected RFCSA and muscle strength (p < 0.0001, Table 1) with an increase in 6MWD in the intervention group (122 ± 161 vs. 46 ± 60 m; p = 0.005; Table 1). Finally, HRQL improved in the intervention group as evidenced by a greater reduction in Epworth sleepiness score, an increase in severe respiratory insufficiency questionnaire sum score and a greater decrease in the hospital and anxiety depression score (Table 1, all p < 0.0001).

**Conclusion**

In patients with OHS, the addition of a hospital home hybrid personalised diet and exercise programme to standard NIV was shown to enhance weight loss as well as, skeletal muscle area and strength, exercise capacity and HRQL.

**Reference**

### Abstract S30 Table 1  
Changes in anthropometrics, blood pressure, peripheral muscle area, peripheral muscle strength and exercise capacity

<table>
<thead>
<tr>
<th></th>
<th>Control Group</th>
<th>Intervention Group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>3 Month</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 Month</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>ANTHROPOMETERS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>141.2±30.7</td>
<td>138.8±34.6</td>
<td>139.3±28.8</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>50.8±7.5</td>
<td>50.3±8.5</td>
<td>51.4±8.2</td>
</tr>
<tr>
<td>NC (cm)</td>
<td>44.0</td>
<td>44.0</td>
<td>48.0</td>
</tr>
<tr>
<td>(42.0–48.0)</td>
<td>(41.0–47.5)</td>
<td></td>
<td>(38.0–49.4)</td>
</tr>
<tr>
<td>WC (cm)</td>
<td>135.5</td>
<td>137.0</td>
<td>132.0</td>
</tr>
<tr>
<td>(129.5–142.0)</td>
<td>(122.0–143.6)</td>
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<td>(127.0–141.6)</td>
</tr>
<tr>
<td>HC (cm)</td>
<td>151.5</td>
<td>151.0</td>
<td>149.0</td>
</tr>
<tr>
<td>(145.3–162.3)</td>
<td>(137.9–160.1)</td>
<td></td>
<td>(134.9–163.7)</td>
</tr>
<tr>
<td><strong>CARDIOVASCULAR</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>125</td>
<td>127</td>
<td>124</td>
</tr>
<tr>
<td>(113-142)</td>
<td>(114-139)</td>
<td></td>
<td>(110-139)</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>69</td>
<td>78</td>
<td>75</td>
</tr>
<tr>
<td>(61-81)</td>
<td>(71-81)</td>
<td></td>
<td>(65-87)</td>
</tr>
<tr>
<td><strong>MUSCLE MASS, MUSCLE STRENGTH &amp; EXERCISE CAPACITY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RF&lt;sub&gt;CSA&lt;/sub&gt;/weight (AU)</td>
<td>8.2 (6.5-9.6)</td>
<td>8.2 (6.1-9.5)</td>
<td>7.7 (6.8-8.5)</td>
</tr>
<tr>
<td>QMVC (kg)</td>
<td>24.5 (16.5-34.3)</td>
<td>25.5 (18.8-35.4)</td>
<td>26.5 (16.7-29.4)</td>
</tr>
<tr>
<td>6MWD (m)</td>
<td>165 (100–288)</td>
<td>275# (123–343)</td>
<td>200 (100–320)</td>
</tr>
<tr>
<td><strong>HEALTH RELATED QUALITY OF LIFE</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESS</td>
<td>12 (8-16)</td>
<td>10# (5-15)</td>
<td>11 (7-14)</td>
</tr>
<tr>
<td>SRI SS</td>
<td>54 (38-69)</td>
<td>49 (42-70)</td>
<td>65 (50-67)</td>
</tr>
<tr>
<td>HAD</td>
<td>13 (10-23)</td>
<td>12 (9-18)</td>
<td>12 (7-18)</td>
</tr>
</tbody>
</table>

Abbreviations: BMI=body mass index; NC=neck circumference; WC=waist circumference; HC=hip circumference; BP=blood pressure; 6MWD=six minute walk distance; RF<sub>CSA</sub>=rectus femoris cross sectional area; QMVC=quadriceps maximal voluntary contraction, ESS=Epworth sleepiness score; SRI SS=severe respiratory insufficiency questionnaire sum score; HAD=Hospital anxiety and depression scale. Data are presented as mean±SD or median (IQR).

∗denotes significant difference from baseline p<0.05, as determined by Wilcoxon Signed Rank test

∗denotes significant difference between groups as determined by ANCOVA
Interventional progress

**S31** SAFETY AND YIELD OF PHYSICIAN LED ULTRASOUND GUIDED TRANSTHORACIC LUNG/PLEURAL BIOPSIES

R Reddy, M Naeem, G Tsaknis. Kettering General Hospital, Kettering, UK

10.1136/thoraxjnl-2015-207770.37

**Introduction** Transthoracic ultrasound is important tool in assessing pleural effusions and guiding placement of chest drains. It also demonstrates pleural-based masses and lung tumours abutting the pleura. Such lesions are suitable for ultrasound guided full core needle biopsy. Percutaneous transthoracic lung biopsy with ultrasound guidance is not widely performed by respiratory physicians.

**Objective** To assess safety and yield of ultrasound guided transthoracic biopsy performed by respiratory physicians.

**Methods** The procedures were carried out in an outpatient or bed side setting between April 2014 and Jun 2015. Apart from checking clotting and omitting antplatelet/anticoagulants no special prior preparations were undertaken. Under real time transthoracic ultrasound, lesions involving pleura or abutting the pleura which were >1.5 cm were sampled 2–3 times with a full core biopsy needle (Biopince 18G). Repeat thoracic ultrasound was done after 10 min to check for pneumothorax. Patients were discharged home around 30 min post procedure.

**Results** 51 patients underwent full core biopsy for suspected peripheral lung (44), pleural based (6) and Mediastinal tumours (1). The biopsies were considered adequate in 47 cases (94%). Diagnosis was achieved in 43 patients with an overall yield of 84% (Table 1) whilst the yield for malignancy was 82% (36/44). Of the 8 patients with a negative biopsy, malignancy was diagnosed at surgery in 2 patients and CTGB (CT guided biopsy) in 6 patients. Complications were minimal with one patient developing a small pneumothorax (2%) and another had a small subcutaneous hematoma. After the introduction of the service the waiting list for CT guided biopsies in our hospital has been eliminated.

<table>
<thead>
<tr>
<th>Abstract S31 Table 1</th>
<th>Malignant</th>
<th>Benign</th>
<th>Nondiagnostic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>36 (70%)</td>
<td>7 (14%)</td>
<td>8 (16%)</td>
</tr>
<tr>
<td>(n = 51)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Vasculitis 1, TB 1,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non specific inflammation 3, other 2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(All proven malignan</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>ct)</td>
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</table>

**Conclusion** Ultrasound guided peripheral lung/pleural mass biopsy can be performed by trained respiratory physicians with excellent yield and very low complication rate. Used appropriately it reduces the waiting list for CTGB.

**REFERENCE**


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**Spoken sessions**

**S32** VIRTUAL BRONCHOSCOPIC NAVIGATION FOLLOWED BY RADIAL EBUS TO BIOPSY PERIPHERAL PULMONARY LESIONS: A PILOT STUDY

N Denny, J Mills, L Brown, SJ Fowler, M Murrayaw. Department of Respiratory Medicine, Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK

10.1136/thoraxjnl-2015-207770.38

**Introduction** Detection of peripheral pulmonary lesions (PPLs) is on the rise but an accurate means of obtaining a tissue diagnosis without high risk of complications is lacking. Virtual bronchoscopic navigation (VBN) guides the bronchoscope under direct vision and, in combination with radial endobronchial ultrasound (R-EBUS) or ultrathin bronchoscopy, may enhance the diagnostic yield of PPLs with a minimal complication rate.

**Aims**

To pilot the use of VBN in the diagnosis of PPLs. To identify patient and lesion characteristics that predict successful VBN.

**Methods** Images from chest CT (slice width 1–1.25 mm) were acquired from patients, and lesion features, including location and presence of a bronchus sign (bronchus contained within PPL), were recorded. CT images were transferred to a portable workstation and Lungpoint Broncus © was used to create a virtual pathway to the PPL. Bronchoscopy was performed with VBN followed by R-EBUS guidance, under conscious sedation, and biopsies obtained. Pre-procedure characteristics, biopsy adequacy, biopsy outcome, 30-day follow up and complications were recorded.

**Results**

The median age of our cohort (n = 7) was 79 and all patients had one or more comorbidities. PPL median size was 28 mm and all were located in sub-segmental bronchi. VBN guided the operator to the correct site in six cases. Adequate biopsies were taken from five patients; four had a positive bronchus sign. Three adequate biopsies received a diagnosis of primary lung cancer; those remaining were negative. One patient with inadequate biopsies underwent transthoracic needle biopsy (TTNB) and was diagnosed with primary lung cancer. No complications occurred in spite of the significant co-morbidity of this patient cohort.

<table>
<thead>
<tr>
<th>Abstract S32 Table 1</th>
<th>Baseline characteristics, biopsy outcome and final diagnosis (n = 7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years, median and range)</td>
<td>79 (67–84)</td>
</tr>
<tr>
<td>Male (n, %)</td>
<td>3 (43)</td>
</tr>
<tr>
<td>Lesion size (mm, median and range)</td>
<td>28 (16–47)</td>
</tr>
<tr>
<td>Location (lobe and n)</td>
<td>Rt upper lobe 2</td>
</tr>
<tr>
<td>Biopsy quality (n, %)</td>
<td>Adequate 5 (71)</td>
</tr>
<tr>
<td>Biopsy outcome</td>
<td>Positive 3</td>
</tr>
<tr>
<td>Final diagnosis</td>
<td>Primary lung cancer 4</td>
</tr>
</tbody>
</table>
tarnished by a high complication rate and is not suitable in patients with significant co-morbidity. Therefore, VBN and R-EBUS are particularly useful where TTNB carries a high risk.

REFERENCES

PERFORMANCE OF EBUS-TBNA IN THE PATHOLOGICAL SUBTYING AND MOLECULAR TESTING OF NON-SMALL CELL LUNG CANCER (NSCLC) IN A UK THORACIC ONCOLOGY CENTRE
H Al-Najjar, M Evison, J Martin, P Barber, P Cobsie, R Booton. University Hospital of South Manchester, Manchester, UK
10.1136/thoraxjnl-2015-207770.39

Introduction The categorisation of NSCLC into squamous and non-squamous subtypes is an important requirement for the optimisation of patient care as this may modify chemotherapy regimens and direct molecular testing. The lung cancer national audit highlights the need to minimise the rate of NSCLC not otherwise specified (NSCLC-NOS).1 The aim of our study was to determine whether samples obtained by endobronchial ultrasound guided-transbronchial needle aspiration (EBUS-TBNA) could be used to pathologically subtype NSCLC and provide sufficient material for molecular testing.

Methods A prospectively maintained database of consecutive patients with suspected lung cancer referred to our unit, a UK regional thoracic oncology centre, was analysed. All patients diagnosed with NSCLC by EBUS-TBNA cytology at our centre between Sept 2013 and Sept 2014 were included in the study.

Results A total of 89 patients were diagnosed with NSCLC using EBUS-TBNA. The pathological subtypes were: n = 46 (51.7%) squamous cell carcinoma, n = 41 (46%) adenocarcinoma and n = 2 (2.2%) NSCLC-NOS. All samples with a new diagnosis of non-squamous subtype were sent for EGFR mutation analysis, with sufficient material in 97% (n = 35/36) and one activating mutation was identified. ALK analysis was successfully performed in all 5 samples in which this was requested. Additional molecular testing was requested in 9 samples with sufficient material in 89% (n = 8/9).

Conclusions EBUS-TBNA cytology can be used to successfully subtype NSCLC and provide adequate material for molecular testing in the majority of cases. The rate of NSCLC-NOS in our study (2.2%) compares favourably with local cancer network figures (13.5%) and national (12.9%) figures.

REFERENCE

METHYLENE BLUE STAINING DIFFERENTIATES NON-SMALL CELL LUNG CANCER TISSUE
P Riddell, 2EL Molloy, 2S Finnegan, 2EP Judge, 1KC Redmond, 1N Mulligan, 2M Maguire, 2S O’Dea, 2J Egan. 1Mater Misericordiae University Hospital, Dublin, Ireland; 2Maynooth University, Maynooth, Ireland
10.1136/thoraxjnl-2015-207770.41

Introduction The early detection of lung cancer during bronchoscopy remains a diagnostic challenge. Chrom bronchoscopy, using vital dyes, has the potential to aid diagnosis by highlighting areas of dysplastic or malignant change. There are limited numbers of studies in this field but results to date are conflicting. Using a novel electrospray system, we delivered targeted methylene blue (MB) to ex vivo human lung cancer tissue. The aim of this study was to identify whether MB provided a differential stain for lung cancer.

Methods Patients undergoing surgical resection were consented to the study. Following lobectomy, fresh sections of cancerous and non-cancerous tissue were obtained. A range of concentrations of MB were applied topically to tissue sections by electrospray atomisation. Following delivery of MB, the tissue was washed with 0.9% saline and images captured. Results were classified in terms of intensity of dye uptake as well as differential staining between normal and cancerous tissue.
Weekly Audiograms Pre-emptively Identify Amikacin Related Ototoxicity in MDR-TB

1A, 1S, 2OM, 3SM, 4D, 5T, 6R, 7L, 1GH. 1London North West Healthcare NHS Trust, London, UK; 2Imperial College London, UK; 3University of Bristol, Bristol, UK; 4Imperial College, London, UK; 5University of Cambridge, Cambridge, UK; 6London Healthcare Trust, London, UK; 7Homerton University Hospital NHS Foundation Trust, London, UK; 8King’s College London, London, UK

Introduction and objectives
Updated WHO guidance recommends at least 8 months of aminoglycoside (AG) for MDR-TB but provides no definitions or monitoring strategies for ototoxicity. Most UK centres perform 2–4 weekly audiograms; we perform weekly audiograms. We retrospectively investigated whether this strategy pre-emptively identifies ototoxicity before significant hearing loss (HL) is evident.

Methods
Patients we treated with amikacin for MDR-TB from 2002–2015, with at ≥4 weekly pure tone audiograms, were included. Audiograms, treatment duration, symptoms, creatinine clearance and outcome were obtained from clinical records. All patients received amikacin at 15 mg/kg per day and had weekly amikacin levels and renal function. Definition of HL was defined as per the ASHA as ≥20 dB loss of pure tone threshold from baseline at one frequency or ≥10 dB at two adjacent frequencies.

Results
31 MDR-TB patients fulfilled selection criteria; 15 female, median age 36 years (IQR: 24–43) and median weight 61.5 kg (IQR: 52–65). 22/31 (70.9%) patients had their first audiogram within 10 days; median 5.5 (IQR: 4–7). The median duration of amikacin treatment was 79.5 days (IQR: 61.75–94) and median total dose of 70.8 g (IQR: 44.4–97.75). 4/31 (12.9%) had moderate-severe baseline hearing loss (HL). A total of 17 (54.8%) patients met the ASHA definition of HL: 7 at 4 kHz, 10 at 6 kHz and 17 at 8 kHz. The median time to meeting ASHA definition of HL among these patients was 59 days (IQR: 41–84.75). 16/31 (51.6%) patients stopped amikacin earlier than planned and 1 continued; 2 (6.5%) due to symptoms of deafness, 2 (6.5%) due to tinnitus and 12 (38.7%) due to asymptomatic high frequency HL on audiograms. Creatinine clearance and trough amikacin levels remained within range for all patients. Regarding outcomes, 17 (54.8%) completed TB treatment, 5 (16.1%) remain on treatment, 4 (12.9%) transferred, 3 (9.7%) were lost to follow up and 1 (3.2%) died.

Conclusions
AGs are important in the treatment strategy of MDR-TB but this must be balanced with the long-term side effects. The ototoxicity of AGs is unrelated to elevated drug levels or contributing factors and is a common adverse effect. Weekly audiograms led to earlier detection of pre-symptomatic amikacin ototoxicity and cessation in 38.7% of patients.
had a highly variable cough frequency during the first 8 weeks of treatment. There was no evidence for an effect of isoniazid resistance, cavitary disease, smear status or smoking on early rates of cough resolution, although there was a trend towards relatively higher cough frequencies in smokers than non-smokers at the end of treatment ($p = 0.100$).

Abstract S37 Figure 1 Objectively-measured cough frequency during treatment of pulmonary tuberculosis

Conclusions Objective cough frequency measurement is feasible in tuberculosis and could provide a novel biomarker of treatment response.

S38 PREDICTIVE ACCURACY AND CLINICAL IMPACT OF XPERT MTB/RIF FOR THE DIAGNOSIS OF SPUTUM SMEAR-NEGATIVE PULMONARY TUBERCULOSIS USING BRONCHOALVEOLAR LAVAGE FLUID

W Ho, DW Connell, A Singanayagam, A Singanayagam, H Donaldson, OM Kon.
Imperial College School of Medicine, Imperial College London, London, UK; St. Mary’s Hospital, Imperial College Healthcare NHS Trust, London, UK

Introduction Sputum smear-negative pulmonary tuberculosis (TB) is increasingly prevalent with bronchoalveolar lavage (BAL) frequently used for diagnostic sampling. Direct molecular testing has reported higher sensitivities compared to smear microscopy. This study aims to assess the predictive accuracy and clinical impact of Xpert MTB/RIF; a PCR-based cartridge assay used to identify M.tbc in BAL fluid samples.

Methods A retrospective evaluation of adult patients ($n = 293$) with suspected pulmonary TB who underwent BAL in a tertiary centre in London between January 2011 and December 2014 were collected. MTB/RIF, smear microscopy, and liquid culture were performed on all sets of BAL fluid. The impact of MTB/RIF on time to TB diagnosis and anti-TB treatment initiation were recorded as markers of clinical impact.

Results 57/293 (19.5%) patients had BAL culture-positive TB for which a significantly higher proportion had positive MTB/RIF results compared to smear microscopy (77.2%; 95% CI 63.8%–86.8% vs. 38.6%; 95% CI 26.3%–52.4%; $p < 0.001$). The specificity of MTB/RIF was 95.7% (92.1%–97.8%) with a negative predictive value (NPV) of 94.6% (90.7%–97.0%), 22/57 (38.6%) culture-positive patients had negative smear microscopy results but positive MTB/RIF results.

Conclusion MTB/RIF used in BAL samples had a higher and more rapid diagnostic accuracy compared to smear microscopy and could replace routine smear microscopy in pulmonary TB diagnosis.

S39 PRELIMINARY RESULTS OF A LATENT TUBERCULOSIS SCREENING AND TREATMENT PROJECT AND THE ROLE OF TB SERVICES IN SECONDARY CARE


Introduction Since July 2014, the London Borough of Newham has offered latent tuberculosis (TB) screening to all recent migrants (residing in the UK less than 5 years), aged 16–50 years, from countries with a TB incidence of greater than 150/100 000 cases/year. All migrants are offered an interferon gamma-release assay (IGRA) when registering with a general practitioner. Active TB is excluded by the GP using chest radiography, blood tests and clinical examination. All IGRA positive patients are tested for HIV, Hepatitis B and C. All patients with-out underlying liver disease, Hepatitis B, C or HIV infection and those who are not immunosuppressed are offered treatment for LTBI with Rifampicin and Isoniazid for 3 months in primary care. Patients with positive results not meeting the above exclusion criteria are referred to the local secondary care service using a standardised referral protocol.

We conducted a retrospective study reviewing records of all patients referred to secondary care from the LTBI screening programme.

Results From July 2014 to March 2015, a total of 5683 patients were offered screening. 3272 proceeded to IGRA testing of which 866 were positive. Of these patients, 138 were referred to the TB clinic. The most common reasons for referral were symptoms suggestive of active TB (26%), abnormal liver function tests (19%) before and after initiation of treatment, an abnormal chest radiograph (CXR) (10%), Pregnancy or breastfeeding (9%), Hepatitis B or C infection (7%) or previously treated latent or active TB (7%). Of those referred, 11 patients were found to have active disease. 6 patients had mediastinal lymph node TB, 4 pulmonary and one patient had TB of the knee.

Conclusion Screening for latent tuberculosis in primary care has identified a significant number of cases of active Tuberculosis, particularly mediastinal TB.
OPTIMISATION OF A HUMAN BCG CHALLENGE MODEL

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Introduction

Tuberculosis remains a significant global disease burden with an estimated 9 million new cases and 1.5 million deaths in 2013. BCG continues to be the only licensed TB vaccine, however it is poorly efficacious against adult pulmonary TB disease and there is a desperate need for a better TB vaccine to provide greater and more consistent protection. Development of such a vaccine has been hampered by the lack of reliable and validated correlates of protection. A human mycobacterial challenge model, using BCG as a surrogate for Mycobacterium tuberculosis challenge would facilitate improved vaccine candidate selection for progression into future field efficacy testing. In this study we evaluate the effect of two BCG strains at two doses to optimise this model.

Methods

40 healthy BCG-naïve adults were assigned to one of four groups to receive intradermal BCG SSI or BCG Tice at standard or high dose. Two weeks following BCG challenge, skin biopsy from the BCG challenge site was performed. Volunteers were followed up for 28 days from challenge to assess reactogenicity and ensure no safety concerns. BCG mycobacterial load was quantified by solid culture and quantitative PCR.

Results

BCG, regardless of strain or dose, was tolerated well and reactogenicity was similar between groups. BCG strain did not significantly affect BCG recovery from skin biopsy, however there was significantly greater recovery from the high dose challenge groups compared with the standard dose. Consistent with previous findings there was an inverse correlation between ex vivo IFN-γ ELISpot responses to PPD and amount of BCG recovered from the skin biopsies.

Conclusions

High dose BCG challenge regardless of strain used, significantly improves the sensitivity of this human mycobacterial challenge model. Practical reasons favour the use of BCG SSI over BCG Tice, as BCG SSI is licensed for intradermal administration in the UK and preparation is more straightforward with less product wastage or variability in dose between vials of BCG SSI. Looking ahead we plan to use this optimised BCG SSI challenge model to evaluate novel TB vaccine candidates in order to improve the selection of which vaccines then progress to expensive field efficacy trials.

INTERSTITIAL LUNG DISEASE MDT PRESENTATIONS

POST VATS LUNG BIOPSY CHANGES THE ORIGINAL HISTOLOGICAL DIAGNOSIS IN 30%


10.1136/thoraxjnl-2015-207770.47

Introduction

NICE recommends MDT presentation of all patients with suspected ILD. Any benefit of representation post VATS biopsy is unknown.

Methods

Our hospital (BHH) provides a regional service for thoracic surgery. All VATS lung biopsies for interstitial lung diseases carried out in 2013 were identified. They were presented post surgery at the ILD MDT where their history, physiology, immunology, original CTs and pathology were reviewed by a fully constituted MDT team including ILD specialist histopathologists, radiologists, clinicians and CNS. The MDT diagnosis was compared with the original specialist pulmonary histopathology report.

Results

71 patients had qualifying VATS biopsies in 2013. In 21 patients (30%) the MDT diagnosis differed significantly from the original histology report. In a further 12 patients the MDT altered a probable to a definite diagnosis. In 3 patients the MDT reduced the confidence of the histological diagnosis. Hypersensitivity pneumonitis was diagnosed much more confidently by the MDT than the histologist alone. The interpretation of necrotising granuloma was a particular problem from the histology alone; the MDT confirming diagnoses of rheumatoid lung, sarcoidosis or no ILD. It was also possible to achieve specific diagnoses in 5 patients whose biopsies were reported as non-specific fibrosis, NSIP (2), UIP (2), HP (1), and in 2 in whom the original report was resolving pneumonia (both HP). In 10/21 patients there was sufficient evidence to classify the UIP as IPF (7), collagen vascular disease UIP (1), chronic HP UIP (1), and drug induced UIP (1). There was often insufficient exposure and immunological data for the MDT to further characterise UIP and NSIP.

Conclusions

The post biopsy MDT changed the diagnosis in 30% compared with the histology report alone. An ILD MDT review with the combination of radiology and pathology and an expert team provided significant extra benefit in terms of a precise diagnosis in patients biopsied with interstitial lung disease in whom the referring physician thought that a diagnosis was not possible without a biopsy. This is not surprising as the histologist is limited by sampling, the radiologist by resolution, and both by the lack of physiology, exposure history and immunology.

HISTOLOGICAL DIAGNOSIS IN 30% INTERSTITIAL LUNG DISEASES- FIRST UK EXPERIENCE

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Introduction

Despite radiological advancements histology is often needed in the diagnosis of Interstitial Lung Disease (ILD). In order to obtain lung biopsies of adequate size and quality patients traditionally undergo a surgical lung biopsy associated with a mean hospital stay of 3.5 days and a complication rate of up to 28%.

We are the first UK centre to have set up a minimally invasive, day case transbronchial cryobiopsy service in the diagnosis of ILDs. Aims To establish a transbronchial cryobiopsy service for ILDs and assess complication rates and diagnostic yield.

Methods

Patients were selected following discussion at the Interstitial Lung Disease Multidisciplinary Team meeting. Only patients in whom significant diagnostic doubt remained after thorough clinic-radiological work up were considered.
All procedures were performed with the patient self-ventilating under deep sedation with propofol using a flexible bronchoscope and 2.4 mm cryoprobe (ERBE). All but one procedure was performed under fluoroscopy guidance. All but the first two cases were performed following intubation with an uncuffed ET tube (Bronchoflex, Rusch). We introduced prophylactic IV tranexamic acid 1 g as premedication and endobronchial adrenaline routinely as part of our protocol after the first 5 cases. 1–5 samples were taken per procedure from several sub-segments of one lobe pre-selected by CT imaging.

Results 14 procedures were carried out on 13 patients. 9 patients were male. Mean age 63, mean predicted TLCO 30%; mean number of biopsies 2.7; mean aggregate biopsy size 624 mm³.

Complications: 2 pneumothoraces requiring chest drain insertion; 1 case of moderate bleeding and 1 case of severe bleeding managed with endobronchial adrenaline and suction only.

All cases were performed as outpatient day cases with patients discharged home 2–4 h after the procedure except the 2 patients requiring chest drains.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
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<th>Number of biopsies</th>
<th>Aggregate biopsy size in mm³</th>
<th>Diagnosis</th>
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<tr>
<td>1</td>
<td>M</td>
<td>66</td>
<td>3</td>
<td>1800</td>
<td>Normal lungparenchyma</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>75</td>
<td>2</td>
<td>118</td>
<td>UIP</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>60</td>
<td>3</td>
<td>410</td>
<td>NSIP</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>66</td>
<td>1</td>
<td>125</td>
<td>Interstitial fibrosis</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>64</td>
<td>1</td>
<td>60</td>
<td>HP</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
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<td>M</td>
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<td>9</td>
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<tr>
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<td>M</td>
<td>41</td>
<td>4</td>
<td>810</td>
<td>OrganisingPneumonia</td>
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<td>11</td>
<td>M</td>
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<tr>
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<td>2000</td>
<td>UIP</td>
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<td>75</td>
<td>Non-diagnostic</td>
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<td>14</td>
<td>F</td>
<td>67</td>
<td>2</td>
<td>pending</td>
<td>pending</td>
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</table>

Conclusions Our transbronchial cryobiopsy service is comparable in complication rates and diagnostic yield with larger case series from established centres outside the UK. Transbronchial cryobiopsy provides potential for minimally-invasive acquisition of sizeable lung biopsies. Further research is needed to establish whether transbronchial cryobiopsy should replace surgical lung biopsy in selected cases.

REFERENCE

Idiopathic Pulmonary Fibrosis (IPF) is a progressive, scarring lung disease with a poor prognosis and median survival of 3 years. It is a heterogeneous disorder with varying rates of progression, which presents a challenge for accurate prognostic prediction. The CPI¹ and the GAP² score are validated scoring systems for prognostic determination in IPF. However, it remains unclear which is the optimal method for accurate prediction of mortality in IPF. Therefore, a comparison of the predictive ability of the GAP score and CPI was undertaken in a cohort of IPF patients.

Methods Baseline data were collected retrospectively from 213 IPF patients (in accordance with ATS/ERS criteria and MDT consensus) from a single centre in the UK between 19th April 2007 and 14th July 2014. Thirty-eight patients were excluded, either because pulmonary function test results could not be obtained or the patient received a lung transplant during follow-up. Gender, age, FVC and DLCO were used to calculate the GAP score whilst FVC, FEV1 and DLCO were used for the CPI. Spearman’s correlation was used to analyse the relationship between GAP score or CPI and survival time. The ability of the scoring systems to predict survival at 1 and 3 years was assessed using ROC curve analysis.
Results Of the 175 patients, 131 (75%) were male with a mean age of 71 ± 8 years (mean ± SD) at presentation. Overall 3-year mortality was 50%. The CPI demonstrated a better correlation with survival ($r^2 = 0.37$, $p < 0.01$) compared to the GAP score ($r^2 = 0.24$, $p < 0.01$). ROC curve analysis for 1-year mortality found that area under curve (AUC) was 0.726 for the GAP score and 0.783 for the CPI. For 3-year mortality AUC was 0.749 for the GAP score and 0.805 for the CPI.

Conclusion These data show that the CPI more accurately predicts survival at presentation and 3-years than the GAP score in a UK IPF cohort.

Introduction Cough is a disabling symptom in IPF which causes significant reduction in quality of life. The mechanisms underlying cough in fibrotic lung disease are not well understood. Polymorphisms in the rs35105950 promoter region of the MUC5B gene have been shown to relate to risk of developing IPF and, in those with disease, have been shown to increase mucin expression in the small airways. A previous small study linked carriage of the minor T allele at rs35105950 with heightened cough in fibrosing lung disease is related to mucin production. Further studies are required to determine the mechanisms underlying the heightened cough response observed in IPF.

Abstract S44 Figure 1 Correlation of GAP score (1a) and CPI (1b) and survival in IPF

References


S45 MUC5B GENOTYPE DOES NOT INFLUENCE COUGH SEVERITY IN IPF


Introduction and objectives We have recently studied platelet activation in idiopathic pulmonary fibrosis (IPF) and found that IPF patients exhibit a significant increase in platelet reactivity. This was demonstrated by an ADP (Adenosine diphosphate) concentration dependent increase in platelet-monocyte aggregates (PMA), platelet P-selectin expression, and platelet fibrinogen binding. We have suggested this may have a potentially important role in the initiation and/or progression of tissue injury in IPF.

Systemic corticosteroid treatment may alter platelet adhesion, as seen with suppression of P-selectin expression in the spontaneously hypertensive rat. We hypothesised that peripherally deposited inhaled corticosteroid may have similar activity. In this study we evaluate the effect of beclomethasone/formoterol pMDI (B/F Fostair) on clinical parameters and biomarkers of platelet activation in IPF.

Methods Twenty non-smoking patients with IPF and no evidence of COPD were randomly assigned to either Fostair 100/6, 2 puffs BD for 28 days or matched placebo inhaler. There was 28 days washout between crossover. Biomarkers, PMA, p-selectin and fibrinogen were measured at baseline and post treatment periods. Clinical outcomes of six minute walk (6MWT), spirometry, average daily activity over 7 days (Sense Wear) and Quality of life (KBILD) were also measured.

Results 17 patients (11 males, mean age 71.2 yrs) completed the study. Table 1 shows the 95% CI on differences between the baseline and two treatments on biomarkers of platelet adhesion obtained from ANOVA and using the Tukey post hoc test for multiple comparisons.

Change from baseline spirometric measurements of FEV1(L), FEV/FVC,% pred FEF25–75 were significantly improved following 28 days B/F by (mean ±SD), 0.88 ± 0.16 L (p = 0.03), 0.03 ± 0.03 (p = 0.03), 12.4 ± 19.1% (p = 0.02) respectively when compared to placebo.

There was no change in quality of life or exercise measures.

S46 AN RCT OF 28 DAY TREATMENT WITH FOSTAIR® PMDI 200/12 BD ON PLATELET BIOMARKERS IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

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Conclusion The effects of B/F in this study may represent delivery of corticosteroid to the peripheral airways ameliorating local injury and altering plateaulet activation. Bronchodilatation may represent an effect on the small airways in IPF. Whether these effects are important in disease progression remains to be established.

REFERENCES

The breath of life: respiratory physiology

S47 NEURAL RESPIRATORY DRIVE RESPONSES TO INCREASES IN CONTINUOUS POSITIVE AIRWAY PRESSURE IN HEALTHY SUBJECTS

Introduction Dynamic hyperinflation (DH) is characterised by an increase in end-expiratory lung volume (EELV) and contributes to exercise limitation in Chronic Obstructive Pulmonary Disease (COPD) patients. Neural respiratory drive (NRD) directly reflects the load-capacity relationship of the respiratory system and is therefore expected to increase with DH. However, there are limited data investigating the effects of isolated increases in EELV on NRD. We hypothesised that 1) increases in EELV induced by continuous positive airway pressure (CPAP) would increase NRD in healthy subjects and 2) with the change in lung volume, NRD to the parasternal intercostal muscles would increase to a greater extent than that to the diaphragm at higher levels of CPAP.

Method CPAP was applied to healthy subjects at 0, 4, 8, 12 and 16 cmH2O in a random order and inspiratory capacity (IC) measured at each CPAP level as an indicator of EELV. Transdiaphragmatic pressure swings (ΔPdi) tidal volume (VT) and respiratory rate (RR) were measured. NRD was assessed with second intercostal space parasternal muscle electromyography (EMGparast) and diaphragm electromyography (EMGdi) using surface electrodes and a multipair oesophageal electrodes, respectively. EMGparast/EMGdi ratio was calculated.

Results 10 healthy subjects were recruited. Increasing levels of CPAP led to a reduction in IC (p < 0.0001, Table 1). Both EMGparast and EMGdi increased with progressive increases in CPAP (Table 1). Interestingly, respiratory rate and tidal volume did not change with the increases in CPAP. Similarly, EMGparast/EMGdi ratio and ΔPdi remained unchanged.

Conclusion This detailed physiological study has demonstrated that escalating levels of CPAP increased EELV, shown by the reduction in IC, in healthy subjects. The increase in EELV was associated with an increase in NRD to both the parasternal intercostal muscles and to the diaphragm. However, contrary to the original hypothesis and observations in COPD patients (O’Donoghue et al., Thorax 2001), NRD was not preferentially distributed to the parasternal intercostal muscles at higher lung volumes. These data indicate that the differential NRD to the parasternal and diaphragm in COPD patients is not solely a consequence of a rise in EELV and alternative mechanisms for the differential NRD should be sought.

REFERENCE

S48 CONTINUOUS POSITIVE AIRWAY PRESSURE TITRATION IN AWAKE OBESE SUBJECTS WITH OBSTRUCTIVE SLEEP APNOEA AND ITS IMPACT ON NEURAL RESPIRATORY DRIVE AND BREATHLESSNESS

Background Continuous positive airway pressure (CPAP) is an effective treatment for obstructive sleep apnoea (OSA). We assessed neural respiratory drive (NRD), as measured by the surface electromyogram of the parasternal intercostals (sEMGparast),...
during awake CPAP titration to quantify the effect of chest inflation on the load of the respiratory system.

**Patients and methods** Obese patients (body-mass-index, BMI >30) with confirmed obstructive sleep apnoea (OSA) were studied and NRD (sEMGaabd) and the surface EMG of the external oblique (sEMGpara) were recorded and normalised to baseline activity (awake, supine). The apnoea-hypopnoea index (AHI) and 95th percentile nocturnal CPAP 14.1 ± 3.8 cmH2O were studied. Awake, sEMGaabd declined by 15.1 ± 1.5% from baseline when CPAP was applied, with the nadir at a CPAP of 10.6 ± 3.4 cmH2O (p = 0.026). Further increase in CPAP levels led to a rise in sEMGpara and breathlessness (mBorg) at lowest sEMGpara 0.9 ± 0.8 points, at CPAP of 20 cmH2O 2.7 ± 2.7 points (p = 0.02).

**Conclusion** The respiratory system is maximally offloaded with subtherapeutic CPAP levels in OSA. Levels of NRD observed at effective CPAP levels are associated with breathlessness which can impact on CPAP compliance.

**Abstract S49 Table 1**

<table>
<thead>
<tr>
<th>Objective</th>
<th>BPD (N = 20)</th>
<th>Healthy Controls (N = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ApEn Tidal Volume</td>
<td>1.31 (0.23)</td>
<td>1.04 (0.28)**</td>
</tr>
<tr>
<td>ApEn Breathing Frequency</td>
<td>1.42 (0.22)</td>
<td>1.24 (0.24)*</td>
</tr>
<tr>
<td>ApEn Minute Ventilation</td>
<td>1.01 (0.29)</td>
<td>0.64 (0.22)**</td>
</tr>
</tbody>
</table>

**Methods** We studied 20 adults (14 female) with unexplained dyspnoea referred for CPET and diagnosed with BPD (by a senior respiratory physiotherapist blinded to ApEn data) and 15 age- and BMI-matched healthy controls. Underlying cardiopulmonary disease was excluded using various investigations (e.g. imaging and echocardiography) prior to referral, in addition to tests performed on the day of CPET; namely pulmonary function and blood gas analysis. ApEn of various ventilatory parameters including tidal volume, breathing frequency and minute ventilation was calculated at rest and during a cycle-ergometer CPET.

**Results** BPD patients had greater dyspnoea (modified BORG) at rest (1.4 ± 1.2 vs 0.2 ± 0.6; P < 0.01) and lower peak oxygen uptake (VO2) (P < 0.01; Table 1). Peak exercise respiratory exchange ratio was similar between groups (1.14 ± 0.17 vs 1.13 ± 0.08, P = 0.84) as were nadir values for ventilatory equivalent for CO2 (28.5 ± 5.2 vs 25.5 ± 3.6, P = 0.07) and end-exercise arterial PCO2 (4.21 ± 0.68 vs 4.1 ± 0.67, P = 0.68). ApEn was significantly greater in the BPD cohort for the duration of the test (Table 1); however differences were not apparent at rest. There was no relationship between ApEn and baseline symptom scores.

**Conclusion** Measurement of ventilatory ApEn in patients referred with unexplained dyspnoea quantified irregularity of breathing pattern and was significantly greater (more irregular) in BPD than controls. These differences were not apparent from resting phase analysis. Quantifying increased dys-regulation in exercise hyperpnoea using ApEn can be applied to ventilatory variables collected during standard CPET, and thus could aid in diagnosis and evaluating treatment response in BPD. Further work should explore how ventilatory ApEn relates to perception of symptoms.

**Introduction and objectives** Opioids are respiratory depressants and heroin/opioid overdose is a major contributor to the excess mortality of heroin addicts. The individual and situational variability of respiratory depression caused by intravenous heroin is poorly understood. The aim of this study was to use advanced physiological monitoring to follow the time course and severity of acute opioid-induced respiratory depression.

**Methods** 10 patients (9/10 with chronic airflow obstruction) undergoing supervised injectable opioid treatment for heroin addiction received their usual prescribed dose of injectable opioid (diamorphine or methadone) (IOT), and their usual prescribed dose of oral opioid (methadone or sustained release oral morphine) after 30 min. The main outcome measures were pulse oximetry (SpO2%), end-tidal CO2% (ETCO2%) and neural respiratory drive (NRD) (quantified using parasternal intercostal muscle electromyography). Significant respiratory depression was defined as absence of inspiratory airflow >10s, SpO2% <90% for >10s and ETCO2% per breath >6.5%.

**Results** ETCO2% indicated significant respiratory depression following IOT in 8/10 patients, with levels increasing from baseline 4.7 (4.5 to 5.4)% to 5.4 (5.1 to 5.7)% at 30 min, p = 0.01. The median (range) peak ETCO2% per breath was 6.9% (5.2 to 7.8).
ARTERIAL OXYGEN CONTENT REFLECTS HAEMOGLOBIN MORE THAN OXYGENATION INDICES IN 440 PATIENTS WITH PULMONARY ARTERIOVENOUS MALFORMATIONS

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ARTERIAL OXYGEN CONTENT REFLECTS HAEMOGLOBIN MORE THAN OXYGENATION INDICES IN 440 PATIENTS WITH PULMONARY ARTERIOVENOUS MALFORMATIONS

Introduction and objectives Our goal was to use a long term model of human hypoxaemia to evaluate factors that reduce arterial oxygen content (CaO₂) and therefore demand higher cardiac outputs to maintain tissue oxygen delivery. This is important for clinical practice; for clinical trials that use cardiac index as a primary outcome measure; and particularly relevant for patients with pulmonary and systemic arteriovenous malformations (AVMs) due to hereditary haemorrhagic telangiectasia (HHT).

Methods Presentation data were evaluated on 497 consecutive patients with pulmonary AVMs due to hereditary haemorrhagic telangiectasia (HHT). Presentation data were evaluated on 497 consecutive patients with pulmonary AVMs due to hereditary haemorrhagic telangiectasia (HHT). Presentation data were evaluated on 497 consecutive patients with pulmonary AVMs due to hereditary haemorrhagic telangiectasia (HHT).

Results There was a four-fold difference in CaO₂ across the 440 patients (range 7.6–27.5, median 17.6) mls of oxygen per decilitre (DL) of arterial blood. SaO₂ ranged from 59–100% (median 94.8%), but CaO₂ did not change appreciably across the SaO₂ quartiles (median CaO₂ 17.1; 18.1; 17.7; 17.8 mls/DL; p = 0.34, Figure 1A). In contrast, CaO₂ was primarily determined by haemoglobin which ranged from 5.9–21.8 g/DL (median 14.1 g/DL). The median CaO₂ across quartiles of haemoglobin were 14.1; 16.7, 18.5; and 20.5 mls/DL (p < 0.0001, Figure 1B). For each 1 g/DL rise in haemoglobin, there was a 10% increase in mls of oxygen per unit blood volume.

Abstract S51 Figure 1 Distribution of arterial oxygen content (CaO₂) across the quartiles of A) oxygen saturation (SaO₂), and B) haemoglobin (Hb) in 440 patients with pulmonary AVMs

Conclusions Currently, in long term conditions, more attention is paid to modest differences in SaO₂ than to haemoglobin. It has been shown that patients with PAVMs maintain CaO₂, and deliver the same amount of oxygen per heart beat (oxygen pulse) before and after correction of hypoxaemia by PAVM embolisation.²,³ For patients where higher cardiac outputs may be detrimental, further attention should be given to minor incremental falls in haemoglobin that substantially reduce arterial oxygen content.

REFERENCES
OUTCOMES FOLLOWING BRONCHIAL ARTERY EMBOLISATION FOR HAEMOPTYSIS IN ADULTS WITH CYSTIC FIBROSIS

Introduction Bronchial artery embolisation (BAE) is recommended as the therapy of choice for massive haemoptysis in cystic fibrosis (CF) but there are no randomised controlled trials of BAE in this setting. Outcomes from BAE are uncertain and the efficacy of BAE in sub-massive haemoptysis is unclear. We performed a single-centre observational study to investigate the role of BAE in CF-related haemoptysis.

Methods All patients with CF undergoing BAE from March 2011 to January 2015 were identified at the time of the procedure. Patient records were reviewed following hospital discharge or death. Severity of haemoptysis was classified as: massive (>240 ml/day or >100 ml/day for ≥2 days), severe (>20 ml/24 h) or mild (<20 ml/24 h). Data were collected on adjuvant therapies, time to recurrence, complications and survival. Results Twenty-seven patients underwent 49 BAE procedures. Mean baseline FEV1-%predicted was 51.0% (SD 19.3). Sixty-three (63.3%) episodes resulted in 8 (16%) deaths. Eight patients (30%) required ≥2 BAEs during the study (range 2–7). Median time to first repeat BAE was 213 (range 18–682) days. Overall, haemoptysis recurred after 31/49 (63%) procedures with no significant difference between massive and sub-massive haemoptysis (61.1% vs 64.5%).

Five patients (18.5%) died during the study and this group had a median FEV1-%predicted of 32% (range 28–82%). Mortality was 3.7% at 30 days following first BAE and 11.1% at six months. Four out of 8 (50%) patients requiring repeat BAE died compared with 1/19 (5%) who needed a single BAE only (p = 0.006).

Conclusion BAE may be life-saving but is associated with considerable morbidity in CF. Need for repeat BAE is associated with increased mortality.

Cognitive function in adults with and without cystic fibrosis related diabetes (CFRD) attending a large UK cystic fibrosis unit

Introduction and objectives On reaching adulthood many cystic fibrosis (CF) sufferers develop cystic fibrosis related diabetes (CFRD). CFRD shares clinical characteristics with type 1 (T1DM) and type 2 diabetes mellitus (T2DM). Impaired glucose tolerance (IGT), T1DM and T2DM have deleterious effects on cognitive performance. Hence, patients with CFRD are hypothesised to show similar impairment. This study aimed to elucidate the nature and severity of any cognitive impairment in patients with CFRD compared to non-diabetic patients with CF and healthy controls matched as closely as possible for age, gender and education level. Patients with CF were also matched as closely as possible on CFTR genotype.

Methods Adult (>16 years old), pancreatic insufficient patients registered to a large UK CF unit who had adequate verbal and written English were eligible. 49 patients with insulin-treated CFRD and 49 CF non-diabetics who had received a normal oral glucose tolerance test (OGTT) within the past 12 months were recruited. 46 healthy matched controls were recruited from relatives of patients and the general population. Cognitive performance was assessed using the Cambridge Neuropsychological Test Automated Battery (CANTAB). Subjective measures of sleep, stress, mood and cognitive functioning were also collected.

Results Matched controls performed better than both groups of patients with CF on tests of visual memory and learning, verbal memory, visual sustained attention, processing speed and executive function. Patients with CFRD performed significantly worse than controls on tests of mental flexibility and processing speed, which is consistent with the pattern of impairment shown in T1DM, and on verbal memory and learning, which is consistent with the pattern of impairment shown in T2DM. Compared to non-diabetic patients with CF, those with CFRD performed worse on tests of visual sustained attention, verbal memory, working memory, and processing speed.

Conclusion CFRD has a negative impact on cognitive performance akin to T1DM and T2DM. Non-diabetic patients with CF also show impaired cognition but to a lesser degree than CFRD. Even modest cognitive impairment in adults with CF may impact upon their self-management skills, health and quality of life.
Towards the clinical application of anti-Pseudomonal bacteriophage: activity is retained following nebulisation with a range of commercially available nebuliser systems

Background and objectives We have recently established safety and efficacy of nasally-inhaled bacteriophage (phage) against Pseudomonas aeruginosa in a murine model with reduced infective burden and inflammatory response demonstrated in bronchoalveolar lavage (Thorax 2012;67:A50–A51 doi:10.1136/thoraxjnl-2012–202678.108). The aim of this study was to assess titre and activity of four phages following exposure to nebuliser systems more applicable to clinical trial use.

Methods Four phage strains (1–4) were nebulised through a) Pari LC Plus (LCP), b) Aeroeclipse II (AE) and c) eFlow Rapid system. All phages retained efficacy post-nebulisation. Nebuliser type affected recovered titres:

- LCP caused significant decrease in titres of phage 1 and 2 within 5 min and phage 3 within 15 min (p < 0.05). Phage 4 titre did not drop.
- AE, despite similar mode of action to LCP, was not as detrimental to titres. Decrease in phage 1 titre was seen within 15 min, phage 2 within 10 min (p < 0.05). Phage 3 and 4 did not decrease (p > 0.05).
- eFlow does not continuously nebulise and recirculate phage, hence changes in titre over time were not recorded. No titre decreases were observed at end of nebulisation (p > 0.05).
- Morphology may play a role in maintenance of phage titre post-nebulisation (1 and 2 Myoviridae, 3 and 4 Podoviridae).

The Figure 1 shows changes in titres of phage 3 over time following nebulisation through each system.

Abstract S55 Figure 1

Conclusions Phage efficacy was retained after nebulisation though titres dropped, greatest for LCP and least for eFlow (which fell within variability of the methodology (± 0.5 log)). We confirm that phage can survive nebulisation and that this mode of administration may therefore be appropriate for future clinical trials.

Moving lentiviral-based gene therapy into a first-in-man CF trial

The UK CF Gene Therapy Consortium has developed a pipeline of vectors to deliver CFTR into the airway epithelium. The first of these (plasmid/liposome complexes) recently completed a Phase Ib trial. Anticipating that increased efficiency of gene transfer will be required, we have developed an F/HIN-pseudo-typed lentivirus which is ~2 logs more efficient in lung gene transfer than non-viral vectors, a single administration lasts for the lifetime of a mouse, and can be repeatedly administered. This vector is targeted for a first-in-man study in 2016, and in preparation for this we have assessed (1) selection of the most efficient promoter/enhancer for lung gene transfer, (2) assessment of toxicity “benchmarked” against the leading non-viral formulation including mapping of integration sites, (3) determination of transduction efficiency which will be used to inform dose-ranging in the trial and characterisation of the cell types transduced by the vector, (4) understanding the impact of pre-existing and acquired anti-viral immunity on transduction efficiency and toxicity, (5) confirmation of CFTR expression and function in relevant models and (6) comparison of vector stability in a jet and single-pass mesh nebuliser. Data will be presented for each of these components, which we believe support progression into human studies. Trial design as well as a regulatory-compliant toxicology study will also be discussed.

Clinical studies in COPD

Short-term clinically important deterioration predicts long-term clinical outcome in COPD patients: a post hoc analysis of the TORCH trial

Background COPD is a progressive disease leading to adverse outcomes such as exacerbations and death. Numerous predictors of these outcomes have been identified, based on observations at single time points, but little is known about disease trajectory as a predictor of long-term outcome. We hypothesised that the occurrence of a composite measure of clinically important deterioration (CID) made up of moderate/severe exacerbations, worsening of FEV1 or St George’s Respiratory Questionnaire (SGRQ) total score measured over 6 months may predict future long-term adverse outcomes.

Method A post hoc analysis of the TORCH data, in all four treatment arms, was performed in 5292 (86.5%) of the 6112...
COPD patients in the study at 6-months (day 182), CID was defined as: decrease of ≥100 mL in post-bronchodilator FEV₁, or increase of ≥4 units in the SGRQ, or a moderate/severe exacerbation. Using day 182 status, we tested the association between the occurrence of any CID type at or before 6 months and outcomes over the next 30 months including: sustained deterioration in FEV₁ and SGRQ scores, moderate/severe exacerbations and mortality. A Cox’s proportional hazards model used day 182 deterioration status with covariates collected at day 182, smoking status and geographical region to estimate future risk. **Results** By day 182, 2870 [54%] patients had experienced a CID (CID+) and 2422 [46%] had not (CID-). 30 months later, the CID+ group had a LS mean post-bronchodilator FEV₁ 117 ml (95% CL 100,134; p < 0.001) higher compared to the CID+ group and the SGRQ total score was 6.4 units (95% CL 5.4, 7.5; p < 0.001) better. Over the same period, post CID+ patients had a 61% (95% CL 50, 72%; p < 0.001) increased risk of a new moderate/severe exacerbation and a 41% (95% CL 15, 72%; p < 0.001) increased risk of all-cause death vs. the CID- group (see Figure 1).

**Abstract S57** Figure 1

**Conclusion** Patients experiencing a clinically important deterioration early in the TORCH trial appeared to be set on a clinical path of sustained deterioration in both health status and FEV₁ and mortality rates among those who survive to discharge. Risk stratification would inform efficient use of resources.

**Background** Exacerbation of COPD is the second commonest reason for hospital admission, with high subsequent readmission and mortality rates among those who survive to discharge. Risk stratification would inform efficient use of services.

**Methods** Consecutive patients admitted with an exacerbation of COPD who survived to discharge were recruited by screening admissions units and searching coding records. Six UK hospitals took part: the derivation and internal validation cohort involved the same two hospitals at different time periods, and the external validation involved four hospitals.

Clinical data, and 90-day death and readmission rates were recorded. Multivariate logistic regression analysis was used to develop a tool to predict 90-day readmission, or death without readmission. Performance was assessed by the area under the receiver operator characteristic (AUROC) curve. **Results** 2,417 patients were analysed (derivation 824, internal validation 824, external validation 791). Female 54.0%, mean (SD) age 72.6 (10.2) years, FEV₁ 45.3 (18.2) %predicted, 90-day readmission or death 38.7%.

In the derivation cohort, the five strongest predictors (odds ratio, 95% confidence interval given for whole population) were: two or more Previous admissions in the preceding year (OR 2.17, 95% CI 1.79–2.66), cor-pulmonale “Right heart failure” (OR 1.53, 95% CI 1.14–2.06), Left heart failure (OR 1.45, 95% CI 1.07–1.97), Two or more previous admissions and eMRCD 5b were assigned a score of 3, eMRCD 5a scored 2, while eMRCD 4 and remaining indices scored 1. The risk of readmission and/or death is shown in Table 1.

The AUROC was: derivation 0.73 (95% CI 0.69–0.77); internal validation 0.68 (95% CI 0.64–0.72); and external validation 0.70 (95% CI 0.66–0.73).

![Graph showing all-cause death in patients with and without a CID](image)

**Abstract S58 Table 1** 90-day death or readmission all patients by PEARL score

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>Readmission or death within 90 days</th>
<th>Death within 90 days of discharge</th>
<th>Readmission within 90 days of discharge</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>0 n 54</td>
<td>7 50</td>
<td>243</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 15.7</td>
<td>2.0 14.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 n 130</td>
<td>15 125</td>
<td>547</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 23.8</td>
<td>2.7 22.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>2 n 164</td>
<td>46 149</td>
<td>462</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 35.5</td>
<td>10.0 32.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3 n 155</td>
<td>58 125</td>
<td>352</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 44.0</td>
<td>16.5 35.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4 n 135</td>
<td>33 120</td>
<td>264</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 51.1</td>
<td>12.5 45.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td>5 n 138</td>
<td>24 127</td>
<td>224</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 61.6</td>
<td>10.7 56.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 n 90</td>
<td>28 83</td>
<td>131</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 68.7</td>
<td>21.4 63.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>7 n 53</td>
<td>14 49</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 70.7</td>
<td>18.7 65.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>8 n 11</td>
<td>6 10</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 84.6</td>
<td>46.2 76.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>9 n 6</td>
<td>3 6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>% 100</td>
<td>50 100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>936 234 844 2417</td>
<td>% 38.7 9.7 34.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Discussion** In patients hospitalised with an exacerbation of COPD the PEARL score is a robust predictor of readmission and death and may be used to inform efficient use of resources according to risk.
USING VENOUS BLOOD GAS ANALYSIS IN THE EFFICACY AND SAFETY OF ACLIDINIUM/FORMOTEROL

Thorax

A36

< 0.001).

than venous (mean pain score 4 (IQR 2

There was good agreement between arterial and venous

Results

234 patients had paired arterial and venous samples.

We calculated the sensitivity and specificity of a VBG pH and

Arterial sampling took more attempts and was more painful

between arterial and venous

Agreement between arterial and venous

pCO2 (kPa) 6.89

Mean Difference

95% Limits of

N

Abstract S59 Table 2 Agreement between SaO2 and SpO2

SaO2 (Mean)

80%).

Arterial sampling took more attempts and was more painful

mean pain score 4 (IQR 2

Table 1) and TDI vs PBO by 297 mL, 145 mL and 1.59

Arterial sampling took more attempts and was more painful than

(1.58 to 2.28)

1.93

-0.54 to 0.11

234

0.001). The exacerbation rate was higher in patients using ICS

290 mL, 135 mL and 1.36 units vs PBO, respectively (all p <

In patients not using ICS, there were improvements with AB/FF

In patients not using ICS, there were improvements with AB/FF

1.58 to 2.28

225

pCO2 (kPa)

pCO2 (kPa)

91.5 would have correctly classified 87% (95% CI 82%

234

patients with SpO2 >80%.

Abstract S59 Table 1 Agreement between arterial and venous

pCO2, pH and HCO3

pH

7.40

(0.09)

29.7

(6.3)

6.89

(2.40)

HCO3 (mEq/L)

29.7

1.93

(2.41)

(6.0)

Mean Difference

80%)

percent saturation*

Oxygen percentage saturation*

-11.12 to 10.78

95% Limits

224

Conclusion Arterial sampling is more difficult and painful than

there is good agreement between pH and HCO3 values derived from venous and arterial blood, and

between pulse oximetry and arterial blood gas oxygen saturations. This could allow the initial assessment of COPD exacerbations to be based on venous blood gas analysis and pulse oximetry, simplifying the care pathway and improving the patient experience.

Efficacy and safety of aclidinium/formoterol fixed-dose combination in patients with COPD, stratified by ICS use

Introduction and objectives This was a secondary analysis, stratified by concomitant inhaled corticosteroid (ICS) use, based on pooled data from ACLIFORM (NCT01462942) and AUGMENT (NCT01437397), two Phase III, 24-week, randomised, double-blind studies of twice-daily aclidinium/formoterol (AB/FF) fixed-dose combination in patients with moderate to severe airflow obstruction.

Methods Patients received twice-daily AB/FF 400/12 μg, AB/FF 400/6 μg, AB 400 μg, FF 12 μg or placebo (PBO). Any baseline ICS use was continued throughout. Assessments: change from baseline in 1-hour morning post-dose and morning pre-dose (tough) forced expiratory volume in 1 s (FEV1) at Week 24 and Transition Dyspnoea Index (TDI) score (pre-planned), rate of exacerbations and adverse events (AEs).

Introduction COPD exacerbations are a common cause of emergency hospital admission in the UK, with an estimated 94,000 per year. Identifying hypercapnic respiratory failure is crucial. Guidelines recommend obtaining arterial blood samples but these are more difficult to obtain than venous samples. Furthermore, administration of local anaesthetic prior to arterial sampling is seldom used. We assessed whether blood gas values derived from venous samples could replace arterial at initial assessment.

Methods Patients treated for a COPD exacerbation had paired arterial and venous samples taken. Bland Altman analyses were performed to assess agreement between arterial and venous pH, pCO2 and HCO3, and between SpO2 and SaO2. The number of attempts and pain scores for each sample were measured.

Results 234 patients had paired arterial and venous samples. There was good agreement between arterial and venous measures of pH and HCO3 (mean difference 0.03 and -0.04, limits of agreement -0.54 to 0.11, and -2.90 to 2.82), and between SaO2 and SpO2 (in patients with a SpO2 of greater than 80%).

We calculated the sensitivity and specificity of a VBG pH and HCO3 to correctly identify an arterial pH of ≥7.35, and an arterial HCO3 of ≥21, as well as a SpO2 to identify a SaO2 of ≥ 92%. A venous pH of 7.34, a venous HCO3 of 21.45 and a SpO2 of 91.5 would have correctly classified 87% (95% CI 82% to 91%), 97% (95% CI 93% to 98%), and 71% (95% CI 65% to 77%), of patients respectively. 96% of patients with an ABG pH of ≥7.35 also had a VBG pH of ≥7.35.

Agreement between arterial and venous

Abstract S59 Table 2 Agreement between SaO2 and SpO2

SaO2 (Mean)

91.2

(6.0)

SpO2 (Mean)

91.0

(4.0)

Mean Difference

95% Limits of

N

91.5 would have correctly classified 87% (95% CI 82% to 91%), 97% (95% CI 93% to 98%), and 71% (95% CI 65% to 77%), of patients respectively. 96% of patients with an ABG pH of ≥7.35 also had a VBG pH of ≥7.35.

Arterial sampling took more attempts and was more painful than venous (mean pain score 4 (IQR 2–5) and 1 (IQR 0–2), p < 0.001).
ANALYSIS OF THE EFFICACY AND SAFETY OF THE COMBINATION OF TIOTROPIUM + OLODATEROL IN PATIENTS WITH COPD BY PREVIOUS USAGE OF INHALED CORTICOSTEROIDS

Rationale Tiotropium (T), a long-acting muscarinic antagonist, and olodaterol (O), a long-acting β2-agonist (both administered twice daily), improved lung function and symptoms over T and O monotherapy. Phase III studies have demonstrated that T+O significantly reduced the rate of exacerbations vs PBO (p < 0.01).1 These effects on lung function were observed irrespective of whether or not patients had reported concomitant use of ICS at baseline (see Table 1). In the ‘ICS usage’ and ‘no ICS usage’ subgroups, there were no statistically significant differences between the combinations and monotherapy treatments in changes in SGRQ total scores from baseline to Week 24, although SGRQ total scores were improved during this period with T+O.

Results In the overall population, all treatments resulted in clinically relevant improvements in lung function, with significant increases with both T+O doses over the individual components (p < 0.01).1 These effects on lung function were observed irrespective of whether or not patients had reported concomitant use of ICS at baseline (see Table 1). In the ‘ICS usage’ and ‘no ICS usage’ subgroups, there were no statistically significant differences between the combinations and monotherapy treatments in changes in SGRQ total scores from baseline to Week 24, although SGRQ total scores were improved during this period with T+O.

Conclusions In patients with COPD, T+O 5/5 μg significantly improved lung function over T 5 μg and O 5 μg monotherapy, irrespective of whether patients had reported ICS use at baseline.

Funding Boehringer Ingelheim.

REFERENCE


Mechanisms of lung injury and fibrosis remodelling on the fly

INHALED CORTICOSTEROIDS

(0.67) vs those who did not (0.36) and AB/FF 400/12 μg significantly reduced the rate of exacerbations vs PBO (p < 0.05; Table 1). The overall AE frequency was similar throughout (range with ICS, 54.8–60.7%; without, 56.0–60.3%). The most common AEs across patient groups were COPD exacerbation, nasopharyngitis and headache, irrespective of ICS use.

Conclusion In this analysis, aclidinium/formoterol 400/12 μg twice daily improved bronchodilation and dyspnoea in patients independent of ICS use and reduced exacerbations in patients using ICS. Combining AB and FF along with an ICS increased bronchodilation vs either monotherapy. AE frequencies were similar between the patient groups, regardless of ICS use.

Abstract S61 Table 1 Change from baseline in morning pre-dose (trough) FEV1 at Week 24 and rate of exacerbations by concomitant ICS use

<table>
<thead>
<tr>
<th>LS mean change from baseline in morning pre-dose (trough) FEV1 at Week 24 by ICS use, mL¹</th>
<th>No ICS use</th>
<th>ICS use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>BID</td>
<td>Placebo</td>
</tr>
<tr>
<td>400/12 μg</td>
<td>98***</td>
<td>47***</td>
</tr>
<tr>
<td>400/6 μg</td>
<td>85***</td>
<td>71***</td>
</tr>
</tbody>
</table>

Rate of exacerbations per patient/year by ICS use²

<table>
<thead>
<tr>
<th></th>
<th>No ICS use</th>
<th>ICS use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>85***</td>
<td>71***</td>
</tr>
</tbody>
</table>
| AB, aclidinium bromide; BID, twice daily; FEV1, forced expiratory volume in 1 s; FF, formoterol fumarate; ICS, inhaled corticosteroid; LS, least squares.

¹Analyses based on the log-linear model.
²Analysis based on the mixed model for repeated measures: treatment effects and treatment comparisons.
³p < 0.05 vs placebo; **p < 0.01 vs placebo; ***p < 0.0001 vs placebo.

Abstract S61 Table 1 Lung function responses at 24 weeks according to baseline ICS usage³

<table>
<thead>
<tr>
<th>Trough FEV1, L</th>
<th>FEV1, AUC0–24, L</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Adjusted mean (SE) change</td>
</tr>
<tr>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>ICS usage</td>
<td>T+O 5/5</td>
</tr>
<tr>
<td></td>
<td>AB/FF 400/12</td>
</tr>
<tr>
<td>No ICS usage</td>
<td>AB</td>
</tr>
<tr>
<td></td>
<td>T</td>
</tr>
<tr>
<td></td>
<td>T+O</td>
</tr>
<tr>
<td></td>
<td>T</td>
</tr>
<tr>
<td></td>
<td>T+O</td>
</tr>
</tbody>
</table>

³p < 0.0001 vs O 5; **p < 0.0001 vs T 2.5; ##p < 0.0001 vs T 5.

Patients were not recorded as receiving LAMA or LABA at baseline in this study.
SE, standard error.

Conclusions In patients with COPD, T+O 5/5 μg significantly improved lung function over T 5 μg and O 5 μg monotherapy, irrespective of whether patients had reported ICS use at baseline.

Funding Boehringer Ingelheim.

REFERENCE


Mechanisms of lung injury and fibrosis remodelling on the fly

USING DROSOPHILA MELANOGASTER TO STUDY PATHOGENIC MUTANTS OF SURFACTANT PROTEIN C

E Mažer, SJ Marciniak. University of Cambridge, Cambridge, UK

Introduction and objectives Surfactant protein C (SFTPc) is secreted by type II pneumocytes to reduce alveolar lining fluid surface tension and thus prevent alveolar collapse at low lung volumes. The immature form of SFTPc must undergo proteolytic

Spoken sessions
processing before being secreted as the mature form, but several
pathogenic SFTPC mutations associated with familial interstitial
lung disease impede this process. Mutations in the C-terminal BRI-
CHOS domain of SFTPC (ΔEx4 and L188Q) lead to retention of
the protein within the endoplasmic reticulum (ER), while other
mutations (e.g. I73T) cause SFTPC mis-trafficking.

Methods To study these mutants in vivo in a genetically tractable
organism, we generated lines of Drosophila melanogaster
expressing wild type or mutant human SFTPC. The transgenic
proteins could be tagged with green fluorescent protein (GFP) to
facilitate in vivo visualisation. These fusion proteins were
expressed under the control of tissue-specific drivers. Compo-
nents of the ER associated degradation (ERAD) machinery or of
the autophagy pathway were depleted in those tissues by RNA
interference. Lines expressing an ER stress reporter or autophagy
reporter were used as readouts for these phenomena.

Results Expression of the BRICHOS mutants ΔEx4 and L188Q
led to the progressive deposition of protein aggregates when
expressed in the fly eye. In contrast, the I73T mutant accumula-
ted in a more diffuse distribution. When expressed in the larval
salivary gland, the BRICHOS mutants where retained within the
cell, in contrast to the wild type protein that was trafficked to
the cell surface. The I73T mutant showed low-level cell surface
and weak intracellular fluorescence. Depletion of the ERAD E3
ubiquitin ligase Hrd1 or its associated E2 ligases failed to affect
mutant protein levels arguing against an important role of ERAD
in the degradation of SFTPC. Accordingly, robust activation of
autophagy was detected in L188Q SFTPC-expressing tissue.
Interestingly, ER stress was not detected.

Conclusion In a Drosophila model of hSFTPC trafficking, autoph-
agy was the major degradation pathway for L188Q mutant SFTPC.

HUMAN MESENCHYMAL STROMAL CELL (HMSC)
REGULATION OF HUMAN MACROPHAGES IN IN VITRO
MODELS OF THE ACUTE RESPIRATORY DISTRESS
SYNDROME (ARDS)
T Morrison, M Jackson, A Kasempltering, C O’Kane, D McAuley, A Kranendonk.
Queen’s University Belfast, Belfast, UK
10.1136/thoraxjnl-2015-207770.69

Background Currently there is no effective therapy which targets
the mechanisms underlying the development of ARDS. MSCs
present a promising candidate therapy and are being tested in clin-
cal trials for ARDS however their mechanisms of effect in ARDS
are not fully understood. Since the alveolar macrophage is key to
orchestrating the alveolar inflammatory response, it was hypothes-
ised that hMSCs increase an anti-inflammatory M2-like phenotype
in human macrophages. The aim of this study therefore was to
determine the effect of MSCs on macrophage phenotype and func-
tion and to elucidate the mechanisms of these effects.

Methods Using an in vitro non-contact co-culture system, human
MSCs and human monocyte-derived-macrophages (MDMs) were
stimulated with E.coli lipopolysaccharide (LPS). Cytokine and
marker expression profiles were examined using ELISAs, multiplex
and flow cytometry. Phagocytic capacity of MDMs was measured
using fluorescent E.coli bioparticles by flow cytometry. For addi-
tional clinical relevance, the ARDS microenvironment was mim-
icked by using bronchoalveolar lavage fluid (BALF) obtained from
patients with ARDS to examine the effect of MSCs.

Results MSCs suppress the production of both pro-inflammatory
and anti-inflammatory cytokines by MDMs stimulated with LPS.
MSCs increase expression of M2 markers CD163 and CD206 and
have no effect on M1 markers CD80 and ICAM-1. Import-
antly, in spite of the immunosuppressive effect on macrophages,
MSCs increase their phagocytic capacity. MSC effects on cyto-
kine secretion and marker expression were maintained in the
presence of BALF from patients with ARDS (Figure 1).

Abstract S63 Figure 1 MSCs decrease secretion of pro-inflammatory
cytokines TNF-α (A) and IL-8 (B) and increase expression of M2
macrophage marker CD206 (C) by MDMs stimulated with BALF from
non-septic (NS) or septic (S) patients of ARDS. (A + B, n = 3–7, Kruskal
Wallis *p < 0.05) (C, n = 4, ANOVA *p < 0.05)

Conclusions Human bone marrow-derived MSCs induce an M2-
like phenotype and suppress cytokine secretion in primary
human MDMs stimulated with LPS or ARDS patient BALF.
Importantly, these effects are coupled with augmentation of mac-
rophage phagocytosis which may be important in the clearance
of bacteria and apoptotic cells. Uncovering the paracrine mech-
nisms responsible for the MSC effects on human macrophages
remain the focus of ongoing work.

Supported by MRC MR/L017229/1, Department of Employment
and Learning.

Some of the materials employed in this work were provided by the Texas
A&M Health Science Centre College of Medicine Institute for Regenerative
Medicine at Scott and White through a grant from NCRR of the NIH, Grant
# P40RR017447.

ALVEOLAR EPITHELIAL TYPE II CELL EXPRESSION OF
VEGF-AXXXA IS CRITICAL FOR DEVELOPMENT OF
IDIOPATHIC PULMONARY FIBROSIS (IPF): AN ANTI-
FIBROTIC ROLE FOR VEGF-AXXXB ANTI-ANGIOGENIC
ISOFORMS?
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Abstract S64 Figure 1 M2 macrophages are recruited into the lung of
IPF patients, and this is associated with increased expression of
M2 macrophage marker CD163 (A) and decreased expression of
M1 macrophage marker CD86 (B) compared with non-fibrotic
controls. In vivo

Conclusions VEGF-AXXXA and VEGF-AXXXB are both pro-
angiogenic and pro-fibrotic, with VEGF-AXXXA being specific
ly higher in fibrotic IPF lungs. By targeting VEGF-AXXXA, we
may be able to block fibrosis and recruit M2 macrophages.
Introduction VEGF has been implicated in the development of IPF. Alternative splicing of the VEGF-A gene generates numerous isoforms. The differential effects of these isoforms, in particular the VEGF-A<sub>XXxb</sub> family, thought to have several opposing functions to the conventional family of isoforms (VEGF-A<sub>XXxa</sub>), have not been considered.

Hypothesis

- The balance of VEGF-A<sub>XXxa</sub>:VEGF-A<sub>XXxb</sub> isoform expression is important in the pathogenesis of IPF.
- VEGF-A<sub>XXxb</sub> isoforms may be protective against the formation of pulmonary fibrosis (PF).

Methods Normal and IPF lung lysates (n = 5) were analysed by western blotting (WB), and ELISA using an antibodies specific for PanVEGF-A and VEGF-A<sub>XXxb</sub> isoforms.

The Bleomycin (BLM)-induced model of PF was used in conjunction with two transgenic (TG) mouse models, developed to explore the role of ATII-derived VEGF in the development of PF: 1) a conditionally inducible, ATII-specific, VEGF knock-out mouse (STCeLL mice) and 2) a TG mouse over-expressing VEGF-A<sub>XXxb</sub> in ATII cells (MMTV-VEGF<sub>165b</sub>).

To explore the therapeutic potential of VEGF-A<sub>XXxb</sub> in PF, wild-type mice were administered intraperitoneal (IP) injections of VEGF-A<sub>XXfib</sub>, commencing 10 days after BLM challenge.

In all experiments fibrosis was assessed histologically using Masson’s Trichrome, with blinded scoring of tissue sections.

Results By WB (n = 3) and ELISA (n = 5) there was no significant difference in PanVEGF-A expression between normal and IPF lung homogenates (t-test, p > 0.05). In contrast, VEGF-A<sub>XXxb</sub> expression was significantly increased in these same IPF samples compared to control, by ELISA (t-test, ****p < 0.0001) and WB (Densitometry: t-test, *p < 0.05).

Specific deletion of VEGF-A from ATII cells of mice ameliorated the development of BLM-induced pulmonary fibrosis (n = 5, Lung fibrosis score: ANOVA with Holm’s Sidak ***p < 0.01). Over-expression of VEGF-A<sub>XXxb</sub> in ATII cells also ameliorated the development of pulmonary fibrosis (n = 6, Lung fibrosis score: ANOVA with Holm’s Sidak ***p < 0.001). Furthermore, delivery of VEGF-A<sub>XXxb</sub>, specifically during the fibrotic phase of the BLM model, also attenuated lung fibrosis development (n = 6, Lung fibrosis score: ANOVA with Holm’s Sidak *p < 0.05).

Conclusion Changes in the bioavailability of ATII cell-derived VEGF-A, namely the ratio of VEGF-A<sub>XXxa</sub>:VEGF-A<sub>XXxb</sub>, appear critical to the development of pulmonary fibrosis. This data suggests that more targeted approach to anti-VEGF-A therapy in IPF should be explored.

Methods Anaesthetised, tracheostomised rats were breathing spontaneously through a 2-way non rebreathing valve. The inspiratory port was connected to a resistance, setting peak tidal tracheal pressure at 50% of maximum (IRB). Quietly breathing animals served as controls. After 6 h of IRB, the mechanics of the respiratory system were assessed with the forced oscillation technique. Bronchoalveolar lavage (BAL) was performed to measure total and differential cell count and total protein levels. Phosphorylation of Src and ERK was detected in lung tissue samples by Western blot analysis at 30 min, 3 and 6 h of IRB. The Src inhibitor PP2 was administered intraperitoneally (1 mg/kg), 30 min prior to IRB, in a subgroup of animals.

Results After 6 h of IRB, increased tissue elasticity was measured, compared to control. Increased BAL cellularity was also found (2-fold increase to control), due to raised numbers of both macrophages and neutrophils. Total protein levels were elevated in BAL fluid. Src activation was detected at 30 min of IRB (3-fold increase to control), while ERK was phosphorylated at 3 and 6 h. Inhibition of Src kinase attenuated the increase in tissue elasticity after 6 h of IRB. Following inhibition of Src kinase, the total cell number after 6 h of IRB was not increased compared to control. Neither macrophage nor neutrophil count was elevated after 6 h of IRB, following Src inhibition. Total protein levels were not altered by Src inhibition. Src inhibition attenuated the activation of ERK only at 3 h of IRB.

Conclusion Src kinase activation partly mediates IRB-induced pulmonary inflammation.

CAFFEINE INHIBITS TGFb ACTIVATION BY EPITHELIAL CELLS, INTERRUPTS FIBROBLAST RESPONSES TO TGFb, AND REDUCES PULMONARY FIBROSIS IN EX VIVO PRECISION-CUT LUNG SLICES

Caffeine (1, 3, 7-tri-methylxanthine) is a common food additive found naturally in many products. It is a non-selective competitive antagonist of G-protein coupled adenosine receptors and can inhibit phosphodiesterases. Caffeine has anti-fibrotic effects in the liver and increased caffeine consumption has been associated with reduced liver fibrosis in patients with chronic hepatitis C infection. The effect of caffeine on pulmonary fibrosis has not been investigated, however, it has been shown to inhibit TGFβ-induced Smad signalling in epithelial cells. This study aimed to investigate the anti-fibrotic effects of caffeine in the lung using lung epithelial cells, fibroblasts and an ex vivo precision-cut lung slice (PCLS) model of fibrosis.

Spoken sessions

THE ROLE OF SRC KINASE IN INSPIRATORY RESISTIVE BREATHING-INDUCED PULMONARY INFLAMMATION

Introductions and objectives Inspiratory resistive breathing (IRB), a hallmark of obstructive pulmonary diseases, is characterised by large negative intrathoracic pressures. IRB is shown to induce pulmonary inflammation in previously healthy rats. Src is a multifunctional kinase that is activated by phosphorylation upon mechanical stress and plays a significant role in inflammatory processes. The aim of our study was to investigate the role of Src in IRB-induced pulmonary inflammation.

Methods Anaesthetised, tracheostomised rats were breathing spontaneously through a 2-way non rebreathing valve. The inspiratory port was connected to a resistance, setting peak tidal tracheal pressure at 50% of maximum (IRB). Quietly breathing animals served as controls. After 6 h of IRB, the mechanics of the respiratory system were assessed with the forced oscillation technique. Bronchoalveolar lavage (BAL) was performed to measure total and differential cell count and total protein levels. Phosphorylation of Src and ERK was detected in lung tissue samples by Western blot analysis at 30 min, 3 and 6 h of IRB. The Src inhibitor PP2 was administered intraperitoneally (1 mg/kg), 30 min prior to IRB, in a subgroup of animals.

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Conclusion Src kinase activation partly mediates IRB-induced pulmonary inflammation.

EX VIVO PRECISION-CUT LUNG SLICES

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Caffeine induced a concentration-dependent decrease in TGFβ activation in iHBECs but had no effect on TGFβ activation in lung fibroblasts. Furthermore, caffeine reduced expression of the TGFβ-inducible genes PAI1 and Col1A1 and reduced TGFβ1 transcript in epithelial cells. Additionally, caffeine reduced TGFβ-induced proliferation of lung fibroblasts and reduced expression of pro-fibrotic genes including COL1A1 and ACTA2. Crucially, ex vivo treatment of fibrotic PCLS from bleomycin treated animals with caffeine caused a dose-dependent reduction in collagen deposition after five days. Caffeine had no effect on collagen deposition in PCLS isolated from saline treated animals nor did caffeine affect tissue viability in PCLS from either saline or bleomycin treated animals.

In conclusion, caffeine has anti-fibrotic effects in the lung via concomitant inhibition of epithelial TGF activation and fibroblast responses to TGFβ.

Conclusions Vitamin D deficiency was highly prevalent in this population of healthy volunteers. The rise in vitamin D levels post LPS exposure may represent mobilisation of vitamin D from fat stores during inflammation though vitamin D metabolism and kinetics are complex and may differ in healthy volunteers and the critically ill. Severe deficiency correlated with increased alveolar inflammation.

Lung infection and primary ciliary dyskinesia

Adult Primary Ciliary Dyskinesia (PCD) has not been well characterised. Patients have varied radiological severity of disease and lung function impairment and limited data is available regarding prognosis. In this retrospective study we describe and characterise a large adult PCD cohort, and identify determinates of disease progression using longitudinal lung function data.

We retrospectively analysed 151 adult patients at a single tertiary centre. Overall mortality was 4.6% over a 7-year median follow-up period. Lung function decline was estimated at 0.49% FEV1/predicted/year. Older age at diagnosis showed moderate negative correlation with FEV1/%predicted at diagnosis ($r = -0.30$; $p = 0.01$) and increased *Pseudomonas aeruginosa* colonisation ($p < 0.01$) but not longitudinal FEV1/%predicted ($\beta = 0.001; (95\% CI:-0.35,0.35)$). Within multivariate mixed models of FEV1 adjusting for ciliary ultrastructure, HRCT scoring of severity of bronchial wall dilatation ($p < 0.01$) and extent of bronchiectasis ($p = 0.03$) showed evidence of modifying the decline in FEV1 with age. Lung function decline additionally differed by ciliary ultrastructure ($p = 0.04$) with patients with microtubular defects having the greatest decline.

Our study reveals a large proportion of adult PCD patients are diagnosed late with lower FEV1 and increased *P. aeruginosa* colonisation at diagnosis. Increased disease burden on HRCT and microtubular defects on ciliary ultrastructure predicts progressive lung function decline. This study highlights the need for early diagnosis alongside prospective multi-centre disease-specific trials to confirm triggers for lung function decline and identify potential novel therapeutic strategies.

Development of an in vitro assay to detect chemically-induced changes in ciliary beat frequency

Techniques are well-established to quantify ciliary beat frequency (CBF), which is often reduced in patients with primary ciliary dyskinesia. This project aims to determine the impact of genetic
polymorphisms in the T2R38 (bitter taste) receptor in response to chemical ligands, which is predicted to lead to changes in CBF, which are transient and small in magnitude. These receptors are of interest as they have been shown to ‘sense’ quorum sensing molecules produced by Pseudomonas aeruginosa (Pa) and may thus be disease modifiers in patients with cystic fibrosis. This work describes the development of a rapid CBF assay with sufficient sensitivity to provide a read-out of airway epithelial cell responses to stimulation in vitro.

Air-liquid interface (ALI) cultures were obtained from surplus clinical diagnostic samples. Cells in ALI were exposed to phosphate buffered saline (PBS; negative control) and adenosine 5'-triphosphate (ATP; positive control). Experiments were conducted in temperature-controlled wells under a 40× light microscope. Cilia were imaged by high-speed video camera and CBF expressed as a ratio of stimulated/basal frequencies.

CBF increased in ALI cultures exposed to ATP (n = 4) but not PBS (n = 3), in experiments at 24–25°C; this effect was not seen at 37°C. Mean ± SEM stimulated/basal CBF ratio was 1.00 ± 0.05 in the PBS-exposed cells, and 1.31 ± 0.08 in the ATP-exposed cells (p = 0.029). Inter-observer variability (n = 2) was lower than within-sample CBF variability (95% limits of agreement from -0.66 to 1.62 Hz). Intra-observer variability was good with 95% limits of agreement between -0.31 to 0.52 Hz.

An assay has been developed to detect rapid changes in CBF in ALI cultures using ATP as a positive control. Further work is being undertaken to a) optimise this assay in epithelial cells in suspension, thus increasing throughput, and b) assess more relevant chemicals and culture media. Once optimised, this assay will be used to study the effects of Pa quorum sensing molecules on ciliated epithelial cells in vitro, from patients of varying TAS2R38 genotypes.

Background Pneumococcal colonisation is a necessary precursor for pneumococcal diseases. Previous studies have suggested that pneumococcal colonisation in children is symptomatic and that there is a relationship between symptom severity/frequency and colonisation density. The literature refers to colonisation in adults as an asymptomatic event but no studies have used robust methodology. Using the Experimental Human Pneumococcal Colonisation (EHPC) model, we investigated whether pneumococcal colonisation (or co-colonisation with a respiratory virus) is symptomatic in healthy adults.

Methods Non-smoking healthy adults aged 18–60 years old were recruited and inoculated intranasally with 0.1 ml per naris of pneumococcus (serotype 6B, 23F) or saline (control). Nasal and non-nasal symptoms were monitored pre-inoculation and for 7 days post-inoculation using a modified Likert score. Symptom severity scoring ranged from 1 (none) to 7 (cannot function). Area under the curve (AUC) was calculated for each participant. Mean values were compared using ANOVA between the groups.

Results Data from 53 participants were analysed. 45 were inoculated with pneumococcus and 8 with saline. In total, 14 became experimentally colonised. Colonised and non-colonised participants reported similar symptom severity scores (Figure 1). Mean severity scores for both nasal and non-nasal symptoms did not significantly differ according to colonisation status (p > 0.05), nor was there any significant association with any particular symptom. In the 14 experimentally colonised participants, density of colonisation did not correlate with symptom severity scores (R² = 0.03, p = 0.89). 6 participants were co-colonised (with pneumococcus and a respiratory virus), although they showed a trend towards experiencing more non-nasal symptoms than other groups, their mean symptom severity was still occasional only (p > 0.05).

EXPERIMENTAL HUMAN PNEUMOCOCCAL COLONISATION IS AN ASYMPTOMATIC EVENT IN HEALTHY ADULTS

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Conclusion In healthy adults pneumococcal colonisation is an asymptomatic event, regardless of density or viral co-colonisation.

Background People with chronic lung diseases, such as Bronchiectasis (BE) and smoking-induced Chronic Obstructive Pulmonary Disease (COPD), are susceptible to lung infections which can exacerbate their disease and can be life threatening. A relatively limited range of pathogens cause infections in these conditions and patients suffer repeated infections. It is unclear why such infections do not elicit protective adaptive immune responses. We wish to better understand immune responses against lung-infecting microbes in people with underlying lung disease since immune responses may be connected to disease pathology and also to protection from infection, and may provide a useful marker of colonisation.

Methods We took peripheral blood samples from 114 BE and 47 COPD patients attending secondary care clinics, and 25 healthy controls, and extracted PBMC and serum. The patients were well-characterised clinically, including their history, aetiology, lung function and longitudinal microbial colonisation. T cell and antibody responses were measured against a panel of common lung-infecting microbial antigens (bacteria, fungi and viruses) using our in-house well-characterised assays (ELISA and ELIspot, respectively). These provided quantitative outputs of specific antibody titre and reactive gamma-interferon-secreting T cells per million PBMC, validated using positive controls. The spumt of patients was cultured, and microbial colonisation defined using prior definitions. Correlations between culture status and bacterial immune responses were analysed.

Results The predominant pathogens varied between BE and COPD as expected (percentages in Table 1). These included Pseudomonas, Haemophilus influenzae, Streptococcus pneumoniae and Moraxella spp. We found that specific IgG antibody responses correlated with bacterial sputum culture data for Pseudomonas ($R = 0.61, \ p = 0.0001$), but not with lung function nor number of exacerbations. In contrast, specific T cell responses did not correlate with microbiology.

Conclusions Our findings suggest that immune responses measured in the blood against potential lung pathogens contribute minimally to protection from infection or pathology. These tests may however help define colonisation status and could be used as surrogate markers of pathogens in the lung. The poor correlation between T cell responses may be a facet of the disease.

Improving lung cancer outcomes

<table>
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<tr>
<th>Abstract S71 Table 1</th>
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Introduction We have collated data from several sources to demonstrate that efforts made over the last 10 years to use data to drive service improvement and improved patient outcomes for UK patients with lung cancer have been successful.

Methods We used data submitted to the National Lung Cancer Audit (NLCA), National Cancer Registration Service (NCRS), Office for National Statistics (ONS) and Society of Cardiothoracic Surgeons (SCTS) from 1995–2013. We calculated numbers and proportions undergoing surgery, case-mix adjusted hazard ratios for death, and actual and predicted (using hybrid analyses) 1-year and 5-year survival for lung cancer patients in England. An international comparison has been made using data from the CONCORD-2 study.

Results In the NLCA, the proportion of NSCLC patients undergoing resection has risen from 14% (2003) to 23% (2013). Over this period, annual primary lung cancer resections have risen from 3,220 to 6,713.

NLCA data, adjusted for age, sex, stage and PS, indicates a gradually falling hazard ratio for death (2013 HR 0.87, 95% CI 0.85–0.89 compared to 2008). ONS data demonstrates a gradual improvement in both 1 yr and 5 yr, and mirrors the increase in the number of resections carried out over the lifetime of the NLCA. Comparison of IYS with other countries suggests that England has passed the survival measured in Denmark in 2004–07 (35%), but still lags behind Canada (42%) and Sweden (46%). In another analysis using NCRS data, comparing stage-specific 1 yr survival in England in 2004–07 and 2012, improvements are most marked in patients with early stage disease.

Conclusion Whilst many changes have taken place in the management of lung cancer over the last 10 years, the close temporal association between the date of the first NLCA report (2005), the numbers of resections carried out and the significant improvements in 1 and 5 yr survival (weighted towards earlier stages) and mortality we report here, would strongly suggest that the NLCA has been successful in its aim to improve standards of care and outcomes for patients. These improvements in survival...
bring England close to parity with other westernised countries, though there is still more work to do.

### Abstract S72 Table 1

<table>
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<tr>
<th>Year</th>
<th>Number of resections</th>
<th>1y survival %</th>
<th>5y survival (%)</th>
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### S73 HEALTHCARE COSTS ASSOCIATED WITH LUNG CANCER DIAGNOSED AT EMERGENCY HOSPITALISATION

**Introduction** The diagnosis of lung cancer at emergency presentation with hospital admission is a poor patient experience and is likely to incur significant cost. Reducing the proportion of patients diagnosed by this route has been identified as a priority by policy makers. The full health-economic impact of this route to diagnosis is not known.

**Aim** To measure the excess healthcare costs attributable to emergency hospital admission in patients diagnosed with lung cancer.

**Methods** Retrospective review of an electronic database of lung cancer patients from 2008–2013. Secondary care costs were acquired from the local NHS Patient Level Information and Costing System (PLICS) with adjustment for inflation. To adjust for survival differences, secondary analyses looked at average costs incurred only while patients remained alive.

**Results** 3,274 consecutively diagnosed patients were included. Mean one and twelve-month costs were £2,400 (95% CI £2,213-£2,493) and £10,009 (95% CI £9,725-£10,285). One month mean costs for patients with emergency admission were higher than for those diagnosed by other routes (£3,499 (95% CI £3,332-£3,667) vs £1,899 (95% CI £1,810-£1,999)). Twelve month mean costs for emergency admissions were lower than for other routes (£8,123 (95% CI £7,704-£8,552) vs £10,870 (95% CI £10,511-£11,211)), but this analysis is heavily influenced by excess mortality within the emergency admission group (1 year survival 14% vs 50% respectively).

Mean costs for survival, only considering costs per patient alive in that month, are shown in Figure 1. Emergency admission was associated with increased mean alive costs compared to other routes at both one month (£3,499 vs £1,899) and 12 months (£15,063 vs £13,233). Adjusted costs accrued between one and twelve months following diagnosis were similar between the two groups (£11,565 vs £11,334).

**Conclusion** Patients diagnosed with lung cancer during an emergency admission incur greater healthcare costs during the first month following diagnosis. Lower longer term costs in these patients seem to be entirely due to the lower survival rates in this poor prognosis group.

In addition to improving patient experience and outcome, strategies to increase earlier diagnosis of lung cancer may reduce the additional healthcare costs associated with this route to diagnosis.
Background The British Thoracic Society guidelines (2015) on the investigation and management of pulmonary nodules recommend the use of two risk prediction tools to assess the likelihood of malignancy in solid pulmonary nodules (Brock model following initial CT and the model described by Herder et al., following PET-CT). Management strategies are suggested on the basis of these risk assessments. The aim of this study was to assess the performance of this algorithm in patients with solid pulmonary nodules recruited from a UK teaching hospital.

Method Patients with solid pulmonary nodules (4–30 mm) were retrospectively identified from the lung cancer MDT and a nodule follow-up clinic (n = 221). All patients had a final diagnosis confirmed by histology or radiological stability on 2-year follow up.

Results The median age was 69 years. The prevalence of malignancy was 37.1% (29.9% primary lung cancer, 7.2% metastatic disease), 25 patients where PET-CT was recommended by the guideline but did not occur were excluded from subsequent analysis.

Ten patients had nodules <5 mm and therefore would have been immediately discharged. All these nodules were benign.

CT surveillance was recommended for 106 patients (37 with nodule <8 mm, 45 with malignant risk of <10% following initial CT, and 24 with malignant risk of <10% following PET-CT). 94% of these 106 patients had benign disease, 2% had primary lung cancer and 4% had metastatic disease.

Surgical/non-surgical treatment was recommended for 58 patients where the malignant risk was >70% following PET-CT. 81% of these patients had primary lung cancer, 10% had metastatic disease and 9% were benign.

For nodules with a malignant risk of between 10 and 70% following PET-CT, the guidelines recommend consideration of biopsy with alternatives of CT surveillance or surgical resection depending on patient preference and fitness. Of the 22 patients with nodules in this range, 36% were benign, 55% primary lung cancer and 9% metastatic disease.

Conclusion The solid nodule algorithm from the BTS guidelines shows good accuracy in discriminating benign from malignant nodules, recommending appropriate management in a high proportion of cases. Further studies should evaluate this and the other management algorithms with prospectively collected data.
Aims and objectives
1. To evaluate four existing models for the probability of malignancy in the target population.
2. To create and validate prediction models for probability of malignancy for patients undergoing oncology follow-up for an indeterminate PN.

Methods
Retrospective data on clinical and radiological characteristics were collected from the medical records of 61 patients with a PN (mean diameter 7 mm, SD 4 mm) that had an active or previous history (within 5 years) of primary lung or extrathoracic malignancy. The gold standard diagnosis of the nodules was established by histology or 2-year stable follow-up.

Three multivariable logistic regression models were evaluated using a leave-one-out cross-validation strategy:
   Model 1: Age, Sex, Smoking status, Emphysema, Nodule diameter.
   Model 2: Age, Sex, Smoking status, Emphysema, CT Texture score.
   Model 3: CT Texture score only.

The models’ performance, measured using the area under the ROC curve (AUC), were reported and further compared to existing clinical models.

Results
The highest AUC, 0.86, was obtained from Model 3 (texture score only). Utilising clinical parameters (Model 2) did not improve performance.

In comparison, AUCs for previously published clinical models were 0.76 (Mayo), 0.84 (Herder), 0.66 (VA) and 0.70 (McWilliams) (Figure 1).

Conclusion
This texture feature model is successful at discriminating benign from malignant nodules in a population of patients undergoing oncology follow-up. While not significantly better than the Herder model (which incorporates PET avidity), this model offers improved risk stratification for PNs in the absence of PET in this patient group.

REFERENCES
1 RSNA 2014, S5C03-05
2 IEEE International Conference doi:10.1109/SMC.2013.663

"STRAIGHT TO CT" IN PRIMARY CARE – IMPROVING THE LUNG CANCER PATIENT JOURNEY
A Nanapragasam, N Maddock, A Mdver, C Smyth, MJ Walshaw. Liverpool Heart and Chest Hospital, Liverpool, UK
10.1136/thoraxjnl-2015-207770.82

Although the advent of rapid access secondary care services has shortened the wait to timely diagnosis in lung cancer, significant delays and congestion can still occur through patients needing to attend clinic before appropriate investigations are organised.

To circumvent this, we primary care colleagues we designed a “straight to CT” system where if a general practitioner is concerned about a patient, or a chest X-ray in the community or emergency department shows suspicious changes, the radiology department automatically offers the patient a CT scan to be performed within 72 h with a same day report. This allows the primary care clinician to reassure patients with normal scans, or where necessary direct appropriately patients with scans showing non-malignant abnormalities. Patients with scans showing possible malignancy are intercepted by the lung cancer team who then organise appropriate further management.

We replaced our one stop rapid access lung cancer clinic with this new service in January 2014 and have now reviewed its use one year on.

468 patients from the local community were eligible for the “straight to CT” service. Of the 246 with a coded X-ray, 222 underwent a 72-hour CT scan (18 of the reminder declined or were not contactable), and of these 127 (57%) showed suspicious abnormalities and were intercepted by the lung cancer team. Of the 222 referred by a concerned clinician, 177 underwent a 72-hour scan (of the remainder 19 were not contactable or declined and the rest were deemed inappropriate) and 60 of these (34%) showed suspicious changes and were intercepted by the lung cancer team. Overall, 401 72-hour scans were performed in 2014: this is similar to the number of scans performed (402) in 2013 using the traditional rapid access clinic model.

As well as empowering primary care, by preventing unnecessary clinic attendance this innovative service has significantly reduced costs and by bringing forward investigations has reduced the lead time to diagnosis (to a mean of 19 days) in our patients. Furthermore, fears that such a service might increase unnecessarily the number of CT scans performed have proved groundless.

We recommend the use of such a service to colleagues to aid timely and economical investigation of patients with a suspected diagnosis of lung cancer.

The smoking gun

PROCESSING OF CIGARETTE GRAPHIC HEALTH WARNING LABELS DECREASE WITH PROLONGED EXPOSURE
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10.1136/thoraxjnl-2015-207770.78

Introduction
Cigarette package graphic health warning labels (GHWL) remain an important means of communicating serious smoking risks. There were significant delays in implementing them in different countries around the world, partly due to tobacco company resistance; additionally, the messages used differed considerably. We expected a reduced cognitive processing of the messages based on the duration since launch. In order to address this question we compared a London (4 years) vs Singapore (8 years exposed) cohort.

Methods
We used a 50-item structured interview; after recording demographics and smoking history, 10 country-specific warning labels were shown. In addition to the emotional response and impact on smoking cessation/prevention, cognitive processing was assessed on a scale from ‘1’ (‘not at all/never’) to ‘5’ (‘all the time/a lot’). Smoking-risk knowledge and their importance in terms of prevention and treatment were elicited.

Results
266 participants were recruited, 163 from London (52 ± 18 years, 54% male, 35% smokers) and 103 from Singapore (58 ± 15 years, p = 0.012; 78% male, p < 0.001; 53% smokers, p = 0.003). Londoners read the labels more carefully and more often; they talked and thought more about them, even with no warning labels were in sight, and they kept packages more often as a reminder about their messages (overall, 2.0 ± 1.3 vs 1.5 ± 1.0, p < 0.001). The processing differences
between the cities were consistent when comparing the London and Singapore smokers (overall, 2.0 ± 1.1 vs 1.6 ± 1.1, \( p < 0.001 \)) and non-smokers (overall, 2.0 ± 1.4 vs 1.4 ± 0.8, \( p < 0.001 \)) (Table 1). Londoners experienced more disgust when viewing the images (79% vs 53%, \( p < 0.001 \)) and felt they were more effective deterrents (51% vs 35%, \( p = 0.011 \)). One-in-five participants in Singapore were unaware of the association between smoking and lung cancer, despite it being the most deterring risk; blindness was the least well-known consequence in London (24%) and Singapore (34%, \( p = 0.075 \)) despite being ranked ahead of stroke, oral cancer, and in smokers, ahead of heart disease for importance to prevent/treat.

### Conclusion

A desensitisation to graphic health warning labels occurs with extended exposure. Non-smokers are prone to the same desensitisation as smokers are. In pre-empting this, the awareness and impact of specific health risks need to be actively utilised, in concerted public health campaigns, to help maintain label efficacy.

**Abstract S77 Table 1** Processing of GHWL; comparing all participants, non-smokers and smokers in London vs Singapore

<table>
<thead>
<tr>
<th>Processing (SD)</th>
<th>All</th>
<th>Non-smokers</th>
<th>Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carefully read</td>
<td>1.8 (1.2)</td>
<td>1.6 (1.3)</td>
<td>2.4 (1.1)</td>
</tr>
<tr>
<td>read labels</td>
<td>1.1 (0.9)</td>
<td></td>
<td>(1.2)</td>
</tr>
<tr>
<td>Often read</td>
<td>1.7 (2.3)</td>
<td>&lt;0.001</td>
<td>1.9 (2.3)</td>
</tr>
<tr>
<td>labels</td>
<td>1.1 (0.9)</td>
<td></td>
<td>(1.2)</td>
</tr>
<tr>
<td>Ever talked</td>
<td>1.5 (2.4)</td>
<td>&lt;0.001</td>
<td>2.0 (2.1)</td>
</tr>
<tr>
<td>about</td>
<td>1.1 (1.1)</td>
<td></td>
<td>(1.2)</td>
</tr>
<tr>
<td>Often think</td>
<td>1.6 (2.4)</td>
<td>&lt;0.001</td>
<td>2.4 (2.1)</td>
</tr>
<tr>
<td>about</td>
<td>1.0 (0.9)</td>
<td></td>
<td>(1.1)</td>
</tr>
<tr>
<td>Inc. when</td>
<td>1.3 (1.8)</td>
<td>&lt;0.001</td>
<td>2.5 (1.7)</td>
</tr>
<tr>
<td>not in sight</td>
<td>0.7 (0.6)</td>
<td></td>
<td>(0.9)</td>
</tr>
<tr>
<td>Kept labels</td>
<td>1.3 (0.8)</td>
<td>0.001</td>
<td>1.0 (1.3)</td>
</tr>
<tr>
<td>as reminder</td>
<td>0.3 (0.2)</td>
<td></td>
<td>(0.3)</td>
</tr>
</tbody>
</table>

**S78 ELECTRONIC CIGARETTE ADVERTISING IMPACTS ADVERSELY ON SMOKING BEHAVIOUR WITHIN A LONDON STUDENT COHORT: A CROSS-SECTIONAL SURVEY**

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10.1136/thoraxjnl-2015-207770.84

**Introduction**

In contrast to tobacco smoking, electronic cigarette (“vaping”) advertisement has been approved in the UK since January 2013. Currently, there are 2.6 million e-cigarette users in the UK. The impact of e-cigarette advertisement on tobacco use has not been studied in detail. We hypothesised that e-cigarette advertisement impacts on smoking behaviour.

**Methods**

A structured survey was constructed to assess the impact of e-cigarette advertising on the perceived social acceptability of cigarette smoking; and, on trying both cigarettes and e-cigarettes (on a scale of 1 to 5”not at all” to ‘a great deal’). The survey was administered between January to March 2015 to London university students, before and after viewing 5 UK adverts including a TV commercial.

**Results**

Data were collected from 106 participants (22 ± 2 years, 66% male), comprising 34 current cigarette-smokers, 57 non-smokers and 15 ex-smokers. There were 17 vapers, 82 non-vapers and 7 ex-vapers. After viewing the adverts, both smokers (2.6 ± 1.1 vs 3.8 ± 1.1, \( p = 0.0002 \)) and non-smokers (3.2 ± 0.7 vs 3.7 ± 0.8, \( p = 0.004 \)) felt e-cigarette advertising increased the social acceptability of smoking; and, both smokers and non-smokers were more likely to try e-cigarettes (3.6 ± 1.0 and 2.6 ± 1.0 respectively, \( p < 0.0001 \)) as well as conventional cigarettes (3.4 ± 1.0 and 1.5 ± 0.9 respectively, \( p < 0.0001 \)). Additionally after viewing, vapers felt e-cigarettes were ‘less effective’ at helping people stop smoking compared to before (3.6 ± 0.7 vs 4.0 ± 0.6, \( p = 0.004 \)).

**Conclusion**

E-cigarette advertising encourages e-cigarette and conventional cigarette use in young smokers and non-smokers. The adverts impact on the social acceptability of smoking without regard to the importance of smoking cessation.

**S79 THE ELECTRONIC CASE-BASED DISCUSSION: A NOVEL TEACHING METHOD APPLIED TO SMOKING CESSATION**

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10.1136/thoraxjnl-2015-207770.85

**Introduction**

Current smoking cessation training in U. K. medical schools fails to equip junior doctors with the skills necessary to effectively combat the leading preventable cause of death and disease. Here I present a novel teaching method using an electronic Case-Based Discussion (eCBD) which streamlines the process of workplace-based assessments, facilitates high-quality learning and provides new insights into what students know about this critically important subject.

**Methods**

An electronic learning module was developed by the author based on existing NICE guidelines. Candidates described a case of a smoker they had seen and were quizzed about the case by the learning module with some instant feedback, then deeper discussion with the author via e-mail. When the candidate was ready a CBD form was completed. Finally feedback was collected using an anonymous, online feedback form.

**Results**

Thirty students and junior doctors have completed the eCBD. The eCBD had excellent feedback with 94% rating the eCBD as “very useful” and 100% feeling more confident in giving smoking cessation advice. Ninety-four percent rated the eCBD as “easier” or “much easier” to arrange and 53% rated it “much better” at assessing knowledge than conventional CBDs.

Analysis of responses revealed deficiencies in knowledge of medications to treat tobacco dependence; 97% knew of nicotine replacement therapy (NRT) but knowledge of some formulations was poor (none mentioned oral strips, 3% microtabs, 17% lozenges); 43% knew of varenicline and 40% bupropion. Only 37% thought that combination NRT was safe and effective and thematic analysis revealed widespread concerns about the risks of overdose. 57% would consider recommending e-cigarettes for selected patients although only 7% had already recommended them to patients.

**Conclusions**

The eCBD can be an effective method of encouraging learning in important and neglected subject areas. It also illustrates an often-wasted opportunity to collect data from online learning modules that could guide curriculum development and facilitate better training in future.
Introduction and objectives Increasing emphasis has been placed on behavioural therapy in smoking cessation efforts. mHealth aims to join today’s arsenal of smoking cessation techniques. Many apps are utilising ‘gamification’ (the use of game design elements in non-game contexts) as a tool to drive positive behaviour change. However, a significant knowledge gap currently remains regarding how gamification can affect health behaviour. Our study seeks to elucidate the motivational mechanisms exploited by gamification in promoting positive health behaviours in the context of smoking cessation, with a view to generating recommendations on how to create effective gamified mHealth interventions.

Methods We conducted a qualitative longitudinal study using a sample of 16 smokers divided into two cohorts. The first cohort used a non-gamified mHealth intervention, whilst the second used a gamified mHealth intervention. The added game components allowed us to isolate the effects of gamification. Each participant underwent 4 one-on-one, semi-structured interviews over a period of 5 weeks. Interviews were transcribed verbatim after which thematic analysis was undertaken.

Results We observed that perceived behavioural control and intrinsic motivation acted as positive drivers to game engagement and consequently positive health behaviour. Importantly, external social influences exerted a negative effect. We identified three critical factors, whose presence was necessary for game engagement; purpose (explicit purpose known by the user), user alignment (congruency of game and user objectives), functional utility (a well-designed game). We summarise these findings in a framework (Figure 1), which we propose to guide the development of gamified mHealth interventions.

Conclusions Our framework outlines the characteristics critical to consider when developing any gamified mHealth intervention to promote a particular health behaviour. Gamification holds the potential for low-cost, highly effective mHealth solutions that may replace or supplement the behavioural support component found in current smoking cessation programmes. Our proposed framework has been built on evidence specific to smoking cessation, but is versatile and can be extended to health interventions in other disease categories. Future research is now required to evaluate the effectiveness of the above framework directly against current behavioural support therapy interventions in smoking cessation.
Lung infection mechanisms

**S82** THE KISS OF DEATH – CALCINEURIN INHIBITORS PREVENT ACTIN-DEPENDENT LATERAL TRANSFER OF ASPERGILLUS FUMIGATUS IN NECROTOTIC HUMAN MACROPHAGES

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Invasive fungal infections are a major cause of mortality in solid-organ transplantation where steroids and calcineurin inhibitors form the core of immunosuppression. Our group has previously shown in established hydrocortisone-based mouse models of invasive aspergillosis that calcineurin inhibitors increase mortality through effects on the innate immune response. As alveolar macrophages present the primary resident innate immune cell in the airways responsible for fungal clearance, we perform a detailed study of the role of the calcineurin pathway in the human macrophage response to A. fumigatus (AF).

We show that the calcineurin-NFAT pathway is highly activated in the human lung transplant alveolar macrophage response to AF with inhibition resulting in impaired fungal clearance. Calcineurin inhibition leads to delayed phagocytosis, reduction in reactive-oxygen species production and an impairment of a novel actin-dependent process of lateral transfer of swollen AF conidia between human macrophages. Further characterisation reveals that transfer of AF occurs during macrophage necroptosis with subsequently around 50% control of germinatio in the receiving macrophage. To understand the calcineurin-dependent mechanism, next generation RNA sequencing was performed which confirms that calcineurin inhibition impairs the macrophage programmed cell death immune response. Utilising phosphoproteomics we additionally show that calcineurin inhibition impairs dephosphorylation of vasodilator-stimulated phosphoprotein (VASP), an important actin regulatory protein which promotes actin filament formation. High-resolution confocal microscopy confirms that VASP strongly co-localises to AF conidia phagocytosis and facilitates lateral transfer through tunnel-like structures. Lastly, we utilise a zebrafish model of invasive aspergillosis to confirm the in-vivo relevance of AF macrophage lateral transfer.

In conclusion our data shows the importance of the calcineurin pathway in the macrophage innate immune response to AF and highlights a novel calcineurin-actin dependent host defense mechanism which may have significant implications on persistence and dissemination within solid organ transplantation. To our knowledge this is the first report of a host-mediated cell-cell transfer mechanism for any pathogen.

**REFERENCE**

with FK506 inhibits maturation in this context. This suggests an inhibitory effect of FK506 on innate antigen presentation to T-cells and may impair the adaptive immune response to invasive aspergillosis in lung transplant recipients.

REFERENCE

S84 SPUTUM NEUTROPHILS BUT NOT INTERLEUKIN-8 (IL-8) OR INTERLEUKIN 17 (IL-17) CORRELATE WITH THE BRONCHIECTASIS SEVERITY INDEX (BSI)

1s Koustas, 1A Peel, 1J Scott, 1J Davison, 1K Jwa, 1S Carnell, 1A Simpson, 1A De Soysa. 1Newcastle University, Newcastle Upon Tyne, UK; 1Adult Bronchiectasis Service, Freeman Hospital, Newcastle Upon Tyne, UK; 1Sir William Leech Centre for Lung Research, Newcastle Upon Tyne, UK

Background Bronchiectasis is a progressive neutrophilic inflammatory lung disease associated with abnormal local cytokine release with possible systemic overspill. Early data suggests that interleukin-17 (IL-17) could be involved in the enhanced infiltration of neutrophils in the lungs, via the induction of IL-8 release, and has emerged as a possible biomarker for other chronic neutrophilic lung diseases.

Aims
1. to investigate the potential use of IL-17 and IL-8 as biomarkers of disease severity in bronchiectasis by utilising a multidimensional clinical severity scoring system, the Bronchiectasis Severity Index (BSI).
2. correlate sputum neutrophils and pathogen status with serum or sputum IL-17 and IL-8 levels.

Methods Spontaneous sputa and sera were collected from stable adult bronchiectasis patients attending a specialist clinic. We quantified both IL-17 and IL-8 concentrations in the pulmonary compartment (sputum) and the systemic compartment (serum) of 119 stable bronchiectasis patients and 26 healthy volunteers. Sputum neutrophils were conducted using standard methods.

Results The mean patient age was 65 years, with 24% in mild BSI, 39% moderate BSI and 46% (43% idiopathic, 24% post infectious). IL-17 in the sputum of bronchiectasis patients was found to be two-fold greater than in serum suggesting “local” release (10 pg/ml vs 5 pg/ml). Statistical analysis revealed a significant correlation between these two variables, suggesting a “spillover” of cytokines from the lungs (p < 0.001).

However, there was no significant difference in serum IL-17 levels between bronchiectasis and healthy subjects (0 ± 2 pg/ml). In addition, no significant correlation was found between IL-8 and IL-17 levels in the sputum of patients. Sputum IL-17 levels were found to have a significant negative correlation with BSI severity scoring, but this was not reproduced when individual BSI parameters were analysed. IL-8 similarly performed poorly in correlating with BSI. In contrast more severe BSI scores were significantly associated with higher% neutrophils in sputa (p = 0.045).

Conclusions The clinical utility of IL-17 and IL-8 as biomarkers for the prediction of disease severity in bronchiectasis patients appears poor. These data may also suggest targeting these chemokines are of limited value. Focus in bronchiectasis may need shifted from neutrophil chemokines to factors that inhibit apoptosis and/or promote neutrophil persistence in the airway.

S85 PNEUMOLYSIN TRIGGERS THE PRODUCTION OF PLATELET-ACTIVATING FACTOR BY HUMAN NEUTROPHILS IN VITRO

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Introduction and objectives Pneumolysin (Ply), the major protein virulence factor of the pneumococcus, has been implicated in the pathogenesis of acute lung injury and acute coronary events, both of which are significant causes of mortality, in severe pneumococcal disease. However, the role of Ply in promoting neutrophil/platelet cross-talk, increasingly recognised as a key event in the immunopathogenesis of inflammation-mediated pulmonary and cardiovascular damage is unknown. This issue has been addressed in the current study, which is focused on the effects of exposure of isolated human blood neutrophils to Ply on the production of the platelet-targeted, pro-inflammatory lipids, platelet-activating factor (PAF) and thromboxane A2 (TXA2).

Methods Neutrophils, isolated from the blood of healthy, adult humans, were suspended at a concentration of 2 × 10⁶/ml in Hanks balanced salt solution and preincubated for 10 min at 37°C followed by addition of recombinant Ply (5–80 ng/ml), or the pneumolysinoid, delta6Ply (80 ng/ml, negative control), or the calcium ionophore, A23187, (2 μM, positive control). After 5 min of incubation, the reactions were terminated and PAF and TXA2 assayed in the cell-free supernatants using sandwich ELISA procedures.

Results These are shown in the accompanying Table 1. Exposure of neutrophils to Ply resulted in dose-related enhancement of production of PAF, which achieved statistical significance at concentrations ≥20 ng/ml of the toxin, while delta6Ply was ineffective, and A23187 extremely potent. Similar, but less impressive effects were noted in the case of TXA2.

Abstract S85 Table 1

<table>
<thead>
<tr>
<th>Agent</th>
<th>PAF (pg/ml)</th>
<th>TXA2 (pg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>4.9 ± 1.2</td>
<td>13.5 ± 1.4</td>
</tr>
<tr>
<td>Ply, 20 ng/ml</td>
<td>9.6 ± 2.4*</td>
<td>16.1 ± 2.0*</td>
</tr>
<tr>
<td>Ply, 40 ng/ml</td>
<td>12.1 ± 3.5*</td>
<td>17.7 ± 2.1*</td>
</tr>
<tr>
<td>Ply, 80 ng/ml</td>
<td>13.1 ± 4.0*</td>
<td>17.7 ± 2.3*</td>
</tr>
<tr>
<td>delta6Ply, 80 ng/ml</td>
<td>5.4 ± 1.0</td>
<td>12.3 ± 1.5</td>
</tr>
<tr>
<td>A23187, 2 μM</td>
<td>37.0 ± 5.3*</td>
<td>28.0 ± 1.4*</td>
</tr>
</tbody>
</table>

*p < 0.05; p < 0.002.

Conclusion Ply, via its pore-forming activity, activates the production of PAF and, to a lesser extent, TXA2, by neutrophils, potentially augmenting pro-inflammatory cross-talk between these cells and platelets, an activity of the toxin which may contribute to the immunopathogenesis of lung and cardiac injury in severe pneumococcal disease.

S86 THE ANTI-INFLAMMATORY EFFECTS OF PNEUMOLYSIN

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10.1136/thoraxjnl-2015-207770.92
The inflammatory response to bacteria requires the interaction of pattern recognition receptors with bacterial surface constituents, and humans deficient in components of inflammatory signalling pathways such as IRAK4 are prone to invasive pneumococcal disease. Pneumolysin is a well-recognised virulence factor for Streptococcus pneumoniae that has multiple effects on the host immune response that are primarily thought to be pro-inflammatory; including causing IL1B release due to pore formation, and epithelial cell layer breakdown. We hypothesised that pneumolysin deficient TIGR4 (a serotype 4 strain) would induce less inflammatory cytokines than wildtype from human monocyte derived macrophages. While both pore forming and non-cytolytic purified pneumolysin induced dose dependent inflammatory cytokine release, the pneumolysin deficient bacteria induced greater TNF and IL6 than wildtype, by qPCR and ELISA measurement of protein. This was reduced by inhibition of phagocytosis with cytochalasin D. Given the pore forming effects of pneumolysin we assessed whether differential cell death contributed to the differences in inflammatory response. While wildtype bacteria caused more cell death at 24 h, inhibition of caspases had no effect on the cytokine response suggesting that apoptosis pathways don’t directly influence the early inflammatory response. Transcriptome analysis confirmed increased pro-inflammatory and interferon gene signalling with the mutant strain, with reduction of the inflammatory and interferon signature with inhibition of phagocytosis. Wildtype bacteria induced less NFkB translocation, but more IRF3 translocation than Δply. An in vivo intranasal mouse infection showed wildtype was more virulent, with more bacteria recovered from bronchoalveolar lavage fluid at 4 h. However, this was associated with reduced TNF compared to Δply. Neutralising TNF intranasally abrogated the difference in bacteria recovered between wildtype and Δply. Thus, the early inflammation dampening effects of pneumolysin released within the phagolysosome may be an important contribution to its virulence by allowing bacterial replication at mucosal surfaces. This may be due to IRF3 mediated inhibition of inflammatory cytokine transcription. Better understanding of the biology of pneumolysin may aid in adjuvant treatment of S. pneumoniae.

New developments in cough

**S87 ARE ORAL STEROIDS EFFECTIVE IN TREATING THE SYMPTOMS OF ACUTE LOWER RESPIRATORY TRACT INFECTION IN NON-ASTHMATIC ADULTS? THE ORAL STEROIDS FOR ACUTE COUGH (OSAC) PLACEBO-CONTROLLED RANDOMISED TRIAL**

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Background The majority of UK adults experience at least one lower respiratory tract infection (LRTI, or acute bronchitis) a year. Despite an absence of evidence in this patient group, some GPs prescribe inhaled or oral corticosteroids. OSAC sought to demonstrate ‘proof of concept’ symptomatic effectiveness of a moderate dose of oral corticosteroid for adults without asthma or COPD with acute LRTI.

**Methods** OSAC was a double blind, placebo controlled RCT set in GP practices in England, powered to investigate if oral prednisolone reduces the duration of moderately bad or worse cough and/or the severity of its associated symptoms, when compared to placebo, by at least 20%. Adults (≥18 years) with acute (≤28 days) cough, for whom same-day antibiotics were not clinically indicated, and without asthma or COPD, received 40 mg oral prednisolone or matched placebo for 5 days. Symptom diaries, completed for up to 28 days, measured two primary outcomes: the duration of moderately bad or worse cough; and the average severity of all symptoms on days 2 to 4 on a scale of 0–6. We sought to demonstrate a minimum clinically important reduction of 20% in each outcome.

**Results** 398 participants were randomised to either prednisolone or placebo tablets (198 and 200 respectively) from 34 UK primary care sites. Attrition was lower than expected, giving over 85% power for the two primary outcomes. Data were analysed on an intention-to-treat basis. The median duration of moderately bad or worse cough was 5 days in both groups (IQRs 2–8 and 3–8 for prednisolone and placebo respectively). Adjusting for trial centre and baseline characteristics, this gave a hazard ratio of 1.11 (95% CI 0.89 to 1.39, p = 0.35). Symptom severity was lower in the prednisolone group (mean 1.99 vs 2.16), adjusted difference -0.090 (-0.212 to 0.003, p = 0.152).

**Conclusions** We found no evidence that a moderately high dose of oral corticosteroid reduced either duration of moderately bad (or worse) cough, or symptom severity at days 2 to 4 in adults without asthma or COPD with LRTI not requiring immediate antibiotic treatment. Lower dose oral or high dose inhaled corticosteroids are also unlikely to be beneficial.
release and changes in the PNE responsiveness to the TRPA1 channel against cinnamaldehyde (100 μM).

**Results** hPDCs undergo a fibroblastic to neuronal phenotypic switch to PNEs which express the sensory neuronal proteins SP and CGRP. Using qPCR we confirm that PNEs express TLR3, TLR4 and TLR7 mRNA and functional expression of TRPA1 and TRPV1 channels. PNEs pre-treated with PolyI:C (2 μg/ml) for 20 mins generated significantly larger inward (-10.8773 pA/pF; p < 0.01) and outward (10.0507 pA/pF; p < 0.01) currents in response to cinnamaldehyde (100 μM) compared to untreated PNEs (-2.347 pA/pF and 2.872 pA/pF respectively). The electrophysiological events elicited by PolyI:C occurred rapidly, were not sustained and appeared independent of alteration in TRP channel gene expression. PNEs incubated with PolyI:C for 24 h released significantly greater IL6 (246.504 pg/ml; p < 0.01) and IL8 (2140.83 pg/ml; p < 0.001) levels compared to untreated PNEs.

**Conclusion** Using a novel human in vitro sensory neuronal model we observed that Poly I:C evoked sensory neuronal hyper-responsiveness with an accompanying pro-inflammatory response. Respiratory viruses may induce similar effects on sensory neurons during exacerbations of airways disease.

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**Spoken sessions**

**S89** HYPERSENSITIVITY TO ADENOSINE TRIPHOSPHATE IN CHRONIC COUGH PATIENTS

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10.1136/thoraxjnl-2015-207770.95

**Introduction** Recent studies have suggested a role for adenosine triphosphate (ATP) activated P2×3 receptors in the pathophysiology of chronic cough. ATP has previously been used as an inhalational challenge substance in asthmatics and COPD patients, with the main focus being on bronchospasm. We have considered whether chronic cough patients are hypersensitive to inhaled ATP compared to healthy volunteers.

**Method** The recognised ERS standardised cough challenge using the Ko-Ko digidoser was performed with ATP and AMP as substrates. 20 Healthy volunteers and 20 chronic cough patients were randomised to the order of challenges. C5 (the concentration of substrate causing at least 5 coughs) was compared for ATP and AMP. Average cough response to ATP was compared between the 2 groups.

**Results** 6 male and 14 female volunteers in each group were randomised to receive cough challenges. Hull Airways Reflux Questionnaire score range was 0–8 in healthy volunteers and 21–52 in chronic cough patients. 1 healthy volunteer had a mild hypersensitivity reaction to ATP with urticaria. 1 patient withdrew after their first challenge due to worsening cough. No other side effects were reported. 2/19 healthy volunteers coughed with AMP, neither achieved C5. 8/20 chronic cough patients coughed with AMP, 2 achieved C5. 1/20 healthy volunteers coughed with ATP with 15 achieving C5. 19/19 chronic cough patients coughed with ATP, 18 achieved C5. The chronic cough patients had a greater cough response at lower concentrations of ATP as demonstrated in Figure 1.

**Discussion** Previous human ATP challenges have documented cough as a symptom but none have objectively measured the cough response in chronic cough patients. We present here the first results demonstrating that chronic cough patients have increased sensitivity to ATP compared to healthy volunteers. This supports a role for ATP driven receptors in the cough reflex arc and supports further research in this area as a target for treatments in chronic cough.

**S90** ‘CHRONIC COUGH, CAUSE UNKNOWN’: A QUALITATIVE STUDY OF PATIENT PERSPECTIVES OF IDIOPATHIC COUGH

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10.1136/thoraxjnl-2015-207770.96

**Introduction and objectives** Idiopathic chronic cough patients have symptoms that persist despite trials of empirical treatment with no underlying cause found. Higher-order brain processes are involved in modulating the cough reflex, but very little is known about the psychological processes underlying idiopathic cough. As the first step in the development of a complex intervention, we sought to elicit an in-depth understanding of patient experience of this condition.

**Methods** Fourteen patients (12 females, mean age = 59 years) participated in qualitative interviews theoretically based upon the comprehensive cognitive-behavioural model. Interviews were thematically analysed and cross-validated using the guidelines outlined by Braun and Clark (2006).

**Results** Eight key themes emerged illustrating the complex, all-encompassing nature of idiopathic cough. ‘Individual vulnerability’ described precipitating factors possibly linked with cough onset. ‘More than just a cough’ highlighted the co-occurrence of severe physical and emotional experiences. ‘Cough in the social sphere’ highlighted the effort of dealing with others’ reactions and concerns about the contagious image. ‘Cough and identity’ described how the cough often defines the person. The occurrence of ‘Vicious circles’ became apparent, contributing to cough maintenance. ‘The battle for control’ highlighted the unpredictable nature of the cough, its subsequent impact and the management strategies employed to counter this. Framing the ‘Cough in
relation to other health conditions’ provided coughers with a point of reference and some coherence to an otherwise confusing condition. The theme ‘At the end of the line’: the cough healthcare journey’ described the care experienced and the continuing search for answers.

Conclusions The onset and persistence of idiopathic cough is complex, involving many interlinking factors. Experimental evidence confirmed previous findings of the involvement of biological (e.g. urge-to-cough sensations) and psychological (e.g. attention) mechanisms. Importantly, it also highlighted the role of the social dimension in how the cough is perceived and managed. These insights suggest a valuable target for future interventions, which accordingly need to take a multi-disciplinary and integrative approach.

REFERENCE

A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSSOVER STUDY TO ASSESS THE EFFICACY OF A SINGLE DOSE OF 100 MG OF VRP700 BY INHALATION IN REDUCING THE FREQUENCY AND SEVERITY OF COUGH IN ADULT PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

1 Satia, 2I Badri, 2T Dockray, 1N Chaudhuri, 2G Brown, 3K Abbott-Banner, 3JA Smith. 1University Hospital of South Manchester, Manchester, UK; 2University of Manchester, Manchester, UK; 3Verona Pharma Plc, London, UK

Background Cough is a common, troublesome symptom in idiopathic pulmonary fibrosis (IPF), but the underlying mechanisms are poorly understood and effective therapies are lacking. VRP700 is thought to inhibit ion-channels found on sensory afferents innervating the airways. We aimed to investigate the efficacy of VRP700 in reducing cough frequency in patients with IPF.

Method A single centre double-blind randomised, placebo controlled crossover study in patients with IPF with chronic cough. Patients were randomised to receive a single inhaled dose of VRP700 (100 mg) or placebo and then crossed-over after a 7 day washout period. The primary endpoint was the number of coughs in the 4 h following the end of nebulisation for VRP700 compared with placebo, measured using an objective cough monitoring system (VitaloJAK, Vitalograph Ltd). Secondary endpoints included urge to cough visual analogue scale (VAS), cough severity VAS, and dyspnoea VAS, recorded at 1, 2 and 4 h post-dose, at the end of the day and 24 hrs post-dose.

Results Twenty five patients were screened, 5 were ineligible and some returned for a 7 day washout period. The primary endpoint was the number of coughs in the 4 h following the end of nebulisation for VRP700 compared with placebo, measured using an objective cough monitoring system (VitaloJAK, Vitalograph Ltd). Secondary endpoints included urge to cough visual analogue scale (VAS), cough severity VAS, and dyspnoea VAS, recorded at 1, 2 and 4 h post-dose, at the end of the day and 24 hrs post-dose.

Conclusions VRP700, administered by nebuliser as a single inhaled dose of 100 mg, did not reduce the frequency and severity of cough in IPF patients with troublesome cough. Instead the inhalation of VRP700 seemed to evoke coughing.

Mechanisms of airway inflammation and remodelling

S92 MATRIX METALLOPROTEINASE-1 ACTIVATION BY MAST CELL TRYP TASE CAUSES AIRWAY REMODELLING AND IS ASSOCIATED WITH BRONCHIAL HYPER-RESPONSIVENESS IN PATIENTS WITH ASTHMA

1 S Naveed, 2 D Clements, 2 D Jackson, 2 D Shave, 2 S Johnston, 1 S Johnson. 1University of Nottingham, Nottingham, UK; 2Imperial College, London, UK

Introduction Matrix Metalloproteinase-1 (MMP-1) is a collagenase, which is present, in its inactive form, in the airways, lung parenchyma and in broncho-alveolar lavage (BAL) fluid of patients with asthma. We hypothesised that MMP-1 could be activated during asthma exacerbations leading to extra-cellular matrix (ECM) processing which contributes to airway remodelling.

Methods Patients with stable, BTS stage 2/3 asthma, and healthy controls underwent Juniper asthma questionnaire, spirometry, methacholine challenge and bronchoscopy. Bronchial washings were processed for MMP-1 protein and activation. A second cohort of 14 patients with mild and 16 with moderate asthma and 10 controls underwent rhinovirus inoculation and had BAL fluid collected 14 days before and 4 days after inoculation. MMP-1 activity was assessed by fluorescent activity assay. ECM was prepared from decellularised airway smooth muscle (ASM) cultures. Cell proliferation was measured by MTT reduction assay and cell counts. Mast cell supernatants were obtained from cultures of HMC-1 cells activated using Phorbol 12-myristate 13-acetate/Ca2+ ionophore.

Results Pro-MMP-1 was expressed more strongly in bronchial washings in asthma than controls (P = 0.0003). After rhinovirus inoculation, asthma symptoms increased and lung function fell. BAL MMP-1 activity increased in asthma patients compared with controls (P = 0.047). MMP-1 protein and activity was positively associated with fall in FEV1 (R square = 0.3618) (P = 0.0039) post viral inoculation. Activated, but not control, mast cell supernatants increased both expression of pro- and active MMP-1 by ASM cell cultures. This was blocked almost completely by inhibitors of tryptase but not chymase or MMPs. Recombinant tryptase activated MMP-1 in vitro. ECM obtained from both control and asthma derived ASM cells treated with activated mast cell supernatants during matrix synthesis and ECM treated directly after decellularisation with active MMP-1 (10 ng/ml) enhanced subsequent ASM growth by 1.5 fold (P < 0.05).

Conclusions MMP-1 expression and activity in bronchial fluid is enhanced during asthma exacerbations and is associated with increased BHR. MMP-1 activation by mast cell tryptase processes ASM derived ECM to enhance ASM growth in-vitro. Our findings suggest that ASM/mast cell interactions during exacerbations may contribute to airway remodelling by generating a pro-proliferative matrix.
PULMONARY MATRIX METALLOPROTEINASES AND SMALL AIRWAYS DISEASE IN COPD – THE ORIGINS OF AIRFLOW OBSTRUCTION?

K Ostridge, N Williams, V Kim, M Bennett, S Harden, L Welch, S Boume, N Coombs, E Elkington, K Staples, T Wilkinson. Southampton NHMRC Respiratory Biomedical Research Unit, Southampton General Hospital, Southampton, UK; Southampton General Hospital, Southampton, UK; and Clinical and Experimental Sciences, University of Southampton Faculty of Medicine, Southampton, UK; Primary Care and Population Sciences, University of Southampton Faculty of Medicine, Southampton, UK.

Abstract S93 Table 1 Linear regression analysis between MMPs and CT measures of disease

<table>
<thead>
<tr>
<th></th>
<th>MMP-1</th>
<th>MMP-2</th>
<th>MMP-3</th>
<th>MMP-4</th>
<th>MMP-5</th>
<th>MMP-6</th>
<th>MMP-7</th>
<th>MMP-8</th>
<th>MMP-9</th>
<th>MMP-10</th>
<th>MMP-12</th>
<th>MMP-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emphysema% (LAA%)</td>
<td>0.01</td>
<td>0.02</td>
<td>0.25**</td>
<td>0.23**</td>
<td>0.15*</td>
<td>0.11</td>
<td>0.34**</td>
<td>0.01</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small airways Disease (E/I MLD)</td>
<td>0.14</td>
<td>0.14</td>
<td>0.53***</td>
<td>0.29*</td>
<td>0.56***</td>
<td>0.36**</td>
<td>0.50***</td>
<td>0.24*</td>
<td>0.00</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchial wall area (PI10)</td>
<td>0.03</td>
<td>0.00</td>
<td>0.00</td>
<td>0.01</td>
<td>0.04</td>
<td>0.01</td>
<td>0.00</td>
<td>0.17*</td>
<td>0.00</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

R² values given. *These values were log transformed to improve normality of residuals. LAA% (n = 31), PI10 (n = 31) and E/I MLD (n = 22). *p < 0.05 **p < 0.01 ***p < 0.001.
Background CRTH2 antagonism has been shown to reduce eosinophilic airway inflammation and improve lung function in patients with severe eosinophilic asthma. To better understand the role of CRTH2 in the pathogenesis of this asthma phenotype, we have carried out a cross-sectional study to investigate the CRTH2 positive cell counts in peripheral blood of patients with severe eosinophilic asthma.

Methods Blood was taken from 12 controls and 33 patients with asthma, 21 of whom met the 2014 ERS/ATS guideline criteria for severe asthma and had historical evidence of eosinophilic airway inflammation as defined before (Pavord et al. Lancet 2012;380:651–9). Th2 were detected as CD3+CD4+CRTH2+, Tc2 as CD3+CD8+CRTH2+, eosinophils as SSC brightly CRTH2+, and basophils as CD123+CRTH2+ by flow cytometry, and numbers presented as total cell counts in peripheral blood. Data were analysed using one-way ANOVA followed by the Newman-Keuls test.

Abstract S95 Figure 1 Comparison of eosinophil, basophil, Th2, Tc2 and total CRTH2+ cell counts in the blood from healthy control and different asthma patients. (p < 0.0001 for CRTH2+ and eosinophils; p < 0.001 for basophils; p < 0.05 for Th2; and p < 0.1 for Tc2. * p < 0.05 between the indicated groups)
Results  CRTH2 cell counts were reasonably repeatable within patients (ICC 0.84; n = 9). Mean ± SD CRTH2+ cell counts were 168 ± 81, 322 ± 191, 710 ± 322 and 290 ± 179 × 106 cells/L in normal controls (n = 12), patients with mild to moderate asthma (n = 12), patients with severe asthma at BTS step 4 (n = 10), and patients with severe asthma at BTS step 5 (n = 11) respectively (Figure 1). Most CRTH2+ cells were eosinophils (Figure 1).

Conclusion  Blood CRTH2+ cells are increased in subjects with severe eosinophilic asthma, mainly because of increased CRTH2+ eosinophils. Eosinophils and basophils numbers are significantly increased in severe eosinophilic asthma at step 4 but not step 5. Th2 and Tc2 cell numbers are less clearly associated with severe asthma. CRTH2+ cell numbers are lower in patients treated with prednisolone.

FREE-LIVING HAEMOPHILUS INFLUENZAE IS ASSOCIATED WITH INCREASED PULMONARY INFLAMMATION

Introduction  The most common pathogen in the lower airway of patients with COPD is *Haemophilus influenzae*. *H. influenzae* has been shown to be linked to inflammation and increased inflammation. Emerging evidence shows that pathogens can exist as either cell-associated or free-living (non-cell associated). We investigated whether detectable free-living *H. influenzae* correlates with pulmonary inflammation.

Methods  Cell-free sputum supernatants samples from 29 COPD patients (24 men), with a mean (range) age of 71 (45 to 88) years were analysed. All samples were collected at stable state and bacterial DNA was extracted, using a commercial assay and then quantified using real time-PCR utilising tagman hydrolysis probes. The *omp* P6 gene from *H. influenzae* was inserted into a positive cloning vector and transformed to generate plasmids. These plasmids were used as standards within the qPCR, allowing the accurate detection of very small levels of *H. influenzae* within the samples. Cytokines were measured using the mesoscale multi-array platform within the same sample set.

Results  Free Living *H. influenzae* was detected in 15/29 (52%) of cell-free samples, with a bacterial load of (geometric mean (95% CI)) of 1.23 × 10^6 gene copies/ml (2.63 × 10^5 to 5.75 × 10^6). Correlations were seen between free-living *H. influenzae* and Interleukin-1 Beta (IL1-β) (r = 0.47, p = 0.01), MMP8 (p = 0.04, r = 0.38), CCL3 (p = 0.002, r = 0.57), CCL13 (p = 0.02, r = 0.54), CCL26 (p = 0.03, r = -0.31), CCL4 (p = 0.04, r = 0.38). No significant correlations were seen between free-living *H. influenzae* and IL8 (p = 0.11, r = -0.30), IL10 (p = 0.10, r = -0.36) or TNF-alpha (p = 0.61, r = -0.12).

Conclusion  Free-living *H. influenzae* is associated with increased pro-inflammatory mediators in the airway. Whether this is related to the pathogenesis of COPD needs to be further investigated.

SEVERITY OF LUNG BUT NOT LIVER DISEASE IMPACTS CARDIOVASCULAR RISK IN ALPHA-1 ANTITRYPSIN DEFICIENCY

Introduction  Alpha-1 antitrypsin deficiency (AATD) is a genetic condition associated with COPD; patients homozygous for the mutant ‘Z’ allele (PiZZ) are predisposed to severe, early-onset emphysema of the lung, and also progressive fibrosis and cirrhosis of the liver. There is a well-known association between COPD and cardiovascular disease, with around 1 in 3 COPD deaths attributed to a cardiac cause. We hypothesised that cardiovascular risk in AATD may be independently modified by the severity of lung and liver disease, through common or related pathophysiological processes.

Methods  Cardiovascular risk was ascertained in 43 patients with PiZZ AATD using QRISK2 score and aortic pulse wave velocity (aPWV). These values were correlated with indicators of lung (FEV1, DLCO, KCO, RV) and structural liver disease (transient elastography and liver ultrasound).

Results  The severity of airflow obstruction (FEV1), emphysema (gas transfer) and gas trapping (RV) all related to cardiovascular risk as assessed by aPWV and QRISK2, Table 1. In contrast, there was no significant association between the presence or increased severity of structural liver disease, as assessed by ultrasound and transient elastography respectively, and either indicator of cardiovascular risk (p < 0.05).

Abstract S97 Table 1

<table>
<thead>
<tr>
<th></th>
<th>FEV1(l)</th>
<th>DLCO (mmol/min/kPa)</th>
<th>KCO (mmol/min/kPa/l)</th>
<th>RV (l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>aPWV (m/s)</td>
<td>-0.459</td>
<td>0.002</td>
<td>-0.516</td>
<td>-0.001</td>
</tr>
<tr>
<td>QRISK2 (% risk)</td>
<td>-0.335</td>
<td>0.043</td>
<td>-0.462</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Conclusions  These findings demonstrate that the severities of emphysema and airflow obstruction are associated with increased cardiovascular risk in AATD. In contrast, there was no association between the severity of structural liver disease and cardiovascular risk. Therefore, in conclusion, cardiovascular risk varies in PiZZ A1AD patients according to disease phenotype.

REFERENCE

Acute exacerbations are cardinal events in the natural history of chronic obstructive pulmonary disease (COPD) and are associated with increased morbidity and mortality. Tele-monitoring interventions are a relatively new field in COPD research and management. Furthermore, the effect of home tele-rehabilitation on COPD exacerbation has not been thoroughly studied. Therefore, we set out to investigate whether a home tele-rehabilitation program would be as beneficial as an outpatient maintenance rehabilitation program, in the context of COPD exacerbations, following completion of a 3-month course of supervised pulmonary rehabilitation.

We studied 137 Caucasian, ambulatory COPD patients. Forty seven patients were assigned to home maintenance tele-rehabilitation (FEV1, %pred = 50 ± 22, mean±SD). Fifteen patients were assigned to twice weekly hospital-based maintenance rehabilitation (FEV1, %pred = 52 ± 17). Forty COPD patients (FEV1, %pred = 52 ± 21), were not assigned to any rehabilitation program and served as controls. Tele-rehabilitation included home exercise reconditioning, self-management techniques, dietary, and psychological advice. Patients were provided with tablets and wireless devices to record and transmit data, related to symptoms, lung function, and vital signs, to a tele-health platform. Patients were followed up for 12 months.

At baseline there were no significant differences amongst the tele-rehabilitation (3.3 ± 3.1), hospital-based rehabilitation (3.4 ± 1.9), or control (3.3 ± 1.6), groups in terms of COPD exacerbations. After 12 months, COPD exacerbations in the group of home tele-rehabilitation were significantly reduced to 1.7 ± 1.7. In the group of hospital-based rehabilitation COPD exacerbations were also significantly reduced to 1.8 ± 1.4. In contrast, in the control group COPD exacerbations remained unchanged (3.5 ± 1.7). There were significant differences amongst the two rehabilitation groups (tele-rehabilitation and hospital-based) and the control group in terms of COPD exacerbations (p < 0.001).

In conclusion, ongoing home tele-rehabilitation with the use of tele-monitoring could significantly reduce COPD exacerbations and seems to be as beneficial as an outpatient hospital-based maintenance rehabilitation program in the context of COPD exacerbations. Thus, tele-rehabilitation may constitute a satisfactory alternative rehabilitative strategy to diminish health care costs.
Conclusions PR as currently delivered gives initial benefits to participants with ILD, however these are not sustained. More tailored approaches to this group are needed to improve the sustainability of response to PR.

**S100** IS IT FEASIBLE TO ASSESS DYNAMIC HYPERINFLATION DURING AN INCREMENTAL TREADMILL TEST IN PATIENTS WITH SEVERE ASTHMA?

1S Majd, 2E Dolmage, 3RH Green, 4P Bradding, 5SJ Singh, 6RA Evans. 1Leicester Respiratory Biomedical Research Unit, University of Leicester, Leicester, UK; 2Respiratory Department, West Park Healthcare Centre, Toronto, Canada; 3Respiratory Department, Glenfield Hospital, Leicester, UK; 4Centre for Exercise Rehabilitation Science, Glenfield Hospital, Leicester, UK. 10.1136/thoraxjnl-2015-207770.106

**Introduction** We wish to investigate whether dynamic hyperinflation contributes to exercise intolerance in patients with severe asthma. It is unclear whether there is an influence by the exercise platform. To begin with, we explored whether performing serial inspiratory capacity (IC) manoeuvres is feasible during a maximal incremental treadmill test in patients with severe asthma.

**Method** Patients with severe asthma (step 4–5 of the British Thoracic Society guidelines), MRC dyspnoea grade ≥2, were recruited from physicians specialising in the care of patients with difficult-to-treat asthma at Glenfield Hospital, Leicester. Patients were excluded if they had both fixed airflow obstruction (FEV₁/FVC <70%) and a smoking history of ≥10 pack years. All participants performed an incremental treadmill test to intolerance, with expiratory gas analysis, designed to produce a linear increase in peak oxygen uptake (VO₂). Patients performed a practice resting inspiratory capacity manoeuvre and then subsequently at rest, during the warm up phase and every two minutes during exercise.

**Results** 18 participants (8 female, mean [SD] 49 [14] yrs, BMI 31 [7] kg/m²; FEV₁/FVC 70 [13]%), 17% were ex-smokers) completed the treadmill test in a duration of 482 [120] s. Observations at peak exercise were: VO₂ 2.0 [0.4] L/min (100 [25]% predicted); ventilation 67 [18] L/min (87 [20]% maximum voluntary ventilation); heart rate 145 [17] beats/min (85 [9]% predicted); Borg Score for breathlessness 7 [2], perceived exertion 17 [3], 16 were predominantly limited by breathlessness. 115 IC manoeuvres were performed with only one data-point missed due to an incomplete manoeuvre. Figure 1 shows the mean end expiratory and inspiratory lung volumes during exercise. Six patients had an inspiratory reserve volume of <500 mls.

**Conclusion** Assessment for dynamic hyperinflation with serial inspiratory capacity manoeuvres during a maximal incremental treadmill test is feasible in patients with severe asthma. The relationship among lung volumes, time and ventilation can be established from rest to peak exercise with minimal practice of the IC manoeuvre or interruption to the test in this patient population.

**REFERENCE**


**S101** DO THOSE PATIENTS WITH A CHRONIC RESPIRATORY DISEASE THAT WALK AT A FASTER WALKING SPEED IMPROVE MORE POST PULMONARY REHABILITATION?

1El Chaplin, 5S Lohar, 3SJ Singh, 2SJ Singh. Centre for Exercise and Rehabilitation Science, Pulmonary Rehabilitation Department, Glenfield Hospital, University Hospitals of Leicester, Leicester, UK; 2School of Sport, Exercise and Health Sciences, Loughborough University, Loughborough, UK. 10.1136/thoraxjnl-2015-207770.107

**Introduction** Several baseline factors influence the response to Pulmonary Rehabilitation (PR). The Incremental and Endurance shuttle walk test is used to prescribe an exercise walking speed for patients with a chronic respiratory disease as part of a PR programme. We wished to explore the speed and duration of baseline endurance performance and observe how this impacted upon changes post rehabilitation particularly around the higher speeds of the endurance shuttle walk test (ESWT).

**Methods** Patients completed a 7 week outpatient PR programme comprising of both endurance and strength training. The endurance training is based on the ESWT speed which is 85% of the individual maximal capacity derived from the incremental shuttle walk test (ISWT). The ISWT and subsequent ESWT were performed at baseline and discharge. Patients were categorised into low (<3.6 km/hr) or high (>3.6 km/hr) speed walkers based on their baseline ESWT performance.

**Results** 990 patients completed the SWT: 567 low speed walkers (mean age 70.9 ± 9.7 years; FEV₁ 1.5 L ± 4.9; BMI 27.6 ± 9.0 kg/m²; MRC 4 (IQR 3–4); ISWT pre 128.4 ± 61.6 m; ESWT pre 166.3 ± 161.5 secs) and 423 high speed walkers (mean age 67.8 ± 9.2 years; FEV₁ 1.62 L ± 3.8; BMI 27.1 ± 14.0 kg/m²; MRC 3 (IQR 2–3); ISWT pre 373.4 ± 103.3 m; ESWT pre 262.4 ± 147.6 secs). Those walking at a higher speed had a significantly higher pre ESWT (p ≤ 0.001). A statistically significant improvement was observed in the ESWT within each group (low: mean change 344.2 ± 401.5 p ≤ 0.001; high: mean change 369.3 secs p ≤ 0.001). However the change in ESWT was not significantly different between the groups (p = 0.3).
SOX2 INITIATES CARCINOGENESIS IN A NOVEL ORGANOTYPIC MODEL OF BRONCHIAL DYSPLASIA

Lung cancer biology and biomarkers

SOX2 INITIATES CARCINOGENESIS IN A NOVEL ORGANOTYPIC MODEL OF BRONCHIAL DYSPLASIA

Abstract S101 Table 1

<table>
<thead>
<tr>
<th></th>
<th>Low speed walkers (n = 567)</th>
<th>High speed walkers (n = 423)</th>
<th>Between group differences (p value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.9 ± 9.7</td>
<td>67.8 ± 9.2</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>1.5 ± 4.9</td>
<td>1.62 ± 3.8</td>
<td>P = 0.7</td>
</tr>
<tr>
<td>MRC (IQR)</td>
<td>4 (IQR 3–4)</td>
<td>3 (IQR 2–3)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.6 ± 9.0</td>
<td>27.1 ± 14.0</td>
<td>P = 0.5</td>
</tr>
<tr>
<td>Pre ISWT (m)</td>
<td>128.4 ± 61.6</td>
<td>373.4 ± 103.3</td>
<td></td>
</tr>
<tr>
<td>Post ISWT</td>
<td>191.8 ± 91.1</td>
<td>415.9 ± 115.0</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Change in ISWT</td>
<td>63.4 ± 66.1</td>
<td>42.6 ± 67.7</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Pre ESWT (secs)</td>
<td>166.3 ± 161.5</td>
<td>262.4 ± 147.6</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Post ESWT</td>
<td>510.5 ± 428.4</td>
<td>631.7 ± 388.5</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Change in ESWT</td>
<td>344.2 ± 401.5</td>
<td>369.3 ± 363.9</td>
<td>P = 0.3</td>
</tr>
</tbody>
</table>

All values are mean (±SD) unless otherwise stated. FEV1, forced expiratory volume in 1 s; MRC, Medical Research Council; IQR, interquartile range; BMI, body mass index; ISWT, Incremental shuttle walk test; m, metres; ESWT, endurance shuttle walk test; sec, seconds.

Conclusion Interestingly, those patients who walk at a faster speed have a greater baseline ESWT performance compared to those patients who walk at a slower endurance speed. However both groups made comparable changes in the ESWT following PR.

Lung cancer biology and biomarkers

SOX2 INITIATES CARCINOGENESIS IN A NOVEL ORGANOTYPIC MODEL OF BRONCHIAL DYSPLASIA

Introduction and objectives Improving the early detection and chemoprevention of lung cancer are key to improving outcomes. The pathobiology of early squamous lung cancer is poorly understood. We have shown in a previous publication that amplification of SOX2 is an early and consistent event in the pathogenesis of this disease but its functional oncogenic potential remains uncertain. We aimed to test the impact of deregulated SOX2 expression in a novel organotypic system that recreates both the molecular and microenvironmental context in which squamous carcinogenesis occurs.

Our objectives are:

1. To develop a 3D in vitro model of bronchial dysplasia that recapitulates key molecular and phenotypic characteristics of the human disease.
2. To test the hypothesis that SOX2 deregulation is a key initiating event in the pathogenesis of bronchial dysplasia.

Methods We use lentiviral transduction to facilitate the inducible activation of SOX2 in immortalised bronchial epithelial cells iBECs. We use lentiviral shRNA and cutting edge CRISPR genome editing technology to introduce specific defects in key tumour suppressor pathways in order to recapitulate the molecular context seen in vitro. We incorporate the genetically manipulated iBECs at the air-liquid interface in a 3-dimensional tissue culture system that also comprises a stromal equivalent with embedded pulmonary fibroblasts and carefully defined media to build an organotypic model of bronchial dysplasia.

Results We develop a model that recapitulates human bronchial dysplasia. SOX2 deregulation does not cause an obvious phenotype in standard tissue culture conditions, but can initiate the dysplastic phenotype in 3D culture systems. Loss of TP53 and PTEN are co-operating genetic events that potentiate the dysplastic phenotype. The alterations in cell signalling pathways recapitulate signatures seen in invasive squamous cell lung cancer.

Conclusions In the appropriate molecular and microenvironmental context acute deregulation of SOX2 expression initiates and drives bronchial dysplasia. This confirms its oncogenic potential in human cells. This model can be used to test the impact of therapeutic agents aimed at chemoprevention and the potential for co-operating genetic lesions to drive disease progression.

S103 SYNTHESIS OF GOLD-BASED NANOMEDICINES TO TREAT NON-SMALL CELL LUNG CANCER

AM Cryer, P Rueca, TD Tietley, AJ Thorley. NHLI, Imperial College London, London, UK

Introduction Lung cancer is the leading cause of cancer death worldwide, with an average 5 yr survival rate of just 9.5% in the UK. The success of current chemotherapy regimens for non-small cell lung cancer (NSCLC), the predominant subtype of lung cancer, is hindered by poor tumour penetration and accumulation, and systemic side effects which significantly affect patient quality of life. The field of cancer nanomedicine seeks to overcome these problems by utilising the unique physicochemical properties of nanoparticles; gold-based nanomedicines (AuNPs) show particular promise as they may be able to offer multimodal therapeutics and diagnostics in a single formulation.

Objectives This study aimed to conjugate cisplatin and pemetrexed, a first line therapy for NSCLC, to AuNPs, and investigate their efficacy on tumour cell proliferation compared to free drug. Furthermore, we investigated whether conjugation to AuNPs abrogated the inflammatory and toxic effects of these drugs on non-cancer human pulmonary epithelial cells.

Methods Cisplatin and pemetrexed were conjugated to AuNPs using heterobifunctional polyethylene glycol (PEG) linkers and were characterised by electron microscopy, ICP-OES, dynamic light scattering and thermogravimetric analysis. The effect of conjugates in in vitro cancer (H226 and A549 cells) and non-cancer (human alveolar type I epithelial cells) cell models were measured by electric cell-substrate impedance sensing (ECIS), MTT assay, ELISA and confocal microscopy.

Results Nanoparticle characterisation confirmed successful conjugation of cisplatin and pemetrexed to AuNPs. Confocal microscopy demonstrated that nanoparticles were internalised by cancer cells and distributed throughout the cytoplasm. Further studies showed that conjugates inhibited cancer cell proliferation significantly more than the respective free drug (Figure 1) and abrogated free drug cytotoxicity in non-cancer alveolar type I epithelial cells (0% cell death vs 30% respectively; 10 μM cisplatin; P < 0.001). Conjugates also attenuated chemotherapy-induced IL-6 release in both cancer and non-cancer cells; 10 μM cisplatin induced 6.6-fold and 7-fold greater IL-6 release compared to equimolar conjugates in H226 and alveolar type I epithelial cells respectively (P < 0.001).

Abstract S101 Table 1
Conclusions We have synthesised gold-based nanomedicines that are more efficacious and biocompatible than free drug in in vitro cell models, suggesting these formulations could have enhanced therapeutic potency and improve patient quality of life.

S104 FACTORS AFFECTING SENSITISING EGFR MUTATION RATE AND CELL TYPE IN STAGE IIIIB/IV LUNG CANCER

Introduction Treatments for advanced lung cancer in patients with a poor performance status are limited. Such patients (PS 3–4) may not be suitable for chemotherapy for NSCLC, but may benefit from chemotherapy if SCLC is confirmed or treatment with an EGFR-TKI if an EGFR sensitising mutation (EGFR-sm) is detected. Estimates of the likelihood of detecting these two subtypes will enable patients to make informed decisions about undergoing biopsy confirmation.

Aim To analyse patient factors that affect the frequency of sensitising EGFR mutations and cell types in patients with stage IIIIB/IV lung cancer.

Method Retrospective review of an electronic database of stage IIIIB/IV lung cancer patients with known cell type from 2008-2013 where a quantified smoking history was available. Where EGFR testing was not performed, the estimated prevalence of EGFR-sm was extrapolated from those patients tested according to cell type. Patients with small cell and large cell lung cancer were presumed to be EGFR wild type.

Results 1033 were identified who fulfilled the inclusion criteria. Cell types were as follows: Adenocarcinoma 31.2%, Squamous Cell 23.5%, Small Cell 22.7%, NSCLC NOS 16.2% and Large Cell 6.4%.

Of 348 (33.7%) undergoing genetic testing, EGFR-sm were found in 39 (11.2%) patients. These included 32 of 241 (13.3%) adenocarcinoma, 6 of 80 (7.5%) NSCLC and 1 of 27 (3.7%) squamous cell. The prevalence of EGFR-sm was estimated for the 384 patients with Adenocarcinoma, NSCLC and Squamous Cell Carcinoma who were not tested.

Table 1 shows the effect of age and pack year smoking history on EGFR mutation status and cell type. Logistic regression analysis shows increasing pack years (p = 0.001) and younger age (p = 0.004) are associated with a lower rate of sensitising EGFR mutations. Increasing pack years is associated with a higher frequency of small cell cancers, but this is not affected by age.

Conclusion Smoking status significantly impacts the likelihood of detecting both EGFR-sm and SCLC, whereas age alters the likelihood of EGFR-sm alone. These data may allow a more informed discussion regarding the likelihood of detecting an actionable result in patients with advanced lung cancer with poor performance when discussing options for biopsy.

S105 MICRODROPLET DIGITAL PCR FOR THE LONGITUDINAL MONITORING OF CIRCULATING TUMOUR DNA BIOMARKERS IN UNSELECTED PATIENTS WITH ADVANCED LUNG CANCER

Introduction and objectives Circulating cell-free tumour DNA (cfDNA) can be detected in patients with solid organ malignancies and has the potential to be used as a non-invasive biomarker. Specific mutational events can be identified in biopsies using targeted next-generation sequencing and individualised microdroplet digital PCR (mdPCR) assays designed to detect and monitor the individualised biomarker in plasma. This can inform
the timing (and sometimes mechanism) of disease progression or treatment failure.

To date this has been demonstrated in patients with EGFR and KRAS mutations.

Our objective was to determine if this approach could be applied to an unselected cohort of patients with advanced non-small cell lung cancer (adenocarcinoma subtype).

Methods Unselected treatment-naive patients with lung cancer were recruited from thoracic oncology clinics. Paired DNA from tumour biopsies and baseline/longitudinal plasma samples was obtained. Targeted next-generation sequencing (NGS) was performed using a 26-gene panel on biopsy-derived DNA. Primer sets and probes for identified mutations were optimised and validated on a the BioRad-QX100 mdPCR system.

Results The NGS data is summarised in Table 1.

CtDNA from plasma has been tested for specific mutations including in PIK3CA, TP53, and BRAF as well as KRAS and EGFR in these patients. In 16 of the 19 patients in which mutations were identified the mutation has also been detected in the plasma. The range of detected MAFs was between <0.1–49.6%.

It was noteworthy that there was discordance between the biomarker response and RECIST1.1 criteria in some patients.

Conclusion It is feasible to perform a targeted NGS analysis on DNA from standard fixed diagnostic lung adenocarcinoma specimens and then validate and use individualised molecular biomarkers for use in a microdroplet digital PCR assay of cell-free circulating tumour DNA. There is potential for this approach to inform clinical decision-making.

This is a robust and low cost means of monitoring treatment response non-invasively and merits further evaluation in a clinical trial.

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### Abstract S105 Table 1 Results of targeted next generation sequencing from cohort of 20 patients

<table>
<thead>
<tr>
<th>Pt Biopsy type</th>
<th>Total DNA loaded (ng)</th>
<th>Mutation 1</th>
<th>Mutation 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Lung biopsy</td>
<td>NK</td>
<td>EGFR exon 19 deletion</td>
<td>33</td>
</tr>
<tr>
<td>2 Pleural fluid</td>
<td>NK</td>
<td>KRAS G12R</td>
<td>28</td>
</tr>
<tr>
<td>3 Bronchial biopsy</td>
<td>33</td>
<td>TP53 P15S</td>
<td>20.42</td>
</tr>
<tr>
<td>4 Bronchial biopsy</td>
<td>26</td>
<td>BRAF V600E</td>
<td>35.1</td>
</tr>
<tr>
<td>5 EBUS</td>
<td>25</td>
<td>KRAS G12V</td>
<td>49.33</td>
</tr>
<tr>
<td>6 EBUS</td>
<td>27</td>
<td>EGFR ex 19 del</td>
<td>63.5</td>
</tr>
<tr>
<td>7 EBUS</td>
<td>33</td>
<td>TP53 K114R</td>
<td>52.97</td>
</tr>
<tr>
<td>8 EBUS</td>
<td>12</td>
<td>TP53 K132E</td>
<td>40.76</td>
</tr>
<tr>
<td>9 EBUS</td>
<td>12</td>
<td>KRAS G12C</td>
<td>13.75</td>
</tr>
<tr>
<td>10 EBUS</td>
<td>33</td>
<td>TP53 R281P</td>
<td>74.19</td>
</tr>
<tr>
<td>11 EBUS</td>
<td>33</td>
<td>KRAS G12C</td>
<td>39.02</td>
</tr>
<tr>
<td>12 Lung biopsy</td>
<td>23</td>
<td>PIK3CA H1047R</td>
<td>28.95</td>
</tr>
<tr>
<td>13 Lung biopsy</td>
<td>3</td>
<td>TP53 R158L</td>
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</tr>
<tr>
<td>14 Lung biopsy</td>
<td>4</td>
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<tr>
<td>15 Lung biopsy</td>
<td>16</td>
<td>TP53 1bp delTPM</td>
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</tr>
<tr>
<td>16 Lung biopsy</td>
<td>33</td>
<td>TP53 E528*</td>
<td>12.88</td>
</tr>
<tr>
<td>17 Lung biopsy</td>
<td>33</td>
<td>EGFR ex 19 del</td>
<td>36.51</td>
</tr>
<tr>
<td>18 Brain biopsy</td>
<td>33</td>
<td>KRAS G12L</td>
<td>52.46</td>
</tr>
<tr>
<td>19 Lymph node</td>
<td>8</td>
<td>No mutation</td>
<td>No</td>
</tr>
<tr>
<td>20 Pleural biopsy</td>
<td>33</td>
<td>TP53 C141Y</td>
<td>62.13</td>
</tr>
</tbody>
</table>

MAF, Mutant Allele Frequency. *Both EGFR and PS3 mutation detected in plasma. **Only two reports of G12L in lung cancer on COSMIC out of >20,000.

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### Nintedanib or pirfenidone?

CONSISTENT EFFECT OF NINTEDANIB ON DECLINE IN FVC IN PATIENTS ACROSS SUBGROUPS BASED ON HRCT DIAGNOSTIC CRITERIA: RESULTS FROM THE INPULSIS® TRIALS IN IPF

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10.1136/thoraxjnl-2015-207770.112

Introduction The two replicate, randomised, placebo-controlled, 52-week INPULSIS® trials assessed the efficacy and safety of nintedanib 150 mg twice daily (bid) in patients with IPF. The primary endpoint was met in both trials; nintedanib significantly reduced the annual rate of decline in FVC compared with placebo, consistent with a slowing of disease progression.

Methods To qualify for the INPULSIS® trials if a surgical lung biopsy was unavailable, patients needed to have a high-resolution computed tomography (HRCT) scan showing honeycombing and/or a combination of reticular abnormality and traction bronchiectasis, without features suggestive of alternative causes. Surgical lung biopsies, if available, were used to confirm eligibility.

A post-hoc subgroup analysis of patients with diagnosis based on honeycombing and/or confirmation of usual interstitial pneumonia (UIP) by biopsy versus patients with no honeycombing and no biopsy was undertaken using pooled data from both trials.

Results 723 patients (425 nintedanib, 298 placebo) had honeycombing and/or confirmation by biopsy and 338 (213 nintedanib, 125 placebo) had no honeycombing or biopsy for diagnosis of IPF. Demographics and baseline characteristics were similar between these subgroups. In patients with honeycombing and/or biopsy, the adjusted annual rate of decline in FVC was -108.7 mL/year with nintedanib and -225.7 mL/year with placebo (difference: 117.0 mL/year [95% CI: 76.3, 157.8]); in patients with no honeycombing or biopsy, it was -122.0 mL/year with nintedanib and -221.0 mL/year with placebo (difference: 98.9 mL/year [95% CI: 36.4, 161.5]). The treatment by subgroup interaction

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20 patients in our test cohort had stage IIIIB/IV lung adenocarcinoma. These included cytology specimens – EBUS, lymph node FNA and pleural effusion, percutaneous biopsies, pleural biopsies and a brain biopsy. The mean quantity of DNA used for targeted resequencing was 23 ng. The lowest read depth for the identified mutations was 1639; in general coverage was >10,000.
The p-value was not significant for the primary endpoint \( (p = 0.81) \) or for the key secondary endpoints of time to first acute exacerbation \( (p = 0.37) \) or change from baseline in St George’s Respiratory Questionnaire total score \( (p = 0.67) \), indicating that the treatment effect of nintedanib was not statistically significantly different between the subgroups.

**Conclusion**
Decline in FVC in placebo arms was virtually identical in patients with A) the presence of honeycombing and/or biopsy confirmation of UIP; and B) the absence of both, but features of “possible UIP” on HRCT. Nintedanib slowed FVC decline equally in both sub-groups. These findings have major implications for diagnosis and clinical trial design.
EFFECT OF BASELINE FVC ON DECLINE IN LUNG FUNCTION WITH NINTEDANIB IN PATIENTS WITH IPF: RESULTS FROM THE INPULSIS® TRIALS

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Introduction The two replicate, randomised, placebo-controlled, 52-week Phase III INPULSIS® trials assessed the efficacy and safety of nintedanib 150 mg twice daily (bid) in patients with idiopathic pulmonary fibrosis (IPF). Patients with forced vital capacity (FVC) ≥50% predicted were included. The primary endpoint, the annual rate of decline in FVC, was significantly reduced in the nintedanib group compared with placebo in both trials, consistent with a slowing of disease progression. Key secondary endpoints were time to first acute exacerbation and change from baseline in St. George’s Respiratory Questionnaire total score, both over 52 weeks. In a pre-specified subgroup analysis of patients with baseline FVC ≥70% versus >70% predicted, the treatment effect of nintedanib on decline in FVC was consistent in both subgroups.

Methods A post-hoc subgroup analysis of patients with baseline FVC >90% versus ≤90% predicted was undertaken using pooled data from the INPULSIS® trials to investigate whether patients with marginally impaired FVC receive the same benefit from nintedanib.

Results 274 patients (nintedanib 166, placebo 108) had baseline FVC >90% predicted and 787 patients (nintedanib 472, placebo 315) had baseline FVC ≤90% predicted. There was no significant treatment-by-subgroup interaction for the primary endpoint (p = 0.5300); in patients with baseline FVC ≤70% versus >70% predicted, the treatment effect of nintedanib on decline in FVC was consistent in both subgroups. Consistent results were observed for changes from baseline in FVC over time (Figure 1). No significant treatment-by-subgroup interaction was observed for the key secondary endpoints. The frequency of adverse events and serious adverse events was comparable between the treatment arms of each subgroup.

Conclusion In a subgroup analysis of pooled data from the INPULSIS® trials, nintedanib 150 mg bid slowed the decline in lung function in patients with IPF independent of degree of lung function impairment at baseline, suggesting that patients with marginally impaired FVC also benefit from treatment with nintedanib.

EFFECT OF CONTINUED TREATMENT WITH PIRfenIDone FOLLOWING A CLINICALLY MEANINGFUL DECLINE IN PERCENT PREDICTED FORCED VITAL CAPACITY IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS (IPF)

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Conclusion In a subgroup analysis of pooled data from the INPULSIS® trials, nintedanib 150 mg bid slowed the decline in lung function in patients with IPF independent of degree of lung function impairment at baseline, suggesting that patients with marginally impaired FVC also benefit from treatment with nintedanib.
Introduction and objectives The clinical course in patients with IPF is characterised by substantial inter- and intra-subject variability in the rates of disease progression, thereby confounding clinical assessments of therapeutic responses in individual patients. We pooled data from three Phase 3 trials to assess the potential benefit of continued treatment with pirfenidone in patients who experienced a ≥10% decline in percent predicted forced vital capacity (%FVC) during the first 6 months of treatment.

Methods Source data included all patients randomised to treatment with pirfenidone 2403 mg/d or placebo in the Phase 3 ASCEND or CAPACITY studies (N = 1247). We selected patients with a ≥10% absolute decline in %FVC by the month 3 or 6 study visit and compared the proportion of patients in the pirfenidone and placebo groups who experienced any of the following during the subsequent 6-month interval: (1) ≥10% absolute decline in %FVC or death; (2) no further decline in %FVC; or (3) death. Observed data were used in the analysis.

Results 34 (5.5%) and 68 (10.9%) patients in the pooled pirfenidone and placebo groups, respectively, experienced a ≥10% absolute decline in %FVC between baseline and month 6 (relative difference, 49.5%). Analysis of outcomes during the subsequent 6-month interval demonstrated that fewer patients in the pirfenidone group compared with placebo experienced a ≥10% decline in %FVC or death (pirfenidone, 2/34 [5.9%] vs. placebo, 19/68 [27.9%]). More patients in the pirfenidone group compared with placebo had no further decline in %FVC (20/34 [58.8%] vs. 26/68 [38.2%]; Table 1). Additionally, there were fewer deaths in the pirfenidone group (1/34 [2.9%]) compared with placebo (14/68 [20.6%]).

Conclusions Among patients who experienced a ≥10% decline in %FVC during the first 6 months of treatment, continued treatment with pirfenidone resulted in a lower risk of %FVC decline or death during the subsequent 6 months. These findings suggest a potential benefit to continued treatment with pirfenidone despite an initial decline in FVC.
Conclusion In the TOMORROW trial, the effect of nintedanib on slowing disease progression in patients with IPF was maintained up to week 76. No relevant changes in the safety and tolerability of nintedanib were observed with treatment up to week 76 compared with week 52.

Pseudomonas: digging for gold or search and destroy?

Abstract S111 Figure 1

Conclusions Pirfenidone treatment reduced disease progression (decline in FVC and TLco) in our total cohort. Our results indicate that patients with rapid decline in FVC may benefit most from pirfenidone. Those declining at less than 200 ml per year may not benefit. These results suggest that further clinical studies are warranted, including patients with evidence of rapid lung function decline with FVC >80% predicted.
explain this is being explored and numbers increased. The results may help determine the best methodology for assessing isolate susceptibility to a phage mix for inclusion in a future clinical trial.

**AN EPIDEMIOLOGICAL REVIEW OF STRAINS OF PSEUDOMONAS AERUGINOSA IN A NON-CYSTIC FIBROSIS BRONCHIECTASIS COHORT**

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10.1136/thoraxjnl-2015-207770.119

**Introduction and objectives** *Pseudomonas aeruginosa* (Pa) is a significant respiratory pathogen. Research in Cystic Fibrosis cohorts has revealed transmissible strains, leading to heightened infection control protocols due to concerns of cross-infection. In patients with Non-Cystic Fibrosis Bronchiectasis (NCFB), the research is more limited. Our objectives were to investigate the strains found in our local NCFB population, and assess the occurrence of shared strains.

**Methods** Patients with NCFB and previous Pa in sputum culture consented to providing sputum for the study and review of their medical notes. Sputum samples from patients were processed in the usual manner and if Pa was isolated, 10 representative colonies per patient were stored for strain typing. Isolates were subjected to Random Amplification of Polymorphic DNA (RAPD). Distinct RAPD types were verified by electrophoresis on an Agilent Bioanalyzer and subsequent cluster analysis using GelCompar II software, and further investigated by Multi-Locus Sequence Typing (MLST).

**Results** Pa was obtained from 46 patients over 12 months providing 459 isolates. Co-existence of multiple strains was observed in two patients. Twenty patients (43%) had unique strains by RAPD and the remaining patients were clustered into 7 subgroups, defined as ≥90% homology by RAPD, using Pearson’s correlation analysis. The largest cluster showed a predominance of one MLST strain type identified as ST-17 (also known as “Clone C”) on the MLST database. In our cohort, 8 patients (17%) harboured Clone C, which is a higher prevalence than observed in previous UK studies of various patient cohorts (typically 2–6% prevalence). MLST analysis of smaller RAPD clusters identified other MLST strain types shared by 2 or 3 patients. As with Clone C, all the observed shared MLST strain types are globally distributed. MLST did not reveal any novel shared strains.

**Conclusions** Our cohort of patients with NCFB shows evidence of shared strains of Pa including a high prevalence of Clone C compared to previous national reports. Whilst the occurrence of shared strains may reflect their global distribution, we cannot rule out cross-infection between patients.

**FEASIBILITY STUDY FOR A RANDOMISED CONTROLLED TRIAL OF PSEUDOMONAS AERUGINOSA ERADICATION TREATMENT IN PATIENTS WITH BRONCHIECTASIS**

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10.1136/thoraxjnl-2015-207770.120

**Introduction** Guidelines recommend Pseudomonas aeruginosa (PA) eradication treatment for new isolation of PA in bronchiectasis patients, but evidence is lacking. We performed a feasibility study to identify how many patients with new PA isolation would be eligible for a future randomised controlled trial (RCT).

**Methods** For 12 months (2013–2014) we piloted a PA “alert” system that would notify the study team when PA was isolated in sputum samples. Patients were reviewed using electronic medical records to classify patients as 1- New PA, having never isolated PA before and therefore eligible for eradication, 2- Relapsed PA, patients having been free from PA and now isolating it again therefore eligible for eradication, 3- Chronic PA, and therefore not eligible for eradication, 4- patients without HRCT confirmed bronchiectasis. Anti-PA IgG antibodies were measured in serum as a predictor of potential eradication success.

**Results** There were 322 PA isolates from sputum over 12 months, in 156 patients. 22 patients presented new PA, 13 patients relapsed PA, 17 chronic PA and 104 patients did not have bronchiectasis (66%). The most frequent diagnoses in the non-bronchiectasis group was COPD.

Overall, 35 patients would have been eligible for a trial of PA eradication on clinical grounds. Of these patients, clearance (negative PA culture at next follow-up sample) was demonstrated in 63%.

PA IgG was positive in all of the patients with chronic PA, and identified those with successful clearance: sensitivity 93% and specificity 54%. A low antibody level was strongly associated with successful eradication (negative likelihood ratio 0.06, successful eradication in 92.3%).

Mortality was very high in this patient group. 9%, 30% and 24% of patients died within 12 months follow-up in the 3 groups respectively.

**Conclusion** This feasibility demonstrates that a future community based RCT of PA eradication would require a large number of centres, and be resource intensive. Major challenges in powering a future study include the low proportion of true first isolates and the high frequency of spontaneous PA clearance. Raised PA IgG was not sufficiently specific to exclude successful eradication, but a low PA IgG suggests a high likelihood of success.

**EFFICACY OF PSEUDOMONAS AERUGINOSA ERADICATION REGIMENS IN NON-CF BRONCHIECTASIS**

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10.1136/thoraxjnl-2015-207770.121

**Introduction and objectives** BTS guidelines recommend to try and eradicate Pseudomonas aeruginosa when first isolated from patients with non-CF bronchiectasis. The aims of this study were to 1) define the different eradication regimens used in our respiratory centre and 2) evaluate their efficacy.

**Methods** The medical notes of adult non-CF bronchiectasis patients who underwent eradication trial for *P. aeruginosa*, between 2007 and 2014, were retrospectively reviewed. Eradication was considered successful if all (and at least 3) respiratory samples collected during the 6-month period following initiation of eradication were free of *P. aeruginosa*.

**Results** During the study period, 67 patients (58% male, average age 63.0 yrs) had at least one eradication trial. The majority of
regimens used combined nebulised colomycin with either oral ciprofloxacin or intravenous antipseudomonal antibiotics as first line therapy. (Table 1, n = 57; 85%). Overall, first eradication attempts were successful in 52% of cases (35/67). Regimens including nebulised colomycin were more effective (n = 23/38; 60%) than those without it (20%; 2/10) (Fisher’s exact test, \( p = 0.04 \)). Longer courses of ciprofloxacin (>3 weeks) did not improve outcome in comparison with shorter (≤3 weeks) courses (\( p = NS \)). Furthermore, intravenous antibiotics were not superior to oral ciprofloxacin (\( p = NS \)). Amongst the 32 patients who failed to eradicate \( P. \) aeruginosa in the first instance, 20 underwent a second attempt. In comparison with first trials, overall success rate of second trials decreased to 35% (n = 7/20). However, this difference did not reach statistical significance (Fisher’s exact test, \( p = 0.3 \)). Nineteen patients, who initially successfully cleared \( P. \) aeruginosa, required a 2nd eradication trial later during the study period. For those patients, the eradication success was 53%, comparable to the first one.

Conclusions Eradication regimens combining systemic and nebulised antibiotics appear more effective than systemic antibiotics alone to achieve \( P. \) aeruginosa eradication in non-CF bronchiectasis patients.

Best of basic science advances

**S116**

GDF-15, THE MIR-542 CLUSTER AND MIR-422A ARE ASSOCIATED WITH MUSCLE WASTING IN INTENSIVE CARE UNIT ACQUIRED PARESIS

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Introduction and aims Intensive care unit acquired paresis (ICUAP) is a common complication of critical illness, associated with significant morbidity and mortality in patients admitted to the ICU. To date, there has been little success in the identification of patients at risk of acute muscle wasting or potential targets for therapeutic intervention.

GDF-15, a TGF-B family member, has been shown to be a potential driver of acute muscle wasting in ICUAP (Crit Care Med 2013;41:982). From previous analyses in ICUAP and other wasting conditions, we hypothesised that pre-surgery expression of microRNAs from the miR-542 family would be higher in patients who would lose significant muscle bulk following surgery, whereas expression of miR-422a would be lower.

Methods A prospective observational study of 40 patients undergoing high-risk cardiothoracic surgery with cardiopulmonary bypass was conducted. Patients underwent pre- and post-operative paired rectus femoris biopsies and blood sampling. Muscle wasting was assessed by ultrasound pre-operatively and at day 7 post surgery. Plasma GDF-15 protein was quantified by ELISA and mRNA and microRNA expression in muscle specimens by RT-PCR.

Main results 52% (21 of 40) patients developed muscle atrophy. Plasma GDF-15 concentration was significantly raised at all sampling time points in patients with significant muscle wasting (wasters) compared to those that did not (non-wasters). miR-542–3p (median 1.9-fold, \( p = 0.0029 \)), miR-542–5p (median 4.5-fold, \( p = 0.0346 \)) and miR-424 (median 4.2-fold, \( p = 0.0040 \)) were higher in pre-operative muscle specimens of wasters compared to non-wasters, whilst miR-422a was lower (median 1.2-fold, \( p = 0.0176 \)). Expression of these miRNAs significantly correlated with change in rectus femoris cross-sectional area over time (see Figure 1).

Conclusions There is a high risk of muscle wasting in ICUAP patients. Plasma GDF-15 concentration and pre-operative expression of specific miRNAs (miR-542–3p, miR-542–5p, and miR-424) are associated with muscle wasting. These data provide further support for the involvement of the p53 stress pathway in muscle wasting in ICUAP patients.
contributes to this susceptibility. This study identifies these microRNAs as potential therapeutic targets in ICUAP.

S117 RSIV. F/HN-MEDIATED GENE THERAPY ENABLES LUNGS TO PRODUCE THERAPEUTICALLY RELEVANT LEVELS OF FVIII

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We have previously shown that lung when treated with Sendai virus-mediated gene transfer can produce secreted proteins and release them into the circulation (Griesenbach et al., Mol Therapy 2002). Despite the high levels of transduction efficiency the gene expression is transient and repeated administration is not feasible due to induction of immune responses. To overcome these barriers we developed a lentiviral vector specifically pseudotyped with the Sendai virus envelope proteins F and HN (rSIV. F/HN) to allow efficient transduction of the airways. Stable expression for >20 months after a single dose and efficient transduction after repeated administration despite detection of anti-rSIV. F/HN neutralising antibodies make the vector an attractive candidate for a large range of disease indications. Here, we first transduced mouse lung with rSIV. F/HN carrying the secreted reporter gene Gaussia luciferase (GLux) or a control gene expression is transient and repeated administration is not feasible due to induction of immune responses. To overcome these barriers we developed a lentiviral vector specifically pseudotyped with the Sendai virus envelope proteins F and HN (rSIV. F/HN) to allow efficient transduction of the airways. Stable expression for >20 months after a single dose and efficient transduction after repeated administration despite detection of anti-rSIV. F/HN neutralising antibodies make the vector an attractive candidate for a large range of disease indications. Here, we first transduced mouse lung with rSIV. F/HN carrying the secreted reporter gene Gaussia luciferase (GLux) or a control vector by nasal instillation (1e6 transduction units (TU)/mouse, n = 6/group). Persistent levels of GLux expression were detectable in lung (3 logs above control) and broncho-alveolar lavage fluid (BALF, 4 logs above control) for at least 12 months. Importantly, even this modest dose of virus lead to significant (p < 0.01) levels of GLux in serum (274 ± 72 RLU/ul, control: 41 ± 6 RLU/ul) which persisted for at least 12 months further supporting the hypothesis that the lung is a suitable, non-invasive factory for production of secreted proteins. Gene therapy strategies for haemophilia have focussed on intravenous or intramuscular delivery of the gene transfer agent. Here, we treated the murine lung with rSIV. F/HN carrying the FVIII cDNA (1.6e8–3.4e8 TU/mouse), or placebo and assessed whether therapeutically relevant levels of FVIII can be produced. Significant (p < 0.05) and dose-related levels of FVIII were detectable in lungs and BALF 10 and 28 days post-transduction. Dose-related levels of FVIII were also detectable in plasma, which reached a therapeutically relevant level of 3% of normal 1 month after gene transfer. These data support the concept that rSIV. F/HN-mediated transduction of lungs can produce therapeutically relevant and persistent levels of recombinant protein in blood.

REFERENCE

S118 CIRCADIAN GLUCOSE PATTERNS IN ADULT CARDIOTHORACIC TRANSPLANT RECIPIENTS

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Introduction New onset diabetes after transplantation (NODAT) is a well-known complication of immunosuppressive therapy and is associated with excess morbidity and mortality. Early identification and treatment of impaired glucose regulation (IGR) is crucial to help prevent or delay the development of NODAT and its associated complications.

Aim To define circadian glucose patterns of cardi thoracic transplant (CTTx) recipients using a continuous glucose monitoring system (CGMS) and compare the findings with conventional tests for diabetes.

Method Cross-sectional study in a CTTx outpatient clinic. CGMS was used to construct circadian glucose profiles. Those with CGMS values in excess of 7.7 mmol/l were asked to complete oral glucose tolerance tests (OGTT) and HbA1c.

Participants Convenience sampling was used to identify 12 stable CTTx recipients (2 heart, 3 single lung and 7 double lung Tx; 9 male; mean [SD] age 58 [8] years, BMI 28.6 [4.9] kg/m², daily prednisolone dose 11.5 [2.2] mg; 4 on tacrolimus vs 8 on cyclosporine; median 477 days since Tx).

Results None had symptoms of hyperglycaemia. CGMS duration range: 37 to 183 hrs/patient. A significant difference was seen between mean morning (06.00–12.00 hrs) and evening (14.00–20.00 hrs) glucose values (5.8 [1.2] vs 7.6 [1.4] mmol/l; p < 0.001, Figure 1). On CGMS data all participants had glucose values >7.7 mmol/l. Three (25%) had glucose values >11.1 and <3.5 mmol/l on CGMS and were diagnosed with impaired glucose tolerance on OGTT. Compared with 9 normal OGTT patients, the IGT group displayed a higher number of hyperglycemic episodes/day and a greater% of time above 7.8 mmol/l. No cases of impaired fasting glycaemia or NODAT were identified using OGTT or HbA1c.

Abstract S118 Figure 1

Circadian Glucose of Participants According to OGTT status

Series 1

Series 2

Series 1 represents patients with IGT and series 2 patients with normal glucose tolerance.

Conclusion Findings of this pilot study emphasise the importance of improving screening for IGR in CTTx recipients. We identified diurnal variation in glucose patterns, with higher glucose values in the afternoon and evening than morning, which has implications for timing of random glucose sampling in clinic. Poor correlation was found between CGMS and conventional diagnostic tests for diabetes which may not be sensitive enough to identify IGR in CTTx recipients. This merits further investigation in a larger cohort.
MICRORNA-200B REPRESSIONS TGF-β1 INDUCED EMT IN BEAS-2B AND PRIMARY BRONCHIAL EPITHELIAL CELLS

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Introduction MicroRNAs (miRNAs) are small non-coding RNAs that function as endogenous gene regulators. They may initiate a process called epithelial-mesenchymal transition (EMT) that leads to aberrant extracellular matrix remodelling and is implicated in a number of airway diseases. Dysregulation of miRNAs has been indicated in chronic lung disorders, the third most common cause of mortality in adults.

Materials and methods NanoString was used to assay the differential expression of miRNAs at 1, 4 and 24 hrs following TGF-β1 treatment of BEAS-2B cells (immortalised primary bronchial epithelial cells) and control. QRT-PCR validated the expression profile of miR-200b. BEAS-2B and PBECs (primary bronchial epithelial cells) were transfected with miR-200b mimics to study expression of EMT markers at mRNA and protein level. MiRNA targets were identified and validated using multiple computational tools and qRT-PCR respectively.

Results nCounter assay allowed identification of novel miRNAs including miR-200 family. MiR-200b mimic transfection (24 hrs) followed by TGF-β1 treatment (48 hrs) demonstrated a significant increase in E-Cadherin (p ≤ 0.05, p ≤ 0.001) and a significant decrease in Fibronectin (p ≤ 0.001, p ≤ 0.01) in BEAS-2B cells and PBECs. Protein studies suggested a similar trend in both the cells. The most prominent targets of miR-200b identified were RHOA, SMURF2, ZNF532 and ZEB2. A significant decrease was observed in ZNF532 (p ≤ 0.01) and ZEB2 (p ≤ 0.001) in miR-200b transfected and TGF-β1 treated BEAS-2B cells (n = 3). Differential expression of mRNA targets was observed in two sets of patient derived PBECs.

Conclusion miR-200b suppressed TGF-β1 induced EMT by maintaining the epithelial framework of BEAS-2B cells and PBECs. Results provide new insights into miR-200b regulation in fibrosis and basis for therapeutic application in lung injury.

SERUM MICRORNA PROFILES IN IPF PATIENTS – BIOMARKERS OR POTENTIAL THERAPEUTIC TARGETS?

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Introduction and objectives Idiopathic Pulmonary Fibrosis (IPF) has limited therapeutic options and predicting the natural history in individual cases is difficult. Exosomes are extracellular microvesicles that are involved in cell-cell signalling. MicroRNA isolated from exosomes has been implicated in several fibrotic models. At present the role of miRNAs in development of lung fibrosis is unclear. We aim to characterise miRNAs isolated from IPF patients and relate these to measures of disease severity.

Methods We assessed exosomes isolated from the serum of IPF patients (n = 8) and aged matched healthy controls (n = 6). Exosomes were characterised by western blot and Nanosight
technology. MiRNA was isolated from these exosomes and profiled using a miRNA PCR assay. Demographic and clinical data was extracted from clinical records. IPF patients were stratified by radiological severity, GAP scoring and rate of progression. Results Exosomes isolated from IPF patients demonstrated decreased fold regulation in antibiotic miRNA such as miR-141 and miR-29 in addition to increases in fibrogenic miRNA such as miR-7 when compared to healthy controls. The degree of up regulation in miR-7 correlates significantly with stratified burden of disease. Interestingly down regulation of miR-155 was also found which has been previously associated with up regulation in mice fibrosis models. Patients had a median follow up of 31 months (IQR 17–43). There was a significant correlation with regards to up regulation of miR-125b with milder disease defined by the GAP score and preservation of FVC.

Conclusion This data identifies novel biomarkers that may provide insights into the natural history and pathogenesis of the disease. Furthermore miR-7 and miR-29 have been implicated in extracellular matrix remodelling with target genes including ECM proteins such as collagens, fibrillins and elastin. Inhibiting up regulated miRNA or supplementing down regulated miRNA may be potential therapeutic targets.

REFERENCE

COPD Weighs Heavily on the Heart

S121 CO-MORBIDITY AND PNEUMONIA RISK IN COPD PATIENTS: A POPULATION DATABASE ANALYSIS OF PRIMARY CARE PATIENTS

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Background Co-morbidities are common in COPD and have been associated with poorer clinical outcomes. Furthermore, patients with COPD are at an increased risk of developing community acquired pneumonia (CAP). We investigated the impact of concurrent co-morbidity on the risk of developing CAP, in a cohort of COPD patients identified from the Hampshire Health Record Analytical database, a local NHS database containing anonymised primary and secondary care records.

Methods Patients defined as having COPD, had a diagnostic Read code [classification of clinical terms for electronic information coding] in their primary care record at any time prior to 1st January 2010 and were aged ≥40 years at the start of the study period. Using clinician-coded diagnoses, CAP episodes which occurred over a 1-year period from the 1st January 2010 were identified using Read and ICD-10 code lists and were defined as taking up to 70 days to resolve. Listed co-morbidities were based on coded entries at any time prior to 1st January 2010.

Results Included were 6707 patients with a complete history in 2010; 55% of patients were men and 36% were current smokers, the mean age was 70 years. 189 patients (2.8%) had at least one CAP episode during 2010. Compared to patients without CAP, patients with CAP were more likely to have ischaemic heart disease (IHD p = 0.005), congestive heart failure (CHF p = 0.021), hypertension (p = 0.017), cerebrovascular disease (CVD p < 0.001), dementia (p < 0.001), and bronchiectasis (p = 0.001). Using logistic regression and controlling for potential confounders, CVD and dementia were independent risk factors for CAP (p = 0.009 and 0.007, respectively), while bronchiectasis trended towards significance (p = 0.073) (Table 1).

Abstract S121 Table 1 Co-morbidities associated with CAP occurrence in COPD

<table>
<thead>
<tr>
<th>Co-morbidity</th>
<th>Odds ratio</th>
<th>95% confidence interval</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHD</td>
<td>1.13</td>
<td>0.89–1.49</td>
<td>0.478</td>
</tr>
<tr>
<td>CHF</td>
<td>1.11</td>
<td>0.95–1.39</td>
<td>0.712</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.18</td>
<td>0.97–1.40</td>
<td>0.276</td>
</tr>
<tr>
<td>CVD</td>
<td>1.73</td>
<td>1.15–2.62</td>
<td>0.009</td>
</tr>
<tr>
<td>Dementia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>1.70</td>
<td>0.95–3.04</td>
<td>0.073</td>
</tr>
</tbody>
</table>

Odds ratios, 95% confidence intervals and p-values were calculated from logistic regression. Separate regression models were used for each co-morbidity, controlling for number of exacerbations in 2010, age, sex, smoking status, included corticosteroid use and HSE diagnoses score.

Conclusion In this large population database analysis, CVD and dementia were identified as being independently associated with an increased risk of CAP. Oro-pharyngeal dysfunction in CVD and use of sedative medications in dementia, may contribute to these findings. Further analysis of the complete cohort, over the full 5-year observation period will allow the formulation of robust conclusions about the important factors of CAP risk in COPD, including the impact of pharmacotherapy, blood markers and functional parameters.

S122 THE EFFECT OF BODY MASS INDEX ON PATIENT OUTCOME IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A RETROSPECTIVE COHORT STUDY USING THE HAMPSHIRE HEALTH RECORD

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Introduction and objectives Chronic obstructive pulmonary disease (COPD) is a systemic disease characterised by persistent airflow obstruction but also has significant extra-pulmonary manifestations, including effects on body mass index (BMI). Nutritional status has been implicated as a predictor of outcome. We aimed to investigate the relationship between BMI and outcomes in a representative sample of UK COPD patients.

Method Patients with a coded GP diagnosis of COPD on or before 31/12/2010 and full data for 3 years or until death were identified from the Hampshire Health Record Analytical database, which collects anonymised routine clinical care data from GP and hospital computer records. Subjects were categorised as underweight, normal, overweight, obese or very obese by WHO standards. Outcomes measured were all-cause death and respiratory-cause hospitalisation and emergency department attendance rate in the following 3 years. Multivariate cox regression modelling was used to estimate hazard ratio (HR) and confidence intervals (CI) adjusted for age, gender, smoking status and FEV1% predicted.
**Results** 10,813 patients were identified (55% male, mean (SD) age 71.07 (±10.48), FEV1%predicted 59.96% (±19.98%). 1677 deaths (15.5%) occurred during the follow-up period. Compared with individuals with a normal BMI, overweight subjects had a higher mortality risk in adjusted analysis (HR = 1.58, 95% CI = 1.31–1.88). The lowest mortality rates were in overweight subjects (HR = 0.72, 95% CI = 0.64–0.81) and very obese subjects had no significant difference (HR = 0.83, 95% CI = 0.68–1.02, p = 0.08).

The relationship between hospitalisation rate and BMI was ‘U’ shaped. Admission rates were highest in the overweight category where 13.3% of subjects had ≥2 admissions compared to 6.2% and 5.3% of overweight and obese subjects respectively.

A similar relationship was observed between BMI and respiratory-cause emergency department attendance. 13.9% of overweight subjects had ≥2 emergency department attendances. The lowest attendance rates were observed in overweight and obese subjects where 6.5% and 5.6% of subjects had ≥2 attendances. Conclusions Underweight COPD patients have the highest death and hospitalisation rates, whilst being overweight or obese appears to have protective effects. There is potential for nutritional supplementation interventions in underweight COPD patients to improve outcomes, and further research into the protective effects of obesity is required.

**Abstract S123 Table 1** Comparison of demographic, respiratory disease-related and cardiovascular risk factors between people with and without COPD

<table>
<thead>
<tr>
<th>No COPD</th>
<th>COPD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number</td>
<td>203</td>
<td>46</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66 ± 1</td>
<td>68 ± 1</td>
</tr>
<tr>
<td>Gender (n (% male))</td>
<td>135 (67%)</td>
<td>37 (80%)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.8 ± 6.9</td>
<td>27.7 ± 5.2</td>
</tr>
<tr>
<td><strong>Respiratory disease-related factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FEV1 % predicted</td>
<td>84 ± 19</td>
<td>68 ± 2</td>
</tr>
<tr>
<td>Recurrent chest infections (n (%))</td>
<td>19 (9%)</td>
<td>6 (13%)</td>
</tr>
<tr>
<td><strong>High sensitivity CRP (mg/L)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1 (0.9–5.4)</td>
<td>4.3 (1.4–7.5)</td>
<td>0.040</td>
</tr>
<tr>
<td><strong>Traditional cardiovascular risk factors</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking status (pack years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>68%</td>
<td>0%</td>
</tr>
<tr>
<td>10–40</td>
<td>26%</td>
<td>59%</td>
</tr>
<tr>
<td>&gt;40</td>
<td>6%</td>
<td>41%</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>2.7±1.0</td>
<td>2.8±1.2</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>135±19</td>
<td>132±20</td>
</tr>
<tr>
<td>Diabetes (n (%))</td>
<td>67 (33%)</td>
<td>8 (17%)</td>
</tr>
<tr>
<td><strong>Coronary artery disease burden</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gensini score</td>
<td>12.5 (8.0–26.8)</td>
<td>22.5 (8.5–46.0)</td>
</tr>
<tr>
<td>Number of vessels affected</td>
<td>2.2 ± 1.0</td>
<td>2.4 ± 1.0</td>
</tr>
<tr>
<td>Total number of lesions</td>
<td>43 ± 2.6</td>
<td>52 ± 2.7</td>
</tr>
<tr>
<td>&lt; Left coronary artery lesions</td>
<td>2.0 ± 1.2</td>
<td>2.1 ± 1.3</td>
</tr>
<tr>
<td>Circumflex lesions</td>
<td>1.0 ± 0.8</td>
<td>1.3 ± 1.0</td>
</tr>
<tr>
<td>Right coronary artery lesions</td>
<td>1.4 ± 1.2</td>
<td>1.7 ± 1.1</td>
</tr>
</tbody>
</table>

FEV1, forced expiratory volume in 1 s; mMRC, modified Medical Research Council dyspnoea scale; CAT, COPD assessment test. Values are mean ± standard deviation, compared with independent t tests, median (interquartile range), compared with Mann-Whitney U tests, or number (%), compared with chi squared tests.

**Conclusions** People with COPD have more severe coronary artery disease than those without. This analysis cannot determine whether this was due to the presence of COPD or the fact that patients with CAD and COPD had much greater cigarette smoke exposure than CAD patients without COPD.

**S124** THE BODE INDEX IS AN INDEPENDENT DETERMINANT OF ARTERIAL STIFFNESS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

**Introduction** COPD is associated with increased cardiovascular events, independent of established risk factors. Arterial stiffness and carotid intima-media thickness (CIMT) are surrogates of cardiovascular risk and we sought to determine their relationship with COPD severity and prognosis in the ERICA (Evaluation of role of inflammation in airways disease) multi-site UK study: the...
largest cohort study focusing on cardiovascular manifestations in COPD. Methods Spirometry, haemodynamic measures (aortic pulse wave velocity (aPWV), augmentation index (AIx), peripheral and central blood pressure (BP)) and CIMT (ultrasound measure of carotid artery intima-media layer thickness) were performed in 729 COPD subjects aged ≥40 years. COPD severity was classified by BODE Index [BMI, Obstruction (FEV1), Dyspnoea (mMRC score), Exercise tolerance (6-minute walk distance)], a validated score based on clinical variables and predictor of mortality in COPD.

Results Mean aPWV was 10.3 (SD 2.6) m/s, Alx 27 (10)%, brachial BP 144/82 (18/11) mmHg, central BP 131/82 (18/11) mmHg, CIMT 0.86 (0.4) mm.

BODE correlated with aPWV (p < 0.0001) and this was maintained when adjusted for study site, age, supine heart rate (HR) mean arterial pressure (MAP), years smoked and cardiovascular comorbidities (MI, stroke, diabetes, peripheral vascular disease), p < 0.0001. BODE was also associated with AIx when adjusted for site, age, seated HR and MAP, years smoked and cardiovascular comorbidities, p < 0.01. The constituent variables of BODE did not have the same significant association with both aPWV and Alx, Table 1.

Abstract Table 1 Comparison of linear regression models of BODE constituent variables, cardiovascular comorbidities and established predictors of arterial stiffness

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>aPWV (m/s)</th>
<th>Augmentation Index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>β coefficient</td>
<td>p-value</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>MAP (mmHg)*</td>
<td>0.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>HR (bpm)*</td>
<td>0.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TPYs</td>
<td>-0.001</td>
<td>0.98</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>0.09</td>
<td>0.01</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>-0.06</td>
<td>0.09</td>
</tr>
<tr>
<td>mMRC (0–4)</td>
<td>0.07</td>
<td>0.09</td>
</tr>
<tr>
<td>6MWd (m)</td>
<td>-0.03</td>
<td>0.5</td>
</tr>
<tr>
<td>MI</td>
<td>-0.01</td>
<td>0.7</td>
</tr>
<tr>
<td>Stroke</td>
<td>-0.01</td>
<td>0.7</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.07</td>
<td>0.03</td>
</tr>
<tr>
<td>PVD</td>
<td>0.1</td>
<td>0.004</td>
</tr>
<tr>
<td>Study site</td>
<td>-0.06</td>
<td>0.09</td>
</tr>
</tbody>
</table>

*Supine for aortic pulse wave velocity (aPWV), seated for Augmentation Index.

An inverse correlation of BODE with central systolic BP (p = 0.003) was observed and this was maintained after adjustment for study site, age and HR p = 0.03. There was no significant relationship between BODE and CIMT.

Conclusions BODE is associated with arterial stiffness in COPD, independent of traditional risk factors. Its negative relationship with systolic pressure suggests increasing arterial stiffness with COPD severity, is independent of blood pressure. The BODE Index composite variables are not on the causal pathway for vascular stiffness, so its positive association likely reflects patient susceptibility to injury from smoke or other irritants in the lungs and vasculature. BODE may also enhance cardiovascular risk stratification in COPD, since its relationship with stiffness was independent of self-reported cardiovascular comorbidities.
understanding of the consequences of Z-alpha-1-antitrypsin expression on cellular dysfunction.

Methods We created YFP tagged wild-type and Z-alpha-1-antitrypsin constructs and expressed them in a cell model along with other fluorescently tagged proteins of interest. Using live-cell imaging including photobleaching techniques, we assessed the relative mobilities of alpha-1-antitrypsin and other ER resident proteins. We further assessed the nature of inter-inclusion protein trafficking by creating a permeabilised cell system in which the cytosol could be manipulated or removed.

Results We have shown that inclusions are translationally active ER fragments in which polymerisation occurs. Using fluorescence recovery after photobleaching (FRAP), we observed that despite inclusions containing immobile polymeric alpha-1-antitrypsin, small ER resident proteins including the ER chaperone BiP are able to diffuse freely within them (Figure 1). We observed that inclusions are physically separated from the tubular ER network but despite this, cargo is transported between inclusions in a cytosol-dependent fashion that is dependent on vesicular trafficking components and may involve the ER-Golgi intermediate compartment (ERGIC).

Conclusions We propose that protein movement between physically separated ER inclusions via ER-ERGIC recycling acts to minimise ER heterogeneity in Z-alpha-1-antitrypsin expressing cells. This may reduce the toxic effects of polymer accumulation via increased availability of, for example, ER chaperones within inclusions and is consistent with in vivo observations of a striking lack of toxicity in cells expressing Z-alpha-1-antitrypsin.
SOLUBLE ADAM33 CAUSES AIRWAY REMODELLING TO A TWO SPECIES PROTEOMICS APPROACH TO

# Methods

A protocol was then applied to dTg minimal BHR and eosinophilia. This low-dose allergen challenge increased in methacholine-induced airway resistance and control mice. Allergen challenge of dTg mice resulted in a significant increase in methacholine-induced airway resistance and eosinophilic airway inflammation compared to HDM-challenged sTg controls. The dTg mice also showed a significant increase in airway inflammatory mediators IL-5, IL-13 and eotaxin, in addition to markers of remodelling.

# Conclusions

This study demonstrates that hsADAM33-MP driven airway remodelling enhances susceptibility to HDM with increases in BHR and inflammation. These functional studies demonstrate, for the first time, a gene-environment interaction involving ADAM33 to cause remodelling and the disproportional inflammatory responses seen in the asthmatic airway. sADAM33 might be a potential target for novel disease-modifying therapies.

**Abstract S129 Figure 1** Expression of hAAT in epithelial lining fluid following treatment with rSIV. F/HN-hAAT. Mice were given between 2e7 and 1.4e8 TU virus and sacrificed 7–10 days post-treatment.
proteome of COPD sputum at exacerbation and stable disease. It suggests a role for MMP-12 in complement regulation and haemostasis in COPD. Thus an important peptide library has been unravelled, providing an ideal tool in developing drugs and understanding COPD pathogenesis.

Main results Axl was the dominant TAM receptor expressed in HD AMs whereas monocytes and MDMs predominantly expressed MerTK. Axl expression was significantly reduced in AMs from patients with asthma compared to HD (p < 0.0001), while mRNA levels of MerTK and Gas6 was similar in both groups. We found no differences in Axl and MerTK expression in monocytes and MDMs from HD and patients with asthma, indicating that the observed differences were restricted to the site of inflammation. In vitro, MDM stimulation with IL-4 or IL-13 downregulated Axl mRNA and protein expression in a time-dependent manner.

Conclusions We have shown for the first time that Axl is the principal TAM receptor expressed in human AMs. Significant reduction of Axl expression in AMs from patients with asthma might be responsible for inefficient clearance of apoptotic cells from the inflamed airways and contribute to persistent airway inflammation. Strategies aimed at restoration of Axl expression or activity may represent a novel therapeutic strategy in asthma and other chronic lung diseases.

REFERENCE

Spoken sessions

AXL RECEPTOR TYROSINE KINASE ON AIRWAY MACROPHAGES HAS A KEY ROLE IN LUNG IMMUNE HOMEOSTASIS

Manchester Collaborative Centre for Inflammation Research, The University of Manchester, Manchester, UK; Institute of Inflammation and Repair, Manchester Academic Health Sciences Centre, University of Manchester and National Institute of Health Research Respiratory and Allergy Clinical Research Facility, University Hospital of South Manchester, Manchester, UK

10.1136/thoraxjnl-2015-207770.136

Rationale Apoptotic cell uptake (efferocytosis) by airway macrophages (AMs) is critical for lung immune homeostasis and is defective in chronic lung diseases, including asthma, although the molecular mechanism behind this remains unknown. The TAM (Tyro3, Axl, MerTK) receptor tyrosine kinases are one of the main receptor classes that mediate efferocytosis but little is known about their regulation and function in inflammatory lung diseases.

Aim To investigate expression profile of TAM receptors and their ligand Gas6 in human AMs and analyse potential defects in TAM receptor expression in chronic lung inflammation.

Methods AMs from the sputum of patients with asthma (BTS step 3–5) (n = 30) or healthy donors (HD) (n = 12) were enriched by plastic adhesion. Monocytes were isolated from matched whole blood samples by CD14 positive selection and differentiated into monocyte-derived macrophages (MDMs). Total RNA was extracted from all purified cell populations and mRNA expression analysed by qPCR. HD MDMs were stimulated with Th2 cytokines in vitro and TAM receptor expression was analysed using qPCR and ELISA.

Main results Axl was the dominant TAM receptor expressed in HD AMs whereas monocytes and MDMs predominantly expressed MerTK. Axl expression was significantly reduced in AMs from patients with asthma compared to HD (p < 0.0001), while mRNA levels of MerTK and Gas6 was similar in both groups. We found no differences in Axl and MerTK expression in monocytes and MDMs from HD and patients with asthma, indicating that the observed differences were restricted to the site of inflammation. In vitro, MDM stimulation with IL-4 or IL-13 downregulated Axl mRNA and protein expression in a time-dependent manner.

Conclusions We have shown for the first time that Axl is the principal TAM receptor expressed in human AMs. Significant reduction of Axl expression in AMs from patients with asthma might be responsible for inefficient clearance of apoptotic cells from the inflamed airways and contribute to persistent airway inflammation. Strategies aimed at restoration of Axl expression or activity may represent a novel therapeutic strategy in asthma and other chronic lung diseases.

REFERENCE
Idiopathic pulmonary fibrosis boldly goes where no disease has gone before

**P1** PRELIMINARY RESULTS FOR ASSOCIATION OF SURVIVAL TIME IN IDIOPATHIC PULMONARY FIBROSIS CASES WITH THE 11P15.5 REGION

Allen RJ, Tobin MD, Wain LV, Braybrooke R, Jenkins G. Department of Health Sciences, University of Leicester, Leicester, UK; School of Medicine, University of Nottingham, Nottingham, UK.

Introduction Idiopathic pulmonary fibrosis (IPF) is a restrictive lung disease of unknown cause. The median survival time after diagnosis is 3–5 years and there are limited treatments available. MUC5AC, MUC5B and TOLLIP in the 11p15.5 region have been shown to be associated with susceptibility to IPF. A variant in TOLLIP (rs5743890) has also been shown to be associated with both susceptibility and survival time however the effects were in opposite directions, i.e. the allele associated with increased susceptibility was also associated with increased survival time.

Methods We performed survival analysis on 612 European cases passing QC using a Cox proportional hazards model adjusting for age, sex, first 10 principal components and study centre. 134 variants were genotyped in a 200 kb region on chromosome 11 covering MUC5AC, MUC5B and TOLLIP.

Results No SNPs in this region reached genome-wide significance (p < 5 × 10^{-8}). The most significant variant was rs6367042 (Hazard Ratio 3.38, 95% CI [1.91, 5.96]; p = 2.74 × 10^{-4}) which is located downstream of MUC5B. The next significant SNP was rs5743894 (Hazard Ratio 0.67, 95% CI [0.54, 0.83]; p = 2.24 × 10^{-4}) located in TOLLIP. For this SNP the allele we found associated with increased survival time has previously been reported as associated with increased susceptibility (showing a similar pattern to that reported for rs5743890) however this SNP has also been previously reported as not being associated with survival time. We found a proxy of rs5743890 (R^2 = 0.698) not to be associated with survival time (p = 0.881).

Conclusions Our results did not replicate those previously reported; however they may support the hypothesis that variants in TOLLIP that increase susceptibility may also increase survival time. In future we will perform a GWAS for susceptibility and survival time and try and replicate the findings.

**P2** PLATELET REACTIVITY AS A POTENTIAL BIOMARKER IN IDIOPATHIC PULMONARY FIBROSIS

Crooks MG, Wright C, Fraser S, Morris AH, Hart SP. Hull York Medical School, Hull, UK.

Introduction and objectives Heterogeneity of idiopathic pulmonary fibrosis (IPF) means it is difficult to identify those at highest risk of progression who are most likely to benefit from treatment. A biomarker that predicts disease activity, prognosis and treatment response would be beneficial. We previously reported increased platelet reactivity in IPF, and here we explore whether platelet reactivity warrants further investigation as a biomarker.

Methods Data were obtained from two studies: Study 1, a study of platelet reactivity in IPF; and Study 2, a pilot randomised-controlled trial of an investigational IPF treatment. Standard protocols were used to measure platelet-monocyte aggregate (PMA) formation, P-selectin expression, and fibrinogen binding in blood samples. Platelet reactivity in IPF was compared with controls. Correlation between platelet reactivity and forced vital capacity (FVC) was assessed. Study 2 data were used to assess the change in platelet reactivity in response to the intervention and correlation between baseline platelet reactivity, symptoms (KBILD) and exercise capacity (6MWD).

Results Study 1 included 13 IPF patients (mean ± SD, Age 70.3 ± 5.8 years, 69% male, FVC 91.9 ± 17.8% predicted) and 12 controls (Age 66.2 ± 10.2, 66.7% males). Study 2 included 19 IPF patients (Age 71.5 ± 8.7, 72% males, FVC 84.4 ± 16.8% predicted). IPF patients demonstrated significantly increased platelet reactivity compared to controls (P < 0.01). Platelet reactivity and FVC did not correlate. In study 2, stimulated platelets expressed significantly less P-selectin in response to the intervention (P = 0.03). Unstimulated PMA formation moderately correlated with KBILD (r = 0.38, P = 0.01), but other platelet markers showed no correlation with symptoms or exercise capacity.

Conclusion IPF patients exhibit increased platelet reactivity compared to controls. The reduction in platelet reactivity in response to an intervention may indicate responsiveness to treatment effect. Although there was no correlation between FVC and platelet activation, further investigation is warranted to assess associations between platelet reactivity and lung function decline and mortality.

**REFERENCE**


**P3** PILOT STUDY TO TEST THE FEASIBILITY OF A PSYCHOLOGICAL SUPPORT WORKSHOP FOR PATIENTS NEWLY DIAGNOSED WITH IDIOPATHIC PULMONARY FIBROSIS (IPF) AND THEIR FAMILIES


Introduction IPF is associated with a poor prognosis, high symptom burden and limited treatment options. Psychological reactions are comparable to those seen in cancer patients, yet support services for IPF patients are less well developed. There is an urgent demand to develop Interstitial Lung Disease (ILD) services that better support the psychological needs of IPF populations. The aim of this pilot study is to characterise the psychological needs of both patients and carers and to test the feasibility of a workshop approach.

Methods Consultant ILD physicians identified patients recently diagnosed with IPF at our Unit, and referred them to the clinical psychologist, including didactic teaching, interactive discussions and experiential learning. Topics covered coping with low mood and anxiety, symptom control and transitions towards the end of life. Four members of the clinical team were present.
Introduction The IPF-PROM development project sought to integrate patients and carers both as participants and co-investigators in the research process. Patients with varied experiences of IPF and members of the multidisciplinary team including a clinical psychologist; research nurses, Patient and Public Involvement Lead and a carer formed the IPF-PROM Research Steering Group (RSG) at the outset of the study.

Methodology Fundamental to PROM development is a robust approach to the item generation process to support the final conceptual framework. The RSG had a key role to ensure patient language was accurately represented. All RSG members:

- Agreed formal terms of reference and role descriptions.
- Reviewed the study protocol.
- Analysed 5 focus groups transcripts individually and collectively identified themes.
- Applied consensus methods to a list of pooled items collated from questionnaires that have been used in studies in IPF populations.
- Assessed the face validity of an electronic Delphi survey administered to patients, carers and healthcare professionals in the UK.
- Analysed the free-text comments captured in the Delphi study using a thematic approach.
- Participated in a Reflective exercise to characterise individual’s perceptions and motivations for continuing involvement in the RSG.

Results RSG members contributed a level of sympathy, insight, compassion and knowledge to the thematic analysis of the focus groups: a dynamic that enhanced the interpretation of transcripts. Emotions evoked by the transcripts were ‘therapeutic’ rather than ‘distressing’. 200 statements were identified for inclusion in the Delphi.

Patient and carers added new and different perspectives on the use of language; rich discussion preceded consensus. Items identified in existing questionnaires (n = 313) were reduced.
QUALITY OF LIFE AND FUNCTIONAL OUTCOMES IN POST-TRANSPLANT IPF PATIENTS AGED OVER 70

P Riddell, S Winward, K Redmond, JI Egan. Mater Misericordiae University Hospital, Dublin, Ireland

10.1136/thoraxjnl-2015-207770.142

Introduction In recent years there has been a large increase in rates of lung transplantation for IPF patients. This has driven by the introduction of the Lung Allocation Score in the US, which prioritises patients based on treatment need and benefit. Increasing rates of transplantation have led to older patients being considered for transplant listing. The aim of this study was to assess the survival, functional capacity and quality of life of IPF patients aged over 70 attending our transplant programme.

Methods Post-transplant IPF patients aged 70 years or older were identified from the National Lung Transplant Registry. Health-related Quality of Life (HRQL) was assessed using the 36-item Medical Outcomes Survey Short Form (SF-36). Functional status was assessed by exercise tolerance, pulmonary function and level of respiratory support. HRQL was compared to published datasets from randomised clinical trials of drug therapy as well as prospective studies in lung transplant recipients.

Results 6 patients met the inclusion criteria, mean age 72.5 ± 0.8 yrs. The mean time from transplant was 3.8 ± 1 yr (range 2.3 – 7.0 yrs). Compared to the BUILD-1 trial (similar age, limited IPF), minimal important clinical differences (MID) were seen across many components of the SF-36 score. These MDIs included physical functioning (+7.1), health perception (+29.2) and vitality (+17). Compared to a post-transplant cohort of younger IPF patients (61.0 ± 1.5 yrs) the mental component score (MCS) was higher in this study (+12.2). These benefits in MCS were maintained when compared to patients in the IFIGENIA study of N-acetylcysteine and the STEP-IPF study of sildenafl. The mean reported exercise tolerance of our patient group was 1.2 km, and no patient required supplementary oxygen or respiratory support. Compared to pre-transplant status large benefits in function were noted (mean pre-transplant 6MWT was 314 ± 91 m with 6 L oxygen/minute).

Conclusion Lung transplantation provides clinically meaningful benefits in HRQL and functional outcomes in patient’s ≥ 70 yrs old. This study highlights that these benefits are comparable to younger IPF patients who receive lung transplant and more beneficial to those reported in drug trials.

REFERENCES

Introduction The INPULSIS® trials assessed the efficacy and safety of nintedanib 150 mg twice daily in patients with idiopathic pulmonary fibrosis. Nintedanib significantly reduced the annual rate of decline in forced vital capacity (FVC) compared with placebo in both trials. Patients who completed the 52-week treatment period and follow-up visit 4 weeks later (n = 807) could receive open-label nintedanib in an extension trial.

Aim To assess the long-term efficacy and safety of nintedanib.

Methods Patients treated with placebo in the INPULSIS® trials initiated treatment with nintedanib in the extension; patients treated with nintedanib continued to receive nintedanib.

Results 734 patients were treated in the extension trial (430 continuing nintedanib; 304 initiating nintedanib). Baseline characteristics were similar between groups. For patients initiating nintedanib, mean (SD) duration of exposure was 16.0 (7.3) months; for patients continuing nintedanib, mean (SD) duration of exposure in the extension was 17.2 (6.6) months, resulting in a mean (SD) duration of exposure across the parent and extension trial of 29.2 (6.6) months. Among all patients treated in the extension, mean (SD) change in FVC from the start of the extension trial was 29.2 (6.6) months. For patients continuing nintedanib, mean (SD) duration of exposure was 16.0 (7.3) months; for patients initiating nintedanib, mean (SD) duration was 11.4 (7.3) months. In total, 92.8% of patients continuing nintedanib and 96.7% initiated on nintedanib had ≥1 adverse event during the extension. The most frequent adverse event was diarrhoea, reported in 63.3% of patients continuing nintedanib and 64.1% of patients initiated on nintedanib.

Conclusion An interim analysis of data from the INPULSIS®-ON extension trial confirmed the efficacy and safety observed in the INPULSIS® trials.

Introduction and objectives Nintedanib (OFEV®) is the second drug licensed for the treatment of Idiopathic Pulmonary Fibrosis (IPF). Evidence from the INPULSIS study demonstrated that it reduced annual FVC decline by approximately 50%. Nintedanib has been available in the UK from October 2014 through the Individual Patient Supply Programme (IPSP); initially for those with FVC >50% predicted, laterly available for all with a diagnosis of IPF regardless of FVC. We present preliminary findings of clinical experience with nintedanib in routine UK clinical practice.

Methods A multi-centre, cohort review was undertaken across 6 NHS Trusts. Data were collected from clinical records of individuals receiving nintedanib for the treatment of IPF from October 2014 to July 2015.

Results 210 patients (161 male) had consented to nintedanib IPSP by July 2015. Mean age (±S. D.) at diagnosis was 70.0 ± 7.7 years. Reasons for starting nintedanib included ineligibility for pirfenidone (FVC >80% predicted: 67 (31.9%) and FVC <50% predicted: 12 (5.7%),) intolerance to pirfenidone 63 (30%), patient preference 54 (25.7%), and clinical progression 72 (34.3%) which required a dose reduction in 11 patients. Other common ADRs included nausea 21 (10.0%), decreased appetite 17 (8.1%) and weight loss 12 (5.7%). The commonest potential adverse drug reaction (ADR) was diarrhoea occurring in 21 (10.0%). Pre-treatment lung function was FVC 72.2 ± 19.0% and DLCO 40.1 ± 17.2% predicted (Domiciliary oxygen was administered to 66 (31.4%) of the cohort.

Mean duration of treatment was 2.4 months (range 0 – 8 months) and 78 patients had completed 3-month follow up. Of these 14/78 patients (17.9%) had discontinued nintedanib due to diarrhoea (5 patients), other GI side effects (3), death/ lung transplant (2/1), miscellaneous reasons (3). The commonest potential adverse drug reaction (ADR) was diarrhoea occurring in 21/78 (26.9%), which required a dose reduction in 11 patients. Other common ADRs included nausea 11/78 (14.1%), abdominal pain 11/78 (14.1%), decreased appetite 7/78 (9.0%), and weight loss 5/78 (6.4%).

Conclusions These data demonstrate that at 3 months follow up, Nintedanib is generally well tolerated when used in routine UK practice in patients with IPF across a wide range of FVC’s. The incidence of diarrhoea at 3 months is much lower than the 12 month reported rate in the INPULSIS study. Ongoing longitudinal follow up of this cohort will further inform our understanding of the use of nintedanib for the treatment of IPF.
EFFECT OF PIRFENIDONE ON GAS TRANSFER IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS
PM George, L Richardson, LA Renzoni, M Kokos, TM Maher, AU Wells, F Chua. Royal Brompton and Harefield NHS Foundation Trust, London, UK
10.1136/thoraxjnl-2015-207770.147

Background Idiopathic pulmonary fibrosis (IPF) is a severe and progressive interstitial lung disease (ILD). Treatment with the anti-fibrotic agent Pirfenidone slows decline in forced vital capacity (FVC). Pulmonary vasculopathy is a relatively common and life-limiting complication of IPF and is frequently associated with a reduction in the diffusing capacity of the lung for carbon monoxide (DLco). However, it is not known what effect Pirfenidone may have on DLco.

Methods We performed a retrospective analysis of patients with diagnoses of IPF on long term Pirfenidone treatment. Lung function data were collected at treatment initiation and then at 12 months, (6–18 months). To assess for a treatment effect, similar data were also collected from an untreated control cohort of biopsy proven IPF patients from the pre-Pirfenidone era managed at the same centre. Data were analysed using Stata.

Results 138 patients were studied; n = 66 patients in the untreated control group and n = 72 patients in the Pirfenidone treated group. The control group had a higher baseline predicted FVC (74.8% v 67.5%) (p < 0.05) but baseline predicted DLco measurements were similar (44% v 40%) (p = 0.19). 12 month relative FVC change was greater in the untreated group; 9.9% (273 mL) (±11.4%) versus 3.9% (123 mL) (±11.9%) (p < 0.005). 12 month relative DLco decline was also greater in the untreated group; 16.4% (±20.5%) versus 7.5% (±17.6%) (p < 0.01). In multivariate analyses, the effect of Pirfenidone treatment had a 6.7% impact on FVC change (2.7–10.6) (p < 0.001) and a 9.0% impact on DLco change (2.5–15.5) (p < 0.01). Right ventricular systolic pressure correlated with baseline predicted DLco (p < 0.005, r² = -0.14).

Discussion In this study we have demonstrated that over 12 months, Pirfenidone confers a reduction in gas transfer decline paralleling that seen for FVC. This treatment effect on DLco may be due to a combination of deceleration in ILD progression paralleling that seen for FVC. This treatment effect on DLco may be due to a combination of deceleration in ILD progression and life-limiting complication of IPF and is frequently associated with a reduction in the diffusing capacity of the lung for carbon monoxide (DLco).

Conclusion Treatment of IPF with Pirfenidone markedly attenuates declines in gas transfer. This is of interest as it may provide insights into mechanisms underpinning disease stabilisation.

PIRFENIDONE POST-AUTHORISATION SAFETY REGISTRY (PASSPORT) – UPDATE AND CONCOMITANT USE OF N-ACETYL CYSTEINE AND/OR CORTICOSTEROIDS
1T Maher, 2V Cottin, 3A Azuma, 4L Groves, 6P Hommel, 5M Sköld, 6S Tomassetti, 7D Koschel. 1Royal Brompton Hospital, London, UK; 2National Reference Center for Rare Pulmonary Disease, Louis Pradel Hospital, Lyon, France; 3Nippon Medical School, Tokyo, Japan; 4Genentech, South San Francisco, CA, USA; 5Karolinska institute, Stockholm, Sweden; 6GB Morgagni Hospital, Forlì, FC, Italy; 7Fachkrankenhaus Coswig, Coswig, Germany
10.1136/thoraxjnl-2015-207770.149

Background PASSPORT is a post-authorisation safety registry for pirfenidone to collect real-world data in EU patients with idiopathic pulmonary fibrosis (IPF). This analysis assessed the safety of pirfenidone as monotherapy and in combination with N-acetylcysteine (NAC) and/or corticosteroids (CS).

Conclusions The decisions of an ILD MDT are limited by the completeness of investigation. We found causes for 50/200 patients with UIP. Pirfenidone was not prescribable for 53% of otherwise suitable patients. If the FVC limit was raised to 90% 32% would still be excluded, including 2 who died of their disease within 12 months. The FVC is often preserved even in terminal IPF.
Methods 109 EU sites dosed 1006 patients. Safety data were recorded at routine clinic visits for up to 2 years. Pirfenidone-associated adverse drug reactions (ADR) were collected.

Results At baseline, mean ± SD age was 70 ± 8.5 years and mean ± SD time since IFP diagnosis was 1.6 ± 2.5 years; 80% of patients were male; supplemental oxygen was used by 27% of patients; mean ± SD FVC was 2.56 ± 0.78 L; mean ± SD predicted FVC was 66 ± 16% (14% had <50% predicted FVC). The most common comorbidities (>10%) were hypertension, gastroesophageal reflux disease, hypercholesterolemia and coronary artery disease.

At this interim analysis, median time on pirfenidone was 7.6 months and total exposure was 803 patient-years. Overall, 67% of patients had ≥1 ADR, most commonly: nausea, 17%; fatigue, 15%; decreased appetite, 13%; decreased weight, 12%; rash, 10%; and diarrhoea, 9%. Of patients who had an ADR, 55% experienced their first ADR within the first 30 days of treatment. Around 5% of patients completed 2 years treatment, 55% are ongoing, 9% died and 21% discontinued because of pirfenidone-related ADRs (most commonly nausea, rash and decreased weight). 11% discontinued for other reasons.

Patients with FVC <50% had a higher discontinuation rate than other patients (48% vs 39%, respectively). The imbalance was mainly driven by higher rates of death and lung transplantation. The discontinuation rate due to pirfenidone ADRs was similar among patients with FVC <50% and ≥50% (20.3% vs 20.9%, respectively).

62% of patients received pirfenidone alone; 11%, 8% and 8% received pirfenidone plus NAC, CS, or NAC+CS, respectively. The remaining 11% had partial use of NAC and/or steroids. ADR incidence was generally consistent for these subgroups except weight decrease and ALT increase, which occurred more often in the pirfenidone+CS group.

Conclusions In this real-world setting, pirfenidone was generally safe and well tolerated as monotherapy or combined with NAC and/or CS. The rate of discontinuation due to pirfenidone-related ADRs was similar regardless of disease severity.

Abstract P13 Table 1 Treatment emergent adverse events in the integrated population compared with the pooled pirfenidone 2403 mg/d and placebo groups in the Phase 3 trials*  

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Integrated population (N = 1299)†</th>
<th>OE = treatment emergent adverse event</th>
<th>OE = treatment emergent adverse event &amp; sun exposure during treatment with pirfenidone; the skin dn</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (range) duration of exposure, yr</td>
<td>Treatment emergent adverse event,%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>1.7 (0.0, 9.9)</td>
<td>37.6</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>35.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>30.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>30.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Idiopathic pulmonary fibrosis</td>
<td>29.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>28.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>28.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>25.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bronchitis</td>
<td>23.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>21.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>21.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>21.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>18.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>15.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight decreased</td>
<td>15.6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>15.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anorexia</td>
<td>15.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Occurring in ≥15% of patients in the cumulative clinical database.
†Includes 2 patients in Study 002 with a diagnosis of “pulmonary fibrosis.”
Conclusions A comprehensive integrated analysis of safety outcomes in a large, well-defined cohort of 1299 patients with IPF who were treated with pirfenidone for up to 9.9 years demonstrated that treatment with pirfenidone is safe and generally well tolerated. These observations provide further evidence to support the long-term clinical safety of pirfenidone in patients with IPF.

Abstract P14 Figure 1 Treatment effect of pirfenidone by baseline lung function

Conclusions In the placebo population, clinically significant disease progression occurs in subgroups with more and less preserved lung function at baseline, underlying the need for early intervention. The magnitude of pirfenidone treatment effect on functional measures was comparable in these subgroups of patients (FVC <80% vs FVC >80%) or GAP I vs GAP II-III stage), supporting the initiation of treatment soon after diagnosis, when pulmonary function is relatively preserved.

Clinical studies of advanced COPD

P15 REGIONAL CEREBRAL ATROPHY AND COGNITIVE FUNCTION IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Background Widespread white matter damage and cognitive impairment have been demonstrated in COPD. However, it remains unclear if regional atrophy is present. We used a simple clinical visual rating scale to measure regional atrophy in a well-characterised population with COPD and compared age-matched controls. We explored correlations with demographics, disease factors and cognitive measures.

Objectives

1. a) To determine if there are significant differences in regional atrophy between COPD patients and age-matched control subjects.
2. b) To investigate whether patient characteristics or measures of disease severity account for group differences in atrophy severity.
3. c) To seek correlations with regional atrophy.

Methods A validated visual analogue MRI grading technique was used to assess the degree of atrophy in multiple brain regions in stable non-hypoxaemic COPD patients (n = 25) and age-matched controls.
matched control subjects (n = 25). This study is a further analysis of a previous case-control multi modal cranial MRI study.1

Main results COPD patients had significantly greater frontal atrophy than control subjects (p = 0.01), this was independent of smoking history, comorbidities and hospital anxiety and depression scores. Cognitive function was significantly worse in the COPD group for executive function, working memory, verbal memory and processing speed. Group differences in atrophy did not seem to account for differences in cognitive function. We were unable to identify meaningful correlations between regional atrophy and disease severity or cognitive function.

Conclusions There is significant frontal brain atrophy in stable non-hypoxaemic COPD patients. This regional atrophy does not appear to be related to disease severity or cognitive function. Further work is needed to identify causative mechanisms behind this structural change.

REFERENCE
1 Dodd JW, Chung AW, van den Broek MD, Barrick TR, Charlton RA, Jones PW. Brain structure and function in chronic obstructive pulmonary disease: a multimodal cranial magnetic resonance imaging study. Am J Respir Crit Care Med. 2012;186:240–245

Introduction COPD is associated with an increased prevalence of osteoporosis with shared risk factors including smoking, low BMI and reduced mobility. However, the risk of future fractures is not routinely considered in the management of COPD. We aimed to quantify future fracture likelihood and identify factors associated with an increased probability of osteoporotic fractures in patients with advanced COPD.

Methods Patients with advanced COPD were prospectively recruited and underwent a ‘comprehensive respiratory assessment’ as previously described.1 The 10 year probability of developing either a major osteoporotic fracture or hip fracture was calculated using the fracture risk assessment tool (FRAX®)2 using routinely collected data including age, gender, weight, height, smoking history, alcohol use, presence of inflammatory arthritis, corticosteroid use, but with the omission of family history and prior history of fractures. High risk was considered to be a ≥20% probability of a major osteoporotic fracture and ≥5% probability of a hip fracture.

Results 181 patients were included: mean (SD) age of 65 (9) years, MRC score 4 (IQR 0), BMI 25.4 (6.9) kg/m², 42% female and 25% current smokers. The mean (SD) 10-year probability for a major osteoporotic fracture was 9.1 (5.1)% and for a hip fracture was 3.5 (3.6)%.

Conclusions

Prospective Risk of Osteoporotic Fracture in Patients with Advanced COPD

**Abstract P15 Table 1** Bilaterally summed composite scores for regional atrophy in the control and COPD group (presented as Mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Control subjects (n=25)</th>
<th>COPD patients (n=25)</th>
<th>P value</th>
<th>Corrected p value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal</td>
<td>5.08 ± 2.68</td>
<td>7.32 ± 3.26</td>
<td>0.01*</td>
<td>0.02*</td>
</tr>
<tr>
<td>Temporal</td>
<td>5.76 ± 3.27</td>
<td>7.72 ± 4.77</td>
<td>0.10</td>
<td>0.06</td>
</tr>
<tr>
<td>Hippocampus</td>
<td>4.60 ± 1.89</td>
<td>5.24 ± 3.06</td>
<td>0.33</td>
<td>0.05</td>
</tr>
<tr>
<td>Parahippocampus</td>
<td>1.69 ± 1.97</td>
<td>3.72 ± 2.75</td>
<td>0.13</td>
<td>0.005</td>
</tr>
</tbody>
</table>

**Generalised linear model multivariate analysis controlling for group differences in Charlson, pack years and HAD scores.**

Quartiles 1 and 4 are the lowest and highest risk. Data are mean (SD). *calculated from DEXA.

**REFERENCE**
1 Steiner MC. Thorax 2015;70(Suppl 3):A1–A254

**Abstract P16 Table 1** Characteristics of patients with advanced COPD divided into quartiles based on FRAX® 10 year major osteoporotic fracture risk

<table>
<thead>
<tr>
<th></th>
<th>Total (n = 181)</th>
<th>Quartile 1 (n = 45)</th>
<th>Quartile 2 (n = 44)</th>
<th>Quartile 3 (n = 44)</th>
<th>Quartile 4 (n = 48)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FRAX major osteoporotic fracture (%)</td>
<td>9.1 (5.1)</td>
<td>4.3 (0.9)</td>
<td>6.6 (0.6)</td>
<td>8.9 (0.73)</td>
<td>16.0 (4.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FRAX hip fracture (%)</td>
<td>3.5 (2.6)</td>
<td>0.7 (0.4)</td>
<td>1.7 (0.9)</td>
<td>3.3 (1.5)</td>
<td>7.8 (4.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV1 (%)</td>
<td>81.0 (14.4)</td>
<td>105.0 (5.6)</td>
<td>80.5 (0.32)</td>
<td>70.0 (0.25)</td>
<td>66.0 (0.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Home oxygen (%)</td>
<td>39%</td>
<td>24%</td>
<td>39%</td>
<td>41%</td>
<td>52%</td>
<td>0.057</td>
</tr>
<tr>
<td>Exacerbations in previous year</td>
<td>4.7 (4.3)</td>
<td>2.8 (2.8)</td>
<td>5.5 (4.9)</td>
<td>4.8 (4.6)</td>
<td>5.5 (5.1)</td>
<td>0.007</td>
</tr>
<tr>
<td>Hospitalisations in previous year</td>
<td>1.3 (2.1)</td>
<td>1.1 (2.7)</td>
<td>1.4 (2.9)</td>
<td>1.3 (1.8)</td>
<td>1.4 (2.1)</td>
<td>0.753</td>
</tr>
<tr>
<td>CAT score</td>
<td>25.8 (6.9)</td>
<td>25.8 (7.7)</td>
<td>24.8 (6.8)</td>
<td>26.8 (6.4)</td>
<td>25.8 (6.7)</td>
<td>0.656</td>
</tr>
<tr>
<td>Incremental Shuttle Walk Test (m)</td>
<td>150 (110)</td>
<td>220 (160)</td>
<td>160 (80)</td>
<td>110 (60)</td>
<td>90 (40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Quadriceps Strength (Kg)</td>
<td>18.5 (7.3)</td>
<td>23.5 (8.6)</td>
<td>20.0 (6.5)</td>
<td>16.9 (4.6)</td>
<td>13.7 (5.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fat Free Mass Index (kg/m²)</td>
<td>16.4 (2.6)</td>
<td>18.0 (2.8)</td>
<td>17.0 (1.9)</td>
<td>15.9 (2.6)</td>
<td>14.8 (2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Skeletal Muscle Index (kg/m²)</td>
<td>6.1 (1.3)</td>
<td>6.7 (1.2)</td>
<td>6.6 (1.2)</td>
<td>5.8 (1.1)</td>
<td>5.4 (1.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Bone Calcium (Kg)*</td>
<td>2.47 (0.62)</td>
<td>2.75 (0.53)</td>
<td>2.65 (0.48)</td>
<td>2.40 (0.52)</td>
<td>2.10 (0.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vitamin D (nmol/l)</td>
<td>29 (26)</td>
<td>30 (28)</td>
<td>29 (24)</td>
<td>34 (28)</td>
<td>22 (25)</td>
<td>0.220</td>
</tr>
</tbody>
</table>

Quartile 1 is the lowest risk and quartile 4 is the highest risk. Data are mean (SD). *calculated from DEXA.
RESPIRATORY IMPACT OF DIABETES MELLITUS IN PEOPLE WITHOUT A PRIMARY DIAGNOSIS OF CHRONIC LUNG DISEASE

S Ruickbie, A Prasad, PW Jones, EH Baker. St George’s, University of London, London, UK
10.1136/thoraxjnl-2015-207770.154

Introduction In the UK, around 3 million people currently have a diagnosis of diabetes mellitus and the prevalence is increasing rapidly. Microvascular and macrovascular complications of diabetes are widely recognised, but the respiratory impact is less well understood. In people with chronic lung disease, diabetes mellitus is associated with worse lung function, impaired health status and more frequent exacerbations (Kinney et al, Diabetes Care. 2014;37:389–95). The aim of our study was to determine the respiratory impact of diabetes in people without a primary diagnosis of chronic lung disease.

Abstract P17 Table 1 Comparison of clinical characteristics, prior respiratory illness, lung function and respiratory symptoms in people with and without diabetes mellitus

<table>
<thead>
<tr>
<th>No diabetes mellitus</th>
<th>Diabetes mellitus</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>175</td>
<td>75</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66 ± 11</td>
<td>67 ± 9</td>
</tr>
<tr>
<td>Gender (n (%) female)</td>
<td>56 (32%)</td>
<td>22 (29%)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>28.2 ± 5.7</td>
<td>32.1 ± 7.7</td>
</tr>
<tr>
<td>Waist:hip ratio</td>
<td>0.94 ± 0.07</td>
<td>0.97 ± 0.07</td>
</tr>
<tr>
<td>Blood glucose mmol/l</td>
<td>5.9 ± 1.7 (45%)</td>
<td>9.0 ± 3.2 (54%)</td>
</tr>
<tr>
<td>HbA1c mmol/mol</td>
<td>41 ± 6 (31)</td>
<td>61 ± 16 (28)</td>
</tr>
<tr>
<td>Diabetic medication (n (%))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>11 (15%)</td>
<td></td>
</tr>
<tr>
<td>Oral hypoglycaemics</td>
<td>51 (68%)</td>
<td></td>
</tr>
<tr>
<td>Insulin (oral hypoglycaemics)</td>
<td>13 (17%)</td>
<td></td>
</tr>
<tr>
<td>Confirmed coronary artery disease</td>
<td>36%</td>
<td>42%</td>
</tr>
<tr>
<td>(Gensini &gt;20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charlson index (excluding diabetes)</td>
<td>3 (2–4)</td>
<td>3 (2–4)</td>
</tr>
</tbody>
</table>

Smoking status (n (%))

<table>
<thead>
<tr>
<th>Never</th>
<th>Ex-smoker</th>
<th>Current smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>41%</td>
<td>46%</td>
<td>13%</td>
</tr>
</tbody>
</table>

Childhood respiratory illness (n (%))

| 30 (17%) | 18 (24%) | 0.139 |

On respiratory medication (n (%))

| 40 (23%) | 16 (21%) | 0.474 |

Prior COPD diagnosis (n (%))

| 22 (13%) | 7 (9%) | 0.314 |

Prior diagnosis of any chronic lung disease (n (%))

| 28 (16%) | 18 (24%) | 0.092 |

Lung function

<table>
<thead>
<tr>
<th>FEV1 (% predicted)</th>
<th>83 ± 21</th>
<th>79 ± 18</th>
<th>0.134</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (% predicted)</td>
<td>91 ± 22</td>
<td>82 ± 17</td>
<td>0.002</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>0.72 ± 0.11</td>
<td>0.76 ± 0.09</td>
<td>0.008</td>
</tr>
</tbody>
</table>

Respiratory symptoms

| Breathlessness (mMRC) | 1.7 ± 0.7 | 2.1 ± 0.9 | 0.001 |
| Cough (%)             | 0.6 ± 1.1 | 1.0 ± 1.3 | 0.005 |
| Phlegm (5)            | 0.4 ± 0.9 | 0.5 ± 1.0 | 0.813 |
| Total CAT score       | 7 ± 5 | 9 ± 7 | 0.024 |

COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; mMRC, modified Medical Research Council dyspnoea scale; CAT, COPD assessment test.

Methods Unselected patients attending for elective coronary angiography March–July 2015 were invited to take part in a prospective observational study (primary aim to investigate the association between coronary atheroma and airflow obstruction). Participants underwent clinical assessment and spirometry prior to the procedure.

Results 250 of 294 (85%) people approached took part. Seventy five (30%) had diabetes mellitus. People with diabetes were of similar age and gender to those without diabetes, but had greater body mass index, central adiposity, blood glucose and HbA1c (Table 1). Despite no differences in history of smoking or respiratory illness (Table 1), people with diabetes had significantly lower forced vital capacity (FVC) and higher forced expiratory volume (FEV1): FVC ratio than those without diabetes. After adjustment for age, gender, body mass index, waist: hip ratio and smoking history, diabetes was an independent predictor of FEV1: FVC (partial eta² 0.03, p = 0.007), but not FVC. People with diabetes had more respiratory symptoms (Table 1). They were more likely to give a history of recurrent chest infections (diabetes 14(19%); no diabetes 11(6%); p = 0.004) and reported more chest infections (diabetes 0.6 ± 1.6; no diabetes 0.2 ± 0.9, p = 0.007) in the past year. After adjustment for age, waist: hip ratio, body mass index, smoking, FEV1: FVC and co-existing respiratory disease, diabetes was an independent predictor of recurrent chest infections (odds ratio 2.81 (95% confidence intervals 1.04–7.73), p = 0.045).

Conclusions Diabetes mellitus is associated with worse lung function, increased respiratory symptoms and more frequent chest infections, independent of smoking and prior respiratory illness. The burden of diabetes-associated respiratory disease on patients and the NHS is likely to increase as diabetes becomes more prevalent.

THE EFFECTS OF ACUTE AND REPEATED BOUTS OF UNILATERAL NEUROMUSCULAR ELECTRICAL STIMULATION ON QUADRICEPS MUSCLE INFLAMMATION IN COPD

P18

1A Gray, 1L Latimer, 2A Parmar, 2P Badding, 2NJ Greening, 2MC Steiner. 1University of Leicester, Leicester, UK, 2University Hospitals of Leicester, Leicester, UK
10.1136/thoraxjnl-2015-207770.155

Introduction and objectives Impaired skeletal muscle function is an important systemic manifestation of COPD which can be improved by exercise training. Non-volitional training using neuromuscular electrical stimulation (NMES) may be an effective training technique in situations where voluntary exercise may be difficult or impractical (e.g. peri-exacerbation or severe ventilatory limitation). Exercise is known to result in both intramuscular and systemic inflammation. However, the cellular response to NMES, which directly depolarises the motor units, is unclear. We investigated the impact of acute and repeated bouts of unilateral NMES in COPD patients.

Methods 16 patients underwent 6 weeks of unilateral NMES 5 times a week for 30 min at 50 Hz at Glenfield Hospital, Leicester. Mean (SD) age was 65 (9) years, FEV1: 50 (22)% predicted, BMI 26.5 (5.2) Kg/m². Isometric quadriceps strength, regional muscle mass (DEXA) and quadriceps thickness (ultrasound) were recorded at baseline and at the end of the intervention. Vastus lateralis muscle biopsies were obtained from both the trained and untrained limbs at baseline, 24 h after the first bout of NMES and at 6 weeks. Venous blood was taken at the same...
time. Biopsies were analysed for neutrophil (neutrophil clastase) and macrophage (CD163) density using immunohistochemistry. ELISA measurements of inflammatory cytokines (IL-6 and TNFα) were performed on blood samples.

**Results** Quadriceps strength increased by 7.6% (p = 0.024), thigh mass by 2.8% (p = 0.185), and quadriceps thickness by 11% (p = 0.002). Muscle biopsies for 11 patients were analysed. Neutrophil density 24 h after a single bout of unilateral NMES significantly increased in both the trained and untrained limb, with larger increase in the stimulated muscle (Table 1). Neutrophil density returned to baseline in the trained limb following training. No changes were seen in muscle macrophage density, serum IL-6 or serum TNFα.

**Conclusion** A single bout of unilateral NMES provokes an intramuscular neutrophilic inflammatory response in both the trained and untrained limb, which are not mediated by changes in circulating IL-6 or TNFα. Neutrophil infiltration returned to baseline in the stimulated leg following training.

**Abstract P18 Table 1** Cellular inflammation in vastus lateralis biopsies following unilateral NMES in both trained and untrained limbs at baseline, 24 hours following first stimulation and 24 hours following 6 weeks training. Data are mean ± SD.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>24 h</th>
<th>6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Trained Leg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophil (Neutrophils/mm²)</td>
<td>3.48 ± 0.87</td>
<td>33.40 ± 11.65*</td>
<td>1.57 ± 0.49**</td>
</tr>
<tr>
<td>Macrophage (Macrophils/mm²)</td>
<td>1.27 ± 1.36</td>
<td>13.10 ± 9.02*</td>
<td>10.97 ± 12.92</td>
</tr>
<tr>
<td><strong>Untrained Leg</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophil (Neutrophils/mm²)</td>
<td>4.87 ± 6.74</td>
<td>0.74 ± 1.41</td>
<td>4.22 ± 10.58</td>
</tr>
<tr>
<td>Macrophage (Macrophils/mm²)</td>
<td>0.78 ± 1.39</td>
<td>8.02 ± 9.03</td>
<td>3.83 ± 5.59</td>
</tr>
</tbody>
</table>

*p-value < 0.05 compared with baseline, **p-value < 0.05 compared with 24 h.

**P19** PREDICTORS OF COPD MORTALITY, 2 YEAR FOLLOW-UP DATA FROM THE ARCADE STUDY

1NS Gale, 1A Albarrati, 1MM Munnery, 2R Singer, 1JR Cockcroft, 1DJ Shale. 1Cardiff University, Cardiff, UK; 2GSK R&D, Pennsylvania, USA

10.1136/thoraxjnl-2015-207770.156

**Background** COPD is a systemic disease with associated comorbidities including cardiovascular disease which have significant impact on morbidity and mortality.1 However, the progression of the disease is not well understood as there are few longitudinal studies of sufficient duration which include outcome data. The aim of this analysis was to evaluate predictors of mortality from the Assessment of Risk in Chronic Airways Disease Evaluation Study (ARCADE), Clinical Trials registration: NCT01656421.2

**Methods** The ARCADE study is a longitudinal observational study of cardiovascular risk and other comorbidities in patients with COPD. Patients were assessed at recruitment and after 2 years including the following outcomes: Spirometry, BMI, St Georges Respiratory Questionnaire (SGRQ), mMRC breathlessness, number of exacerbations and 6 min walk distance (6MWD). A sample of blood was analysed for the inflammatory mediator fibrinogen.

**Results** At baseline 524 patients with COPD, confirmed with spirometry, were recruited to the study. Thus far, at the 2 year follow up there have been 47 deaths. According to hospital records, causes of death were: respiratory n = 22 (including acute exacerbations/respiratory infections (n = 12) and pneumonia (n = 10)), cardiovascular n = 9, cancer n = 10, septicaemia n = 3 and unknown n = 4.

At baseline the subjects who did not survive were similar to survivors in age, gender and BMI, but had greater airflow limitation, worse SGRQ, more breathlessness, more exacerbations and lower 6MWD, fibrinogen was also higher (Table 1). Using logistic regression of the objective markers which differed between the groups; FEV1% predicted, number of exacerbations, 6MWD and fibrinogen were entered into the model. Of these Fibrinogen (p = 0.013) and 6MWD (p = 0.024) were significant predictors of mortality (X2 (4) = 18.678, p = 0.001).

**Abstract P19 Table 1** Baseline characteristics of patients

<table>
<thead>
<tr>
<th></th>
<th>Survivor</th>
<th>Non-survivor</th>
<th>p =</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. Exac per year</td>
<td>2 (1–3)</td>
<td>2.5 (1.5–4)</td>
<td>0.022</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>3.6 ± 1.0</td>
<td>4.1 ± 1.3</td>
<td>0.002</td>
</tr>
</tbody>
</table>

*p-value < 0.05 compared with baseline, **p-value < 0.05 compared with 24 h.

**Conclusions** The follow up mortality rate was 9%, with the majority of deaths due to respiratory causes, followed by cancer and cardiovascular events. The non-survivors had poorer objective and patient reported outcomes. Further follow-up of this cohort will provide greater power to predict outcomes.

**REFERENCES**


A DATABASE APPROACH TO DOSE SCORE CALCULATION AS A TOOL TO IDENTIFY ‘AT RISK’ CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS THROUGH CLINICAL RECORDS

1LA Rigge, M Johnson, O Cullford, N Williams, L Josephs, M Thomas, T Wilkinson. 2NIHR CLAHRC Wessex, University of Southampton, Clinical and Experimental Sciences & University Hospital Southampton NHS Foundation Trust, Southampton, UK; 3NIHR CLAHRC Wessex, Methodological Hub, Southampton, UK; 4University of Southampton, Clinical and Experimental Sciences & University Hospital Southampton NHS Foundation Trust, Southampton, UK; 5NIHR CLAHRC Wessex, University of Southampton, Primary Care and Population Sciences, Southampton, UK

10.1136/thoraxjnl-2015-207770.157

Establishing how best to target resources remains a challenge within COPD as this is a heterogeneous patient group with complex needs often poorly reflected by routinely collected clinical measurements such as FEV1.

Jones et al. created the DOSE score (dyspnoea (MRC score), obstruction (FEV1 percentage predicted), smoking status and exacerbation number in a year) (Table 1) a validated, clinically useful measure of risk stratification in COPD which utilises data already routinely collected in Primary Care for QOF review.

By using a collaborative approach with informatics, statistical and clinical input we developed a database approach to calculating a DOSE score using routinely collected and coded Primary and Secondary Care data. A local NHS database holding anonymised clinical records for over one million patients was used to identify a cohort of over 13,000 patients with codes diagnostic of COPD.

Microsoft Structured Query Language Server was used to identify, cleanse and standardise the required clinical information and calculate the DOSE score, creating a series of functions that can be replicated across other database management systems.

Date of FEV1 percentage predicted was taken as the index date for DOSE score calculation. Where only FEV1 was recorded, a percentage of predicted FEV1 was calculated using available height and age data.

Read codes (the routine coding system used in primary care) and ICD-10 codes were used to compile lists identifying those symptoms, diagnoses and prescriptions indicative of COPD exacerbations. These lists were applied in the year prior to the chosen FEV1 value and, functions were written to cluster those events felt to be reflective of a single exacerbation.

Read codes reflecting MRC score and smoking status closest in time to the index FEV1 measurement were combined with the above measurements, generating a complete score in approximately 10,000 patients. Partial scores were created for a further 1500 patients with incomplete data for the individual score components.

This approach provides a simple way for clinicians to risk stratify their COPD population without increasing their clinical workload. This gives an opportunity to identify those at highest risk of hospital admission and death and proactively allocate resources accordingly.

Poster sessions

THE APPLICABILITY OF CURRENT CARDIOVASCULAR RISK SCORES AND CARDIOVASCULAR SURROGATES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A CASE-CONTROL STUDY

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10.1136/thoraxjnl-2015-207770.158

Background COPD is a complex multi-morbid disorder with significant cardiac mortality. Despite this, current cardiovascular scoring systems do not include COPD in their risk prediction models. The aims of this study were to assess whether differences in cardiovascular surrogate markers exist in COPD and to further our understanding of the relationship of COPD to cardiovascular structure and function.

Methods This post-hoc cross-sectional analysis utilised baseline data from two randomised controlled trials (n = 36 and 54). 26 COPD patients were matched for global cardiovascular risk with 26 controls with normal lung function using QRISK2, a validated scoring system for predicting the 10-year risk of cardiovascular disease in a United Kingdom population. Patients underwent cardiac magnetic resonance imaging, arterial stiffness and lung function measurements.

Results Pulse wave velocity (PWV) (mean difference +1.0 m/s, 95% CI 0.02–1.92; p = 0.045) and total arterial compliance (TAC) (mean difference -0.27 mL/m²/mmHg, 95% CI -0.39, -0.15; p < 0.001) were adversely affected in COPD compared to the control group matched for cardiovascular risk. In the whole cohort (n = 90) QRISK2 (β = 0.046, p = 0.017) and FEV1 (β = 0.013, p = 0.022) were associated with PWV in multivariate analysis. The relationship between QRISK2 and PWV appeared to be modified by COPD, where the interaction term reached borderline significance (p = 0.060). FEV1 (β = 0.005, p = 0.004) was also associated with TAC in multivariate analysis. Cardiac chamber size and stroke volume was decreased in COPD compared to controls. The mean difference in left ventricle stroke volume index (LVSVI) and left and right end diastolic volume index was -10.3 ml/m² (95% CI -15.1, -5.5, p < 0.001), -14.1 ml/m² (95% CI -21.9,-6.3 p < 0.001) and -13.0 ml/m² (95% CI -23.3, -2.6 P < 0.015) respectively, which were shown to be associated with airflow limitation in multivariate models. In the COPD group associations were found with lung hyperinflation (LVSVI: β = 0.075, p = 0.032; Left atrial size: β = -0.129, p = 0.047) and fibrinogen (TAC: β = 0.716, p = 0.030).

Conclusion Surrogates for cardiovascular outcomes are adversely affected in COPD compared to a group matched for global cardiovascular risk, suggesting that current scoring systems may be suboptimal for cardiovascular risk prediction in COPD.
DISTRIBUTION AND PREDICTION OF 10-YEARS RISK FOR CORONARY HEART DISEASE IN COPD

1A Albarrati, 1M Munnery, 2JR Cockcroft,
1Cardiorespiratory Medicine, Cardiff University, Cardiff, UK

Introduction Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in COPD in excess of the effect of smoking. Clarification of cardiovascular risk factors could clarify the extra risk and lead to appropriate clinical management. We hypothesise that COPD increases the 10 year risk for CVD in patients free of clinically overt CVD.

Methods Using data from ARCADE study, 382 stable patients with COPD free from CVD and 143 controls were assessed for; lung function (forced expiratory volume (FEV1), forced vital capacity (FVC) and their ratio), blood pressure (BP), BMI, aortic pulse wave velocity (PWV) and number of exacerbations. In addition, medical and smoking history were recorded and used to calculate the Framingham risk score (FRS).

Results Patients with COPD had greater FRC, 24 (8) than controls, 19 (9), p < 0.001. The majority of patients were at high risk, 72%, while only 7% were at low risk. There was no difference between genders. Post hoc analysis showed patients at high risk of CVD had greater aortic stiffness, 10.2 (2.4) m/s compared to patients at low, 8.3 (2) m/s and moderate risk, 9.1 (2) m/s, p < 0.001. The FRS was related to age, r = 0.39, p < 0.001, waist circumference, r = 0.11, p = 0.026, and number of exacerbations, r = 0.10, r = 0.039, but was not related to FEV1.

Conclusion The majority of our patients were at high risk of developing fatal and non-fatal cardiovascular events. Early identification of cardiovascular risk factors and aggressive management would contribute to lowering the incidence of CVD in COPD.

REFERENCE
Background Pulmonary artery distensibility and pulsatility has been studied in patients with COPD using cardiac MRI (CMRI). However, pulmonary artery pulse wave velocity (PA-PWV) using the ‘QA’ method2 in CMRI has not been studied in this population. We hypothesised that patients with COPD have a higher PA-PWV compared to healthy individuals.

Methods This interim analysis includes 23 COPD and 12 healthy volunteers (current or ex-smokers free from respiratory disease). All participants underwent spirometry to measure FEV1, FVC and their ratio, oxygen saturations, heart rate, peripheral mean arterial pressure (MAP), 6-minute-walk-distance (6MWD) and cardiac MRI to measure PA-PWV.

MRI studies were performed using a 3.0T GE Signa HDx MRI scanner (GE Healthcare). Phase-contrast cross-sectional images of the pulmonary artery using steady-state free precession sequence were obtained, approximately 2 cm above the pulmonary valve, under free-breathing conditions.

Results Patients with COPD and the healthy individuals were similar in age and gender (Table 1). Patients with COPD had impaired lung function, greater PA-PWV (3.37 ± 0.6 1.41 ± 0.4 <0.001), heart rate and mean arterial pressure than the healthy individuals. Male patients with COPD had greater PA-PWV (3.63 ± 0.45) than females (3.11 ± 0.59) p = 0.042. PA-PWV did not relate to age, lung function, resting oxygen saturations, heart rate or peripheral MAP.

Abstract P23 Table 1

<table>
<thead>
<tr>
<th></th>
<th>COPD (n = 23)</th>
<th>CONTROLS (n = 12)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE (yrs)</td>
<td>65.8 ± 7.3</td>
<td>66.8 ± 7.1</td>
<td>0.713</td>
</tr>
<tr>
<td>GENDER (male:female)</td>
<td>11:12</td>
<td>6:6</td>
<td>0.903</td>
</tr>
<tr>
<td>FEV1/FVC (L)</td>
<td>0.55 ± 0.14</td>
<td>0.75 ± 0.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEV1 % predicted</td>
<td>59.2 ± 17.6</td>
<td>105.8 ± 12.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SMOKING (pack years)</td>
<td>39.0 ± 29.9</td>
<td>12.2 ± 8.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resting Heart Rate (bpm)</td>
<td>68 (9)</td>
<td>62 (7)</td>
<td>0.034</td>
</tr>
<tr>
<td>Peripheral MAP (mmHg)</td>
<td>100.1 ± 9.7</td>
<td>95.6 ± 10.5</td>
<td>0.236</td>
</tr>
<tr>
<td>PA-PWV (m/s)</td>
<td>3.37 ± 0.6</td>
<td>1.41 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>388.2 ± 127.7</td>
<td>536.8 ± 49.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion Pulmonary artery PWV measured using CMRI ‘QA’ method showed that COPD patients have a stiffer pulmonary artery than healthy individuals. Further analysis will investigate the association between pulmonary artery stiffness and cardiac function.

REFERENCES
Objectives Recognising the end of life phase in chronic non-malignant lung conditions remains a challenge which has been proposed as a major barrier to ensuring effective end-of-life care in this population. Our aims were threefold. Firstly, to establish whether patients who died of causes related to their lung condition could have been predicted to have been in the last 6–12 months of their lives. Secondly, to evaluate the standard of care they received leading up to their death. Finally, to compare end-of-life care received by patients with chronic obstructive pulmonary disease (COPD) and interstitial lung disease (ILD).

Methods A retrospective review of deaths due to COPD and ILD over a 26 month period in two acute hospitals in South Wales using paper and electronic health records. Gold Standards Framework (GSF) prognostic indicators of poor prognosis were identified, and ‘standards of care’ evaluated in the 12 months preceding death.

Results 119 cases were analysed. 83% of patients could have been identified as ‘approaching end of life’ (AEOL) using GSF criteria. ‘Standards of care’ were variably met: do not attempt cardiopulmonary resuscitation (DNACPR) forms were completed in 93% of cases, Advanced care planning, establishing preferred place of care and use of specific end-of-life care documentation took place in <1%, 7% and 14% respectively. COPD patients had more indicators of poor prognosis than patients with ILD but received fewer ‘standards of care’.

Conclusions The majority of patients in our study could have been identified as AEOL and therefore ought to have been in receipt of the ‘standards of care’. There is a need to improve recognition of patients that are AEOL in order that they receive better end-of-life care. Further investigation to confirm or refute the discrepancy in care between COPD and ILD patients is necessary. Research into the best means of identifying, and subsequent provision of care, for patients with non-malignant respiratory disease is also required.

Abstract P25 Figure 1 Clinical indicators of severity

REFERENCE

MEASURING THE VALUE OF A CONSULTANT-LED COMMUNITY RESPIRATORY (CORE) MULTIDISCIPLINARY TEAM (MDT) IN A DEPRIVED INNER CITY AREA: ACHIEVING PARITY IN RESPIRATORY CARE FOR HOUSEBOUND SICK PATIENTS

Introduction The shift of chronic respiratory disease management to the community has stimulated development of multidisciplinary community respiratory services (CORE-MDT). Measuring the value of these services is challenging but is important for quality improvement and commissioning. This retrospective analysis of the activity of an inner city community respiratory service documents the nature of the caseload, interventions made and their impact on usual care provision.

Method The CORE-MDT, accepting referrals from GPs and three acute hospital trusts, is based at three localities and includes respiratory nurses, physiotherapists, quit-smoking advisors, clinical psychologists and respiratory consultant support. Care is delivered at home with hospital in-reach during every admission. A bespoke iPad App database (Handbase) was designed for information documentation and sharing from case management and consultant-led MDT discussion of patients. A retrospective analysis of records was made of sequential referrals from Sept 2014 to March 2015. Demographics, disease severity, comorbidities, social deprivation, duration of management, nature of intervention and healthcare resource utilisation over 6/12 were documented. Hospital data allowed estimation of bed-day savings based on average length of stay for acute exacerbations of COPD (AECOPD).

Results Records from 83 patients (most with COPD) were reviewed. Mean [SD] FEV1: 0.98 [0.38]L. Patients had multiple comorbidities, high smoking prevalence, deprivation and isolation (Table 1). Mean [SD] duration of CORE team management: 5.2[4.9]months. ~50% of patients were then discharged to usual care. 17/34 (50%) completed pulmonary rehabilitation, 11 saw a psychologist and 6/12 (50%) achieved smoking cessation. Mortality was 6%. Hospital bed-days usage (p = 0.001) and GP visits (p = 0.02) were reduced during active case management compared to the year before referral. Discriminant analysis of 105 AECOPD reduced GP workload with an estimated £58 000 savings in admission avoidance for (p = 0.03), 30 patients with baseline hypoxia <92% or ≥2 admissions in the year prior to CORE management HRG DZ-21K: £2000/admission).

Conclusions The service has improved quality of care for these complex sick patients and generated significant savings in GP workload and admission avoidance which should underpin service commissioning and provision. The use of Handbase has facilitated consistency in evidence-based care and record-keeping, information sharing and evaluation of CORE-MDT activity.
Abstract P26 Table 1  Demographic details, interventions and outcomes

<table>
<thead>
<tr>
<th>DEMOGRAPHIC DETAILS</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>AGE  Mean (SD, range) years</td>
<td>75 (1.2; 52–96)</td>
</tr>
<tr>
<td>Gender  M: F</td>
<td>40:43</td>
</tr>
<tr>
<td>DEPRIVATION (Multiple index of Deprivation 2010)</td>
<td>69/83 (83%) lived in least deprived</td>
</tr>
</tbody>
</table>

DISEASE SEVERITY

| Mean FEV1 (SD) n = 83 | 0.98 (0.38) |
| Mean FEV1% predicted (SD) n = 75 | 43.9 (17.2) n = 75 |
| Mean MRC Dyspnoea Score (SD) n = 83 | 3.8 (0.8) |
| Mean (SD; range) SaO2 on room air on referral | 93.3% (3.5; 84–99) |

Number with SaO2 <92% on room air on referral (%): 17 (20%)

Number on LTOT (%): 29 (35%)

Number of Medical Co-morbidities Mean (SD; range) n = 81: 3.5 (2.1, 0–11)

Healthcare Utilisation in 1 year prior to referral:

- Mean No of Hospital Admissions (SD; range): 0.9 (1.1; 0–5)
- Mean No of GP visits/telephone calls (SD; range): 4.8 (3.8; 1–17)

Psychosocial Factors

- Lives alone: 32 (39%)
- ESH: 12 (14%)
- Serious Mental Illness: 27 (33%)
- Anxiety: 25 (30%)
- Depression: 25 (30%)

INTERVENTIONS AND OUTCOMES over 6 months

| Mean Duration (months) under CORE team (SD; range) | 5.2 (4.9; 1–22) |
| Mean number of visits/month (SD; range) | 1.19 (0.9; 0.2–5) |
| Referral to other agencies (TOTAL 81) |  |

- QUIT smoking: 12
- Pulmonary Rehabilitation (PR): 34
- Clinical Psychologist: 11
- Nutritionist: 5
- Social Services: 7
- ICTT, Age concern, SHINE (Fuel Poverty Service) | 12 |
- Attempting or Quit smoking | 7/12 |
- Assessed/Attending/Attended PR | 26/34 |
- Completed PR | 17/34 |
- Total Episodes of Domiciliary Acute | 105 |
- exacerbation of COPD Management |

Management Outcomes

| Remains under active case management | 27 |
| Inactive on list | 12 |
| Discharged | 43 (52%) |
| Did not engage | 6 |
| Died | 5/83 (6%) |

Health Care Resource Utilisation

Mean hospital beddays per month (SD; range) n = 69

| 1 year prior to CORE team referral | 0.86 (1.44; 0–8.83) |
| during CORE team management | 0.63 (2.5; 0–18) p = 0.01 |
| Mean Number of GP visits per month (SD; range) n = 51 | 0.33 (0.5; 0–3) p = 0.02 |
Non-IPF ILDs: diagnosis and management

P28 REAL WORLD MDT DIAGNOSIS OF IDIOPATHIC PULMONARY FIBROSIS

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10.1136/thoraxjnl-2015-207770.165

Idiopathic pulmonary fibrosis (IPF) is the commonest idiopathic interstitial lung disease (ILD). The diagnosis is determined by a usual interstitial pneumonitis (UIP) pattern on high resolution computed tomography (HRCT). Current guidelines advocate lung biopsy in patients with diagnostic uncertainty though biopsy can afford significant morbidity and mortality. We aimed to evaluate our practice in diagnosing IPF in relation to these guidelines.

Methods We evaluated our experiences in a multidisciplinary team (MDT) setting in a UK tertiary referral centre of 104 patients referred with a presumed diagnosis of IPF between November 2012 and July 2014.

Results After MDT discussion, 48.5% patients had definite UIP and 51.4% had possible UIP or fibrotic non-specific interstitial pneumonitis (NSIP) based on ATS/ERS criteria. Of the fifty-three patients with possible UIP/NSIP, fifteen (28%) patients had a lung biopsy. Twelve out of fifteen patients had UIP on biopsy (80%). One patient died and one suffered with chronic pain post-biopsy (13%). In the remaining thirty-eight (72%) patients, biopsy was not possible due to comorbidities or patient choice.

Of the thirty-eight patients with radiological diagnosis of possible UIP/NSIP, thirteen (34%) patients were deemed to have a clinical diagnosis of probable IPF after MDT discussion based on disease progression and age. Two (5%) patients were subsequently diagnosed as having a connective tissue disease and twenty-three (60%) patients were clinically diagnosed as NSIP based on response to immunosuppression and stability of lung function.

Conclusions Surgical lung biopsy is considered the gold standard based on response to immunosuppression and stability of lung function.

Abstract P29 Table 1 Pre-MDT diagnoses and consensus diagnoses following MDT discussion

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Pre-MDT Diagnosis</th>
<th>Consensus diagnosis</th>
<th>1 year transplant free survival</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Asbestosis</td>
<td>10</td>
<td>1.5</td>
<td>11</td>
</tr>
<tr>
<td>CPFE</td>
<td>26</td>
<td>4.0</td>
<td>33</td>
</tr>
<tr>
<td>CT-ILD</td>
<td>79</td>
<td>12.1</td>
<td>68</td>
</tr>
<tr>
<td>Drug Related ILD</td>
<td>16</td>
<td>2.5</td>
<td>14</td>
</tr>
<tr>
<td>Hypersensitivity pneumonitis</td>
<td>63</td>
<td>9.7</td>
<td>71</td>
</tr>
<tr>
<td>IPF</td>
<td>150</td>
<td>23.0</td>
<td>130</td>
</tr>
<tr>
<td>No ILD</td>
<td>2</td>
<td>0.3</td>
<td>65</td>
</tr>
<tr>
<td>NSIP</td>
<td>47</td>
<td>7.2</td>
<td>73</td>
</tr>
<tr>
<td>NSIP/UIP Spectrum</td>
<td>12</td>
<td>1.8</td>
<td>6</td>
</tr>
<tr>
<td>Organising pneumonia</td>
<td>11</td>
<td>1.7</td>
<td>11</td>
</tr>
<tr>
<td>Other (including vasculitis, DIP, LAM etc)</td>
<td>33</td>
<td>5.1</td>
<td>39</td>
</tr>
<tr>
<td>Pulmonary Langerhans Cell Histiocytosis</td>
<td>5</td>
<td>0.8</td>
<td>7</td>
</tr>
<tr>
<td>RB-ILD</td>
<td>10</td>
<td>1.5</td>
<td>13</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>84</td>
<td>12.9</td>
<td>74</td>
</tr>
<tr>
<td>Unclassifiable ILD</td>
<td>103</td>
<td>15.8</td>
<td>45</td>
</tr>
<tr>
<td>Total</td>
<td>651</td>
<td>100.0</td>
<td>651</td>
</tr>
</tbody>
</table>


Introduction The weekly Bristol Interstitial Lung Disease (BILD) multidisciplinary team (MDT) meeting decides consensus diagnoses for patients from around the South West. A database records cases at the time of discussion. Referrals have increased since the advent of novel agents for Idiopathic Pulmonary Fibrosis, prompting this retrospective review of the MDT experience.

Aims Establish the range of cases referred, determining the proportion for whom MDT discussion leads to changes in diagnosis and which variables influence this. Examine IPF patients, identifying differences between those prescribed Pirfenidone or otherwise.

Methods For all cases recorded in the MDT database between 1/1/2013 and 1/1/2015, the pre-MDT differential diagnosis and consensus diagnosis, dates of referral/discussion, referral source, demographics, investigation results, the number of discussions and dispensing of Pirfenidone were reviewed. For patients with multiple entries, initial differential diagnoses were compared to final consensus. Outcome measures of interest were change in diagnosis and decision to use Pirfenidone in IPF patients.

Results 846 discussions occurred (651 individual patients) over this period. Pre/post MDT diagnoses are shown in the Table 1. 78% of cases were discussed within 2 weeks of referral. 25% were discussed more than once (range 1–5). 57.0% of IPF cases were external referrals vs 32.3% overall.

Diagnosis changed following discussion for 44.1% of patients. Pre-MDT diagnosis of IPF changed for 36.7%. Logistic regression suggests pre-MDT differential diagnosis and age at referral are main influences on change in diagnosis.

Overall mean age was 65.5 years (17–91), 58.1% male. For IPF cases, mean age was 74.4 years, 76.9% male. Pirfenidone was prescribed to 46.2% of IPF cases; median time to dispensing 61 days. 6MWD was greater where Pirfenidone was given (284 m vs 249 m, p = 0.03); however lung function and HRCT pattern did not differ. 12-month mortality was 6.7% in the Pirfenidone group, 27.1% where not given (p = 0.002).
Conclusion Specialist MDT discussion influenced changes in diagnosis in 44.2% of patients. The majority of IPF cases discussed are external referrals. This has implications for design and delivery of specialist ILD services.

Case selection for Pirfenidone does not appear based on lung function differences. This has implications for guidelines for its use.

Abstract P30 Figure 1 Showing data plots and average fitted quadratic curve for FVC of patients who received IV Cyclophosphamide therapy. FVC (litres); Time relative to treatment (months)

Abstract P31 A RETROSPECTIVE ANALYSIS OF INTERSTITIAL LUNG DISEASE SCREENING IN A REGIONAL CENTRE FOR PATIENTS WITH SCLERODERMA

Background Interstitial Lung Disease (ILD) and Pulmonary Arterial Hypertension (PAH) are the major sources of morbidity and mortality amongst patients with Scleroderma. Specific autoantibodies, anti-Scl70 and anti-centromere (ACA), are associated with ILD and PAH respectively. Screening for ILD and PAH using annual pulmonary function testing (PFT), High Resolution Computed Tomography (HRCT) and Echocardiography respectively, is recommended by the BTS ILD Guidelines, 2008. However, the predictive value of autoantibodies and clinical screening for ILD and PAH, remains unclear in regional centres managing patients with Scleroderma. We hypothesised that an objective scoring system would elucidate lung phenotypes amongst the cohort and confirm original radiology reports for these patients, whilst patients autoantibody profiles would serve a clinical purpose in management. We retrospectively compared identification of ILD by a specialist ILD radiologist, against the use of predictive autoantibody profiling, for the detection of ILD.

Methods 99 patients with Scleroderma, managed in Nottingham, were identified from clinic lists (n = 68) or the pathology database (n = 31). Autoantibody profiles (n = 77), including Extractable Nuclear Antigens (ENA) and Myositis Immunoblot, were accessed using the Nottingham University Hospitals Trust pathology database. Existing and accessible HRCT scans (n = 69), were evaluated, by a radiologist with a special interest in connective tissue disease-ILD. The Scleroderma Lung Study scoring system was employed, evaluating ground glass opacity, fibrosis, bronchiectasis and honeycombing in three anatomical zones. A binary logistic regression model evaluated the role of autoantibodies in ILD diagnosis.
**Results** On re-evaluation of HRCT (n = 69), eight scans had no evidence of ILD. 49 scans had evidence of ILD (NSIP = 41; UIP = 5; non-specific pattern of ILD = 3). Following comparison with the initial reporting radiologists’ reports, twelve patients, with no previous diagnosis of ILD, were identified with the NSIP phenotype. The autoantibody model, using positive ACA and anti-Scl70 status, correctly classified 64.5% of cases overall (n = 62; p = 0.05).

**Conclusions** The role of objective HRCT evaluation, by a specialist radiologist, is superior in the detection of ILD, even in the ubiquitous NSIP phenotype, when compared to general radiology review and predictive autoantibody profiling of the same patients.

**P32 ROLE OF NON ACID AND PROXIMAL REFUX IN SCLERODERMA-ASSOCIATED INTERSTITIAL LUNG DISEASE**

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**Background** Oesophageal involvement is extremely common in patients with scleroderma. This prospective observational study (NCT02136394) addresses the relationship between gastro-oesophageal reflux (GORD) and scleroderma-associated interstitial lung disease (SSc-ILD), and evaluates the clinical utility of non-invasive tests of microaspiration.

**Materials and methods** We present preliminary results of the first 27 enrolled patients (median age 59 [min/max 35/79], median FVC = 74% [38/128%], median DLCO = 39% [21/72%], female 70%, diffuse SSc 33%). Collected clinical data included 24 hr impedance (carried out off PPI), respiratory (K-BILD and Leicester cough questionnaires) and GORD symptom questionnaires (UCLA SCTC GIT 2.0 Questionnaire, Reflux Disease Questionnaire RDQ), as well as full lung function test data. Pepsin levels were measured in saliva in all patients, and in a subset of 6 patients in bronchoalveolar lavage (BAL).

**Results** Non acid reflux and proximal reflux were detected in 54% and 49% of patients, respectively. In the subgroup of patients with normal DeMeester score (i.e. global impedance index of acid exposure), 66% had non acid reflux episodes. The DeMeester score (median 14.2 [min/max 0.8/156]) was correlated with total scores GORD questionnaire scores (e.g. RDQ, r = 0.68 p = 0.003; GIT 2.0, r = 0.68 p = 0.004), but not with K-BILD, Leicester questionnaire, or saliva pepsin. Proximal reflux episodes were moderately correlated with the Leicester total score (r = -0.76 p = 0.002) and with saliva pepsin (r = 0.46 p = 0.05). Saliva pepsin (median concentration 2.34 ng/ml [2.34/12.4]) was correlated with the impedance cough index association (r = 0.53, p = 0.02). BAL pepsin was present in all six cases (median concentration 2.34 ng/ml [2.34/12.4]) and was correlated with FVC (r = -0.8, p = 0.04). Lung function test parameters were not correlated with saliva pepsin, but were significantly, if loosely, correlated with impedance measures of acid exposure in the recumbent position (e.g. % time of exposure, r = -0.43 p = 0.04).

**Conclusions** Proximal and non acid reflux are highly prevalent in the SSc-ILD population and are associated with a high symptom burden. Pepsin is measurable in BAL of SSc-ILD patients and suggests microaspiration into the lungs, although larger numbers are needed to confirm these findings and define whether saliva pepsin measurement could represent a useful non invasive marker of microaspiration.

**P33 RITUXIMAB AS RESCUE THERAPY IN ADVANCED PROGRESSIVE SYSTEMIC SCLEROSIS ASSOCIATED INTERSTITIAL LUNG DISEASE**

M Kokosi, P Saunders, K Karagiannis, F Chua, TM Maher, EA Renzoni, AU Wells. Royal Brompton Hospital, London, UK.

**Introduction** Severe interstitial lung disease associated with systemic sclerosis (SSc-ILD) often has an inexorable progressive course. Prevention or retardation of disease progression (as seen in both SLS and the FAST trials) is the only realistic treatment goal in most cases. Rituximab is a B-lymphocyte depleting monoclonal antibody which has proven efficacy in a spectrum of treatment-refractory interstitial lung diseases. Data on the impact of rituximab therapy on SSc-ILD outcomes are limited.

**Methods** 18 patients with severe progressive SSc-ILD, despite conventional immunosuppression, were studied retrospectively. Serial change in FVC and DLco was quantified as percentage relative change from baseline, Pulmonary function trends pre (3–17 months) and post (3–11 months) Rituximab therapy were compared using paired t-testing.

**Results** 18 patients (four male), with a median age 57.5 (±15.9) received treatment with rituximab between 2012 and 2014. The median follow-up period was 7.96 (range 3.1–11.2) months. One patient died from heart failure. Rituximab was well tolerated. At the time of rituximab treatment, patients had severe pulmonary function impairment (median FVC 50.5%, range 36–84%; median DLco 25%, range 14–41%). On paired testing, there was a reduction in serial FVC decline following Rituximab therapy (-10.1% ± 7.8% versus -1.5% ± 8.7%, p = 0.01) and a similar reduction in serial DLco decline (-15.6% ± 16.8% vs. 1.0% ± 27.2%, p = 0.05).

**Conclusion** The addition of Rituximab was associated with a significant reduction in serial pulmonary function decline in patients with advanced progressive SSc-ILD, not controlled by intense conventional immunomodulation. These findings provide further support for the use of Rituximab as rescue therapy in severe SSc-ILD.

**P34 SARCOIDOSIS AND CO-EXISTENT ASPERGILLUS LUNG DISEASE**

S Gudur, E Nuttall, C Harris, N Chaudhuri, C Leonard, E Muldoon. University Hospital of South Manchester, Manchester, UK.

**Introduction** Sarcoidosis is a multisystem disorder which affects the lungs and in a small percentage of cases may result in fibrosis and cystic cavitating lesions. Chronic pulmonary aspergillosis (CPA) typically affects patients with underlying lung conditions; immunosuppressive therapy is not recommended due to risk of progression or spread of Aspergillus infection. Sarcoid patients...
are often significantly debilitated when they develop co-existent Aspergillus lung disease. They can present with worsening breathlessness, weight loss and significant haemoptysis. There is no consensus on how to best treat patients diagnosed with Sarcoidosis and CPA.

Methods A retrospective review of patients diagnosed with Sarcoidosis and CPA was performed. Cases were identified from a database held of patients diagnosed with CPA group in our specialist clinic. Patient demographics, presentation, laboratory parameters, radiology results were recorded and data analysed.

Results 38 patients with sarcoidosis were diagnosed with CPA from 2009 – March 2015. 33/36 (63%) were male. 14/36 (38%) patients were affected by breathlessness with MRC dyspnoea score ≥3. 15/36 (41%) of patients were on maintenance Prednisolone between 5 – 10 mg/day and 3 patients on other steroid sparing agents. 12/28 patients had obstructive spirometry and average predicted gas transfer factor at 49% (range 20 – 75%).

33/36 (91%) had CPA defined by presence of serum precipitins and 50% of patients had aspergillomas detected in the cavities on radiology. 27/36 (75%) of patients were on antifungal therapy. On regular follow-up, antifungal therapy was titrated based on serum azole levels and as tolerated.

4/36 (11%) patients had been treated for proven TB and 2/36 were on empirical treatment until TB diagnosis was excluded when there was clinical and radiological deterioration.

Conclusions Although sarcoidosis has slight female predominance, in this cohort of patients with CPA and sarcoid 63% were males. Many of the patients had significant lung disease with high MRC dyspnoea scores, and obstructive spirometry often with low gas transfers. The management of CPA in the setting of sarcoidosis is complex due to the risk of immunosuppression and interactions with antifungal therapy. Close working between specialties is important in optimising such patients, to ensure the best patient outcomes.

Results Multivariate analysis and modelling of all presenting features was performed. Patients were characterised into four groups—limited no treatment, limited requiring steroids, chronic but stable and chronic progressive steroid dependent. Overall the treatment rate was 50.4% in this cohort. In the chronic cohort 32% required steroid sparing agents. Initial analysis confirmed previously known prognostic indicators including Scadding CXR stage, age >40 and presence of EN OR 0.24 (0.13 – 0.45), p < 0.0001 at diagnosis. Additional predictors of prognosis included IgG levels, positive skin prick testing and vitamin D levels. In the group with elevated levels of IgG (IQR 15.7–19.8) at assessment the treatment rate was 77.1% OR 3.3 (1.5 to 7.6) p value 0.004. In the group with positive SPT, only 17.4% required treatment, OR 0.21 (0.07–0.62), p value 0.005.

Conclusions These results indicate possible new markers of progression in terms of treatment and disease progression in sarcoidosis. Phenotyping sarcoid patients in this way may be valuable in designing future clinical trials in sarcoidosis.

REFERENCE

1 Neville E, Walker AN, Geraint James D. Prognostic factors predicting the outcome of sarcoidosis: an analysis of 818 patients. QJM 1983;4525–533
are needed to determine the long-term outcome in this patient cohort, such as decline in PFTs, quality of life and mortality.

**REFERENCE**


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**Acute exacerbations of COPD and acute NIV**

**P37**

**FRAILTY AND ITS RELATIONSHIP TO MORTALITY IN PATIENTS RECEIVING ACUTE NON-INVASIVE VENTILATION (NIV) FOR RESPIRATORY FAILURE IN A DISTRICT GENERAL HOSPITAL**

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10.1136/thoraxjnl-2015-207770.174

**Introduction**

NIV is a treatment for acute respiratory acidosis in patients admitted with exacerbations of COPD. BTS audits have demonstrated that NIV is frequently used for other conditions, functional dependency is common and in-hospital mortality is high. Tools to prognosticate outcome from acute use of NIV tend to be disease-specific. Targeting the use of NIV to those who are most likely to benefit from it should be a clinical and ethical priority. Frailty relates to patient outcome in clinical settings including elderly patients with COPD and critical care admissions. We hypothesised that patients with higher frailty scores who receive NIV for acute respiratory failure have inferior outcomes, compared to those assessed as being less frail.

**Methods**

Prospective study of patients receiving acute NIV for respiratory failure; over 15 months. The respiratory physiotherapists manage all such patients and collect data into the EPR. An additional item of data was collected – the Clinical Frailty Scale (CFS). All analyses were by episode apart from demographics and mortality which were by individual.

**Results**

89 patients received 110 episodes of acute NIV, median age 79, (range 23–97) years. Diagnoses: COPD (56%), Pneumonia and ‘other’ (30%), cardiogenic pulmonary oedema (4%), obesity-related (4%), chest wall/neuromuscular (7%). At initiation of NIV: median pH 7.26, PaCO2 9.8 kPa, PaO2 8.5 kPa.

Duration of hospital stay, median 16.3 days, in-hospital mortality (28%). CFS median score 6, range (2–8). There was no correlation between CFS and age. CFS was statistically significantly higher in those who died (either during their index admission or during follow-up) than in those who survived – see Figure 1. Patients with a CFS of 7 or 8 had an in-hospital mortality of 40% and a total mortality of 80%. By contrast those with a CFS of less than 7 had an in-hospital mortality of 24% and a total mortality of 46%.

**Conclusions**

Patients receiving acute NIV who are very frail (CFS 7 or 8) are less likely to experience a mortality benefit. These data should inform discussions and decision-making about use of NIV.

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**P38**

**IMPROVED MORTALITY AND OUTCOMES FOR PATIENTS REQUIRING NON-INVASIVE VENTILATION MANAGED IN A DEDICATED HYPER ACUTE MEDICAL UNIT**

1 Buttle, H Chreif, H Woods, S Lohani. Darent Valley Hospital, Dartford, UK

10.1136/thoraxjnl-2015-207770.175

**Introduction**

Non-invasive ventilation (NIV) improves survival and outcomes in hypercapnic (type 2) respiratory failure. Following below average performance in a district hospital in the BTS national NIV audit, NIV delivery moved from acute medical and respiratory wards to a new hyper-acute medical unit (HAMU) providing level 1 nursing care and NIV. The unit is supervised by Respiratory Physicians and a dedicated NIV-
trained nursing team, to improve outcomes for acutely unwell patients. A close working relationship with the Critical care team, and physical proximity to the Intensive care unit ensures rapid joint assessment and transfer of complex patients requiring invasive monitoring or intubation.

**Aims and objectives** To compare NIV success and mortality for patients with acute type 2 respiratory failure requiring NIV, before and after introduction of HAMU.

**Method** Data was collected for all patients in acute type 2 respiratory failure requiring NIV, for nine months before (2011–2012) and after (2012–2013) the HAMU was opened. Baseline characteristics (age, gender, performance and smoking status) were recorded. NIV success and mortality were compared and analysed. Patients requiring intubation on admission were not included.

**Results** Baseline characteristics in both groups were similar, and comparable to national figures. NIV was successful in 56% (28/53) before, improving to 74% (43/58) after (p < 0.05). National success rates from BTS 2013 data were 66.5%. All-cause mortality improved from 42% (22/53), to 24% (14/58) (p < 0.05). National all-cause mortality rate was 34% in 2013. Transfer to Critical care was low in both groups (1/53 pre, and 1/53 post).

**Conclusions** NIV success and mortality rates improved significantly following opening of the HAMU. Following establishment of the HAMU, success rates are also clearly better than national comparators for 2013. NIV delivery in a dedicated unit with highly trained nurses and dedicated respiratory medical input improves outcomes in acute Type 2 Respiratory failure.

**P39**

**Noninvasive PH with Transcutaneous PCO2 Monitoring as an Alternative to Arterial Line Sampling: A New Patient Friendly Approach to Monitoring Acute NIV**

I Adejumo, J Khan, M Sovani. Nottingham University Hospital NHS Trust, Nottingham, UK

Arterial blood gas measurement is a standard way to initiate and monitor Noninvasive ventilation (NIV) in acute hypercapnic respiratory Failure. It is painful for patients and time and resource intensive for staff.

In a pilot study we have demonstrated that transcutaneous CO2 monitoring provides reliable CO2 measurements in patients with Acute Hypercapnic Respiratory Failure (AHRF). Moreover this is less painful and preferred by patients. van Oppen et al., Respir Care. 2014 Nov 18. pii: respcare.03335.

PCO2 time trends were concordant. Mean PCO2 bias was -2.33 mm Hg (95%LOA -9.60 to 5.03) mmHg, r = 0.89 (p < 0.001). Initiation of transcutaneous monitoring was less painful than the arterial equivalent (p = 0.008).

Particularly in patients with AHRF due to COPD exacerbation pH plays an important role in initiating and guiding therapy. We explored whether TcCO2 can be used to predict pH thereby minimising the need for repeated arterial blood gas measurements in this patient group.

Based on Henderson Hasselbalch equation pH = 6.1 + log (HCO3/CO2).

In the pilot study mentioned above Non-invasive pH was determined using ptcCO2 and predicted bicarbonate. Reference bicarbonate was recorded from ABG taken at NIV initiation. TcCO2 was monitored continuously over 12 h using Radiometer TOSCA TCM4. PaCO2 was obtained from arterial blood samples at 0, 4, 8 and 12 h. Mean pH bias was 0.012 (95%LOA -0.070 to 0.094), r = 0.84 (p < 0.001).

We have subsequently reviewed records for 38 patients who received Acute NIV for AHRF. We retrospectively looked at change in pH, bicarbonate and CO2 over 24, 48 and 72 h.

**REFERENCE**

1. van Oppen JD, Daniel PS, Sovani MP. What is the potential role of transcutaneous carbon dioxide in guiding acute noninvasive ventilation? Respir Care. 2015;60:484-91

**Table 1**

<table>
<thead>
<tr>
<th>Phenomenon</th>
<th>in 24 hr</th>
<th>in 48 hr</th>
<th>in 72h</th>
</tr>
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<tbody>
<tr>
<td>Median absolute change</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>absolute increase in pH</td>
<td>0.11</td>
<td>0.12</td>
<td>0.15</td>
</tr>
<tr>
<td>absolute increase in HCO3</td>
<td>0.70</td>
<td>1.60</td>
<td>4.15</td>
</tr>
<tr>
<td>absolute reduction in CO2</td>
<td>1.85</td>
<td>2.21</td>
<td>2.47</td>
</tr>
</tbody>
</table>

Using these data and Henderson Hasselbach equation we can show that in the first 48 h change in pH is almost exclusively explained by change in CO2 (Pearsons Correlation coefficient for change in CO2 and pH = 0.84; p < 0.05).

Therefore in patients with pure Respiratory Acidosis transcutaneous CO2 would provide trend for pH as well as CO2, thereby minimising the need for arterial blood gas measurement and improve patient comfort.

**REFERENCE**

1. van Oppen JD, Daniel PS, Sovani MP. What is the potential role of transcutaneous carbon dioxide in guiding acute noninvasive ventilation? Respir Care. 2015;60:484-91

**P40**

**Should Provision of Acute Inpatient Non-Invasive Ventilation in a District General Hospital Be Exclusively a Respiratory Consultant-Led Service?**

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10.1136/thoraxjnl-2015-207770.177

Poster sessions

Thorax 2015;70(Suppl 3):A1–A254 A95
Introduction Non-invasive ventilation (NIV) may be used for a number of specific clinical indications in the context of acute type 2 respiratory failure. Prior to October 2013, any doctor at or above ST3 level could initiate NIV on a patient if it was deemed necessary. It was noted in a number of cases the use of NIV was inappropriate and not as per the clinical guidelines. In October 2013 a new guideline was implemented within the Trust whereby all decisions to start patients on NIV must be discussed with and approved by the Respiratory Consultant on-call.

This study was conducted to evaluate the impact of the guideline implementation on the outcome for patients treated with NIV.

Methods Retrospective analysis of data from Inpatient NIV database of patients receiving acute NIV over a 2-year period (one year before and one year after the implementation of the new guidelines). Comparison was drawn between the data from two years for all-cause mortality and mortality specifically in those with COPD.

Results A total of 280 cases were identified over the 2-year period (140 male, 140 female). All-cause mortality was found to be lower overall in the post-intervention group (38.9% post-intervention compared to 48.3% pre-intervention). This was further analysed based on whether or not patients had COPD. Overall there was statistically significant higher mortality in non-COPD patients compared to COPD patients both before and after intervention with p values of 0.023 and 0.0096 respectively. There was significantly lower mortality in COPD patients post-intervention compared to pre-intervention (p = 0.0237). There was also lower mortality in non-COPD patients after intervention but this was not statistically significant.

Conclusion Mortality for NIV patients was considerably lower after strict implementation of the local guideline. It shows that Respiratory Consultant-led decisions enable more appropriate use of this treatment and better outcomes for patients. It also highlights the importance of education in NIV initiation for general medical doctors.

REFERENCE

Discussion and conclusion Patients coming for weaning from trachy-ventilation represent a complex group with diverse aetiology and have multiple comorbidities. Their stay in a high dependency area is unpredictable and the LOS varies considerably. While a third of patients remained successfully weaned at one year they carry a high in-hospital and 1 year mortality. LOS is influenced by the complexity of discharge planning often including patients from outside our catchment area. Our RCU like many others are not staffed to look after more than 2 trachy-ventilated patients at any one time which combined with prolonged stay slows down patient flow form ICU. This highlights the need for dedicated units for weaning with a team that is able to look after complex needs in hospital and coordinate complex discharges.

P41 OUTCOMES OF PATIENTS TRANSFERRED TO RESPIRATORY CARE UNIT (RCU) ON TRACHEOTOMY VENTILATION: A 4 YEAR EXPERIENCE
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10.1136/thoraxjnl-2015-207770.178

Background RCU in Leeds admits patients who had tracheostomy in ICU as part of acute admission and are slow to wean from ventilation. We looked at the long-term outcomes of attempted weaning from ventilator support in terms of survival and level of support at discharge. We also looked at length of stay (LOS), underlying diagnosis and comorbidities.

Methods Thirty one patients admitted to RCU as a step-down from ICU between October 2011 and July 2014 were included. Patients were identified using database and data was collected from electronic records and inpatient notes. Patients were excluded if they had tracheostomy inserted on a previous admission.

Results The demographics, length of stay on RCU and primary diagnosis leading to respiratory failure and intubation are described in Table 1. All except one patient had significant other comorbidities including muscular dystrophies, MND, COPD, IHD, etc. The average number of days spent in ICU after tracheostomy prior to step-down was 19+-15. Eight (26%) patients died in hospital. Seventeen patients (55%) were discharged without any ventilatory support after decanulation, 3 required overnight NIV and 3 were discharged with tracheostomy ventilation. At 12 months post-discharge 16 (52%) patients were dead; 11 (35%) were not on any ventilatory support; 3 were continuing to be ventilated via trachostomy, 1 remained on NIV.

P42 FACTORS AFFECTING THE DURATION OF ACUTE NON INVASIVE VENTILATION REQUIRED IN PATIENTS WITH ACUTE HYPERCAPNIC RESPIRATORY FAILURE
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10.1136/thoraxjnl-2015-207770.179

Introduction and objectives Factors predicting the likelihood of failure of NIV, i.e. requirement of intubation or death, have been well documented with low pH shown to be the most important factor. Factors affecting the duration of NIV required in those patients who receive ward base treatment without the need for intubation have not been established. This study aimed to identify factors which influence the duration of NIV required in acute hypercapnic respiratory failure.

Methods A retrospective analysis of 123 consecutive episodes of acute hypercapnic respiratory failure requiring NIV between June 2013 and June 2014 was carried out. Correlation between duration of NIV treatment and a number of variables, namely
admission creatinine, pH, worst arterial carbon dioxide level (CO2) and presence and severity of chronic kidney disease (CKD) was assessed by simple linear regression.

**Results** There was a statistically significant regression coefficient between worst observed CO2 and the duration of NIV (fitted equation: NIV Duration = 4.281 + 14.357 × Worst CO2, p = 0.019). The plotted linear relationship showed an increase in duration of NIV treatment of 14.35 h for every 1 kPa increase in CO2 above 6 kPa. The admission creatinine and severity of CKD did not significantly alter the duration of NIV required. The presence of acute kidney injury was also not significant. The pH value did not significantly alter the duration of NIV treatment.

**Conclusion** This survey shows that the level of CO2 influences the duration of acute NIV required, in that for every 1 kPa rise in CO2, the duration of acute NIV treatment rises by 14.35 h. The other studied variables do not correlate with treatment duration.

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**P43 HOW APPROPRIATELY IS NIV USED AS A CEILING OF TREATMENT?**

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10.1136/thoraxjnl-2015-207770.180

**Background** Treatment Escalation Plans (TEPs) were introduced at the Royal United Hospitals Bath (RUH) in 2013 to help physicians document decisions regarding ceilings of treatment. In implementing a TEP, a patient may be deemed unsuitable for resuscitation and/or Intensive Care Unit (ICU) but remain a potential candidate for ward-based non-invasive ventilation (NIV). However as ward-based NIV is indicated in relatively few respiratory conditions this option should only be available to a small cohort of patients. This study examines how appropriately patients have NIV cited as a ceiling of treatment, using 2002 BTS acute NIV guidelines as a benchmark.

**Method** We collected data from medical, surgical and geriatric wards at the RUH on three separate days between November 2014 and June 2015. In patients with a TEP who were deemed unsuitable for CPR, we recorded a) the ceiling of treatment decision b) reason for admission and c) co-morbidities. We reviewed how many patients with NIV as a ceiling of treatment had an indication in accordance with BTS guidelines.

**Results** 658 patient notes were reviewed. 109/658 patients were deemed not suitable for ICU but had NIV as a ceiling of treatment. 64/109 patients (59%) had an indication in accordance with BTS guidelines, while 45/109 patients (41%) were non-compliant. There was variation in compliance between specialties (General Medicine 60% compliant, Elderly Care 54% compliant and Surgery 33% compliant). The Respiratory ward was the most compliant (100%).

**Conclusions** Whilst NIV can offer significant survival benefits to patients with certain conditions (eg COPD exacerbations, obesity hypoventilation syndrome and chest wall disease) national BTS audits have repeatedly shown that ward-based NIV is often used unsuccessfully outside of these indications. The current study demonstrates that over 40% of patients admitted to our hospital inappropriately have NIV set as their ceiling of treatment, albeit with some variability between wards and specialties. This suggests that further education is required about the potential limitations of NIV, particularly for non-respiratory specialists who often make TEP decisions.

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**P44 CHRONIC OBSTRUCTIVE PULMONARY DISEASE EXACERBATION AND RESPIRATORY ACIDOSIS: PATIENT OUTCOMES AT 6 MONTHS**

1S Jackson, 2TM McKeever, 3G Hesdon, 4G Housley, 5C Reynolds, 6W Kinnear, 3TW Harrison, 7AM Kelly, 8DE Shaw. 1Nottingham University Hospitals NHS Trust, Nottingham, Nottinghamshire; 2Division of Epidemiology, University of Nottingham, Nottingham, UK; 3Respiratory Research Unit, Division of Respiratory Medicine, University of Nottingham, Nottingham, UK; 4East Midlands Academic Health Sciences Network, Nottingham, UK; 5Joseph Epstein Centre for Emergency Medicine Research, Western Health, St Albans, Victoria, Australia

10.1136/thoraxjnl-2015-207770.181

**Introduction** Recognition of hypercapnic respiratory failure is a vital part of the assessment and management of the patient with an acute exacerbation of chronic obstructive pulmonary disease (COPD). Several studies have demonstrated that respiratory acidosis in the context of an acute exacerbation is associated with worse inpatient outcomes. Our study compares the outcomes of patients admitted with an acute exacerbation, between those with respiratory acidosis and those who had a normal pH and PaCO2 on arterial blood gas (ABG) analysis.

**Methods** Patients requiring hospital treatment for an acute exacerbation of COPD had an ABG taken on admission. Patients were subsequently assessed for the following outcomes: inpatient...
mortality, outpatient mortality up to six months after discharge and hospital re-admission rates in the six months post discharge. Chi-squared test was applied to assess the relationship between respiratory acidosis and our outcomes.

**Results** 234 patients had an admission ABG and were subsequently followed up to the point of death or six months post discharge. Patients with a PaCO2 of >6 Kpa were 2.33 times (95% CI 1.11 to 4.96) more likely to die in hospital as compared to those patients with a normal value. Patients with a lower arterial pH (<7.35) were 2.32 times (95% CI 1.07 to 4.96) more likely to die in hospital as compared to those with a pH of >7.35. The increased risk in mortality was only seen for in-hospital mortality and there was no association with death in the 6 months following discharge, hospital re-admission or readmission for a respiratory problem.

**Conclusion** This data supports previous studies that suggest hypercapnia and respiratory acidosis are associated with increased inpatient mortality, therefore further demonstrating the usefulness of pH and PaCO2 as prognostic markers for inpatient outcomes. However our study does suggest that patients with respiratory acidosis on admission, who survive until discharge from hospital, do not have an increased risk of six month mortality or readmission compared to those with a normal admission ABG.

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**P45 PRACTICAL USE OF THE DECAF SCORE: CAN WE IMPROVE OUTCOMES IN ACUTE EXACERBATION OF COPD ADMISSIONS?**

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10.1136/thoraxjnl-2015-207770.182

**Background** Acute exacerbations of COPD (AECOPD) are the second most common cause of emergency hospital admission in England and are associated with an inpatient mortality rate of 4.3%. The Dyspnoea, Eosinopenia, Consolidation, Acidemia and Atrial Fibrillation (DECAF) Score, is an effective prognostic tool that predict mortality in AECOPD admissions. This scoring system is easy to apply during admission and has performed better than existing prognostic tools. We aim to appraise the efficacy of DECAF score in our busy respiratory and medical admissions unit.

**Method** Hospital admissions with AECOPD from Dec 2014 to Mar 2015 are prospectively reviewed and DECAF score applied to each patient. Morbidity and mortality indicators were then correlated with both total DECAF scores and each predictive index.

**Results** 78 admissions were reviewed, 60% were male and the mean age was 72.7 years. Average length of stay was 15.3 days and 12 patients died in hospital. Our results were comparable with previous studies, with inpatient mortality highest in those with DECAF scores of 3–5 (92%) and lowest in those with scores of 0–1 (0%). Higher DECAF scores were also associated with use of non-invasive ventilation (43%). Furthermore, each individual predictive index within the DECAF score was independently related to an increased mortality rate. There was 44% mortality in patients with atrial fibrillation and 30% mortality in patients with dyspnoea score of eMRC 5B. In-hospital mortality rate increased with each DECAF score (Figure 1).

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**P46 FREQUENCY OF COPD EXACERBATIONS IN THE GERMAN DACCORD REGISTRY**

1P Kardos, 2R Buhl, 3C-P Créée, 4C Vogelmeier, 5C Mailaender, 6H Worth. 1Group Practice and Centre for Allergy, Respiratory and Sleep Medicine, Red Cross Mainz Hospital, Frankfurt, Germany; 2Pulmonary Department, Mainz University Hospital, Frankfurt, Germany; 3Department of Sleep and Respiratory Medicine, Evangelical Hospital Goettingen-Weende, Bovenden, Germany; 4Department of Respiratory Medicine, University of Marburg, Marburg, Germany; 5Novartis Pharma GmbH, Nuremberg, Germany; 6Fachzertum Fuerth, Fuerth, Germany

10.1136/thoraxjnl-2015-207770.183

**Introduction** In patients with COPD, exacerbations are among the most relevant safety measures. In this analysis of data from the observational DACCORD study, we report the frequency of exacerbations in a COPD population.

**Methods** To get insights into occurrence and frequency of exacerbations, data from 4,123 patients were obtained from 349 primary and secondary care centres in Germany. To be eligible for entry into DACCORD, all patients had to have a COPD diagnosis (consistent with the German Disease Management Programme definition), and had to have a change in bronchodilator maintenance medication, prior to entry. Data collected included history and treatment of exacerbations 6 months prior to inclusion, and for the duration of follow-up. Exacerbations were defined based on prescription of oral corticosteroids and/or antibiotics or on hospitalisation.

**Results** Mean age of the patients was 65.7 years; 36.9% of patients had severe or very severe airflow limitation (GOLD 2010). In the 6 month period prior to study inclusion, 26.4% of the patients had at least one exacerbation. Fewer patients in the subgroup with CAT30 (16.7% vs 47.9%). Interestingly, 45% of...
all exacerbators received inhaled corticosteroids (ICS) compared to 38.7% of the non-exacerbators. ICS treatment in patients with an exacerbation history in the 6 months prior to study inclusion was more frequent in patients with a duration of disease >1 year compared to those with disease duration.

In the interim-analysis of 4,123 patients that have completed the 1st year of the observational period, 25.5% had at least one exacerbation during follow-up. In the subgroups CAT30, 22.0% and 40.2% of the patients had at least one exacerbation, respectively. A hospital stay was required for 3.5% of the patients who experienced an exacerbation of the total cohort during 12 months follow-up compared to 4.3% in the 6 month prior to the study.

Conclusion At baseline, the prevalence of patients reporting at least one exacerbation in this large real life COPD cohort was low and seems to be unchanged during 1 year follow-up.

**Abstract P47 Table 1**

<table>
<thead>
<tr>
<th>Strategy</th>
<th>PPV (95% CI)</th>
<th>Sensitivity (95% CI)</th>
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<tbody>
<tr>
<td>AECOPD hospitalisation code</td>
<td>26.5% (21.5-32.2%)</td>
<td>1.8% (1.6-2.0%)</td>
</tr>
<tr>
<td>AECOPD code</td>
<td>1.9% (1.8-2.1%)</td>
<td>27.0% (26.2-27.8%)</td>
</tr>
<tr>
<td>Generic hospitalisation code</td>
<td>15.5% (14.5-16.6%)</td>
<td>29.9% (28.5-31.1%)</td>
</tr>
<tr>
<td>AECOPD code &amp; generic hospitalisation code</td>
<td>47.5% (41.3-53.4%)</td>
<td>15.4% (14.8-16.1%)</td>
</tr>
</tbody>
</table>

Conclusions Primary care electronic healthcare databases are not sufficient to accurately identify hospitalisations for AECOPD. Future studies should use HES data linked with primary care records to study AECOPD which result in hospitalisation.

Sponsored by MRC and GSK.

**REFERENCE**


**P48 IDENTIFYING EXACERBATIONS USING SYMPTOMS: READING BETWEEN THE LINES**

Introduction Exacerbations of COPD are associated with significant morbidity and mortality; however there is no clear consensus to the definition of an exacerbation and this remains subjective. Furthermore, it has been challenging to identify an individual biomarker, be it biological or physiological to identify an exacerbation, although identification of exacerbation phenotypes improves this. Most, if not all, patients report increase in symptoms during an exacerbation, measured using the visual analogue scale, performed on a 100 mm line ranging from no symptoms to worst ever symptoms. However, it is unclear if there is a linear relationship with the increase in VAS symptoms and the onset of an exacerbation. In this study, we seek to mathematically model relationships with the VAS and symptoms of dyspnoea, sputum production, sputum purulence and cough in patients with COPD at stable state and during exacerbations.

Methods Patients with COPD with completed assessments of VAS during both stable state and exacerbations were studied. An exacerbation was defined according to healthcare utilisation and increased symptoms. Classifier algorithms (Waikato Environment for Knowledge Analysis software) were run to predict the value of an exacerbation and multiple cross validation was used to assess the predictive accuracy. The Naïve Bayes (based on conditional probability), Multi-layer Perceptron (neural networks), J48 (decision tree) and Random Forest classifier were each run to model relationships.

Results Data from 149 COPD subjects was collected, with 180 instances of an exacerbation recorded. The mean (SD) VAS (mm) for cough, dyspnoea, sputum production and purulence at baseline was 35 (27), 47 (27), 33 (27) and 28 (25) respectively. At exacerbation there was a significant increase (p < 0.001) for all these parameters compared to stable state (mean difference,
95% CI for VAS cough, VAS dyspnoea, sputum production and purulence was 26 mm (20–32); 25 mm (19–30); 25 mm (19–31) and 25 mm (18–31) respectively.

The J48 classifier decision tree had the most predictive accuracy (80%) of identifying an exacerbation (Figure 1), based on VAS and score.

Conclusion Unbiased mathematical modelling of the VAS may be useful in determining a true exacerbation event. The addition of characterisation based upon VAS may enhance the ability to identify exacerbations.

Abstract P48 Figure 1  Decision tree classifier using VAS for identification of an exacerbation of COPD

Abstract P49 Table 1  Univariate associations between patient factors and service use (in-patient admission and GP consultations) during a three month period

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Background There is a high prevalence of anxiety and depression among people with Chronic Obstructive Pulmonary Disease (COPD). Anxiety and depression are frequently associated with increased service use, particularly hospital admission; other demographic and health variables are also known to be significant in this relationship. However, less is known about the nature of these relationships when COPD is advanced. The aim of this study was to identify the relationship between anxiety and depression and service use in patients with advanced COPD, together with the role of key demographic and health variables.

Methods A well-characterised population-based cohort of patients with advanced COPD completed the Hospital Anxiety and Depression Scale (HADS) and reported hospital and community service use and experiences. Patient demographics and health variables were also collected. Univariate analyses of associations between service use and anxiety, depression, health variables and demographics were carried out using data collected over a three month period.

Results 235 patients recruited: mean age 71.6 (SD 10.3); 61% male; mean MMRC dyspnea scale 3.68 (SD 1.040); mean CAT score 23.4 9 (SD7.5). Anxiety and depression scores (HADS) were higher than population norms. Univariate associations (Table 1) were identified between anxiety and contact with a GP (p = 0.021) and depression and in-patient admission (p = 0.017). Other variables crudely associated with GP service use, were the number of exacerbations managed at home (p = 0.006), co-morbidities (p = 0.014) and the CRQ dyspnea, physical and emotional domains (p = 0.014, 0.011 and 0.032 respectively). Crude associations were also found between inpatient admissions and the number of exacerbations at home (p = 0.034) and the CRQ dyspnea domain (p = 0.014).
Conclusion Patients with advanced COPD and co-morbid anxiety were more likely to have had contact with their GP. Those with co-morbid depression were more likely to have had an inpatient admission. Variables associated with these relationships may include health related quality of life, co-morbidities and exacerbations managed at home. On-going work will validate these conclusions by analysing data collected over an 18 month period. Supportive interventions targeting patients with comorbid anxiety and depression may ameliorate the effects of psychological morbidity and reduce admissions.

Introduction and objectives Chronic Obstructive Pulmonary Disease (COPD) is the second most common cause of emergency admission to hospital in the UK. Following an exacerbation there is a high risk of recurrence. Early identification and prompt treatment of exacerbations have been shown to reduce risk of hospital admission.

Methods Patients were enrolled following a hospital admission for an exacerbation of their underlying COPD. They were followed prospectively for 12 weeks and monitored by SleepMinder TM (Resmed) technology recording Nocturnal Respiratory Rate (NRR). Some of the 15 patients completed the study period and recorded >75% of study data. Of these 8 patients had further exacerbations. Median time post discharge for an exacerbation was 56.5 days (IQR 41–67). There were no differences in baseline demographics between those who had an exacerbation and those that did not however there was a trend towards increased BMI, baseline CAT score and length of stay. Of the 8 patients who had an exacerbation a clear signal in NRR could be identified, by visual inspection, in 5 (62.5%) around the time of recorded health care contact. The average time from a signal to health care contact was 6.6 days indicating a window of opportunity for intervention. There was no significant trend between change of CAT score and length of stay. Of the 8 patients who had an exacerbation a clear signal in NRR could be identified, by visual inspection, in 5 (62.5%) around the time of recorded health care contact. The average time from a signal to health care contact was 6.6 days indicating a window of opportunity for intervention. The was no significant trend between change of CAT score and change of NRR indicating patients may be unaware of impending exacerbation.

Conclusions SleepMinder TM technology assessing nocturnal respiratory rate may have use in a real time clinician led connected health setting to trigger early intervention and prevent readmission following discharge.

REFERENCE

P51 ADVANCING QUALITY (AQ) REDUCING VARIATION AND IMPROVING QUALITY AND OUTCOMES FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) IN THE NORTH WEST OF ENGLAND

Introduction and objectives COPD patients in the North West of England die 15 years earlier than expected.

Advancing Quality is a programme of work where a common approach supports quality improvement that focuses on clinical pathways.

Methods A regional clinical expert group agreed the AQ COPD evidence based measures (clinical interventions) in February 2013.

The AQ COPD clinical interventions are:
Within 4 Hours Hospital Arrival: Oxygen - Bronchodilator - Corticosteroid - Antibiotic Therapy.

Following an initial pilot, AQ COPD went live in September 2014. AQ is a proven approach to improve quality, providing standardisation and transparency for providers and commissioners.

Results Trusts aim to deliver all the interventions that the patient is eligible for, this is known as the Appropriate Care score (ACS). More patients are receiving “perfect care” with AQ, (see Figure 1).

Abstract P51 Figure 1 Advancing Quality (AQ) reducing variation and improving quality and outcomes for patients with COPD in the North West of England

Trusts participating in AQ had a mean LOS of 4.7 days compared to 5.7 days for non-participating trusts and average bed days for patients re-admitted in participating trust was 5.5 days compared to 11.8 days in non-participating trusts. Trusts participating saw their readmission rate fall to 20.1% over the period (a reduction of 9%).

Conclusion A regional standardised approach, focused on a small but significant set of clinical interventions, can have a significant impact on improving patient care and outcomes.
In 2015/16 North West CCGs have commissioned AQ COPD across 15 of the 21 Acute Trusts. An AQ incentive framework was also developed for providers and commissioners that supports “doing the right thing” collaborative events ensure that ongoing sharing of best practise happens and we have future plans to expand into Primary and Community Care.

**Occupational lung disease**

**P52 Epidemiology of occupational extrinsic allergic alveolitis reported to SWORD 1996–2014**

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10.1136/thoraxjnl-2015-207770.189

Introduction Worldwide, the true epidemiology of occupational EAA is poorly understood. Data from national reporting schemes offers one method of examining the changing demographics of this disease, and comparing the most commonly reported causes.

Methods Data was obtained for all cases of occupational EAA reported to the UK Surveillance of Work-related and Occupational Respiratory Disease (SWORD) scheme since 1996. The likely causative agents for each reported case were grouped into categories, and data compared for the earliest and latest available 5-year time periods (1996–2000 and 2010–2014). An estimate of the annual incidence of occupational EAA was calculated from the estimated number of cases in each time period divided by the average UK working population at that time (data from the Office for National Statistics).

Results Data for the early and late 5-year time periods are presented in Table 1. The estimated incidence of occupational EAA was similar for the two time periods, but there has been a notable change in reported causation. Occupational EAA due to metalworking fluid, coolant or oil mist exposure has become the most commonly reported cause, responsible for almost a third of all cases. Over the same time period, EAA in mushroom workers has fallen from the joint commonest cause to no reported cases at all.

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</tbody>
</table>

Discussion The estimated annual incidence of occupational EAA in the UK has remained relatively stable at approximately 1–2 cases per million workers. Although this is likely to represent an underestimate, it is similar to the estimated incidence from reporting schemes in Australia, Catalonia, and the Czech Republic, but an order of magnitude lower than that reported in Finland. Over the last 20 years, EAA due to metalworking fluid exposure has emerged as the most commonly reported cause in the UK. This change has not been noted in other published reporting schemes, where EAA due to agricultural exposures remains the most common aetiology.

**P53 Determination of specific IgE antibodies to mouse proteins in laboratory animal workers**

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Introduction Laboratory animal workers are at increased risk of developing specific IgE antibodies to laboratory animal proteins. The major allergen for mouse is Mus m 1 which is predominantly found in the urine. Specific IgE to mouse is determined using either a commercial skin prick test solution of mouse epithelium or ImmunoCAP for either mouse urine or epithelium. Specific IgE to Mus m 1 is used for routine diagnostic testing.

The aim of this study was to compare sensitisation using both ImmunoCAP and skin prick test as well as compare mouse urine and epithelium as allergens. At present there is no gold standard for sensitisation to mouse allergens.

Methods Laboratory workers exposed to mice were recruited to the SPIRAL (Safe Practice in Reduction of Allergy in Laboratories) study. Sensitisation was determined by the presence of specific IgE to Mus m 1 and mouse epithelium using ImmunoCAP (Phadia) (positive result ≥0.35 kU/l) and by skin prick test to mouse epithelium (positive result is a saline adjusted mean wheal diameter of ≥3 mm).

Results Of the participants (321), 11 (3%) were positive by skin prick test, 34(11%) with specific IgE to Mus m 1 and 35 (11%) with a positive specific IgE to mouse epithelium.

There were 25/321(8%) participants with a discordant result between SPT and specific IgE to Mus m 1 (Table 1). There were 14 participants with a discordant result between specific IgE to Mus m 1 and mouse epithelium (Table 1).

<table>
<thead>
<tr>
<th>Mus m 1 specific IgE positive</th>
<th>Mus m 1 specific IgE negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPT positive</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>SPT negative</td>
<td>24</td>
<td>286</td>
</tr>
<tr>
<td>Total</td>
<td>34</td>
<td>289</td>
</tr>
<tr>
<td>Mouse epithelium positive</td>
<td>26</td>
<td>9</td>
</tr>
<tr>
<td>Mouse epithelium negative</td>
<td>5</td>
<td>286</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>295</td>
</tr>
</tbody>
</table>

Abstract P52 Table 1 Demographics of occupational EAA reported to SWORD between 1996–2000 and 2010–2014

Abstract P53 Table 1 Specific IgE to Mus m 1 and mouse epithelium in laboratory animal workers
Discussion Laboratory animal workers may have specific IgE antibodies to either Mus m 1 or mouse epithelium. Diagnostic tests for mouse sensitisation may require testing to both Mus m 1 and mouse epithelium to ensure we do not miss any sensitised cases. Skin prick tests appear higher rates of false negative than anticipated and are therefore less reliable in clinical practice if used alone.

**P54 RESPIRATORY SYMPTOMS, LUNG FUNCTION AND QUALITY OF LIFE IN BRITISH FOUNDRY WORKERS**

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Introduction Foundry work is associated with exposure to potentially harmful substances that may cause occupational asthma (OA).

Aim To record respiratory symptoms, lung function and health-related quality of life (HRQoL) in a group of exposed British foundry workers, and investigate their associations and causes.

Method A workplace-based study was conducted, where participants were delivered a researcher-administered questionnaire in order to record individual job exposures, respiratory and general health, and HRQoL (the EQ-5D). Spirometry was performed using a Ndd Easy on-PC Spirometer according to ATS/ERS guidelines. Fractional exhaled nitric oxide (FENO) was measured using a NOBreath device to ATS standards.

Results 351 (65%) of a possible 539 workers participated. 350 (99.7%) were men, with a mean age of 42.4 (SD 12.5) years. The average length of employment in the foundry industry was 14.8 (SD 12.7) years. Twenty-one (6%) workers self-reported a diagnosis of current asthma, and six (1.7%) self-reported COPD.

139 (40%) participants had at least one respiratory symptom, of which wheeze was the most prevalent (n = 114, 33%). One-in-five participants reported work-related respiratory symptoms (WRRS) (n = 69, 20%), of which work-related cough was the most prevalent (n = 45, 13%; Table 1). Significantly more workers reporting WRRS were ever smokers (chi squared = 5.1, p = 0.02).

### Abstract P54 Table 1 Demographic data for British foundry workers with and without work-related respiratory symptoms (WRRS)

<table>
<thead>
<tr>
<th>Variable</th>
<th>WRRS (n = 69)</th>
<th>No WRRS (n = 282)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (SD)</td>
<td>41.1 (12.3)</td>
<td>42.7 (12.5)</td>
</tr>
<tr>
<td>Length of employment, years (SD)</td>
<td>15.4 (12.3)</td>
<td>14.7 (12.8)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>25 (36)</td>
<td>71 (25)</td>
</tr>
<tr>
<td>Ever smoker, n (%)</td>
<td>48 (70)</td>
<td>154 (55)*</td>
</tr>
<tr>
<td>Self-reported current asthma, n (%)</td>
<td>8 (12)</td>
<td>13 (5)</td>
</tr>
<tr>
<td>FEV1/FVC &lt;0.75, n (%)</td>
<td>3 (4)</td>
<td>31 (11)</td>
</tr>
<tr>
<td>Mean% predicted FEV1 (SD)</td>
<td>98.3 (10.5)</td>
<td>98.4 (14.1)</td>
</tr>
<tr>
<td>Mean% predicted FVC (SD)</td>
<td>103.1 (9.8)</td>
<td>103.6 (12.8)</td>
</tr>
<tr>
<td>Mean% predicted PEF (SD)</td>
<td>106.2 (17.1)</td>
<td>108.3 (18.2)</td>
</tr>
<tr>
<td>Mean FENO, ppb (SD)</td>
<td>31.1 (24.2)</td>
<td>29.9 (29.0)</td>
</tr>
<tr>
<td>Mean EQ-5D VAS (SD)</td>
<td>76.6 (15.8)</td>
<td>83.5 (11.0)**</td>
</tr>
</tbody>
</table>

*p = < 0.05, **p = 0.001.

155 (44%) workers had a FENO above 25 ppb, the suggested ATS cut off for a low probability of eosinophilic airway inflammation. No difference in FENO was found between those with and without WRRS (chi squared for FENO above or below 25 ppb = 1.50, p = 0.22).

However, WRRS were associated with significantly lower mean scores on the EQ-5D visual analogue scale (VAS; 77 vs 84, p = 0.001, 95% CI 2.89 – 11.01). In contrast, no difference in VAS was observed between those with and without an obstructive lung defect (FEV1/FVC <0.7), (mean 83 vs 82, p = 0.63, 95% CI -5.48 – 3.33).

Conclusion Work-related respiratory symptoms among foundry workers were common and associated with impaired HRQoL. More work is required to better understand the cause of such symptoms in foundry workers, and their relationship with workplace exposures.

**P55 THE OCCUPATIONS ASSOCIATED WITH COPD RISK IN THE LARGE POPULATION-BASED UK BIOBANK COHORT STUDY**

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Introduction and objectives COPD is one of the leading causes of morbidity and mortality worldwide. Exposure to occupational hazards is an important and preventable risk factor. However, the contribution of each occupation to COPD risk in a general population is uncertain. Our aim was to investigate the association of COPD with occupation in a large UK population-based study.

Methods Between 2006 and 2010 the UK Biobank cohort recruited 502,649 subjects aged 40–69 years. COPD cases were defined by spirometry-based FEV1/FVC <LLN according to ATS/ERS guidelines. Individual current occupation was coded using the Standard Occupation Classification (SOC) 2000. Prevalence ratios (PRs) and 95% confidence intervals (CIs) of COPD for exposure to each SOC-coded job were estimated using a robust Poisson model adjusted for sex, age, study centre and lifetime tobacco smoking.

Results Of the 353 SOC-coded jobs reported by 228,614 current working participants several occupations showed a significantly increased COPD risk. The occupations at highest COPD risk were Seafarers (PR = 2.64;95% CI:1.59–4.38), Coal mine operatives (PR = 2.30;95% CI:1.00–5.31), Cleaners (Industrial: PR = 1.96;95% CI:1.16–3.31 and Domestic: PR = 1.43;95% CI:1.28–1.59), Roofers/tilers (PR = 1.86;95% CI:1.29–2.67), Packers/bottlers/canners/fillers (PR = 1.60;95% CI:1.15–2.22), Food, drink and tobacco process operatives (PR = 1.46;95% CI:1.11–1.93), Floorers and wall tillers (PR = 1.41;95% CI:1.00–2.00), Postal workers/couriers (PR = 1.35; 95% CI:1.15–1.59), Labours in building and woodworking trades (PR = 1.32; 95% CI:1.04–1.68), School mid-day assistants (PR = 1.32; 95% CI:1.01–1.74), and Kitchen/catering assistants (PR = 1.30; 95% CI:1.10–1.53). Associations were similar in analyses restricted to never smokers and to subjects never reporting a doctor’s diagnosis of asthma.

Conclusions Selected occupations are associated with increased COPD risk in a large cross-sectional population-based UK study. Further analyses to investigate the underlying occupational hazards are planned. Occupational health surveillance among these occupations should be strengthened.
CROSS-SECTIONAL STUDY OF PREVALENCE OF SENSITISATION TO MOUSE ALLERGENS IN LABORATORY ANIMAL WORKERS: THE SPIRAL (SAFE PRACTICE IN REDUCING ALLERGY IN LABORATORIES) STUDY

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Introduction
At least 12000 people work with laboratory animals in the UK. Approximately 15% of exposed employees develop specific IgE sensitisation and 10% clinical symptoms of occupational rhinitis and asthma due to laboratory animal allergy (LAA). Individually ventilated cages (IVCs) are increasingly replacing conventional open cages (primarily for mice welfare); whilst this can be associated with lower levels of ambient aeroallergen levels no corresponding reduction in incidence of LAA is apparent. The SPIRAL (Safe Practice In Reducing Allergy in Laboratories) study is a large multi-centred study designed to increase understanding of the complex association between workplace exposure to mouse allergens and development of sensitisation, and to evaluate the risk of working with mice today.

Methods
A cross-sectional study of animal workers at UK medical research institutions is underway. Primary outcome is a comparison of prevalence of sensitisation to mouse proteins in those working in IVC only and those working in mixed facilities (open cages +/- IVCs). Participants complete a detailed online questionnaire including questions about work tasks and practices. Skin-prick tests to common aeroallergens and various animal proteins are performed and blood samples analysed for serum specific IgE to Mus m 1 (mouse urinary protein) and mouse epithelium. Aeroallergen sampling for particulate matter and Mus m 1 is undertaken concurrently to provide objective exposure measurements (results presented elsewhere).

Results
507 participants have been recruited to date. Analyses were restricted to those with less than 5 years exposure to mice

<table>
<thead>
<tr>
<th>Variable</th>
<th>Not sensitised n (%)</th>
<th>Sensitised n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years (median (range))</td>
<td>26.2 (11.8, 61.2)</td>
<td>24.9 (21.8, 27.4)</td>
</tr>
<tr>
<td>Male</td>
<td>79 (31.1)</td>
<td>4 (40.0)</td>
</tr>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>154/201 (76.6)</td>
<td>6 (60.0)</td>
</tr>
<tr>
<td>Ex</td>
<td>28/201 (13.9)</td>
<td>0</td>
</tr>
<tr>
<td>Current</td>
<td>19/201 (9.5)</td>
<td>4 (40.0)</td>
</tr>
<tr>
<td>Atopic*</td>
<td>56/198 (28.3)</td>
<td>7/10 (70.0)</td>
</tr>
<tr>
<td>Older siblings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>112/201 (55.7)</td>
<td>3 (30.0)</td>
</tr>
<tr>
<td>1</td>
<td>72/201 (35.8)</td>
<td>4 (40.0)</td>
</tr>
<tr>
<td>2</td>
<td>11/201 (5.5)</td>
<td>1 (10.0)</td>
</tr>
<tr>
<td>3+</td>
<td>6/201 (3.0)</td>
<td>2 (20.0)</td>
</tr>
<tr>
<td>Years worked with mice</td>
<td>2.12 (0, 4.98)</td>
<td>2.57 (1.10, 4.15)</td>
</tr>
<tr>
<td>No previous occupational exposure to mice</td>
<td>142/201 (70.7)</td>
<td>8 (80.0)</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>24/24 (100)</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>82/90 (91.1)</td>
<td>8/90 (8.9)</td>
</tr>
<tr>
<td>C</td>
<td>32/32 (100)</td>
<td>0</td>
</tr>
<tr>
<td>D</td>
<td>26/27 (96.3)</td>
<td>1/27 (3.7)</td>
</tr>
<tr>
<td>E</td>
<td>27/28 (96.4)</td>
<td>1/28 (3.6)</td>
</tr>
<tr>
<td>F</td>
<td>11/11 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Job title</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Technician</td>
<td>57/59 (96.6)</td>
<td>2/59 (3.4)</td>
</tr>
<tr>
<td>Scientist</td>
<td>132/140 (94.3)</td>
<td>8/140 (5.7)</td>
</tr>
<tr>
<td>Other</td>
<td>13/13 (100)</td>
<td>0</td>
</tr>
<tr>
<td>Cage type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVC only</td>
<td>109/199 (54.8)</td>
<td>4 (40.0)</td>
</tr>
<tr>
<td>Open/mixed</td>
<td>90/199 (45.2)</td>
<td>6 (60.0)</td>
</tr>
<tr>
<td>Work related symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>25/201 (12.4)</td>
<td>5 (50.0)</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>41/201 (20.4)</td>
<td>7 (70.0)</td>
</tr>
<tr>
<td>Asthma</td>
<td>6/201 (3.0)</td>
<td>3 (30.0)</td>
</tr>
</tbody>
</table>

* saline-adjusted wheal of ≥3mm to grass, house dust mite or cat on skin prick testing
(n = 212); of these, 10 (5%) participants were sensitised to mouse proteins. Prevalence of sensitisation was 3.5% in IVC only facilities and 6.3% in open cage/mixed facilities. Although numbers are small, a history of atopy to common aeroallergens and the site at which people worked appears to be associated with risk of sensitisation. Reporting of symptoms of laboratory animal allergy was as anticipated. (Table 1).

**Methods**

We studied the antibody and cellular immune response in fanciers attending pigeon shows. 77 completed a questionnaire of symptoms, performed spirometry and gave a blood sample, 32 of whom had symptoms of acute PFL. Peripheral Blood Mononuclear Cells and serum were extracted from the blood, and T cell and antibody responses were measured against pigeon serum and mucin using in-house well-characterised assays (ELISA and ELIspot, respectively), as well as flow cytometry and multiplex cytokine assays. These provided quantitative outputs of specific antibody titre and reactive T cells per million PBMC, validated using positive controls.

**Results**

Correlations between immune responses and disease symptoms were analysed.

**Conclusions**

Pigeon fanciers have high levels of antigen exposure and demonstrate intense antibody and cellular immune responses, but these correlate minimally with clinical symptoms. The pathogenesis of PFL is complex and may involve an inflammatory cell-antibody axis.
Conclusions In summary, our study demonstrates that laboratory animal workers carry out animal allergens on their skin when they leave the animal facility at the end of the day. The implications of these findings will be considered in the development of safe working practices in prevention of laboratory animal allergy within the context of the SPIRAL study.

Background Laboratory animal workers face the risk of developing an IgE-associated respiratory allergy to airborne proteins, such as Mus m 1 (mouse urinary protein). Approximately 15% of exposed employees will develop IgE sensitisation and 10% clinically apparent disease. We have recently embarked on a large study called SPIRAL (Safe Practice In Reduction of Allergy in Laboratories) to gain a greater understanding of laboratory animal allergy (LAA) and to determine whether we can devise a code of safe practice to prevent, as far as possible, the future occurrence of LAA.

Aim To determine personal exposure to Mus m 1 within animal facilities where mice are housed exclusively in open cages and exclusively in individually ventilated cages (IVC).

Methods Selected employees wore Casella Apex pumps (2 L/min) during their full shifts to collect inhalable particulate onto fluoropore membrane (1 μm), 25 mm filters using IOM sampling heads.82 filters from an IVC facility and 56 filters from an open cage facility were analysed for Mus m 1 using a commercial sandwich enzyme linked immunoassay (Indoor Biotechnology).

Results The range of Mus m 1 levels within the IVC facility was 0.00–66.33 ng/m³ and in the open cage facility was 3.89–305.59 ng/m³. 11 (13%) of samples from the IVC facility and 50 (89%) of samples from the open cage facility had a Mus m 1 exposure level greater than 5 ng/m³. Additionally, there was substantial variation when task specific sampling was carried out over short periods of time compared with full shift sampling. Further analyses will allow us to identify which tasks were associated with highest levels of exposures.

Conclusions The majority of samples from the open cage facility were above 5 ng/m³, a figure previously suggested to limit or reduce incidence of LAA. Although use of IVCs has been shown to reduce exposure to Mus m 1, we found several samples above 5 ng/m³. Exposure to high allergen levels will be influenced by cage type, variation in individual working practices and carrying out of specific “high-risk” tasks; some of these factors may be modifiable and these results may be used to change practice.

Introduction Statutory periodic health surveillance (HS) of workers can identify early cases of occupational asthma. Information about its uptake in the UK, and its content when carried out, are lacking.

Methods A telephone survey of employers, and their occupational health professionals, was carried out in three sectors with the potential for producing exposures, which may result in the development of occupational asthma (bakeries, wood working, motor vehicle repair).

Results 457 organisations participated (31% response rate); 77% employed less than 10 people, 17% between 10 and 50 and 6% more than 50. Risk assessments were common (67%) and 14% carried out any form of occupational asthma HS, rising to 19% if only organisations reporting asthma hazards and risks were considered. HS was carried out by both in-house (31%) and external providers (69%). Organisational policies were often used to define surveillance approaches (80%), but shared with the occupational health provider only in one third of cases.

Conclusions This study has provided new insights into the real world of health surveillance for occupational asthma in the UK. We consider that future work could and should define more practical, evidence based and simple approaches to HS, by working with the end users to develop interventions that meet their needs. This will ensure maximal uptake of high quality HS approaches and consistency.

Introduction Exposure at work to inhaled respirable crystalline silica (RCS) has previously been linked with silicosis, tuberculosis, lung cancer and COPD. Whilst the risk of developing silicosis is largely a function of cumulative lifetime RCS exposures, current workplace exposures contribute to this risk.

Methods A cross sectional GB based workplace study of brick manufacturers was carried out, in order to identify a subsequent longitudinal cohort. Participating worksites were using silica to make bricks for various uses. Consenting workers were asked to complete an interviewer led questionnaire, undergo lung function testing and complete a full occupational history including details of lifetime exposure to RCS. Consenting workers had a PA Chest Radiograph using a mobile facility, and levels of RCS exposure in the personal breathing zone were taken.

Results 189 workers took part, with a mean age of 45.9 years and 22 years median (range 0.08–47) years worked overall in industry. Three had radiological evidence of silicosis (ILO standards used; 2 definite and one probable case). Respiratory symptoms were common; for example 14.3% reported cough, 21.2% wheeze in the last 12 months, 14.3% reported ever having asthma. 13.2% reported at least one work related respiratory
symptom. Mean lung function values were as follows; mean (SD) percentage predicted FEV₁ 98.1 (15.2) and FVC 102.4 (13.9).

Fourteen workers had measured airways obstruction (as defined by an FEV₁/FVC <0.7); in this cross sectional analysis its presence did not significantly relate to current smoking status or lifetime duration of RCS exposure, although was significantly associated with an increased time worked in the current work area. Airways obstruction was also associated with the reporting of a diagnosis of (ever having) asthma and wheeze in the last 12 months.

Conclusions This cross sectional study of silica exposed brick workers has identified a cohort for longer term follow up. Future work will allow the development of dose response relationships, corrected for other relevant factors, between cumulative RCS exposure and FEV₁ decline and will assist in the development of workplace interventions to reduce the health risks associated with RCS exposure in this group of workers.

**Abstract P62 Figure 1** Key to exposures: 1 = gold mining, 2 = foundry work, 3 = talc processing, 4 = mixed exposures, 5 = silicon carbide processing, 6 = potash mining, 7 = carbon black mining

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**P62 A COMPARISON OF THE RELATIVE EFFECTS OF EXPOSURE ON FEV₁ AND FVC IN OCCUPATIONAL COPD**

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**Introduction and objectives** A wide range of occupational exposures to dusts and fumes are known to cause COPD. Little is known about the underlying pathophysiology as few studies have measured gas transfer or included CT scans. It is not known whether the relative degree of small airway disease and emphysema is similar to that seen with smoking or varies by causative agents. The modifying effect on lung function of pneumoconiosis, that is a feature of several accepted or possible causative agents of occupational COPD, is also uncertain.

**Methods** We have reviewed papers investigating exposure-response relationships for FEV₁ and FVC to a range of occupational dusts and fumes. We examined the ratio of the slopes of the regression equations relating exposure to FEV₁ and FVC for the occupational exposures and for cigarette smoking.

**Results** We identified 15 papers dealing with exposure to coal mine dust (5 papers), silica-containing dusts (8 papers) and other dusts (2 papers). The relative effects of exposure on FEV₁ and FVC are shown in Figure 1, together with the relative effects of smoking on FEV₁ and FVC obtained from the same papers. It should be noted that as FEV₁ is lower than FVC, an equal reduction in FEV₁ and FVC with exposure (ratio = 1) still leads to airflow obstruction. Cigarette smoking had an effect on FEV₁ that was approximately twice the effect on FVC. Coal mine dust was associated with a similar ratio of effect though with greater variability. Studies on silica-containing dusts had a more equal effect on FEV₁ and FVC. That was also the case for the two studies of non-silica containing dusts (carbon black and potash mining).

**Conclusions** COPD associated with exposure to silica-containing dusts appears to be associated with a more restrictive abnormality than COPD associated with cigarette smoking and coal dust, possibly because of a modifying effect of associated lung fibrosis.
timepoint analysis was more affected. With only 2 readings, sensitivity was reduced for all scores. Specificity was unaffected by data reduction (Table 1).

Abstract P63 Table 1 Sensitivity and (specificity) at each randomisation and data reduction

<table>
<thead>
<tr>
<th>Oasys score</th>
<th>ABC score</th>
<th>Timepoint analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-Randomisation</td>
<td>75 (84)</td>
<td>69 (93)</td>
</tr>
<tr>
<td>Randomisation 1</td>
<td>67 (73)</td>
<td>61 (89)</td>
</tr>
<tr>
<td>Randomisation 2</td>
<td>72 (68)</td>
<td>55 (86)</td>
</tr>
<tr>
<td>Randomisation 3</td>
<td>86 (86)</td>
<td>69 (93)</td>
</tr>
</tbody>
</table>

Conclusion Specificity was not reduced by adding random errors to the peak flow measurements nor through data reduction. Sensitivity was reduced, relatively more for the timepoint analysis, but in 2/3 randomisations it was preserved for the Oasys and ABC systems. Oasys analysis is robust despite decreasing data quality and quantity.
Asthma phenotyping and biomarkers

**P66** CAN WE IDENTIFY ASTHMA AND COPD OVERLAP SYNDROME (ACOS) FROM A SEVERE DIFFICULT ASTHMA CLINIC PATIENT COHORT?

R Singal. Barts Health NHS Trust, London, UK

Introduction Asthma-COPD Overlap Syndrome (ACOS) is characterised by persistent airflow limitation with several features usually associated with asthma and several features usually associated with COPD, which can be difficult to define. In response to the document produced by GINA and GOLD (2014) there is a need for further studies to identify the proportion of ACOS patients within treatment centres. Patients with features of ACOS are reported between 15–55% and have outcomes that are far worse than COPD or asthma alone.1

Objectives To locally identify the proportion and current management of ACOS patients within a tertiary treatment centre.

Method The study was carried out retrospectively reviewing patient data over a 6 month period from electronically documented clinic letters, discharge summaries, pathology and lung function results. Patients included were identified from a severe difficult asthma clinic list at a large tertiary centre in London.

Results 101 patients were reviewed with a mean age of 49.1 years. Table 1 identifies patients with chronic airflow limitation with a cohort of 6.9% (n = 7) diagnosed as asthma and COPD; showing fixed airway obstruction (n = 6), mean age 54.6 years. There are no patients receiving LABA mono therapy, however 7.9% patients have no ICS in their treatment plan.

Conclusion This review of severe difficult asthma clinic patients highlights the challenge in identifying ACOS patients. Spirometry results contributed are of limited value in diagnosis between asthma, COPD and ACOS; reversibility testing would be more indicative for future work. Interestingly we have a relatively young patient population on high BDP doses and some potentially at risk due to no ICS treatment. Further prospective studies in the form of patient questionnaires is required in order to identify detailed clinical history to aid earlier diagnosis and management.

REFERENCE

1 Diagnosis of Diseases of Chronic Airflow Limitation: Asthma, COPD, and Asthma – COPD Overlap Syndrome (ACOS). GINA and GOLD, 2014

**P67** BRONCHIECTASIS IN SEVERE UNCONTROLLED ASTHMA

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Introduction and objectives Bronchiectasis can contribute to severe and difficult to control asthma. It is important to recognise bronchiectasis in asthmatics and treat them accordingly. In order to estimate the presence of bronchiectasis in severe asthma, and the relation with the clinical and functional parameters we studied 40 patients with severe uncontrolled asthma, in a stable condition.

Methods The symptoms, the duration of asthma diagnosis, the number of exacerbations/year, cycles of corticosteroids and antibiotic treatment/year, spirometry, and bronchial colonisation were estimated. High resolution computed tomography (HRCT) was performed to evaluate the presence and extent of bronchiectasis. HRCT were studied by an expert thoracic radiologist, according to Smith scale for bronchiectasis (score 0–24), taking a score≥3 as radiologically significant.

Results Forty patients were studied, 28 women, mean age (±SD) 57.9 years (±12.4), 32 non smokers. Mean ACT score was 14.2 (±4.9).

The main symptoms were: cough (92%), wheezing (95%), dyspnea (92%), sputum production (72%) of which mucoid (52%), mucopurulent and purulent (48%). Mean duration of asthma diagnosis was 16.5 (±11.5) years, exacerbations: 4.4 (±2.7)/year, corticosteroid per os cycles/year: 4.4 (±3.1), antibiotic cycles/year: 2.8 (±2.2).

In 27 patients (67.5%) bronchiectasis was diagnosed: Smith score: 5.2 (±4.2).

The mean FEV1 was 72.6% (±21.1) of predicted, FVC 79.1% (±19.4), FEV1/FVC ratio 67.3 (±9.7). Nine patients (22.5%) were colonised with pathogens, 6 of whom with Pseudomonas Aeruginosa. Patients with sputum production had a higher Smith score compared to those without expectoration (6.3 ± 4.2 vs 2.3 ± 2.2 respectively Z = 2.8, p = 0.005). In addition, patients with pathogens in sputum cultures had a higher Smith score compared to those with normal flora (10 ± 4.2 vs 3.8 ± 3 respectively, Z = 3.5, p < 0.0001) (Figure 1).
Introduction and objectives

Asymptomatic chronic bronchitis is common in patients with severe uncontrolled asthma. Sputum production and pathogen isolation in sputum culture may indicate the presence of this comorbidity and the need of antibiotics as an additional treatment.

Methods

We reviewed Leicester difficult asthma clinic letters to evaluate the heterogeneity within this population. We sought to: a) compare asthmatics with and without recurrent infections using a case-control approach and b) phenotype asthmatics with recurrent infections. A 1:1 case-control ratio was used. 71 cases and 71 controls were identified. The antibiotic use, physiology, CT imaging, and pathogen isolation in sputum cultures and in patients with normal flora were evaluated. Model based cluster analysis was performed to phenotype the cases with no evidence of infection in each subphenotype, the host microbiome and response to antimicrobials are required.

Results

Three subphenotypes of asthma with recurrent infections have been identified. Further immunopathological studies to evaluate the mechanism of infection in each subphenotype, the host microbiome and response to antimicrobials are required.

Conclusion

Three subphenotypes of asthma with recurrent infections have been identified. Further immunopathological studies to evaluate the mechanism of infection in each subphenotype, the host microbiome and response to antimicrobials are required.

Abstract P67 Figure 1  Smith score in patients with pathogens in sputum cultures and in patients with normal flora

No correlation was found between the extent of bronchiectasis and the lung function parameters. The severity of bronchiectasis (Smith score) was correlated to the number of antibiotic cycles/year ($p = 0.002$, $r = 0.48$). In addition, a lower ACT score was related with a higher asthma exacerbation rate ($r = 0.52$, $p = 0.001$).

Conclusion

The evidence of bronchiectasis on HRCT is common in patients with severe uncontrolled asthma. Sputum production and pathogen isolation in sputum culture may indicate the presence of this comorbidity and the need of antibiotics as an additional treatment.
strongly with sputum and blood eosinophil counts, and are most useful when a moving average is taken over approximately 9 days. Further studies are required to determine if daily FeNO measurements may have a role in predicting loss of asthma control or exacerbations.

**P70** BLOOD EOSINOPHIL COUNTS IN NORMAL CONTROLS WITH NO HISTORY OF ALLERGIC DISEASE


Background The beneficial effect of corticosteroids and anti-interleukin (IL)-5 on exacerbations of airway disease becomes apparent at blood eosinophil counts above 0.15 × 10^9/L, well within the normal range. One potential explanation is that the upper limit of the normal range is artificially high because studies have included patients with allergic disease and eosinophilic inflammation. We have assessed the normal range for blood eosinophil counts in volunteers with no self-reported history of allergic disease and compared this with the findings from a more traditional control population.

Methods We recruited 78 volunteers (15 male) with a mean age of 38.8 years. Volunteers with a self-reported history of asthma, allergic rhinitis and/or eczema were excluded. The differential cell count was carried out using a symex XN analyser and serum IgE measured using automated enzyme immunoassay by Phadia ImmunoCAP equipment. Result were compared with an unscreened population (n = 120) used to calculate our local normal ranges.

Results One outlier value of 0.79 × 10^9/L, (>5 SD above the mean) was excluded from further analysis. In the remainder the mean blood eosinophil count was 0.15 × 10^9/L with an upper limit of normal range of 0.27 × 10^9/L. Volunteers with no self-reported history of allergic disease but an IgE >120 iu/L and/or positive specific IgE to house dust mites or grass were not statistically different. The mean blood eosinophil count in the laboratory population was 0.19 × 10^9/L (p = 0.018 vs our population) and the upper limit of normal range 0.42 × 10^9/L.

Conclusions The upper limit of the normal range for blood eosinophil count is lower in a population who have no clinical history of allergic disease.

**P71** THE RELATIONSHIP BETWEEN THE LEICESTER COUGH QUESTIONNAIRE, EOSINOPHILIC AIRWAY INFLAMMATION AND ASThma PATIENT RELATEd OUTCOME MEASURES IN SEVERE ASThma

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Background Severe asthma is characterised by a variety of symptoms which include chronic cough, although the mechanisms responsible are poorly understood. Modulation of cough reflex sensitivity by eosinophilic airway inflammation is considered likely but has not been well studied. Likewise the impact of chronic cough on patients health status is not well known as existing asthma patient related outcome instruments such as the Juniper Asthma Control Score (ACQ-6), Asthma Quality of Life Questionnaire (AQLQ) were not primarily designed to capture cough and its related morbidity in asthma. We sought to evaluate (i) the Leicester Cough Questionnaire (LCQ) in a severe asthma population, (ii) the relationship between the Leicester Cough Questionnaire (LCQ) and the ACQ-6, AQLQ and (iii) airway inflammation in sputum in severe asthma patients.

Methods 312 patients [mean (SD) age of 60.4(16.2) years, median (IQR) GINA treatment score 5(4–5) and median (IQR) sputum eosinophil percentage of 3.0(0.5–16.6)] attending the Leicester difficult asthma service were evaluated with the LCQ, ACQ-6 and AQLQ at a single clinical visit. Induced sputum samples were also acquired at the same visit for differential cell count.

Results The LCQ demonstrated the following distribution properties: mean 15.30, standard deviation 4.49, range 4.04–21 and 10th percentile point of 8.52. Domain specific scores were LCQ (physical) 5.30(1.55) and LCQ (social) 5.19(1.67). There were modest correlations between LCQ and ACQ-6 (r = -0.60; p < 0.001) but not with AQLQ (r = -0.067). There was no correlation between LCQ and sputum eosinophils/neutrophils.

Discussion Severe asthma is associated with a high degree of cough related morbidity that appears to be independent of eosinophilic airway inflammation and not captured fully by available patient reported outcome instruments. Further research is required to determine the validity of the LCQ and its responsiveness in severe asthma populations.

**P72** T2 BIOMARKERS RELATE TO EXACERBATIONS AND CONTROL IN REFRACTORY ASTHMA

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Background T2 biomarkers have been shown to predict responsiveness to corticosteroids and possibly relate to asthma exacerbations and control. T2 biomarkers in the form of fraction exhaled nitric oxide (FeNO), peripheral blood eosinophils (PBE), and serum periostin are easier to measure and probable surrogate markers for induced sputum eosinophilia (ISE). The relationships between PBE, FeNO and periostin particularly in refractory asthma have been conflicting. A composite score of T2 biomarkers has also been postulated to predict exacerbations and may be more sensitive.1

Aim To explore the relationship between the T2 biomarkers individually, and in the form of composite score to asthma exacerbations and control.

Methods Unselected consecutive patients with confirmed diagnosis of refractory asthma (ATS) attending a tertiary severe asthma centre were recruited following an informed consent. Participants were evaluated for the following: demographics, exacerbations requiring corticosteroids in the preceding 12 months, asthma control questionnaire (Juniper ACQ7), lung function, FeNO, PBE, and periostin measurement. The composite T2 score of all the 3 biomarkers was calculated as previously reported (reference). Statistical analyses were conducted using MedCalc software.

Results One-hundred and fifteen patients were recruited with mean age 45 yrs, 88 (69.8%) females, mean inhaled corticosteroids (BDP equivalent) = 1,647 µg/day, on maintenance OCS =
63 (55%), mean FEV1 = 2.0 L (SD 1.8–2.1), FEV1% pred = 68%, and mean FEV1/FVC ratio = 71% (SD = 68–74).

A significant positive correlation between FeNO and PBE was observed (r = 0.39, p = 0.004), but not with periostin. Only FeNO significantly correlated to exacerbations (r = 0.42, p = 0.0008) and only periostin correlated significantly to ACQ7 score (r = 0.33, p = 0.0053). In addition, the biomarkers composite score significantly correlated with exacerbations (r = 0.4, p = 0.0031) (Figure 1), but not ACQ7.

**Conclusion**
In real life settings, FeNO correlated with historical exacerbations and the T2 composite score displayed a dose response correlation with exacerbations frequency. Periostin correlated with ACQ7 but not exacerbations. Further research is required to confirm these findings.

**REFERENCE**

**P73**
A PILOT STUDY TO INVESTIGATE THE USE OF SERUM INHALED CORTICOSTEROID CONCENTRATION AS A POTENTIAL MARKER OF TREATMENT ADHERENCE IN SEVERE ASTHMA

**Background**
Inhaled anti-inflammatory therapy is fundamental to asthma management, but adherence is very poor. This increases the risk of exacerbations and poor symptom control. Currently there is no direct way of assessing adherence to inhaled steroids accurately. The primary aim of this project was to determine whether liquid chromatography tandem mass spectrometry could be used to detect fluticasone propionate (FP) in human serum as a potential aid to therapeutic monitoring. The secondary aim was to relate serum levels of FP to markers of asthma severity.

**Methods**
We collected blood samples over an 8 hr period from inpatients with severe asthma on a stable dose of inhaled FP. Following baseline (trough) sampling, patients were observed using their inhaler, with inhaler technique documented. Subsequent samples were obtained 1, 2s, 4 and 8 hrs post inhalation. Demographic details and spirometry were also recorded.

**Results**
Thirteen patients were recruited: 8 males, 5 females; age range 22–64 yrs; FEV1 range 53–101% predicted; 10 patients on 1000 mcg/day, and three on 2000 mcg/day FP. The mean concentration of FP at 1 hr post inhaler (peak in 7/13 patients) was 95.5 (SD 89.1) ng/L. The mean pre-dose trough concentration was 32.9 (SD 41.5) ng/L. Two patients were noted to have poor inhaler technique; these patients had some of the lowest serum FP levels recorded. The FEV1% predicted was found to be strongly correlated with the peak serum FP concentration (Pearson’s r = 0.8, p = 0.001).

**Conclusion**
We have demonstrated that FP can be detected in the blood of patients with severe asthma following directly observed therapy; this could have a potential future application as a direct measure of adherence and perhaps inhaler technique. We also demonstrated a profound effect of reduced lung function predicting low serum FP levels. Future work will explore whether poor absorption reflects relatively poor efficacy in the most severe patients.

**P74**
PREVALENCE OF SPECIFIC ANTIBODY DEFICIENCY IN SEVERE ASTHMA

**Introduction**
Patients with asthma are prone to recurrent infective exacerbations, due to viral or bacterial infections. We have previously presented retrospective data, demonstrating
significantly reduced lung function in severe asthma patients with specific antibody deficiency. The prevalence and impact of specific antibody deficiency in this patient group is not known. **Aim** We aimed to determine the prevalence of specific antibody deficiency and its association with markers of disease severity. **Methods** We prospectively collected data from all new patients attending the regional severe asthma clinic. We recorded demographic details and markers of disease severity including: BTS treatment step, inhaled corticosteroid (ICS) dose, spirometry, blood and sputum eosinophil count, radiological findings such as bronchiectasis and bronchial wall thickening, exacerbations in the last year and ITU admissions. Specific antibody levels to *Haemophilus influenzae* (Streptococcus Pneumoniae <0.35 μg/ml to at least 6 of the 12 serotypes classed as deficient) were measured. **Results** Data for 53 patients (39F), mean (SD) age 49.6 (15.9) years were available. Mean (SD) FEV1 was 69 (22)% predicted, ICS dose 1914 (1337) micrograms, and BMI 31.5 (8.6) kg/m2. All were at BTS step 3–5. Information on specific antibody levels was available for 43 and 45 patients for *H Influenzae* and *S pneumoniae* respectively and for both in 42 patients. Overall out of the 42 patients 35 (83%) were deficient to one or both the organisms. Of these 13 (31%) were deficient to *H Influenzae* alone, 5 (12%) to *S pneumoniae* alone, and 17 (40.5%) to both. Looking at each organism separately 23 (51%) were deficient to *H influenzae*, 5 (12%) to *S pneumoniae* to *H influenzae* alone, 8 (19%) to both. Of the 32 patients for whom data were available 20 (62.5%) had 7 or more exacerbations in the preceding year and two thirds of these had bronchial wall thickening on their CT scans. A third of patients (30%) reported at least one ITU admission. The presence of specific antibody deficiency did not correlate with any clinical or radiological findings. **Conclusion** Specific antibody deficiency to *H influenza* and *S pneumoniae* is remarkably common in moderate to severe asthma. Further studies are required to determine the clinical significance of this finding.

**Abstract P74 Table 1** Prevalence of specific antibody deficiency and associated patient characteristics

<table>
<thead>
<tr>
<th>Antibody Levels</th>
<th>Prevalence Bronchial wall thickening on CT chest</th>
<th>Bronchiectasis on CT chest</th>
<th>≥7 Exacerbations past year</th>
<th>Total ITU admissions</th>
<th>Percentage predicted FEV1 (%)</th>
<th>Inhaled steroid (BDP equivalent) μg</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>n</em> = 45</td>
<td><em>n</em> (%)</td>
<td><em>n</em> (%)</td>
<td><em>n</em> (%)</td>
<td><em>n</em> (%)</td>
<td><em>n</em> (%)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Total <em>H. influenzae</em> deficient</td>
<td>30 (70)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>H. influenzae</em> deficient alone</td>
<td>13 (31)</td>
<td>8 (23)</td>
<td>5 (3) - 14</td>
<td>4 (3) - 17</td>
<td>3 (1) - 18</td>
<td>57 (16)</td>
</tr>
<tr>
<td>Total <em>S. pneumoniae</em> deficient</td>
<td>23(51)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>S. pneumoniae</em> deficient alone</td>
<td>5 (12)</td>
<td>3 (8.5)</td>
<td>2 (2) - 6</td>
<td>1 (0) - 4</td>
<td>0 (2) - 0</td>
<td>77 (8)</td>
</tr>
<tr>
<td>Combined Deficiency</td>
<td>17 (40)</td>
<td>11 (31)</td>
<td>6 (10) - 17</td>
<td>8 (3) - 33</td>
<td>4 (2) - 24</td>
<td>73 (23)</td>
</tr>
<tr>
<td>Competent Specific Antibody Levels</td>
<td>7 (13)</td>
<td>2 (8)</td>
<td>3 (2) - 8.5</td>
<td>2 (3) - 6</td>
<td>0 (3) - 0</td>
<td>70 (32)</td>
</tr>
</tbody>
</table>

**Introduction** The relationship between immunological biomarkers and evidence of lung damage has not been established in asthmatics that are sensitised to fungi. We sought to determine what features of allergic fungal airways disease were related to adverse radiological outcomes by the use of cluster analysis. **Method** Factor analysis was used to determine the significance of different clinical and immunological variables, the number of clusters present and cluster membership (*n* = 423). The presence of radiological indicators of lung damage and inflammation were then assessed between these groups. **Results** Three clusters were identified. Cluster 1 (37.1%) were obese, had late onset and minimal eosinophilic disease, cluster 2 (40.9%) had late onset eosinophilic disease and cluster 3 (22%) had early onset, atopic disease. Sensitisation to *A. fumigatus* was more prevalent in cluster 3 (94.2%; sIgE *A. fumigatus* 10.2 kUA/L (1.31–35.4)), compared to cluster 1 (44.9%; sIgE *A. fumigatus* 0.16 kUA/L (0.03–0.94)) and cluster 2 (45.7%; sIgE *A. fumigatus* 0.25 kUA/L (0.06–1.36)). Cluster 3 had a greater degree of airflow obstruction (p < 0.001), bronchectasis (69%, p < 0.001), tree in bud (32.4%, p < 0.001), collapse/consolidation (48.6%, p<0.007) and fibrosis (31.7%, p < 0.05) than any of the other groups. **Conclusion** This cluster analysis demonstrates that sensitisation to *A. fumigatus*, in addition to the other known clinical phenotypes, identifies asthmatics most at risk of developing fixed airflow obstruction and radiological features of airway inflammation and damage.
**Methods** We retrospectively reviewed referrals with respiratory symptoms and dysphonia to the upper airway service at the Royal Brompton, over a 12 month period to 2015. PVD was identified according to accepted criteria: no structural or neurological laryngeal disease, discrepancy between laryngeal status and voice quality, temporary loss of volitional control over phonation, e.g. frequently reported as secondary to dyspnoea), normal voicing on vegetative manoeuvres (e.g. coughing) and positive psychological factors associated with onset of symptoms. Perceptual voice quality was rated using the GRBAS scale.

**Results** Ten female patients were identified as having PVD (70% type 2, 20% type 3, 10% type 1). All patients had preserved spirometric indices but daily symptoms of dyspnoea and dysphonia. Respiratory diagnoses at referral included chronic cough (20%), difficult asthma (50%) and unexplained dyspnoea (30%), with symptoms of between 2 months and 15 years’ duration. The majority of patients (70%) were receiving treatment with either oral +/- inhaled corticosteroid prior to referral. Perceptual voice quality varied among patients, but in all cases normal voice was restored by the end of the first treatment session, leading to subjective reduction in breathlessness. Relevant psychological factors were identified as an underlying cause of the voice disorder.

**Conclusion** PVD is an under-recognised cause of treatment-refractory respiratory symptoms in patients with altered voice quality. Prior to referral, these symptoms are often attributed to the use of inhaled corticosteroid, yet accurate diagnosis and targeted therapy permits rapid restoration of normal voice and symptomatic improvement. This case series underpins the importance of collaborative working between SLT and respiratory medicine to ensure patients receive timely and appropriate specialist treatment.

**REFERENCE**

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**P77 HYPOXIC CHALLENGE TESTING FOR FITNESS TO FLY IN SEVERE ASTHMA**

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**Introduction and objectives** Commercial airline travel poses a recognised risk to patients with respiratory disease, including those with asthma. Hypoxic challenge testing (HCT) is typically employed to mitigate this risk by dictating in-flight oxygen requirement. The objective of this work was to evaluate the role of HCT in patients with severe asthma.

**Methods** A retrospective analysis was performed of all BTS/SIGN Step 5 asthmatics in whom air travel is being considered and should certainly be recommended in those with impaired lung function.

**Abstract P77 Figure 1**

**Conclusions** In patients with severe asthma, baseline oxygen saturation level is poorly predictive of the need for in-flight oxygen. Our findings indicate that a HTC should be considered for all BTS/SIGN Step 5 asthmatics in whom air travel is being considered and should certainly be recommended in those with impaired lung function.

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**P78 STUDY OF MORTALITY IN SEVERE AND DIFFICULT TO TREAT ASTHMA**

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10.1136/thoraxjnl-2015-207770.215

**Introduction** The National Report on Asthma Death (NRAD 2014) highlighted important shortcomings related to asthma management and an important number of patients still die from asthma. However, the mortality rate and causes of mortality in the severe asthma services has not been previously reported.

**Aim** To study what patients with severe asthma die from and what is their risk of mortality.

**Methods** All patients attending our severe asthma service who had died between March 2009 and December 2014 were identified. We retrieved data from case notes, GP, local hospitals and local database using a pre designed proforma which included cause of death, place of death, age at time of death, clinical details on asthma duration, lung function, biomarkers, medication, exacerbations including hospitalisation and co-morbidities. Causes of death was obtained from death certificates and when available coroner’s post-mortem reports.

**Results** Of the 520 patients attended our service between January 2009 and December 2014, there were 24 deaths (4.6% over 72 months, 0.7% annually). The mean age of death was 51 yrs (range 21–69), 17/24 (71%) were females. 30% had poorly
controlled asthma with a mean predicted FEV1 of 54%, 13/24 (61%) were on a maintenance dose of oral corticosteroids (mean dose 19 mg/day). The mean inhaled corticosteroids was 1006 μg. The cause of death was not known in 6 cases, with majority of cases died from non-asthma causes (78%) with cardiovascular disease being the most common. Asthma was the cause of death in 4/18 (22%) cases. Co-morbid diseases were prevalent particularly those that form the metabolic syndrome. Non-concordance with asthma medications and smoking history (current and ex-smokers) were also common (50% and 60% respectively).

Conclusion Although death is a rare event in our severe asthma service (0.7%), patients did die prematurely (mean age 51 yrs) usually from non-asthma causes, but asthma still accounted for death in the fifth of this group. Larger multicentre study with control data will be needed to confirm these findings and look for drivers and predictors of mortality in severe asthma.

New markers of lung physiology

**P79** COMPARISON OF CF AND NON CF LCI RESULTS USING THE EXHALYZER D AND INNOCORM DEVICES

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10.1136/thoraxjnl-2015-207770.216

Background Multiple breath washout (MBW) is a pulmonary function test that allows measurement of lung clearance index (LCI), a marker of ventilation heterogeneity. LCI is increasingly being considered as a clinical trial outcome measure. The Exhalzyer D N2 washout (N2/ExD, Ecomedics AG, Switzerland) is the recommended technique by the ECFS CTN. Mostly our group’s experience with LCI uses the Innocor™ gas analyser (Innovision, Denmark), SF6 as a tracer gas (SF6/Inn). To understand the N2/ExD technique, the aims of this study were to compare a) intra-test variability; b) LCI values c) LCI and FEV1 for the two techniques.

Methods 21 CF (14F, mean 20 ± 12 yrs) and 10 non-CF (8F, mean 28 ± 10 yrs) have completed MBW trials with the 2 techniques in random order in the same visit; methods previously described (Horsley et al. 2009, Jensen et al. 2013).

Results Intra-test CoV (2–3 repeats) was similar for SF6/Inn and N2/ExD (3.57 vs 3.78 CF, ns). LCI was significantly higher with N2/ExD than with SF6/Inn in both CF (14.05 vs 9.33; p = 0.005) and non-CF (7.08 vs 6.64, p = 0.04). Both techniques show a significant correlation for LCI and FEV1%, although the regression slopes were significantly different (p < 0.0005); much steeper for N2/ExD.

Conclusions LCI values cannot be used interchangeably between the Innocor™ and Exhalzyer D. In non CF, there was a statistically significant difference, with higher values in the N2/ExD. The difference was much greater in CF and increased as LCI did. In the context of similar intra-test variability, the hypothesis that this may translate into improved power in future clinical trials needs to be tested. Sponsored by a non-restricted grant from Novartis.

**REFERENCES**

1 Horsley AR, Gustafsson PM, Macleod KA. et al. Lung clearance index is a sensitive, repeatable and practical measure of airways disease in adults with cystic fibrosis. Thorax 2008;63:135–46


**P80** EXTRAPOLATING LUNG CLEARANCE INDEX (LCI) FROM SHORTENED MEASUREMENTS


10.1136/thoraxjnl-2015-207770.217

Introduction and objectives Shortened multiple breath washouts (MBW) are attractive in young children, where a long test time may not be tolerable (Thorax 2013;68:586–7). Lung clearance index (LCI) is usually calculated at 1/40th of the starting concentration (LCIstd), but in shorter MBWs the LCI is calculated at 1/20th of the starting concentration (LCI0.5). LCI0.5 and LCIstd are closely correlated but not interchangeable, and so we calculated an extrapolated full LCI (LCIex) from LCI0.5. Our hypothesis was that extrapolated LCI (LCIex) will better reflect LCIstd than LCI0.5 and be more sensitive to intervention.

Methods Condition-specific equations for cystic fibrosis (CF), primary ciliary dyskinesia (PCD) and asthma, and an overall equation for all 3 groups, were developed to convert LCI0.5 to LCIex from data previously analysed (n = 90, Thorax 2014;69 [Suppl1]A166). LCIstd, LCI0.5 and LCIex were then calculated for new cohorts (n = 70, 20 asthma, 30 CF, 20 PCD), and LCIex was compared to LCIstd. CF patients receiving IV antibiotics (n = 17) and asthma patients receiving triamcinolone (n = 32) also had LCIstd, LCI0.5 and LCIex calculated and compared. The upper limit of normal for LCIstd was calculated from healthy controls. LCIex was compared to LCIstd with a Bland-Altman plot.

Results In CF, at higher LCIs, the spread between LCIex and LCIstd grew but there was no bias. For PCD and asthma agreement remained very good. There was no significant difference between LCIstd and LCIex. Results for positive and negative prediction of LCIstd for LCI0.5 and LCIex are shown in the Table 1. LCIex and LCIstd were also sensitive to interventions in asthmatic and CF patients, although in general LCIex had better p values.

Conclusions LCIex performed better than LCI0.5 in predicting results of LCIstd. However, LCIex did not always reflect LCIstd, particularly in CF, so the two cannot be used interchangeably in lung disease.

<table>
<thead>
<tr>
<th>Abstract P80 Table 1</th>
<th>LCIcorrectly categorised (%)</th>
<th>Sensitivity to intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCIstd</td>
<td>True positive</td>
<td>True negative</td>
</tr>
<tr>
<td>LCIex</td>
<td>37</td>
<td>26</td>
</tr>
<tr>
<td>LCI0.5</td>
<td>38</td>
<td>26</td>
</tr>
</tbody>
</table>

PLOS One 2013;8:e56868
P81 FEASIBILITY OF MEASURING LUNG CLEARANCE INDEX (LCI) IN A CLINIC SETTING IN PRESCHOOL CHILDREN WITH A RANGE OF AIRWAY DISEASES

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Introduction and objectives LCI is a measurement of lung function (in particular distal airway disease) derived from the multiple breath washout (MBW) test (Eur Resp J 2013; 41:507–22). Although practical in a research setting, feasibility in a clinic setting (with limited time and without using sedation) in young children is not known. We looked at success rates of LCI, and LCI0.5 (a shortened washout which can be accomplished more quickly) in preschool children (aged 2–6 years) with recurrent wheeze (Eur Resp J 2008; 32:1096–110), cystic fibrosis (CF), recurrent cough/infections, and healthy controls. Our hypothesis (based on other research performed in this field (Thorax 2012; 68:586–587) was that shortened LCI0.5 would be more feasible than full LCI, and that the test would be more feasible in older preschool children than younger.

Methods 62 preschool children median age 3.9 (2.07–5.95) years, 34 male, (n = 21 with wheeze, n = 11 CF, n = 2 PCD, n = 22 other, n = 5 healthy controls) performed MBW test during a routine outpatient visit. Wheeze was doctor diagnosed or parent reported via wheeze questionnaire.

Results 66% of children successfully completed either the LCI or LCI0.5. Completion according to age group is shown in Figure 1. LCI success rate in wheezers was 67%, healthy controls 100%, CF 82%, PCD 100% and recurrent cough/infections 50%. Success rate was identical between males and females (61%), and was similar comparing LCI0.5 (42/62) to full LCI (38/62). Three of the four that only completed LCI0.5 were less than 3.5 years old.

Conclusions LCI is a feasible test in the clinic setting for preschool children; however success rates under 3 years of age in all disease groups are very low. Use of the shortened washout (LCI0.5) marginally improves success rates, but may improve test completion in the youngest children.

Abstract P81 Figure 1

P82 LUNG CLEARANCE INDEX (LCI) AND GENOTYPE-PHENOTYPE CORRELATIONS IN PRIMARY CILIARY DYSKINESIA (PCD)

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Introduction and objectives Mutation type may affect clinical phenotype in PCD, as shown by differences in forced expiratory volume in 1 s (FEV1) (AJRCCM 2015;191:316–324). LCI, measured using multi-breath washout (MBW) is raised in PCD (AJRCCM 2013;188:545–549) but the relative sensitivities of the two physiological measurements is disputed (Thorax 2015;70:339–345, and 305–306). We hypothesised that LCI would be more sensitive to genotype-phenotype differences in PCD.

Methods MBW (using sulphur hexafluoride MBW with a photoacoustic gas analyser) and spirometry were performed in 77 PCD patients (mean age 16.4 years (range 4–62.2), 33 males, mean FEV1 z score -2.09 (range -5.33–1.59)). 44 had outer dynein arms (ODA) defects, or both inner (IDA) and ODA, 18 had microtubular defects (either transposition or microtubule disorganisation with absent IDA), 15 had normal ultrastructure (diagnosis made on either genetics (n = 10), low nasal NO, clinical phenotype and consistent dyskinesia on light microscopy).

LCI is worst in other defects group than dynein arm defects (p = 0.01) or normal ultrastructure (p = 0.0002). FEV1 is better in normal ultrastructure than dynein arm (p = 0.04) and other defects (p = 0.007).

Abstract P82 Figure 1
(n = 1), or low nasal NO, clinical phenotype and an affected sibling (n = 3)). There was no significant difference in age or gender composition between the 3 groups.

**Results**

Patients with normal ultrastructure had significantly higher FEV₁ and lower LCI, indicating milder disease. Those with ODA +/- IDA had a more normal LCI than those with microtubular defects (Figure 1), but similar FEV₁.

**Conclusions**

PCD patients with normal ultrastructure have the milder disease, and those with microtubular defects more severe. Differences were more apparent on LCI than FEV₁, suggesting LCI may be more sensitive to worse distal small airway disease in PCD.

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**P83**

REMOTE PULMONARY FUNCTION TESTING – COMPUTER GAMING IN THE RESPIRATORY WORLD

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**Introduction**

Lung function testing by spirometry has remained unchanged for over 50 years, despite limitations including patient technique, discomfort, cost and training. Non-invasive, remote lung volume measurement is an alternative approach. This has been explored in the past using structured light, accelerometers and impedance pneumography, but these have often been costly and of limited validity.

We use a novel approach to remote assessment (~2 metres) using a 3D time-of-flight depth camera – similar to those found in many home gaming consoles. This pilot developmental data was generated from patients in a clinical setting.

**Methods**

Patients were recruited from a general respiratory physiology laboratory. Spirometry was performed according to ATS/ERS standards using an unmodified pneumotachograph (nSpire Health, Longmont, CO, USA). A Kinect V2 time-of-flight depth sensor (Microsoft, Redmond, WA, USA) was used to reconstruct 3D models of the subject's thorax to estimate volume-time and flow-time curves for both Forced and Slow Vital Capacity and their associated measurements (Figure 1, technical details in1).

These results were correlated with simultaneous recordings from the pneumotachograph, and error values calculated to assess the accuracy of the technique.

**Results**

Data were available from 53 patients, with 40 having usable data. Mean age 62.8 yrs (SD 16.2), BMI of 26.8 (SD 5.5). 41.5% male. 54.7% of patients had obstructive lung diseases, and 28.4% fibrotic lung disease. Mean FVC was 91.3% predicted (SD 26.4%), Mean FEV1 83.1% (SD 28.9%).

The model estimates were highly correlated with spirometric values for FVC ($\lambda = 0.999$), FEV₁ ($\lambda = 0.947$), VC ($\lambda = 0.999$), IC ($\lambda = 0.997$) and TV ($\lambda = 0.962$).

Univariate analysis demonstrated no patient characteristics predictive of discrepancy from spirometric values for FVC or VC.

**Conclusions**

We describe a pilot data from the initial development of a new technique for non-invasively assessing lung volume and pulmonary function measurements. It correlates to within 30 ml for FVC and 10 ml for VC. This has a wide range of potential applications, including screening, home monitoring of respiratory disease, assessment of lung function in those unable to complete pneumotachography and gating controls for radiological imaging techniques.

**REFERENCE**


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**Abstract P83 Figure 1**

(A) Reconstructed chest surface and volume estimation from reference plane. (B) Volume-time curves (FVC and SVC) comparing spirometer values and Kinect calculation
THE INSPIWAVE (TM) TRIAL ON ADULT HEALTHY VOLUNTEERS – INSIGHTS GLEANED FROM POSTURAL STUDIES

Introduction Current techniques used to monitor Functional Residual Capacity (FRC) present significant clinical limitations which often restrict patients to those who are conscious, cooperative and mobile. There is a clinical need for an operator independent device that is able to simultaneously and continuously monitor FRC in mechanically ventilated patients, the morbidly obese and infants. The InspiWave™ is one such device which utilises a sinusoidal Nitrous Oxide (N2O) tracer gas technique to non-invasively monitor various parameters of cardiopulmonary function, including end tidal alveolar volume (VA) and Bohr deadspace volume (VD). This study evaluates the performance of the InspiWave™ in estimating lung volume using two unique postural change protocols in healthy volunteers.

Method 5 subjects were asked to adopt 3 stationary postures (sitting upright, supine, 45° elevation) using a tilt table. 21 subjects adopted a different protocol, with a single transition phase between sitting and supine.

Results In the first protocol (n = 5), VA estimations were consistently smaller at supine than at sitting (31%). At 45° elevation, VD estimations were the smallest of all three postures. Comparison of absolute flow signal (Δ|Flow dt|) data at the point of postural transition with VA estimations by the device (n = 21) yielded a Pearson’s correlation (r) of 0.453 (p < 0.05).

Conclusion Estimations by the InspiWave™ demonstrated acceptable correlation between absolute flow signal change and device estimation, suggesting good accuracy. FRC changes by approximately 25% from sitting to supine, due to added pressure from abdominal contents on the diaphragm when gravity shifts with postural change. Data from this study closely mirrored this value (31%), demonstrating a good degree of device performance. VD estimations were smallest at 45° elevation of the three postures which may be due to airways being kept more open, consistent with respiratory benefits of the 45° “beach chair position”. Postural studies provide an alternative over conventional comparative studies with reference techniques (such as body plethysmography) in assessing device performance, when comparing variables which are not entirely equivalent.

REFERENCE


Abstract P84 Figure 1 Alveolar Volume (A) and Deadspace Volume (B) estimated by the device at three different postures. Averaged data of participants (n = 5) shown in traces with circle markers (●), error bars represent standard deviation. Normalised data relative to the upright sitting position plotted with square markers (■), error bars represent 95% confidence interval

Background The 6MWT is a simple, reproducible test of exercise performance. Lettieri et al.1 proposed a composite index of the product of the lowest oxygen saturation (SpO2) and distance walked – the distance–saturation product (DSP). Pimenta et al.2 calculated the differences between actual SpO2 and 100% every two seconds, and produced the desaturation-distance ratio (DDR-1). Ijiri et al.3 simplified Pimenta’s methodology, using the SpO2 at the end of each minute (DDR-2).

Aim To compare the different methods of calculating the composite index.

Methods We retrospectively analysed 48 6MWT datasets, obtained using standard methodology. SpO2 was recorded every second using a Minolta 300B pulse oximeter and analysed using Visi-Download (Stowood Scientific, Oxford). The DSP and DDR's was calculated by each method. Additionally, data using Pimenta’s method, was calculated using one second data intervals (DDR-3). Data are given as median (IQR).

Results 41/48 patients were male. Group age was 63 (53 to 73) years, FEV1%pred 68.4% (41.3 to 82.3), distance walked 390 m (321.3 to 477.5), baseline SpO2 95% (93 to 96) and decline in SpO2 was -4% (-2 to -8). DSP was 324.6 (278.8 to 419.4) m%, DDR-1 was 8.90 (4.98 to 13.27), DDR-2 was 16.83 (9.14 to 24.8) and DDR-3 was 8.90 (4.99 to 13.66). Bland-Altman

REFERENCE


Conclusions 1) there is no significant difference between DDR-1 and DDR-3, both providing an accurate assessment of changes in SpO₂ during exercise and allowing for the different storage capabilities of pulse oximeters; 2) the simplest index (DSP), showed poorer correlations compared to the DRRs, perhaps reflecting the simplicity of the index; 3) the conceptual idea of a composite index of distance walked and changes in SpO₂ during a 6MWT needs further investigation in a range of different clinical settings.

REFERENCES

Diagnosis and management of paediatric lung disease

P87 REPEAT SURVEY OF VITAMIN K PRESCRIBING PATTERNS AND BONE HEALTH SURVEILLANCE IN UK PAEDIATRIC CF CENTRES

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Introduction and objectives CF bone disease is multi-factorial; UK guidelines for screening and treatment of CF bone disease are published. 1 Despite evidence of a key role for Vitamin K in bone formation, there is limited agreement on supplementation in CF. A previous 2005/06 survey 2 of bone health surveillance and Vitamin K use in CF reported wide variation in practice. The current survey aimed to ascertain practice 10 years on.

Methods Questionnaires were sent via email to all 25 UK paediatric CF centres. Data were collected on use of vitamins A, D, E and K including preparation, dose and criteria for Vitamin K supplementation. In addition, information was obtained on bone health surveillance including use of dual-energy X-ray absorptiometry (DXA) scanning to measure bone mineral density (BMD).

Results A 60% questionnaire response representing 2805 CF children was collected. All centres reported that >90% pancreatic insufficient patients receive multivitamin supplements and 12/15 centres reported >90% patients receive additional Vitamin E.

Only 3 centres routinely supplement Vitamin K, with only 1 reporting that >90% patients receive Vitamin K. Criteria for prescribing Vitamin K were deranged liver function (10/15), clotting (5/15), low Vitamin K levels (2/15), and low BMD (3/15). Vitamin K dosage varied from 0.3–10 mg/day, with most (12/15) prescribing 10 mg/day. Menadione was mainly (10/15) used with some using Phytomenadione for younger patients. Four centres used AquaDEKs, whilst three reported limitations in prescribing AquaDEKs due to formulary constraints.
All centres measured vitamin D levels and 14/15 (94%) routinely perform DXA scans. Dietary calcium intake was assessed in 11/15 centres.

**Conclusion** Bone health surveillance is routinely undertaken in all paediatric CF centres, with Vitamin D levels and BMD (by DXA) measurement universal. Vitamin K prescribing (criteria and dose) is still heterogeneous. A Cochrane review of routine vitamin K supplementation in CF concluded that evidence is currently limited to two small trials, with further evidence needed to establish optimal dose and long-term benefit.

**REFERENCES**


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**P88 THE EVALUATION OF EXOPHIALA IN PAEDIATRIC CYSTIC FIBROSIS**

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10.1136/thoraxjnl-2015-207770.225

**Introduction** The increasing prevalence of fungal pathogens in paediatric cystic fibrosis (CF) is challenging current practice. Whilst respiratory growth and colonisation with *Exophiala*, a saprophytic fungus is documented; the susceptibility, clinical manifestation and management is unclear.

**Aim** To evaluate the clinical manifestation of *Exophiala* and the role of antifungal therapies in paediatric CF.

**Setting** Royal Manchester Children’s Hospital provides tertiary care for 182 patients and shared care for 170 patients encompassing a diverse range of genotypes.

**Population** Fifteen patients have yielded *Exophiala* positive sputum swabs on routine screening over 24 months.

**Measures** Objective measures of disease severity and demographics; age, gender, BMI (Z-score), lung function, hospital admissions are assessed against *Exophiala* growth and co-existing pathogens. Antifungal treatment regimens are described and compared.

**Analysis** Significant clinical manifestation of *Exophiala* and evidence of eradication in CF is described.

**Results** Data reveals no significant difference in sex ratio (♂:♀) though distribution is skewed towards older patients 46.7% (n = 7) ≥15 years, 26.6% 12–14 years, 12.5% 10 years, 12.5% 5–7 years.

**Two distinct categories of carriage are evident; sporadic growth (n = 9) and colonisation (n = 6).** All positive sputa contained ≥2 organisms suggesting coexisting colonisation. 73.3% of all patients and 100% percent of patients colonising *Exophiala* had coexisting colonisation of *Candida albicans*. 100% of patients colonising *Exophiala* also had a drop in BMI and Z-score from diagnosis to date of study. They also had a rate of >9 admissions/year. Lung function tests revealed variation independent of carriage.

Symptomatic carriage of *Exophiala* was treated with triazoles; voriconazole, itraconazole and posaconazole though 50% of blood triazole levels were below therapeutic range. One patient cleared *Exophiala* without antifungal treatment. No further growth was noted following itraconazole treatment on initial growth in another patient. Colonisation was treated successfully with intravenous voriconazole, though re-colonised 4 months later. Colonisation was evident in 2 patients despite 6–12 months of oral voriconazole but was eradicated on switching to oral posaconazole.

**Conclusion** Data from this single centre study suggests that some paediatric CF patients may be more susceptible to fungal infections. *Exophiala* carriage manifestation varies and may affect height and weight. *Exophiala* eradication can be achieved.
Towards a protocol for the management of very severe chronic lung disease

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Background While corticosteroids appear effective in reducing respiratory support requirements of babies with very severe chronic lung disease of prematurity (CLD), controversy remains regarding the most appropriate route, timing, preparation and dosage. Using Delphi methodology, consensus was reached involving 4-weekly pulses of methylprednisolone for 3 days at 500 mg/m² in ventilator-dependent, or close to ventilation, babies in diffuse lung disease of childhood (Cunningham S., et al. Am J Respir Crit Care Med 189;2014:A4664). Use of hydroxychloroquine and azithromycin also reached consensus.

Aims and objectives To describe the features of those babies who received methylprednisolone, hydroxychloroquine and azithromycin (“consensus treatment”) for severe CLD compared to those who did not in order to inform the drafting of a protocol.

Methods A prospective database detailing care of babies with severe CLD referred to the CLD service at Nottingham Children’s Hospital Jan 2009–Dec 2014 was used.

Results 147 children were referred to the service; 4 babies received consensus treatment. Those receiving consensus treatment were ventilated for longer 39(sd 4.6) versus 8(sd 16.8) days (p < 0.001). Children receiving consensus treatment were significantly older at discharge 245(65) versus 95(45.3) days and were discharged with higher oxygen requirements 1.0(0.4) vs. 0.3(0.2) litres).

Conclusions Babies with very severe CLD were successfully treated with consensus treatment. A change in practice toward discharge at higher oxygen delivery rates in such babies was safe. Further experience will refine the objective criteria for considering consensus treatment and would inform the design of a future randomised controlled trial.

Post-infective obliterative bronchiolitis acquired beyond the first 3 years of life

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Introduction Obliterative bronchiolitis (OB) is a rare form of chronic obstructive lung disease that follows a severe insult to the lower respiratory tract, resulting in fibrosis of the small airways. In the non-transplant paediatric population, adenovirus infection is the most common cause. The initial infective insult occurs in the early years and the diagnosis requires a history of acute severe bronchiolitis/viral pneumonia in previously healthy children in the first 3 years of life. Though there has been a case report of post-infectious OB in an adult female,1 to our knowledge, there are no published cases in children acquired after 3 years of age.

Aim We describe two previously healthy older boys with normal immunological investigations who developed post-infectious OB.

Cases The first patient had severe adenovirus pneumonia aged 7, requiring ventilation, oxygen and bronchodilator therapy. In view of atopic background (nut allergy and paternal asthma) inhaled corticosteroids were initiated at discharge. A year later he presented with productive cough, debilitating shortness of breath on exertion, moderately reduced PEFR but no wheeze. He did not respond to Amoxicillin or step-up asthma treatments. CXR and exercise test were normal and pulmonary function tests (PFT) did not show evidence of reversibility. A mixed growth of typical respiratory pathogens were isolated in sputum and treated with prolonged oral antibiotic course. High resolution chest CT (HRCT) showed air trapping in the right upper lobe consistent with OB.

The second patient developed severe mixed mycoplasma and adenovirus pneumonia aged 3.5, followed by persistent left lower lobe collapse and wet cough requiring intravenous antibiotics and physiotherapy. His left lower lobe re-expanded, but his HRCT revealed air trapping consistent with OB. He continued to have intermittent chest infections with various typical respiratory pathogens isolated in sputum requiring oral and intravenous antibiotics. His PFTs are stable with moderately reduced FEV1/FVC.

Both patients are maintained on regular chest physiotherapy and intermittent antibiotics.

Conclusion Post-infectious OB can develop in healthy children older than 3 years.

Reference

Real-time online analysis of volatile organic compounds in the exhaled breath of preschool children

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Introduction Investigating airway inflammation and pathology in preschool children is challenging from both a technical and ethical standpoint and as such we urgently need to identify and validate novel, non-invasive techniques. Analysis of exhaled volatile organic compounds (eVOC) has been successfully employed using conventional, offline mass spectrometry in preschoolers (van de Kant 2013). However, real-time, instant analysis of eVOC in this age group would be an important advance in the field of ‘breathomics’. We sought to assess whether real-time online analysis of eVOC was feasible in preschool children attending our hospital.

Methods Breath samples were taken from preschool children (aged between 1 and 6 years) attending the emergency department or an acute medical ward at our hospital. Children breathed room air tidally via a facemask and eVOC were analysed instantly by Proton-Transfer-Reaction time-of-flight mass spectrometry (PTR-ToF-MS) coupled to Loccioni breath collection apparatus. Capnography data was simultaneously recorded. The mass spectra were analysed using a Matlab programme coded for adult patients and the spectra for mass channel (m/z) 59 (acetone) were inspected. Total counts for all mass channels were summed.

Results Eight children (median age 42 months, range 14–59 months) participated, of which five (median age 40 months) were able to produce analysable results. The total median count from the summation of all mass channels was 157,465 ncp (number of counts per second) ranging from 4,831 to 200,319 ncp. The Figure 1 below demonstrates a spectrum for m/z 59 and capnography trace from one of the participants. The patterns of both traces are comparable.
**Poster sessions**

**Abstract P92**

**Figure 1** Spectrum for m/z 59 (1a) and capnography trace (1b). ncps = number of counts per second

**Discussion** The comparability of the traces for the spectrum of m/z 59 and capnography suggests that real-time PTR-ToF-MS is detecting eVOC which relate to end-tidal breathing. The traces are likely offset due to the lag between end-tidal exhalation and the sample reaching the apparatus. This feasibility study has demonstrated that real-time analysis of eVOC is possible in preschool children in an acute setting. Further work is needed to determine the most accurate way of analysing the spectra to be able to apply this novel, non-invasive method of investigating airway inflammation and pathology in preschool children.

**REFERENCE**


**P93**

**THE PRACTICALITIES OF USING ALLERGEN-IMPERMEABLE BED COVERS IN CHILDREN WITH MITE ALLERGIC ASTHMA**

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**Objective** As part of a randomised double-blind placebo-controlled study in children with mite-allergic asthma, mite-impermeable bedding encasings were evaluated in terms of reduction in allergen exposure and patient/parent acceptability.

**Methods** Physician diagnosed asthmatic children (3–17 years) were recruited following an exacerbation of asthma. Mite-sensitised children were randomised to either mite-impermeable encasings for the mattress, pillow and duvet (Astex Pristine; ACP Manchester, UK) or placebo encasings (100% polycotton; Musbury fabrics, Rossendale, UK), in a double-blind manner. Vacuumed dust samples were collected from the child’s mattress prior to fitting the encasings and at 12 months, stored at -20°C, then analysed for mite allergen content (Der p 1) by enzyme-linked immunosorbent assay (Indoor Biotechnologies, Cardiff, UK). Questions aimed at assessing the practicalities of using the encasements were asked of parents by an interviewer blind to their allocation, 8–12 months later.

**Results** 284 children (mean age 7.7 years; 65.8% male) were randomised (146 active; 136 placebo). There was an 84% decrease in Der p 1 levels in child’s mattress in those using the mite-impermeable encasings, which was not seen in the Placebo group (p < 0.001). Data on ‘use of bedding encasements’ were obtained from 232 participants. Significantly more families in the active group reported that the duvet slipped within its cover, compared to the placebo group (32.2% vs 5.3% respectively, p < 0.001) and that it was “noisy” (14.4% active vs 0.9% in placebo, p < 0.001). Some reported the extra covers made them too warm (3.4% active vs 1.8% placebo, p = 0.64). Overall 31 (26.3%) using the mite-impermeable encasings rated them as “uncomfortable” compared with 2(1.8%) in the placebo group (p < 0.001). Furthermore, 30(25.4%) children in the mite-impermeable group said they would prefer to have the encasings removed, compared to 3(2.6%) in the placebo group (p < 0.001). There was no difference in the numbers of families who stated that they would continue to use the encasings if it were of benefit to the child, (87.3% mite-impermeable vs 89.35% placebo p = 0.68)

**Conclusions** Mite-impermeable encasings can significantly reduce mite allergen levels in the bed. Despite some practical issues, most families are willing to use this intervention if it is of benefit to their child’s asthma.

**P94**

**EFFECT OF HYDROXYUREA ON NOCTURNAL AND AWAKE OXYGEN SATURATION IN CHILDREN WITH SICKLE CELL DISEASE**

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10.1136/thoraxjnl-2015-207770.231

**Introduction** Sickle cell disease (SCD) causes lifelong morbidity and reduced life expectancy. Resting hypoxaemia and intermittent nocturnal oxygen desaturation are often seen in children with SCD, which may contribute to morbidity associated with vaso-occlusive episodes. Treatment with hydroxyurea reduces the frequency and severity of vaso-occlusive episodes but the impact of hydroxyurea on oxygen saturation and sleep apnoea is unknown.

**Objective** To look for any difference in baseline oxygen saturation asleep and awake and the frequency of intermittent nocturnal desaturation after starting hydroxyurea in children with SCD.

**Methods** A retrospective review of children who were commenced on hydroxyurea between March 2006 and July 2014 attending two UK sickle-respiratory clinics. Data was collected from overnight sleep studies and averaged pulse oximeter spot check recordings in clinic notes when awake from a) 6 months before starting hydroxyurea and b) up to 2 years after. Lung function and haemoglobin changes were also noted over the same time periods.

**Results** Forty six children (25 male) with a median age of 10 years (range 5–19 years) were started on hydroxyurea. Haemoglobin and HbF rose significantly on hydroxyurea as expected (Table 1). After starting hydroxyurea the average overnight oxygen saturation increased from median of 93.5% to 95.2% (p = 0.01) and the median daytime spot oxygen saturation rose from 93.5% to 96.3% (p = 0.001). There was no significant change in the median intermittent nocturnal 3% oxygen desaturation index (ODI), nocturnal PCO₂ or spirometry.

**REFERENCE**

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10.1136/thoraxjnl-2015-207770.231
Conclusion In children with SCD, the use of hydroxyurea was associated with a significant increase in awake and nocturnal baseline oxygen saturation, but no change in intermittent nocturnal desaturation indices or lung function. This preliminary data suggests that improving oxygen saturation may be an important outcome of hydroxyurea therapy with potential benefits in reducing not only vaso-occlusive crises but future respiratory morbidities. This hypothesis would need to be tested by a prospective multicenter trial.

REFERENCE

P95 GROWTH AND NUTRITION IN ATAXIA TELANGIECTASIA

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10.1136/thoraxjnl-2015-207770.232

Background Ataxia telangiectasia (A-T) is a rare multisystem disease with high early mortality from lung disease and cancer. Nutritional failure adversely impacts outcomes in many respiratory diseases. Several factors influence nutrition in children with A-T including carabolism during recurrent infections and inadequate oral intake (fatigue, difficulties with chewing or swallowing, poor appetite, and nausea due to medications). We hypothesised that children with A-T have progressive growth failure.

Methods Data was collected prospectively on weight, height and body mass index (BMI) at the national paediatric A-T specialist clinic in Nottingham. Adequacy and safety of oral intake was assessed. Nutritional advice was given at each multidisciplinary review.

Results 92 children (46 girls) (33 once, 37 twice, 20 thrice, 1 child four times and 1 child 5 times) had 176 measurements since 2009. Median (range) age was 9.2 (1.5 to 18.4) years. Weight, height and BMI Z-scores were respectively -0.84 (-8.34 to 3.58), -0.98 (-5.85 to 3.66) and -0.24 (-4.45 to 2.75). Weight, height and BMI Z-scores inexorably declined over time.

Conclusion There is a remorseless decline in growth over time. There is an urgent need for new strategies, including an understanding of why growth falters. Undernutrition adversely affects acute and chronic lung health. Outcomes for late gastrostomy insertion in AT are poor (Leighton Greif OJRD 2011;210). We suggest early proactive consideration of gastrostomy from age 8 years upwards in order to prevent respiratory deterioration.

Abstract P94 Table 1 Change in haematological and respiratory indices with hydroxyurea

|                        | Before Median (Interquartile range) | On Hydroxyurea Median (Interquartile range) | *P value
|------------------------|-------------------------------------|------------------------------------------|---------
| Hb (g/L)               | 76 (69.5–86.5)                      | 83 (72.7–87.7)                           | 0.04    |
| HbF (%)                | 6.1 (3.7–12.9)                      | 8.8 (6.1–16)                             | <0.001  |
| Average overnight      | 93.5 (08–97)                        | 95.2 (93–98)                             | 0.01    |
| SpO2 (%)               | 84 (77.4–89)                        | 87 (83–91)                               | 0.009   |
| Mean overnight PCO2 (Kpa) | 5.7 (4.7–6.2)                  | 5.5 (5.2–6.0)                            | 0.3     |
| Exp. nocturnal         | 93.5 (91–97)                        | 96.3 (94–98)                             | 0.001   |
| % FVC                  | 70 (61.5–83.5)                      | 73 (68–88)                               | 0.6     |

*P values based on Wilcoxon matched-pairs signed rank test.

Abstract P95 Figure 1

Poster sessions

P96 INTERSTITIAL LUNG DISEASE CAUSED BY STING-ASSOCIATED VASCULOPATHY WITH ONSET IN INFANCY (SAVI)

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Introduction An increasing number of monogenic auto-inflammatory conditions known as primary type I interferonopathies are being recognised. We present a case of the newly described condition, stimulator of interferon gene (STING) associated vasculopathy with onset in infancy (SAVI), with significant respiratory involvement.

Presentation A male infant, born to healthy non-consanguineous parents, presented to his local hospital with tachypnoea, intermittent fever and failure to thrive from 5 weeks of age. Over the following months, episodes of increased respiratory effort, cough and fever were attributed to infection. He subsequently developed a papular rash in discrete clusters over his back. At presentation to our centre at 7 months of age, he was tachypnoeic but not hypoxaemic. A chest radiograph showed extensive airspace shadowing with chest computed tomography demonstrating interstitial changes. Bronchoalveolar lavage was negative for infection. Laboratory tests revealed microcytic anaemia, raised inflammatory markers, positive anti-nuclear antibody, raised IgA and IgG and abnormal lymphocyte proliferation. A lung biopsy showed a mixed pattern of inflammation, with type 2 pneumocyte hyperplasia and endothelial tubuloreticular
inclusions on electron microscopy. Given the combination of interstitial lung disease, skin rash and likely vasculopathy, SAVI was suspected. This was confirmed on genetic testing with a heterozygous somatic mutation (c.463G >A, p. V155M) in exon 5 of the TMEM173, the gene encoding STING.

Treatment Treatment with pulsed methylprednisolone was commenced without improvement. He gained weight with supplemental feeding but had persistent tachypnoea, subsequently becoming hypoxaemic requiring low flow oxygen therapy. He commenced on a trial of monthly intravenous immunoglobulin (IVIg) with evidence of clinical efficacy awaited. We are considering the use of the Janus kinase inhibitor, baricitinib, as a specific targeted therapy to block interferon signalling.

Conclusion SAVI is a recently described interferonopathy in which lung involvement is a major clinical feature with subsequent significant morbidity and mortality. Twelve patients have been reported so far in the literature, with overall poor response to glucocorticoids and disease modifying anti-rheumatic drugs. In the context of failure to thrive, fevers, rash and interstitial lung disease in early life, we urge clinicians to consider SAVI as a differential diagnosis and to seek testing for TMEM173 mutations.

P97 UPTAKE OF THE EMERGENCY SALBUTAMOL INHALER IN NORTH EAST ENGLAND SECONDARY SCHOOLS FOLLOWING AMENDMENT OF THE HUMAN MEDICINES REGULATIONS

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10.1136/thoraxjnl-2015-207770.234

Introduction and objectives As a result of amendments to The Human Medicines Regulations 2012, schools have been permitted since 1st October 2014 to purchase salbutamol inhalers to be used by children diagnosed with asthma and prescribed an inhaler, where parents have given written permission for the emergency inhaler to be used. This regulatory change may represent a useful step in facilitating access to emergency asthma treatment in schools.

This study provides the first published data on the number of schools that have availed of this new power, through an assessment of uptake of the emergency salbutamol inhaler in secondary schools in North East England.

Methods We compiled a list of all free-to-attend schools within the 12 local authorities in North East England using listings on local authority websites. We limited our study to schools which served 16 year old mainstream pupils in order to aid interpretation of our results. Postal letters were sent to invite the included schools to complete a brief online or postal questionnaire asking if the school had an emergency salbutamol inhaler for use by pupils in an asthma emergency. Data was collected between November 2014 and May 2015.

Results Of 153 schools included in the study, 103 questionnaire responses were received. We excluded the response of 1 school due to lack of clarity. Of the remaining 102 responses, 45 (44%) indicated that the school had an emergency salbutamol inhaler available, while 57 (56%) indicated that the school did not have such an inhaler. The proportion of schools in which emergency salbutamol inhalers were available varied by local authority from 0% to 71%.

Conclusions Despite the change in legislation, 56% of schools included in this study did not possess an emergency salbutamol inhaler. More needs to be done to increase the level of uptake of the emergency salbutamol inhaler to enable schools to better respond to asthma emergencies.

P98 THE RELATIONSHIP BETWEEN INVASIVE AND NON-INVASIVE MEASURES OF INFLAMMATION IN CHILDREN WITH SEVERE THERAPY-RESISTANT ASTHMA


Background Children with severe therapy-resistant asthma (STRA) are refractory to treatment despite optimal management. Assessment of airway inflammation to phenotype these patients can enable targeted therapy. Samples obtained at bronchoscopy provide the most direct measure of lower airway inflammation; however, non-invasive measures (induced sputum and exhaled nitric oxide (FeNO)) are of greater clinical utility. We have previously demonstrated a poor relationship between blood and bronchoalveolar lavage (BAL) eosinophilic phenotype using clinical cut-offs for children (blood eosinophils 1.0 × 10⁹/L). Recent studies of the anti-IL-5 antibody mepolizumab have used a lower cut point (0.3 × 10⁹/L) for blood eosinophils. The aim of this study was to assess the concordance between BAL and non-invasive measures of inflammation.

Methods 113 children (aged 4–17 years) with STRA underwent bronchoscopy at the Royal Brompton Hospital. They had all previously been assessed and potentially modifiable factors such as poor adherence had been addressed. Inflammation was measured invasively using BAL cytology and non-invasively by blood eosinophils, induced sputum and exhaled nitric oxide (FeNO). The eosinophilic phenotype was defined as BAL eosinophils >1.19%; blood eosinophils ≥0.3 × 10⁹/L; sputum eosinophils ≥2.5%; and FeNO >35ppb. The relationship between measures was assessed using Spearman rank correlation and Receiver Operator Characteristic (ROC) curves were constructed to determine which cut points best determined BAL eosinophilia and positive and negative predictive values (PPV and NPV) calculated.

Results The predominant phenotype in all samples was eosinophilic. There was 75.6–77.8% concordance between the eosinophilic phenotype in BAL and each of the non-invasive measures.

Abstract P98 Table 1 The predictive value of peripheral blood eosinophils, sputum eosinophils and FeNO for BAL eosinophilia

<table>
<thead>
<tr>
<th>Blood eosinophils (×10⁹/L)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;0.15</td>
<td>89.8</td>
<td>60</td>
<td>84.1</td>
<td>71.4</td>
</tr>
<tr>
<td>≥0.3</td>
<td>80</td>
<td>68</td>
<td>85.2</td>
<td>56.7</td>
</tr>
<tr>
<td>≥0.45</td>
<td>59.3</td>
<td>84</td>
<td>89.7</td>
<td>46.7</td>
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<tr>
<td>Sputum eosinophils, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;6</td>
<td>90.9</td>
<td>38.5</td>
<td>78.9</td>
<td>62.5</td>
</tr>
<tr>
<td>≥2.5</td>
<td>78.8</td>
<td>61.5</td>
<td>83.9</td>
<td>53.3</td>
</tr>
<tr>
<td>≥5</td>
<td>63.6</td>
<td>69.2</td>
<td>84</td>
<td>42.9</td>
</tr>
<tr>
<td>FeNO (ppb)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;23</td>
<td>84.9</td>
<td>62.5</td>
<td>83.3</td>
<td>65.2</td>
</tr>
<tr>
<td>&gt;35</td>
<td>79.2</td>
<td>75</td>
<td>87.5</td>
<td>62.1</td>
</tr>
</tbody>
</table>

PPV = positive predictive value, NPV = negative predictive value.
Blood and BAL eosinophils had the strongest correlation ($r = 0.57$, $p < 0.001$, $n = 84$). Weaker correlations were found between the other measures. The most promising predictor of BAL eosinophilia was a blood eosinophil count of $0.15 \times 10^9/L$ (PPV 84.1, NPV 71.4) (Table 1). 

**Conclusions** These results suggest that blood eosinophils at a lower cut-point may be a useful measure of lower airway inflammation. However, this is still a relatively invasive test in children and there is little data available about longitudinal stability of blood eosinophils.

**REFERENCES**


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**P99**

**COLONISATION WITH FILAMENTOUS FUNGI AND ACUTE EXACERBATIONS IN CHILDREN WITH ASTHMA**

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10.1136/thoraxjnl-2015-207770.236

**Background** Children with asthma are frequently sensitised to fungi and recent observations suggest that fungal sensitisation may be associated with more severe asthma in children. Aspergillus fumigatus airway colonisation in adults with asthma is associated with reduced lung function. There is a paucity of data on fungal sensitisation in children with asthma. The role of fungi in exacerbation prone asthma has not been previously investigated. Our study aim was to evaluate the association between fungal airway colonisation and exacerbation prone asthma in children.

**Methods** Children aged 5–16 years with stable asthma who attended for a routine hospital outpatient appointment and children with an acute exacerbation of asthma who attended for urgent care to an acute admissions unit were recruited to the study. We obtained a sputum sample either via nebulisation with hypertonic saline in children with stable asthma or nebulisation with 0.9% saline in children with acute asthma. Sputum culture was focused to detect filamentous fungi, in particular Aspergillus and Penicillium species. Culture and sensitisation results were compared with clinical assessment data.

**Results** Fifty five children were recruited to the study; 26 with acute asthma and 29 with stable asthma (17 BTS step 4–5). There was no difference in demographics between the two groups (Table 1). Sixteen children (29%) were culture positive for filamentous fungi, either Aspergillus fumigatus (81.3%) or Penicillium (18.7%). One child with stable asthma harboured two different filamentous fungi, A. niger and A fumigatus. Children with acute asthma were more likely to be culture positive for filamentous fungi than children with stable asthma (42.3%, $n = 11 v 17.2%$, $n = 5$ respectively, $p = 0.041$). Of the five children with stable asthma who were culture positive for filamentous fungi, three were BTS step 4–5.

**Conclusions** Significantly more children with acute asthma had filamentous fungi isolated from their sputum compared to children with stable asthma. Aspergillus fumigatus was the most common fungus isolated. The potential role of fungal airway colonization in triggering asthma attacks in children merits further investigation.

**REFERENCES**

Conclusion VC and TH improved the children’s MDI technique which was reflected on better asthma control. VC children could not, however, maintain the acceptable IF through their MDI which is critical for aerosol lung deposition. An inhaler training tool available to patients at any time can be helpful.

Best of science advances

P101 PERIPHERAL BLOOD TYPE 2 INNATE LYMPHOID CELL COUNT IN PATIENTS WITH SEVERE EOSINOPHILIC ASTHMA

**Background** A subgroup of patients with severe asthma have persistent eosinophilic airway inflammation despite treatment with high intensity corticosteroid treatment. One possible explanation for this pattern of disease is involvement of a type 2 innate lymphoid cells (ILC2s) dependant and relatively corticosteroid resistant pathway generating type 2 cytokines such as IL-5 and IL-13. The presence of high numbers of ILC2s in the nasal polyps commonly associated with severe eosinophilic asthma supports this view. We have carried out a cross-sectional study testing the hypothesis that ILC2 counts are increased in peripheral blood of patients with severe eosinophilic asthma.

**Methods** Blood was taken from 9 controls and 33 patients with severe eosinophilic asthma. 23 of whom met the 2014 ERS/ATS guideline criteria for severe asthma and had historical evidence of eosinophilic airway inflammation as defined before (Pavord et al., Lancet 2012;380:651–9). ILC2 were measured as lineage-CD45+CD127+CRTH2+ by flow cytometry and numbers presented as total cell counts and percentage peripheral blood mononuclear cells.

**Results** ILC2 counts were repeatable within patients (ICC 0.97; n = 6). Mean ± SD ILC2 counts were 566 ± 379, 323 ± 224, 437 ± 628 and 429 ± 421 cells/mL (Figure 1A) and 0.034 ± 0.022, 0.02 ± 0.017, 0.020 ± 0.028 and 0.019 ± 0.014% of total lymphocytes (Figure 1B) in normal controls (n = 9), patients with mild to moderate asthma (n = 10), patients with severe asthma at BTS step 4 (n = 12), and patients with severe asthma at BTS step 5 (n = 11) respectively.

**Conclusion** Type 2 innate lymphoid cells are scarce in peripheral blood but can be measured consistently. We found no evidence of increased counts in peripheral blood from patients with severe eosinophilic asthma.
NE as a primary efficacy endpoint in clinical trials or as a marker of inflammation within the clinic has been hampered by the lack of a robust and simple to use assay. ProteaseTag™ Active NE Immunoassay specifically measures only active NE in clinical samples, is quick and easy to use (<3 h) and has no dependency on a kinetic readout. ProteaseTag™ technology is currently being transferred to a lateral flow device for use at Point of Care.

P103 INHIBITION OF ASTHMA-RELATED IMMUNOLOGICAL RESPONSES BY CULTURED EPITHELIAL CELL LINES


10.1136/thoraxjnl-2015-207770.240

Background Previous studies have shown that constitutive and IgE-mediated histamine production by human lung mast cells is inhibited by a transferable factor produced by the airway epithelium. We have tested the hypothesis that a similar interaction exists between epithelial cell and mast cell lines. We have also investigated the effect of co-culture of epithelial cell lines and Tp2 cells on interleukin (IL)-13 production.

Methods A549 or BEAS-2B cells were grown to confluence overnight. Media was removed and LAD2, HMC1.2 or human-derived ex-vivo T-cells added for 16 h. For transwell experiments epithelial cells were added to a 24-well plate, replaced with fresh media after 16 h and mast cells media added to the insert, maintaining the mast cell/epithelial/volume ratio. Wells, and transwell insert media, were then centrifuged, supernatants harvested and mediator release quantified by histamine or IL-13 ELISA.

Results Neither mast cell line consistently produced histamine in response to IgE and anti-IgE. Flow cytometry suggested that this was due to absence of the high-affinity IgE receptor FceRI. Constitutive histamine production by HMC1.2 was reduced from 191 ± 13 ng/10⁶ cells by 60.9% (95% CI 54.1, 67.8; p < 0.0001) when co-cultured with A549 and 21% (95% CI 14.2, 28.1; p < 0.0001) with BEAS-2B cells. Similar findings were seen with the LAD2 mast cell line. Constitutive IL-13 production by Tp2 cells was reduced from 18000 ± 1800 pg/10⁶ cells by 68.6% (95% CI 62.0, 75.1; P < 0.0001) by A549 and 59.9% (95% CI 53.3, 66.5; p < 0.0001) by BEAS-2B. Epithelial inhibition was similar when cells were separated by a transwell suggesting involvement of a transferable factor.

Abstract P103 Figure 1

- 24-hour constitutive histamine (left) and IL-13 (right) release from mast or T-cells in the presence or absence of epithelial cell lines

Conclusion Epithelial cell lines inhibit a range of asthma-related immunological responses, probably by producing an inhibitory substance.

P104 STRUCTURAL AND CELLULAR RELATIONSHIPS IN THE PERIPHERAL LUNG: COMBINING MICRO-CT AND IMMUNOHISTOCHEMISTRY

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10.1136/thoraxjnl-2015-207770.241

Introduction and objectives The peripheral lung contains a range of structural elements (small airways, blood vessels and lymphatics) together with infiltrating inflammatory cells. These components exist together in complicated spatial arrangements. Lung disease is frequently accompanied by changes in both lung architecture and the number and distribution of inflammatory cells. Light microscopy has been the conventional technique of choice in understanding these changes and relationships but provides only 2-D representations of a complex 3-D network.

We selected to use micro computed tomography (μ-CT) to image structural elements in the peripheral lung. We aimed to reconstruct the 3-D architecture by combining the μ-CT data with immunohistochemistry (IHC) to positively identify the principal structural elements and inflammatory cells.

Methods Human lung tissue was fixed in formalin, embedded in paraffin wax and subjected to μ-CT scanning. The tissue was then sectioned and immunostained for pancytokeratin (airways), collagen IV (blood vessels), D2-40 (lymphatic vessels) and CD68 (macrophages). The resulting images were used to guide the segmentation of the 3-D μ-CT image stack. IHC, using neurofilament antibodies, was also used on multiple lung samples to attempt to identify nerve fibres in the parenchymal tissue.

Results The main structural elements of the lung periphery could be identified, segmented out and their 3-D architecture examined. Macrophages were found throughout the tissue in large quantities and were most concentrated around the blood vessels and lymphatics. Lymphatic vessels were especially dense in the pleural region and elsewhere were intertwined with blood vessels. Despite being readily identifiable in bronchial samples, nerve fibres were not identified using IHC in the parenchyma.

Conclusions Combining μ-CT and IHC provides a robust method to positively identify important structural elements of the peripheral lung and to localise inflammatory cells in 3-D, thus allowing a detailed review of their spatial relationships. Alternative methodologies may however be advantageous regarding identifying parenchymal nerve fibres for reconstruction. μ-CT and IHC together create a highly accurate 3-D reconstruction but this method remains time consuming; advances in automation and improved tools are required to fully exploit the research potential.

P105 IDENTIFICATION OF ‘LARGE’ ALVEOLAR MACROPHAGES AND PULMONARY INTRA-VASCULAR MACROPHAGES IN COPD PATIENTS

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10.1136/thoraxjnl-2015-207770.242

Background A population of small macrophages with increased pro-inflammatory activity has been reported in COPD sputum. We have investigated macrophage size in the alveoli of COPD
patients using immunofluorescence for the markers CX3CR1 and CD68.

**Methods** Formalin fixed paraffin embedded tissue blocks were obtained from an area of the lung as far distal to the tumour as possible from COPD patients, smokers (S) and healthy non-smokers (HNS) undergoing lung resection for lung carcinoma. Sections were labelled with an anti-CX3CR1 antibody and detected using an Alexafluor conjugated secondary antibody. Immunohistochemical detection of CD68 (enzymatic non-biotin amplification technique) confirmed the macrophage phenotype of CX3CR1+ cells.

**Results** All CX3CR1+ cells expressed CD68. The diameters of COPD macrophages were greater than controls (Table 1). Intra-vascular CX3CR1+CD68+ macrophages were observed in COPD and S (Table 1).

<table>
<thead>
<tr>
<th>Abstract P105 Table 1</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>COPD (n = 9) S (n = 9) HNS (n = 6)</td>
</tr>
<tr>
<td>25th percentile (µm)</td>
</tr>
<tr>
<td>Median (µm)</td>
</tr>
<tr>
<td>75th percentile (µm)</td>
</tr>
<tr>
<td>Vessels with intra-vascular macrophages (%)</td>
</tr>
</tbody>
</table>

The Kruskal-Wallis test with application of Dunn’s post-test was used to determine the statistical significance of differences observed in the alveolar macrophage diameter between the three groups. *p < 0.0001 against COPD.

**Conclusion** Increased macrophage size in COPD may be linked to altered function. Pulmonary intravascular macrophages have been observed in other mammalian species and may promote pulmonary inflammation through direct release of cytokines into the pulmonary circulation.

**P106** **TISSUE FACTOR PATHWAY INHIBITOR (TFPI) IS CLEAVED BY MULTIPLE PROTEASES IN COPD LUNGS TO AFFECT CIRCULATING TFPI LEVELS**

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**Background** Tissue factor pathway inhibitor (TFPI) attenuates intravascular coagulation, a function limited by its proteolysis. Airway inflammation in COPD is associated with protease activity and intravascular thrombotic events, yet the link between proteolysis of TFPI in the airways and intravascular thrombosis in COPD is unexplored.

**Aims** To explore the presence and processing of TFPI in COPD airways and its relationship to plasma TFPI levels.

**Methods** COPD sputum and blood were collected at exacerbation and when stable. In vitro cleavage of TFPI was explored by incubation with proteases and Western blotting. TFPI presence and cleavage in sputum was detected by Western blotting. To determine the main protease/s involved in TFPI cleavage, sputum was spiked with recombinant TFPI in the presence of protease inhibitors, followed by Western blotting.

**Results** TFPI was cleaved in vitro by Matrix Metalloproteinase (MMP)-12, Neutrophil Elastase (NE) and urokinase-type plasminogen activator (uPA) to <20.

**Conclusion** TFPI is cleaved by NE in COPD airways, leading to lower circulating levels. Further studies are needed to determine if lower circulating TFPI levels lead to increased intravascular thrombotic events in COPD.

**P107** **FUNCTIONAL SIGNIFICANCE OF THE NITRIC OXIDE-ASYMMETRIC DIMETHYLARGININE-DIMETHYLARGININE DIMETHYLAMINOHYDROLASE (NO-ADMA-DDAH) AXIS IN TGF-β MEDIATED EPITHELIAL-MESENCHYMAL TRANSITION**

HK Lota, JM Leiper. Nitric Oxide Signalling Group, MRC Clinical Sciences Centre, Imperial College London, London, UK

**Background** Transforming growth factor (TGF)-β is a key mediator of epithelial-mesenchymal transition (EMT), a pathogenic
Sleep services: current delivery and future directions


P108 QUALITY OF LIFE, DIET AND EXERCISE MEASUREMENTS IN OBESE INDIVIDUALS WITH AND WITHOUT VENTILATORY FAILURE


Introduction Obesity is associated with reduced quality of life (QOL), particularly physical health. In addition obesity has been linked to reduced exercise and high calorie diet. We aimed to describe these factors in obese individuals with and without ventilatory failure, and investigate the hypothesis that ventilatory failure would have a negative impact on QOL.

Methods QOL, diet and exercise was assessed as part of an open cross-sectional study of ventilatory failure in obese subjects referred either for assessment of sleep disordered breathing or bariatric surgery.

The SF-12 was completed; a validated questionnaire to assess QOL giving summary scores for physical health (PCS) and mental health (MCS), and compared to data from a large non-obese UK cohort. Participants underwent actigraphy (SenseWear BodyMedia) and from this the daily energy expenditure was estimated. A sedentary lifestyle was defined as <5000 steps/day.

Results 72 individuals with a mean age of 52.0 years (SD 8.9) and median BMI of 46.7 kg/m² (IQR 39.5, 52.6) participated in the study. Median duration of actigraphy was 23.2 days (IQR 21.2, 23.4).

Arterial base excess was significantly and weakly correlated to MCS (r = 0.33, p = 0.01) but not to PCS (r = 0.05, p = 0.74).

Conclusions Obesity had a large negative impact on both physical and mental QOL not reproducibly reported elsewhere. Ventilatory failure was only a weak predictor of mental, but not physical QOL scores. The majority of participants were sedentary and dietary calorie intake was higher than the recommended daily allowance for most women and a significant number of men. Actigraphy energy expenditure estimates exceeded patient reported dietary intake, which is probably due to patient underreporting. This highlights the clinical importance of considering mental health, physical activity and diet together when obese individuals are seen in a tertiary centre.

REFERENCE


Poster sessions

Abstract P108 Table 1 Results of SF-12, actigraphy, food frequency questionnaire and arterial blood gasses

<table>
<thead>
<tr>
<th>N</th>
<th>Study mean or median</th>
<th>SD or IQR</th>
<th>95% confidence interval of difference from comparison mean</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>PCS</td>
<td>72</td>
<td>38.0</td>
<td>11.3</td>
<td>-16.4, -11.3</td>
</tr>
<tr>
<td>MCS</td>
<td>72</td>
<td>41.2</td>
<td>10.6</td>
<td>-10.2, -5.0</td>
</tr>
<tr>
<td>Energy expenditure (kCal)</td>
<td>72</td>
<td>2977</td>
<td>566</td>
<td></td>
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<tr>
<td>Daily steps</td>
<td>72</td>
<td>3169</td>
<td>2141</td>
<td>5242</td>
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<tr>
<td>Dietary energy (kCal)</td>
<td>72</td>
<td>2434</td>
<td>1760</td>
<td>3348</td>
</tr>
<tr>
<td>Men</td>
<td>41</td>
<td>2434</td>
<td>1760</td>
<td>3348</td>
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<tr>
<td>Women</td>
<td>31</td>
<td>2434</td>
<td>1760</td>
<td>3348</td>
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<tr>
<td>Arterial base excess (mmol/l)</td>
<td>72</td>
<td>2.08</td>
<td>2.41</td>
<td>48.6% had a raised arterial base excess (&gt;2 mmol/l)</td>
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<tr>
<td>Arterial PaCO₂ (kPa)</td>
<td>72</td>
<td>5.57</td>
<td>0.80</td>
<td>22.2% had a raised PaCO₂ (&gt;6 kPa)</td>
</tr>
</tbody>
</table>
Predicting Difficult Mechanical Ventilation in Obese Patients Undergoing Laparoscopic Surgery: An Observational Study

D Hallsworth, R Wingate, A Klucniks, A Manuel. Oxford Centre for Respiratory Research, Oxford Biomedical Research Centre, Churchill Campus, Oxford University Hospitals NHS Trust, Oxford, UK

10.1136/thoraxjnl-2015-207770.246

Introduction

Morbid obesity and super obesity are associated with increasingly negative effects on respiratory parameters, but beyond BMI itself the physical predictors of difficult intraoperative ventilation have not been demonstrated. We performed a study to identify criteria for the prediction of difficult intraoperative mechanical ventilation in obesity patients.

Method

We performed an observational study of 48 obese patients (BMI >35 kg/m²) undergoing laparoscopic surgery (bariatric, upper gastrointestinal and gynaecological). Patients with conditions likely to affect respiratory compliance, e.g. thoracic or spinal deformity were excluded.

We analysed biometric measurements such as age, sex and BMI, waist, hip and neck circumferences, waist: hip ratio, STOP-BANG scores, presence of obstructive lung disease and pre-operative oxygen saturation measurements. Respiratory mechanics were assessed pre- and post-pneumoperitoneum using standard Pitot pneumotachograph measurements, including tidal volumes, peak pressures, positive end-expiratory pressure and dynamic respiratory compliance.

Differences in ventilator strategy (e.g. volume-control versus pressure-control and tidal volume delivered) were analysed post-hoc.

Results

See Figures 1 and 2. Our study demonstrated a statistically significant correlation between BMI and increased peak pressures both pre- and post-pneumoperitoneum (p < 0.01).

Abstract P109 Figure 1 Showing relationship between BMI and Peak Pressure. Peak Pressure: cmH₂O, BMI: kg/m². Our study demonstrated a statistically significant correlation between BMI and increased peak pressures both pre- and post-pneumoperitoneum (p < 0.01).

The difference between volume-controlled and pressure-controlled strategies were analysed and shown not to be significant.

Conclusion

Our novel study shows increasing BMI has a negative influence on respiratory mechanics of the anaesthetised obese patient. It is important to stress that while BMI is the strongest predictor of increased peak pressure and reduced respiratory compliance, patient positioning and lung recruitment can have positive effects on respiratory mechanics. Further studies are needed to help identify predictors of difficult ventilation in obesity.

A Review of Persistent Hypercapnia and Subsequent Referral for Obese Patients Admitted into an Intensive Care Unit

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10.1136/thoraxjnl-2015-207770.247

Introduction

Obesity hypoventilation syndrome (OHS) is increasingly common but data detailing the prevalence, outcome and long-term management, in patients admitted to the ICU, are limited. Indeed, we aimed to assess the prevalence of persistent hypercapnia in obese patients admitted to ICU and subsequent referral rate for specialist long-term management of sleep disordered breathing.

Methods

A retrospective analysis of data that was prospectively entered into an electronic patient record was conducted, from May 2011 to May 2014, at a University Hospital. Obesity was defined as a body mass index (BMI) (>35 kg/m²) and hypercapnia as an arterial partial pressure of carbon dioxide (PaCO₂) >6 kPa. All patients meeting both criteria were reviewed to assess whether these patients were referred to the regional sleep and ventilation unit.

Results

A total of 5014 patients were ventilated in critical care of which 240 (5%) had obesity with persistent hypercapnia (age 49 ± 14 years, BMI 41.5 ± 6.7 kg/m², PaCO₂ 7.5 kPa). 27% percent (65/240) were referred for assessment of sleep disordered breathing. Referred patients were more likely to have respiratory comorbidity (p < 0.001) and were more obese (ΔBMI 3.1 kg/m², p < 0.001) but of similar age (p = 0.977) and degree of hypercapnia (p = 0.474). Patients referred for assessment of sleep disordered breathing had improved survival compared to those who were not referred (980 days v 1271 days, log rank test p = 0.004, Figure 1).
Abstract P110 Figure 1

Conclusions Rates of obesity and persistent hypercapnia are high in survivors of critical illness. However, patients are frequently not referred for specialist respiratory assessment. Survival is increased in patients referred for long-term management, although this data needs to be interpreted with caution as this could be the result of referral bias and a prospective study is now required.

P111 RESPIRATORY FLOW LIMITATION IN THE ABSENCE OF OBSTRUCTIVE SLEEP APNOEA Responds to CPAP THERAPY

B Chakrabarti, S Emegbo, S Craig, J Heseltine, T Wright, N Duffy, JF O'Reilly. University Hospital Aintree, Liverpool, UK

Background The Apnoea–Hypopnoea index (AHI) is regarded as a gold standard diagnostic marker of Obstructive Sleep Apnoea Syndrome (OSAS). However, a number of patients present with excessive daytime sleepiness (EDS), yet exhibit a raised Respiratory Disturbance Index (RDI), comprising of flow limited breaths in the presence of a normal AHI (<5 events/hr). We sought to evaluate the benefits of CPAP in this “Flow Limitation” cohort compared to a matched population of OSAS subjects.

Results 27 subjects (Mean age 47 (SD 8) years; ESS 17(4); 48% male; BMI 35.60 (8.12)) presented to our Sleep Service with EDS and undertook a cardio-respiratory polysomnograph, demonstrating an RDI >15 and AHI <5 (Mean RDI 16 (4); AHI 3 (2); ODI 5(3)) 25 subjects were subsequently treated with CPAP. At “6-week compliance” visits, 20 (80%) were deemed compliant with CPAP (mean nightly usage 6.03 (1.47) hrs; pre-CPAP ESS 18(3) falling to 9 (4) following CPAP. Within the Flow Limitation cohort, statistically significant associations were observed between CPAP compliance and Female gender (100 v 55%), higher BMI (36.61 v 31.56), higher pre-CPAP ESS (18 v13) and lower Pulse Transit Time PTT (300.90 v 316 ms).

This “Flow Limitation” cohort was compared with an age/ gender matched “OSAS “cohort (ESS 15(5); BMI 38.33 (7.80) AHI 58.16 (25.79) ODI 48 (23)). 26 OSAS subjects were treated with CPAP with 19 (70%) deemed compliant (nightly usage 5.25 (3.55) hrs; pre-CPAP ESS 16 (5) falling to 10(5) following CPAP. Whilst the mean PTT of the OSAS cohort was lower than the “Flow Limitation” cohort, this did not reach statistical significance (298.85(15.04) v 306.44 (18.36) ms; ANOVA; p = 0.1) yet the PTT Deceleration Index (DI), a surrogate of physiological arousal, was significantly higher in the OSAS cohort (59.05 (29.33) v 36.32(23.69)/hour; ANOVA; p = 0.003).

Conclusion “Sleepy” subjects exhibiting an elevated Flow Limitation Index in the presence of a normal AHI appear to demonstrate a response to CPAP therapy comparable to that observed in OSAS. Female gender and a higher BMI appear to predict compliance with therapy, whilst the utility of Pulse Transit Time in guiding decision making in “sleepy” subjects with a normal AHI merits further study.

P112 CPAP ROLE ON THE PERIOPERATIVE OUTCOMES OF PATIENTS WITH OBSTRUCTIVE SLEEP APNOEA

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Background Obstructive sleep apnoea (OSA) has been previously reported as an independent risk factor for intra and post operative adverse events.

Early diagnosis of sleep disordered breathing and initiation of CPAP treatment was suggestive to improve operative outcomes.

Objectives To determine the prevalence of sleep apnoea in a surgical population and establish the role of CPAP on peri-operative outcomes in patients with OSA.

Methods A retrospective study was performed in a university hospital between 1st June 2013 and 1st June 2015 and included 160 surgical patients investigated for OSA. Sleep apnoea was defined as dip rate >10 events/hour associated with a desaturation of 4% below the baseline. Statistical analysis was performed with STATA v10 software.

Results From 160 surgical patients included, 33.1% (53) were females and average age was 54 years. Prevalence of OSA was 44.3% (71/160) and 12.5% (20/160) had severe OSA defined as a dip rate >30 events/hour.

Following sleep investigations, 68 patients had surgical interventions: 48.5% (33/68) trauma and orthopaedics, 17.6% (12/68) general surgery, 10.2% (7/68) urology, 8.8% (6/68) gynaecology, 7.3% (5/68) colorectal, 4.4% (3/68) ENT. From 68 patients undergoing surgical procedures, 44.1% (30/68) were diagnosed with OSA and started on CPAP prior to surgery.

Peri-operative adverse events were not significantly related to OSA when compared to non OSA patients: intra operative desaturations (23.3% vs 26.3%) and prolonged recovery stay (53.3% vs 55.2%).

OSA patients had a lower hospital stay compared to non OSA group (1.7 vs 3.1 days).

Conclusions We have identified a high prevalence of sleep apnoea of 44% in surgical population. CPAP treatment was found effective in improving operative outcomes of patients with OSA, further studies being needed to confirm these results. Routine pre-assessment screening for OSA followed by sleep investigations for initiation of CPAP prior to surgery is recommended.

REFERENCES
2 Gross JB, et al. Practice guidelines for the perioperative management of obstructive sleep apnea: ASA task force on perioperative management of OSA. Anesthesiology 2014;120
P113 CLINICAL USE OF ADAPTIVE SERVO-VENTILATION ACROSS THE UK: RESULTS OF A POSTAL SURVEY

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Introduction Adaptive Servo-Ventilation (ASV) is used to treat central sleep apnoea (CSA), but evidence for its use is limited. A large trial, SERVE-HF, randomised patients with CSA and left ventricular heart failure to ASV or control. Their results led to a field safety notice in May 2015, advising ASV is contraindicated in patients with symptomatic chronic heart failure and reduced ejection fraction. Sleep Centres therefore reviewed ASV in clinical practice; we sought information about ASV use in the UK.

Methods A survey was sent to 187 UK sleep centres, asking about the use of ASV.

Results Seventy-five surveys were returned (40% response rate). ASV was not used in 53% of centres.

Of the 47% (n = 35) of sleep centres using ASV, the average number of patients on ASV per centre was 13 (range 1–69). For comparison, the average number on CPAP was 3368 (range 100–12000).

Of the 454 patients using ASV, the reasons are shown in Table 1.

<table>
<thead>
<tr>
<th>N (total 454)</th>
<th>%</th>
<th>CSA with Cheyne Stokes Respiration (CSR)</th>
<th>Central</th>
<th>Mixed sleep apnoea</th>
<th>Reasons not stated/unclear</th>
<th>Complex sleep apnoea</th>
<th>Due to opioid/narcotic use</th>
<th>Other causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>149</td>
<td>33</td>
<td>CSA with Cheyne Stokes Respiration (CSR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>126</td>
<td>28</td>
<td>“Central”</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61</td>
<td>13</td>
<td>Mixed sleep apnoea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61</td>
<td>13</td>
<td>Reasons not stated/unclear</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>5</td>
<td>Complex sleep apnoea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>5</td>
<td>Due to opioid/narcotic use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>3</td>
<td>“Idiopathic”/other causes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Following the field safety notice, 66% of centres reviewed patients in clinic. Others contacted patients by phone (45%) or in writing (31%), or used a combination of these. Five centres did not contact their patients and five centres had to run between one and two additional clinics to review their ASV patients. Some repeated echocardiography.

Seventy-two (48%) CSA-CSR patients were advised to stop using ASV. Fifteen chose to continue, 32 changed to CPAP/NIV, 14 stopped ASV, 11 were not specified.

Clinicians rated ASV as very useful (26%), quite useful (23%) and occasionally useful (49%).

Conclusions There is a wide range of clinical ASV use in sleep centres across the UK; many do not use it. Apart from SERVE-HF, there are few randomised clinical trials to inform who would benefit from ASV. Use may be determined by case series, expert opinion and individual response. This highlights the need for further research in this area.

P114 CAN A DEDICATED ‘FAST TRACK’ SLEEP SERVICE SUCCESSFULLY ESTABLISH VOCATIONAL DRIVERS ON CPAP WITHIN FOUR WEEKS OF REFERRAL?

BAM Downie, G Gids, M Tomlinson, SD West. Newcastle Regional Sleep Service, Freeman Hospital, Newcastle Upon Tyne, UK

Introduction and objectives Sleepiness due to Obstructive Sleep Apnoea (OSA) can impair driving, and OSA has been implicated in road traffic accidents. DVLA guidelines state that those with “sleepiness sufficient to impair driving” should cease driving until they have been investigated and treated. This may have a significant effect on the ability of vocational drivers to earn a living. Fear of lengthy investigations and licence regulations may deter these patients from seeking treatment. We developed a dedicated service that aimed to diagnose OSA and successfully establish vocational drivers on CPAP within 4 weeks of referral.

Methods The service was advertised to local GPs, encouraging identification of vocational drivers at point of referral. Patients were seen by a nurse specialist and underwent domiciliary sleep studies, returning the following day for results and CPAP therapy. Those who were not identified via GP referral were fast-tracked from first clinic appointment. Compliance and Epworth Sleepiness Score (ESS) were evaluated after one week of treatment on CPAP, or as soon as the patient could attend thereafter.

Results Between September 2014 and July 2015, 29 drivers were referred; one failed to attend. Fifteen held a type 1 drivers’ licence and 13 a type 2 licence. At presentation, the mean age was 48 years (range 25–61), mean BMI was 34 (27–51) and mean ESS was 10 (0–21). Sleep studies showed a mean ODI of 30 (0–93), with moderate or severe OSA in 18 (64%). Twenty two patients were commenced on CPAP (79%). Seventeen patients attended for review on CPAP, a mean of 16 days after initiation. Mean ESS was 5.4 and mean CPAP usage was 5.3 h/night. Of these, six people were reviewed between six and eight days after CPAP initiation; their mean compliance was 6.2 h/night (4.1–8.3). Mean time from referral (or first clinic visit) to review on CPAP was 33 days.

Conclusion A fast track service is practical and effective at diagnosing OSA and establishing vocational drivers on CPAP. There were some delays due to patient non-attendance or re-scheduling. It is vital that GPs are aware of the service and refer patients as vocational drivers.

P115 OUTCOMES OF SLEEP STUDIES AND TARGETED THERAPIES IN PATIENTS WITH MYOTONIC DYSTROPHY: A COHORT STUDY

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Patients with myotonic dystrophy (DM) have complex respiratory and neurological disease. Sleepiness is common. We describe a prospective cohort study of patients with DM and response to sleep treatments.
Methods DM patients with daytime sleepiness or symptoms of respiratory failure were referred to the Regional Sleep Centre. They were admitted overnight for sleep study and respiratory assessment. If there was central hypoventilation causing respiratory failure, or obstructive sleep apnoea (OSA), they were offered non-invasive ventilation (NIV) or continuous positive airway pressure (CPAP) respectively. People without sleep disordered breathing with daytime sleepiness were assessed for modafinil, an alerting drug.

Results From May 2011 to May 2015, 120 people with DM had investigations. Mean age was 47 (SD 13, range 18–74), mean BMI 28 kg/m² (7, 16–53) and mean Epworth Sleepiness Score 13 (5, 2–24). Mean Muscular Impairment Rating Scale was 3.85 (0.7, 2–5).

Mean FEV1 was 70% predicted (SD 22), FVC 68% predicted (27), with a >15% supine fall in FVC in 18%. PI max, PE max was 3.85 (0.7, 2)

Score 13 (5, 2

35% of the total cohort gained benefit from CPAP, NIV or modafinil, an alerting drug.

Conclusions DM is a heterogeneous disorder, with varying BMI, sleepiness, muscular and respiratory impairment. Overall, only 35% of the total cohort gained benefit from CPAP, NIV or modafinil and continued with this therapy.

Abstract P116 Figure 1 Patient characteristics. ESS = Epworth Sleepiness Score, ODI = Oxygen Desaturation Index, AHI = Apnoea Hypopnoea Index

Discussion and conclusion In contrast to the meta-analysis (Greenburg et al. 2009) in which 62% had residual disease in our cohort 80% had clinical cure and they had a lower post-op ODI (7.1) in spite of comparable weight loss. Even though our patients had similar pre-op BMI but the mean pre-op ODI was less than most reported studies the reason for which is not clear but might be responsible for a much higher cure rate.

REFERENCE

P116 IMPACT OF BARIATRIC SURGERY ON OSAS: A 4-YEAR EXPERIENCE

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Background Obstructive Sleep Apnoea Syndrome (OSAS) is common in morbidly obese patients. Previous studies indicate bariatric surgery reduces the severity of OSAS but may not cure it. We explored the impact bariatric surgery on patients who were observed on CPAP prior to surgery.

Methods All morbidly obese patients who underwent bariatric surgery at our institution between June 2010 and May 2014 who underwent sleep study (SS) or oximetry prior to bariatric surgery were included. The primary end point was cure (oximetry off CPAP showing either ODI less than 5 or ODI 5–15 with ESS <10 and no other symptoms of SDB) from OSAS. Secondary end points were weight loss achieved, improvement in OSAS and improvement in ESS. All data were obtained from electronic bariatric surgery and sleep service databases.

Results 184 patients underwent bariatric surgery. 97 (52.7%) had SS or oximetry prior to surgery. (Figure 1) Mean ODI was 25 (95% CI 19–30) and ESS 12 (95% CI 10–13). Out of 46 patients considered for CPAP, 45 continued using CPAP peri-operatively, one discontinued after failed trial, 20 (43.4%) patients were considered cured from OSAS by 12–24 months, 17 (36.9%) patients became asymptomatic and returned CPAP were considered to be cured clinically but not had SS post surgery. At 12 months post bariatric surgery, there were significant (P < 0.0001) reductions in various parameters; means of difference in ODI 34, ESS 10 and BMI 17.8.

P117 COMPARISON OF THE EFFECTS OF CONTINUOUS POSITIVE AIRWAY PRESSURE AND MANDIBULAR ADVANCEMENT DEVICES ON SUBJECTIVE DAYTIME SLEEPINESS IN PATIENTS WITH OBSTRUCTIVE SLEEP APNEA: A NETWORK META-ANALYSIS

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Background Obstructive sleep apnoea (OSA) is associated with increased daytime sleepiness. Previous meta-analyses have shown that both continuous positive airway pressure (CPAP) and mandibular advancement devices (MADs) reduce the Epworth Sleepiness Score (ESS), a common measure of daytime sleep propensity. However, no meta-analysis has yet identified which treatment is superior in reducing ESS, perhaps due to a lack of studies directly investigating the two treatments. In addition, the effect of CPAP usage on ESS has yet to be thoroughly explored.

Methods We searched Medline and the Cochrane Library up to the end of May 2015 to identify randomised controlled trials in OSA investigating the effect of CPAP and/or MADs against each other or an inactive control (IC, placebo or no treatment) on ESS. A network meta-analysis was used to incorporate both
direct and indirect evidence to estimate the difference between the three treatment groups on ESS. Meta-regression was used to assess the influence of CPAP usage and average baseline patient characteristics on the effect of CPAP compared to ICs.

**Findings** A total of 67 studies comprising 6873 patients were included in the meta-analysis. Of these, 51 (5898 patients) assessed CPAP against an IC. CPAP and MADs were estimated to reduce ESS by 2.5 (95% CI 2.1,2.9) and 1.7 (95% CI 1.1,2.3) points respectively compared to an IC. CPAP was estimated to reduce the ESS by a further 0.8 points compared to MADs (95% CI 0.1,1.4; p = 0.015). However, there was some suggestion of publication bias in favour of CPAP which may have inflated this effect. There was no evidence that studies reporting higher CPAP usage also reported larger treatment effects.

**Interpretation** Both CPAP and MADs are effective treatments for reducing daytime sleepiness in patients with OSA. CPAP appears to be the most effective treatment and should be recommended for more severe or sleepier OSA patients. However, MADs are a suitable second-line treatment should CPAP not be tolerated.

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**P118 FACTORS AFFECTING CONCORDANCE WITH CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP) IN OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS)**

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10.1136/thoraxjnl-2015-207770.255

**Introduction and objectives** The benefits of continuous positive airway pressure in the treatment of obstructive sleep apnoea syndrome have been well established. Despite this, CPAP adherence remains a significant issue resulting in many patients not receiving adequate treatment. A number of variables have been suggested as contributing to non-concordance, however study results have been inconsistent. Studies assessing long term concordance, suggest severity of OSAS and sleepiness to be good predictors of this. This scientific survey looked at the influence of co-morbidity and the severity of OSAS as represented by apnoea hypopnoea index (AHI) at diagnosis and usage and concordance with CPAP.

**Methods** Data from 230 patients completing annual follow up after initiation of CPAP by 31st December 2014 was collected retrospectively. The presence and severity of co-morbidity was assessed by the Adult Co-morbidity Evaluation- 27 (ACE-27) score. CPAP usage per day was averaged over the preceding year. The association between usage and initial AHI (data available for 207 patients) was analysed by linear regression. The association between usage and ACE-27 score was analysed by ANOVA.

**Results** The regression coefficient for initial AHI against CPAP usage shows a statistically significant effect (p = 0.00126) fitted equation: concordance = 4.161 + 0.024 × AHI). There was no significant difference in CPAP usage between different ACE-27 groups. Further analysis of individual co-morbidities revealed significance in four categories; cardiac arrhythmia (p = 0.031), coronary artery disease (p = 0.006), congestive heart failure (p = 0.045) and malignancy (p = 0.001).

**Conclusion** AHI at diagnosis remains a strong determinant of CPAP concordance at 1 year. Severity of co-morbidity cannot be conclusively demonstrated to influence usage however further studies into overall and specific co-morbidities are warranted.

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**Phenotypes and response to treatment in COPD**

**P119 CHARACTERISING NON-EOSINOPHILIC COPD**

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10.1136/thoraxjnl-2015-207770.256

**Background** Phenotypes of COPD are increasingly recognised, with classification centred on inflammation and in particular microbes and inflammatory markers within the airways and peripheral blood. Studies focusing on eosinophilic inflammation in COPD have shown the validity of airway and peripheral eosinophilia as a marker to direct treatment with corticosteroids. However, the majority of COPD patients have low sputum and peripheral eosinophils, with a large proportion showing raised sputum neutrophils at exacerbation and stable state. The characteristics of this ‘Non-eosinophilic’ group are less well defined, making the identification of biomarkers and target pathways for drug development more challenging.

**Methods** Baseline data from patients with COPD, previously recruited to a study identifying biomarkers was analysed using SPSS (SPSS version 22, IBM Corp, released 2013, Armonk, NY). A cut off of 3% sputum eosinophils was used to distinguish ‘Eosinophilic’ and ‘Non-eosinophilic’ groups. Parametric and non-parametric analyses were performed where appropriate.

**Results** Of 149 patients, 96 had <3% sputum eosinophils, with a median age of 69.5 years (47–88 range). There were no differences in gender and proportion of smokers between the two groups. There was an increase in percentage sputum neutrophils in the non-eosinophilic group (mean difference 13%, 95% confidence interval 9–17%, p = 0.01). The non-eosinophilic patients had more exacerbations/person/year compared to the eosinophilic group (3.52 vs. 3.11); this was independent of inhaled corticosteroid use. There were more significant co-morbidities in the non-eosinophilic group compared to the non-eosinophilic group (78% vs. 61%, p < 0.01). Co-morbidity was defined as the presence of cardiovascular disease, endocrine disorders, depression, or musculoskeletal disease.

There were more positive sputum cultures in the non-eosinophilic group compared to the eosinophilic group (33% vs. 11%, p = 0.16). There was also an increase in colony forming units in the non-eosinophilic group compared to the eosinophilic group (mean fold difference 0.4, 95% CI 0–0.8, p = 0.05).

![Abstract P119 Figure 1](image-url) Venn diagram showing relationship of characteristics of eosinophilic (a) and non-eosinophilic (b) COPD, using absolute numbers
Conclusions Non-eosinophilic COPD subjects have more exacerbations, with more co-morbidities and bacterial burden (see Figure 1). Further work is required to understand the pathogenesis of this phenotype.

**Poster sessions**

### P120

**REAL LIFE DISTRIBUTION OF COPD SEVERITY IN THE GERMAN DACCORD REGISTRY: LUNG FUNCTION IS THE MAIN DRIVER OF CLASSIFICATION IN GOLD GROUP C AND D**

1H Worth, 1R Buhl, 1C-P Crie, 1P Kardos, 1C Maalaender, 1CF Vogelmeier. 1Facharztforum Fuertth, Fuertth, Germany; 1Pulmonary Department, Mainz University Hospital, Mainz, Germany; 1Department of Sleep and Respiratory Medicine, Evangelical Hospital Goettingen-Weende, Boeveden, Germany; 1Novartis Pharma GmbH, Nuremberg, Germany; 1Department of Respiratory Diseases, University of Marburg, Marburg, Germany

Introduction Currently there is limited real-life data available regarding the distribution of COPD patients using the GOLD 2011 criteria. The German DACCORD registry that collects data from a large ‘real life’ population sample was used to categorise COPD patients according to GOLD 2011.

Methods To be eligible for entry into DACCORD, all patients had to have a diagnosis of COPD (consistent with the German Disease Management Programme definition), and, prior to entry, to have either newly initiated bronchodilator maintenance medication, or to have a bronchodilator added to their maintenance regimen. No other inclusion criteria were applied, and the only exclusion criterion was a diagnosis of asthma. In primary and secondary care, data were collected from 4,123 COPD outpatients, including spirometry, exacerbations, CAT and mMRC.

Results The mean age of patients was 65.7 years with 40.3% of patients still working and 73.3% patients with duration of disease ≥1 year. Based on mMRC 0–1, 37.2% of patients had few symptoms (A and C); using CAT <10, only 9.0% were categorised into these two groups. 32.5% of the patients were assigned to C and D groups solely due to FEV1 <50%.

After 12 months, 41.4% patients in GOLD A were categorised in a higher GOLD category, while 42.7% of GOLD D patients were categorised in a lower GOLD category (GOLD categorization based on CAT). 67.6% of patients categorised as D at baseline due to exacerbation history alone were categorised as GOLD B after 1 year follow-up.

Almost 80% of GOLD B patients were still categorised as GOLD B after the observation period of 12 months and were therefore the most stable subgroup with regards to COPD severity according to GOLD 2011 (Figure 1).

<table>
<thead>
<tr>
<th>GOLD 2011 at 12 months</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D1*</th>
<th>D2*</th>
<th>D3*</th>
</tr>
</thead>
<tbody>
<tr>
<td>(N of total)</td>
<td>370 (94.9%)</td>
<td>2,164 (54.3%)</td>
<td>1,259 (32.5%)</td>
<td>606 (43.9%)</td>
<td>169 (43.9%)</td>
<td>160 (43.3%)</td>
</tr>
<tr>
<td>A</td>
<td>282 (73.9%)</td>
<td>136 (6.3%)</td>
<td>68 (3.4%)</td>
<td>2 (0.2%)</td>
<td>7 (2.2%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>B</td>
<td>174 (66.4%)</td>
<td>142 (5.1%)</td>
<td>310 (11.3%)</td>
<td>15 (6.1%)</td>
<td>114 (43.9%)</td>
<td>68 (25.7%)</td>
</tr>
<tr>
<td>C</td>
<td>124 (5.3%)</td>
<td>30 (1.3%)</td>
<td>14 (0.5%)</td>
<td>7 (2.7%)</td>
<td>2 (0.2%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>D1*</td>
<td>805 (51.9%)</td>
<td>23 (1.3%)</td>
<td>176 (11.0%)</td>
<td>42 (2.7%)</td>
<td>533 (33.1%)</td>
<td>5 (0.3%)</td>
</tr>
<tr>
<td>D2*</td>
<td>599 (50.2%)</td>
<td>32 (1.0%)</td>
<td>405 (13.2%)</td>
<td>12 (0.4%)</td>
<td>50 (8.4%)</td>
<td>22 (3.7%)</td>
</tr>
<tr>
<td>D3*</td>
<td>365 (54.0%)</td>
<td>7 (0.8%)</td>
<td>65 (9.4%)</td>
<td>15 (2.3%)</td>
<td>61 (9.0%)</td>
<td>11 (1.7%)</td>
</tr>
</tbody>
</table>

Abstract P120 Figure 1

### P121

**CHARACTERISTICS OF COPD PATIENTS WITH AND WITHOUT MAINTENANCE TREATMENT AT BASELINE, BY GOLD STAGE: TONADO**

1S Korn, 1R Abrahams, 1L Grönke, 1L Korduki, 1V Amatto, 1R Buhl. 1Pulmonary Department, Mainz University Hospital, Mainz, Germany; 3Morgantown Pulmonary Associates, Morgantown, West Virginia, USA; 3Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany; 3Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, Connecticut, USA

Introduction The efficacy and safety of the once-daily combination of tiotropium (T), a long-acting muscarinic antagonist (LAMA), and olodaterol (O), a long-acting β2-agonist (LABA), for the treatment of chronic obstructive pulmonary disease (COPD) has been established. We investigated whether there was a difference in the characteristics of COPD patients with and without baseline maintenance treatment.

Methods Two replicate, randomised, 52-week, double-blind, parallel-group, Phase III trials (NCT01431274; NCT01431287; n = 5162) assessed the efficacy and safety of once-daily treatment with T+O (2.55 μg; 5/5 μg; Respimat® inhaler) compared to the individual components. Baseline characteristics of COPD patients within Global initiative for Chronic Obstructive Lung Disease (GOLD) subgroups 2 and 3/4, with/without maintenance treatment (prior LABA, LAMA or both at baseline), are presented, based on data from the pooled set.

Results Most patients received baseline maintenance treatment (3037 vs 2121) and of those, there was a greater proportion of GOLD 3/4 compared to GOLD 2 patients (52.58% vs 47.42%, respectively). An opposite trend was observed in patients not receiving maintenance treatment (GOLD 3/4, 45.87% vs GOLD 2, 54.13%). The proportion of current smokers was lower in GOLD 3/4 than GOLD 2 patients, as expected (Table); nevertheless, irrespective of GOLD stage, there was a greater proportion of smokers without maintenance treatment than with maintenance treatment (42.81% vs 32.86%, respectively). As expected, pulmonary function was reduced in GOLD 3/4 compared to GOLD 2 patients, although it appeared comparable between patients with and without maintenance treatment. Of the patients with maintenance treatment, a considerably greater proportion received inhaled steroids compared to those without prior LAMA/LABA treatment (69.67% vs 15.51%, respectively).

Furthermore, a smaller proportion of patients without prior LAMA/LABA treatment received short-acting β-adrenergics compared to those with maintenance treatment (Table 1). Of the GOLD 3/4 patients without baseline maintenance treatment, 43.4% were not receiving any other pulmonary medication.
Poster sessions

**Abstract P121**

<table>
<thead>
<tr>
<th>Characteristics of COPD patients with or without maintenance treatment at baseline, by GOLD stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients with</strong></td>
</tr>
<tr>
<td><strong>maintenance treatment</strong></td>
</tr>
<tr>
<td>(n = 3037)</td>
</tr>
<tr>
<td><strong>GOLD 2</strong></td>
</tr>
<tr>
<td><strong>Patients</strong></td>
</tr>
<tr>
<td><strong>Male</strong></td>
</tr>
<tr>
<td><strong>Mean age, years (SD)</strong></td>
</tr>
<tr>
<td><strong>Age group, years</strong></td>
</tr>
<tr>
<td>&lt;65</td>
</tr>
<tr>
<td>65–&lt;75</td>
</tr>
<tr>
<td>75–&lt;85</td>
</tr>
<tr>
<td>≥85</td>
</tr>
</tbody>
</table>

**Smoking history**
- **Smoker**
  - Yes: 1440 (47.4) vs. 1157 (54.2), p = 0.001
  - No: 183 (9.2) vs. 14 (0.7), p < 0.001

**Post-BD pulmonary function**
- **Mean FEV1 (SD)**
  - GOLD 2: 1.689 (0.418)
  - GOLD 3/4: 1.026 (0.293)
- **Mean% predicted**
  - GOLD 2: 81.2 (7.94)
  - GOLD 3/4: 77.8 (8.18)

**Pulmonary medication at baseline**
- **Anti-cholinergic (long acting/inhaled)**
  - Yes: 1440 (47.4) vs. 1157 (54.2), p = 0.001
  - No: 156 (5.1) vs. 128 (7.2), p = 0.01
- **Anti-cholinergic (short acting/inhaled)**
  - Yes: 156 (5.1) vs. 128 (7.2), p = 0.01
  - No: 1070 (74.3) vs. 1322 (82.8), p = 0.001

**Conclusion**
A high proportion of GOLD 3/4 patients not receiving maintenance treatment were not receiving any other pulmonary medication. One could hypothesise that these patients had either been diagnosed recently or that they were not treated according to current COPD guidelines.

**Background**
Most COPD patients will deteriorate over time, so a key aim of COPD management is to minimise this risk. We developed a composite endpoint of three aspects of worsening: COPD exacerbations, clinically important deteriorations (CID) in lung function and health status. This method was applied in a post hoc analysis of TORCH, a 3-year, double-blind, placebo-controlled trial in moderate/severe COPD that compared salmeterol 50 mcg/fluticasone propionate 500 mcg combination (SFC) with placebo (PBO), salmeterol 50 mcg (SAL) alone and fluticasone 500 mcg alone. In this analysis, SFC was compared with SAL to test whether the addition of inhaled corticosteroids (ICS) reduced the risk of a CID beyond their known effect on exacerbations.

**Method**
The overall analysis was performed in 6112 patients, 3054 treated with SFC and SAL. A CID was defined as a decrease ≥100 mL in post-bronchodilator FEV1, an increase (worsening) in St George’s Respiratory Questionnaire (SGRQ) total score of ≥4 units, or an on-treatment moderate/severe exacerbation. The time to the first deterioration of each component and the composite endpoint was analysed using a Cox’s proportional hazards model with covariates of: treatment, smoking status and geographical region; baseline values for FEV1 and SGRQ score were included for those individual component endpoints. The analysis was performed on the intention-to-treat (ITT) population and in patient categorised into GOLD grades I/II and III/IV.

**Results**
A similar percentage of patients in both treatment groups eventually experienced ≥1 category of deterioration during the 3-year trial. The Hazard Ratios (HR) show that compared to SAL, SFC significantly reduced the time to first worsening of COPD exacerbations, clinically important deteriorations (CID) in lung function and health status.
FEV₁ and SGRQ (Table 1). The benefit of SFC over SAL was seen with the composite endpoint in the ITT population and both GOLD subgroups.

**Conclusion** This post hoc analysis showed that, although most patients eventually experienced one of the three measures of deterioration, SFC significantly reduced the risk of a first composite CID compared to SAL. This added benefit of ICS was equally present in patients with mild/moderate or severe/very severe COPD.

**Abstract P123 Table 1**

<table>
<thead>
<tr>
<th></th>
<th>GOLD A/B</th>
<th>GOLD C/D</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2259</td>
<td>2903</td>
</tr>
<tr>
<td>Age (years), mean ± SD</td>
<td>64.3 ± 8.6</td>
<td>63.8 ± 8.0</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>1576 (69.8)</td>
<td>2186 (75.3)</td>
</tr>
<tr>
<td>Ex-smoker, n (%)</td>
<td>1348 (59.7)</td>
<td>1906 (65.7)</td>
</tr>
<tr>
<td>Post-bronchodilator FEV₁, (L), mean ± SD</td>
<td>1.73 ± 0.44</td>
<td>1.1 ± 0.37</td>
</tr>
<tr>
<td>Post-bronchodilator FEV₁, (% predicted), mean ± SD</td>
<td>62.9 ± 8.2</td>
<td>39.9 ± 11.6</td>
</tr>
<tr>
<td>Reversibility (mL), mean ± SD</td>
<td>193 ± 158</td>
<td>154 ± 131</td>
</tr>
<tr>
<td>Baseline maintenance medication, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICS</td>
<td>871 (38.6)</td>
<td>1575 (54.3)</td>
</tr>
<tr>
<td>ICS without LABA</td>
<td>165 (7.3)</td>
<td>255 (8.8)</td>
</tr>
<tr>
<td>ICS plus LABA</td>
<td>706 (31.3)</td>
<td>1320 (45.5)</td>
</tr>
<tr>
<td>LABA</td>
<td>904 (40.0)</td>
<td>1489 (51.3)</td>
</tr>
<tr>
<td>LAMA</td>
<td>768 (34.0)</td>
<td>1072 (36.9)</td>
</tr>
<tr>
<td>Xanthines</td>
<td>153 (6.8)</td>
<td>363 (12.5)</td>
</tr>
</tbody>
</table>

SD, standard deviation; FEV₁, forced expiratory volume in 1 s; LAMA, long-acting muscarinic antagonist.

**P124 A RANDOMISED, PARALLEL-GROUP STUDY TO EVALUATE THE EFFECT OF UMECLIDINIUM ADDED TO INHALED CORTICOSTEROID/LONG-ACTING BETA-AGONIST COMBINATION THERAPY IN SUBJECTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

**Rationale** To evaluate efficacy and safety of adding umeclidinium (UMEC), a long-acting muscarinic antagonist (LAMA), to inhaled corticosteroid (ICS)/long-acting β-agonist (LABA) in patients with moderate-to-very severe chronic obstructive pulmonary disease (COPD) for 12-weeks.

**Methods** Multicentre, randomised, double-blind, parallel-group study. Inclusion criteria included diagnosis of COPD, modified Medical Research Council Dyspnoea score ≥2 (i.e. patients symptomatic on ICS/LABA), post-salbutamol forced expiratory volume in one second (FEV₁) ≤70% predicted and FEV₁/forced vital capacity ratio of 1 at Day 85; other endpoints included 0–6 h weighted mean FEV₁, rescue medication use, COPD assessment test (CAT) score, and transition dyspnoea index (TDI) score. Adverse events (AEs) were also investigated.

**Results** In the UMEC+ICS/LABA and PBO+ICS/LABA groups, 119 and 117 patients were randomised, respectively, receiving fluticasone/salmeterol (40%), budesonide/formoterol (43%), and other ICS/LABA, including generics (17%). Compared with PBO+ICS/LABA, UMEC+ICS/LABA resulted in statistically significant improvements in change from baseline trough FEV₁ at Day 85 and 0–6 h weighted mean FEV₁ at Day 84 (Table 1). UMEC+ICS/LABA resulted in a statistically significant reduction in change from baseline mean puffs/day of rescue salbutamol over Weeks 1–12 versus PBO+ICS/LABA, but not for percentage of rescue-free days. Change from baseline in CAT score at Day 84 was statistically significantly different for UMEC+ICS/LABA versus PBO+ICS/LABA, but TDI score was not significantly different for UMEC+ICS/LABA versus PBO+ICS/LABA; the study was not powered for these endpoints. Incidence of AEs was similar with UMEC+ICS/LABA and PBO+ICS/LABA; n = 45 (38%) and n = 49 (42%), respectively. The most common AEs were nasopharyngitis (13–15%) and headache (3–7%).
**Abstract P124 Table 1** Endpoint results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Diff. vs PBO (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UMEC + ICS/LABA (N=119)</td>
<td>0.123 (0.071, 0.174)</td>
</tr>
<tr>
<td>PBO + ICS/LABA (N=117)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusions**
UMEC+ICS/LABA improved lung function and reduced rescue medication use (mean puffs/day) and CAT score in patients with COPD versus PBO+ICS/LABA. No additional safety concerns were identified with UMEC+ICS/LABA.

Funded by GlaxoSmithKline (NCT02257372).

**COI Statement**
ARS, JR, AC, WAF, CQZ and YSP are employees of GSK and hold stocks/shares in GSK.

---

**Abstract P125 Table 1**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No prior LABD treatment</th>
<th>Prior LABD treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>T+O</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T+O</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T</td>
</tr>
</tbody>
</table>

**Rationale**
Tiotropium plus olodaterol (T+O) is a novel once-daily combination of the long-acting muscarinic antagonist (LAMA) tiotropium (T) and the recently approved long-acting β2-agonist (LABA) olodaterol, for use as maintenance treatment in chronic obstructive pulmonary disease (COPD). These post hoc analyses of data from the two pivotal 1-year TONADO studies determined whether treatment with a long-acting
bronchodilator (LABD) prior to randomisation affected the lung-function benefits of T+O 5/5 μg (via Respimat®) compared to T 5 μg (via Respimat®).

**Methods** In the studies, 2124 patients had not received prior LABD treatment (T+O n = 426; T n = 454) and 3038 patients had (T+O n = 603, T n = 579; 60.6% LAMA, 78.8% LABA). Baseline characteristics for all patients and a sub-group with Global initiative for chronic Obstructive Lung Disease (GOLD) 2 lung-function impairment are presented in the Table 1. Forced expiratory volume in 1 s (FEV1) area under the curve from 0–3 h (AUC0–3) response (change from baseline) and trough FEV1 response were primary end points in the studies.

**Results** Comparable responses for both FEV1 AUC0–1 and trough FEV1 were observed in patients previously treated and untreated with LABD (see Table 1). The between-treatment differences (adjusted mean response [SE]; mL) for no prior LABD and prior LABD treatment, respectively, were: 116 (13) and 105 (11) for FEV1 AUC0–1, and 76 (14) and 49 (11) for trough FEV1. In the GOLD 2 subgroup, the between-treatment differences (adjusted mean response [SE]; mL) for no prior LABD and prior LABD treatment, respectively, were: 114 (19) and 123 (17) for FEV1 AUC0–1, and 79 (20) and 61 (18) for trough FEV1.

**Conclusions** Our analyses demonstrate the robust lung-function efficacy of T+O, compared to T alone, independent of the requirement for, or prior use of, LABD. These findings suggest a benefit of combination therapy over the mono-product as a first-line maintenance treatment.

**Funding** Boehringer Ingelheim.

---

**Table 1** Spirometric and symptomatic variables in symptomatic patients with COPD (baseline E-RS >10)

<table>
<thead>
<tr>
<th>Change from baseline in normalised FEV1 vs placebo, mL</th>
<th>Aclidinium 400 μg</th>
<th>Tiotropium 18 μg</th>
<th>Aclidinium vs tiotropium</th>
<th>Tiotropium 18 μg</th>
<th>Aclidinium vs tiotropium</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1, AUC0–1</td>
<td>150*</td>
<td>87*</td>
<td>63†</td>
<td>140**</td>
<td>106*</td>
</tr>
<tr>
<td>FEV1, AUC12–24h (night-time)</td>
<td>157**</td>
<td>67*</td>
<td>90†</td>
<td>153**</td>
<td>90**</td>
</tr>
<tr>
<td>FEV1, AUC12 (day time)</td>
<td>147**</td>
<td>112**</td>
<td>35</td>
<td>126*</td>
<td>123*</td>
</tr>
<tr>
<td>Morning pre-dose (trough) FEV1</td>
<td>136**</td>
<td>68*</td>
<td>68†</td>
<td>137*</td>
<td>70*</td>
</tr>
<tr>
<td>E-RS Total Score over 6 weeks</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-2.15*</td>
<td>-0.98</td>
</tr>
<tr>
<td>(% reduction)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.25*</td>
<td>-0.11</td>
</tr>
<tr>
<td>Night-time symptom severity over 6 weeks</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.23*</td>
<td>-0.09</td>
</tr>
<tr>
<td>(% reduction)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.31%</td>
<td>-0.23%</td>
</tr>
</tbody>
</table>

*p < 0.05 vs placebo; †p < 0.0001 vs placebo; ‡p < 0.05 vs tiotropium.

<table>
<thead>
<tr>
<th>&lt;br&gt;P126 Efficacy of aclidinium bromide compared with tiotropium and placebo in symptomatic patients with moderate to severe chronic obstructive pulmonary disease (COPD): post-hoc analysis of a phase IIIB study</th>
<th>&lt;br&gt;1J Beier, 2RM Róż, 3FC Chueco, 3EG García Gil. 1Insaf Respiratory Research Institute, Wiesbaden, Germany; 2ISPL Centrum Medyczne, Białystok, Poland; 3AstraZeneca PLC, Barcelona, Spain</th>
</tr>
</thead>
</table>

**Abstract P126**

**Introduction and objective** Maintaining bronchodilation and symptom control throughout the day and night is an important COPD therapeutic aim. Here, we compare 24-hour lung function and symptom control in symptomatic patients with moderate to severe COPD treated with aclidinium or tiotropium, two long-acting, muscarinic antagonists.

**Methods** This was a post-hoc analysis of a 6-week, double-blind, Phase IIIb study comparing aclidinium 400 μg BID with tiotropium bromide 18 μg QD or placebo in patients with moderate to severe COPD (NCT01462929). Symptomatic patients were defined as having an EXAcerbations of Chronic pulmonary disease Tool-Respiratory Symptoms (E-RS) baseline score ≥ 10 units. Primary endpoint: change from baseline in normalised FEV1 AUC over 24-hours post-morning dose (AUC0–24/12h) at Week 6. Other endpoints: change from baseline in morning pre-dose (trough) FEV1 and change from baseline in FEV1 AUC0–12h, E-RS, early-morning and night-time symptoms, and limitation of early-morning activities.

**Results** A total of 277/414 symptomatic patients were included; mean age was 62.1 years, 54.5% were current smokers, baseline FEV1 1.41 ± 0.48 L. At Week 6, aclidinium 400 μg BID improved FEV1 over 24 h from baseline vs placebo (Table 1). During the night-time period, aclidinium 400 μg BID improved FEV1 from baseline vs tiotropium 18 μg QD. At Week 6, improvements in trough FEV1 from baseline were observed with aclidinium vs tiotropium and placebo. Aclidinium improved E-RS total score from baseline vs tiotropium and placebo. Moreover, aclidinium improved early-morning and night-time symptom severity from baseline vs tiotropium and placebo over the treatment period (see Table 1 for all results described above). Limitation of early-morning activities caused by COPD symptoms was also improved with aclidinium vs tiotropium and placebo (p < 0.05). Tolerability has been previously reported (Beier COPD 2013) where adverse events (AEs) were similar in each arm, few anticholinergic AEs or serious AEs occurred in any group, and aclidinium was well tolerated.

**Conclusions** Aclidinium 400 μg BID improved bronchodilation, particularly during the night-time period, as well as early morning, daily and night-time symptoms, and early-morning limitation of activity in symptomatic patients compared with either tiotropium 18 μg QD or placebo.

10.1136/thoraxjnl-2015-207770.263
**P127 SUPERIORITY OF GLYCOPRYRONIUM VERSUS TIOTROPIUM IN EARLY ONSET OF BRONCHODILATION IN PATIENTS WITH MILD TO SEVERE COPD – THE FAST STUDY**

1H Watz, 2C Malaaender, 3A-M Kirsten. 1Pulmonary Research Institute at Lung Clinic Grosshadern, Grosshadern, Germany; 2Novartis Pharma GmbH, Nuremberg, Germany

10.1136/thoraxjnl-2015-207770.264

**Background** Glycopyrronium (GLY) has demonstrated efficacy similar to open-label and single-blinded tiotropium (TIO) in the treatment of COPD and fast onset of bronchodilation action. 1,2 The double-blinded FAST study compared the efficacy of GLY with TIO in serial spirometry and bodyplethysmography measurements to allow for a more intensified characterisation of the earlier onset of action.

**Methods** In this multicenter, randomised, double-blinded, double-dummy, cross-over study patients (pts) with moderate-to-severe COPD received single-dose of both once-daily GLY 44 µg and TIO 18 µg via the Breezhaler® and Handihaler® devices, respectively. Primary endpoint was the forced expiratory volume in one second (FEV1) AUC~2h. Further endpoints included inspiratory capacity (IC), residual volume (RV), functional residual capacity (FRC) and specific airway resistance (sRaw), all measured by bodyplethysmography.

**Results** Of 152 pts randomised (mean age: 61.8 yr, mean post-BCF50 48.3%; 99.3% completed the study. After inhalation of the single dose, GLY demonstrated superiority to TIO in early bronchodilation i.e. FEV1 AUC~2h (least squares mean (LSM) = 0.037 L, p = 0.0006). Both treatments showed similar improvements in IC, RV, and FRCPleth. Over the first 90 min after dosing, GLY also showed statistically significant improvement in sRaw compared to TIO with a difference of 0.184 kPa*s at the time point 90 min (LSM, p = 0.006).

**Conclusion** GLY showed effective bronchodilation and was superior to double-blinded TIO in terms of early onset of bronchodilation. Both GLY and TIO showed similar improvements in static lung volume parameters; however GLY was superior in reduction of sRaw early after inhalation.

**REFERENCES**

**P128 POOLED SAFETY ANALYSIS OF ADJUDICATED SERIOUS ADVERSE EVENTS WITH THE COMBINATION OF TIOTROPIUM + OLODATEROL**

1R Buhl, 2K Tetzlaff, 3Z Korádi, 4C Vogelmeier, 5L McGregor. 1Pulmonary Department, Mainz University Hospital, Mainz, Germany; 2Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany; 3Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, Connecticut, USA; 4Department for Respiratory Diseases, University of Marburg, Marburg, Germany; 5Centre for Infection and Immunity, School of Medicine, Dentistry and Biomedical Sciences, Queen’s University Belfast, Belfast, UK

10.1136/thoraxjnl-2015-207770.265

**Rationale** This analysis aimed to obtain a comprehensive and objective safety assessment of the combination of tiotropium (T), a long-acting muscarinic antagonist, with olodaterol (O), a long-acting β2-agonist, (T+O) in patients with moderate to very severe chronic obstructive pulmonary disease (COPD).

**Methods** Data from two, 52-week, pivotal Phase III trials investigating T+O 5/5 µg and T+O 2.5/5 µg versus T 2.5 µg, 5 µg and O 5 µg were pooled, and patient narratives and profiles of serious adverse-event (SAE) reports were reviewed by an independent Adjudication Committee. The committee members independently assessed all SAEs to determine if any deaths, hospitalisations or intubations were respiratory-related, cardiovascular-related, cerebrovascular-related or other event-related. For an SAE adjudicated as respiratory-related, determination was made if it was related to COPD or pneumonia. For an SAE adjudicated as cerebrovascular-related, determination was made if it was related to stroke or other cerebrovascular events. Incidences of the composite end point (death, hospitalisation and intubation for respiratory-, cardiovascular-, cerebrovascular- or other-related events) and the individual components of this end point were evaluated.

**Results** The safety population for the primary analysis included patients from two trials (NCT01431274 and NCT01431287) in which 799/3162 (15.5%; range across treatments: 14.3–16.5%) had any adjudicated event of interest. As expected in a moderate to very severe COPD population, most SAEs were respiratory-related (8.1%; 420 patients). Eighty-three (1.6%) patients had cardiovascular-related SAEs and 27 (0.5%) had cerebrovascular-related SAEs; 363 (7.0%) had SAEs that were adjudicated as non-respiratory-, non-cardiovascular- or non-cerebrovascular-related. Most adjudicated SAEs (763 patients; 14.8%) were hospitalisations, while there were 26 (0.5%) patients with intubation and 75 (1.5%) with fatal SAEs (86 [1.7%] had fatal SAEs when including vital status follow-up).

**Conclusions** The adjudicated analysis of SAEs demonstrated that the risk of having an event (composite end point of hospitalisations, intubations and death whether related to respiratory, cardiovascular, cerebrovascular or other cause) was similar for T+O 2.5/5 µg compared to T+O 2.5/5 µg or any of the monotherapy components. Similar conclusions can be drawn for the individual events of hospitalisations, intubations and death.

| Abstract P128 Table 1 Summary of adjudicated SAEs: combined data (n [%]) |
|------------------|------------------|------------------|------------------|------------------|------------------|
|                  | O 5 µg | T 2.5 µg | T 5 µg | T+O 2.5/5 µg | T+O 5/5 µg |
| Total number of patients | 1038 | 1032 | 1033 | 1030 | 1029 |
| SAEs                           |       |       |       |       |       |
| Any adjudicated           | 171    | 148    | 162    | 157    | 161    |
| (16.5)                   | (14.3) | (15.7) | (15.2) | (15.6) |       |
| Any respiratory-related   | 85     | 82     | 84     | 78     | 91     |
| (8.2)                    | (7.9)  | (8.1)  |       |       |       |
| Key respiratory-related   | 78     | 74     | 70     | 69     | 83     |
| (7.5)                    | (7.2)  | (6.8)  |       |       |       |
| COPD-related              | 67     | 63     | 65     | 53     | 71     |
| (6.5)                    | (6.1)  | (6.3)  |       |       |       |
| Pneumonia-related         | 15     | 15     | 9      | 9      | 22     |
| (1.4)                    | (1.5)  | (1.6)  |       |       | (2.1)  |
| Other respiratory-related | 7      | 10     | 17     | 11     | 11     |
| (0.7)                    | (1.0)  | (1.6)  |       |       | (1.1)  |
| Cardiovascular-related    | 15     | 13     | 19     | 17     | 19     |
| (1.4)                    | (1.3)  | (1.8)  |       |       | (1.8)  |
| Any cerebrovascular       | 6      | 6      | 5      | 5      | 5      |
| (0.6)                    | (0.6)  | (0.5)  | (0.5)  | (0.5)  | (0.5)  |
| Stroke-related            | 3      | 3      | 3      | 4      | 4      |
| (0.3)                    | (0.3)  | (0.3)  | (0.4)  | (0.4)  | (0.2)  |
| Other cerebrovascular-related | 4      | 4      | 0      | 1      | 3      |
| (0.4)                    | (0.4)  | (0.0)  | (0.1)  | (0.3)  | (0.3)  |
| Non-respiratory, non-cardiovascular or non-cerebrovascular-related | 78     | 67     | 74     | 73     | 71     |
| (7.3)                    | (6.5)  | (7.2)  |       |       |       |
WHAT IS THE PATIENT’S PREFERENCE: TIOTROPiUM MONOTHERAPY OR FIXED-DOSE INDACATEROL/GLYCOPYRRONIUM COMBINATION THERAPY? - THE FAVOUR STUDY

P Kardos, 1 I Hagedorn. Allergy, Respiratory and Sleep Medicine, Red Cross Maingau Hospital, Frankfurt, Germany
10.1136/thoraxjnl-2015-207770.266

Introduction and objectives Shared decision-making for drug and inhaler-device use improves adherence and outcomes in COPD. Physicians are encouraged to involve patient’s opinion in choosing drugs and inhalers. It remains unclear, however, whether the superior effect on FEV1 shown for the fixed-dose combination of indacaterol/glycopyrronium (IND/GLY) compared to tiotropium (TIO) translates into medication preference by patients.

The present study was conducted to evaluate the overall preference for IND/GLY and TIO respectively, in patients who are still symptomatic under a TIO treatment.

Method This multicenter, cross-over, open-label study randomised COPD patients with moderate to severe airflow limitation and a CAT score of ≥10 to either receive 4 weeks o.d. IND/GLY (110/50 μg) followed by 4 weeks o.d. TIO (18 μg) or vice versa in a 1:1 ratio. To determine patient’s treatment preference and satisfaction as secondary and explorative objectives, respectively, several validated and new questionnaires were used. As primary endpoint, FEV1 1 h post-inhalation after 4 weeks was investigated.

Results Of 88 patients (mean age, 65 years; post-bronchodilator FEV1, 57.7% predicted; mean CAT score, 17.6) randomised, 87 patients completed the study. After 4 weeks treatment, 1 h post-inhalation FEV1 was significantly higher with IND/GLY compared to TIO (LSM difference, 81 ml; p = 0.0017). Importantly, a higher proportion of patients preferred IND/GLY (69.4%) over TIO (30.6%) at the end of the study. Reduction of dyspnea was mentioned as an important or very important reason for favouring IND/GLY by 91.5% of the patients.

Conclusion This study indicated that beyond FEV1, patients reported outcomes improve with the dual bronchodilator IND/GLY compared to TIO monotherapy. Further studies are needed to investigate how the favoured treatment option translates into improved adherence and long term treatment outcomes.

INTRODUCTION AND OBJECTIVES

Introduction and objectives Fluticasone propionate/salmeterol (FP/SAL), can be delivered by metered-dose inhaler (MDI) or dry powder inhaler (DPI). The choice of device may affect adherence to and effectiveness of treatment. Although only 1000 mcg/day DPI is licensed for the treatment of COPD in the UK, the MDI and lower doses are regularly used in real-world practice. The aim of this study was to compare the effectiveness and safety of FP/SAL MDI or DPI at two doses (500 and 1000 mcg/day) in COPD patients.

METHODS

Historical, matched cohort study using the Optimum Patient Care Research Database in patients with COPD, aged >35 years and initiating with FP/SAL via either MDI or DPI. Conditional Poisson regression and conditional logistic regression were used respectively to compare the rate of moderate/severe COPD exacerbations and the odds of diagnosis of pneumonia and diabetes mellitus (including anti-diabetic drug prescriptions) between MDI and DPI during one year outcome period. Models were adjusted for the respective baseline values of the outcome variable of interest where possible. Addition of LAMA therapy during the outcome period was compared using conditional logistic regression.

RESULTS

472 and 1172 patients initiated on FP/SAL at 500 mcg/day and 1000 mcg/day, respectively. The rate of moderate/severe COPD exacerbations was significantly lower for patients prescribed FP/SAL versus DPI.

Abstract P130 Table 1 Moderate/severe exacerbations, pneumonia and diabetes mellitus during the outcome period for patients initiating on FP/SAL at 500 mcg/day and mcg/day via MDI versus DPI

<table>
<thead>
<tr>
<th></th>
<th>Initiating at 500 mcg/day FP/SAL</th>
<th>Initiating at 1000 mcg/day FP/SAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N = 472 (100%)</td>
<td>N = 1172 (100%)</td>
</tr>
<tr>
<td></td>
<td>MDI</td>
<td>DPI</td>
</tr>
<tr>
<td></td>
<td>N = 236 (100%)</td>
<td>N = 236 (100%)</td>
</tr>
<tr>
<td></td>
<td>N = 586 (100%)</td>
<td>N = 586 (100%)</td>
</tr>
<tr>
<td>Number of all moderate/severe COPD exacerbations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0, n (%)</td>
<td>137 (58.1)</td>
<td>121 (51.3)</td>
</tr>
<tr>
<td>1, n (%)</td>
<td>56 (23.7)</td>
<td>59 (25.0)</td>
</tr>
<tr>
<td>2–3, n (%)</td>
<td>35 (14.8)</td>
<td>35 (14.8)</td>
</tr>
<tr>
<td>4+, n (%)</td>
<td>8 (3.4)</td>
<td>21 (8.9)</td>
</tr>
<tr>
<td>Rate ratio (95% CI)</td>
<td>0.72 (0.55, 0.95)</td>
<td>1.10 (0.93, 1.30)</td>
</tr>
<tr>
<td>Adjusted rate ratio (95% CI)</td>
<td>0.71 (0.54, 0.93)</td>
<td>1.11 (0.94, 1.30)</td>
</tr>
<tr>
<td>No. of exacerbations</td>
<td>231 (97.9)</td>
<td>232 (98.3)</td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>5 (2.1)</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td>Odds ratio (95% CI)</td>
<td>1.25 (0.33, 4.76)</td>
<td>1.33 (0.30, 5.88)</td>
</tr>
<tr>
<td>Adjusted odds ratio (95% CI)</td>
<td>0.87 (0.59, 1.43)</td>
<td>1.05 (0.80, 1.39)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of exacerbations</td>
<td>214 (90.7)</td>
<td>211 (89.4)</td>
</tr>
<tr>
<td>Yes, n (%)</td>
<td>22 (9.3)</td>
<td>25 (10.6)</td>
</tr>
<tr>
<td>Odds ratio (95% CI)</td>
<td>1.05 (0.80, 1.39)</td>
<td>1.05 (0.80, 1.39)</td>
</tr>
<tr>
<td>Adjusted odds ratio (95% CI)</td>
<td>0.88 (0.40, 1.92)</td>
<td>1.10 (0.71, 1.69)</td>
</tr>
</tbody>
</table>
Efficacy of Tiotropium and Olodaterol Combination in Patients with COPD on β-Blockers

E Derom, S Kom, A Hamilton, VC Amatto, Y Zhao, F Maltais. Ghent University Hospital, Ghent, Belgium; University Medical Center, Johannes Gutenberg University, Mainz, Germany; Boehringer Ingelheim, Burlington, Ontario, USA; Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim, Germany; Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, Connecticut, USA; Centre de Recherche, Institut Universitaire de Cardiologie Et de Pneumologie de Québec, Québec, Canada

Poster sessions
10.1136/thoraxjnl-2015-207770.268

Rationale The efficacy and safety of a new once-daily combination with tiotropium (T), a long-acting muscarinic antagonist, and olodaterol (O), a long-acting β2-agonist, was established for the treatment of chronic obstructive pulmonary disease (COPD) in the TONADO studies (NCT01431274; NCT01431287). This analysis evaluates the efficacy of the combination in a subpopulation of patients receiving β-blockers in these studies.

Methods Two replicate, randomised, double-blind, parallel-group, 52-week, Phase III trials assessed the efficacy and safety of T+O (2.5/5 μg; 5/5 μg; via Respimat® inhaler) once daily compared to the monocomponents. Key primary end-point data for the combined analysis of the replicate trials in patients with COPD receiving β-blockers during treatment are presented.

Results 5136 patients were evaluable; 556 (10.8%) received β-blockers. At 24 weeks, similar improvements in mean forced expiratory volume in 1 s (FEV1) area under the curve from 0–3 h (AUC0–3) responses for T+O compared to monocomponents were seen across β-blocker subgroups (Table 1), with no significant treatment interaction effect observed. A similar trend was observed with trough FEV1 and quality of life scores.

Conclusions While the β-blocker patient group analysed was small, these data demonstrated similar sustained improvements in lung function, irrespective of β-blocker use. These data support the efficacy of T+O in this patient group.

Funding Boehringer Ingelheim.

Abstract P131 Table 1 Efficacy of T+O versus monocomponents by β-blocker use

<table>
<thead>
<tr>
<th>Treatment comparison, μg</th>
<th>β-blockers (N = 556)</th>
<th>No β-blockers (N = 4580)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment</td>
<td>Adjusted mean FEV1, AUC0–3 L [95% confidence interval]</td>
<td></td>
</tr>
<tr>
<td>T+O 2.5/5 – 0.5</td>
<td>0.114 [0.06, 0.169] 0.129 [0.111, 0.147]</td>
<td></td>
</tr>
<tr>
<td>T+O 2.5/5 – T 5</td>
<td>0.078 [0.02, 0.131] 0.114 [0.097, 0.132]</td>
<td></td>
</tr>
<tr>
<td>T+O 2.5/5 – O 5</td>
<td>0.122 [0.069, 0.174] 0.114 [0.096, 0.132]</td>
<td></td>
</tr>
<tr>
<td>T+O 2.5/5 – T 2.5</td>
<td>0.108 [0.058, 0.158] 0.113 [0.095, 0.130]</td>
<td></td>
</tr>
<tr>
<td>T+O 2.5/5 – T 5</td>
<td>0.085 [0.034, 0.136] 0.099 [0.081, 0.117]</td>
<td></td>
</tr>
</tbody>
</table>

Poster sessions
10.1136/thoraxjnl-2015-207770.269

Aim To characterise disease burden, health care resource utilisation (HCRU), and costs among a cohort of COPD patients newly prescribed maintenance therapy in UK general practice.

Method A retrospective cohort of COPD patients aged ≥40 yrs and newly prescribed COPD monotherapy (long acting beta-agonists [LABA] or long acting muscarinic antagonist [LAMA]), dual therapy (LABA+LAMA; LABA+inhaled corticosteroid (ICS); LAMA+ICS) or open triple therapy (LAMA+LABA+ICS) between 1/1/2009 and 30/11/2012 was identified from UK Clinical Practice Research Datalink (CPRD).

Results A total of 39,639 COPD patients were included (54% male, mean age 68 yrs (SD: 11)). LABA+ICS (39%) and LAMA (34%) were the most commonly initiated LABD; 13% were first exposed to LABD as part of an open triple regimen (Table 1). Patients initiating an ICS-containing regimen had a higher exacerbation rate (moderate or severe) in the 12 months prior to maintenance therapy initiation (LABA+ICS: 0.74 per PY [95% CI: 0.72–0.75]; LAMA+ICS: 0.86 per PY [0.82–0.90] and LABA+LAMA+ICS: 0.83 per PY [0.80–0.85]) compared to patients on bronchodilators alone (LAMA: 0.55 per PY [0.54–0.57]; LABA: 0.56 per PY [0.54–0.59]; LAMA+LABA: 0.50 per PY [0.44–0.56]). Patients on open triple therapy demonstrated the highest rates of non-COPD related hospitalisations. The annual per patient cost ranged from £2,139 (LABA) to £2,876 (LAMA+LABA+ICS); approximately half were due to GP visits and a third resulted from non-COPD related hospitalisations (Table 1).

Abstract P132 Table 1 Annual per patient health care utilisation costs 12 months prior to LABD initiation

<table>
<thead>
<tr>
<th>LABA</th>
<th>LAMA</th>
<th>LABA</th>
<th>LABA</th>
<th>LAMA</th>
<th>LAMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>LABA</td>
<td>LABA+ICS</td>
<td>LABA+ICS</td>
<td>LABA+ICS</td>
<td>LABA+ICS</td>
<td>LABA+ICS</td>
</tr>
<tr>
<td>(N = 289)</td>
<td>(N = 13511)</td>
<td>(N = 525)</td>
<td>(N = 15374)</td>
<td>(N = 2370)</td>
<td></td>
</tr>
<tr>
<td>Total costs</td>
<td>£2,139</td>
<td>£2,223</td>
<td>£2,240</td>
<td>£2,334</td>
<td>£2,410</td>
</tr>
<tr>
<td>GP visits</td>
<td>£1,230</td>
<td>£1,249</td>
<td>£1,237</td>
<td>£1,224</td>
<td>£1,313</td>
</tr>
<tr>
<td>All exacerbations</td>
<td>£173</td>
<td>£192</td>
<td>£179</td>
<td>£247</td>
<td>£287</td>
</tr>
<tr>
<td>Non-COPD</td>
<td>£709</td>
<td>£759</td>
<td>£795</td>
<td>£811</td>
<td>£703</td>
</tr>
<tr>
<td>hospitalisations</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Treatment</td>
<td>£27</td>
<td>£23</td>
<td>£29</td>
<td>£51</td>
<td>£106</td>
</tr>
</tbody>
</table>
Conclusion Patients with a higher baseline exacerbation rate were more likely to receive ICS-containing therapies compared to those taking bronchodilators alone. Across all maintenance therapy groups, GP visits and non-COPD related hospitalisations were the primary driver of total costs.

Pulmonary rehabilitation and physical activity

A MULTIDISCIPLINARY PATIENT EDUCATION PROGRAMME SIGNIFICANTLY IMPROVES ASTHMA CONTROL AND QUALITY OF LIFE IN PATIENTS WITH SEVERE ASTHMA

RD Daly, LJ Holmes, H Scanlon, D Ryan, RM Niven. University Hospital South Manchester, Manchester, Greater Manchester

10.1136/thoraxjnl-2015-207770.270

Background The impact of severe asthma upon quality of life is significant, as a consequence of unpredictable hospitalisations and life-threatening attacks. It is unknown whether patient education programmes in severe asthma improve self-management, quality of life or measures of asthma control.

A 12 week patient education programme was piloted within a severe asthma multi-disciplinary team. Sessions were 2 h duration fortnightly. The aim of the programme was to enable patients to gain greater insight into their disease, treatment options and lifestyle management with emphasis on improving asthma control and quality of life.

Aims Our aim was to assess the effect of the introduction of this programme upon participant’s asthma control and quality of life.

Methods Prospective data collection was performed, including Asthma Quality of Life Questionnaire (AQLQ), Asthma Control Questionnaire (ACQ) and Hospital Anxiety and Depression (HAD) at week 1 and 12. Patient Satisfaction Evaluation forms were completed to facilitate ongoing programme development.

Results 21 patients entered with 16 (76%) completing the 12 week programme (12 female, 4 male). Dropout was attributed to difficulty attending on a regular basis. There was an improvement in mean total AQLQ of 1.3 (minimal clinically important difference >0.5). There was notable improvement in the AQLQ domains; symptoms (0.8) and emotional (0.7). Mean ACQ improved by 0.7 (p < 0.05), mean HAD anxiety and depression scores fell but this did not reach statistical significance (Table 1).

Conclusion A multidisciplinary patient education group for severe asthma patients significantly improves quality of life and asthma control. Longitudinal studies are required to determine impact upon exacerbations and hospitalisations.

P134 EXERCISE RESPONSES TO ONE-LEGGED CYCLING IN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS

1TS Reilly, 2S Majid, 3B Popat, 4Yu Greening, 5TE Dolmage, 6S Agrawal, 7FA Woodhead, 8RA Evans. 1University of Leicester, Leicester, UK; 2University Hospitals Leicester, Glenfield General Hospital, Centre for Exercise and Rehabilitation Science, Leicester, UK; 3University Hospitals of Leicester NHS Trust, Glenfield Hospital, Leicester Respiratory Biomedical Research Unit, Leicester, UK; 4West Park Healthcare Centre, Toronto, ON, Canada; 5University Hospitals Leicester, Glenfield General Hospital, Department of Respiratory Medicine, Leicester, UK

10.1136/thoraxjnl-2015-207770.271

Introduction Pulmonary Rehabilitation is recommended for patients with Idiopathic Pulmonary Fibrosis (IPF) although the magnitude of benefit appears less compared to those with other chronic lung diseases. Patients with IPF may not be able to sustain high-intensity training to induce physiological change due to a ventilatory limitation to exercise. One strategy to circumvent this in COPD has been to reduce the exercising muscle mass by cycling one leg at a time during the same exercise session. Randomised controlled trials have shown greater improvements in exercise capacity after training using one-legged cycling (OLC) compared to two-legged cycling (TLC). We, therefore, compared OLC to TLC responses during incremental and constant work rate (CWR) exercise in patients with IPF.

Methods Patients were recruited from a tertiary referral centre if they met the current NICE diagnostic criteria for IPF with a MRC dyspnoea grade ≥2. Exclusion criteria included a requirement for long-term oxygen therapy. Participants completed four Cardiopulmonary Exercise Tests (CPETs) to intolerance on a cycle ergometer with expired gas analysis. The tests were completed on separate days: 1) two-legged maximal incremental test (TLC-ICE); 2) one-legged maximal incremental test (OLC-ICE); 3) two-legged CWR (TLC-CWR) test at 70% peak power achieved on the TLC-ICE; 4) one-legged CWR (OLC-CWR) test at 35% TLC-ICE peak power.

Results Twelve participants (11 male, mean [SD] 73 [8] yrs, BMI 30.6 [4.8] kg/m2, FVC% predicted 71.8 [20.3]%, resting SpO2 98 [1]%) completed all four CPETs demonstrating a ventilatory limitation to exercise (92 [14]% maximum voluntary ventilation [MVV]). Although the OLC-ICE peak oxygen uptake (peak VO2) was significantly lower than the peak VO2 TLC-ICE (p < 0.001) the OLC: TLC was high at 0.85. The OLC-CWR was endured for more than twice the TLC-CWR (p < 0.001) at the same muscle-specific power leading to almost double the work being performed (Table 1).

Abstract P133 Table 1

<table>
<thead>
<tr>
<th></th>
<th>AQLQ Total</th>
<th>AQLQ Symptoms</th>
<th>AQLQ Activity</th>
<th>AQLQ Emotional</th>
<th>AQLQ Enviro</th>
<th>ACQ 6</th>
<th>HAD Anxiety</th>
<th>HAD Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(mean)</td>
<td>(mean)</td>
<td>(mean)</td>
<td>(mean)</td>
<td>(mean)</td>
<td>(mean)</td>
<td>(mean)</td>
<td>(mean)</td>
</tr>
<tr>
<td>Week 1</td>
<td>2.6</td>
<td>2.7</td>
<td>2.6</td>
<td>2.9</td>
<td>3.08</td>
<td>3.9</td>
<td>9.6</td>
<td>9.1</td>
</tr>
<tr>
<td>Week 12</td>
<td>3.9</td>
<td>3.5</td>
<td>3.1</td>
<td>3.6</td>
<td>3.22</td>
<td>3.2</td>
<td>8.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Change from baseline</td>
<td>11.3</td>
<td>0.8</td>
<td>0.5</td>
<td>0.7</td>
<td>0.10</td>
<td>0.7</td>
<td>0.7</td>
<td>1.6</td>
</tr>
<tr>
<td>p value</td>
<td>p = 0.06</td>
<td>p = 0.04</td>
<td>p = 0.1</td>
<td>p = 0.07</td>
<td>p = 0.3</td>
<td>p = 0.05</td>
<td>p = 0.27</td>
<td>p = 0.18</td>
</tr>
</tbody>
</table>

The patient evaluation forms demonstrated significant patient satisfaction with the programme, highlighting the positive impact that the sessions have had upon their life.
Conclusion OLC at the same muscle-specific power compared to TLC enabled patients with IPF to almost double the work in a simulated exercise training session. Future research should investigate OLC as a potentially efficacious aerobic training strategy for patients with IPF.

REFERENCES
1 Bjorgen SJ. Eur J Appl Physiol 2009;106:501–507
2 Dolmage TE. Chest 2008;133:370–376

Introduction and objectives Pulmonary rehabilitation (PR) is recommended by the British Thoracic Society for patients that suffer from COPD; it is typically delivered in supervised sessions. Daily physical activity (PA) is often recorded as an outcome following PR, with variable results. National guidelines recommend that older adults should accumulate 150 min of moderate intensity activity in bouts of 10 min or more. We wanted to objectively measure the amount and intensity of PA, which patients actually accumulate during 1 PR session. This is the first study to profile PA during a PR exercise class in this way and could be useful for home training and general PA advice.

Methods We conducted a prospective study on patients diagnosed with COPD that were enrolled for PR at Glenfield Hospital, Leicester. 12 PR sessions include walking [85% speed derived from the incremental shuttle walk test (ISWT)], leg/arm bike, and resistance training. We placed Sense-Wear™ monitors (SWM) on the patients’ arm during session 2 only. Analysis took place on Innerview™ computer software.

Results The patient cohort consisted of 20 patients: 60% female, mean age of 70.1 years (SD – 8.3 years), BMI 28.6 (SD 7.9), FEV1/FVC ratio 60.8 (SD 17.3), 90% of the patients were either smokers or ex-smokers. The baseline ISWT of the group was 199.5 (SD 145.0) metres.

Table 1 shows that in our cohort, patients were exercising in the 0–1.5 METs range for 52% of the time (sedentary activity), 1.5–3 METs – 31% of the time (light activity) and for 17% of the time, they were exercising above 3 METs (moderate activity).

Conclusion The results highlight that, early in the PR programme COPD patients were not achieving 10 min of moderate intensity activity during 1 PR session, as recommended in national guidance. However, documented inaccuracies of the SWM, for instance at slow speeds of walking and when the arm is fixed may account for these results. Future work should aim to discover if the time spent above 3 METs increases later in the programme. In addition, we could use the PA profile of each patient to tailor home and class training progression.

Introduction NICE recommends community PR as an essential component of chronic obstructive pulmonary disease (COPD) management, although nationally mean uptake is only 13%.2 PR has been proven to improve quality of life and to be cost effective.1 Our team routinely assess and refer COPD inpatients to PR, however, many decline referral. We piloted an inpatient exercise class with the objective of increasing referrals to PR and explored the reasons patients declined referral.

Methods Patients admitted with an acute exacerbation of COPD during 2013–2014 were given the opportunity to attend a Physiotherapy-led exercise class twice weekly. Baseline referral and completion rates to PR were calculated over two separate months during 2013–2014 and comparisons made with rates for the class attendees.

Results Baseline referral rate to PR was calculated at 25%. 50 patients were offered in-patient exercise during the study; 30 agreed (60%). PR referral rate for patients who attended the in-patient class was 57% compared with 40% of those who did not. Baseline PR completion rate was 15%. In those exposed to in-patient exercise, completion rose to 18%. In the group declining inpatient exercise only 13% completed PR. The reasons for declining subsequent referral to PR are outlined in Figure 1.
Abstract P136 Figure 1  Reasons why patients who attended the inpatient exercise class declined subsequent referral to community PR

Discussion  Whilst not achieving statistical significance the referral rate to PR was higher amongst patients exposed to an inpatient exercise class, suggesting an effect on the initial uptake to PR may be improved with this intervention. Completion rates of PR were similar but sample size was insufficient to reliably detect this and it is acknowledged this was a small preliminary study. As an improvement in referral rate to PR was observed the feasibility of providing a routine exercise class warrants further investigation in a larger cohort. Further investigation is also required into why many patients decline PR referral and find it difficult to express reasons why.

REFERENCES
1 NICE. CG101 Chronic Obstructive Pulmonary Disease-(Update), 2010

‘I REALLY LIVE FOR COMING HERE’. THE EFFECT OF A LONG-TERM SINGING GROUP ON CONTROL OF BREATHLESSNESS, SOCIAL EMPOWERMENT AND PSYCHOLOGICAL WELLBEING OF PATIENTS WITH RESPIRATORY DISEASE: A QUALITATIVE STUDY

Introduction Community singing programs may improve quality of life for breathless people with long-term respiratory disease but there has been limited formal exploration of its social and psychological importance. This qualitative study aimed to investigate the impact of a long-term weekly singing group on empowerment, breathlessness, psychological wellbeing and social engagement of respiratory patients at an inner city London hospital.

Methods Patients attending a weekly, 1-hour singing group led by a music therapist and open to all patients with respiratory disease were recruited. Demographic, disease severity and self reported health care resource utilisation data were collected from those who consented to participate. Semi-structured interviews (Figure 1), were used to collect qualitative data which were analysed using grounded theory methodology.

Results 16 patients (4M:12F, mean (range) age 72.6 (50–92) years) were interviewed. Diagnoses included COPD (11/16), asthma (2/16), bronchiectasis (2/16) and fibrosis (1/16) with mean (±SD, range) FEV1 1.31 (± 0.54, 0.69–2.58) litres, FEV1 54% predicted (± 22.01 range 26% – 96%). All were non-smokers (ex-smokers 12/16); 12/16 (75%) had previously attended pulmonary rehabilitation. 10/16 lived alone and 8/16 had a history of mental health comorbidity requiring treatment. Duration of singing group attendance (mean±SD) was 15.3 ± 6.5 months. Four themes were identified from the qualitative analysis of the semi-structured interviews: 1. ‘Control of Symptoms’, 2. ‘Community and Friendship’, 3. ‘Psychological Benefits’, 4. ‘Mastery of Illness’. The singing group improved breathlessness symptoms, enabled access to further sources of support and formed new friendships. Self reported primary care (GP) visits were (non-significantly) fewer in the year following commencement of singing. There was no difference in hospital admissions in the year after starting singing compared to the year before.

Conclusion The singing group had a profound impact on this group of patients with moderate chronic respiratory disease, a high prevalence of anxiety and depression and social isolation. The dominant effects were improving mood, providing a sense of mastery (control) over breathing to better cope with breathlessness, and tackling social isolation. These findings should help to inform commissioners of the value of singing groups as an effective, low-cost, non-pharmacological long-term therapy for patients with chronic respiratory disease.

P137 EARLY VS DELAYED REHABILITATION: A RANDOMISED CONTROLLED TRIAL

Introduction  Providing outpatient Pulmonary Rehabilitation (PR) following hospitalisation for an acute exacerbation of Chronic Obstructive Pulmonary Disease (AECOPD) has been found to improve exercise capacity, quality of life and a reduction in unplanned hospital admissions and mortality (Puhan, 2011). These positive effects, although studied in the short term, have led to national and international guidelines supporting the provision of post exacerbation PR (PEPR). However, uptake is poor with less than 10% of hospital discharges for AECOPD completing PEPR (Jones, 2014).

Discussion  Whilst not achieving statistical significance the referral rate to PR was higher amongst patients exposed to an inpatient exercise class, suggesting an effect on the initial uptake to PR may be improved with this intervention. Completion rates of PR were similar but sample size was insufficient to reliably detect this and it is acknowledged this was a small preliminary study. As an improvement in referral rate to PR was observed the feasibility of providing a routine exercise class warrants further investigation in a larger cohort. Further investigation is also required into why many patients decline PR referral and find it difficult to express reasons why.

REFERENCES
1 NICE. CG101 Chronic Obstructive Pulmonary Disease-(Update), 2010
The aim of this study was to establish whether delaying the offer of rehabilitation would be effective and acceptable to patients who have recently been hospitalised for an AE of their COPD.

Methods A randomised controlled trial was conducted. Patients were randomised to PEPR or delayed PEPR (D-PEPR) following hospitalisation for an AECOPD. Both programmes were the same, consisting of twice weekly, six-week hospital based programme (exercise and education). PEPR commenced within four weeks of hospital discharge and D-PEPR commenced 7 weeks after. The primary outcome was the Incremental Shuttle Walking test (ISWT), secondary outcomes were the Endurance Shuttle Walking Test (ESWT).

Results Thirty six patients consented and were assessed (14 male, mean (SD) age 66.03 (7.64) years, FEV1 1.18 (0.48) litres, ISWT 225 (160.77) metres, ESWT 222 (151.09) seconds). We observed important improvements in the PEPR group. However, only 6 patients out of 12 assessed in the D-PEPR group remained during the control time prior to the programme commencing of which 3 patients went on to complete all of D-PEPR (Table 1).

Abstract P139 Table 1 Mean changes with 95% CI for patients who completed pulmonary rehabilitation

<table>
<thead>
<tr>
<th></th>
<th>Early PR (n = 14)</th>
<th>D-PEPR at 7 weeks (n = 6)</th>
<th>Post D-PEPR (n = 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISWT (Metres)</td>
<td>28.67 (51.49 to 5.85)*</td>
<td>13.33 (52.97 to 26.31)</td>
<td>40.00 (139.37 to 59.37)</td>
</tr>
<tr>
<td></td>
<td>p = 0.427</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ESWT (Seconds)</td>
<td>250.10 (407.98 to 23.20 (259.87 to 23.20 (259.87 to 283.33 (1302.90 to 283.33 (1302.90 to 92.16)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>213.47</td>
<td></td>
<td>736.23</td>
</tr>
</tbody>
</table>

Conclusion PEPR is effective and no natural recovery was observed. Although small numbers, acceptability and completion for D-PEPR was even worse than PEPR. D-PEPR does not seem a feasible alternative to PEPR.

REFERENCE

P139 INVESTIGATING THE PROFILE OF PHYSICAL ACTIVITY IN COPD PATIENTS 7 DAYS POST DISCHARGE FROM A RESPIRATORY-RELATED ADMISSION. DOES BRIEF ADVICE HAVE AN EFFECT?

P. Kanabar, V. Warrington, L. Houchen-Wolloff, S. Singh. Centre for Exercise and Rehabilitation Science, University Hospitals of Leicester NHS Trust, Leicester, UK

Introduction and objectives There is a relationship between Physical Activity (PA) and both readmissions and mortality.1 PA in COPD in the immediate period following hospital admission and discharge has not received much attention. This study aimed to investigate the profile of PA in the 7 days following discharge from a respiratory-related admission. Additionally, we explored whether brief PA advice (given as part of a self-management (SM) manual) would improve the rate of recovery, compared to usual care.

Methods The study was a Randomised Controlled Trial. Those randomised to UC were discharged with standard treatment and follow-up addition, those allocated to the SM group received brief advice PA advice in the form of a SM manual (SPACE FOR COPD). All patients wore the ‘Sensewear’ armband (SWA) monitor for 7 days post-discharge for 12 waking hours/day. Outcomes collected were: Total Energy Expenditure (TEE), Steps, Physical Activity Level (PAL) and time spent in light, moderate and vigorous activity.

Results Activity data was collected on 25 patients with COPD, UC = 10, SM = 15. Mean (SD) Age-67.7(7.2) years, FEV1-1.01(0.43) L, MRC grade-3.8 (1. X), 14 Females, 11 Males. Figure 1 shows the serial measures of steps over 7 days. There were no significant differences in physical activity at baseline between the groups. There was little fluctuation in steps over 7 days and the change was not significant from Day 1–Day 7, within each group. Furthermore, there was no significant difference between the groups. This was the same for all of the other activity monitor data.

Abstract Figure 1

Conclusion We found there was no improvement in steps in the 7 days post-discharge, despite PA advice given in the SM group. It may be that the advice was too brief or that 7 days was not long enough to witness an effect. Further research is required to investigate the effects of an exacerbation and SM interventions on PA; capturing PA data prior to, during and after an admission would be of value.

REFERENCE
1 Puhan MA, Scharplatz M, Troosters T, Steurer J. Respiratory rehabilitation after acute exacerbation of COPD may reduce risk for readmission and mortality – a systematic review. Respir Res. 2005;6:54

P140 EFFECTS OF INDACATEROL/GLYCOPYRRONIUM ON LUNG FUNCTION AND PHYSICAL ACTIVITY IN PATIENTS WITH MODERATE TO SEVERE COPD

H. Watz, 2C. Mallaender, 1A-M Kirsten, 1Pulmonary Research Institute at Lung Clinic Grosshansdorf, Grosshansdorf, Germany, 2Novartis Pharma GmbH, Nuernberg, Germany

Introduction and objectives There is a relationship between PA and both readmissions and mortality.1 PA in COPD in the immediate period following hospital admission and discharge has not received much attention. This study aimed to investigate the profile of PA in the 7 days following discharge from a respiratory-related admission. Additionally, we explored whether brief PA advice (given as part of a self-management (SM) manual) would improve the rate of recovery, compared to usual care.

Methods The study was a Randomised Controlled Trial. Those randomised to UC were discharged with standard treatment and follow-up addition, those allocated to the SM group received brief advice PA advice in the form of a SM manual (SPACE FOR COPD). All patients wore the ‘Sensewear’ armband (SWA) monitor for 7 days post-discharge for 12 waking hours/day. Outcomes collected were: Total Energy Expenditure (TEE), Steps, Physical Activity Level (PAL) and time spent in light, moderate and vigorous activity.

Results Activity data was collected on 25 patients with COPD, UC = 10, SM = 15. Mean (SD) Age-67.7(7.2) years, FEV1-1.01(0.43) L, MRC grade-3.8 (1. X), 14 Females, 11 Males. Figure 1 shows the serial measures of steps over 7 days. There were no significant differences in physical activity at baseline between the groups. There was little fluctuation in steps over 7 days and the change was not significant from Day 1–Day 7, within each group. Furthermore, there was no significant difference between the groups. This was the same for all of the other activity monitor data.

Conclusion We found there was no improvement in steps in the 7 days post-discharge, despite PA advice given in the SM group. It may be that the advice was too brief or that 7 days was not long enough to witness an effect. Further research is required to investigate the effects of an exacerbation and SM interventions on PA; capturing PA data prior to, during and after an admission would be of value.

REFERENCE
1 Puhan MA, Scharplatz M, Troosters T, Steurer J. Respiratory rehabilitation after acute exacerbation of COPD may reduce risk for readmission and mortality – a systematic review. Respir Res. 2005;6:54
Rationale Indacaterol/glycopyrronium (IND/GLY, QVA149) is a combination of a long-acting beta-2 agonist and a muscarinic receptor antagonist for the once-daily treatment of COPD. Here we assessed the effects of indacaterol/glycopyrronium on lung function and physical activity compared with placebo.

Methods We performed a randomised, two-period, cross-over study (21 days of treatment separated by a wash-out period of 14 days) with IND/GLY 110 μg/50 μg or matching placebo. Lung function was measured by slow and forced spirometry. Physical activity was measured by an activity monitor (Bodymedia SenseWear Armband) over the last week of each treatment period. The primary endpoint was peak inspiratory capacity (IC) at the end of each treatment period (i.e., on Day 21). The co-primary endpoint was physical activity level as defined by daily activity-related energy expenditure (kcal/day). Secondary endpoints included number of steps per day, duration of at least moderate activity per day, peak IC and FEV1 on Day 1, trough IC on Day 1, and trough IC and FEV1 on Day 21.

Results 194 patients (mean age 63 years; mean postbronchodilator FEV1 61.6% predicted), were randomised; 183 patients completed the study (21 days of treatment separated by a wash-out period of 14 days) with IND/GLY 110 μg/50 μg or matching placebo. Compared with placebo, IND/GLY improved lung function and physical activity in patients with moderate to severe COPD.

Conclusion Compared with placebo, IND/GLY improved lung function and physical activity in patients with moderate to severe COPD.

Abstract P140 Table 1

<table>
<thead>
<tr>
<th></th>
<th>IND/GLY vs PBO</th>
</tr>
</thead>
<tbody>
<tr>
<td>IC (Day 21)</td>
<td>p = 0.0101; 95% CI: 0.158–0.246</td>
</tr>
<tr>
<td>trough</td>
<td>p = 0.001; 95% CI: 0.151–0.245</td>
</tr>
<tr>
<td>IC (Day 1)</td>
<td>p = 0.0101; 95% CI: 0.219–0.297</td>
</tr>
<tr>
<td>peak</td>
<td>p = 0.001; 95% CI: 0.189–0.251</td>
</tr>
<tr>
<td>FEV1 (Day 1)</td>
<td>p = 0.001; 95% CI: 0.102–0.170</td>
</tr>
<tr>
<td>peak</td>
<td>p = 0.001; 95% CI: 0.244–0.311</td>
</tr>
<tr>
<td>FEV1 (Day 21)</td>
<td>p = 0.0199; 95% CI: 1.724–71.701</td>
</tr>
<tr>
<td>trough</td>
<td>p = 0.0199; 95% CI: 0.004–0.043</td>
</tr>
<tr>
<td>Activity related energy expenditure (kcal/day)</td>
<td>p = 0.0228; (SD = 2457.95)</td>
</tr>
<tr>
<td>Co-primary</td>
<td>Duration of at least moderate activity per day (min/day)</td>
</tr>
<tr>
<td>p = 0.001; 95% CI: 0.0399</td>
<td>p = 0.2637; 95% CI: -3.333 – 12.098</td>
</tr>
</tbody>
</table>

P142 REDUCED ALL CAUSE HEALTHCARE UTILISATION AFTER BREATHING RETRAINING FOR DYSFUNCTIONAL BREATHING

Introduction There are few controlled studies to prove the effectiveness of breathing retraining in the management of
dysfunctional breathing (Cochrane 2013) and only one observational study which shows a reduction in Emergency Room attendance (Hagman 2011) as a measure of the efficacy widely reported in clinical practice.

Method Using all consecutive unselected patients referred to a single Respiratory Physiotherapy Unit with 2 experienced practitioners between April 2012 – April 2013, a historical control was used to examine the healthcare utilisation of this group. The incidence of all cause new Out Patient referrals, A+E visits, and admissions in the six month period prior to treatment was compared to the six months after the study period. Extraction of data was by review of notes and computerised search of hospital events with anonymised patient data. In addition to this information on baseline characteristics, response to treatment, and comorbidities were also examined.

Results 67 patients were recorded, 2 were duplicate referrals and excluded from further analysis. The majority were referred by the Respiratory Service, but 27 by General Practice and senior nurses. Mean age was 58 (SD 15.6) and male to female ratio 30 to 37 respectively. 93% had one or more comorbidities, the most frequent being asthma in 49%. 58 patients attended for breathing retraining with an average Nijmegen score of 26.31 (SD 10.28).

In the 6 months after physiotherapy, new outpatient referrals fell by 56% (from 70 to 31), A+E visits fell by 17% (30 to 25) but admissions rose by 35% (20 to 27). The overall reduction of secondary care visits was 31% (120 to 83). Exploratory analysis using Wilcoxon matched-pairs signed rank test showed statistical significance in the outpatient referral group only (p < 0.01).

Conclusion While this is crude data based on limited numbers in a single site, the size of effect is noteworthy, suggesting efficacy of intervention. Healthcare utilisation was not restricted to Respiratory service, in keeping with the multi-symptomatic nature of this condition. The rise in admissions is in contrast but did not relate to respiratory symptoms in this ageing population over a 24 month period. Further study is warranted.

REFERENCES


Abstract P143 Table 1 Table showing the strength of the relationship between quadriceps function (endurance and SEP) and parameters across a number of functional tests

<table>
<thead>
<tr>
<th>Functional parameter</th>
<th>Isokinetic Endurance</th>
<th>Strength-Endurance Product</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>r²</td>
</tr>
<tr>
<td>6MWT</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distance</td>
<td>-0.185</td>
<td>0.034</td>
</tr>
<tr>
<td>Minimum SpO₂</td>
<td>-0.519</td>
<td>0.269</td>
</tr>
<tr>
<td>Desaturation</td>
<td>0.470</td>
<td>0.221</td>
</tr>
<tr>
<td>Maximum perceived breathlessness</td>
<td>0.558</td>
<td>0.312</td>
</tr>
<tr>
<td>Distance-saturation product</td>
<td>-0.285</td>
<td>0.081</td>
</tr>
<tr>
<td>Incremental CPET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak VO₂ (L)</td>
<td>-0.217</td>
<td>0.047</td>
</tr>
<tr>
<td>Peak VO₂ (ml/kg)</td>
<td>-0.364</td>
<td>0.133</td>
</tr>
<tr>
<td>VO₂ @ anaerobic threshold (L)</td>
<td>-0.064</td>
<td>0.004</td>
</tr>
<tr>
<td>VO₂ @ anaerobic threshold (ml/kg)</td>
<td>-0.563</td>
<td>0.317</td>
</tr>
<tr>
<td>Endurance CPET</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak VO₂ (ml)</td>
<td>-0.275</td>
<td>0.075</td>
</tr>
<tr>
<td>Activity data</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical activity level</td>
<td>-0.312</td>
<td>0.097</td>
</tr>
<tr>
<td>Total energy expenditure</td>
<td>-0.179</td>
<td>0.032</td>
</tr>
<tr>
<td>Resting energy expenditure</td>
<td>0.189</td>
<td>0.036</td>
</tr>
<tr>
<td>Active energy expenditure</td>
<td>-0.336</td>
<td>0.113</td>
</tr>
</tbody>
</table>
limited added value of a combined "SEP" was evident. The clinical meaning of endurance measures remain unclear.

REFERENCES

A COMPARISON OF SHUTTLE WALKING TEST ENDPOINTS IN EXERCISE STUDIES IN PATIENTS WITH COPD

S Singh, F Maitas, L Tombs, WVA Fahy, M Vahdati-Bolouiri, JH Riley. Centre for Exercise and Rehabilitation Science, University Hospitals of Leicester NHS Trust, Glenfield Hospital, Leicester, UK; Centre de Pneumologie, Institut Universitaire de Cardiologie Et de Pneumologie de Québec, Université Laval, Sainte-Foy, Canada; Precise Approach LTD (Contingent Worker Who Is Working on Assignment at GSK), Uxbridge, UK; GlaxoSmithKline, Uxbridge, UK.

Background: The Minimal Clinically Important Difference (MCID) for pharmacotherapy for the endurance shuttle walking test (ESWT) has been reported by Pepin et al. 1 Two performance measures, change in time (45–85 s), and percentage change from baseline (13–15%) are investigated here.

Objective: To review endurance outputs in two exercise studies combined in this post-hoc analysis, and compare two different measures of performance MCID, exercise time in seconds and as a percentage change.

Methods: The effect of umeclidinium (UMEC 62.5 mcg)/vilanterol (VI 25 mcg), VI (25 mcg) and UMEC (62.5 mcg) compared with placebo in exercise endurance, using the ESWT across two 12-week cross-over studies enrolling hyperinflated COPD patients (FRC >120%) was investigated. All ESWTs were performed at 80% VO2 max derived from a baseline incremental SWT. ESWT time (in seconds) and % change from baseline were reported and compared at Day 2 and 84, 3 h post-dose. Analysis was performed using a repeated measures model with covariates of study, period walking speed, visit by mean walking speed and visit by treatment. Combining this test with simple remote technology it can be determined whether they are intentionally or non-intentional non-adherence, and can show technique and timing errors.

Results: Baseline exercise endurance times (EET) and on-treatment change from baseline as seconds and percentage are presented in Table 1. UMEC/VI showed mean changes (95% CI) from placebo at both timepoints, whereas for change from baseline EET only the Day 2 analysis vs placebo showed a result greater than the MCID. MCID as percentage change from baseline may be a more meaningful measure of response to bronchodilators than MCID in seconds because it reflects a patient’s baseline exercise tolerance. No additional safety concerns were identified.

Funding: GSK Clinicaltrials.gov: NCT01328444, NCT01323660

REFERENCE

Asthma treatment

USING FRACTIONAL EXHALED NITRIC OXIDE (FENO) SUPPRESSION AND INHALED COMPLIANCE ASSESSMENT (INCA) TO IDENTIFY AND MANAGE NON-ADHERENCE IN DIFFICULT ASTHMATICS

LG Heaney, KJ Hetherington. Queen’s University Belfast, Belfast, UK

Abstract P144 Table 1

<table>
<thead>
<tr>
<th></th>
<th>UMEC (62.5mcg)</th>
<th>VI (25mcg)</th>
<th>UMEC/VI (62.5/25mcg)</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 89</td>
<td>297.1 (159.4)</td>
<td>303.5 (130)</td>
<td>307.7 (162.6)</td>
<td>328.1 (182.1)</td>
</tr>
<tr>
<td>N = 140</td>
<td>20.4 (7.7)</td>
<td>27.3 (6.3)</td>
<td>27.3 (6.3)</td>
<td>27.3 (6.3)</td>
</tr>
<tr>
<td>N = 321</td>
<td>307.7 (162.6)</td>
<td>307.7 (162.6)</td>
<td>307.7 (162.6)</td>
<td>307.7 (162.6)</td>
</tr>
</tbody>
</table>

REFERENCE

Introduction: The identification of intentional and non-intentional non-adherence in patients with "difficult" asthma and establishing who should respond well to inhaled steroid treatment is essential to prevent the inappropriate escalation of inhaled corticosteroids (ICS) and the initiation of complex biological therapies. One week FeNO suppression testing can identify non-adherence and ascertain which patients who should achieve good asthma control with better adherence to standard treatment. Combining this test with simple remote technology it can be determined whether they are intentionally or non-intentionally non-adherent, and can show technique and timing errors.

Methods: The INCA device was developed by Professor Richard Costello in conjunction with Vitalograph and is designed to work with the Accuhaler inhaler. The INCA device time and date stamps the activation of a microphone and records a sound file of the inhaler being used; these sound files can then be transferred to the computer and uploaded onto a server where they are analysed by an algorithm. Within the Belfast City Hospital 40 patients have carried out the one week FeNO suppression testing, 20 of those in combination with INCA technology. This testing is relatively simple and is part of the Medical Research Council funded Refractory Asthma Stratification Programme and is currently being piloted in five specialist Difficult Asthma Centres in the UK.
Results Within the 40 patients there were 23 non-suppressors (ie adherent patients) and 17 suppressors (ie non-adherent patients). With the patients using the INCA technology, the server highlighted technique errors; for example, not activating the drug blister or exhaling into the mouthpiece, as well as erratic timing issues. At subsequent follow up appointments these issues were emphasised and addressed by using patient-friendly print outs showing the usage of the inhaler, with the addition of alarm reminders and behavioural cues to encourage adherence.

Conclusion FeNO Suppression and INCA testing is an effective method of identifying and managing non-adherence with the capability of encouraging improved technique and timing also having the capability to be used as a long term behavioural assistance to adherence to ICS.

P146 PRESCRIBING RESPIRATORY MEDICINES WITHOUT MAKING A DIAGNOSIS OF ASTHMA IN UK PRIMARY CARE

Introduc4on and objectives Despite asthma being one of the most prevalent worldwide chronic diseases, there remains a wide variation in prevalence. The United Kingdom’s (UK) National Review of Asthma Deaths suggests avoidable factors play a part in as many as three-quarters of cases of asthma death. There is need to highlight and address many aspects of asthma care including the variation in diagnosis across all ages to enable appropriate treatment and improve symptom control. Here we investigate the relationship between prescribing respiratory medications and making the diagnosis of asthma, in UK primary care.

Methods GP recorded data were collected from 72 UK general practices participating in the pilot British Lung Foundation asthma management program in 3 health authority areas (two Clinical Commissioning Groups in England and one Health Board in Scotland). A retrospective analysis was undertaken of the Optimum Patient Care Research Database. This included data on child and adult patients (aged between 0 and 89) in receipt of asthma medication without a diagnosis of a chronic respiratory disease, classified by the absence of a QoF recorded asthma diagnosis. Asthma medications prescribed in the previous 12 months were identified (beta2-agonists, inhaled corticosteroids, cromones or montelukast).

Results 39,124 patients received at least one respiratory medication in the 12 months prior to data collection. Of these, 9,761 (25.0%) had no clinical diagnosis ever recorded for asthma or COPD. 3,655 patients were prescribed 2 or more respiratory medications without a coded respiratory disease and 982 patients had a lower respiratory tract infection recorded within the same period.

Conclusion These results raise concern about over and under-treatment of children and adults in whom no diagnosis of asthma or any other chronic respiratory disease has been made. It is important that future Primary Care studies highlight the importance of early accurate diagnosis before starting treatment. Also, we suggest the present UK national prevalence and morbidity data are likely to underestimate the total burden of asthma within the Primary Care setting.
who had been prescribed ≥12 SABA inhalers without an asthma review (as coded by QOF) were identified.

**Results** 94,955 asthma patients met the inclusion criteria, of which 12661 (13%) were children. LABAs with no ICS had been prescribed to 402 patients (0.4%). A total of 5032 patients (5.3%) had been prescribed ≥ 12 SABA inhalers, ranging from 13–136 inhalers of which 1965 (39%) had not had an asthma review. Among these, 117 were children, 0.92% of the total.

**Conclusion** These data, covering a large GP population, suggest evidence of non-guideline recommended prescribing which might contribute to increased risk to asthma patients. Prescribers should consider implementing system alerts to identify and review such prescribing behaviours.

**REFERENCE**


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**P148**

ONCE-DAILY TIOTROPIUM RESPIMAT® ADD-ON TO AT LEAST ICS MAINTENANCE THERAPY REDUCES EXACERBATION RISK IN PATIENTS WITH UNCONTROLLED SYMPTOMATIC ASTHMA

D Dusser, R Buhl, M Castro, HAM Kerstjens, P Paggiaro, M Engel, P Moroni-Zentgraf, H Schmidt, HAM Kerstjens, Royal Devon & Exeter Hospital, Exeter, UK; University of Cape Town, Cape Town, South Africa; Respiratory Pathophysiology and Rehabilitation Unit, University of Pisa, Pisa, Italy; Center for Genomics and Personalized Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA; TA Respiratory Diseases, Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim Am Rhein, Germany; Global Biometrics and Clinical Applications, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an Der Riss, Germany; University of Groningen, Department of Pulmonary Medicine, University Medical Center Groningen, Groningen, The Netherlands

Background A reduction in the risk of asthma exacerbation may provide improvements in clinical burden, patient experience and healthcare costs. In Phase III trials, once-daily tiotropium Respimat® add-on to at least ICS improved lung function in patients with symptomatic asthma. We investigated exacerbation risk in each trial.

Methods Five Phase III, double-blind, placebo-controlled, parallel-group trials in patients with symptomatic asthma. Patients received tiotropium Respimat® 5 µg or placebo Respimat® each as add-on to at least ICS maintenance therapy (Table 1). Pre-planned co-primary or secondary end points were time to first severe exacerbation and time to any asthma worsening.

Results Mean baseline% of predicted FEV1, ACQ-7 score and ICS dose (µg) were: 56.0 ± 13.1, 2.6 ± 0.7 and 1198 ± 539 in PrimoTinA-asthma® (two replicate trials); 75.1 ± 11.5, 2.2 ± 0.5 and 660 ± 213 in MezzoTinA-asthma® (two replicate trials); and 77.7 ± 11.9, 2.1 ± 0.4 and 381 ± 78 in GraziaTinA-asthma®. Tiotropium Respimat® 5 µg reduced risk of severe asthma exacerbation by at least 21% in all three severity cohorts (Table 1) and risk of asthma worsening versus placebo Respimat® in all trials, with a statistically significant reduction in PrimoTinA-asthma®.

Conclusion Once-daily tiotropium Respimat® 5 µg add-on to at least ICS maintenance therapy consistently reduced exacerbations across asthma severities and so may be a beneficial add-on option to reduce current and future exacerbation risk.

**Abstract P148 Table 1** Risk of severe asthma exacerbation in PrimoTinA-asthma®, MezzoTinA-asthma® and GraziaTinA-asthma®

<table>
<thead>
<tr>
<th>Trial</th>
<th>Background medication</th>
<th>Tiotropium Respimat® 5 µg</th>
<th>Placebo Respimat®</th>
<th>HR* (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PrimoTinA-asthma®</td>
<td>ICS + LABA (&gt;800 µg budesonide or equivalent)</td>
<td>0.79 (0.62, 1.00)</td>
<td>0.034</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MezzoTinA-asthma®</td>
<td>ICS (400–800 µg budesonide or equivalent)</td>
<td>0.72 (0.45, 1.14)</td>
<td>0.164</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GraziaTinA-asthma®</td>
<td>ICS (200–400 µg budesonide or equivalent)</td>
<td>0.25 (0.03, 2.24)</td>
<td>0.216</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p Hazard ratio, time to first severe exacerbation (vs placebo, <1 favours tiotropium Respimat®)

1D Halpin, E Bateman, P Paggiaro, E Blleecker, M Engel, P Moroni-Zentgraf, H Schmidt, HAM Kerstjens, Royal Devon & Exeter Hospital, Exeter, UK; University of Cape Town, Cape Town, South Africa; Respiratory Pathophysiology and Rehabilitation Unit, University of Pisa, Pisa, Italy; Center for Genomics and Personalized Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina, USA; TA Respiratory Diseases, Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim Am Rhein, Germany; Global Biometrics and Clinical Applications, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an Der Riss, Germany; University of Groningen, Department of Pulmonary Medicine, University Medical Center Groningen, Groningen, The Netherlands

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**P149**

ONCE-DAILY TIOTROPIUM RESPIMAT® ADD-ON TO AT LEAST ICS IN ADULT PATIENTS WITH SYMPTOMATIC ASTHMA: POOLED SAFETY ANALYSIS

D Halpin, E Bateman, HAM Kerstjens, P Paggiaro, M Engel, P Moroni-Zentgraf, U Ursal, E Bateman, Pulmonary Department and Adult Cystic Fibrosis Center, Université Paris Descartes, Sorbonne Paris Cité, Cochin Hospital, AP-HP Paris, Paris, France, Pulmonary Department, Main University Hospital, Mainz, Germany; Division of Pulmonary and Critical Care Medicine, Washington University School of Medicine, St. Louis, Missouri, USA; University of Groningen, Department of Pulmonary Medicine, University Medical Center Groningen, Groningen, The Netherlands; Respiratory Pathophysiology and Rehabilitation Unit, University of Pisa, Pisa, Italy; TA Respiratory Diseases, Boehringer Ingelheim Pharma GmbH & Co. KG, Ingelheim Am Rhein, Germany; Global Biometrics and Clinical Applications, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach an Der Riss, Germany; Department of Medicine, University of Cape Town, Cape Town, South Africa

Background A high proportion of patients with asthma are symptomatic despite at least ICS maintenance therapy. Five trials aimed to evaluate the safety of tiotropium Respimat® compared with placebo Respimat®, each as add-on to at least ICS in adult patients with symptomatic asthma.

Methods Five Phase III and one Phase II randomised, double-blind, placebo-controlled, parallel-group trials. PrimoTinA-asthma® (48 weeks): tiotropium Respimat® 5 µg add-on to ICS + LABA (≥800 µg budesonide or equivalent); MezzoTinA-asthma® (24 weeks): tiotropium Respimat® 5 µg or 2.5 µg add-on to ICS (400–800 µg budesonide or equivalent); GraziaTinA-asthma® (12 weeks): tiotropium Respimat® 5 µg or 2.5 µg add-on to ICS (200–400 µg budesonide or equivalent); Study 342 (16 weeks): tiotropium Respimat® 5 µg add-on to ICS (400–800 µg budesonide or equivalent). Pooled safety data are presented.

Results 1929 patients received tiotropium Respimat® (PrimoTinA-asthma®, n = 456; MezzoTinA-asthma®, n = 1036; GraziaTinA-asthma®, n = 309; Study 342, n = 128). Frequency

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**Poster sessions**
of AEs in >2% of patients was comparable in the tiotropium Respimat® 5 μg, tiotropium Respimat® 2.5 μg and placebo Respimat® groups (Table 1). No deaths occurred. 110 (5.7%) and 55 (4.4%) patients receiving tiotropium Respimat® and placebo Respimat®, respectively, reported drug-related AEs (cardiac AEs were rare: tiotropium Respimat®, 7 [0.4%]; placebo Respimat®, 3 [0.2%]). One drug-related serious AE (asthma) was reported with tiotropium Respimat®.

### Abstract P149 Table 1

<table>
<thead>
<tr>
<th></th>
<th>Tiotropium Respimat® 5 μg (n = 1256)</th>
<th>Tiotropium Respimat® 2.5 μg (n = 673)</th>
<th>Placebo Respimat® (n = 1260)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure, patient-years</td>
<td>705.42</td>
<td>371.08</td>
<td>708.04</td>
</tr>
<tr>
<td>Any AE</td>
<td>732 (58.3)</td>
<td>350 (52.0)</td>
<td>712 (61.3)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>51 (4.1)</td>
<td>12 (1.8)</td>
<td>56 (4.4)</td>
</tr>
<tr>
<td>AEs by preferred term</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>326 (26.0)</td>
<td>106 (15.4)</td>
<td>384 (30.5)</td>
</tr>
<tr>
<td>Decreased PEF rate</td>
<td>158 (12.6)</td>
<td>58 (8.6)</td>
<td>207 (16.4)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>98 (7.8)</td>
<td>51 (7.6)</td>
<td>118 (9.4)</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>49 (3.9)</td>
<td>29 (4.3)</td>
<td>67 (5.3)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>43 (3.4)</td>
<td>9 (1.3)</td>
<td>27 (2.1)</td>
</tr>
<tr>
<td>Headache</td>
<td>41 (3.3)</td>
<td>19 (2.8)</td>
<td>49 (3.9)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>31 (2.5)</td>
<td>17 (2.5)</td>
<td>33 (2.6)</td>
</tr>
<tr>
<td>Influenza</td>
<td>29 (2.3)</td>
<td>1 (0.1)</td>
<td>25 (2.0)</td>
</tr>
</tbody>
</table>

 AE = adverse event, HR = hazard ratio

**Conclusion**

Once-daily tiotropium Respimat® add-on to at least ICS maintenance therapy in adult patients demonstrates a safety profile comparable with that of placebo and is well tolerated across severities of symptomatic asthma.

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**P150**

**ONCE-DAILY TIOTROPium RESPIMAT® REDuces RISK of SEVERE ASTHMA EXACERBATION and ASTHMA WORsENING IN SYMPTOMATIC ASTHMA, INDEPENDENT OF ALLERgIC AND INFLAMMATory STATUS**

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**Background**

Four trials explored whether tiotropium Respimat® add-on to at least ICS is effective in the T1/2 phenotype, determined by high serum immunoglobulin E (IgE) and blood eosinophil values, in reducing risk of severe asthma exacerbation and asthma worsening in adult patients with moderate or severe symptomatic asthma.

**Methods**

Four Phase III, double-blind, placebo-controlled, parallel-group trials. PrimoTinA-asthma® (two 48-week trials; NCT00776984/NCT00772538; n = 912); tiotropium Respimat® 5 μg or placebo Respimat® add-on to ICS + LABA (>800 μg budesonide or equivalent); MezzoTinA-asthma® (two 24-week trials; NCT01172808/NCT01172821; n = 2100); tiotropium Respimat® 5 μg, tiotropium Respimat® 2.5 μg or placebo add-on to ICS (400–800 μg budesonide or equivalent). Patients had symptomatic asthma requiring treatment with at least ICS for ≥4 weeks before screening; COPD was excluded. Subgroups of allergic and inflammatory status (IgE and eosinophils) were used to analyse risk of severe exacerbation and asthma worsening, post hoc. Cox regression modelling analyses, adjusted for treatment, IgE or eosinophils and treatment by IgE or eosinophil interaction, were applied to calculate hazard ratios and 95% confidence intervals across IgE (2–2000 μg/L) and eosinophil (0.05–7.00 × 10^9/L) values.

**Results**

Severe exacerbation: in PrimoTinA-asthma®, tiotropium Respimat® 5 μg reduced risk in terms of hazard ratio versus placebo Respimat® up to an IgE level of ~1000 μg/L, and consistently across all eosinophil values. In MezzoTinA-asthma®, tiotropium Respimat® 5 μg and 2.5 μg reduced risk versus placebo consistently across all IgE and eosinophil levels. Asthma worsening: in PrimoTinA-asthma®, tiotropium Respimat® 5 μg reduced risk in terms of hazard ratio versus placebo Respimat®, independent of IgE and eosinophil values. In MezzoTinA-asthma®, tiotropium Respimat® 5 μg reduced risk versus placebo across all IgE and eosinophil values. Tiotropium Respimat® 2.5 μg reduced risk versus placebo across all IgE values and at eosinophil values <3.00 × 10^9/L.

**Conclusion**

Tiotropium Respimat® add-on to ICS ± LABA reduces risk of severe exacerbation and asthma worsening in patients across severities of symptomatic asthma and a broad range of IgE and eosinophil values, suggesting efficacy independent of underlying allergic/eosinophilic inflammation. Once-daily tiotropium Respimat® may have potential as add-on to at least ICS maintenance therapy in patients with symptomatic asthma, independent of T1/2 phenotype.
µg budesonide or equivalent) received once-daily tioR 5 µg or placebo Respimat®. In two 24-week trials (MezzoTinA-asthma®: NCT01172808/NCT01172821), patients on ICS (400–800 µg budesonide or equivalent) received once-daily tioR 5 µg or 2.5 µg, twice-daily salmeterol 50 µg via hydrofluoroalkane metered-dose inhaler (active comparator) or placebo (identical devices in a double-dummy protocol). Pre-planned analyses (pooled data) of time to first severe exacerbation and time to first episode of asthma worsening were performed in TH2-low and TH2-high subgroups: total serum immunoglobulin (IgE) ≤ or >430 µg/L (179.2 IU/L); blood eosinophils ≤ or >0.6 × 10⁹/L (600/µL).

Results 912 patients with severe asthma received tioR 5 µg or placebo Respimat®: 205/182 were reported with IgE >430 µg/L and 99/87 with an eosinophil count of >0.6 × 10⁹/L. 2100 patients with moderate asthma received tioR 5 µg or 2.5 µg, salmeterol or placebo: 319/320/319/326 were reported with IgE >430 µg/L and 104/103/111/107 with an eosinophil count of >0.6 × 10⁹/L. Time to first severe exacerbation was longer with tioR versus placebo (Table 1) in patients with severe or moderate asthma, independent of IgE and eosinophils (interaction p values Cox regression 0.169 and 0.754, respectively, for PrimoTinA-asthma®; analyses not performed for MezzoTinA-asthma® because of low incidence of severe exacerbations). Time to first asthma worsening was longer with tioR versus placebo (Table 1) in patients with severe or moderate asthma, independent of IgE (interaction p values 0.998 [PrimoTinA-asthma®] and 0.041 [MezzoTinA-asthma®]) and eosinophils (interaction p values 0.251 [PrimoTinA-asthma®] and 0.125 [MezzoTinA-asthma®]).

### Abstract P151 Table 1 Risk of severe asthma exacerbation and asthma worsening in PrimoTinA-asthma® and MezzoTinA-asthma®

<table>
<thead>
<tr>
<th>All comparisons versus placebo Respimat® or placebo HFA-MDI, hazard ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum IgE (µg/L)</td>
</tr>
<tr>
<td>≤430</td>
</tr>
<tr>
<td>PrimoTinA-asthma® (ICS + LABA)</td>
</tr>
<tr>
<td>TioR 5 µg</td>
</tr>
<tr>
<td>QD</td>
</tr>
<tr>
<td>MezzoTinA-asthma® (ICS)</td>
</tr>
<tr>
<td>TioR 5 µg</td>
</tr>
<tr>
<td>QD</td>
</tr>
<tr>
<td>TioR 2.5 µg</td>
</tr>
<tr>
<td>QD</td>
</tr>
<tr>
<td>Salmeterol®</td>
</tr>
<tr>
<td>p = 0.594</td>
</tr>
</tbody>
</table>

| MezzoTinA-asthma® (ICS) |
| TioR 5 µg | 0.88 | 0.83 | 0.90 | 0.70 |
| QD | p = 0.495 | p = 0.220 | p = 0.410 | p = 0.170 |
| TioR 2.5 µg | 0.45 | 0.81 | 0.60 | 0.81 |
| QD | p < 0.001 | p = 0.157 | p < 0.001 | p = 0.691 |
| Salmeterol® | 0.60 | 0.84 | 0.71 | 0.92 |
| p = 0.009 | p = 0.231 | p = 0.009 | p = 0.714 |

*Defined as either a progressive increase in symptoms or a decline of ≥30% in best morning PEF for ≥2 consecutive days; †Plus placebo HFA-MDI BID; ‡Salmeterol HFA-MDI 50 µg BID plus placebo Respimat®. QD, BID, twice-daily; HFA-MDI, hydrofluoroalkane metered-dose inhaler; QD, once-daily; tioR, tiotropium Respimat®.

Conclusion Once-daily tiotropium Respimat® add-on to at least ICS reduced the risk of severe exacerbation and asthma worsening in patients with moderate or severe symptomatic asthma, independent of TH2 phenotype.

**P152 FLUTICASONE FURATE (FF)/VILANEROL (VI) ONCE DAILY REDUCES ASTHMA SYMPTOMS BOTH DAY AND NIGHT**


10.1136/thoraxjnl-2015-207770.289

Introduction and objectives FF/VI is the first once daily inhaled corticosteroid/long-acting β₂-agonist combination available for the treatment of asthma. Results from five phase III studies that have previously been presented demonstrated a sustained 24 h improvement in lung function and improvement in symptom-free 24 h periods.

Methods Post-hoc analyses of diary card data from these studies were performed to examine whether there was any difference in the contribution of the day and night time symptom-free period to the 24 h symptom-free period. The diary card scale used is described below.

Day-time Symptom Score:
- 0 = No symptoms during the day
- 1 = Symptoms for one short period during the day
- 2 = Symptoms for two or more short periods during the day
- 3 = Symptoms for most of the day which did not affect my normal daily activities
- 4 = Symptoms for most of the day which did affect my normal daily activities
- 5 = Symptoms so severe that I could not go to work or perform normal daily activities

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 day or night the patient needed to record a score of 0.

Results The post-hoc analyses demonstrated that the improvements in day and night time symptom–free periods were similar to the 24 h symptom free periods. See Figure 1 below.

Conclusions In general benefits in symptom free days and symptom free nights contributed to the benefit of FF/VI over comparator groups in terms of 24 h symptom free periods.
and, with pressurised metered-dose inhalers (pMDIs), the failure to inhale “slowly”. We present an easy to remember “2–3–4” training paradigm, designed to address these errors, that was used in an open-label, cross-over study comparing patient handling of fluticasone propionate/formoterol (FP/FORM; flutiform®) breath-actuated inhaler (BAI) and pMDI devices. Here we present the pMDI data.

Methods The study was carried out in 311 patients (≥12 years) with persistent asthma (64%), COPD (28%), or both asthma and COPD (8%) of patients. Patients were randomised to one of two sequences (BAI/pMDI or pMDI/BAI). Patients were trained to correctly use each device prior to an assessment of correct handling according to prespecified criteria. Eight steps were assessed including, but not limited to: exhale ≥2s; inhale ≥3s; hold breath ≥4s; the 2–3–4 technique. Patients were assessed on a single device (BAI or pMDI) at each visit, with 7–21 days between the two visits.

Results Overall, 77.2% of patients demonstrated correct performance of all steps of FP/FORM pMDI use at their first attempt post-training (N = 307); a further 14.0% required 2 attempts. 99.3% of patients were successfully trained within 15 min. Step 2 (Removes cap) and steps 4–6 (Places upright in mouth; starts inhaling and actuates; inhales for at least 3 s) were considered critical steps, and 82.4% of patients demonstrated correct performance of all 4 critical steps at their first attempt post-training. 96.1%, 87.6% and 95.8% of patients correctly followed each component of the “2–3–4” training paradigm with the pMDI at the first attempt post-training (exhale ≥2s, inhale ≥3s; hold breath ≥4s, respectively).

Conclusions Almost all patients can be rapidly taught to use a pMDI (within 15 min) using a simple training method suitable for all clinical settings. An easy to remember, sequential “2–3–4” paradigm is effective in encouraging patients to exhale to residual volume, to inhale slowly, and to breathe hold satisfactorily: manoeuvres that are frequently performed incorrectly without such instruction.

Sponsor Mundipharma Research Ltd.

Abstract P154 Table 1

<table>
<thead>
<tr>
<th>Inhaler technique variables</th>
<th>Spiromax</th>
<th>Turbohaler</th>
<th>p-value(^{1})</th>
<th>Odds ratios ((95% CI)^{3})</th>
<th>Rate ratios ((95% CI)^{4})</th>
<th>Treatment difference ((95% CI)^{5})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhaler mastery achievement, stage 1, n (%)(^{a})</td>
<td>Yes</td>
<td>454 (94)</td>
<td>418 (87)</td>
<td>&lt;0.001</td>
<td>3.77</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>27 (6)</td>
<td>63 (13)</td>
<td>(2.05–6.95)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Inhaler mastery maintenance, stage 2, n (%)(^{b})</td>
<td>Yes</td>
<td>89 (59)</td>
<td>82 (53)</td>
<td>0.316</td>
<td>1.26</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>62 (41)</td>
<td>72 (47)</td>
<td>(0.80–1.98)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Total HCP-observed errors, mean (SD)</td>
<td>—</td>
<td>0.50 (0.67)</td>
<td>0.81 (1.10)</td>
<td>—</td>
<td>0.61</td>
<td>—</td>
</tr>
<tr>
<td>HCP-observed mastery assessed by independent video review, n (%)</td>
<td>Yes</td>
<td>122 (81)</td>
<td>92 (60)</td>
<td>(0.001)</td>
<td>2.84</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>29 (19)</td>
<td>62 (40)</td>
<td>(1.69–4.76)</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Change in 6-item Asthma Control Questionnaire, week 12, mean (SD)</td>
<td>—</td>
<td>-0.22 (0.95)</td>
<td>-0.36 (1.05)</td>
<td>—</td>
<td>0.13</td>
<td>—</td>
</tr>
</tbody>
</table>

\(^{a}\)In stage 1, 493 patients were randomly assigned to either empty Spiromax followed by empty Turbohaler or empty Turbohaler followed by empty Spiromax. Achieving inhaler mastery was defined as the absence of HCP-observed errors by the end of step 3 of a 6-step standardised inhaler training protocol for empty Spiromax compared to empty Turbohaler inhalers; \(^{b}\)In stage 2, 305 out of 395 patients (61.9%) patients were eligible for the full analysis set. Maintaining inhaler mastery was defined as the absence of HCP-observed errors after 12 weeks of inhaler use; \(^{1}\)The p-value for the treatment comparison is based on chi-square, \(p < 0.05\) considered statistically significant; \(^{2}\)Logistic regression; \(^{3}\)Negative binomial regression; \(^{4}\)Analysis of variance; \(^{5}\)Confidence interval; HCP: Health care professional; SD, standard deviation.

P154 EVALUATION OF INHALER TECHNIQUE MASTERY FOR BUDESONIDE FORMOTEROL SPIROMAX® COMPARED WITH SYMBICORT TURBOHALER® IN ADULT PATIENTS WITH ASTHMA: PRIMARY RESULTS FROM THE EASY LOW INSTRUCTION OVER TIME [ELIOT] STUDY

Introduction and objectives Technical errors in the use of inhalers are associated with poor asthma control. This study evaluated achievement of mastery in a training environment using a randomised cross-over design (stage 1), followed by randomisation into a prospective 12-week trial to assess maintenance of mastery in patients receiving inhaled corticosteroids (ICS)/long-acting β₂-agonists (LABA) via SPIROMAX versus ICS/LABA received via TURBOHALER (stage 2).

Methods Patients with asthma were randomised to a 6-step training protocol using empty Spiromax and empty Turbohaler devices. The proportion of patients achieving and maintaining inhaler mastery, respectively defined as the absence of health care professional (HCP)-observed errors by training step 3 (instructional video) in stage 1, and the absence of HCP-observed errors after 12 weeks of inhaler use in stage 2, were analysed using logistic regression. The maintenance of independent expert video-observed inhaler mastery was analysed using logistic regression. Total observed errors (HCP and technology) were analysed using a negative binomial regression model. Vitalsograph Pneumatic Spirometry results were compared using a Mann Whitney U test.

Results A total of 493 (89.1%) patients (stage 1) and 305 (61.9%) (stage 2) were eligible for the full analysis set. The odds of maintaining inhaler mastery were not significantly different...
for patients using either inhaler, although achieving inhaler mastery was significantly greater in patients using Spiromax compared with Turbohaler at baseline. A higher, non-significant percentage of patients using Spiromax maintained inhaler mastery (assessed by HCPs). This result was supported by significantly higher odds of maintaining mastery when HCP errors were calibrated using independent video assessment in patients using Spiromax (consented videos available for 243/305 patients [79%]). Maintaining inhaler mastery improved asthma control in both treatment groups and was not significantly different (Table 1).

Conclusions The proportion of patients achieving inhaler mastery at baseline was significantly greater for Spiromax compared with Turbohaler; no significant difference was found in inhaler mastery at 12 weeks. Patients using Spiromax made significantly fewer errors overall (HCP-observed and HCP-technology-observed) than patients using Turbohaler. Maintaining inhaler mastery improved asthma control in both treatment groups. Independent video assessment can assist HCPs in evaluating device mastery, and is proposed as the gold standard in such studies.

Introduction and objectives FF/VI is the first once daily inhaled corticosteroid/long-acting β2-agonist combination available for the treatment of asthma. Data from five phase III studies that have previously been presented have generally demonstrated a sustained 24 h improvement in lung function and improvement in rescue-free 24 h periods compared with placebo (P), FF alone or fluticasone propionate (FP). Due to differences in study comparators, duration of study and primary endpoints, integration of the study results has not been possible therefore each study is considered separately.

Methods Post-hoc analyses of diary card data from the 5 studies were performed to examine whether there was any difference in the contribution of the day and night time rescue medication use to the 24 h rescue-free period. Patients recorded in an electronic diary card the number of inhalations of rescue salbutamol/albuterol inhalation aerosol used during the day and night.

To be counted as rescue-free during the day or night the patient needed to record a no use of rescue medication during that period.

Results The post-hoc analyses demonstrated that the improvements in day and night time rescue –free periods were similar to the 24 h rescue free periods. See Figure 1 below.

Conclusions In general the benefit of FF/VI on rescue free 24 h periods is reflected in the improvements seen in day and night time rescue use.

Abstract P155 Figure 1
P156 OVERUSE OF INHALED CORTICOSTEROIDS IN ASTHMA PATIENTS WITH CONCURRENT EXERCISE-INDUCED LARYNGEAL OBSTRUCTION

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10.1136/thoraxjnl-2015-207770.293

Introduction Exercise induced laryngeal obstruction (EILO) causes asthma-like respiratory symptoms (i.e. shortness of breath and wheezing) and EILO is therefore difficult to distinguish from asthma in the clinic, resulting in a diagnostic dilemma in symptom based asthma management. We aimed to elucidate if the symptom contribution from EILO affected treatment strategy in patients suffering from both asthma and EILO compared with patients suffering from asthma only.

Methods We included 28 consecutively referred subjects with verified asthma, of which 11 had concurrent EILO. At baseline and at a one-year follow-up, all subjects underwent a thorough work-up consisting of a detailed clinical interview including asthma medication history, ACQ and mini-AQLQ scores, and diagnostic tests including spirometry, Mannitol and Methacholine bronchoprovocation tests, and fractional exhaled nitric oxide. Further, all subjects underwent a continuous laryngoscopy during exercise (CLE) test verifying the severity or absence of any concurrent EILO.

Results Subjects who suffered from both asthma and EILO were prescribed higher doses of inhaled corticosteroids (ICS) as a result of the baseline work-up (P = 0.016) and were reduced in ICS doses at time of follow-up (P = 0.027) and reported a significant decrease in ACQ-scores at one-year follow-up (P = 0.016). In subjects with asthma only, there were no significant changes in ACQ scores at time of follow up despite of comparable asthma severities between groups at time of referral.

Conclusion EILO is a relevant differential diagnosis when managing patients with respiratory symptoms in a tertiary asthma clinic. Symptoms arising from EILO are difficult to distinguish from asthma symptoms, resulting in an ostensible overuse of ICS in patients with EILO. Further studies are needed to establish the clinical consequences and the optimal treatment strategy in this patient group.

REFERENCE

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P157 INDIVIDUAL PATTERNS OF INHALER USE AND HEALTH OUTCOMES IN ADOLESCENTS WITH ASTHMA

1S Howard, 1M Patel, 1AR Lang, 1C Youle, 1H Vyas, 1D Shaw, 1S Sharples. 1University of Nottingham, Nottingham, Nottinghamshire

10.1136/thoraxjnl-2015-207770.294

Abstract P157 Table 1 Forced Expiratory Volume (FEV1) Spirometry values for four of the seven participants pre and post study

<table>
<thead>
<tr>
<th>Participant</th>
<th>Pre Study</th>
<th>Study Period</th>
<th>Post-Study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FEV1 (L)</td>
<td>AM Adherence</td>
<td>PM Adherence</td>
</tr>
<tr>
<td>P1</td>
<td>2.15 28</td>
<td>73 71</td>
<td>76 3.1</td>
</tr>
<tr>
<td>P2</td>
<td>4.76 0</td>
<td>93 97</td>
<td>90 5.43</td>
</tr>
<tr>
<td>P3</td>
<td>2.86 23</td>
<td>93 94</td>
<td>92 2.88</td>
</tr>
<tr>
<td>P4</td>
<td>2.36 118</td>
<td>67 66</td>
<td>68 2.61</td>
</tr>
</tbody>
</table>

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P158 THE COST OF STEROID INDUCED MORBIDITY AMONG SEVERE ASTHMA PATIENTS IN THE UK

1L Barry, 1S Sweeney, 1C O’Neill, 1C Patterson, 1D Price, 1L Heaney. 1National University of Ireland, Galway, Ireland; 2Queens University of Belfast, Belfast, UK; 3University of Aberdeen, Aberdeen, UK

10.1136/thoraxjnl-2015-207770.295
Introduction Patients with severe asthma are estimated to comprise 5–10% of the total asthma population but contribute disproportionately to the overall burden of disease. A growing body of evidence exists that implicates steroid exposure in morbidity and healthcare costs among this group.

Aim This study sought to quantify the additional healthcare costs associated with steroid exposure among patients with severe asthma.

Methods Data on patients severe asthma (GINA treatment step 5 with ≥4 prescriptions/year oral corticosteroids, \( n = 808 \)) was obtained from the Optimum Patient Care Research Database (OPCRD) database along with age and gender matched mild/moderate asthma patients (GINA treatment step 2/3, \( n = 3975 \)) and non-asthmatic controls (rhinitis only, \( n = 1865 \)). Data included details of all scheduled and unscheduled healthcare consultations and details of prescribed medicines. Data on service use were extracted for the two most recent years for which observations were available. Healthcare contacts were monetised using unit costs extracted from the Personal Social Services Research Unit’s reference costs and for drugs using Prescription Cost Analysis data. All costs were expressed in their 2013 equivalents. Sensitivity analyses related to identification of staff providing specific consultations or activity, and high/low estimates based on assumptions used were produced. Mean high/low healthcare costs over two years by group were estimated and compared as were costs estimated separately for healthcare contacts and prescribed medicines.

Results As shown in Table 1 mean per patient drug, healthcare activity and combined drug and activity costs were significantly higher for the severe asthma group relative to the mild/moderate group with asthma and the non-asthma controls in both high and low cost scenarios. The mean difference in combined cost between the severe and non-asthma controls groups was between £5,031 (low cost) and £5,545 (high cost) depending on the cost scenario and £4,098 (low cost) and £4,510 (high cost) compared to the mild asthma group.

Abstract P158 Table 1  Mean (SD) per patient healthcare costs over 2 years

<table>
<thead>
<tr>
<th></th>
<th>Severe asthma ((n = 808))</th>
<th>Mild/moderate asthma ((n = 3975))</th>
<th>Non-asthma controls (rhinitis only) ((n = 1994))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescribed medicines (Mean)</td>
<td>£3447</td>
<td>£972</td>
<td>£514</td>
</tr>
<tr>
<td>(SD)</td>
<td>£5606</td>
<td>£1619</td>
<td>£1178</td>
</tr>
<tr>
<td>Activity- Low cost (Mean)</td>
<td>£4229</td>
<td>£2606</td>
<td>£2131</td>
</tr>
<tr>
<td>(SD)</td>
<td>£4296</td>
<td>£3267</td>
<td>£2807</td>
</tr>
<tr>
<td>Total – Low cost (Mean)</td>
<td>£7676</td>
<td>£3578</td>
<td>£2645</td>
</tr>
<tr>
<td>(SD)</td>
<td>£7490</td>
<td>£3899</td>
<td>£3254</td>
</tr>
<tr>
<td>Activity – High cost (Mean)</td>
<td>£5085</td>
<td>£3951</td>
<td>£2474</td>
</tr>
<tr>
<td>(SD)</td>
<td>£5364</td>
<td>£4225</td>
<td>£3259</td>
</tr>
<tr>
<td>Total – High cost (Mean)</td>
<td>£8533</td>
<td>£4023</td>
<td>£2988</td>
</tr>
<tr>
<td>(SD)</td>
<td>£8206</td>
<td>£4791</td>
<td>£3924</td>
</tr>
</tbody>
</table>

Conclusions Patients with severe asthma matched by age and gender have significantly greater direct healthcare costs compared to patients with mild/moderate asthma and non-asthmatic subjects.
sought to assess the usage of bone protection in steroid dependant asthmatics.

**Method**
A retrospective analysis of patients admitted for a systematic assessment of asthma over a 12 month period at the Royal Brompton hospital was performed. Steroid dependence was defined as daily maintenance oral glucocorticoid for over three months. Other inflammatory conditions requiring corticosteroids resulted in study exclusion.

**Results**
151 patients were admitted for a systematic assessment over a 12 month period. The mean age of subjects at assessment was 46 years of age (± 27 SD) and the majority were female (77%). Fifty four subjects (36%) were steroid dependent at the time of admission. The average daily dose of prednisolone prescribed was 12.5 mg (±5.9 SD). Two thirds of steroid dependent patients had been on corticosteroids for over 12 months (36/54).

At the time of referral 11 patients were on Bisphosphonates and 34 on vitamin D replacement. The systematic assessment encompassed a DEXA scan in 49 of the steroid dependent subjects; half demonstrated normal bone density (26/54), one third had osteopenia (16/54) and seven subjects had osteoporosis. Forty Six subjects had vitamin D levels checked and the mean levels were 48 nmol/L (±27 SD).

Bisphosphonates were stopped in seven patients with normal bone mineral density (13%), continued in 3 subjects and started during assessment in 4. Vitamin D supplementation was continued in 30 subjects, stopped in 2 and started in 5 subjects with osteopenia and low vitamin D levels.

**Conclusions**
In a cohort of oral glucocorticoids steroid dependant asthmatics over half have normal bone mineral density. While calcium and vitamin D supplementation occurs in the majority of subjects bisphosphonate are often used unnecessarily in a predominantly pre-menopausal and female population. Clearer guidelines for the investigation and monitoring of bone protection in steroid dependent asthmatics are required.

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**Lung cancer management**

**P161 HOW HAS THE SURGICAL TREATMENT OF LUNG CANCER IN THE UK EVOLVED OVER THE LAST TWO DECADES? – AN ILLUSTRATIVE SURGEON’S EXPERIENCE**

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10.1136/thoraxjnl-2015-207770.298

**Background/introduction**
The practice of lung cancer surgery in the UK has seen many changes over the last 20 years, with innovations in surgical technique and investigatory modalities together with significant organisational changes.

**Aims/objectives**
To assess how these changes have impacted on an individual Consultant surgical practice spanning this era.

**Method**
We have retrospectively reviewed a single-surgeon practice from consultant appointment to the present (1997–2015) comprising 1708 consecutive lung cancer operations: 962 (56%) lobectomy, 296 (17%) sublobar resection, 250 (15%) extended resection, 157 (9%) pneumonectomy, 43 (3%) open/close. Concurrently, 710 surgical staging procedures were performed. We analysed trends with time in type of procedure; open/close rates and in-hospital mortality.

**Results**
1557 anatomic resections were performed (87 cases/year, 67–130) with no significant decrease in the annual workload. There were significant changes in the types of surgical procedures performed over the time period: a significant decrease in pneumonectomy rate (p < 0.001), mirrored by an increasing use of sleeve-resections (p = 0.088); an increase in the proportion of anatomical resections by video assisted thoracic surgery (VATS) (p < 0.001), an overall increasing number of anatomical segmentectomies (p < 0.001), with a stable rate of wedge resections (mean 6.3%, p = 0.908). There has been a significant decrease in surgical mediastinal staging, particularly after 2010 (p < 0.001) with a significant reduction in the open/close rate, particularly after 2004 (4.8 vs. 0.65%, p < 0.001). Overall the in-hospital mortality rate has significantly decreased (from 7.1% in 1998 to 2.9% in 2015, p = 0.004).

**Conclusion**
There has been significant evolution in lung cancer surgery over the last two decades, which are illustrated in this individual surgeon’s practice. Whilst increased surgical experience may partly explain the changes, other important factors include: a change in the biology of lung cancer from central squamous to peripheral adenocarcinomas with earlier tumour detection, facilitating more VATS and lung-sparing surgery; improved perioperative care and the use of lesser resections, reducing mortality; and new techniques in staging (CT-PET, EBUS) reducing the need for surgical staging and the number of futile thoracotomies.
CT FOLLOW UP AFTER SURGERY FOR LUNG CANCER – SHOULD THE AVAILABILITY OF RADIO-SURGERY PROMPT A CHANGE IN SCREENING PROTOCOL TO DETECT EARLY INTRACEREBRAL RECURRENCE?

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10.1136/thoraxjnl-2015-207770.299

Although routinely performed, the optimal screening regimen for recurrent disease after curative surgery for lung cancer has yet to be agreed. Radio-surgery has improved prognosis for patients with limited intra-cerebral metastases, however screening for intracerebral recurrence has little evidence base. Local protocol is to perform CT head/chest/abdomen pre surgery and CT chest/abdomen at 3, 12 and 24 months after surgery. We proposed that the addition of CT head to the post-surgical protocol would enable earlier detection of intra-cerebral recurrence, facilitating timely treatment.

CT head was added to standard post surgical surveillance programme in February 2015. CT reports were reviewed prospectively and we report data to June 2015. For comparison, retrospective data for all patients currently enrolled in screening was also reviewed.

All 222 CT scans for the 115 patients undergoing post-surgical surveillance were reviewed. 28 of these have been performed since our protocol changed to include CT head.

In total, 22 patients (19%) had recurrent disease. 2 patients had isolated intracerebral recurrence. This represents 9% of all patients with recurrent disease and these patients would not be identified on previous screening protocol. This is in line with findings from previous work.

Four cases of symptomatic intra-cerebral recurrence were identified prior to protocol change. Only one of these patients was eligible for radio-surgery. Since protocol change, one case of asymptomatic isolated intra-cerebral recurrence has been detected through screening; this patient was thereafter treated with radio-surgery.

Our results show that isolated intra-cerebral recurrence would be missed on the previous screening protocol. These preliminary results suggest that the addition of CT head in post operative surveillance enables earlier identification of these patients. The earlier detection of intracerebral recurrence as a result of screening may increase referrals for radio-surgery, with potential for improved survival.

Site of recurrent disease after surgery

- Isolated intracerebral recurrence
- Intracerebral and extracerebral recurrence
- Extracerebral recurrence only

Abstract P162 Figure 1

REFERENCES

OUTCOMES FROM A NOVEL NURSE LED TELEPHONE CLINIC POST THORACIC SURGERY


10.1136/thoraxjnl-2015-207770.300

Background Moore et al. reported that nurse led initiatives can reconfigure care, making it more responsive to individual needs, increasing patient satisfaction and reducing hospital visits. Nurse-led telephone follow up clinics post surgery have evidence of patient satisfaction and reduction in post-op complications, but this is not a routine intervention post thoracic surgery. Prior to establishing our clinic, patients were discharged after thoracic surgery with a surgical outpatient appointment at 6 weeks and no routine community follow up. These patients had often undergone complicated surgery, and been discharged with chest drains or on strong opioids.

Methods All patients discharged after surgery were contacted by telephone up to a maximum of a week after discharge with a further follow up call 2 weeks later if needed. A protocol of open questions was used to identify post-op difficulties at an early stage, facilitate referral to community teams, improve patient experience and provide additional information.

Results and conclusion 29 patients were contacted over a 6 month period, following discharge after thoracic surgery; VATS, lobectomy, sleeve/wedge resection, pneumonectomy and pleurectomy. Each call lasted up to 20 min, equating to a maximum 10 h of nurse time.

Telephone clinic highlighted a number of medical issues that required intervention and prevented GP and hospital appointments/admissions. Commonly reported symptoms included pain, shortness of breath, fatigue, constipation, weight loss and inability to sleep. In most cases simple advice and reassurance could be given. In 3 cases, medication was organised (antibiotics, laxatives, analgesia). A referral to the GP or community services was organised in 4 cases. Patient satisfaction was high however further evaluation over a longer period is needed. Additional study is necessary to explore the cost implications and the monetary value of avoiding admissions.

REFERENCES

SMOKING AT THE TIME OF CURATIVE-INTENT LUNG CANCER SURGERY INCREASES PERIOPERATIVE COMPLICATIONS: IS THERE A ROLE FOR ELECTRONIC CIGARETTES?

1ST Lugg, 2T Tikka, 2P Agostini, 1A Ken, 2J Webb, 2E Adamas, 2E Bislay, 2S Steyn, 2MS Kalkat, 2PB Rajesh, 2DR Thickett, 2E Naida. 1Centre for Translational Inflammation Research, University of Birmingham, Birmingham, UK; 2Department of Thoracic Surgery, Heart of England NHS Foundation Trust, Birmingham, UK

10.1136/thoraxjnl-2015-207770.301
Introduction Smoking is a risk factor for postoperative pulmonary complications (PPCs) following curative-intent surgery for lung cancer. Risk modification is via smoking cessation; the role that electronic cigarettes (e-cigarettes) have in preoperative tobacco replacement is a debated topic.

Aims Investigate the impact of smoking on postoperative outcome including long-term survival. Assess current smoking habits and attitudes towards preoperative smoking cessation, with emphasis on e-cigarette use.

Methods A prospective observational study was carried out on all patients following curative-intent lung cancer resection in a regional thoracic centre over 4 years. Preoperative smoking status was self-reported by all patients. PPCs were assessed daily in hospital using the Melbourne group scale. Other data included patient demographics, hospital length of stay (LOS), intensive treatment unit (ITU) admission and mortality data. To assess smoking habits, a questionnaire was given to 105 patients attending the preoperative assessment unit.

Results Of 460 patients, 24% were current smokers, 12% ex-smokers 6 weeks duration, and 11% never smoked Compared to never smokers, current smokers had significantly longer hospital LOS in days (9, CI 7–11 vs. 6, CI 4–8; p < 0.001), higher frequency of PPCs (22% vs 2%, p = 0.001) and ITU admissions (14% vs. 0%; p < 0.005). Compared to never smokers, the trend was for reduced survival in current smokers from 1–3 years, but the survival lines converged after this (median follow-up 30 vs. 31 months; p = 0.31). The questionnaire found 24/105 patients were smokers, of these 80% patients had previously tried to quit but only 38% had been specifically approached by health-care professionals about smoking cessation. When asked if they would consider stopping smoking immediately if supplied an e-cigarette, 54% said yes.

Conclusions Preoperatively, 1 in 4 patients continue to smoke; the majority have attempted to quit and failed. Current smokers have higher postoperative morbidity with no significant survival difference within our follow-up period. Current methods of preoperative smoking cessation in this population are ineffective; patients appear willing to use e-cigarettes. Further research in this field is urgently needed.

REFERENCE

RESULTS OF THE NORTHUMBRIA DIRECT ACCESS CXR PROJECT
M Weatherhead, Wansbeck Hospital, Ashington, UK
10.1136/thoraxjnl-2015-207770.302

Northumbria Healthcare (NHCT) traditionally had a low number of patients presenting with early stage lung cancer leading to low resection rates. In addition a high number of patients presented through the emergency route rather than through target clinics.

A local initiative was developed to try to improve the local presentation and diagnosis rates. The Northumbria initiative utilised primary care education, a social marketing project and a direct access CXR project which ran for 12 months.

The assessment criteria for direct access CXR were based on NICE guidance and patients meeting these criteria could self-present for a CXR.

- Is the patient over 50
- Has the patient had a chest x-ray in the last 3/52
- Has the patient developed a new and persistent cough for more than 3/52
- Has the patient had persistent chest pain for more than 3/52
- Has the patient had blood in their phlegm

Results Over 12 months 768 CXR examinations were carried out. 751 people presented a cough, 192 with chest pain and 33 with haemoptysis.

18 CT’s were requested due to a suspicious CXR and 52 people had a follow up CXR. 19 of these 70 were reviewed in a chest clinic.

4 lung cancers were detected, 2 of which were early stage and the patients had radical treatment. 5 pulmonary nodules were identified, for which interval follow-up was planned.

Conclusion The Northumbria Walk-in project proved successful in terms of delivering a campaign message to the local population. The trust communications team won a regional award for the best “low budget” campaign for this project.

The detection rate for lung cancer was not higher than one would expect from performing CXR’s on a population of similar age with a smoking history and on current evidence did not provide evidence for continuing the walk in CXR programme.

However, over the 2 years while this project was being developed and awareness of cancer was targeted there was a 6% rise in the rate of early stage lung cancer locally suggesting that the combined awareness raising approach both locally and nationally has had some effect on presentation rate.

THE FREQUENCY OF CHEST RADIOGRAPHS PRIOR TO THE ONSET OF LUNG CANCER SYMPTOMS
MPT Kennedy, O Walkowiak, MEJ Callister. Leeds Teaching Hospitals NHS Trust, Leeds, UK
10.1136/thoraxjnl-2015-207770.303

Introduction Previous data has shown wide variation in the frequency of CXRs requested by GPs that is not explained by case mix factors. The relationship between threshold for CXR request and lung cancer characteristics at diagnosis is unknown. Aim To analyse the frequency of CXRs prior to the development of lung cancer symptoms according to stage at presentation.

Method Retrospective review of an electronic database of lung cancer patients, excluding small cell, from 2010–2013. The dates of all CXRs in the three years before the first appointment with the lung cancer team were recorded. The frequency of CXRs was compared using Mann-Whitney U test with normal approximation.

Results 1750 patients were included. 589 had early stage disease (I/II) and 1161 had late stage disease (III/IV). The frequency of CXRs from 36 to 6 months prior to diagnosis is shown in Figure 1 according to stage at diagnosis. Patients subsequently diagnosed with early stage cancer had significantly more CXRs performed during this period compared to late stage patients (1.70 vs 0.92, p < 0.001).

Poster sessions
Background and objectives With increasing use and fidelity of CT scans the workload relating to surveillance of indeterminate lung nodules is ever increasing and is burdensome in terms of out-patients appointments and/or clinical administrative time. In July 2014 we established a virtual nodule clinic (VNC) for reviewing indeterminate lung nodules. A proforma within our hospital electronic patient record is completed which automatically generates written communication for both the patient and the GP informing of the findings of the latest CT result and any follow-up required. The patients are not seen in clinic unless they request. The clinic template allows review of 40 cases per session.

The objectives of this study are to review the impact of the VNC on concordance with Fleischner guidelines and timeliness of communication of results.

Methods We retrospectively reviewed 50 consecutive nodule follow-up scans performed in November 2013 prior to establishment of VNC and 49 consecutive cases reviewed in VNC in November 2014. Concordance with Fleischner guidelines and date from CT scan to patient/GP being informed was reviewed.

Results Demographics were similar between groups.

The VNC has improved concordance with Fleischner guidelines in lung nodule surveillance by 40%. Prior to the VNC, 52% of patients had surveillance concordant with Fleischner guidelines. Following the introduction of the VNC, 92% of patients had follow-up concordant with Fleischner guidelines.

Median time from the date of CT scan to the patient/GP being informed of CT results was 5 weeks. None of the cases reviewed in VNC contacted us to request a face to face consultation despite this being offered within the written communication to patients.

Conclusion The introduction of a virtual nodule clinic has significantly improved concordance with published guidelines for radiological follow-up of indeterminate lung nodules. It has also allowed a significant reduction in the number of ‘unnecessary’ out-patient appointments within the lung cancer service. VNC ensures effective and timely communication of scan results to patients and GPs.

Abstract P167 Table 1 A comparison between patients seen prior to the VNC and those reviewed in the VNC

<table>
<thead>
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<th>Prior to VNC (November 2013)</th>
<th>Reviewed in VNC (November 2014)</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>50</td>
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<tr>
<td>n</td>
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<td>Age (mean)</td>
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<td>Male 50%</td>
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<tr>
<td>Gender</td>
<td>Male 49%</td>
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<tr>
<td>Female 50%</td>
<td>Female 51%</td>
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<tr>
<td>Mean Size of Nodule (Diameter in cm)</td>
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<td>Mean Size of Nodule (Diameter in cm)</td>
<td>7.05</td>
</tr>
<tr>
<td>Concordance with Fleischner Guidelines</td>
<td>52% (26/50)</td>
</tr>
<tr>
<td>Concordance with Fleischner Guidelines</td>
<td>92% (45/49)</td>
</tr>
</tbody>
</table>

Conclusion

The ‘REAL WORLD’ IMPACT OF THE NEW BTS LUNG NODULE SURVEILLANCE GUIDELINES

J Thomas, S Grundy. University Hospital Aintree, Liverpool, UK

10.1136/thoraxjnl-2015-207770.304

Background and objectives The BTS published new guidelines for the investigation and management of pulmonary nodules in June 2015. These replace the Fleischner guidelines and are based on an improved evidence base produced predominantly from recent lung cancer screening trials.

The BTS guidelines suggest no radiological follow-up for nodules smaller than 5 mm or <80 mm³ and limit CT follow-up to 12 months when volumetric analysis is used. The guidelines recommend use of the Brock Model (full with spiculation) to estimate the probability of malignancy in nodules ≥ 8 mm. The Brock group also published a parsimonious model which requires fewer clinical variables to calculate risk with almost equivalent accuracy.

The objectives of this study are to establish the impact of the new guidance on the number of patients requiring radiological follow-up and the total number of scans recommended. We also studied any differences between the 2 Brock risk models.

Methods We retrospectively reviewed 99 consecutive patients who were reviewed for indeterminate lung nodules. Their follow-up recommendations were calculated using 3 methods: 1)
FDG PET-CT scans are a valuable tool in the diagnosis and staging of lung cancer, but their growing use in other diseases can cause resource issues, and in some cases they may be ordered by non-specialists further congesting use in other diseases. The new BTS guidelines will significantly reduce both the number of patients requiring radiological follow up for indeterminate nodules and also the total number of scans required overall.

Conclusion The new BTS guidelines will significantly reduce both the number of patients requiring radiological follow up for indeterminate nodules and also the total number of scans required overall. Even assuming worst case scenario in terms of clinical risk factors there is very little difference between Brock (full) and Brock (parsimonious). This needs assessing in a larger population with clinical outcomes evaluated.
radiotherapy, chemotherapy for SCLC), sixteen (37%) patients with palliative intent (radiotherapy, chemotherapy, brachytherapy), and ten (23%) patients received best supportive care (BSC) only. Of the five patients with PS 3, one received palliative radiotherapy and the other four BSC. Patients treated with curative intent had 71% survival at six months, 65% survival at 12 months: survival rates significantly higher compared with those receiving palliative treatment or BSC (p = 0.02). There was no survival difference between palliative treatment and BSC (p = 0.81) (Figure 1).

Abstract P170 Figure 1 Kaplan-Meier curves with survival stratified by treatment

Conclusion When a tissue diagnosis of lung cancer is pursued in those aged 75 and older, most patients will receive specific cancer treatment and this data informs clinical discussions about curative intent outcomes. In those who are PS 3 at baseline, BSC only is the likely outcome, and pursuing tissue diagnosis may not be appropriate.

P171 A LOCAL CANCER NETWORK ROOT CAUSE AUDIT OF 62-DAY LUNG CANCER PATHWAY BREACHES

O Eneje, N Kumar, D Powrie, B Yung, M Lawson, Basildon University Hospital NHS Foundation Trust, Basildon, UK; Southend University Hospital NHS Foundation Trust, Southend, UK; Broomfield Hospital, Chelmsford, UK

10.1136/thoraxjnl-2015-207770.308

Introduction Over several years there has been an ongoing rise in 62-day Lung Cancer pathway referrals initiated by GPs as two-week wait referrals (2WW). This was particularly marked in 2014 and breach rates increased across the East of England SCN. Within the Essex Lung Cancer Network an audit of these breaches was undertaken by three Trusts to look for common themes and to share best practice.

Methods Data were collected for all pathways that failed to meet the 62-day target across three NHS Trusts in Essex to identify any predictive factors for breaching the pathway. A standard proforma was used for abstraction. Results were analysed using GraphPad Prism 6 (La Jolla, CA).

Results In 2014 a total of 1,419 2WW referrals were received by the three Trusts of which 13–23% were diagnosed with lung cancer. Between 19% and 54% breached the 62-day target (89 of 246 pathways). The median length of the breached pathways varied from 86–88 days by Trust. Trusts did not appear to differ significantly by end treatment after pathway breach. There were generic common themes within the breached pathways of each Trust but for the two worst performing Trusts specific pathway issues were identified. In one Trust it was clear that time delays to perform CT guided lung biopsies with a 2.75 relative risk of breaching if a pathway involved a CT biopsy (95% CI 1.6–4.6, p < 0.0001). At another Trust a high proportion of breached pathways had a bronchoscopy as the first test but went on to have further diagnostic biopsies by other methods.

Conclusion Many of the diagnostic delays were due to complex patient pathways needing multiple diagnostic tests. However for two Trusts significant problems were highlighted for targeted quality improvement plans. Selecting the best test to give diagnostic and staging information is vital particularly when services are stretched and capacity is reached.

P172 TRAINING NURSES IN SAMPLING AND ACQUISITION OF SPECIMEN DURING EBUS GUIDED TRANSBRONCHIAL NEEDLE ASPIRATION

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10.1136/thoraxjnl-2015-207770.309

Introduction EBUS has now become the standard of choice for mediastinal staging and in the diagnosis of paratracheal and peribronchial lesions. EBUS is usually performed as a 2 person procedure, one to locate and align the bronchoscope and a second to carry out node sampling. Whilst these have traditionally both been medical personnel, with the increase in use of this procedure and alterations in the training and availability of medical staff, we wished to look at the feasibility of empowering nurses to perform needle aspiration during EBUS.

Methods We provide a regional service for EBUS, carrying out over 420 procedures per year, often in technically difficult cases where local hospital EBUS has been unhelpful. From January 2015 we trained a band 5 registered nurse in needle aspiration, who randomly assisted in the procedure in 93 cases up to June 2015. We report our experience in these 93 cases.

Results These 93 patients were referred from 12 hospitals and 20 had undergone previous undiagnostic procedures (6 EBUS, 14 bronchoscopy). The mean age was 67 years (range 27 – 87) and 50 were male. 82 were performed under local anaesthesia using lignocaine spray and intravenous midazolam (1 – 10 mg; mean 4 mgs) and the remaining 11 under general anaesthesia. 200 lymph nodes (2R, 4R, 4L, 7, 10R, 10L, 11R) and 13 lung lesions were biopsied. Results were as follows: Adequate samples were obtained in 99% (91/93) and the NSCLC - NOS rate was 2%, 31 adenocarcinoma, 10 squamous cell carcinoma, 10 small cell carcinoma, 1 NSCLC - NOS, 1 large cell neuroendocrine carcinoma, 1 soft tissue lesion (repeat EBUS showed myxoid spindle cell mesenchymal lesion), 1 breast carcinoma, 19 nonspecific benign nodes, 15 sarcoïd and 2 TB. There were no complications.

Conclusion Our findings suggest that with motivated staff and adequate training, it is possible for nurses to perform needle aspiration during EBUS procedure with excellent results. This could be adopted as the method of choice by other centres as EBUS services continue to expand.
Background Southmead Hospital is a large teaching Hospital in the South West of England. GP two week wait (TWW) referrals to the respiratory department are sent via a standardised pro-forma with one of a number of reasons for referral selected. We conducted this project both to evaluate how we are currently investigating patients referred with haemoptysis and to identify whether our diagnostic pathway for patients for these patients could be optimised. We were particularly interested as to whether bronchoscopy is diagnostically helpful in this cohort of patients.

Methods We looked at all TWW referrals between 13/6/13 and 2/4/15 (825 referrals) and selected those who were referred for haemoptysis (110 patients). The clinical course of these patients was tracked retrospectively by looking at our electronic record system and clinical letters.

Results Overall 109 of the 110 patients identified had a CT scan – this was normal in 31 patients. In the remainder of cases the CT was suggestive of malignancy in 38 of the 78 abnormal scans. The remainder of CT scans had positive findings that were not suggestive of malignancy. Of the 31 patients who had a normal scan, 22 patients underwent bronchoscopy. 40 patients had abnormal CT scan that were not suggestive of malignancy. 25 of these patients went on to have bronchoscopy. In our cohort of patients all bronchoscopies were either normal or showed non specific findings. 16 patients who had an eventual diagnosis of lung malignancy had an initial CT scan suggestive of malignancy.

Conclusion Our project demonstrates that currently 58% of patients referred with haemoptysis via the TWW system go on to have a bronchoscopy. In our cohort of patients all bronchoscopies were either normal or showed non-specific changes. All patients with lung malignancy had a prior CT that was suggestive of malignancy and did not require a bronchoscopy other than as a potential means of obtaining tissue. We suggest that bronchoscopy may not be necessary in patients referred with haemoptysis who have a normal CT scan. We feel this will change our local practice and may enable us to better target this investigation to patients who will benefit from it.

Introduction In Salford, annual 2WW referrals rose from 235 in 2010/11 to 248 (2011/12) and 281 (2012/13) but fell to 249 in 2013/14 as the result of a 5 month pilot1 of our CATCH protocol (Community Access To CT Chest) allowing abnormal “low risk” CXR reports to trigger a GP request for a fast track CT scan. This audit reviews the performance of CATCH for a whole year of activity from 1st May 2014 to 30th April 2015.

Methods The CATCH d-base and electronic patient record were used to identify the patients and dates of CXR and CT examinations in addition to CXR/CT scan reports and final diagnoses. The number of 2WW referrals was determined for the same time period using the cancer waiting times d-base.

Results A total of 117 patients entered the CATCH protocol of which the majority of CXRs demonstrated the presence of a well-defined (47%) or ill-defined opacity (14%) and a further 18% revealed abnormality at the hilum. The remaining CXRs (21%) raised concerns about fat pads, atelectasis or pleural abnormality. For the 115 patients having a CT scan, the findings confirmed cancer in 9%, solitary pulmonary nodule (25%), infection/inflammation (15%), atelectasis (10%), pleural plaque (10%), fat pad (5%) and in 11% the CT scan was normal.

Following CATCH CT scan, 53 (46%) patients required no follow up, 33 (29%) generated urgent referral, 16 (14%) non-urgent referral to the chest clinic, 11 (10%) required follow up surveillance imaging. Timelines for CATCH management are detailed in Table 1. Mean time from CT report to cancer diagnosis was 61.1 days (range 23 to 187) and total number of 2WW referrals for 2014/15 was 234.

Conclusions Following the introduction of CATCH to the Salford Lung Cancer Service, 2WW referrals have fallen further to manageable numbers. The pick-up rate for cancer is only small and reflects the low risk abnormality detected on CXR. The relatively long diagnostic times for cancer reflect the processing of small nodules detected within this select group of patients.

REFERENCE

P174 CATCH - A YEAR IN PROFILE AND FURTHER REDUCTIONS IN 2WW REFERRALS
1VTY Ng,2A Walsham,3A Sharman,5SCO Taggart,3Manchester University Medical School, Manchester, UK; 4Salford Royal NHS Foundation Trust, Salford, UK
10.1136/thoraxjnl-2015-207770.311

P175 USE OF A VIRTUAL CLINIC TO IMPROVE THE LUNG CANCER PATIENT JOURNEY
A Narapragasam, N Maddock, C Smyth, MJ Walshaw. Liverpool Heart and Chest Hospital, Liverpool, UK
10.1136/thoraxjnl-2015-207770.312

In 2014 with our primary care colleagues we introduced a ‘Straight to CT’ system for out-patients with a radiological or clinical suspicion of lung cancer. The CT was done on behalf of primary care, and only patients who had a CT suspicious of lung cancer, were automatically taken by the lung cancer team. Such scans are reviewed by a cancer clinician, who makes a provisional next best test plan, and this empowers a telephone clerk by a highly specialised lung cancer nurse. The assessment
results were available, nearly double the rate in Asia (12%). Further, 67% of UK oncologists, compared to 51% of all respondents, reported that treatment decisions were not affected by EGFR mutation subtype. Conclusion Despite the high levels of EGFR mutation testing in the UK, the survey found that more than one in five patients with advanced NSCLC do not receive treatment personalised for cancer type and mutation subtype, even though evidence shows this improves survival and quality of life. These findings suggest there is incomplete implementation of UK guidelines. Further research is needed to discover what factors contribute to oncologists not following established guidelines in the UK. These data were originally presented at the European Lung Cancer Conference, 2015. Annals of Oncology, Volume 26, Supplement I, 2015.

REFERENCE

Managing pleural disease

Poster sessions

P177 COST EFFECTIVENESS OF AMBULATORY MANAGEMENT OF SPONTANEOUS PNEUMOTHORAX
C Pillay, B Shah, M Naeem, R Reddy. Kettering General Hospital, Kettering, UK
10.1136/thoraxjnl-2015-207770.314

Introduction Hospital admissions due to a primary diagnosis of spontaneous pneumothorax (SP) have an annual incidence of 11.2 per 100,000.1 It is estimated there are around 7200 emergency hospital admissions annually for pneumothorax in NHS. We have previously demonstrated pneumothorax patients requiring intercostal drains can be managed safely as outpatients with a Pneumostar device (similar to Heinlich valve).2 Methods All patients with primary spontaneous pneumothorax (PSP) and secondary spontaneous pneumothoraces (SSP) with a good performance status (WHO scale of 0–1) requiring an intercostal drain were eligible for outpatient management. SP patients presenting to hospital between July 14 and June 15 were analysed to see what percentage could be managed on the ambulatory pathway. The number of bed days saved was calculated from the total number of days patients spent in the community with the chest drain. The savings were then extrapolated to whole of NHS.

Results 50 episodes (in 44 patients) of SP presented to hospital between July 14 and June 15. 36 episodes required a chest drain insertion. 20 of these 36 episodes (55%) were managed on the ambulatory pathway. The number of bed days saved was calculated to be 137 days, with a histological rate of 89%. Our 62 day breach rate is 6%. The new process also provides a 42% cost saving for primary care.

Conclusions We have shown that the use of a virtual clinic can target and speed up the diagnostic pathway for patients with lung cancer. It also makes more efficient use of scarce NHS resources, by ensuring that patients only attend the hospital for necessary investigations.

We recommend the use of this innovative service to other clinicians charged with managing this common and distressing disease.
**Abstract P177 Table 1**

<table>
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<tr>
<th>Document Type</th>
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<tr>
<td>Attendance at ambulatory care</td>
<td>-6800 (£N = 34)</td>
</tr>
<tr>
<td>Chest x-ray</td>
<td>-949 (£N = 36)</td>
</tr>
<tr>
<td>Pneumostat Device</td>
<td>-588 (£N = 21)</td>
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<tr>
<td>Overall savings</td>
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</table>

**REFERENCES**


**Abstract P178**

**AMBULATORY CARE OF PRIMARY SPONTANEOUS PNEUMOTHORAX WITH A PNEUMOSTAT DEVICE – COST EFFECTIVE AND SAFE**

*M Samuel, 2P Sivakumar, 2AW et al.*


**Introduction and objectives** A Heimlich Valve attached to an intercostal drain facilitates the ambulatory management of primary spontaneous pneumothorax (PSP) and in selected individuals permits outpatient care. We have 3 years of experience in doing this with Atrium’s Pneumostat device. We ascertained the safety and cost effectiveness of this ambulatory pathway.

**Methods** We conducted a retrospective evaluation of all patients presenting with a PSP from March 2013 to December 2014. Data was collected on management, length of stay (LOS) and complications. Outpatients with a Pneumostat are advised to attend the chest clinic 24 h after bubbling stops for review for drain removal, or earlier if any concerns. Medical bed days saved was calculated as time at home with the device in situ, as standard BTS care would require an inpatient stay with a drainage bottle.

**Results** 73 patients presented with a PSP; 34 patients required chest tube drainage, 24 of which were managed as an outpatient with a Pneumostat. The median LOS in the outpatient group was 1.0 day (IQR 0.0–2.0 days) vs 3.5 days (IQR 1.3–7.0 days) in the inpatient group. A total of 98 bed days were saved using the device. Based on a cost of £25.70 per Pneumostat and £312 per bed day, the overall saving was £29,959.20. Patients who required thoracic surgery were kept on the “inpatient waiting list” and could be admitted directly from home.

In the outpatient group, there was 1 drain site infection, 1 drain displacement and 1 patient failed to attend follow-up but returned a week later with a resolved pneumothorax.

**Conclusion** Pneumostat devices have recently been withdrawn from use in the United States by FDA decree. Although legal in the UK and supported by the MHRA, a Certificate of Medical Necessity is required to purchase the devices and there is no alternative “all-in-one” solution that attaches to a standard chest drain. Our data shows that this device is safe in uncomplicated PSP and confers significant financial savings. These benefits should not be overlooked and a consensus statement is required to ensure their continued use in the UK.

**Abstract P179**

**THE EFFECTIVENESS OF CHEMICAL PLEURODESIS AGENTS IN SPONTANEOUS PNEUMOTHORAX: A SYSTEMATIC REVIEW**


**Introduction and objectives** Spontaneous Pneumothorax (SP) is a common pathology. Recurrence rates (RR) for Primary SP (PSP) are often quoted as approximately 30% (individual studies reporting anywhere between 17 and 49%), with less data available on Secondary SP (SSP) recurrence rates. Recurrence prevention at first episode remains controversial. International guidelines suggest pleurodesis for non-resolving air leak or recurrence prevention at second episode. There are numerous candidate agents for chemical pleurodesis.

This study aimed to comprehensively review the existing literature regarding chemical pleurodesis as a treatment modality.

**Methods** The systematic review methodology was based on the PRISMA approach and principles. Literature searches of multiple databases (PubMed, Embase, Medline, Web of Science, Cochrane Library) used combinations of terms including “spontaneous”, “pneumothorax”, “chemical”, “talc”, “tetracycline”, “minocycline”, “iodopovidine”, and “blood”. Abstracts were reviewed for relevance by two authors, who subsequently assessed and extracted data from the full articles.

**Results** Of 522 abstracts reviewed; 427 were excluded (e.g. case reports, letters, reviews, animal models or basic science articles); an additional 4 papers included via back-referencing. 99 full text papers were reviewed; 58 were excluded for the following reasons:

**Abstract P179 Table 1**

<table>
<thead>
<tr>
<th>Study</th>
<th>Medical/Surgical</th>
<th>Intervention agent (# cases)</th>
<th>Control (# cases)</th>
<th>PSP/SSP (# cases)</th>
<th>Co-Intervention</th>
<th>Recurrence rate (agent/control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light (1990)</td>
<td>M</td>
<td>Tetracycline (113)</td>
<td>Drainage only (116)</td>
<td>46/183</td>
<td>Nil</td>
<td>25%/41%</td>
</tr>
<tr>
<td>Almind* (1989)</td>
<td>M</td>
<td>Talc (29) vs tetracycline (33)</td>
<td>Drainage only (34)</td>
<td>7/125</td>
<td>Thoracoscopy (no intervention)</td>
<td>8%/13%/36%</td>
</tr>
<tr>
<td>Tschopp (2002)</td>
<td>M</td>
<td>Talc (61)</td>
<td>Drainage only (47)</td>
<td>10/80</td>
<td>Thoracoscopy (no intervention)</td>
<td>5%/34%</td>
</tr>
<tr>
<td>Chen (2006)</td>
<td>S</td>
<td>Minocycline (103)</td>
<td>Saline (99)</td>
<td>20/20</td>
<td>VATS - bullectomy</td>
<td>2%/8%</td>
</tr>
<tr>
<td>Chung* (2007)</td>
<td>S</td>
<td>Talc and Dextrose (42) vs Dextrose alone (49)</td>
<td>Drainage only (50)</td>
<td>14/10</td>
<td>Thoraco-scopic bleb resection/cautery</td>
<td>2%/0%/6%</td>
</tr>
<tr>
<td>Agarwal (2011)</td>
<td>M</td>
<td>Iodopovidone (20)</td>
<td>Talc (15)</td>
<td>10/25</td>
<td>Nil</td>
<td>0%/0%</td>
</tr>
<tr>
<td>Alayouty (2011)</td>
<td>S</td>
<td>Minocycline (42)</td>
<td>Abrasion (40)</td>
<td>8/20</td>
<td>VATS - bullectomy</td>
<td>0%/5%</td>
</tr>
<tr>
<td>Chen (2013)</td>
<td>M</td>
<td>Minocycline (106)</td>
<td>Drainage only (108)</td>
<td>21/40</td>
<td>Nil</td>
<td>29%/49%</td>
</tr>
</tbody>
</table>

*Three arms of trial.
Introduction and objectives Indwelling pleural catheters (IPC) are well established in the management of malignant pleural effusions. However, there is some reluctance in its use in patients receiving chemotherapy due to a hypothetical increased risk of infection. There are no prospective trials primarily examining IPC safety in chemotherapy. Retrospective series suggest a similar IPC-related complication rate in chemotherapy and non-chemotherapy patients.1,2 Our primary study objective is to determine the safety of IPC insertion in chemotherapy.

Methods We conducted a retrospective analysis of all patients who underwent IPC insertion for malignant pleural effusion at our trust from September 2010 to December 2014. Data was collected on IPC insertion and removal, tumour type, systemic chemotherapy, pleural infection and other complications.

Results 104 patients were identified, (Table 1) 43 in chemotherapy group and 61 in non-chemotherapy group. The incidence of pleural infection in chemotherapy group vs non-chemotherapy group, 4 (9.3%) vs 4 (6.5%) respectively, was not statistically different; with iodopovidone less so (13%). Of 27 retrospective case series (n = 4,990), seven were reasonable quality, finding good efficacy of adding talc or silver post-bullectomy (RR: 1 to 2%); better than minocycline or acromycin post-bullectomy (3 and 4%) or talc post-electrocoagulation (5%). The remaining 20 were poorer quality with high risk of bias, assessing 7 different agents.

Conclusions Numerous agents have been used for chemical pleurodesis for spontaneous pneumothorax. Chemical pleurodesis post-surgical treatment or via thoracoscopy appears most effective. Evidence for definitive success rates of each agent is limited by the small number of randomised and comparative trials.

<table>
<thead>
<tr>
<th>Patient demographics, interventions and outcomes</th>
<th>Chemotherapy with IPC in-situ</th>
<th>No chemotherapy with IPC in-situ</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>43</td>
<td>61</td>
</tr>
<tr>
<td>Mean age (yrs)</td>
<td>64</td>
<td>68</td>
</tr>
<tr>
<td>Cancer primary</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung (Small cell)</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Lung (Non-small cell)</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Breast</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Other</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>Median duration IPC in-situ (days)</td>
<td>69 (13–283)</td>
<td>28 (2–413)</td>
</tr>
<tr>
<td>Mean duration of concurrent chemotherapy (days)</td>
<td>76 (2–480) (~4 cycles)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleural infection</td>
</tr>
<tr>
<td>Cellulitis</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Drain blockage</td>
</tr>
<tr>
<td>6-month Mortality</td>
</tr>
</tbody>
</table>

Abstract P180 Table 1

Introduction CHEMOTHERAPY Pleural Catheter Safety in Patients Undergoing CHEMOTHERAPY

P180

C Chan Wah Hak, P Sikakumar, L Ahmed, Respiratory Medicine, St. Thomas’ Hospital, Guy’s and St Thomas’ NHS Foundation Trust, London, UK

Methods Prospective data is collected for patients undergoing insertion of IPCs at a tertiary pleural referral centre. Pre-procedure thoracic ultrasound is performed in all patients and a grading of septations is made; no septations, mild (<4), moderate (4–9), severe septations (>9). Immediate, early (30 days) complications as well as six month follow-up data are recorded. This study is a retrospective analysis of this prospectively maintained database.

Results A total of 47 patients with complete datasets were identified between 2013–2014; 34% (16/47) had mild/moderate/severe septations (n = 7, 5, 4 respectively) and 66% (31/47) had no septations. There was no significant difference in the number of patients achieving resolution of pleural effusion and

REFERENCES


pleurodesis whereby the IPC could be removed according to the presence of septations (pleurodesis in those with no septations 16%, 5/31 vs. 13%, 2/16 in those with septations, \( p = 1.0 \)). There were no patients in either group in whom the drain was removed due lack of drainage in the context of a persistent pleural collection. There was no significant difference in overall complication rate according to the presence of septations (16%, 5/31, in the no septation group vs 13%, 2/16, in the septation group, \( p = 1.0 \)).

**Conclusion**
These results suggest that the presence of septations on the pre-insertion thoracic ultrasound do not affect the rate of pleurodesis or drain removal due to lack of drainage and persistent pleural effusion. The numbers in the study are small and a limitation is the lack of assessment of post-procedure breathlessness in our patients (e.g. with a visual analogue scale). The presence of septations should not deter consideration of IPC insertion in the management of malignant pleural effusions.

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**P182**

**PROPHYLACTIC DOXYCYCLINE FOLLOWING INDWELLING PLEURAL CATHETER INSERTION FOR MALIGNANT PLEURAL EFFUSIONS**

E Nuttall, H Balata, M Al-Aloul, M Evison, J Holme. University Hospital South Manchester

**Introduction**
The insertion of indwelling pleural catheters (IPCs) allows outpatient based management of malignant pleural effusions. This group of patients frequently require chemotherapy and there is concern over infection rates from IPCs which has the potential to delay or prevent such treatment. The infection rate was reported as 10% in a prospective trial of IPCs. In our tertiary pleural service we have elected to routinely prescribe 7 days doxycycline 100 mg once daily following IPC insertion. This study examined our infection rates using this practice.

**Method**
Data was collected from a tertiary respiratory and pleural service. Prospective data is collected on all patients undergoing IPC insertion at UHSM. Immediate post-procedure data is collected and a further clinical and case-note review undertaken at 6 months. Pre-defined immediate (post-procedure), early (30 days) complications are recorded. Infection is defined as the prescription of antibiotics (oral or intravenous) for suspected or confirmed pleural infection or drain-site cellulitis. This study is a retrospective review of the prospectively maintained database. To ensure six months of follow-up data for all patients the analysis was restricted to patients undergoing IPC insertion prior to 31/12/2014.

**Results**
62 patients with complete datasets underwent IPC insertion between 01/01/2013 and 31/12/2014. All patients received 7 days of prophylactic doxycycline at a dose of 100 mg OD. One patient (1.6%) suffered drain site cellulitis requiring antibiotics within 30 days of insertion. There were two cases (3.2%) of pleural infection treated with antibiotics (both within 30 days of insertion and required intravenous antibiotics and admission). In these cases the IPCs were not removed but it did fall out in one case where the patient developed delirium with infection.

**Conclusion**
The infection rate in this prospectively collected data is lower than rates reported in large prospective randomised controlled clinical trials. This may suggest a benefit from the routine use of prophylactic antibiotics. A randomised controlled trial of prophylactic antibiotics versus no antibiotics following IPC insertion may be warranted.
Aims
1. To develop and implement a modified WHO surgical checklist for use in PI; specifically thoracoscopy (TS) and chest drain (ICD) insertion.

Methods
Adverse events for TS were identified using a locally developed TS database (previous 3 years data) and ICD events were identified using our unit’s BTS National audit data. Following a MDT discussion we developed and implemented a modified WHO checklist for the specific risks of TS and ICD. The checklists follow the three-part structure recommended by the WHO; 1. Sign in (before arrival to procedural area), 2. Time out (before starting), 3. Sign out (before leaving).

Checklist effectiveness was reviewed 6 months following implementation.

Results
Pre-implementation
For TS there were a small number of adverse events (mistaken identity of an abnormal ECG in patients with similar names, delay in pre-procedure blood results, ECG not performed, intravenous fluids not readily available, kinked ICD, thromboprophylaxis not prescribed); most events led to delayed procedure only.

For ICD insertion, several avoidable patient safety issues were identified: 5.6% no support nurse available; insufficient documentation of observations pre (13.7%) and post (5.6%) ICD insertion.

Post-implementation
No adverse events recorded in TS and an improvement in ICD patient safety issues (procedure not done without support present, observations documented in 42% of cases). Team-working and communication reported to have improved.

However, ICD checklist completion rate was poor (53%), with form retrieval rates in TS low compared to reported completion rates (66.7% v 100%). Forms were generally incomplete.

Conclusion
Most adverse events identified were due to system errors despite previously available safeguards. Well-designed procedural checklists can improve patient safety. Paper versions were not fully completed therefore we have incorporated an electronic version of the checklist into the procedural database, which has to be completed before the procedure starts.

REFERENCES

P185
EVALUATION OF THE LENT PROGNOSTIC SCORE IN A LARGE TERTIARY PLEURAL SERVICE
H Balata, N Anwar, P Foden, M Al-Aloul, J Holme, M Evison. University Hospitals of South Manchester, Manchester, UK
10.1136/thoraxjnl-2015-207770.322

Introduction and objectives
Reliable predictors of survival in malignant pleural effusions (MPE) have far reaching applications in clinical practice, not least tailoring individual treatment strategies. The ‘LENT’ score (pleural fluid Lactate dehydrogenase; Eastern Cooperative Oncology Group performance score; Neutrophil-to-lymphocyte ratio; Tumour type) was developed and validated as a clinical prognostic scoring system from three international prospective patient databases. The aim of this study was to evaluate the LENT score in a further UK population of patients with MPE, geographically separate from those in the original study.

Methods
Our hospital is a large tertiary centre for a physician-led pleural service (including medical thoracoscopy), a regional mesothelioma centre and a regional thoracic surgical centre. A retrospective study of all patients with positive (i.e. diagnostic for malignancy) pleural cytology or histology from 2010 to 2014 was undertaken. This timeframe allowed a minimum of 12 months follow-up for all patients. Survival data was obtained from national death registries. All patients in whom all LENT criteria were available were included in the analysis. A Kaplan-Meier curve and a Cox regression model were used to assess the LENT risk category. Harrell’s C statistic was used to assess the accuracy of the regression model and mortality rates at time points of interest were calculated.

Results
The LENT score was calculated for 101 patients diagnosed with MPE. The median survival (days, IQR) for the low (n = 18), medium (n = 54) and high risk (n = 29) groups were: 254 (152–602), 102 (40–301) and 16 (7–42). In the high risk group, only 31% of patients survived 1 month and 7% survived 6 months. There is a statistically significant difference in the survival times in the different risk groups according to the log-rank test (p < 0.001). Harrell’s C statistic in this cohort is 0.69 (see Figure 1).

Abstract P185 Figure 1

Conclusions
The LENT scoring system has again been shown to be a good tool for predicting survival in patients with MPE when applied to a geographically distinct cohort of patients to the original study. The LENT score continues to be a clinically valuable tool in the assessment of patients with MPE.

REFERENCE

P186
CHEST DRAIN CARE BUNDLE IMPROVES CHEST DRAIN INSERTION IN DISTRICT GENERAL HOSPITAL
H Steer, J Hutton, S Graham, R Jones. Gloucestershire NHS Trust, Gloucester, UK
10.1136/thoraxjnl-2015-207770.323
Introduction and objectives Chest drain insertion is a common advanced procedure with a significant associated risk of pain, distress and serious complications. Nationally, audit and patient safety work has highlighted a number of safety concerns around chest drain insertion.

Previous audit work has demonstrated poor levels of documentation; particularly around use of pre-medication, use of ultrasound guidance and consent. This has obvious potential consequences for patient safety and thus is an important target for improvement work.

Method National best practice standards were identified through review of national guidance. This work quantifies current standards of documentation in Gloucestershire against national best practice standards. Drain insertion was prospectively analysed over a 3 month period to establish baseline standards of documentation. A combination of accessible and easy-to-read guidelines, education and the introduction of a chest drain bundle were introduced. Chest drain insertion was then re-audited over a further 3 month period and assessed for improvement.

Results The data set included 24 pre-intervention and 23 post-intervention. Results demonstrated an improvement in many areas of documentation. Prior to the intervention, documentation was found to be poor; especially in areas related to consent, use of ultrasonography, pre-medication, post-procedure advice, details regarding length and size of drain and investigations requested. Overall the results showed improvement in most areas of documentation.

The care bundle demonstrated improvement in documentation compared to the classical “freehand” documentation. However, only 40% of cases used the new proforma due to a mixture of staff rotation and an unexpectedly high proportion of drains inserted in non-targeted areas including the emergency department, theatre and intensive care.

Outcomes were also compared against the recent national findings from the 2015 British Thoracic Society Pleural Procedures audit. Use of the chest drain bundle created improved compliance with several key standards; particularly written consent, bedside ultrasonography, nursing chest drain observation and care on designated respiratory ward.

Conclusion The chest drain care bundle improves documentation of this important procedure. This is important to ensure uniformity in clinical “best” practice, aid communication and protect patients. Further improvements can be made by more widespread education and access to the care bundle.

Abstract P186 Figure 1 Comparison of written consent obtained pre-intervention, post-intervention, when proforma exclusively used and national average. Target = 98%

Abstract P186 Figure 2 Comparison of use of bedside ultrasonography pre-intervention, post-intervention, when proforma exclusively used and national average. Target = 100%

Abstract P186 Figure 3 Comparison of use of nursing drain observation sheets pre-intervention, post-intervention, when proforma exclusively used and national average. Target = 100%

Abstract P186 Figure 4 Comparison of care on respiratory ward pre-intervention, post-intervention and national average. Target = 100%
Aim We wished to establish the use of the modified WHO safety checklist for all pleural procedures throughout the trust, excepting those done in emergency situations.

Methods We completed audits to review the implementation of the checklist. This was following writing trust guidelines, extensive teaching and presentations throughout the trust and to multiple departments on its use over a three-year period. We completed retrospective, spot check audits for one month of all pleural procedures in November 2013 and then re-audit in November 2014.

Results In 2013 the checklist was used in 14/40 of cases (35%) overall, 47% of medical patients) and re-audit showed similar results with its use in 20/47 (38%).

Discussion Following Route Cause Analysis of 2 never events, a modified WHO safety checklist was identified as a potential way of preventing future similar adverse events in our trust. Despite numerous teaching sessions and discussion in other fora we have seen that it is still not being used in the majority of cases. We feel that the use of safety checklists should be considered for all procedures that have the potential for serious harm and will continue to strive towards implementing this within our trust. It is possible that if it were to be nationally mandated or included in national guidelines that this would bring further weight towards its use.

Abstract P187 Figure 1

REFERENCES

P188 SURVEY OF USE OF SAFETY CHECKLISTS AND STANDARDISATION OF PRACTICE IN THORACOSCOPY CENTRES IN THE UK

T Duncan, S Clarke, J Hoyle. North Manchester General Hospital, Manchester, UK

10.1136/thoraxjnl-2015-207770.325

Introduction and objectives Safety checklists have been part of routine surgical practice for some time with evidence for reduction in morbidity and mortality. The use of such checklists in physician led interventions is more of a novelty. Several recent papers have been published outlining the introduction of safety checklists in the field of cardiology and gastroenterology. The 2013 BTS bronchoscopy guidelines include an adapted WHO surgical checklist, but there are no such recommendations in the BTS pleural disease guidelines. A literature search did not reveal any evidence of use of safety checklists within the area of local anaesthetic thoracoscopy.

Our department set out to adapt and introduce a safety checklist for use on our thoracoscopy list, and to ascertain whether such practice is common place on UK thoracoscopy lists. Additionally, we looked to assess whether other aspects of thoracoscopy practice were standard across the UK.

Method A checklist for use in thoracoscopy was adapted from the WHO surgical checklist. Additions specific to thoracoscopy included assessment of drain function post procedure.

A brief survey was sent out electronically to 23 medical thoracoscopy practitioners throughout the UK. Questions assessed whether a safety checklist was in use, whether such practice is common place on UK thoracoscopy lists. Additionally, we looked to assess whether other aspects of thoracoscopy practice were standard across the UK.

Results A 35% response rate was achieved. 75% of participants were using pre procedure checklists. 63% of respondents had experienced issues with equipment malfunction or sterility. 75% of respondents had experienced significant clinical complications; death (12.5%), pleural space infection (50%), bleeding (25%), other (25%). MRSA screening was carried out in 50% of centres whilst prophylactic antibiotics were used in 25%.

Conclusions Amongst the responders there was a high rate of use of pre-procedure checklists. This may not be representative of practice throughout the UK due to the relatively low response rate. A significant proportion of respondents had experienced equipment related complications, something that is likely to be picked up during routine safety checks prompted by a checklist.

The survey results suggest a lack of consistency in practice across the UK and more prescriptive guidelines may be beneficial.

P189 DEVELOPMENT OF PATIENT-CENTRED OUTCOMES FOR A PLEURAL DISEASE SERVICE

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A Addenbrookes Hospital, Cambridge, UK

10.1136/thoraxjnl-2015-207770.326

Introduction and aim There are no standardised methods for developing patient-centred service outcomes. We recognised the need for locally derived outcomes for a new pleural disease service.

Methods A survey was administered to patients who had had a pleural or ascitic drain/aspiration. The survey combined open and closed questions e.g What is important to you? We carried out emotional mapping in half of the subjects with the aim of gaining more in depth information on patient experience (see NHS institute website). We held a structured discussion with one patient’s relative to explore the themes more broadly.

Patients were identified from three acute areas, over a six week period. They were typical of patients from the medical take and respiratory ward. The survey and emotional mapping were carried out with patients face-to-face by the project lead.

Themes from the survey and emotional mapping were identified. The most common themes from the data were discussed in the structured discussion.

Thorax 2015;70(Suppl 3):A1–A254
Results 18 patients were surveyed (4 after ascitic procedures), 9 had emotional mapping. The mean overall service rating was 4/5. The graph above represents both responses to the question ‘What is important to you?’ and themes that emerged from emotional mapping.

More detailed insight was gained from the discussion with one patient’s relative, this was triangulated with the other data to give a clearer picture of what was most important to patients. Similar themes were combined to form 5 final patient-centred outcomes that were important to patients (see Figure 1 attached). E.g. ‘Be treated as an INDIVIDUAL’ encompassed good interpersonal relationships and personal choice, and ‘Receive the RIGHT INFORMATION’ for consent, medical care and managing waiting.

Discussion These five outcomes were developed for a specific service. The data has come from a relatively small number of patients from a specific cohort, but they seem credible, and may be more widely applicable. The next step is to measure the service against these outcomes before and after the. A new patient survey has been designed to measure these outcomes. It will be administered before and after the start of the new service.

Home non-invasive ventilation

DEVELOPMENT OF A RESPIRATORY QUESTION SET FOR REMOTE MONITORING IN MOTOR NEURONE DISEASE (MND)

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University Hospital of South Manchester, Manchester, UK

10.1136/thoraxjnl-2015-207770.327

Background Benefits of tele-monitoring (TM) of home non-invasive ventilation (NIV) in MND have been reported. Question sets for other respiratory conditions may not be transferrable. This work sought to develop questions transmitted via tablet device (Docobo Careportal®) allowing patients to inform clinicians of respiratory status, illness progression and NIV issues.

Methods Modified Delphi methodology was used involving 4 stages: initial expert panel with clinicians (EP1), trial of questions and feedback sessions (FS) with patients, second panel with professionals (EP2), 21 questions were developed at EP1 and trialled with 9 patients (male = 7; mean = 58 years; mean illness duration = 52 months) for 8 weeks. FS were conducted after the trial to examine face validity, clarity and relevance. Each question was deemed clear if at least there was 80% agreement.18 questions were retained, 3 modified, 2 deleted and 5 added. EP2 repeated the process, the resulting final question set contained 26 items of which 17 generate a notification. Patients completed questions weekly, appropriateness of alerts was checked by phone call; the panel specified some notifications to be of greater clinical importance requiring intervention or further observation. It was possible to review reported issues against overnight oximetry and patient ventilation interaction data.

Results For 12 weeks, 10 patients using NIV male = 7; mean (SD) age = 62 (8) years; median illness duration = 16.3 months, completed the final question set weekly. 210 alerts (geometric mean 15.3, IQ range 11–24.) were generated for; sleep quality, alertness, tiredness, NIV compliance, secretion clearance difficulty, increased secretions, and increased dyspnoea. 34 interventions resulted as described in the bar chart: the median number of interventions per patient was 2 (range = 0–9). The data has come from a relatively small number of patients from a specific cohort, but they seem credible, and may be more widely applicable. The next step is to measure the service against these outcomes before and after the. A new patient survey has been designed to measure these outcomes. It will be administered before and after the start of the new service.

SURVIVAL IN PATIENTS WITH CHRONIC TYPE 2 RESPIRATORY FAILURE: A COMPARISON OF OBESITY HYPOVENTILATION SYNDROME, COPD AND OVERLAP SYNDROME

A Jothieswaran, M Mascareno, S Bokhari, N Chaudhry, TW Felton, AM Bentley. University Hospital of South Manchester, Manchester, UK

10.1136/thoraxjnl-2015-207770.328

Introduction and objectives Home non-invasive ventilation (NIV) is established for the treatment for patients with obesity-related type 2 respiratory failure. Long-term outcomes for the use of NIV in patients with chronic hypercapnic COPD and “overlap syndrome” are less certain. Our objective was to
compare the long-term survival of patients with obesity hypoventilation syndrome (OHS), COPD and overlap syndrome who were established on NIV.

**Methods** All patients with a diagnosis of COPD, OHS and overlap syndrome were identified retrospectively from a patient database. Overlap syndrome was defined as COPD and either OHS or obstructive sleep apnoea resulting in chronic type 2 respiratory failure. The diagnosis was defined at the time NIV was established from medical assessment and respiratory physiology. All patient data was anonymised. A Kaplan-Meier survival analysis was performed. Median survival was estimated for each of the three groups. Survival was compared using Mantel-Cox test, Gehan-Breslow-Wilcoxon test and Log-rank test.

**Results** In total 463 patients were established on NIV. NIV was initiated on 158 patients with COPD (51% female, 49% male, mean age at set up 66 years), 269 patients with OHS (46% female, 54% male, mean age 62 years) and 36 patients with overlap syndrome (48% female, 52% male, mean age 66 years). The Kaplan-Meier survival curves for the three groups are shown. A clinically and statistically significant difference in survival was observed between the three groups (p < 0.0001). Patients with COPD had the worst long term survival compared with patients with OHS and the overlap syndrome. The median survival was 49 months for patients with COPD, 92 months for patients with overlap syndrome and 141 for patients with OHS.

**Conclusion** Evidence for domiciliary NIV in patients with OHS is well established. There is emerging evidence to support the use of NIV in patients with chronic hypercapnic COPD and low body mass index. Patients with overlap syndrome are a heterogeneous group representing a spectrum from predominately COPD to predominately OHS. Further studies are required to establish if patients with overlap syndrome benefit from NIV and to identify potentially modifiable risk factors associated with a poor outcome.

**REFERENCE**
patients often reside outside of formal health-care environments. Tracheostomy tubes generally need to be changed monthly. Our unit undertakes the majority of tube changes in the patient’s home. There are little data evaluating the safety of this procedure outside of the hospital.

**Method** We conducted a retrospective review of domiciliary tracheostomy tube changes on ventilator dependent patients. Concurrently all HMV-UK network centres were sent a basic electronic survey. Data collection took place during December 2014.

**Results** E-Surveys were sent to 37 centres. Responses were received from 12 (32%). 75% (n = 9) of those responding undertake the majority of tracheostomy changes in the community, 1 centre brings patients into hospital, 2 others do not routinely manage T-HMV patients. Tube changes undertaken at home, are frequently but not exclusively completed by trained professionals including care support workers. 5 areas reported that family members undertake some domiciliary tube changes.

The notes of 11 ventilator dependent T-HMV patients were reviewed. Each patient had a mean 9.2 domiciliary tube changes undertaken by the respiratory outreach team. 72% (n = 66) of changes took place without complication or incident. Of the 26 changes which had documented complications, 69% related to minor bleeding only, 3 described moderate bleeding. 5 changes were associated with incidents. 3 of these related to difficulty inserting a new tube with 1 patient requiring a smaller diameter replacement tube. 1 patient, erroneously, had a wrong diameter tube inserted, this was not replaced as the patient found it more comfortable and continued to ventilate effectively. 1 change was associated with loss of speech for 24-hours post procedure. Nobody was admitted or harmed as a direct result of a tube change at home.

The notes of a further patient were reviewed. Approximately 50 domiciliary tube changes were undertaken by her brother without supervision or involvement of health care workers. There were no documented complications or admissions as a result of these changes.

**Conclusion** Domiciliary tracheostomy tube change by trained personnel on ventilator dependent patients is safe and effective.

**Introduction** HMV can be initiated and monitored as either inpatient or outpatient. There is little evidence for best practice in this field and inpatient ventilation beds are a scarce resource. We evaluated patients, with sub-optimal HMV, admitted to our tertiary unit for adjustments to consider whether these admissions were successful, and hence an effective use of resources.

**Methods** Patients were identified from our ventilation unit’s database. Notes, oximetry and ventilator download from pre-admission, pre-discharge and post-discharge were retrospectively analysed.

**Results** In a 6-month period (June–December 2013) 30 patients were admitted to our unit for adjustments of HMV. 43% were female. Obesity related sleep disorder formed the majority of underlying conditions (53%), with musculoskeletal deformities (20%) and neuromuscular conditions (10%) also frequently seen. Median length of stay was 2 days. HMV was discontinued during admission in 2 cases in line with patient wishes. 19 (63%) were deemed to have had successful admissions, defined as normalisation of at least one abnormal ventilation parameter (pCO2 >6.0, desaturations >14/hr, time below 90% of >30 min, mean saturations of <88%, usage >6 hrs, leak <50 L/min). Of the 19 successful admissions, 6 showed sustained improvement post-discharge. 11 (37%) admissions were deemed unsuccessful, poor baseline usage and missed outpatient appointments were observed in this group. Noteworthy improvements were made to oximetry parameters during admission, although not all of these were maintained post-discharge (Table 1).

**Abstract P194 Table 1**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre Adm</th>
<th>Pre Dis</th>
<th>Post Dis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desaturation &gt;14/hr</td>
<td>8 (27%)</td>
<td>2 (7%)</td>
<td>4 (13%)</td>
</tr>
<tr>
<td>Sats &lt;80%</td>
<td>23 (77%)</td>
<td>6 (20%)</td>
<td>18 (60%)</td>
</tr>
<tr>
<td>Mean Sats &lt;88%</td>
<td>9 (30%)</td>
<td>3 (10%)</td>
<td>2 (7%)</td>
</tr>
</tbody>
</table>

Ventilator leak and usage information was available for 22 (73%) patients. Excess leak (50 >L/min) was seen in 10 patients pre-admission, only 1 patient had excess leak post-discharge. Pre-admission usage of <2 h/night was seen in 6 patients, only 1 showed sustained improvement in usage. 8 patients were admitted with usage of 2–4 h, 4 improved post discharge usage to >6 h and only 1 showed deterioration in usage.

**Conclusion** Admitting patients for adjustments to HMV can improve ventilation parameters yet only some of these improvements are maintained after discharge. There appears to be a subset of patients who do not benefit from inpatient admissions, particularly patients with poor baseline usage. We suggest careful selection of patients to ensure effective use of limited resources.

**Abstract P193 Figure 1** Chart detailing the outcome of 92 domiciliary tracheostomy changes on ventilator dependent patients
Introduction Non-invasive ventilation (NIV) in motor neurone disease (MND) is an evidence-based therapy, recommended by NICE. A single centre randomised trial of 41 patients underpins much of current practice, it was suggested our patient cohort may differ from those in the original trial work.

Methods Retrospective review of all patients offered NIV from 01.01.2013 to 30.06.2015. Data was taken from the initial neuromuscular referral, and NIV set-up. Demographics were compared with the Newcastle study (Table 1). Twelve month survival, and/or death post NIV initiation were assessed.

Results Sixty-three patients were offered trial of NIV; 5 declined admission, and 7 declined NIV. Fifty-one patients were discharged with NIV, of whom 4 rapidly discontinued ventilation. Forty-seven patients were followed as NIV users, 35 for at least a year or to death.

Fifty-seven percent were documented as having bulbar symptoms, the severity of which were not formally assessed. Twenty-nine percent received formal carer support at NIV initiation. Of the 35, 24 (68.6%) died within one year of NIV commencement, and median survival for all deaths was 177 days (range 4–630 days). Patients who died were significantly more likely to have bulbar dysfunction (18/24, p = 0.003) with a trend to reduced survival, median 149 vs. 239.5 days non-bulbar (p = 0.09). Twenty patients are alive at data collection, current median survival 292 days (range 7–793 days) and this data will affect results. Those with carers in place had a significantly lower ALSFRS-R score (48.9) vs (90.5), p = 0.008 and shorter median survival (135 days). Of those dying or surviving at least a year, 22/35 (63%) were issued with cough-assist support (18/22 mechanically in/exsufflation).

Conclusions Our cohort and outcomes are similar to those in the Bourke trial. Patients with bulbar disease, and/or pre-existing care input may have worse survival. Current users will be followed up to complete the dataset for survival. The impact of bulbar disease, cough augmentation and carer need remain uncertain. Ways to better assess and support these groups should be sought, and adequately powered randomised trials in these areas developed.

<table>
<thead>
<tr>
<th>Abstract P195 Table 1</th>
<th>NIV trials for MND (January 2013–June 2015)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trial of NIV (n=51)</td>
</tr>
<tr>
<td>Age, years</td>
<td>66±7.9</td>
</tr>
<tr>
<td>Age &gt; 75 years</td>
<td>9/35 (26%)</td>
</tr>
<tr>
<td>Sex, male</td>
<td>30/31 (96%)</td>
</tr>
<tr>
<td>Bulbar signs at trial NIV</td>
<td>29 (57%)</td>
</tr>
<tr>
<td>PaCO₂ kPa</td>
<td>9.2±2.8</td>
</tr>
<tr>
<td>PaO₂ kPa</td>
<td>6.3±3.3</td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.8±4.7</td>
</tr>
<tr>
<td>Mean sleep SpO₂ %</td>
<td>89.4±3.3</td>
</tr>
<tr>
<td>% Sleep SpO₂ &lt;90%</td>
<td>29.6±30.5</td>
</tr>
<tr>
<td>ALSFRS-R score [0-120]</td>
<td>50±49.9</td>
</tr>
<tr>
<td>Carers required at home</td>
<td>15/29 (51.7%)</td>
</tr>
<tr>
<td>Oxygen issued with NIV</td>
<td>8±15.6kPa</td>
</tr>
<tr>
<td>IAP, cmH₂O</td>
<td>14±4.3</td>
</tr>
<tr>
<td>EPAP, cmH₂O</td>
<td>5±1.4</td>
</tr>
<tr>
<td>Face / Nasal Interface</td>
<td>6/45</td>
</tr>
</tbody>
</table>

Legend: Data are number (%) or mean (SD). PaCO₂ = arterial partial pressure of oxygen, PaO₂ = arterial partial pressure of carbon dioxide. ALSFRS-R = Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised (score/120). IAP = Inspiratory Positive Airway Pressure, EPAP = Expiratory Positive Airway Pressure.

P196 A LOCAL DOMICILIARY NON-INVASIVE VENTILATION (NIV) SERVICE REDUCES LENGTH OF HOSPITAL STAY FOR PATIENTS UNABLE TO WEAN FROM NIV

A Lane, S Hatlov, P Murray, Ashford & St Peter’s Hospitals NHS Foundation Trust, Chertsey, UK
10.1136/thoraxjnl-2015-207770.333

Background NIV is a clinically proven treatment for acute hypercapnic respiratory failure. Most patients are fully weaned from NIV before discharge from hospital but some with chronic ventilatory failure require long term NIV at home. Historically, these patients would need to wait for inpatient transfer to a tertiary centre for NIV titration. Due to the high demand for tertiary care beds, this could take days to weeks. By this time, patients would frequently be optimised and stable on domiciliary NIV settings and only require transfer for equipment issue. A local domiciliary NIV service was commissioned in April 2012 to provide an integrated secondary care and community service closer to home and to reduce delayed discharge.

Method Data were collected prospectively from 83 consecutive patients between October 2006 and May 2014 (395.6 weeks) from patients on a respiratory ward, unable to fully wean and requiring domiciliary NIV on discharge.

Results See Table 1.
Efficacy of a Local Domichiary Non-Invasive Ventilation (NIV) Service for Motor Neurone Disease (MND): Patient Survival, Safety and Satisfaction

A. Lane, J. Tollit, R. Lewis, P. Murray, Ashford & St. Peter’s NHS Foundation Trust, Chertsey, UK; Respiratory Care Team, Virgin Care, Chertsey, UK; Woking & Sam Beare Hospices, Woking, UK

10.1136/thoraxjnl-2015-207770.334

Background NIV is an established treatment for MND patients with ventilatory failure and improves survival by an average of 219 days.1 NHS England (2013)2 recommend that MND patients are managed by complex weaning and ventilation centres. However, many patients find travel to hospitals difficult and distressing and therefore will not consider NIV. A Domiciliary NIV service was set up in April 2012 to provide integrated care in patients’ homes. A small prospective audit was carried out to investigate survival rates, adverse events and satisfaction with the service.

Method Data were collected prospectively from 18 consecutive patients between April 2012 and June 2015 (169 weeks). NIV was started on onset of reported symptoms. All assessments, titration onto NIV and treatment was carried out in patients’ homes.

Results 12 of 16 (75%) patients returned satisfaction questionnaires. 8 of 12 (67%) scored the service 10 (highly recommended) on the visual analogue scale, 4 patients left this blank. 100% responded that they had confidence and trust in the team and preferred to be seen at home. No adverse events were reported by these patients.

Discussion NIV survival with home based care is comparable with the current literature. Of the patients who died, the longest survival was 339 days, 60 days under median survival for those still alive. The reason for this is unclear but may be partly explained by 3 patients with bulbar involvement in this group. Further investigation into this cohort may reveal differences, such as long term feeding. Analysis is required to establish if home care is cost effective.

Abstract P197 Table 1 Survival and days spent on NIV

<table>
<thead>
<tr>
<th></th>
<th>All patients n = 18</th>
<th>Still receiving NIV n = 8</th>
<th>Died n = 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis to NIV (days)</td>
<td>359 (30–2076)</td>
<td>376 (334–1448)</td>
<td>359 (30–2076)</td>
</tr>
<tr>
<td>Survival from NIV (days)</td>
<td>181 (66–1004)</td>
<td>399 (66–1004)</td>
<td>184 (90–339)</td>
</tr>
<tr>
<td>Survival from diagnosis (days)</td>
<td>690 (142–2413)</td>
<td>711 (224–2413)</td>
<td>652 (142–2572)</td>
</tr>
</tbody>
</table>

Data are median (range).

Conclusion MND patients requiring NIV can be safely and effectively managed in a home setting and find this preferable to hospital care. This patient centred model could increase the number of patients offered NIV, subsequently improving uptake.

REFERENCES


Managing Ventilatory Failure in Patients on LTOT: A Case Series of Outcomes using NIV


10.1136/thoraxjnl-2015-207770.335

Background Long term Oxygen therapy (LTOT) has been shown to have survival benefits in patients with COPD when therapeutic levels are achieved (PO2 >8.0 kPa, saturations >92%). But for some patients, loss of hypoxic ventilatory drive, can lead to development of worsening ventilatory failure and symptomatic hypercapnia during oxygen titration. Current guidelines recommend use of nocturnal NIV in conjunction with LTOT to clinically stable patients who develop a respiratory acidosis and/or a rise in PaCO2 by >1 kPa (7.5 mmHg) during an LTOT assessment on two repeated occasions, but the evidence for this approach is lacking. We present a case series of patients on LTOT who were commenced on NIV for this indication, and look at arterial blood gas outcomes, survival time and hospital admissions.

Methods Patients on both LTOT and NIV were identified using our local database and medical notes were reviewed. Results were analysed using a paired T-test and expressed as means with standard deviations.

Results A case series of 15 patients with COPD on LTOT and NIV were identified. The mean (range) age was 68 (53–83) and mean FEV1% predicted was 29%. Mean (SD) pre-treatment pH on LTOT was 7.36 ± 0.67 and post treatment with NIV pH 7.41 ±0.38, p = 0.089. Mean LTOT pCO2 was 8.09 kPa (±1.25), and post LTOT/NIV treatment levels dropped to 7.03 kPa (±0.85), p = 0.001; with a significant improvement in PO2 from 7.26 kPa (±0.64) to 8.87 kPa (±1.15) p < 0.005. PaO2 increased to therapeutic range (> 8.0 kPa) in 80% of patients after commencing NIV with LTOT.

Mean (SD) number of hospital admissions in the 12 months before and after the introduction of LTOT/NIV significantly reduced from 0.87 (±0.74) to 0.27 (±0.59), p = 0.023 (Figure 1). In patients with COPD, the mean survival time from starting NIV in addition to LTOT was 30 months.

Abstract P198 Table 1 Hospital admissions pre and post-treatment with NIV of patients on LTOT

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD) admissions (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before NIV/LTOT</td>
<td>0.87 (±0.74)</td>
</tr>
<tr>
<td>After NIV/LTOT</td>
<td>0.27 (±0.59)</td>
</tr>
</tbody>
</table>

Abstract P198 Figure 1

Conclusion The addition of NIV to LTOT therapy can facilitate therapeutic oxygen delivery, whilst managing hypercapnia. Concurrent NIV and LTOT use can also reduce hospital admissions and increase survival times.
**P199** DOES AVERAGE VOLUME ASSURED PRESSURE SUPPORT (AVAPS) VENTILATION IMPROVE SAFETY IN MOTOR NEURONE DISEASE?

TS Buttle, S Nathoo, J Kindred, S Banerjee. Medway Maritime Hospital, Gillingham, UK

10.1136/thoraxjnl-2015-207770.336

Average volume-assured pressure support (AVAPS) is a novel way to deliver NIV. In this mode, a target tidal volume is set, and the device adjusts the pressure support to reach that volume. A particular potential benefit is that it may adapt to disease progression, as in patients with progressive Motor Neurone Disease. NICE guidance (2010) recommend follow up every 3 months. We propose to investigate if this new technology improves safety during the initial period of ventilator support.

**Aim**

1. To identify the trend in pressure support and hours of use of AVAPS ventilation in patients with ventilatory failure due to MND.
2. Look at compliance and tolerability on patients with AVAPS.

**Methods** Retrospective review of case notes and downloads from the ventilators of 6 patients identified to have started on AVAPS due to ventilatory failure secondary to MND. Average AHI, IPAP, EPAP, hours of use, compliance during first three months were reviewed.

**Results** There was no significant change in IPAP (Mean 14.78 at 1 month, 14.98 at 3 months) or EPAP (5.91 at 1 month, 6.57 at 3 months). Average use (6 hrs 44 min at one month rising to 8 hrs 48 min at three months) and compliance (percent greater than 4 h 77.6% at 1 month to 89.5% at 3 months) did show positive trends but did not reach significance.

**Abstract P199 Table 1 Summary of NIV usage**

<table>
<thead>
<tr>
<th></th>
<th>Month 1</th>
<th>Month 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>AHI</td>
<td>6.98</td>
<td>4.8</td>
</tr>
<tr>
<td>IPAP</td>
<td>14.78</td>
<td>14.98</td>
</tr>
<tr>
<td>EPAP</td>
<td>5.91</td>
<td>6.57</td>
</tr>
<tr>
<td>Avg use</td>
<td>06:44</td>
<td>08:30</td>
</tr>
<tr>
<td>Avg hrs when using</td>
<td>06:44</td>
<td>08:48</td>
</tr>
<tr>
<td>% &gt;4hrs</td>
<td>77.6</td>
<td>89.5</td>
</tr>
</tbody>
</table>

**Conclusions** This study shows an increase in average hours of use and compliance in the first 3 months of use. Tidal volumes and pressure support remain preserved. This initial data would suggest no benefit in providing the more expensive AVAPS machine compared to standard BiPAP S/T mode. Larger prospective studies looking at disease progression and ventilation usage in MND are warranted.

**P200** DOMICILIARY NOCTURNAL NIV IN COPD – STILL CONTROVERSIAL?

J Barnacle, CME Longley, V Padmanaban, S Elkin, SAA Bloch. Imperial College Healthcare NHS Trust, London, UK

10.1136/thoraxjnl-2015-207770.337

Non-invasive ventilation (NIV) following acute exacerbations of COPD resulting in decompensated type 2 respiratory failure (T2RF), the evidence for the long-term use of nocturnal NIV to prevent readmission or improve survival is controversial and has often been contradictory. Therefore clinicians are faced with the difficult question of what to do with COPD patients who are admitted with severe exacerbations requiring NIV and are considered at high risk of future decompensation. We hypothesised that domiciliary nocturnal NIV, established following an acute admission with decompensated T2RF delayed readmission.

**Methods** We performed a retrospective case note analysis of patients started on domiciliary NIV following acute admission to a busy central London acute trust. Indication for NIV and success of treatment were assessed. Time between admissions prior to establishing domiciliary NIV and time to 1st readmission were compared.

**Results** 18 patients were identified from our database. (2 were excluded: 1 returned their machine immediately, the other never attended for any follow-up at our hospital.) To our knowledge the patients were not admitted to other hospitals in the year pre or post the index admission – the admission at which NIV was initiated. The mean age of the 16 remaining patients was 70 ± 12 years; 9 were female, 8 male. Indication for NIV in 13 patients was COPD with resistant or recurrent T2RF, 1 had COPD plus sarcoidosis and the remaining 2 had COPD plus obesity hypventilation. NIV was shown to be successful in reducing pCO2 between discharge and first follow up (mean reduction 0.84 ± 1.17 kPa p = 0.01). There was a trend towards delayed 1st readmission following initiation of NIV, when compared to the time between previous admission (Kaplan-meier survival analysis. p = 0.09 Figure 1).

**Conclusion** Domiciliary NIV for high risk patients with decompensated T2RF in COPD is often used because of concerns of leaving the condition untreated when objectively NIV improved the patient’s pCO2 furthermore there are no consistently ratified guidelines. The data presented here suggest that NIV may help to delay readmission to hospital. The results of ongoing randomised trials are eagerly awaited.
Double pneumonia and other infections

P201 LIVING YOUR LIFE WITH BRONCHIECTASIS: AN EXPLORATION OF PATIENTS AND CARERS INFORMATION NEEDS INFORMING DEVELOPMENT OF A NOVEL INFORMATION RESOURCE

KLM Hester, 1J Newton, 2A DeSoysa, 1T Ragley, 1Newcastle University, Newcastle Upon Tyne, UK; 2The Newcastle Upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne, UK

Introduction/background Bronchiectasis is a chronic lung condition, causing breathlessness and chronic productive cough, with intermittent infective exacerbations. Patients often have recurrent hospital admissions, poorer quality of life, and significant fatigue. Treatment concordance can be problematic. There is little patient information currently available, yet information and education could support patients to self-manage, improve understanding and optimise engagement with treatment. Previous exploratory interviews with patients suggested that a lack of credible patient information was available and that having information could help patients learn to live with and manage their condition.

Aims/objectives
1. To further identify, explore and understand the information needs of patients with bronchiectasis and their carers.
2. To co-develop, with the user group, a novel patient information resource.

Methods In-depth interviews were conducted with 17 people who have bronchiectasis and 9 carers. Three focus group style workshops were subsequently held with 11 patients and 3 carers in total. All were recruited from respiratory clinics in the North of England. Interviews and workshops were audio-recorded and transcribed and thematic analysis was undertaken to identify common themes.

Results Ages ranged from 33 to 78 years, including both newly diagnosed and longstanding patients. The focus of the interviews was to identify, explore and understand information needs. A core mediating issue emerged, however: what it means to learn to live your life with bronchiectasis. Embedded in this journey are issues around developing support and coping mechanisms, how people learn to connect with information and how they start to take back control and develop new, active, partnerships with the medical team.

Using these qualitative data in the workshops, we co-developed a novel online and paper-based information resource for patients and their families. This resource is currently being piloted in a feasibility study comparing use of the resource to usual care.

Conclusions Understanding patient and carer experiences of living with bronchiectasis, the biographical disruption(s) that it imposes and the ways in which patients and carers connect with health information over time, has enhanced our understanding of their information needs and how these could be met. The outcomes of the feasibility study are expected in March 2016.

P202 ASSESSMENT OF BRONCHIECTASIS SCORING SYSTEMS: A LONG TERM COHORT STUDY

HC Ellis, 1S Cowman, 1M Fernandes, 1R Wilson, 1M Loebinger. 1Host Defence Unit, Royal Brompton Hospital, London, UK; 2St. George’s, University of London, London, UK

Introduction Bronchiectasis is a chronic, disabling illness with an unpredictable clinical course. Two multidimensional scores have been developed to predict mortality in bronchiectasis: the bronchiectasis severity index (BSI) and the FACED score.1,2 This study is a retrospective cohort study aiming to compare these scores and test their ability to predict long-term mortality in bronchiectasis.

Methods Data was obtained for 74 subjects with bronchiectasis who had previously taken part in research at our centre. BSI and FACED scores were calculated and outcomes were ascertained after a median of 18.8 years follow-up. Receiver operator characteristic (ROC) curves for mortality were generated and survival between groups compared using univariate Cox proportional hazards analysis.

Results Both scoring systems had similarly excellent predictive power for 5-year mortality, with area under the ROC curve (AUC) 0.79 for BSI and 0.8 for FACED. Both scores were also able to predict 15-year mortality (Figure 1), with the FACED score showing superior predictive power (AUC 0.82 vs 0.69 P = 0.0495). For both scores subjects with high scores had an increased risk of death compared to the low scoring group (hazard ratio (HR) for death 3.6 for BSI P = 0.07, 12.5 for FACED P < 0.001). The intermediate scoring FACED group was also at an increased risk of death (HR 5.9 P < 0.001), whereas the intermediate BSI group was not (HR 1.4 P = 0.58). The BSI tended to assign higher scores; accordingly the high BSI group was larger (33 vs 6 subjects) with a lower mortality (57% vs 83%) than the equivalent FACED group.

Abstract P202 Figure 1

Conclusion This study demonstrates the ability of the BSI and FACED score to predict mortality in bronchiectasis over a far longer period than previously described. Such tools will be
valuable for stratification in clinical trials and for identifying individuals in a higher risk group for intensified treatment.

REFERENCES

P203 WITHDRAWN: A DESCRIPTION OF IMMUNOLOGICAL AND SPECIFIC ANTIBODY PROFILE IN A COHORT OF NON-CF BRONCHIECTASIS PATIENTS
GM Miller. North Tees & Hartlepool NHS Foundation Trust, Stockton-on-Tees, UK

P204 RISK FACTORS FOR REQUIRING INTRAVENOUS ANTIBIOTIC THERAPY DELIVERED IN HOSPITAL FOR EXACERBATIONS OF BRONCHIECTASIS
1P Palani Venu, 1P Bedi, 2K Turnbull, 2AT Hill. Royal Infirmary of Edinburgh, Edinburgh, UK; 2MRC Centre for Inflammation Research, Edinburgh, UK

Introduction Recurrent exacerbations requiring IV antibiotic therapy are a feature of advanced bronchiectasis. Our group has previously established the safety and efficacy of domiciliary antibiotic therapy compared to inpatient hospital treatment for exacerbations of bronchiectasis. In this study we aimed to identify factors at presentation that could predict the requirement for inpatient antibiotic therapy compared to domiciliary antibiotic therapy.

Methods We assessed the management of bronchiectasis exacerbations referred to a specialist respiratory unit over a 1-year period (April 2013 to 2014). All patients received 10 to 14 days IV antibiotic therapy and were assessed at the beginning and end of their treatment course. We assessed demographic data, treatment outcomes, morbidity, mortality and 30-day readmission rates. Logistic regression analysis was performed to identify factors predictive of the treatment modality used.

Results A total of 72 patients were treated with 131 courses of IV antibiotic therapy. Thirty-six cases (27.5%) were managed as inpatients, 20 cases (15.2%) required initial admission and subsequently received early supported discharge (ESD) to complete IV antibiotic therapy at home and 75 cases (57.2%) received domiciliary IV antibiotics.

Logistic regression showed that Charlson Co-morbidity Index was independently predictive of the requirement for inpatient antibiotic therapy (p = 0.03). White Cell Count at presentation was also positively associated with the requirement for inpatient antibiotic therapy approaching statistical significance (p = 0.05).

There were no mortalities in the ESD or domiciliary antibiotic groups but 2 mortalities (5.6%) were noted in the inpatient group (Table 1). Morbidity in the inpatient, ESD and domiciliary antibiotic groups were 8.3%, 5.0% and 2.9% respectively (p = 0.40). The median length of stay before early supported discharge was 7 (interquartile range 7–9) days. Thirty-day readmission rates were 11.1%, 25.0% and 2.7% respectively (2 × 3 Chi-square; p < 0.05). Total bed days saved from ESD and domiciliary antibiotic therapy was 1153 days (interquartile range 9–14).

Conclusions Our study has demonstrated that the Charlson Co-morbidity Index is the independent risk factor that predicts the need for inpatient intravenous antibiotic therapy in exacerbations of bronchiectasis. Those patients that received domiciliary treatment received it safely.

Abstract P204 Table 1 Biochemical indices, Morbidity, Mortality and 30-day readmission between treatment groups

<table>
<thead>
<tr>
<th></th>
<th>Inpatient (n = 36)</th>
<th>Early supported discharge (n = 20)</th>
<th>Domiciliary (n = 75)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WCC (Median)</td>
<td>Pre 9.6</td>
<td>12.5</td>
<td>8.1</td>
</tr>
<tr>
<td></td>
<td>Post 8.3</td>
<td>7.8</td>
<td>7.1</td>
</tr>
<tr>
<td>CRP (Median)</td>
<td>Pre 21</td>
<td>34.5</td>
<td>13.5</td>
</tr>
<tr>
<td></td>
<td>Post 10</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>ESR (Median)</td>
<td>Pre 29</td>
<td>50</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td>Post 28</td>
<td>32</td>
<td>18.5</td>
</tr>
<tr>
<td>Morbidity</td>
<td>8.3% (3)</td>
<td>5% (1)</td>
<td>2.9% (2)</td>
</tr>
<tr>
<td>Mortality</td>
<td>5.6% (2)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Access related complications</td>
<td>2.8% (1)</td>
<td>5% (1)</td>
<td>1.3% (1)</td>
</tr>
<tr>
<td>Anaphylaxis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Readmission within 30 days</td>
<td>11.1% (4)</td>
<td>25% (5)</td>
<td>2.7% (2)</td>
</tr>
</tbody>
</table>

P205 ADMISSION TRENDS AND OUTCOMES OF INDIVIDUALS WITH BRONCHIECTASIS ADMITTED TO ADULT GENERAL CRITICAL CARE UNITS IN ENGLAND, WALES AND NORTHERN IRELAND
1V Navaratnam, 2C Muirhead, 1RB Hubbard, 3A De Soyza. 1Division of Epidemiology and Public Health, University of Nottingham, Nottingham, UK; 2Institute of Health and Society, Newcastle University, Newcastle, UK; 3Institute of Cellular Medicine, Newcastle University & Sir William Les Che Centre, Newcastle, UK

Introduction Whilst studies suggest increasing incidence and mortality from bronchiectasis in UK, there are sparse data on outcomes of individuals with bronchiectasis admitted to intensive care (ICU). We investigated trends in bronchiectasis admissions to ICU and estimated outcomes in patients with bronchiectasis admitted to ICU compared to a better studied group, i.e. Chronic Obstructive Pulmonary Disease (COPD).

Methods We used data from the Intensive Care National Audit and Research Centre (ICNARC), a database of patient outcomes from adult critical care units across England, Wales and Northern Ireland. 95% of adult critical care units contribute data to ICNARC which includes information from 1.5 million individuals. Admissions from bronchiectasis and COPD from 1/1/2009 to 31/12/2013 were extracted. Bronchiectasis admissions included patients whose primary or secondary reason for admission was exacerbation of bronchiectasis, excluding people with cystic fibrosis. COPD admissions were those whose primary or secondary reason for admission was either COPD with acute lower respiratory infection; or COPD with acute exacerbation. Patients with COPD-bronchiectasis overlap were excluded. ICU mortality was defined as status on leaving ICU.

Results There were 614,352 admissions across 219 critical care units during the study period, 536 (0.1%) of which were from...
EXPERIENCE OF ESTABLISHING FUNDING FOR A HOME IV SERVICE FOR BRONCHIECTASIS

A Booth, A McCleary, RA Thomas. York Hospitals NHS Trust, York, UK

10.1136/thoraxjnl-2015-207770.342

Background The benefit of intravenous (IV) antibiotics in bronchiectasis has been established, and IV antibiotics can be safely delivered in a domiciliary setting. We report on the experience of obtaining funding through the CCG to establish a service delivering IV antibiotics safely and effectively to people with bronchiectasis at home.

Methods The model for home IV antibiotics involved a vascular surgeon placing a PICC line on day one under guided ultrasound, and an initial review by specialist nurse and physiotherapist. The specialist nurse administered the first dose. Education on line care, anaphylaxis and potential complications was provided. Drugs were delivered via a homecare company, Calea, and home IV doses were administered by specialist nurses from the homecare company. At the end of the course patients were reviewed by the specialist bronchiectasis nurse.

Results Negotiations with the CCG agreed funding for the service with 7.5 h of specialist nurse time and to meet the costs of the homecare company. Between July 2014 and July 2015 9 patients underwent 10 IV courses. A total of 132 days IV antibiotics were given, with 96 (73%) being given at home. This saved bed days, at an estimated saving of £26,400. Seventy seven home visits were conducted by the homecare company specialist nurses at a cost of £5625 and the homecare drug cost was £6134 (total £11,759 or £1,175 per course). Overall cost savings amounted to approximately £20,266 for the ten courses, or £2,026 per course. One patient had to return to hospital for replacement of their line due to mechanical phlebitis, but was still able to complete the entire course. Qualitative feedback is being sought via patient questionnaires, and has proved very positive.

Conclusion Administering IV antibiotics at home for people with bronchiectasis is safe, reduces inpatient bed days and is cost effective.

REFERENCES


THORACIC INVOLVEMENT IN IGG4-RELATED DISEASE

1. RM Ansty, 1P Corcoran, 1E Culver, 1A Takeda, 1R Halifax, 1P Palladis, 2TN Cargill, 2CD Manginis, 2E Barnes, 1NM Rahman. 1Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Trust, Oxford, UK; 2Translational Gastroenterology Unit, Oxford University Hospitals NHS Trust, Oxford, UK

10.1136/thoraxjnl-2015-207770.343

Background and objectives IgG4-related disease (IgG4-RD) is a systemic fibro-inflammatory disorder originally described in association with autoimmune pancreatitis (AIP), usually but not always in the context of elevated serum IgG4 levels. Thoracic manifestations of IgG4-RD include mediastinal lymphadenopathy, lung nodules or masses, interstitial lung disease, bronchiectasis and pleural disease.

Poster sessions

Abstract P205 Table 1 Crude admission rates, Poisson regression modelling of admissions, mortality and median ICU length of stay in people with Bronchiectasis and Chronic Obstructive Pulmonary Disease (COPD)

<table>
<thead>
<tr>
<th>Year</th>
<th>Bronchiectasis</th>
<th>COPD</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>121</td>
<td>3126</td>
</tr>
<tr>
<td>2010</td>
<td>136,877</td>
<td>3223.6</td>
</tr>
<tr>
<td>2011</td>
<td>137,062</td>
<td>3146.9</td>
</tr>
<tr>
<td>2012</td>
<td>137,062</td>
<td>3318.9</td>
</tr>
<tr>
<td>2013</td>
<td>136,877</td>
<td>3289.5</td>
</tr>
<tr>
<td>2014</td>
<td>137,062</td>
<td>3497.8</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Year</th>
<th>Crude admission rate per 100,000 person years (95% CI)</th>
<th>Crude admission rate ratio (95% CI)</th>
<th>Number of ICU deaths (%) on ICU* (IQR)</th>
<th>Median length of stay on ICU* (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>74</td>
<td>97,457</td>
<td>3204.6 (3094.2–3318.9)</td>
<td>1.00</td>
</tr>
<tr>
<td>2010</td>
<td>78</td>
<td>114,207</td>
<td>3217.8 (3115.5–3223.6)</td>
<td>1.01 (0.96–1.05)</td>
</tr>
<tr>
<td>2011</td>
<td>108</td>
<td>128,659</td>
<td>3049.9 (2956.0–3146.9)</td>
<td>0.95 (0.91–1.00)</td>
</tr>
<tr>
<td>2012</td>
<td>155</td>
<td>137,062</td>
<td>3193.4 (3100.2–3289.5)</td>
<td>0.99 (0.95–1.04)</td>
</tr>
<tr>
<td>2013</td>
<td>121</td>
<td>136,877</td>
<td>3398.7 (3302.4–3497.8)</td>
<td>1.08 (1.01–1.11)</td>
</tr>
</tbody>
</table>

*p for trend = 0.022

*p value for likelihood ratio test. *length of stay in days.
The authors’ regional IgG4-RD service is one of the largest UK-based units treating patients with this condition. Specialist clinics and multidisciplinary team meetings operate alongside an active research programme. We aimed to describe the frequency with which thoracic abnormalities – either as a symptomatic presenting feature of IgG4-RD or an incidental asymptomatic finding on imaging – were present in a prospectively recruited patient cohort.

Method and results Patients referred to the authors’ IgG4-RD service from 2005 onwards and confirmed as having a diagnosis of IgG4-RD were included. Diagnoses were made using established clinical criteria (HSORt for AIP and Japanese International Consensus Diagnostic Criteria for systemic disease); tissue specimens were assessed using the Boston histopathological consensus criteria where available. Patients were followed prospectively; clinicopathological data relating to presentation and clinical progress were stored in a secure database with the consent of participants. In patients without symptomatic thoracic manifestations of IgG4-RD, routine clinical imaging (CXR and CT) was reviewed where available for evidence of incidental asymptomatic disease.

61 IgG4-RD patients with thoracic imaging available were included; mean age at diagnosis was 60.3 years (SD 14.6). 43 (70.5%) patients were male. The majority of patients (85.2%) presented with features of intra-abdominal disease. 6 patients (9.8%) had evidence of symptomatic thoracic disease on the basis of clinical presentation, radiology and/or histology. A further 15 (24.6%) patients had abnormal imaging suggestive of asymptomatic thoracic IgG4-RD.

Conclusion A significant proportion of IgG4-RD patients have evidence of symptomatic and asymptomatic thoracic manifestations of this multi-system disease. Respiratory physicians should consider IgG4-RD in their differential diagnosis for a range of pulmonary presentations, particularly where there is co-existing extra-thoracic organ involvement. Making a diagnosis of IgG4-RD impacts on access to established therapeutic options including corticosteroids and rituximab to which the disease is responsive in the inflammatory phase.

Abstract P208 Figure 1

P209 THE BURDEN OF HOSPITAL ACQUIRED PNEUMONIA: A COHORT STUDY

Introduction VAP is a common nosocomial infection with various known strategies for prevention, including CPT. Conflicting evidence regarding CPT for VAP prevention exist since CPT may cause desaturation and respiratory muscle fatigue.

Objectives To determine the efficacy of CPT, compared with standard care, in preventing the onset of VAP among mechanically ventilated adult ICU patients, its effect on ICU mortality, length of ICU stay, and duration of mechanical ventilation.

Inclusion criteria Controlled trials on adult mechanically ventilated ICU patients, given CPT for VAP prevention, compared with standard care.

Search strategy An electronic search in PubMed, EMBASE, CENTRAL, BioMedCentral, Elsevier Health, and Herdin was done. Reference lists were checked manually.

Study manoeuvres The authors arrived at a consensus and the Cochrane risk of bias tool was used for evaluation.

Statistical analysis Mantel-Haenszel method using the Review manager 5.3.

Results Twenty studies were found, and 10 were retrieved for review. Five studies were included, representing 595 patients. Evaluation of the included studies found 1 study with low risk of bias, 2 studies with high risk, and 2 studies with unclear risk. Overall combined meta-analysis of all 5 studies found no difference in VAP incidence between the 2 groups (RR 0.80, 95% CI 0.52 to 1.23, P = 0.05). A subgroup analysis done excluding the studies with high risk of bias still showed no difference in VAP incidence (RR 0.96, 95% CI 0.62 to 1.50, P = 0.86). CPT made no significant difference on ICU mortality (RR 0.97, 95% CI 0.57 to 1.97, P = 0.07), duration of ICU stay (RR 0.36, 95% CI -1.83 to 2.55, P = 0.10), and duration of mechanical ventilation (RR 0.23, 95% CI -0.74 to 1.21, P = 0.14).

Conclusions It is not recommended to perform routine CPT on mechanically ventilated adult ICU patients to prevent the onset of VAP as this is associated with potential harm and unnecessary costs. The authors recommend that more trials with low risk of bias be conducted on CPT for VAP prevention.
Abstract P209 Table 1  Association between clinical and demographic features of cohort and death at 30 days

<table>
<thead>
<tr>
<th>Demographic feature</th>
<th>Number of individuals (n = 790) (%)</th>
<th>Number of deaths at 30 days (n = 240) (%)</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>394 (49.9)</td>
<td>111 (46.2)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Male</td>
<td>396 (50.1)</td>
<td>129 (53.8)</td>
<td>1.23 (0.91–1.67)</td>
<td>1.38 (0.96–1.99)</td>
</tr>
<tr>
<td><strong>Age category (years)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;70</td>
<td>184 (23.3)</td>
<td>27 (11.3)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>70–79</td>
<td>182 (23.0)</td>
<td>58 (24.2)</td>
<td>2.72 (1.63–4.55)</td>
<td>2.30 (1.28–4.14)</td>
</tr>
<tr>
<td>80–89</td>
<td>305 (38.6)</td>
<td>113 (47.1)</td>
<td>3.42 (2.14–5.48)</td>
<td>3.18 (1.86–5.43)</td>
</tr>
<tr>
<td>≥90</td>
<td>119 (15.1)</td>
<td>42 (17.5)</td>
<td>3.17 (1.82–5.52)</td>
<td>3.23 (1.71–6.10)</td>
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<tr>
<td><strong>Admitted from nursing home</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>734 (92.9)</td>
<td>218 (90.8)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>56 (7.1)</td>
<td>22 (9.2)</td>
<td>1.54 (0.88–2.68)</td>
<td>1.47 (0.75–2.91)</td>
</tr>
<tr>
<td><strong>Charlson Index Score</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>186 (23.5)</td>
<td>29 (12.1)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1</td>
<td>178 (22.5)</td>
<td>49 (20.4)</td>
<td>2.06 (1.23–3.44)</td>
<td>1.94 (1.09–3.44)</td>
</tr>
<tr>
<td>2–3</td>
<td>248 (31.4)</td>
<td>79 (32.9)</td>
<td>2.53 (1.57–4.08)</td>
<td>2.15 (1.27–3.66)</td>
</tr>
<tr>
<td>≥4</td>
<td>178 (22.5)</td>
<td>83 (34.6)</td>
<td>4.73 (2.89–7.74)</td>
<td>4.34 (2.50–7.53)</td>
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<tr>
<td><strong>Consolidation on CXR</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>138 (17.5)</td>
<td>35 (14.6)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>Yes</td>
<td>386 (48.9)</td>
<td>132 (55.0)</td>
<td>1.53 (0.98–2.37)</td>
<td>1.48 (0.92–2.39)</td>
</tr>
<tr>
<td><strong>Timing of HAP antibiotics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Admission or ≤48 h of admission</td>
<td>192 (24.3)</td>
<td>59 (24.6)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>2–4 days from admission</td>
<td>169 (21.4)</td>
<td>42 (17.5)</td>
<td>0.75 (0.47–1.19)</td>
<td>0.81 (0.48–1.39)</td>
</tr>
<tr>
<td>≥5 days from admission</td>
<td>429 (54.3)</td>
<td>139 (57.9)</td>
<td>1.08 (0.75–1.56)</td>
<td>0.87 (0.57–1.33)</td>
</tr>
<tr>
<td><strong>White cell count (quintiles)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤3.9</td>
<td>191 (24.2)</td>
<td>47 (20.0)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>4.0–10.9</td>
<td>189 (23.9)</td>
<td>53 (22.1)</td>
<td>1.19 (0.76–1.89)</td>
<td>1.01 (0.59–1.67)</td>
</tr>
<tr>
<td>11.0–14.6</td>
<td>190 (24.1)</td>
<td>61 (25.4)</td>
<td>1.45 (0.93–2.27)</td>
<td>1.20 (0.72–2.02)</td>
</tr>
<tr>
<td>≥14.7</td>
<td>190 (24.1)</td>
<td>69 (28.8)</td>
<td>1.74 (1.12–2.72)</td>
<td>1.38 (0.83–2.35)</td>
</tr>
<tr>
<td>Missing</td>
<td>30 (3.8)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>C Reactive Protein (quintiles)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤45</td>
<td>187 (23.7)</td>
<td>41 (17.1)</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>46–87</td>
<td>186 (23.5)</td>
<td>60 (25.0)</td>
<td>1.70 (1.06–2.69)</td>
<td>1.90 (1.12–3.22)</td>
</tr>
<tr>
<td>88–174</td>
<td>187 (23.7)</td>
<td>73 (30.4)</td>
<td>2.28 (1.45–3.59)</td>
<td>2.42 (1.42–4.12)</td>
</tr>
<tr>
<td>≥175</td>
<td>185 (23.4)</td>
<td>55 (22.9)</td>
<td>1.51 (0.94–2.41)</td>
<td>1.56 (0.90–2.70)</td>
</tr>
<tr>
<td>Missing</td>
<td>45 (5.7)</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*Odds ratio adjusted for all variables in table.*

Background  Hospital acquired pneumonia (HAP) is a common nosocomial condition, especially in the elderly population. We aimed to describe clinical and demographic features of patients diagnosed with HAP (excluding ventilator associated pneumonia) in a large teaching hospital and investigate the association of these features with 30 day mortality.

Methods  We used electronic medical records to identify all individuals with a physician diagnosis of HAP between 1/11/2014 and 31/4/2015. We extracted information on demographics, radiographic and laboratory findings, antibiotic prescriptions and mortality. HAP was defined as either diagnosis of pneumonia after 48 h of admission or hospital admission within the preceding 10 days. 30 day mortality was defined as death within 30 days of first being prescribed antibiotics for HAP. Logistic regression was used to generate odds ratios for death at 30 days, stratified by clinical and demographic features. White cell count and C Reactive Protein (CRP) levels were divided into quartiles.

Results  There were 790 people with a diagnosis of HAP during the study period. 396 (50.1%) were male and mean age at admission was 78.0 years (standard deviation [SD] 13.1). 56 (7.1%) people were admitted from a nursing home. 706 (89.4%) patients were admitted under medical specialities. 186 (23.5%) had a Charlson Index Score of 0, and 62 (7.9%) had dementia coded as a co-morbid illness. 48.9% of patients were reported to have consolidation on chest radiograph, whilst 19.9% were reported to have clear lungs. 598 (75.7%) patients had been admitted to hospital for at least 48 h prior to starting antibiotics for HAP, with a median stay of 5 days in hospital prior to starting antibiotics for HAP (Interquartile range [IQR]: 2 to 11). 240 (30.4%) patients died within 30 days of first being prescribed antibiotics for HAP. Features strongly associated with increased mortality at 30 days were older age, higher Charlson Index Score and high CRP (see Table 1).

Conclusion  Our findings suggest that HAP poses a substantial burden to secondary care services and carries a high mortality rate.

P210  COMMUNITY ACQUIRED PNEUMONIA- SEVERITY AND MORTALITY

K. Tariq, P. McDermott, S. Sunny, H. Burhan, J. Hadcroft. Royal Liverpool and Broadgreen University Hospitals, Liverpool, UK 10.1136/thoraxjnl-2015-207770.346

Background  Community acquired pneumonia (CAP) is a common cause of hospital admissions and carries a high mortality rate. Risk stratification through clinical assessment, underlying chronic lung disease, SIRS and CURB65 helps identify patients at moderate to high risk of mortality. Despite prompt and appropriate management, a significant number of patients (18.3%) die in hospital (BTS Adult CAP audit 2009/10).

Aims and objectives  We wished to determine our hospital’s CAP mortality rate and ascertain the proportion of patients with a high likelihood of death, as predicted by high CURB-65 scores, markers of severe infection (SIRS criteria) and underlying chronic respiratory disease.
Methods Case notes of all patients admitted with CAP over a 3 month period were requested and 175 were obtained. Information was gathered on the presence of underlying chronic lung conditions, CAP severity/mortality markers (SIRS and CURB65 scores) and mortality.

Results At least one underlying chronic pulmonary condition was found in 45.1% (n = 79), the commonest being COPD (n = 56). CURB65 score was 0 to 1 in 39.4% (low risk), 2 in 27.4% (moderate risk), 3–5 in 17.2% (high risk) and not done in 16% (n = 28). SIRS criteria were met in just under half of the cases (48.5% n = 85).

An in-patient mortality review during this study period showed that 8% (n = 14) CAP patients died in hospital within 30 days. An association of these patients with background lung condition, CURB65 and SIRS is shown in Table 1.

Conclusion We showed an improvement in mortality figures compared with the BTS National CAP adult audit 5 years ago (8% vs 18.3%). A significant number of these patients have an underlying chronic lung disease which predisposed them to developing CAP. The highest mortality was seen in patients with a high CURB65 score with SIRS response.

Mortality Chronic lung disease CURB65 SIRS SIRS and/or CURB65 2–5

<table>
<thead>
<tr>
<th>Numbers</th>
<th>Yes</th>
<th>No</th>
<th>0–1</th>
<th>2–5</th>
<th>Yes</th>
<th>No</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td>1</td>
<td>7</td>
<td>5</td>
<td>9</td>
<td>8</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>12.6%</td>
<td>4.2%</td>
<td>1.4%</td>
<td>9%</td>
<td>5.9%</td>
<td>10%</td>
<td>9%</td>
<td>7%</td>
<td></td>
</tr>
</tbody>
</table>

Abstract P210 Table 1 Characteristics of CAP patients who died in hospital within 30 days (n = 14)

P121 IMPACT OF DOOR-TO-RADIOGRAPH TIME ON PNEUMONIA MANAGEMENT

JM Dudziak, KL Scott, A Ashton, R Varia. Whiston Hospital, Prescot, Merseyside, UK
10.1136/thoraxjnl-2015-207770.347

Introduction Pneumonia continues to be associated with significant mortality.1 The diagnostic gold standard remains the Chest X-Ray (CXR). Quality indicators such as door-to-antibiotic or door-to-radiograph time are monitored as surrogate outcome measures.

Objective To assess the impact of CXR availability at first clinician contact in cases where initial antibiotics were delayed.

Methods We interrogated the time of initial consultation, radiographs and diagnosis for 57 CAP patients between March 2013 and February 2014 whose initial antibiotics were delayed beyond 4 h.

Results The median age was 77 (interquartile range 67–85), 32 (53%) were female. Presentation was to the ED in 45 (79%) and to the GP assessment unit (GPAU) in 12 (21%) cases. 37 (65%) cases had SIRS, 45% had a CURB-65 score of 3 or above.

CXR reports were compatible with pneumonia in 44 (77%) cases, but only 11 (19%) had a CXR at time of first doctor contact. Interestingly, a reported consolidation was not associated with an initial diagnosis of pneumonia (p = 1.0000, Fisher’s exact test, two-tailed p).

Median time to first clinician contact was 2:14 h (ED 2:03 h, GPAU 4:33 h). Overall, 20 patients (35%) had a diagnosis of pneumonia after the initial consultation, 7 (58%) in GPAU and 13 (29%) in the ED. CXRs were obtained within 4 h in 49 (86%) cases. Median time to diagnosis was 7:06 h (ED 8:35 h, GPAU 5:54 h). CXR availability at first clinician contact differed significantly – GPAU 50%/6 vs ED 11%/5 (p = 0.0068, Fisher’s exact test, two tailed p).

Discussion There were significant delays to diagnosis, despite most CXR reports indicative of pneumonia. The absence of a CXR on initial clinician contact may contribute to the poor diagnostic accuracy seen in this case series. Notably the 4 h door-to-radiograph target set by BTS was largely met. We will deploy the GPAU pneumonia care bundle in the ED, which was shown to improve door-to-radiograph time (CURECAP, reported previously). The efficacy of this intervention will be the subject of further studies.

REFERENCES

P212 MICROBIOLOGICAL SAMPLING IN COMMUNITY-ACQUIRED PNEUMONIA: DO WE FOLLOW THE GUIDELINES AND DOES IT HELP OUR PATIENTS?

1 S Sunny, 2 P McDermott, 3 K Tarig, 1 J Hadcroft, 1 J Folk. 1 Medical Microbiology, Liverpool Clinical Laboratories, Royal Liverpool University Hospital, Liverpool, UK; 2 Respiratory Medicine, Royal Liverpool University Hospital, Liverpool, UK
10.1136/thoraxjnl-2015-207770.348

Introduction Community-acquired pneumonia (CAP) is a common cause for hospital admission and carries a high mortality rate. Choosing the correct antibiotic can be challenging and “atypical” pathogens, such as Mycoplasma pneumoniae and Chlamydia pneumoniae, are not eliminated by some frontline empirical agents. Identification of the infecting organism through microbiological sampling can help to tailor antibiotic therapy and substantially improve patient outcomes. Guidelines exist (NICE, BTS, trust) that recommend which patients should undergo microbiological sampling. We wished to determine whether these guidelines were followed in our trust in patients admitted with CAP.

Methods We reviewed the notes of adult patients admitted over a 15-week period (February–May 2014) with a clinical code of pneumonia. Further information was obtained from hospital systems, including Telepath (used by the Microbiology department) and from ‘Advancing Quality’ data available for these patients.

Results 175 patients were identified with CAP. Blood cultures (BCs) were indicated in 89 patients according to trust guidelines (based on Systemic Inflammatory Response Syndrome (SIRS) criteria, CURB-65 score, immunocompromised; data sufficient in 147) and appropriately collected in 55 (61.8%). However, only 4 had positive (clinically significant) BC results. Sputum samples were sent for 31 patients (17.7%, n = 175) and only 19% had significant bacterial growth. All patients transferred to intensive care (ITU; 3.4%) were screened appropriately for urinary pneumococcal antigen (UPA) and urinary legionella antigen (ULA), with 1 positive UPA result. 6 (of 10) UPA and 7 (of 12) ULA samples appeared to be sent inappropriately for non-ITU patients and were rejected by the laboratory. Serum samples were sent for Mycoplasma testing in 7 patients, despite this
service being superseded by testing by polymerase chain reaction (PCR)-testing of nose/throat swabs, for which only 1 was sent for the entire cohort.

Conclusion While BC collection was frequent, compliance with local guidance was less than desired. Sampling to rule out atypical pathogens in CAP appeared to be low and, occasionally, inappropriate. Although positive detection rates were low, further work appears to be indicated to optimise patient outcomes in CAP by increasing awareness amongst clinicians of tests available and ensure appropriate sampling for atypical pathogen screening.

**P213 CXR FOLLOW-UP AFTER COMMUNITY ACQUIRED PNEUMONIA (CAP): OUTCOMES OF ADHERENCE TO GUIDELINES**

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10.1136/thoraxjnl-2015-207770.349

**Introduction and objectives** BTS Community Acquired pneumonia (CAP) guidelines require a chest radiograph (CXR) 6 weeks after discharge in high risk patients. This is the hospital team’s responsibility. Malignancy is reported in 1.7% of patients.

We wanted to assess how this was organised across our trust and the outcomes, aiming to improve organisation of the service.

**Methods** Patients were identified via retrospective review of local NIV/COPD and critical care ICNARC databases. Xrays and reports were reviewed and eRecords interrogated for appointments, follow-up CXR and outcomes.

**Results** 102 patients were identified between December 2013 to January 2015, (mean age 69 and 56 female patients). Only 54 patients had the follow up CXR. 16 patients did not need local follow-up for a variety of reasons: co-morbidities; current malignant diagnosis; CXR clear pre-discharge or usual residence outside geographical area. 7 patients did not attend the organised follow up appointment. Ultimately, 25 patients had no follow up plans made.

The majority of follow-up CXRs were organised by the hospital team (n = 53) compared to discharge correspondence instructions to GP to request a CXR (n = 14). The hospital requested CXR were significantly more likely to be undertaken, with 88% completed versus 57% from requests to GP (p < 0.05 Chi-square).

The majority of CXRs showed resolution of changes (n = 38/54), 3 patients had lung or pleural malignancy diagnosed, 2 patients are having on-going nodule follow-up and 1 patient had atypical mycobacterium diagnosed. 10 patients to date have incomplete resolution of their changes. These end-points were after 62 CXRs, 7 Ct scans, 2 bronchoscopies and 1 pleural biopsy.

**Conclusion** There is room for improvement within our trust to improve this parameter for CAP patients. This would be best fulfilled by automatic request at time of discharge follow CAP.

The follow up clearly requires increasing amounts of work and administration. How does the NHS keep up with guideline requirements and clinical outcomes in the ageing population?

The finding of 5.5% (3/54) new malignancy shows the importance of follow-up and is higher than published reports.

**P214 ARRHYTHMIAS IN PNEUMONIA: A REVIEW OF INCIDENCE, OUTCOMES AND MANAGEMENT**

**Background** Community-acquired pneumonia (CAP) has high mortality, from 5 to 18.3%. Arrhythmias are a recognised significant complication. Growing evidence associates this treatable complication with increases in mortality. No review has summarised data on mortality or ways to improve outcome.

**Aims** This review aimed to define the extent of the problem, collate and appraise evidence regarding outcomes and management, and identify gaps in understanding.

**Methods** Narrative review using a systematic protocol. Medline, ProQuest, Web of Science were searched for papers reporting adults with CAP complicated by arrhythmia. 382 articles were assessed and excluded based on title (348), abstract (27) and full text (6), leaving 11. Review of bibliographies added 3, totalling 14. These were appraised and coded, with Newcastle-Ottawa scores assigned.

**Results** Three reviews and 11 primary studies were included: 10 Cohorts (4 prospective, 6 retrospective) and one case series. One meta-analysis of cardiac events identified a pooled incidence of 4.7% for CAP inpatients developing arrhythmia. N-O scores ranged from 5 to 9, Median 7.5. Outcomes reported: Incidence; 30 and 90 day mortality; Re-hospitalisation; predisposing factors. Only one paper commented on treatment.

**Discussion** There is high quality evidence of a link between CAP and arrhythmogenesis. Data linking it to mortality suggest a strong association with worse outcome. This review was limited by its single reviewer. Some evidence was limited by retrospective study designs and biased populations. The strengths of this review lie in its reproducible systematic methods and clear outlining of gaps in our understanding of this phenomenon, particularly regarding best management.

**Abstract P214 Figure 1**
Conclusion New arrhythmia complicating CAP is a recognised phenomenon that carries morbidity and mortality. Notably, no research has been reported on how best to manage this complication – reflected by the guidelines for the respective diseases in isolation. The next step is to look at how this complication is managed and identify the best approach to improve patient outcomes.

REFERENCES

Epidemiology in lung disease

P215 THE EPIDEMIOLOGY OF PNEUMOTHORAX IN ENGLAND (1968–2011)
10.1136/thoraxjnl-2015-207770.351

Introduction and objectives Spontaneous Pneumothorax (SP) is a common pathology. Incidence rates are quoted as 16–24 and 1.2–6 per 100,000 cases per annum for males and females respectively, based on two studies in single centres (45 years ago, USA; 30 years ago, Sweden) and 4-year periods of national data in UK (1991–4) and France (2008–2011).

The aim of this study is to determine the incidence and recurrence of spontaneous pneumothorax in a larger dataset in England.

Methods An all-England Hospital Episode Statistics (HES) dataset from 1968–2011 was used to determine the incidence of Spontaneous Pneumothorax using International Classification of Diseases codes as the main diagnosis in a hospital admission. A record-linked HES dataset (only available from 1999–2011) was used to distinguish between Primary and Secondary Spontaneous Pneumothorax (PSP and SSP) and to determine the risk of a second pneumothorax within specified time intervals. SSP was defined as the patient having a diagnosis of a chronic lung disease (e.g. COPD, emphysema, lung malignancy, asthma, bronchiectasis, sarcoidosis) made at any time covered by the linked data.

Results and discussion From 1968–2011, in a population of 50 million, there were a total of 246,534 episodes of spontaneous pneumothorax (no data for 1986–89). In 1999–2011, the average annual incidence was 9.1 per 100,000 males and 3.2 per 100,000 females for PSP; 11.9 and 4.7 for SSP; and 21.0 and 7.9 for SP overall. The incidence of SP appears to be increasing (Figure 1): it was 12.5 (95% confidence interval 12.2–12.8) in 1999 and 13.6 (13.3–13.9) in 2011. It is unclear whether this reflects a true rise in new cases, better reporting or increasing recurrence rates.

The overall risk of recurrence is 13.5% within 1 year (18.7% within 5 years). Recurrence is more common in SSP than PSP at 1 year (16.1% vs 10.6%) and 5 years (21.2% vs 14.7%).

Conclusions This is the largest epidemiological study of pneumothorax to date. These data only cover hospitalised pneumothorax, and therefore may be a conservative estimate of the true burden of disease. Pneumothorax appears to be increasing in incidence.

P216 DURATION OF TOTAL AND EXCLUSIVE BREASTFEEDING, TIMING OF SOLID FOOD INTRODUCTION AND RISK OF ALLERGIC DISEASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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10.1136/thoraxjnl-2015-207770.352

Background Allergic diseases are the leading causes of chronic illness in children and young adults in the UK.

Aim To undertake a comprehensive review of the evidence on the effect of breastfeeding (BF) duration and timing of solid food introduction on the risk of wheeze, atopic dermatitis, rhinoconjunctivitis, food allergy, allergic sensitisation and measures of lung function or bronchial hyper-responsiveness.

Methods We carried out a systematic review following the PRISMA guidelines (International Prospective Register of Systematic Reviews [PROSPERO] CRD42013003802). We included intervention, cohort, case-control and cross-sectional studies. Following literature searches (July 2013), study eligibility, data extraction and risk of bias assessments were conducted independently by two investigators. Random effects meta-analyses were used to pool results. Five levels of comparison of total or exclusive BF duration were used to assess disease risk in children at age 0–4 yrs, 5–13 yrs or 15+ yrs: ‘never vs ever’; ‘>1–2 months vs. <1–2 months’; ‘>3–4 months vs. <3–4 months’; ‘>5–7 months vs. <5–7 months’; and ‘>8–12 months vs. <8–12 months’. Exclusive BF (EBF; BF without formula or solid food supplementation) was categorised as ‘>0–2 months vs. <0–2 months’, ‘>3–4 months vs. <3–4 months’ and ‘>5+ months vs. <5+ months’, and SFI as ‘>3–4 months vs. <3–4 months’. Publication bias was assessed using Egger’s asymmetry test.

Results Of 16,289 identified studies, 564 met the inclusion criteria and were eligible for analysis. We found reduced risk of wheezing in children aged 5–14 yrs with longer BF or EBF duration, which was dose-dependent, but there was evidence of publication bias (BF and odds of recurrent wheezing P = 0.007). Similar results were found for recurrent wheeze at age 5–14 yrs but not in other ages. Measures of lung function were also increased with increased BF or EBF duration. We found no
Introduction Chronic mucus hypersecretion (CMH) is associated with COPD development and progression. CMH presence across adult life is dynamic, influenced by factors such as smoking behaviour. CMH is usually considered a binary phenotype and the potential influence of longitudinal CMH pattern on concurrent FEV1 decline has not been explored. We investigated how longitudinal prevalence of CMH relates to concurrent FEV1 decline.

Methods The MRC National Survey of Health and Development consists of a sample of men and women born in one week in March 1946 within England, Scotland and Wales. Smoking behaviour, MRC questionnaire defined CMH, height, weight and pre-bronchodilator spirometry were recorded at three ages: 43, 53 and (60–64) years.

We used the number occasions that CMH was positively reported (0–3) as a measure of longitudinal prevalence of CMH. Multilevel models adjusted for sex were used to analyse the relationship between longitudinal prevalence of CMH and concurrent FEV1 decline (between ages 43 and (60–64)), allowing both intercept and slope to vary according to the longitudinal prevalence of CMH score. Height, weight and mean FEV1 at age 43 years were then included in the model. Smoking status (current, ex and never-smoker) and number of cigarettes smoked daily were included as time-varying covariates capable of influencing both intercept and slope.

Results 1960 individuals contributed data to the multilevel model: 46% male; 59% ever-smoker and mean FEV1 at age 43 years = 3.00 L. 13% reported CMH ≥ once between ages 43 and 60–64 years. After full adjustment, longitudinal prevalence of CMH was significantly associated with both a lower FEV1 at age 43 (intercept p < 0.001) and a faster decline (slope p = 0.003) (See Table 1). For each additional occasion CMH was reported there was an additional 3.2 ml/yr decline in FEV1 (p = 0.003) i.e. presence of CMH on all three occasions was associated with an additional 9.6 ml/year FEV1 decline compared with those without CMH on any occasion.

Conclusion Longitudinal prevalence of CMH is associated with concurrent FEV1 decline independent of concurrent smoking history. Rather than CMH being solely an airway disease phenotype, the longitudinal course of CMH may represent a biomarker of concurrent disease activity.
Background Developing a comprehensive picture of the burden of asthma in the UK will enable informed national decisions about care provision and planning. We sought to provide the first UK-wide estimates of the epidemiology, healthcare utilisation and costs of asthma.

Methods We undertook analyses of national health surveys, routine healthcare and administrative datasets over the period 2010–12. Economic modelling was carried out to estimate costs. Estimates were calculated for each nation and the UK as a whole.

Results The UK lifetime prevalence of patient-reported symptoms suggestive of asthma in 2010–11 was 30.7% (95% Confidence Intervals [CI] 29.2–32.2; equivalent to ~18,949,516 people), lifetime prevalence of patient-reported physician-diagnosed asthma was 15.9% (95% CI 14.7–17.1; ~10,841,030 people), annual prevalence of patient-reported physician-diagnosed-and-treated asthma was 9.1% (95% CI 8.0–10.2; ~5,765,237 people), annual prevalence of GP reported-and-diagnosed asthma was 8.2% (95% CI 8.2–8.2; ~5,215,607 people) and annual prevalence of GP reported-and-diagnosed-and-treated asthma was 6.0% (95% CI 6.0–6.0; ~3,946,796 people). In 2011–12, asthma resulted in an estimated: 6,392,670 primary-care consultations; 1,864 (317 paediatric and 1,547 adult) intensive-care unit episodes; 93,916 inpatient-care episodes; 1,547 adult) intensive-care unit episodes; 36,800 disability living allowance (DLA) claims; and 1,160 deaths. The estimated cost of asthma in the UK was at least £1.1 billion in 2011–12: 75% of this was for primary-care (60% prescribing and 15% consultations), 13% for DLA claims, and 10% for hospital care.

Conclusions We found that asthma is very common, affecting at least 3.95 million people, and that it is responsible for substantial morbidity, healthcare and societal costs in the UK. Setting ambitious targets for improving asthma outcomes is paramount and resources should be targeted to improving community-based prescribing decisions and reducing the risk of asthma exacerbations and associated hospitalisations and deaths.

Funding Asthma UK, with additional support from the Edinburgh Health Services Research Unit and Farr Institute, UK.

Potential Impact of Air Pollution Coverage in the Media on Respiratory Disease Admissions

Objective The UK CF Registry annual reports include comparisons between centres on key outcomes such as FEV1 using rankings. While illustrating the distribution between centres, they promote the assumption that those with the highest measures provide “better” care. We hypothesised a more scientific approach based on statistical “process control” using funnel plots and adjustment for case-mix may help to identify exceptional CF care services in terms of clinically meaningful outcomes.

Methods We extracted data from annual reviews (2007–2012) on the CF Registry. Our outcomes included FEV1 (% predicted) at 15 years and change in FEV1 between 18 and 21 years. Funnel plots were generated with confidence limits at 2 and 3 standard deviations (SD). Centres with mean values outside these limits are said to display “special cause variation” -variability outside what one would expect. Outcomes were then adjusted for case mix (including gender, genotype, pancreatic sufficiency and socioeconomic deprivation) and analysed using funnel plots.

Results 31 paediatric centres provided FEV1 data on 15 year olds between 2007 and 2012. Funnel plots of unadjusted FEV1 (% predicted) showed few centres with evidence of special cause variation (2SD limits). Initial case-mix adjustment reduced the number of centres outside these limits to 3. We also identified 28 adult centres providing sufficient data to calculate change in respiratory admission levels sourced from Nottingham University Hospitals Trust data (ICD10 codes J39 – J9999).

2. Time series of levels of media coverage were generated by applying kernel density estimation at a range of bandwidths (using linear and exponential kernels at bandwidths of 1, 10, 25, 50 and 100 days) to daily counts of online news articles featuring pollution and air quality issues over the period 01.01.2013 – 09.04.2014.

3. Predictive model accuracies were compared following integration of these time series of media coverage levels as an additional predictor.

Results Of the predictive models tested, random forests parameterized provided optimal results for air-quality predictors. When predicting daily respiratory admissions, the model’s accuracy was 19.90% better than simply predicting mean daily admissions, with an average root mean square error (RMSE) of 7.5031. However, on introduction of the media-coverage variable, RMSE was reduced to 7.3210, representing a 21.85% improvement over mean prediction. While this reflected a slight improvement in admissions forecasting, a corrected t-test suggested these differences were not statistically significant, with a p-value of 0.0633.

Conclusion Initial results indicate that consideration of media coverage may offer minor improvements in predicting respiratory admissions, but this effect was not statistically significant. While such a relationship requires further investigation, models informed by media coverage cannot currently be considered to be accurate enough for use in a practical setting. Better media data collection may improve prediction accuracy.
FEV1 (% predicted) between 18–21 years. While there was some evidence of special cause variation (at 2SD limits) in prior to case-mix adjustment, after adjustment none were outside the 2SD limits. None of the centres were outside the 3SD limits in either analysis. Conclusion In conclusion the work to-date illustrates that funnel plots can be used to explore potential differences in FEV1 between specialist centres. Case-mix adjustment models should develop into a useful tool for making centre comparisons which can continue to be used by stakeholders. This is early work, however, and we need to bear in mind that by examining outcomes in small populations risk missing true differences due to low statistical power. Further work is required to assess whether any observed differences are due to chance or are related to the care patients receive.

P221 EVALUATION OF EXACERBATION FREQUENCY AND RE-HOSPITALISATION, AND RISK FOR SUBSEQUENT EXACERBATIONS IN ASTHMA PATIENTS IN A UK PRIMARY CARE SETTING
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10.1136/thoraxjnl-2015-207770.357

Introduction and objective Exacerbations occur in all asthma patients but disproportionately impact those with more severe disease. This study aimed to describe the frequency of exacerbations by asthma severity and the risk for future exacerbation. Methods In a retrospective cohort of asthma patients in the CPRD (2009–2011), we defined asthma severity based on asthma medication use and exacerbation history; index date was asthma medical code date. Asthma severity was determined by asthma medication use and exacerbation history during the 12 months preceding the index date. Exacerbations were ascertained during the 12-month follow-up period and were defined as an asthma-related accident and emergency (A&E) department visit or hospitalisation, or any oral corticosteroid (OCS) prescription with an asthma medical code recorded within ±2 weeks. A proportional hazard model was developed to evaluate the risk for subsequent exacerbations associated with the type of exacerbation (OCS vs. ED/hospitalisation). Results A total of 211,807 patients with asthma were identified in CPRD during the study period. The mean age was 45 years and females made up 58% of the study population. Of these patients, 17,785 (8.4%) and 3,592 (1.7%) experienced ≥1 exacerbations, respectively during the follow-up period. The proportion of patients experiencing ≥1 or ≥2 exacerbations increased with severity and prior exacerbation frequency (Table 1). Among 1,900 patients with an asthma-related hospitalisation, 2.3%, 3.3%, and 3.8% experienced asthma-related readmissions within 30-, 60-, and 90-days, respectively. When limited to patients with more severe disease, the readmission rates increased significantly, up to three times in those with a history of ≥2 exacerbations. Compared to an OCS defined exacerbation, an A&E visit or hospital admission was associated with a 30% greater risk for any subsequent exacerbation (HR = 1.3, 95% CI 1.15–1.44), after adjusting for gender, disease severity, atopy, and exacerbation history. Conclusion Asthma exacerbations remain a burden for patients with severe asthma or a history of frequent exacerbations. Additionally, patients should be managed carefully after an asthma exacerbation as they are at higher risk for subsequent exacerbations and readmission. (GSK-funded; WEUSKOP7092).

P222 RATES OF HOSPITALISATION AFTER DIAGNOSIS OF LUNG CANCER: A LINKED AUDIT AND HOSPITAL EPISODE STATISTICS STUDY
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10.1136/thoraxjnl-2015-207770.358

Much of the research in lung cancer is concerning survival or treatment rates and little is known about the rate of hospitalisation (emergency/elective) following the diagnosis of lung cancer. Newly diagnosed English patients from the National Lung Cancer Audit database (NLCA), 2007–2011, were linked with Hospital Episode Statistics (HES) data to provide details on their subsequent hospital admissions. Hospitalisations for receipt of chemotherapy or cardiothoracic surgery were excluded to ensure only non-treatment related admissions were included. We only included patients included who survived at least 30 days after their first presentation to a physician to exclude more advanced disease. We calculated rates and rate ratios (RR) of elective and emergency admissions per person-year (ppy) by patient features including sex, age, performance status and co-morbidity.

Among 92,482 patients, there were 261,121 non-treatment related hospitalisations with rate of 2.92 admissions ppy (95% CI, 2.91–2.93). Emergency admissions constituted 57% of all admissions at a rate of 1.66 admissions ppy while the elective admission rate was lower at 1.26 admission ppy. Adjusted RRs in Table 1 show that males were approximately 20% more likely than females to be admitted through either route (RR 1.17, 95% CI 1.16 – 1.18 for emergency and 1.20 (1.18–1.21) for elective). Worsening performance status, co-morbidity and advanced stage were all associated with higher emergency admissions while there was no strong association with age. For elective admissions pattern were similar yet associations were weaker and performance status did not show a linear association with admissions. Increasing socioeconomic deprivation was associated with a moderate increase emergency admission rates but a decrease elective admission rates.

The rate of emergency admissions was higher than the rate of elective admissions following diagnosis of lung cancer. Sex, worsening performance status, advanced stage and co-morbidity were all independently associated with admissions with similar patterns for emergency and elective admissions. However, being from a more deprived socioeconomic class was associated with more emergency admissions and fewer elective admissions. Reason for these findings could be related to variation in receiving treatment in these groups or treatment related side effects leading to more emergency admissions.

P223 VALIDITY AND INTERPRETATION OF SPIROMETRY FOR PATIENTS IN PRIMARY CARE
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10.1136/thoraxjnl-2015-207770.359

Background Previous studies have questioned the validity and interpretation of spirometry undertaken in primary care. Knowing that data are accurate is important as many respiratory diseases are diagnosed and managed in primary care. Additionally researchers use data entered into electronic health records both
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Abstract P222 Table 1  Rate of emergency and elective admissions following lung cancer diagnosis per person year (n = 261,121 admissions)

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<tr>
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<th>Emergency Admissions</th>
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<th>Elective Admissions</th>
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<tr>
<td></td>
<td>Rate per person year (95% CI)</td>
<td>Adjusted Rate Ratio (95% CI)</td>
<td>Rate per person year (95% CI)</td>
</tr>
<tr>
<td>Overall</td>
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<td>1.26 (1.25–1.27)</td>
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<td>Sex</td>
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<tr>
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<td>1.42 (1.40–1.44)</td>
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<td>5</td>
<td>1.75 (1.73–1.77)</td>
<td>1.14 (1.13–1.16)</td>
<td>0.79 (0.77–0.80)</td>
</tr>
</tbody>
</table>

†Rate Ratios adjusted for sex, age, performance status, stage, co-morbidity and socioeconomic quintile.

as single measurements and to track changes in lung function over time. We aimed to determine whether spirometry undertaken in primary care for patients suspected to have COPD was of sufficient quality, and was correctly interpreted.

Methods As part of previous studies to validate the recording of COPD diagnosis and exacerbations of COPD in the clinical practice research datalink (CPRD) we obtained additional information from GPs which included spirometry traces. In this subset, a respiratory physician assessed spirometry traces for: 1) quality and 2) diagnostic interpretation. We used logistic regression to assess predictors of GPs interpretation of spirometric traces with the outcome of COPD diagnosis confirmed by respiratory physician adjudication of spirometry traces as correct and age, sex and previous record for asthma as covariates.

Results We obtained spirometry traces for 306 patients, of which 221 (72.2%) were conducted in primary care. 96.3% of traces were of adequate quality such that a valid interpretation could be made. Of those traces which were of adequate quality and conducted in primary care, and in whom a GP diagnosis of COPD had been made (N = 218), 73.4% showed obstruction, suggestive of COPD (Table 1). There was some evidence that correct interpretation of spirometry (either as obstructive, restrictive or normal) was influenced by a previous asthma diagnosis (OR 0.49, 95% CI 0.26–0.93). There was no evidence that correct interpretation was modified by age (OR 0.98, 0.96–1.01) or sex (OR 1.28, 0.69–2.38).

Abstract P223 Table 1  Interpretation of spirometry for patients diagnosed with COPD in primary care (N = 218)

<table>
<thead>
<tr>
<th>Respiratory physician spirometry interpretation</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>50 (22.9%)</td>
</tr>
<tr>
<td>Obstructive</td>
<td>358 (72.5%)</td>
</tr>
<tr>
<td>Restrictive</td>
<td>8 (3.7%)</td>
</tr>
<tr>
<td>Mixed obstructive and restrictive</td>
<td>2 (0.9%)</td>
</tr>
</tbody>
</table>

Conclusions Spirometry is performed in primary care to a high standard. Interpretation in patients with suspected COPD in primary care is moderate. Efforts should be made to improve spirometry interpretation for high quality patient care, and for research. As quality of spirometry measurements were high, researchers could use actual recorded values of FEV₁ and FVC.
However should exercise caution with using interpretation of spirometry values documented in primary care records.

P224 THE ASSOCIATION BETWEEN DEGREE OF AIRFLOW LIMITATION AND DEGREE OF CORONARY ARTERYATHEROMA IS NOT ATTRIBUTABLE TO SMOKING HISTORY

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10.1136/thoraxjnl-2015-207770.360

Introduction Prevalence of coronary artery disease (CAD) in chronic obstructive pulmonary disease (COPD) is 16–53% (Smith and Wrobel. Int J Chron Obstruct Pulmon Dis. 2014;9:871–888), with ~25% COPD patients dying from cardiovascular disease. Diverse studies demonstrate ~2-fold increased risk of CAD in COPD after adjustment for known cardiovascular risk factors. By contrast, in asthma increased CAD risk appears to be restricted to smokers (Colak et al. Am J Respir Crit Care Med. 2015 Apr 27). Our objectives were to investigate the association between airflow limitation and severity of coronary artery atheroma in patients undergoing coronary angiography and to determine the effect of smoking on this relationship.

Methods Patients attending for elective coronary angiography March–July 2015 underwent clinical assessment and spirometry prior to the procedure. Coronary artery disease burden was quantified from angiograms using the Gensini score (Needland et al. Am Heart J 164:547–552). A single rater (Professor of Interventional Cardiology), blinded to clinical diagnosis, determined number and severity of lesions. Blinded repeats were performed and ratings compared to clinical reports to ensure reliability. A nonlinear score was assigned to each lesion based on the severity of stenosis and a multiplier applied depending on lesion location in the coronary tree. Lesion scores were summed to derive total score, which was log-transformed for analysis.

Results 233 people (age 66 ± 10 years (mean±SD), 69% male) had FEV1 82 ± 21% predicted, FVC 89 ± 21% predicted, number and severity of lesions. Blinded repeats were performed and ratings compared to clinical reports to ensure reliability. A nonlinear score was assigned to each lesion based on the severity of stenosis and a multiplier applied depending on lesion location in the coronary tree. Lesion scores were summed to derive total score, which was log-transformed for analysis.

Conclusions People with more severe airflow limitation have more coronary atheroma, but smoking does not appear to be a direct determinant of this relationship. Shared comorbid disease (e.g. dyslipidaemia) between COPD and CAD may be more important than smoking in determining the association, supporting the hypothesis that COPD and CAD are part of a multi-morbid disease complex.

REFERENCES

P225 IDENTIFYING ASTHMA PATIENTS IN WALES USING LATENT CLASS ANALYSIS OF ROUTINE DATA

M Al Sallakh, 1SE Rodgers, 1RA Lyons, 2A Sheikh, 1GA Davies. 1College of Medicine, Swansea University, Swansea, UK; 2Usher Institute of Population Health Sciences and Informatics, The University of Edinburgh, Edinburgh, UK
10.1136/thoraxjnl-2015-207770.361

Background The Wales Asthma Observatory aims to produce current estimates of asthma prevalence and disease burden using routine data. In the absence of a feasible gold standard to validate case definitions, latent class analysis (LCA) can be employed.

Objectives To estimate the prevalence of treated asthma in Wales using LCA of routine health data.

Methods We performed LCA using observed variables of asthma-related healthcare diagnostics and utilisation in the fiscal year 2011–2012 for a random sample of 98,042 individuals in the Secure Anonymised Information Linkage (SAIL) databank. The observed variables were chosen if they exhibited expected distributions. Diagnostic performance of each of the observed variables was calculated. The model was tested for stability over multiple time windows and small area configurations. Since COPD can be misdiagnosed as asthma, a separate LCA was performed to identify COPD patients and cross-validate the asthma model.

Abstract P224 Table 1 Univariate and multivariate relationships between log Gensini score, lung function and clinical variables

<table>
<thead>
<tr>
<th></th>
<th>Univariate analysis</th>
<th>Multivariate analysis (ANOVA)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pearson’s correlation</td>
<td>R value</td>
</tr>
<tr>
<td>FEV₁ % predicted</td>
<td>-0.149</td>
<td>0.036</td>
</tr>
<tr>
<td>FVC predicted</td>
<td>-0.116</td>
<td>0.105</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>-0.157</td>
<td>0.027</td>
</tr>
<tr>
<td>Age</td>
<td>0.192</td>
<td>0.007</td>
</tr>
<tr>
<td>Waist to hip ratio</td>
<td>0.129</td>
<td>0.071</td>
</tr>
<tr>
<td>Body mass index</td>
<td>-0.157</td>
<td>0.027</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.052</td>
<td>0.469</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>-0.056</td>
<td>0.436</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.145</td>
<td>0.049</td>
</tr>
<tr>
<td>HbA₁c</td>
<td>0.053</td>
<td>0.705</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.156</td>
<td>0.02</td>
</tr>
<tr>
<td>hsCRP</td>
<td>-0.022</td>
<td>0.759</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>0.078</td>
<td>0.285</td>
</tr>
<tr>
<td>Charlson index</td>
<td>0.231</td>
<td>0.001</td>
</tr>
<tr>
<td>Pack year smoking history</td>
<td>0.080</td>
<td>0.259</td>
</tr>
<tr>
<td>Number of chest infections in last year</td>
<td>-0.141</td>
<td>0.047</td>
</tr>
<tr>
<td>ANOVA (categorical variables) F statistic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>8.6</td>
<td>0.004</td>
</tr>
<tr>
<td>Ever smoked</td>
<td>1.4</td>
<td>0.261</td>
</tr>
<tr>
<td>Childhood respiratory illness</td>
<td>0.6</td>
<td>0.432</td>
</tr>
<tr>
<td>Recurrent chest infections</td>
<td>3.0</td>
<td>0.084</td>
</tr>
</tbody>
</table>

FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; LDL, low density lipoprotein; HbA₁c, glycated haemoglobin; hsCRP, high sensitivity C reactive protein; ANOVA, analysis of variance.
Results Our LCA model estimated the prevalence of treated asthma in Wales in 2011–2012 as 8.9% (95% CI: 8.7%–9.1%), which was higher than estimates from the Quality and Outcome Framework (6.9%), but lower than both the prevalence of self-reported treated asthma estimated by the Welsh Health Surveys in 2011 (11.0%) and 2012 (10.0%) and the prevalence of ‘GP reported and treated asthma’ from the ‘True Costs of Asthma in the UK’ project (13.0%). In our model, prescription of any asthma medication had the highest accuracy among other observed variables (sens. = 99%; spec. = PPV = NPV = 100%), while asthma diagnosis variable had a lower accuracy (sens. = 66%; spec. = 94%; PPV = 51%; NPV = 97%). In the same sample, COPD prevalence was 2.0% (95% CI: 1.9%–2.1%) with only 2.8% of those classified as asthmatics were also classified as having COPD.

Conclusion Our LCA model provides a reasonable, data-driven, reference identification of people with treated asthma in Wales. Further work is needed to explore potential reasons for the observed differences in the estimates from other sources.

### Abstract P226 Table 1

<table>
<thead>
<tr>
<th>Age [years]</th>
<th>HIV positive (N = 181)</th>
<th>HIV negative (N = 68)</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 (43–56)</td>
<td>44 (38–52)</td>
<td>P = 0.006</td>
</tr>
<tr>
<td>Using antiretroviral therapy</td>
<td>92%</td>
<td></td>
</tr>
<tr>
<td>CD4 count [cells/μL]</td>
<td>617 (458–839)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>79%</td>
<td>68%</td>
</tr>
<tr>
<td>Current smoker</td>
<td>28%</td>
<td>33%</td>
</tr>
<tr>
<td>FEV1</td>
<td>3.43 (0.86)*</td>
<td>3.20 (0.78)*</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>4.24 (1.06)*</td>
<td>3.87 (0.98)*</td>
</tr>
<tr>
<td>SGRQ Total score</td>
<td>12 (6–29)</td>
<td>8 (3–18)</td>
</tr>
</tbody>
</table>

Values median (IQR) or% unless otherwise stated. *mean (SD).

Significantly higher SGRQ scores were observed in HIV positive participants than HIV-negative participants with a median total SGRQ score of 12 for those with HIV infection and 8 for the HIV negative participants (p = 0.03). In a linear regression (log scale) model, HIV infection was associated with a 62% increase (95% CI 1.19–2.21, p < 0.01) in SGRQ in unadjusted analysis and 48% increase (1.08–2.02, p = 0.01) in a multivariable analysis adjusting for age, gender and smoking status.

Conclusions Despite widespread use of ART, HIV infection is independently associated with impaired respiratory health status. This does not appear to result from current smoking or obstructive lung disease.

### P227 LUNG CANCER DIAGNOSIS AT EMERGENCY ADMISSION – HOW DOES DORSET COMPARE?

Introduction Survival for lung cancer patients in the UK is worse than in comparable countries, at least partly because they present with more advanced disease. Recent data suggest that rural residence is associated with an increased risk of early death in lung cancer.

As our region encompasses rural areas, we investigated rates of emergency admission at the three major hospitals in our region and factors which may lead to this.

Methods We retrospectively identified new presentations of lung cancer as emergencies from August to October 2014. We gathered patient demographics, mortality and GP presentation data and compared them with local lung cancer database data for the same time period.

Results We identified 41 new lung cancer diagnoses in this period, from a total of 119 new diagnoses. This gives an emergency diagnosis rate of 34.5%, comparable to national figures of 39%. However, there was significant variation (21–43%) between the three sites.

When analysed by gender, only 30% of male diagnoses were made at emergency presentation, compared with 41% of females. Unfortunately our sample size was not large enough to demonstrate statistical significance (p = 0.22).

GP data were available for 28 patients, of whom 17 had reported symptoms to their GP. The median duration between
first reporting symptoms to the GP and being admitted as an emergency was only 4 days.

As expected, staging in emergency patients was significantly higher than in those diagnosed as outpatients (Figure 1, □ indicates p < 0.001). Mortality at 3 months was comparable: 56% compared with 13% (p < 0.001).
Ten patients (none with cenocepacia) are using inhaled antibiotics (3 colistin, 1 Colobreathe, 2 TOBI, 2 Cayston, 1 ceftazidime, 1 alternating Cayston and Promixin).

Conclusion This study shows that a significant proportion of our Burkholderia spp infected patients have organisms that are sensitive to currently available inhaled antibiotics. Given our positive experience, and with the expected availability of new inhaled antibiotics in the near future, perhaps the time has come to formally look at the use of inhaled anti-microbial therapy in this small but important cohort of CF patients.

P230 INVESTIGATING THE ROLE OF CHEST PHYSIOTHERAPY IN THE COLLECTION OF SPUTUM SAMPLES FROM INDIVIDUALS WITH CYSTIC FIBROSIS (CF)

R Dacie, R Howlin, M Carroll, G Connett. University of Southampton, Southampton, UK

Introduction Chronic respiratory infection is responsible for the majority of the morbidity and mortality of CF patients. In order to guide treatment regimes and improve understanding of the pathophysiology of CF, airway secretions are sampled and analysed. Sputum is usually the selected method of sampling.

Often, large quantities of sputum are required to facilitate comprehensive laboratory testing. Hence, when designing studies, it is important to consider the quantity of sputum likely to be produced by patients and to ensure that the composition of the sputum samples is not altered by the procedure by which they are obtained.

This study aimed to investigate the effect of chest physiotherapy on the quantity and composition of sputum samples collected from individuals with CF. It was hypothesised that physiotherapy would increase the quantity of sputum produced, reduce the salivary content and alter the microbiological content.

Methods Clinically stable adults with CF were recruited at outpatient clinics and randomised into group A (physiotherapy group, n = 21) or group B (no physiotherapy group, n = 25).

Laboratory processing of the samples involved determining sample weights and counting human cells (alive respiratory cells, dead respiratory cells and squamous cells). The dissolved sputum was also transferred onto plates of cetrimide agar for culturing Pseudomonas aeruginosa. Colony-forming units (CFUs) were counted on the plates after 24 h.

Results Samples from the physiotherapy group had significantly greater weights than the no physiotherapy group (p < 0.001). When considering the total number of cells per gram of sputum, there was no statistical difference between the two groups (p = 0.396). However, the numbers of squamous cells per gram, and dead respiratory cells per gram were both significantly greater in the no physiotherapy group (p = 0.039 and p = 0.001 respectively). There were no significant differences between numbers of alive respiratory cells per gram (p = 0.487) or CFUs (p = 0.459).

Conclusion Whilst physiotherapy was found to increase the quantity of sputum collected, there were significant differences in sputum composition, suggesting that the two groups represent samples from different niches. Hence, when planning a study involving sputum analysis, the procedure by which the sample is obtained has to be considered when interpreting the results.

P231 A PROSPECTIVE COHORT STUDY OF INTEGRATED PALLIATIVE CARE OF CYSTIC FIBROSIS (CF)

SJ Bourke, R Mackley, Z Booth, S Doe, A Anderson, S Rice, AD Gascogne, R Quibell. Royal Victoria Infirmary, Newcastle Upon Tyne, UK

10.1136/thoraxjnl-2015-207770.367

There are 140 deaths in the UK each year from CF, often on a transplant waiting list and often without specialist palliative care. A palliative physician and nurse joined our team in 2011, providing palliative care in parallel with standard CF care. We undertook a prospective study documenting symptoms and outcomes, the views of the CF team and the experience of the palliative specialists.

Over 3 years, 28 (10%) of 282 patients at our Centre had palliative input; their mean age was 31 (range 18–47) years and mean FEV1 was 0.86 L (24%); 17 (61%) died - 6 were on a transplant waiting list, 10 were unsuitable, and one died post transplantation; 4 had had transplantation and no longer needed palliative input, 7 are in on-going care; 15 (88%) of deaths were on the CF ward and 2 at home. All patients who died had had palliative care. The main symptoms were breathlessness, cough, pain, vomiting, fatigue and low mood. The mean palliative assessment score was high at 2.9, indicating that life was dominated by symptoms. Palliative interventions included opioid, benzodiazepine, anti-emetic and anti-depressant medications and non-pharmacological interventions included relaxation techniques, massage, acupuncture and cognitive therapy. A survey was completed by 16 members of the CF team: all felt that palliative specialists should be part of the team and rated the model of care highly with a mean score of 4.1 (scale 1–5); 11 thought that patients had found input very helpful and 5 helpful; one patient declined a palliative consultation. The palliative specialists had increased their knowledge of CF, found it useful to meet patients earlier and had no difficulty in providing palliation in parallel with standard CF care. Their workload was high and they identified additional needs of bereavement counselling and managing the effects of deaths on other CF patients.

This integrated model was successful in overcoming barriers to specialist palliative care. Palliative specialists have improved their knowledge of CF and the CF team have learnt palliative skills.

P232 TOO SWEET FOR TOO LONG?


10.1136/thoraxjnl-2015-207770.368

Background Cystic fibrosis related diabetes (CFRD) is associated with deterioration in clinical status. Lung function and nutritional status deteriorate up to 2–4 years before a diagnosis of CFRD based on the oral glucose tolerance test (OGTT). Timely detection and treatment is crucial.

Aims To evaluate:

- adherence to CFRD screening guidelines and
- whether identifying stages of progressive Cystic Fibrosis Insulin Deficiency (CFID) using the extended OGTT altered management
- trends in weight, BMI and FEV1 in CFRD as compared to CF controls.
Methods Retrospective analysis using patients’ records. 7 patients with CFRD were compared to matched CF controls using mean z-scores for weight, BMI and FEV1.

Results Records of 59 children (23 males) were analysed, 21 children between 5–10 years and 38 >10 years. In the younger group, 80% (n = 17) had both HbA1c and random glucose tested as per our guidelines. Of 38 patients aged >10 years, 78% (n = 30) were screened by OGTT of whom 16% (n = 5) had the standard test. Table 1 summarises the results and shows the degree of glucose impairment on OGTT and the related grade of cystic fibrosis insulin deficiency (CFID).

Conclusions Adherence to screening guidelines needs to be improved. Patients with CFRD have a significant declining trend in weight, BMI and FEV1 compared to controls. Some patients with CFID were commenced insulin on clinical grounds rather than results of extended OGTT. Whether treatment at earlier stages of CFID will slow down the rate of decline needs to be explored, but we have reverted back to the standard OGTT for the present.

Abstract P232 Table 1 The degree of cystic fibrosis insulin deficiency (CFID) in patients (>10 years) undergoing the extended OGTT

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Result</th>
<th>Glucose in mmol/L</th>
<th>2 hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 (20)</td>
<td>Normal</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>11 (36)</td>
<td>CFID1</td>
<td>≥2.2</td>
<td>&lt;11.1</td>
</tr>
<tr>
<td>6 (20)</td>
<td>CFID2</td>
<td>≥1.1</td>
<td>&lt;11.1</td>
</tr>
<tr>
<td>7 (23)</td>
<td>CFID3</td>
<td>&lt;7</td>
<td>≥11.1</td>
</tr>
<tr>
<td>0 (0)</td>
<td>CFID4</td>
<td>≥7 with fasting hyperglycaemia</td>
<td></td>
</tr>
</tbody>
</table>

The mean weight and BMI z scores for those with CFRD compared to controls were -0.64 vs -0.02 (p = 0.005) and -1.26 vs -0.03 (p = 0.0001). There was a lower trend in FEV1 in CFRD, 1.871 (73.06%) vs 2.351 (89.03%). 3 patients with CFID3 and 1 with CFID1 later commenced insulin based on clinical grounds.

Conclusions Adherence to screening guidelines needs to be improved. Patients with CFRD have a significant declining trend in weight, BMI and FEV1 compared to controls. Some patients with CFID were commenced insulin on clinical grounds rather than results of extended OGTT. Whether treatment at earlier stages of CFID will slow down the rate of decline needs to be explored, but we have reverted back to the standard OGTT for the present.

REFERENCE
1. Mycobacterium abscessus. Suggestions for infection prevention and control. CF Trust, 2013
TEMOCILLIN FOR BURKHOLDERIA INFECTION IN CYSTIC FIBROSIS

S Ajab, J Marlow, K Delisle, M Walshaw, M Ledson. Liverpool Heart and Chest Hospital, Liverpool, UK
10.1136/thoraxjnl-2015-207770.371

Introduction
Burkholderia spp infection in cystic fibrosis (CF) confers a worse prognosis, with increased morbidity and mortal- ity. Treatment can be problematic because strains are often resistant to many of the commonly available intravenous antibiotics, leading to a search for new therapies. We have studied the use of Temocillin, a derivative of Ticarcillin with promising in-vitro activity against Burkholderia spp, in the treatment of acute exacerbations in CF patients infected with Burkholderia spp.

Methods
We have used Temocillin in IV form, often in combination, in acute respiratory exacerbations in CF patients attending our large adult unit who are chronically infected with Burkholderia spp. We present our two year data, looking at the subspecies treated, length of treatment, improvement in clinical parameters, and co-antibiotic use.

Results
Nineteen courses of IV Temocillin were administered to 7 CF patients (mean age 29 years, [range 23–42 years], 2 males, 1 infected with B Cenocepacia, 6 with B Multivorans.) All patients completed their treatment without complication.

Median length of Temocillin treatment was 9.7 days (range 3–16 days), and most patients finished their therapy as outpatients (mean inpatient stay 5.2 days). All patients had clinical improvement, with all gaining weight (mean 3 kg [range 6.5 to 0.9]) and most increased spirometry (mean change in FEV1% predicted 6 [17 to -3]).

As regards the efficacy of co-antibiotic use, the 11 courses accompanied by Ceftazidime had a mean 3% improvement in FEV1, 8% with Meropenem (6 courses) and 9% with Colomycin (2 courses).

Discussion
This clinical study has shown that Temocillin is well tolerated by CF patients and is associated with clinical improvement in those infected with Burkolderia spp when given in combination with other antibiotics. Temocillin adds to the limited antibiotic armamentarium available to treat these difficult infections in CF patients and we recommend its use to other clinicians.

REFERENCE

Clinical studies in cough

P236 PSYCHOLOGICAL PROFILE OF INDIVIDUALS PRESENTING WITH CHRONIC COUGH

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10.1136/thoraxjnl-2015-207770.372

Introduction and objectives
Between 20–40% of patients seen in respiratory clinics with chronic cough have an ‘idiopathic cough’ with persistent symptoms that are refractory to treatment and have no obvious underlying pathology. Adverse consequences of chronic cough are well documented in the literature, but relatively little is known about this patient population. We aimed to investigate the association of psychological factors, identified as important in the medically unexplained, persistent symptom literature, with chronic cough.

Methods
Eighty-nine participants (63 female, mean age = 59) took part. Sixty-seven patients attending a specialist cough clinic (idiopathic; n = 25, explained cough; n = 42) and 22 normal controls were asked to complete questionnaires; all participants completed the Hospital Anxiety and Depression Scale, Big Five Inventory (Personality), Chalder Fatigue Scale and Patient Health Questionnaire-15. Cough patients also completed the Illness Perception Questionnaire-Revised. Appropriate statistical analyses were conducted comparing the participant groups.

Results
Idiopathic coughers displayed significantly higher levels of neuroticism (p < 0.05), anxiety (p < 0.05), depression (p < 0.001), fatigue (p < 0.001) and somatic physical symptoms (p < 0.005) than controls. In comparison to explained coughers, significantly higher depression (p < 0.005) and fatigue (p = 0.01) scores were reported by idiopathic coughers, who also had significantly more negative illness perceptions (p < 0.005). Specifically, they had strong beliefs regarding negative consequences, lower illness coherence and higher emotional representations. Explained coughers only differed significantly to the control group in the increased levels of fatigue reported (p < 0.05).

Conclusions
Many psychological factors are associated with chronic cough and seem to differentiate between the two patient groups. The prevalence of neuroticism, negative affect, negative illness beliefs and increased physical symptom reporting suggest a patient profile of idiopathic cough similar to that of other medically unexplained symptoms. This, as well as the novel and significant finding of the prevalence of fatigue, should be considered in consultations and developing novel interventions.

Abstract P234 Table 1

<table>
<thead>
<tr>
<th>Lung transplantation</th>
<th>Non pulmonary complications following treatment with Temocillin</th>
</tr>
</thead>
<tbody>
<tr>
<td>GVT:</td>
<td>Non pulmonary complications following treatment with Temocillin</td>
</tr>
<tr>
<td>Gastro-oesophageal Reflux disease (GORD) (16)</td>
<td>Cardiovascular: Hypertensive disease (7)</td>
</tr>
<tr>
<td>Nissen fundoplication (12)</td>
<td>Malignant Disease: Post-transplant</td>
</tr>
<tr>
<td>Bowel obstruction (4)</td>
<td>Myocardial infarction (1)</td>
</tr>
<tr>
<td>Oesophageal candidiasis (3)</td>
<td>Squamous and basal cell carcinoma - Skin (5)</td>
</tr>
<tr>
<td>Oesophageal fistula (1)</td>
<td>Oesophageal candidiasis (1)</td>
</tr>
<tr>
<td>Gastrointestinal bleed (1)</td>
<td>Gastric adenocarcinoma (1)</td>
</tr>
<tr>
<td>Duodenitis (1)</td>
<td>Vulvar intraepithelial neoplasia (1)</td>
</tr>
<tr>
<td>Renal:</td>
<td>Musculoskeletal complication:</td>
</tr>
<tr>
<td>Chronic kidney disease (CKD) (14)</td>
<td>Cardiovascular</td>
</tr>
<tr>
<td>(requiring renal transplantation)</td>
<td>Steroid related Diabetes (2)</td>
</tr>
<tr>
<td>Haemodialysis - 1</td>
<td>Osteopenia (10)</td>
</tr>
<tr>
<td>Acute Kidney injury (3)</td>
<td>Osteopenia (10)</td>
</tr>
<tr>
<td>Vertebral compression fracture (1)</td>
<td>Adrenal related Diabetes (1)</td>
</tr>
<tr>
<td>Endocrine:</td>
<td>Secondary hyper-parathyroidism (1)</td>
</tr>
</tbody>
</table>

*Poster sessions*
INTRODUCTION AND OBJECTIVES Few studies have investigated cough frequency in neurological patient groups, in which cough may be impaired or increased in the presence of aspiration. This study aimed to (1) validate the Leicester Cough Monitor (LCM) on a stroke unit, where background coughs might contaminate one patient’s cough recordings; and (2) observe cough frequency longitudinally in a convenience sample of acute stroke survivors.

METHODS To validate the LCM, 15-minute recordings were made from 5 patients on a stroke unit. LCM results were compared with real-time cough counts by a researcher present in the room (visual and auditory). To observe cough frequency longitudinally, 21 stroke survivors underwent 24-hour LCM recordings at baseline (<2 weeks post stroke), week 1 and 4. Participants (14 men, mean (SD) age 60 (15) years) had moderate stroke impairment (median (IQR) NIHSS score 8 (5, 11)) with cortical (n = 9), subcortical (n = 9), brainstem (n = 2) and cerebellar (n = 1) strokes. Five randomly selected recordings were analysed by a second researcher, blinded to subject characteristics and not present during the recordings.

RESULTS In the validation study, the real-time observer counted 67 subject coughs plus 81 background coughs in total. The LCM returned a subject cough count of 68, not significantly different to the observer’s count (p = 0.99) with excellent agreement (ICC 0.996, 95% CI: 0.967, >0.999). Inter-rater reliability for LCM hourly cough counts was good (ICC 0.973, 95% CI: 0.789, 0.997). In the longitudinal cohort, average cough frequency was higher at baseline and reduced over time, with wide individual variability (Table 1) and higher cough frequency during day-time. There were no significant associations between cough frequency and sex, age, stroke site, stroke severity, swallowing safety, smoking status or ACE-inhibitor use.

CONCLUSIONS This study is limited due to the small sample size and should be regarded as exploratory. It was possible to validate the LCM for application on an acute stroke unit. The findings might serve hypothesis-generation: For example, is cough frequency after stroke increased, indicating sub-clinical levels of swallowing impairment and aspiration threat, which trigger frequent protective coughs?

Abstract P237 Table 1 24-hour cough frequency (median, range) following acute stroke. Baseline assessments were conducted within 2 weeks of stroke

<table>
<thead>
<tr>
<th>24-hour cough frequency</th>
<th>Baseline (n = 21)</th>
<th>Week 1 (n = 20)</th>
<th>Week 4 (n = 17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of coughs</td>
<td>118 (4, 375)</td>
<td>60 (6, 217)</td>
<td>56 (1, 186)</td>
</tr>
<tr>
<td>Hourly coughs</td>
<td>5 (0, 16)</td>
<td>2 (0, 9)</td>
<td>2 (0, 8)</td>
</tr>
<tr>
<td>Day time coughs</td>
<td>86 (4, 282)</td>
<td>30 (6, 159)</td>
<td>41 (1, 108)</td>
</tr>
<tr>
<td>Hourly day time coughs</td>
<td>6 (0, 20)</td>
<td>2 (0, 11)</td>
<td>3 (0, 8)</td>
</tr>
<tr>
<td>Night time coughs</td>
<td>21 (0, 112)</td>
<td>18 (0, 58)</td>
<td>9 (0, 90)</td>
</tr>
<tr>
<td>Hourly night time coughs</td>
<td>2 (0, 11)</td>
<td>2 (0, 6)</td>
<td>1 (0, 9)</td>
</tr>
</tbody>
</table>

*Day time: 08:00–22:00, night time: 22:00–08:00.

Abstract P238 Table 1

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Treatment</th>
<th>Adjusted geometric mean (90% credible intervals)</th>
<th>Ratio of adjusted geometric means</th>
<th>% Increase from placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 h cough count</td>
<td>GSK2339345</td>
<td>120.5</td>
<td>1.26 (1.01, 1.54)</td>
<td>26%</td>
</tr>
<tr>
<td>Placebo</td>
<td>152.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8 h cough count excluding transient coughs</td>
<td>GSK2339345</td>
<td>153.9</td>
<td>1.02 (0.87, 1.19)</td>
<td>1.6%</td>
</tr>
<tr>
<td>Placebo</td>
<td>151.5</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Based on data from 14 subjects – 21 8h counts per treatment due to replicate period. Transient coughs are the number of coughs occurring in the first 2 min following each dose.
Conclusion There was no evidence of an anti-tussive effect of GSK2339345 over the 8 h analysis for any subject, despite cough frequency being highly reproducible within patients. Inhalation of GSK2339345 had a pro-tussive effect in all subjects following actuation of the device, not seen with placebo. The novel cough challenge methodology warrants further investigation as a development tool.

**P239 LOW PREVALENCE OF EXTRA-THORACIC AIRWAY HYPER-RESPONSIVENESS IN UK PATIENTS WITH CHRONIC REFRACTORY COUGH**

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10.1136/thoraxjnl-2015-207770.375

**Introduction** Prior research indicates that chronic refractory cough (CRC) is associated with a high prevalence of extra-thoracic airway hyper-responsiveness (EAHR). This heightened laryngoconstrictor reflex can be characterised using standard bronchoprovocation tests (e.g. histamine or hypertonic saline); whereby attenuation in the inspiratory component of the flow-volume curve is evaluated in response to escalating doses of the stimulus.

**Aims and objectives** To determine the prevalence of EAHR in a cohort of CRC patients in the UK undergoing cough assessment, and to relate EAHR to other disease characteristics.

**Methods** Data was retrospectively evaluated for all CRC patients completing cough assessment with histamine bronchoprovocation challenge, between 2013 and 2015. EAHR was defined by a 25% dose-responsive fall in the mid-inspiratory flow (PC25FIF50) in response to ≤ 8 mg/ml histamine. EAHR data was compared with other simultaneous investigation results, including overnight pH/impedance results and co-existing nasal disease.

**Results** We studied 57 adult CRC patients (n = 42, female; 74%), mean ±SD age 54.6 ± 12.4 years, BMI 28.2 ± 5.9 kg/m², reporting a duration of cough 5.5 years (0.8–50) with a median cough VAS score of 57 (16–90). The majority of patients (56%) reported cough without other respiratory symptoms, whereas 12 (21%) reported cough with dyspnoea and wheeze. Evidence of EAHR was found in three patients (5.3%). At a reduced cut-off (PC20FIF50 ≤ 16 mg/ml) the prevalence of EAHR was greater (12%) (Figure 1). Patients with a positive EAHR test at this cut-off were younger (p < 0.01, mean age 44 yrs versus 56 yrs) and more likely to report respiratory dyspnoea and wheeze (p < 0.05). In patients completing an overnight reflux study (n = 52), 32 (62%) had evidence of reflux. 21 (37%) patients had co-existing nasal disease. However, presence of reflux or nasal disease was not predictive of EAHR (both p > 0.05).

**Conclusion** EAHR was not prevalent in CRC patients, completing assessment at a specialist cough service, when using a standard histamine bronchoprovocation test. Differences from prior published data may be explained by methodological differences, specifically the application of stringent control of the measures of reproducibility of inspiratory flow parameters and dose response criteria.

**REFERENCES**


**P240 VALIDATION OF THE LEICESTER COUGH QUESTIONNAIRE IN PULMONARY TUBERCULOSIS**

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10.1136/thoraxjnl-2015-207770.376

**Introduction and objective** Cough is prominent in pulmonary tuberculosis (TB) and transmits infection, yet no tool has been validated for assessing cough symptoms. We evaluated the Leicester Cough Questionnaire (LCQ) for measuring cough-related quality of life (QOL) in TB.

**Method** The face validity of the LCQ was evaluated by structured interviews with patients and a multi-disciplinary team (MDT) discussion (respiratory physicians and nurses). Consecutive patients with TB completed the LCQ just before or within 7 days of starting therapy; a subgroup completed a repeat questionnaire approximately two weeks after the first. Internal reliability (inter-relatedness between items), concurrent validity (association with cough severity visual analogue scale [VAS] score and 24-hour cough frequency measured with the Leicester Cough Monitor), and responsiveness were evaluated.

**Results** The MDT and patients thought the LCQ to be relevant, comprehensive and useful in TB and no modifications were suggested. Forty patients completed the questionnaire before (n = 29) or just after (n = 11) the start of treatment. Internal reliability of responses was high (Cronbach’s α = 0.93). LCQ scores were correlated with both the VAS (Spearman’s ρ = -0.69 [95% confidence interval -0.83 to -0.46], p < 0.00001) and 24-hour cough frequency (ρ = -0.36 [-0.62 to -0.04], p = 0.023), and were worse pre-treatment in culture-positive compared to culture-negative disease (median 12.4 [IQR 8.5–17.4] vs 18.7 [17.8–19.6] respectively, p = 0.052). There was no evidence of association with other markers of disease severity (spu tum smear positivity, lung cavities and radiographic extent of disease), but a trend towards worse LCQ scores amongst current smokers than non-smokers (12.6 [8.3–14.4] vs 17.1 [11.1–21.0] respectively, p = 0.075).
All patients who repeated the questionnaire appeared adherent to TB medication. There were substantial improvements in LCQ responses after a median of 14 (10–14) days’ treatment (n = 12; median IQR score 9.1 [8.1–14.5] at baseline, 18.3 [14.5–19.4] at two weeks, median improvement 5.1 [1.8–9.7], p = 0.003; Figure 1). The effect size of the change in LCQ scores was 1.17.

Poster sessions

Abstract P240 Figure 1 Changes Leicester Cough Questionnaire score during early treatment of pulmonary tuberculosis

Conclusion The LCQ is a valid instrument for evaluating cough-related QOL in TB and may be a useful outcome measure to evaluate therapy.

P241 THE FEASIBILITY AND VALIDITY OF OBJECTIVE COUGH MONITORING IN CHILDREN USING AN ADULT COUGH DETECTION SYSTEM

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Background In young children the evaluation of symptoms is almost wholly reliant upon parental reporting. Cough is extremely common in childhood and a tool to objectively measure cough frequency would be clinically beneficial. To date paediatric cough monitoring systems have relied on manual cough counting which is time consuming and costly. The VitaloJAK™ (Vitalograph, UK) is a custom built 24 hr semi-automated cough monitoring device that has been used successfully to quantify cough in adults. Using the VitaloJAK™ we tested the feasibility of 24 hr cough recordings in children and tested existing compression software for cough quantification.

Methods Children (age 2–14 years) with acute or chronic cough were asked to wear VitaloJAK™ cough monitor for a maximum of 24 h. Feedback about the device was obtained from the child/carer were appropriate. All recordings were manually counted and also processed through the compression software.

Results 40 children (21 male; mean age 8 yrs) wore the monitor for a median of 22.25 h (0.38 – 24 hrs). Children who wore the monitor as out-patients with chronic cough generally wore the monitor for longer (median 23.07 hrs) than those who were in-patients with acute symptoms (median 12.59 hrs; p = 0.06). Twenty-nine children (73%) wore the monitor for >12 h and 22 for >22 hrs including during the night. Eighteen (45%) children reported the monitor was heavy/bulky and eleven (28%) said at times it restricted some normal daily tasks (bending/stooping/using the toilet). Neither length of time the monitor was worn for, nor complaints about the size or restricting nature of the monitor, were age dependent. No serious adverse events were reported. One recording was excluded due to technical problems. Recordings demonstrated wide variability in frequency from 2 to 2712 coughs per recording (median 72). Following compression a median of 98.5% (85.7–100) of coughs were retained.

Conclusions VitaloJAK™ semi-automated cough monitor can be used in children to accurately measure cough frequency. As with many medical interventions, it was not tolerated by all children for long periods, however the majority of children were able to wear it for >12 h.

P242 THE ORDER EFFECT OF EXPERIMENTAL OESOPHAGEAL ACIDIFICATION ON COUGH REFLEX SENSITIVITY IN CHRONIC COUGH PATIENTS AND HEALTHY VOLUNTEERS

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10.1136/thoraxjnl-2015-207770.377

Background One of the mechanisms thought to be involved in the triggering of chronic cough is gastroesophageal reflux. We aimed to compare the effects of oesophageal acid infusion on cough reflex sensitivity in chronic cough (CC) patients with healthy volunteers (HV).

Method In a randomised, double-blind, placebo-controlled, crossover study, 0.15 M hydrochloric acid/saline was infused in the distal oesophagus of each subject. Each infusion treatment was separated by a washout period of at least 7 days. Single dose inhalation capsaicin challenge (C5) was used to measure cough reflex sensitivity before (baseline), immediately after (t = 0 mins) and 90 min, 180 min and 24 hrs post infusion. Data were analysed using Generalised Estimating Equation (GEE) models.

Results Ten CC patients (mean age 56.0 ± 11.0 years, 8 females) and twelve HV (mean age 26 ± 8.3 years, 7 females) completed the study. Overall, CC patients had a more sensitive cough reflex than HV (geometric mean ratio 0.46; ratio 0.05, Table 1). Furthermore, there was a significant order effect (acid-saline vs saline-acid); CC patients appeared to be sensitised to acid infusion when given first (p-value = 0.039), but not second (p-value = 0.245), whereas HV cough responses were not influenced by the infusion order (all p-values > 0.05).

Conclusions In our experience, distal oesophageal acid infusion did not sensitise the cough reflex in either CC patients or HV. Notably, the order of the infusions heavily influenced the cough responses of CC patients compared to HV. Future study designs need to be cognisant of order effects and if cross-over designs are used, test for the presence of these.
ASSESSING THE EFFECT OF PH ON CITRIC ACID COUGH CHALLENGES IN CHRONIC COUGH PATIENTS AND HEALTHY VOLUNTEERS

Z Rai, H Fowles, J Howard, A Morice. Hull and East Yorkshire NHS Foundation Trust, Hull, UK

10.1136/thoraxjnl-2015-207770.379

Introduction Citric acid has been used for over 6 decades in cough challenge studies, however despite this, the mechanism of its tussive effect is still not fully understood. We assessed the cough response to citric acid solutions, at different levels of acidity (pH) to determine what role this plays in the induction of cough. Healthy volunteers and chronic cough patients were compared.

Methods 20 chronic cough patients and 20 healthy volunteers were recruited and underwent three cough challenges at 48 h apart. Each visit involved 5 repeated inhalations of a 300 mM citric acid solution. Whilst the concentration of the citrate cation was kept constant, the pH was varied by titration with sodium hydroxide, to achieve pH 3, 5 and 6. These represent the Pka values of the individual acid moieties within citric acid. The total number of coughs elicited per study day was recorded.

Results Participants were gender matched, each group consisting of 12 females. Two participants withdrew and were not included in the analysis. In healthy volunteers, 60% of people coughed at pH3 (average coughs 9), 30% of people coughed at pH5 (average coughs 3), and 10% of people coughed at pH6 (average coughs 0). In contrast, 74% of chronic coughers coughed at pH 3 (average coughs 16), 89% coughed at pH 5 (average coughs 18) and 63% coughed at pH 6 (average coughs 7). Thus there was a clear dose response to decreasing pH in healthy volunteers but not in chronic cough patients. The standard deviation of cough challenge on an individual day was determined to explore the variability of response to inhalation challenge. At pH 3 CC vs HV was x vs y, at pH 5 × 1 vs y1 and at pH 6 × 2 vs y2 (p > 0.01).

Discussion As we have previously reported, chronic cough patients are hypersensitive to citric acid challenge. However the response to individual challenge is much more variable than in HV, suggesting the cough reflex circuitry in these patients is ‘unstable’. This was particularly shown at higher pH where cough was virtually abolished in healthy volunteers but not chronic cough patients. It has been widely suggested that cough hypersensitivity resides in up regulation and interplay of different peripheral receptors. That a single stimulus increases the variability of response in a pathological state suggests that hypersensitivity to citric acid resides in a complex central rather than peripheral mechanism.

Asthma quality improvement

THE IMPACT OF “SEVEN DAY WORKING” ON RESPIRATORY INPATIENT ACTIVITY AT ST HELENS AND KNOWSLEY NHS TRUST. – “THE SLOW DRIFT MODEL”

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10.1136/thoraxjnl-2015-207770.380
St Helens and Knowsley NHS trust (STHK) have re designed the acute pathway for medical admissions. Investment in Consultant numbers has allowed the Acute Medical Admissions (MAU) team and the speciality teams to provide robust Consultant input to their areas Monday to Sunday. Speciality Consultants have been released from the acute medical take and traditional Physician of the day (POD) activities. Advantages of a Consultant led seven day service include: Greater parity of service across seven days a week; high level of clinical competence ensuring rapid and appropriate decision making; improved outcomes for patients; skilled judgement and performance leading to the most effective working and more efficient use of resources; and GP access to the opinion of a fully trained doctor.

Respiratory Consultant numbers have increased from 5 to 8 (7.5 WTE). 90 PA’s have been invested in the service. The inpatient service is resourced with 64 inpatient beds. General principles have been applied to the inpatient service. These include: Each Consultant provides daily review, in the form of 3 ward rounds and 2 board rounds, to their allocated patients; rounds are performed in the first half of the day to aid patient flows and discharges; Consultants provide cross cover during leave; and weekends are covered on a 1 in 8 basis. Alteration to outpatient and elective services has also occurred.

Results 160% increase in weekend Respiratory discharges and 48% increase in overall Respiratory discharges, with no increase in bed base. Significant fall in Respiratory length of stay. 50% improvement in MET calls per discharge reflecting improved quality of care. Significant fall in readmissions. Positive feedback from patients, relatives and staff. Additional benefits include improved elective and outpatient productivity due to less clinic cancellations enforced by the traditional POD model of acute medical activity. Outpatient activity has increased by 50% and elective (Bronchoscopy) activity by 35%. Improved junior doctor support and education are also achieved. Significant decrease in departmental complaints.

Discussion The “slow drift” model presented here offers significant advantages over traditional working practices for both efficiency and outcome. The return on investment contributes to cost improvement programs.

Introduction and objectives Despite the large socioeconomic burden of severe asthma, few studies have focused specifically on the patient experience of living with and managing severe asthma. Patient-related factors including behavioural, psychological and social factors complicate the management of the condition.

This study aimed to explore these experiences in individuals with severe asthma to understand how to support effective self-management.

Method Semi-structured interviews were conducted with participants recruited from a difficult asthma service at Step 4–5 of the BTS/SIGN guidelines. Recruitment occurred until theoretical saturation was achieved. Interviews were transcribed verbatim and coded, supported by NVivo software (Version 10). Thematic analysis was performed.1

Results 29 interviews were completed (44% male, mean age 49.45 (13.64) years, BMI 31.65 (5.48) kg/m², 4 smokers). Five themes describe the experience of living with and managing severe asthma:

**Impact of asthma.** Debilitating breathlessness was described impacting on many areas of participants lives, including relationships, work and family life.

**Day to day management of asthma.** Self-regulatory behaviours were described such as monitoring peak flow and pacing. However, these behaviours and the implied restrictions could induce distress and dissatisfaction. This limited self-management behaviours in-between the acute phases of illness.

**Confidence to manage symptoms.** Participants reported confidence to manage acute events, but the unpredictability of symptoms and fear of inducing symptoms appeared to undermine their confidence to manage symptoms.

**Challenges to effective self-management.** There were further multiple challenges to effective self-management, such as; understanding of disease; perceptions of asthma by others; reluctance to accept hospitalisation and the unpredictability of symptoms.

**Beliefs about medication.** There was conflict around long term oral steroids. Most participants resolved this by balancing the necessity of the medication versus the concerns they held about the long term effects of maintenance. There was little comment regarding inhaled medications.

Conclusion Strategies are needed to enhance acceptance and confidence in self-management behaviours. This should encompass all aspects of the disease, not solely the acute phases, to minimise daily distress and increase effective self-management to improve the health status for this severe population.

REFERENCE
1 Braun V. Using thematic analysis in psychology. Qualitative Research in Psychology. 2006;3:77–101
Successful contact was made with 112 patients; 50 then attended clinic. Contact was unsuccessful for 212 patients; 59 then attended clinic. Due to a lack of contact details, no contact was attempted in 133 patients; 31 then attended clinic subsequently. The relative increase in clinic attendance following contact was 1.95 when compared to the no contact group, and 1.6 compared to the unsuccessful contact group. Unsuccessful contact produced a relative increase of 1.2 compared to no attempted contact.

### Abstract P246 Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Number of patients</th>
<th>Number who attended clinic subsequently</th>
<th>Percent of group that attended clinic subsequently</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total DNAs</td>
<td>457</td>
<td>140</td>
<td>31%</td>
</tr>
<tr>
<td>No contact</td>
<td>133</td>
<td>31</td>
<td>23%</td>
</tr>
<tr>
<td>Unsuccessful contact attempted</td>
<td>212</td>
<td>59</td>
<td>28%</td>
</tr>
<tr>
<td>Successful contact</td>
<td>112</td>
<td>50</td>
<td>45%</td>
</tr>
</tbody>
</table>

### Conclusion

Telephoneing patients following a missed asthma clinic appointment is relatively resource intensive method of doubling clinic attendance. In the unsuccessful contact group, telephone calls were frequently not answered or were voicemail messages were not responded to. Yet there does appear to be a small benefit in attendance rates in this group compared to the no contact group. Because the groups were not randomised confounding factors may be present. Services that provide prospective reminders and perhaps use a free text service may be more effective and less labour intensive.

### Reference


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**Poster sessions**

**P248** SELF-REPORTED ACTIVITY LEVELS, BARRIERS AND FACILITATORS TO EXERCISE IN SEVERE ASTHMA

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10.1136/thoraxjnl-2015-207770.384

**Introduction and aim**: The association between physical inactivity and increased morbidity is well documented. It is widely recognised that patients with respiratory disease often have decreased exercise capacity, and therefore may be at increased risk of co-morbidities such as cardiovascular disease, depression and obesity. The latter have been found to be highly prevalent within severe asthma populations.

In recent years there has been a greater emphasis placed on co-production and service user involvement in shaping interventions for patients with chronic diseases. The aim of this study was to gather self-reported activity levels of severe asthma patients and to determine barriers and facilitators to exercise, in order to focus future interventions.

**Method**: Fifty two patients (40 females) aged 18 to 65 years with a confirmed diagnosis of severe asthma following systematic multidisciplinary assessment took part in this study. Patients completed an activity questionnaire anonymously during their clinic visits. The questionnaire included a mixture of open and closed questions that assessed the level and attitudes to physical activities and exercise.

**Results**: 48/51 (94%) of respondents rated themselves as less active than their peers, and 21/49 (43%) did not participate in any exercise. There was a strong theme of fear of exercise induced exacerbation and breathlessness in 21/52 (40%) of patients, with 21/52 (40%) reporting feeling unsafe to exercise, and 33/52 (63%) reporting exercise induced worsening of their asthma symptoms. 45/52 (87%) wanted to become more active. Patients reported a strong preference for exercising alone or with a health professional present as opposed to group activities or classes. Swimming and walking were the activities patients were most likely to show an interest in.

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**P247** THE PREVALENCE OF ASTHMA AND LEVEL OF TREATMENT IN CURRENT OR FORMER HEROIN SMOKERS

BH Vlies, N Lewis-Burke, L Davies, PP Walker. Aintree University Hospital, Liverpool, UK

10.1136/thoraxjnl-2015-207770.383

**Introduction**: We have reported an association between heroin smoking and early onset severe COPD/emphysema and from this screening study reported a COPD prevalence of approximately one third in heroin smokers attending a community drug centre. However, respiratory symptoms were common in people who did not have COPD and a previous report showed a high level of wheeze and bronchial hyper-responsiveness in opiate smokers/insufflators. Therefore, we examined our cohort to determine asthma prevalence and level of symptoms and treatment in this group.

**Methods**: Current and former heroin smokers were recruited from a community-based drug service in Merseyside and completed spirometry with reversibility testing, MRC and CAT score and smoking, drug use, health and treatment questionnaires. They were not selected because of the presence of symptoms. Asthma was defined by either airflow obstruction that normalised with bronchodilatation or airflow obstruction with an FEV1 that improved by ≥9% with bronchodilatation (7 subjects), or a diagnosis of asthma before age 25 or before the subject had smoked heroin for 2 years (28 subjects).

**Results**: 107 heroin smokers completed the study, the majority of whom had also smoked cigarettes, cannabis and crack. 35/107 (33%) met our diagnosis of asthma and we compared them with 42 heroin smokers with neither COPD nor asthma. The asthma subjects had a significantly lower mean FEV1 (3.26 L vs 3.73 L and 83% vs 97% predicted) and FEV1/FVC (0.71 vs 0.81). Mean age was 42 years and duration of cigarette, cannabis and crack smoking was similar as were MRC and CAT scores. Symptoms were very common in the asthma group – cough 23 (66%), wheeze 23 (66%) and breathlessness 26 (74%) but this was similar to the non-asthmatics. Only 11 (31%) were prescribed short-acting beta-agonists and/or inhaled steroids and only 2 (6%) a long-acting beta agonist despite 32 (92%) having a prior diagnosis of asthma.

**Conclusions**: In an unselected group of current/former heroin smokers the prevalence of asthma was high at 33% and similar to the number diagnosed with COPD. Further detailed assessment of this cohort may be valuable and different methods of engaging with this undertreated and hard-to-reach group worthy of examination.
Conclusion This data suggests the main barrier to increasing physical exercise in severe asthma was fear/anxiety of worsening asthma symptoms particularly breathlessness. More research is required to investigate the relationship between this fear of exercise and objective measures of asthma worsening.

REFERENCES

Background and objective Patients with severe asthma remain highly symptomatic despite high dose anti-inflammatory treatment. Level of asthma control is often assessed in the clinical setting with the asthma control questionnaire (ACQ). Separate components of the ACQ focus on different aspects of control. A high score on the third question (Q3) demonstrates activity limitations and may be caused by factors other than asthma such as physical deconditioning, concomitant cardiac disease and dysfunctional breathing patterns, leading to an over-estimation of the severity of asthma. This could potentially lead to overtreatment. The aim of this study was to determine whether patients with severe asthma had a continuously high ACQ score, predominated by the third question despite treatment.

Methods In a group of severe asthma patients, referred to the Royal Brompton hospital in London, UK, an evaluation of ACQ as monitoring tool was performed from May to July 2015, at an index clinic (v3) and two previous attendances (v1–2). The patients suffered from severe asthma (step 4 or 5 BTS/SIGN guideline treatment) and change in ACQ score over time (total and Q3) was compared with other measures of asthma severity such as medication burden and lung function.

Results Forty three patients (n = 27 females, 61.4%) of mean (SD) age: 56 (11) years were included. The total ACQ score (median (range)) at index was 2.67 (0.17–5.50), the ACQ score on Q3 was 3.00 (0.00–6.00) and mean (SD) FEV1 percent of predicted was 61.9 (±23.78). The total ACQ score was lower at index visit than the first visit (-0.17 (-1.83–1.50); p = 0.041). A change in ACQ score in Q5 was found (p = 0.019), whereas Q3 was unchanged. A change in FEV1 percent predicted was -0.62 (±12.11). A correlation between FEV1 percent predicted and both total ACQ score (p < 0.01) and Q3 ACQ score (p < 0.01) was found. There was no correlation between the changes in these three parameters.

Conclusion In patients with severe asthma there is a significant improvement in total ACQ score over three visits, but no improvement in exercise induced symptoms (Q3). This can be correlated with the fact that Q3 can reflect other symptoms than asthma.

P249 LONGITUDINAL EVALUATION OF PHYSICAL ACTIVITY IMPAIRMENT USING THE ASTHMA CONTROL QUESTIONNAIRE (ACQ) IN SEVERE ASTHMA

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Introduction and objectives Missed clinic appointments are a huge financial burden on the NHS, with an average of 6.9 million outpatient appointments being missed each year.1 The difficult asthma clinic at our inner city hospital is no exception to this trend. Many factors are likely to contribute to missed appointments, which can be summarised in with in socioeconomic deprivation indices. We wanted to confirm whether there is an association between missed appointments and socio-economic deprivation. We hypothesised that non-attenders lived in areas with worse deprivation scores.

Method We compared deprivation scores of English postcodes of clinic attenders and non-attenders of a ‘difficult asthma clinic’ between 2011–2014 inclusive. Indices of multiple deprivation scores were using census related data and Townsend Index via UK data service ©University of Essex and University of Manchester. This provides a validated, relative measure of deprivation across small localities in England to enable comparison. A higher score represents an area with worse socio-economic deprivation, maximum score = 100. Mann-Whitney two-tailed tests to compare non-paired non-parametric data were performed in Prism version 6 (GraphPad).

Results The median deprivation score of postcodes of non-attenders (n = 458) was 60.69, whereas for attenders it was 51.12 (n = 505), with a p value of <0.0001.

Conclusion These results strongly suggest socioeconomic deprivation has a negative impact on attendance rates at this specific
Tuberculosis in older versus younger adult patients: a retrospective comparison of patient characteristics and treatment outcomes at a major UK referral centre


Introduction and objectives Tuberculosis (TB) in older persons presents challenges related to diagnosis, management, comorbidities and polypharmacy potentially contributing to increased morbidity and mortality. This retrospective cohort review compares the baseline characteristics, diagnosis, management and outcome between older patients (OPs) (over 65 years) and younger patients (YPs) (25–35 years).

Method All patients ≥65 years treated at Northwick Park Hospital during 2002–2014 were identified from London TB register; a comparison group of patients aged 25–35 years were randomly selected. Clinical, microbiological, radiological and biochemical parameters together with management and outcomes were obtained from electronic records. Characteristics of patients were compared between the two groups using Chi-squared and Kruskal-Wallis tests; analyses were performed using Stata (Stata Corp, 2013).

Results The comparison groups comprised 313 patients aged ≥65 years and 339 patients aged 25–35. Demographics, site of disease, TB culture, treatment regimens and outcomes are recorded in Table 1. 35.6% of OPs and 29.6% of YPs were symptomatic for >2 months at review in secondary care. Median duration to starting treatment from review was 17 days (IQR: 4–57) in OPs compared to 2 (IQR: 1–19) in YPs (p = 0.001). 44.8% of OPs experienced drug toxicity compared to 27.3% of YPs (p = <0.001). Gastrointestinal symptoms affected 24.8% and 9.6% of OPs and YPs respectively (p = <0.001). There was no difference in prevalence of rash (4.8% in OPs) or drug induced liver injury (6.4% of OPs, p = 0.32). Comorbidities were higher in OPs, with diabetes associated arthralgia (2.4% of OPs,) or drug induced liver injury (6.4% of OPs, p = <0.001). Mortality was 16.0% amongst OPs, versus 9.1% with no deaths amongst YPs (both p = <0.001).

Conclusion These data characterise the delays in presentation and treatment initiation in older patients who also experience a more complicated treatment course with an increased side effect profile, more variation from standard quadruple therapy, lower completion rates and poorer outcomes. This, together with longer inpatient stays impacts patients, but also has financial implications for services.

A retrospective evaluation of the diagnostic utility of adenosine deaminase in pleural tuberculosis in a low-prevalence area

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Introduction and objectives Pleural fluid adenosine deaminase (pfADA) is a validated diagnostic marker for pleural tuberculosis (TB) in high prevalence areas, with good sensitivity and specificity reported at a threshold of 40 U/L. However, in north-west Europe pfADA is not routinely measured, due to a lack of evidence as to its diagnostic utility in areas of low TB prevalence. The aim of this study is to assess the sensitivity and specificity of pfADA in a low-prevalence area, evaluating its diagnostic value for pleural TB.

Methods A retrospective analysis considered all pfADA-tested suspected pleural TB patients within one hospital trust from 2009–2015. This cohort was then divided into two groups: those with a confirmed diagnosis of pleural TB and those without pleural TB. Those without pleural TB were used as a control group, to determine the sensitivity and specificity of pfADA at various thresholds.

Results Of 156 patients tested for pfADA, 25 had confirmed pleural TB and 131 did not, with mean pfADA levels of 71.7 (±25.2) and 19.8 (±22.4), respectively. On a Receiver Operating Characteristic (ROC) curve (Figure 1), pfADA of 30 U/L has a sensitivity of 100%, specificity 83%, positive and negative predictive values of 53% and 100% respectively. At a threshold of 40 U/L, sensitivity was 88% with a specificity of 88%. The calculated area under ROC curve is 0.949 (95% CI 0.91–0.982).

Abstract P252 Figure 1

Conclusion Although the positive predictive value of pfADA may be lower in areas of low TB prevalence, its negative predictive value is unaffected, retaining its value as a worthy screening test to exclude pleural TB, allowing focus on obtaining adequate culture samples and biopsies in suspected pleural TB.
Abstract P251 Table 1  This table shows the demographics, site of diseases, treatment regimens and outcomes of older versus younger patients with the relevant p values. R = rifampicin, H = Isoniazid, Z = Pyrazinamide, E = Ethambutol, M = Moxifloxacin

<table>
<thead>
<tr>
<th></th>
<th>Age 25-35 years (n=339)</th>
<th>Age 65+ (n=313)</th>
<th>P-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>119 (35.2%)</td>
<td>136 (43.5%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Male</td>
<td>220 (64.9%)</td>
<td>177 (56.6%)</td>
<td></td>
</tr>
<tr>
<td>Ethnic origin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Indian</td>
<td>246 (72.6%)</td>
<td>177 (56.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pakistani</td>
<td>12 (3.5%)</td>
<td>13 (4.2%)</td>
<td></td>
</tr>
<tr>
<td>Nepalese</td>
<td>17 (5.0%)</td>
<td>5 (1.6%)</td>
<td></td>
</tr>
<tr>
<td>Sri Lankan</td>
<td>12 (3.5%)</td>
<td>10 (3.2%)</td>
<td></td>
</tr>
<tr>
<td>Afghan</td>
<td>4 (1.2%)</td>
<td>8 (2.6%)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>30 (8.9%)</td>
<td>39 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>11 (3.2%)</td>
<td>50 (16.0%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7 (2.1%)</td>
<td>11 (3.5%)</td>
<td></td>
</tr>
<tr>
<td>Born in the UK</td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>No</td>
<td>322 (95.0%)</td>
<td>272 (87.5%)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>17 (5.0%)</td>
<td>39 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>Site of TB</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>84 (24.8%)</td>
<td>127 (40.6%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Extrapulmonary</td>
<td>231 (68.1%)</td>
<td>160 (51.1%)</td>
<td></td>
</tr>
<tr>
<td>Both</td>
<td>24 (7.1%)</td>
<td>26 (8.3%)</td>
<td></td>
</tr>
<tr>
<td>Sputum smear</td>
<td></td>
<td></td>
<td>0.28</td>
</tr>
<tr>
<td>Positive</td>
<td>31 (12.9%)</td>
<td>28 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>210 (87.1%)</td>
<td>140 (83.3%)</td>
<td></td>
</tr>
<tr>
<td>TB Sensitivity</td>
<td></td>
<td></td>
<td>0.01</td>
</tr>
<tr>
<td>Negative culture</td>
<td>105 (33.9%)</td>
<td>111 (43.0%)</td>
<td></td>
</tr>
<tr>
<td>Fully sensitive</td>
<td>184 (59.4%)</td>
<td>142 (55.0%)</td>
<td></td>
</tr>
<tr>
<td>Isoniazid resistant</td>
<td>18 (5.8%)</td>
<td>4 (1.6%)</td>
<td></td>
</tr>
<tr>
<td>MDR</td>
<td>2 (0.7%)</td>
<td>1 (0.4%)</td>
<td></td>
</tr>
<tr>
<td>XDR</td>
<td>1 (0.3%)</td>
<td>0 (0.0%)</td>
<td></td>
</tr>
<tr>
<td>Initial regimen</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RHZE</td>
<td>298 (90.0%)</td>
<td>69 (51.9%)</td>
<td></td>
</tr>
<tr>
<td>RHZM</td>
<td>13 (3.9%)</td>
<td>32 (24.1%)</td>
<td></td>
</tr>
<tr>
<td>RHEM</td>
<td>6 (1.8%)</td>
<td>7 (5.3%)</td>
<td></td>
</tr>
<tr>
<td>RHE</td>
<td>0 (0.0%)</td>
<td>10 (7.5%)</td>
<td></td>
</tr>
<tr>
<td>RHM</td>
<td>0 (0.0%)</td>
<td>6 (4.5%)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>14 (4.2%)</td>
<td>9 (6.8%)</td>
<td></td>
</tr>
<tr>
<td>Outcome</td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Completed – non-</td>
<td>227 (67.0%)</td>
<td>141 (45.1%)</td>
<td></td>
</tr>
<tr>
<td>pulmonary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Completed – pulmonary</td>
<td>82 (24.2%)</td>
<td>105 (33.6%)</td>
<td></td>
</tr>
<tr>
<td>Died</td>
<td>0 (0.0%)</td>
<td>50 (16.0%)</td>
<td></td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>11 (3.2%)</td>
<td>2 (0.6%)</td>
<td></td>
</tr>
<tr>
<td>Stopped</td>
<td>1 (0.3%)</td>
<td>7 (2.2%)</td>
<td></td>
</tr>
<tr>
<td>Transferred</td>
<td>18 (5.3%)</td>
<td>8 (2.6%)</td>
<td></td>
</tr>
</tbody>
</table>

† P-values for comparisons of proportions from Chi-squared test (or Fisher’s exact test if frequency <5)
Introduction East London has one of the UK’s largest cohorts of Drug Resistant Tuberculosis (DR-TB). This paper aims to provide insight into the recent behaviour of DR-TB in a multi-ethnic urban TB clinic.

Methods A retrospective study was conducted on all patients with DR-TB between 2007 and 2013. Statistical analysis was performed using Fisher’s Exact Test.

Results 179 cases were identified: 126 patients had Isoniazid mono-resistance (H-Mono), 3 had poly-resistance including Isoniazid, and 37 patients had multi-drug resistant TB (MDR-TB). There were 6 cases of Rifampicin mono-resistance, 1 Ethambutol mono-resistance, and 6 Pyrazinamide mono-resistance.

H-Mono and MDR-TB were more prevalent in males (58% and 57% respectively). H-Mono predominated in younger age groups (mode age group 25–29) whilst MDR-TB had a more uniform age distribution (Figure 1). The ethnicities of patients with DR-TB reflected the local population (Indian Subcontinent: 57% of H-Mono and 52% MDR-TB; Africa: 16% for both; Caucasian: 11% and 16% respectively; Other: 16% for both).

Conclusion H-mono and MDR-TB shared many demographical features, but in this cohort there were significant differences in age distribution, previous diagnosis of TB and country of origin. A significant proportion of patients did not match the typical profile of DR-TB, highlighting the importance of culture to exclude drug-resistance in all individuals.

Conclusion H-mono and MDR-TB shared many demographical features, but in this cohort there were significant differences in age distribution, previous diagnosis of TB and country of origin. A significant proportion of patients did not match the typical profile of DR-TB, highlighting the importance of culture to exclude drug-resistance in all individuals.
Introduction Anti-TNFα treatment is associated with a significant risk of LTBI reactivation (median onset 12 weeks for infliximab). Patients are therefore recommended to undergo prior LTBI screening but current NICE and BTS guidance differ in their approach. In particular, the BTS places more emphasis on demographic factors (age, ethnicity, birth outside the UK) in stratifying risk and does not mandate routine IGRA use.1 We describe the effect of local Trust screening protocol, incorporating IGRA, in the diagnosis and decision to start anti-TB chemoprophylaxis in a large cohort of patients being worked-up for anti-TNFα therapy.

Abstract P255 Table 1 Characteristics of patients included in the study

<table>
<thead>
<tr>
<th>Screening with IGRA test (n=472)</th>
<th>positive (n=27)</th>
<th>negative (n=445)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean ±SD)</td>
<td>48±13</td>
<td>39±13</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black African</td>
<td>2</td>
<td>22</td>
</tr>
<tr>
<td>Indian subcontinent</td>
<td>4</td>
<td>29</td>
</tr>
<tr>
<td>White UK born</td>
<td>9</td>
<td>270</td>
</tr>
<tr>
<td>White non UK born</td>
<td>8</td>
<td>68</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>56</td>
</tr>
<tr>
<td>Indication for anti-TNF therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>4</td>
<td>34</td>
</tr>
<tr>
<td>Crohn’s Disease</td>
<td>5</td>
<td>168</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>7</td>
<td>134</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>7</td>
<td>79</td>
</tr>
<tr>
<td>Other</td>
<td>4</td>
<td>30</td>
</tr>
<tr>
<td>Anti-TNF therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>12</td>
<td>222</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>2</td>
<td>40</td>
</tr>
<tr>
<td>Etanercept</td>
<td>6</td>
<td>37</td>
</tr>
<tr>
<td>Golimumab</td>
<td>0</td>
<td>18</td>
</tr>
<tr>
<td>Infliximab</td>
<td>7</td>
<td>128</td>
</tr>
<tr>
<td>LTBI Tx</td>
<td>19</td>
<td>8**</td>
</tr>
<tr>
<td>No LTBI Tx</td>
<td>2*</td>
<td>443</td>
</tr>
<tr>
<td>LTBI diagnosed by BTS protocol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>No</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>No data available</td>
<td>5</td>
<td>59</td>
</tr>
<tr>
<td>Active TB diagnosis</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

* Diagnosis based on CXR and/or clinical assessment
** History of active, fully treated TB in the past
Methods Data on adult patients undergoing LTBI screening before anti-TNFα commencement were collected prospectively between Jan ’13 and Dec ’14. The local screening protocol included clinical assessment, chest X-ray (CXR) and an ELISpot-TB assay. Where required, routine chemoprophylaxis was isoniazid for 6 months (anti-TNFα was started ≥1 month). Clinical follow-up data was obtained for 6 months post anti-TNFα commencement.

Results 472 patients received anti-TNFα for a minimum of 6 months after LTBI screening. According to the local protocol 21 cases (4.5%) received chemoprophylaxis vs. 66 patients (14%) who would have received chemoprophylaxis if the BTS guideline had been applied (Table 1). Moreover, 5 white, UK born, patients were identified that would not have been risk stratified to receive chemoprophylaxis according to the BTS. 2 cases receiving adalimumab for psoriasis developed active TB during the follow-up period. Both had negative IGRA at screening and were not given chemoprophylaxis however, both would have received treatment according to the BTS protocol. One case resulted from a subsequent TB exposure. The other had an abnormal screening CXR. This result was not appropriately followed up hence the case did not necessarily represent protocol failure per se.

Conclusions These preliminary data illustrate the benefit of an LTBI screening IGRA based protocol by decreasing the need for chemoprophylaxis by 69% if BTS recommendations had been applied.

REFERENCE

Abstract P256 Table 1

<table>
<thead>
<tr>
<th>Clinical outcomes</th>
<th>Symptoms group</th>
<th>Screening group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adverse outcome:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Neurological sequelae</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Significant structural</td>
<td>9*</td>
<td>0</td>
</tr>
<tr>
<td>Lung disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TB arthritis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Ileocaecal stricture</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>14/89 (16%)</td>
<td>0/106 (0%)</td>
</tr>
<tr>
<td><strong>Good outcome:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal CXR</td>
<td>54</td>
<td>84</td>
</tr>
<tr>
<td>no symptoms</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor CXR changes</td>
<td>19</td>
<td>20</td>
</tr>
<tr>
<td>Symptoms not due to TB</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>75/89 (84%)</td>
<td>106/106 (100%)</td>
</tr>
</tbody>
</table>

*1 also had neurological sequelae n = 195/209.

Conclusion TB is not a benign disease in children. This study shows that clinical outcomes are significantly worse in those who present with symptoms compared with those identified through screening and reminds us of the importance of identifying children at risk of TB infection early.

Poster sessions

P257 MODERN DAY SCROFULOUS SWELLINGS: BREAST TUBERCULOSIS IN EAST LONDON


Introduction Breast tuberculosis (TB) is rare and diagnosis may be delayed. It was first described in 1829. Incidence is highest in TB endemic areas. Here we describe a series of cases diagnosed in East London (UK).

Methods We conducted a retrospective study of all patients treated at our institution for breast TB between 2005 – 2015. Data including demographics, symptoms, microbiological, histological diagnoses and treatment outcomes were recorded.

Results 35 cases of breast TB were identified (1 male). Mean age at diagnosis was 33 years (range 16 – 63). 24 patients were from the Indian subcontinent, 3 Asian other, 7 Black-African and 1 Middle Eastern; no patients were Caucasian. Three patients were lactating, two were pregnant. Four patients had a previous
history of TB and one was HIV positive. All patients presented with a breast lump, 58% in the upper outer quadrant. 25 patients initially presented to their general practitioner (GP), of which 24 were referred to breast clinic and 1 directly to TB clinic. Eight cases presented to hospital. In two cases there was insufficient data. The breast lump was associated with skin changes in six cases, inverted nipple in three, discharge in one, and 49% had ipsilateral axillary lymphadenopathy. Erythrocyte sedimentation rate and C-reactive protein was raised in 84% and 53% cases respectively. Thirty percent of patients had abnormal mammography, 68% abnormal ultrasound breast findings. 25 out of 35 cases had biopsies/fine needle aspirations (FNA), all of these were sent for culture; 17 were culture positive with 3 drug resistant cases. Nine cases had necrotising granulomatous changes on histology, of which 1 was positive for Ziehl-Neelsen (ZN) stain, 9 cases had non-necrotising granulomas, of which 2 were ZN positive, and 7 cases had inflammatory changes only (none were ZN positive). All patients received at least three antituberculous drugs. Median treatment duration was six months, leading to complete resolution of breast TB.

**Conclusion** This case series highlights the difficulty in diagnosing breast TB. Raising awareness of the classical presentation of breast TB amongst GPs and breast services may improve diagnosis and treatment of this rare disease.

**REFERENCE**


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**Poster sessions**

**P258 Multi-drug resistant tuberculosis monitoring guidance: are we following the national guidelines?**


10.1136/thoraxjnl-2015-207770.394

**Introduction** Multi-drug Resistant Tuberculosis (MDR-TB) is a form of TB that is resistant to the two most powerful first-line anti-tuberculosis antibiotics available, rifampicin and isoniazid. Between 2004 and 2011, the proportion of cases of MDR-TB increased from 1.2% to 1.6%, of which it has remained stable over the past 3 years. Due to the complexity of treatment regimens used for MDR-TB, national monitoring guidelines have been developed to aid monitoring for adverse effects during treatment. A previous study identified that prior to the development of these monitoring guidelines the incidence of adverse effects associated with MDR TB medicines was high.2

**Objective** To establish whether national guidelines for the monitoring of MDR-TB medicines at a tertiary centre are being adhered to.

**Results** 9 patients with MDR-TB were included in the audit. The findings (see Table 1) show that baseline monitoring was not undertaken in the majority of patients. Whilst on-going monitoring was predominantly undertaken in over 80% of occasions, the audit standard was not met.

**Conclusions** Despite the presence of national guidance to support the monitoring of complex regimens for MDR-TB, this audit shows that monitoring of these in a tertiary centre is below the audit standard. Whilst adherence to on-going monitoring parameters were usually undertaken in over 80% of instances, it is of particular concern that baseline monitoring was significantly below the audit standard. Pharmacists are ideally placed to support the safe and effective monitoring of these often toxic medicines. The development of a pharmacist to support the TB clinics and specifically to support the monitoring of patients with MDR-TB could significantly improve this adherence and reduce the risk of adverse effects as a result of sub-optimal monitoring.

**REFERENCE**


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**P259 Central nervous system tuberculosis: diagnostic difficulties**


10.1136/thoraxjnl-2015-207770.395

**Introduction** Central nervous system (CNS) tuberculosis (TB) is difficult to diagnose. There is often a delay in diagnosis and a lack of robust diagnostic criteria.

**Methods** We conducted a retrospective study of all patients treated at our institution for CNS TB from 2009–2014 excluding those with HIV co-infection. Data including demographics, symptoms, microbiological and radiological features was recorded.

**Results** 53 cases of CNS TB were identified. The mean age was 36 (4 months – 81 years). Most patients were from the Indian Subcontinent (70.9%), 10.8% were from South East Asia, 1.8% from Africa, 10.9% were UK born and 5.5% were unknown. Symptoms and signs at presentation included headache (67.3%), fever (49%), confusion (34.5%), focal neurological deficit (27.3%), weight loss (27.3%), night sweats (23.6%), altered GCS (23.6%) and seizures (20%). 29% of patients also had pulmonary TB, 11% had TB lymphadenopathy and 11% had miliary TB.

89% of patients had a CT head, of which 42.8% were reported normal, 28.5% reported tuberculosis, 14.2% hydrocephalus and 20.4% exhibited other abnormalities. 87% had an MRI head, of which 10% were normal, 39.6% reported tuberculomas, 33% meningeal enhancement, 6% hydrocephalus, and 23% demonstrated other abnormalities.

Lumbar puncture (LP) was performed in 73% of cases, and CSF protein was elevated in 73% of these. The WCC was elevated in 60% with 63% having a predominant lymphocytosis.
CSF Glucose was documented in 80% of cases and levels were low (<2.5 mmol/L) in 47%. TB PCR was performed on 15 samples (38%), 2 (13%) were positive. Five CSF samples were not sent for AFB or culture. No samples were smear positive, 26% of CSF samples were culture positive; one was Isoniazid resistant.

7 patients died (one death attributed to TB chemotherapy), 3 became fully dependent for all activities of daily living and 6 patients had significant cognitive or neurological deficit.

Conclusions CNS TB causes significant morbidity and mortality. CSF examination should always be performed if feasible. Imaging by MRI should be considered in all patients with suspected TB meningitis in view of the much higher diagnostic yield compared to CT.

Following NICE 2015 63 non-pulmonary contacts would not have been seen. None of these had LTBI or TB disease. Of the remaining 307 contacts/new entrants 47(15%) had a positive Mantoux of whom 11(4%) had LTBI and 4(1%) TB disease.

Conclusions 37% more children will be investigated and treated for TB infection/disease under the new NICE TB guideline. In a 12 month period in our clinic this represents 33 additional children with 1 extra case of TB disease and 2 cases of LTBI identified.

**P260**

**POTENTIAL IMPACT OF THE 2015 NICE CONSULTATION GUIDELINE FOR TUBERCULOSIS ON THE NUMBER OF CHILDREN ASSESSED AND TREATED FOR TB INFECTION AND DISEASE IN THE UK**

L Turnbull, C Bell, F Child. Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK

10.1136/thoraxjnl-2015-207770.396

**Background** NICE Tuberculosis (TB) guideline 2015 recommends all children, regardless of BCG status, with Mantoux ≥5 mm induration receive treatment for latent TB once active TB has been excluded. The 2011 version defines a positive Mantoux as ≥6 mm (no prior BCG) and ≥15 mm (prior BCG). NICE 2011 recommends screening of household contacts of all cases of TB compared with the 2015 guideline which recommends screening of contacts of pulmonary TB only.

**Objectives** To establish the impact of the change in NICE recommendations on the number of children assessed and treated for latent TB infection (LTBI) or TB disease in our department.

**Methods** We performed a retrospective analysis of all children.

**Results** 445 patients were referred, 75 with symptoms, 138 new entrants, 63 non-pulmonary contacts and 169 pulmonary contacts.

Of those with symptoms, 5 had positive Mantoux (NICE 2011) compared with 18 (NICE 2015). In this group 0/75 were treated for LTBI and 7/75 for TB disease.

Results of patients referred for contact tracing/new entrant screening are shown in Table 1. Two contacts with LTBI and 1 with TB disease (all IGRA positive) would have been missed by the 2011 guideline but identified in 2015.

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Mantoux</th>
<th>LTBI</th>
<th>TB disease</th>
<th>No LTBI or TB disease</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>Positive 9</td>
<td>3</td>
<td>2</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative 3</td>
<td>1</td>
<td>352</td>
<td>356</td>
<td></td>
</tr>
<tr>
<td>2015*</td>
<td>Positive 11</td>
<td>4</td>
<td>32</td>
<td>47</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative 1</td>
<td>0</td>
<td>259</td>
<td>260</td>
<td></td>
</tr>
</tbody>
</table>

*Non-pulmonary contacts not included in 2015 data.

**Abstract P260 Table 1** Number of patients referred for contact tracing or new entrant screening by Mantoux test result and TB disease status.
Introduction and objectives Skeletal tuberculosis (TB) accounts for about 10% of extrapulmonary tuberculosis in Europe and the USA. Outcomes and duration of treatment are less well described than pulmonary TB. We sought to identify characteristics and outcomes for patients diagnosed with skeletal TB in the two hospitals in our trust.

Methods Cases of TB treated in our NHS trust from 1/1/2011 to 31/12/2013 with site of disease including bone and/or spine were included. Data was obtained from the Enhanced TB Surveillance Database and case note review. Patients with a positive alternative diagnosis were excluded. TB affecting other body systems was defined as imaging abnormalities with exclusion of alternative diagnoses.

Results 34 patients (20 males), mean age 42.7 years, were identified. 29 (85%) were born outside the UK. No patients were HIV positive (test not offered/refused in 11%). Sites of disease are shown in Table 1. 13 (38%) of patients had the diagnosis made via non-surgical biopsy (either radiological or bedside), 6 (18%) through surgical biopsy, and 5 (15%) of patients having the diagnosis made through sampling from another site (usually pulmonary). The remainder of patients (10) either had a clinical-radiological diagnosis or the diagnosis made overseas, with 4 of those patients undergoing a non-diagnostic biopsy. Mean length of treatment was 10 months. At end of treatment 9 (40%) of spinal TB patients had ongoing back pain and 4 (33%) of patients with appendicular joint involvement had residual stiffness.

Conclusions Bedside or image guided procedures have a role in the diagnosis of skeletal TB; about 30% will also have pulmonary TB which may be more accessible for diagnosis. Sending for TB culture during surgery is important. After appropriate treatment a proportion of patients have residual pain and stiffness.
Hospitals NHS Trusts between 2010–2014 were extracted. HIV-negative individuals with ≥2 positive sputum samples or ≥1 positive bronchoalveolar lavage were included. Demographic, clinical, radiological, microbiological, management and outcome data was obtained from electronic records.

**Results**
1190 NTM sputum samples were identified from 822 individuals. 152 individual patients met inclusion criteria for analysis. Table 1 describes cohort demographics.

Within the cohort 48/152 (32%) were treated for NTM disease. All treated subjects and 74/104 (71%) non-treated subjects met international guidelines for diagnosis of NTM infection, which included positive clinical, radiological (cavities or bronchiectasis +/- nodules or infiltrates) and microbiological criteria. Mycobacterium avium complex (MAC) was the most commonly isolated (68/152; 45%) and treated organism (21/48; 44%) followed by Mycobacterium kansasii (11/48; 23%). 19/48 (40%) completed treatment (median duration: 17 months [IQR: 12–24]). 10/48 (21%) remain on treatment (median duration: 18 months [IQR: 11–36]). 11/48 (23%) stopped treatment due to side effects and 13/48 (27%) were either lost to follow up or treated for Mycobacterium tuberculosis.

Of those treated, 29/48 (60%) culture converted; 23/29 (79%) remain negative at 12 months post culture conversion. Of 19/48 who completed treatment, 5/19 (26%) had symptomatic or radiological disease progression compared to 11/28 (39%) who did not complete treatment. 11/48 (23%) patients died within the treatment group. Within the untreated subjects who met international guidelines for NTM infection (74/104), mortality was 19/74 (26%) (p = 0.83).

Discussion
NTM is a challenging disease with only 39% of eligible subjects receiving treatment and a high associated mortality. Furthermore, only 40% starting treatment completed it and the 21% who remain on treatment have been treated for a median duration of 18 months to date. Unlike similar HIV-negative UK cohorts, MAC pulmonary disease is the most prevalent.

**Abstract P264 Table 1**

Demographic characteristics of NTM positive individuals managed between 2010 and 2014 at ICHT and NWLH Trusts

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Notes</th>
<th>Treated (n = 48)</th>
<th>Non-treated (n = 104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Median (IQR)</td>
<td>63 (54–76)</td>
<td>70 (56–79)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male (%)</td>
<td>28 (58)</td>
<td>60 (58)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>White (%)</td>
<td>25 (52)</td>
<td>51 (49)</td>
</tr>
<tr>
<td></td>
<td>Black (%)</td>
<td>5 (10)</td>
<td>10 (10)</td>
</tr>
<tr>
<td></td>
<td>Asian (%)</td>
<td>14 (29)</td>
<td>21 (20)</td>
</tr>
<tr>
<td></td>
<td>SE Asian (%)</td>
<td>0 (0)</td>
<td>5 (5)</td>
</tr>
<tr>
<td></td>
<td>Other (%)</td>
<td>2 (4)</td>
<td>8 (8)</td>
</tr>
<tr>
<td></td>
<td>Unknown (%)</td>
<td>2 (4)</td>
<td>9 (9)</td>
</tr>
<tr>
<td>Imunosuppression</td>
<td>n (%)</td>
<td>22 (47)</td>
<td>27 (27)</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>n (%)</td>
<td>5 (10)</td>
<td>10 (10)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>n (%)</td>
<td>2 (4)</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Symptoms at diagnosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>38 (81)</td>
<td>73 (70)</td>
<td></td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>14 (29)</td>
<td>28 (27)</td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>19 (40)</td>
<td>17 (16)</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>6 (13)</td>
<td>20 (19)</td>
<td></td>
</tr>
<tr>
<td>Haemoptysis</td>
<td>6 (13)</td>
<td>17 (16)</td>
<td></td>
</tr>
<tr>
<td>Night sweats</td>
<td>10 (21)</td>
<td>8 (8)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>6 (13)</td>
<td>14 (14)</td>
<td></td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>0 (0)</td>
<td>7 (7)</td>
<td></td>
</tr>
</tbody>
</table>

**Diagnosis and management of pulmonary arterial hypertension**

**P265**

THE CLINICAL UTILITY OF BIOMARKERS ASSOCIATED WITH INFLAMMATION AND ENDOTHELIAL DYSFUNCTION IN CTEPH

1C Hadinnapola, 1M Southwood, 1J Hernandez-Sanchez, 1K Sheares, 1S Preston, 1D Jenkins, 1N Morell, 1M Toshner, 1J Pepeke-Zaba. 1Papworth Hospital, Cambridge, UK; 1University of Cambridge, Cambridge, UK

Introduction
Chronic thromboembolic pulmonary hypertension (CTEPH) is a rare form of pulmonary hypertension. Inflammation, defective angiogenesis and endothelial dysfunction have been implicated in its pathogenesis. We assessed the prognostic utility of biomarkers, related to these processes, in pulmonary endarterectomy (PEA) assessment.

Methods
80 patients with CTEPH had serum samples taken immediately prior to PEA and a subset (n = 54) also at follow-up after PEA. 20 healthy volunteers and 20 patients with idiopathic pulmonary arterial hypertension (IPAH) served as controls. Samples were processed on a custom-designed Luminex multiplex array. Biomarker levels were correlated to haemodynamics and functional assessments. Material removed during PEA and explanted lungs of CTEPH and IPAH patients were additionally analysed using immunostaining.

Results
Compared to healthy controls Pre PEA samples showed increases in interleukin (IL)-8, -10, tumour necrosis factor α (TNFα), high sensitivity C-reactive protein (hsCRP) and angiopeitin 2 (Ang2). Vascular endothelial growth factor (VEGFc) was higher in healthy controls.

Following PEA (6.00 ± 1.83 months), improvements in haemodynamics and six-minute walk distance were observed compared to baseline (Table 1). Additionally, there were decreases in Ang2 and Endoglin.

Preoperative Ang2 levels were independently associated with baseline pulmonary vascular resistance (PVR) with multiple linear regression (p = 0.0001). A similar association was found in IPAH subjects (p < 0.05).

Ang2 expression was demonstrated in the endothelium of distal pulmonary arteries in both IPAH and CTEPH notably in areas of small vessel vasculopathy and in neovessels found in the PEA specimens.

The clinical utility in predicting small vessel vasculopathy and residual CTEPH post-PEA surgery was assessed using a cross validation approach. Baseline Ang2 was a necessary component of the best multiple linear model for predicting PVR at follow up (along with baseline PVR, WHO class, age and the use of PAH targeted therapy) r² = 0.39, q² = 0.35.

Conclusion
We found only modest increases in any marker of inflammation in CTEPH, they were not normalised by PEA or correlated to disease severity. By comparison Ang2 correlated with haemodynamics and has utility in predicting postoperative outcomes.
Poster sessions

Abstract P265 Table 1  Characteristics and biomarker assessment of CTEPH and control subjects

<table>
<thead>
<tr>
<th></th>
<th>CTEPH Pre PEA</th>
<th>CTEPH Post PEA</th>
<th>Healthy controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median</td>
<td>95% CI</td>
<td>Median</td>
</tr>
<tr>
<td>Age</td>
<td>63.59</td>
<td>58.6–66.2</td>
<td>64.09</td>
</tr>
<tr>
<td>IL-6 (pg/ml)</td>
<td>0.13</td>
<td>0.13–0.13</td>
<td>0.13</td>
</tr>
<tr>
<td>IL-8 (pg/ml)</td>
<td>7.22</td>
<td>4.76–9.34</td>
<td>4.12</td>
</tr>
<tr>
<td>IL-10 (pg/ml)</td>
<td>1.85</td>
<td>1.29–2.96</td>
<td>1.44</td>
</tr>
<tr>
<td>TNFα (pg/ml)</td>
<td>9.69</td>
<td>7.89–11.10</td>
<td>9.21</td>
</tr>
<tr>
<td>hsCRP (pg/ml)</td>
<td>2.86</td>
<td>2.23–3.91</td>
<td>0.72</td>
</tr>
<tr>
<td>VEGFα (pg/ml)</td>
<td>157.68</td>
<td>121.21–244.79</td>
<td>142.37</td>
</tr>
<tr>
<td>VEGFd (pg/ml)</td>
<td>30.51</td>
<td>6.90–50.36</td>
<td>27.72</td>
</tr>
<tr>
<td>Ang2 (pg/ml)*</td>
<td>1266.79</td>
<td>1079.31–1649.42</td>
<td>757.07</td>
</tr>
<tr>
<td>BNP (pg/ml)</td>
<td>25.47</td>
<td>18.13–28.79</td>
<td>24.87</td>
</tr>
<tr>
<td>Endoglin (pg/ml)*</td>
<td>242.30</td>
<td>209.53–285.24</td>
<td>117.22</td>
</tr>
<tr>
<td>ProBNP (pg/ml)</td>
<td>575.00</td>
<td>131.1–1142</td>
<td>234.00</td>
</tr>
<tr>
<td>RAP (mmHg)</td>
<td>8.00</td>
<td>7.00–8.00</td>
<td>7.00</td>
</tr>
<tr>
<td>CI (L/min/m²)*</td>
<td>44.50</td>
<td>39.50–47.00</td>
<td>26.00</td>
</tr>
<tr>
<td>WHO class*</td>
<td>3</td>
<td>3–3</td>
<td>2</td>
</tr>
</tbody>
</table>

*Variables different between Pre and Post PEA samples.
**Variables different between Post PEA and healthy control samples.

Introduction Airway obstruction has been demonstrated in patients with Pulmonary Arterial Hypertension Associated with Congenital Heart Disease (CHD-APAH), but the cause is unknown. The vasoactive mediator endothelin-1 is a potent vasoconstrictor that induces smooth muscle proliferation in pulmonary arterial hypertension. Endothelin-1 also has the potential to cause bronchoconstriction when present in the airways, though this has not been demonstrated in CHD-

P266 DO ENDOTHELIN-1 AND INFLAMMATION PLAY A ROLE IN AIRWAY OBSTRUCTION IN PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH CONGENITAL HEART DISEASE?  

1AT Low, 2SJ George, 2AB Millar, 1RMR Tulloh. 1University Hospitals Bristol, Bristol, UK; 2University of Bristol, Bristol, UK
10.1136/thoraxjnl-2015-207770.402

Abstract P266 Table 1  Serum and induced sputum cytokine and endothelin-1 levels for CHD-APAH patients, CHD patients and healthy controls

<table>
<thead>
<tr>
<th>Analyte (pg/ml)</th>
<th>CHD-APAH</th>
<th>CHD</th>
<th>Healthy control</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum (n = 56)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL1β</td>
<td>1 (0.52–2.4)</td>
<td>0.36 (0.22–1.18)</td>
<td>0.43 (0.04–0.70)</td>
<td>0.0314*</td>
</tr>
<tr>
<td>IL6</td>
<td>2.70 (1.96–3.97)</td>
<td>1.69 (1.2–1.88)</td>
<td>1.53 (1.02–1.86)</td>
<td>0.0005*</td>
</tr>
<tr>
<td>IL8</td>
<td>12.3 (10.5–15.5)</td>
<td>8.62 (6.78–15.28)</td>
<td>9.26 (6.12–12.18)</td>
<td>0.0161*</td>
</tr>
<tr>
<td>IL10</td>
<td>0.71 (0.26–1.01)</td>
<td>0.65 (0.54–1.18)</td>
<td>0.47 (0.18–0.76)</td>
<td>0.1119</td>
</tr>
<tr>
<td>TNFα</td>
<td>12.9 (10.82–15)</td>
<td>11.97 (8.8–14.42)</td>
<td>10.95 (7.38–12.36)</td>
<td>0.0411*</td>
</tr>
<tr>
<td>VEGF</td>
<td>78.9 (47.7–101.9)</td>
<td>89.6 (58.5–115.9)</td>
<td>41.3 (27.7–72.0)</td>
<td>0.0232*</td>
</tr>
<tr>
<td>ET-1</td>
<td>2.43 (2.13–3.30)</td>
<td>1.43 (1.16–1.72)</td>
<td>1.48 (1.20–1.77)</td>
<td>0.0001*</td>
</tr>
<tr>
<td>Sputum (n = 30)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IL1β</td>
<td>18.2 (12.2–33.1)</td>
<td>45.4 (22.7–61.3)</td>
<td>36.4 (22.2–106.2)</td>
<td>0.2126</td>
</tr>
<tr>
<td>IL6</td>
<td>10.6 (5.4–57.6)</td>
<td>14.7 (9.6–35.2)</td>
<td>16.6 (6.4–29.2)</td>
<td>0.7559</td>
</tr>
<tr>
<td>IL8</td>
<td>712.4 (447.1–1246.4)</td>
<td>746.0 (602.5–2335.5)</td>
<td>893.4 (348.1–2780.1)</td>
<td>0.9851</td>
</tr>
<tr>
<td>IL10</td>
<td>0.64 (0.46–0.9)</td>
<td>0.74 (0.6–0.9)</td>
<td>0.6 (0.4–1.5)</td>
<td>0.6519</td>
</tr>
<tr>
<td>TNFα</td>
<td>5.89 (4.6–7.9)</td>
<td>8.36 (4.66–17.7)</td>
<td>5.09 (3.66–14.84)</td>
<td>0.5719</td>
</tr>
<tr>
<td>VEGF</td>
<td>323.6 (150.6–376.2)</td>
<td>314.5 (196.8–464.6)</td>
<td>295.7 (255.6–454.4)</td>
<td>0.9645</td>
</tr>
<tr>
<td>ET-1</td>
<td>0 (0–0.82)</td>
<td>0.56 (0–0.82)</td>
<td>0.98 (0.55–1.1)</td>
<td>0.1810</td>
</tr>
</tbody>
</table>

Data presented as median (IQR).  
P values calculated by Kruskal-Wallis.  
*Post hoc comparison showing CHD-APAH levels significantly greater than CHD and significantly greater than healthy controls (p < 0.05).  
**Post hoc comparison showing CHD-APAH and CHD levels significantly greater than for healthy controls (p < 0.05).  
APAH = Associated pulmonary arterial hypertension, CHD = Congenital heart disease, ET = endothelin, IL = interleukin, TNF = tumour necrosis factor, VEGF = vascular endothelial growth factor.
APAH. Systemic inflammation also occurs in CHD-APAH but associated airway inflammation has not been investigated. This study investigates the relationship between inflammation, endothelin-1 and airway dysfunction in CHD-APAH patients. 

**Methods** 58 patients were prospectively recruited: 20 CHD-APAH, 20 CHD and 18 healthy controls. Exclusion criteria were pre-existing lung disease, significant smoking history, scoliosis and Down’s syndrome. Participants performed full lung function tests and provided serum and induced sputum samples at a single visit. Serum and sputum cytokines were measured by multiplex bead assay array and endothelin-1 levels measured by enzyme linked immunosorbent assay. Induced sputum was also assessed for total and differential cell counts.

**Results** Serum cytokines and endothelin-1 levels were significantly elevated in patients with CHD-APAH in comparison to CHD and healthy controls (See Table 1). There were no significant differences in sputum cytokine or endothelin-1 levels between the 3 groups, with no differences in total or differential cell counts. A significant correlation between serum endothelin-1 levels and FEF25–75 was found for CHD-APAH patients ($r = -0.6017$, $p = 0.0083$ Spearman). There were no significant correlations between measures of airway obstruction and serum cytokine levels.

**Conclusions** There is evidence of systemic inflammation in CHD-APAH patients but serum cytokines did not correlate with measures of airway dysfunction, and there was no evidence of airway inflammation. This suggests that inflammation does not play a role in airway obstruction in this patient group. Serum endothelin-1 is significantly elevated in CHD-APAH patients, and this did correlate with measures of airway obstruction. While elevated endothelin-1 in the pulmonary vessels may affect the adjacent airways, induced sputum endothelin-1 was not elevated. Whether serum endothelin-1 can cause bronchoconstriction without being associated with raised levels in the airways is unclear and requires further investigation.

**REFERENCE**

1 Brash L, Church C, Gibbs JS, Howard LSGe, Johnson MK, Welsh DJ, Wilkins MR, Newby DE, Peacock AJ. Apelin improves cardiac output in patients with pulmonary arterial hypertension. Submitted to ERS 2015 Conference
Results GDF-15 mRNA and protein levels were raised in the lung homogenates of the MCT rat compared to controls (p < 0.05). Immunohistochemistry revealed GDF-15 was localised in the endothelial cells and to a lesser extent in the PASMCS of these animals. GDF-15 levels in the serum of the MCT treated rats was higher than that in those treated with vehicle control (771 ± 345 vs. 411 ± 305, p < 0.05). Serum GDF-15 was correlated with RV/LV+S weight in the MCT treated group (Pearson r = 0.66, p < 0.05). Immunohistochemistry also revealed an increase of phospho-TGFβ activated kinase 1 (TAK1) in PASMCS of the MCT rat. In HPASMCs GDF-15 (1 ng/ml) treatment resulted in an increase in proliferation over baseline at 72 h (Figure 1). GDF-15 was also able to induce phosphorylation of TAK1 in HPASMCs.

Conclusions GDF-15 is over-expressed in the lung vasculature of MCT rats, mimicking human disease. GDF-15 was associated with the degree of right ventricular hypertrophy in these animals. GDF-15 downstream signalling molecule phosphorylated TAK-1 is present in increased levels in the vasculature of the MCT rat. In vitro GDF-15 treatment caused proliferation of HPASMCs and activation of TAK-1. Further investigation of this pathway is required to determine its relevance to human disease.

Poster sessions

P269 PERIOPERATIVE OUTCOMES IN PATIENTS WITH PULMONARY HYPERTENSION UNDERGOING NON-CARDIAC NON-OBSTETRIC SURGERY IN A DESIGNATED UK PULMONARY HYPERTENSION CENTRE


10.1136/thoraxjnl-2015-207770.405

Introduction and objectives Patients with pulmonary hypertension (PH) represent an extremely high-risk surgical group, with previous reported mortality 7–18%, and predicting perioperative risk is difficult. The aim of this study was to characterise a current cohort of patients with pulmonary hypertension undergoing surgery in a National UK Designated PH centre and to determine predictors of adverse events.

Methods Consecutive patients with PH undergoing non-cardiac, non-obstetric surgery were identified by matching theatre and PH databases between 1st April 2008 and 1st April 2015. Demographics, recent echocardiogram, right heart catheterisation, B-natriuretic peptide (BNP), six-minute walk test (6MWT) and World Health Organisation functional class (WHO-FC) on last clinic visit was recorded. Anaesthetic and perioperative details; post-operative management, short-term morbidity and 28-day outcome were recorded. Data are mean±SD or median (range).

Results 37 procedures requiring anaesthesia were identified in 32 patients with PAH (7 idiopathic PAH, 1 PVOD, 24 CHD-PAH, 4 CTD-PAH) and 1 CTEPH. Average age was 44.4 ± 13 years, 27(84%) were female. Baseline preoperative WHO-FC was II (3, 9%), III (28, 88%), IV (1, 3%). Baseline 6MWT distance was 317 ± 68 m; BNP 200 (12-2027) ng/L; RV systolic pressure (RVSP) 85 ± 16 mmHg, tricuspid annular planar systolic excursion (TAPSE) 18 ± 7 mm. Cases including oesophagogastroscopy (n = 4), dental extraction (n = 8) under general anaesthesia (GA) were classified as minor; 6 (16%) including mastectomy, laparotomy and fasciotomy as major surgical procedures. Almost all (95%) were performed under GA; most were elective procedures and were monitored on the high dependency or intensive care unit post-operatively. Cardiovascular perioperative complications occurred in 6 cases (16%) including death in 2 patients (5.4%) in the days following surgery, in both cases related to PH crises, resulting in right ventricular (RV) failure. Baseline parameters of RV function including RVSP, TAPSE and the presence of a pericardial effusion were associated with adverse events.

Conclusion Perioperative mortality in patients with PH remains high, even in the current era. If surgery is deemed essential, PH centres with experts in cardiothoracic anaesthesia and ICU should be involved in preoperative planning with the PH multidisciplinary team guiding appropriate selection of patients, considering pulmonary haemodynamics and indices of RV function, as well as surgical factors.

P270 IDENTIFYING THE OPTIMAL D-DIMER CUT OFF VALUE FOR RULING OUT PES IN AN AMBULATORY CARE SETTING

FA Khan, K Ryanna, E Bailie, Y Vali. Glenfield Hospital, Leicestershire, UK

10.1136/thoraxjnl-2015-207770.406

Introduction Patients attending the ambulatory pulmonary embolism (PE) clinic at the Glenfield Hospital are risk stratified into low, intermediate and high risk based on the BTS scoring. Those with a low or intermediate pre-test probability go on to have a microlatex D-dimer assay and if this is greater than 0.5 ug/mL, imaging in the form of CTPA or VQ scan is carried out.

It has been suggested that using a higher cut off value of D-dimer may improve specificity without affecting sensitivity for a PE.

Methods Data was collected for 2139 consecutive patients who presented to the ambulatory PE clinic between June 2010 and Dec 2014. For each of these patients, age, BTS clinical probability, D-dimer results and final diagnosis was recorded.
Receiver operating characteristics (ROC) curve analysis was performed separately for patients with low and intermediate probability, and the optimum cut-off value to exclude PE determined.

**Results** Of the 2139 patients, prevalence of PE was 3.2% (50/1535) in the low, 14.2% (63/443) in the intermediate and 26% (42/161) in the high probability group. No patients with a D-dimer of <0.5 ug/mL who were discharged without any radiological investigations have returned with a missed diagnosis of PE.

ROC curve analysis showed the optimum D-dimer cut off value in low risk patients was 0.52, and 0.57 in patients with an intermediate risk.

<table>
<thead>
<tr>
<th>Criterion (low risk)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;0.52</td>
<td>100%</td>
<td>49%</td>
<td>100%</td>
</tr>
<tr>
<td>&gt;0.8</td>
<td>92%</td>
<td>71%</td>
<td></td>
</tr>
<tr>
<td>&gt;1</td>
<td>84%</td>
<td>78%</td>
<td>99.4%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Criterion (int risk)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;0.57</td>
<td>100%</td>
<td>37%</td>
<td>100%</td>
</tr>
<tr>
<td>&gt;0.8</td>
<td>83%</td>
<td>62%</td>
<td></td>
</tr>
<tr>
<td>&gt;1</td>
<td>76%</td>
<td>67%</td>
<td>94.7%</td>
</tr>
</tbody>
</table>

**Conclusion** The optimum D-dimer value must be chosen in the context of missed PEs versus scanning fewer people and thus avoiding unnecessary radiation and using resources more efficiently. A higher D-dimer of 1.0 ug/mL would have correctly avoided 161 scans and subsequently saved over £19,000.2 This must be offset however against patients being incorrectly diagnosed and often ending up in hospital with complications. Using the same cut off of 1.0 ug/mL would have missed a total of 22 PE’s during the study period. Based on this the conventional D-dimer cut off value of 0.5 ug/mL is most appropriate for patients attending the ambulatory PE clinic.

**REFERENCES**

**Abstract P271 Table 1**

<table>
<thead>
<tr>
<th>Criterion (low risk)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-adjusted D-dimers (low risk)</td>
<td>94%</td>
<td>48%</td>
<td>99%</td>
</tr>
<tr>
<td>Age-adjusted D-dimers (int risk)</td>
<td>90%</td>
<td>37%</td>
<td>95%</td>
</tr>
<tr>
<td>Age adjusted (low and int risk)</td>
<td>91%</td>
<td>45%</td>
<td>98%</td>
</tr>
<tr>
<td>Conventional 0.5</td>
<td>100%</td>
<td>49%</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Conclusion** The optimum D-dimer value must be chosen in the context of missed PEs versus scanning fewer people and thus avoiding unnecessary radiation and using resources more efficiently. An age-adjusted D-dimer in patients above the age of 50 would result in PEs being missed, and a conventional cut off value of 0.5 ug/mL is most appropriate for patients in an ambulatory care setting.

**REFERENCES**
Results In 5 patients (4%), PE was confirmed after imaging. The mean age was 50 years with 68.5% female patients. The most common presenting complaint was chest pain followed by dyspnoea. In 59% of the cases the Wells score was not documented. D-Dimer was negative in 94.5% of patients with unnecessary measurement in 11% of these. In 20% of patients who had radiological investigations for PE, D-dimer was negative. ECG and CXR were performed in most of cases with abnormal findings in 11% and 15% respectively. 77% of patients underwent CTPA, 21% had a V/Q scan, and 2% had V/Q scan followed by CTPA. The mean time to scan was 1.5 days with minimum of 1 day and maximum of 4 days. All confirmed PEs were identified by CTPA and were provoked by risk factors such as recent surgery, recent pregnancy, oral contraceptives, previous documented VTE. Domi-

ciliary enoxaparin was administered in 89% of patients pending CTPA or VQ. All confirmed PEs were subsequently treated with warfarin. No complications occurred, including bleeding events, recurrent VTEs, readmissions for anticoagulation related events, or deaths related to PE.

Conclusions Our experience shows that selected patients with suspected PE can be safely managed as outpatients in our trust. Closer adherence to the pathway may prevent a number of unnecessary scans (i.e. PE can be safely excluded when Wells score low and D-Dimer negative without a scan). Our protocol and pathways are being updated to incorporate PESI criteria to safely identify ambulatory patients, and to use of rivaroxaban in preference to warfarin for confirmed PE.

Conclusion Compared to the ESC 2014 guidelines, recurrence rates and complications at 2 years are much lower. The classification of provoked and unprovoked events led to the diagnosis of unknown pathologies. Although only an initial study, this shows that secondary follow-up decreases adverse consequences.

Treatment options in cystic fibrosis

P274 MOVING FROM RESCUE TO PREVENTION: REAL WORLD EVIDENCE OF REDUCTION IN IV ANTIBIOTIC REQUIREMENT FOLLOWING IMPROVEMENT IN ADHERENCE TO MAINTENANCE NEBULISED TREATMENT IN AN ADULT CYSTIC FIBROSIS CENTRE

1ZH Hoo, 2R Curley, 3C Carolan, 4C Hinchliffe, 5M Hutchings, 6MJ Campbell, 7MJ Wildman.

1ScHARR, University of Sheffield, Sheffield, UK; 2Adult CF Centre, Northern General Hospital, Sheffield, UK;

Background Adherence to preventative nebulised therapy is associated with better health and lower costs for rescue treatment. However, adherence with nebulised treatment is generally poor and there is currently no systematic adherence intervention for people with CF. The Sheffield Adult CF centre has embarked on various pilot projects in this area, culminating in an NHS programme grant awarded in 2014 to develop such a systematic adherence intervention. We hypothesised that the pilot projects would have improved the adherence levels and health outcomes among people with CF receiving care at the CF centre.

Objectives To determine overall change in nebuliser adherence and health outcomes among the cohort of people with CF receiving care at Sheffield from 2013 to 2014.

Methods Demographic data, spirometry, BMI, annual total intravenous antibiotics days and prescription details were obtained by reviewing patient notes. Adherence was measured with I-neb and calculated as a percentage of the agreed regimen in 3 months of I-neb data.

Results Of the 84 patients (40 male, 44 female), 83 were available for follow-up at the 2 year mark. Fifty patients (59.5%) had a provoked event whilst 32 (38.1%) were unprovoked- 2 patients had inadequate history to assess. Patients with unprovoked events were investigated further to screen for an underlying malignancy. Three patients (9.38%) were diagnosed with malignancies within 6 months of their PE. Of the unprovoked, 26 underwent a thrombophilia screen with 4 (12.5%) testing positive. Of 83 patients followed to 2 years, 7 (8.4%) had a recurrence (mean 17 months). Two (2.4%) developed chronic thromboembolic pulmonary hypertension whilst 3 (3.6%) developed post-thrombotic syndrome.

Abstract P274 Table 1

<table>
<thead>
<tr>
<th></th>
<th>2013 data</th>
<th>2014 data</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 166)</td>
<td>(n = 170)</td>
</tr>
<tr>
<td>People on I-neb (%)</td>
<td>92 (55%)</td>
<td>101 (59%)</td>
</tr>
<tr>
<td>People with ≥3 months of I-neb data (%)</td>
<td>83 (50%)</td>
<td>85 (50%)</td>
</tr>
<tr>
<td>Median % I-neb nebuliser adherence (IQR)</td>
<td>40.5 (20.2–66.8)</td>
<td>49.5 (23.1–77.8)</td>
</tr>
<tr>
<td>Median age in years (IQR)</td>
<td>25 (19–31)</td>
<td>26 (20–32)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>75 (45%)</td>
<td>79 (46%)</td>
</tr>
<tr>
<td>Pancreatic insufficiency (%)</td>
<td>138 (83%)</td>
<td>136 (80%)</td>
</tr>
<tr>
<td>CF related diabetes (%)</td>
<td>38 (23%)</td>
<td>41 (24%)</td>
</tr>
<tr>
<td>Median % predicted FEV1 (IQR)</td>
<td>79 (56–95)</td>
<td>79 (56–93)</td>
</tr>
<tr>
<td>BMI (IQR)</td>
<td>22.0 (19.7–24.6)</td>
<td>22.7 (19.8–24.9)</td>
</tr>
<tr>
<td>Median IV days (IQR)</td>
<td>14 (0–41)</td>
<td>14 (0–28)</td>
</tr>
<tr>
<td>Total IV days</td>
<td>3970</td>
<td>3313</td>
</tr>
</tbody>
</table>
Results 15 people were excluded from the analysis for both years. The cohort increased from n = 166 in 2013 to n = 170 in 2014, with a similar increase in the number of people with I-neb data for ≥3 months (n = 83 in 2013, n = 85 in 2014). Median nebuliser adherence improved from 40.5% in 2013 to 49.5% in 2014. The median FEV1 remained stable at 79% while BMI improved slightly from 22.0 in 2013 to 22.7 in 2014. The total IV days reduced by 657 from 3970 in 2013 to 3313 in 2014; a potential saving of around £156,000.

Conclusion Although adherence remains a challenging issue, these data suggest the potential of benefits of improved adherence. More work will be needed to examine the adherence data in more detail and to collect further longitudinal data to determine if there is a clear trend of improvement.

### Poster sessions

#### P275 PREVALENCE AND STRAIN TYPING RESULTS OF GRAM-NEGATIVE EMERGING BACTERIAL PATHOGENS IN PATIENTS ATTENDING A LARGE UK ADULT CF CENTRE

1HD Green, 1R Bright-Thomas, 1D Kenna, 1AM Jones. University Hospital of South Manchester, Manchester, UK; 2Public Health England, London, UK

10.1136/thoraxjnl-2015-207770.411

Introduction In recent years Gram-negative bacterial emerging pathogens (EP) have been noted to infect the airways of patients with CF. Prevalence of EP is increasing but much remains unknown. This study aimed to determine prevalence of EP at a large adult UK centre and whether these organisms may be capable of cross infection.

Methods Prevalence of Burkholderia multivorans; Stenotrophomonas maltophilia and Achromobacter; Ralstonia and Pandorea species was calculated in October 2013 and 2014. Strain typing was performed on EP isolated from patients from January 2008 to present using pulsed-field gel electrophoresis following restriction with XbaI. Epidemiology of patients with shared strains was analysed by reviewing patient addresses, outpatient appointments, admissions, paediatric centres and asking patients about their social behaviours.

Results In October 2013, 358 patients had at least 1 sputum culture result in the previous 12 months and were included in the prevalence calculation. This increased to 368 patients in October 2014. Prevalence of most EP increased between 2013 and 2014. EP prevalence in 2014 ranged from 1.9% (Ralstonia species) to 6.2% (B. multivorans) (Table 1). 96 patients had ≥1 isolation of an EP between January 2008 and July 2015. Of these, 20 (21%) had ≥2 strains of EP isolated from their sputum within that timeframe. To date, strain typing has been performed on 97 of 115 identified isolates from 96 patients. Shared strains of EP in unrelated patients with epidemiological connections other than place of home residence were found in cases of infection with Achromobacter, Ralstonia and Pandorea species. Shared strains of B. multivorans were found in a sibling pair, an unrelated pair with no temporal overlap in positive cultures and in 4 patients with no clear opportunities for cross infection to have occurred.

Conclusions Prevalence of EP is low at our centre but is slowly increasing. History of EP infection appears to be a risk factor for infection with other EPs. Shared strains of Achromobacter, Ralstonia and Pandorea species have been identified in our centre in patients with epidemiological connexions. Numbers are too small to establish whether cross infection or a common environmental source is responsible.

### Abstract P275 Table 1 Prevalence of Gram-negative bacterial emerging pathogens at Manchester Adult Cystic Fibrosis Centre 2013 and 2014

<table>
<thead>
<tr>
<th>Organism</th>
<th>Prevalence October 2013, % (number of patients)</th>
<th>Prevalence October 2014, % (number of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkholderia multivorans</td>
<td>6.4 (23)</td>
<td>6.2 (23)</td>
</tr>
<tr>
<td>Achromobacter species</td>
<td>4.5 (16)</td>
<td>5.1 (19)</td>
</tr>
<tr>
<td>Stenotrophomonas maltophilia</td>
<td>3.4 (12)</td>
<td>4.6 (17)</td>
</tr>
<tr>
<td>Pandorea species</td>
<td>2.2 (8)</td>
<td>2.4 (9)</td>
</tr>
<tr>
<td>Ralstonia species</td>
<td>1.4 (5)</td>
<td>1.9 (7)</td>
</tr>
</tbody>
</table>

#### P276 THE PREVALENCE OF TICARCILLIN HYPER-SUSCEPTIBLE PSEUDOMONAS AERUGINOSA ISOLATES FROM NON CYSTIC FIBROSIS BRONCHIECTASIS PATIENTS COMPARED TO PATIENTS WITH CYSTIC FIBROSIS AND CONTROLS

1IT Hettiarachchi, 1T O’Sullivan, 1M Wootton, 1J Duckers, 1R Dhillon. Public Health Wales, Cardiff, UK; 2Cardiff University, Cardiff, UK; 3Cystic Fibrosis Centre, University Hospital of Llandough, Cardiff, UK

10.1136/thoraxjnl-2015-207770.412

Background and aims Pseudomonas aeruginosa (PsA) is associated with considerable morbidity and mortality in Non-Cystic Fibrosis bronchiectasis (NCFB) and Cystic Fibrosis (CF) patients. Ticarcillin, a carboxypenicillin, is occasionally used in NCFB and CF to treat pulmonary exacerbations. In CF, a subpopulation of PsA exists that is hypersusceptible to ticarcillin (Tichs) \textit{in vitro}, (minimum inhibitory concentration [MIC] <4 μg/ml). This phenotype, is associated with reduced MICs to β-lactams, fluoroquinolones, tetracyclines and a degree of resistance to aminoglycosides.

The aim of this study was to investigate whether this Tichs strain exists in NCFB patients and compare this to the prevalence rates from CF and control cohorts. We also assessed whether this strain correlated with enhanced susceptibility to temocillin and other anti-pseudomonal antibiotics.

Methods 18 isolates of PsA from NCFB patients, 23 PsA isolates from CF patients and 18 PsA isolates from controls with no chronic lung disease were analysed. MICs for each isolate were determined by agar dilution using ISO20776-1 for the antibiotics listed in Table 1 and interpreted using EUCAST breakpoints.

Results The NCFB isolates had the highest prevalence of the Tichs strain of the three cohorts we tested, with a prevalence of 76%, compared to a prevalence of 48% in the CF cohort and 0% in the controls. Resistant strains of PsA were more prevalent in the CF cohort compared to the NCFB and control cohorts, except for temocillin and ticarcillin where the CF and NCFB cohorts had lower MICs compared to the control cohort (Table 1).

The Tichs strain in NCFB and CF was associated with reduced MICs to all antibiotics apart from ciprofloxacin in comparison to the non-Tichs strain. In CF, the Tichs strain was also associated with increased MICs to gentamicin.

Conclusion Our data supports the existence of a Tichs strain of PsA in NCFB patients, which existed in greater prevalence compared to our CF cohort. This appears to correlate with reduced MICs to temocillin, to which PsA would normally be resistant.
Therefore, temocillin may provide a useful alternative to the current anti-pseudomonal antibiotics in treating NCFB and CF patients.

**Abstract P276 Table 1**  
MIC range, MIC 50, MIC 90 and% resistant *P. aeruginosa* isolates for Cystic Fibrosis (CF), Non Cystic Fibrosis Bronchiectasis (NCFB) and controls (C).

<table>
<thead>
<tr>
<th></th>
<th>Meropenem</th>
<th>Ceftazidime</th>
<th>Ticarcillin</th>
<th>Temocillin</th>
<th>Ciprofloxacin</th>
<th>Gentamicin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MIC Range</strong></td>
<td>CF NCFB C</td>
<td>CF NCFB C</td>
<td>CF NCFB C</td>
<td>CF NCFB C</td>
<td>CF NCFB C</td>
<td>CF NCFB C</td>
</tr>
<tr>
<td></td>
<td>0.008-16</td>
<td>0.008-16</td>
<td>0.01-25</td>
<td>0.25-128</td>
<td>2-16</td>
<td>128-64</td>
</tr>
<tr>
<td></td>
<td>0.032-8</td>
<td>0.032-8</td>
<td>0.125-64</td>
<td>0.125-64</td>
<td>0.064-4</td>
<td>64-256</td>
</tr>
<tr>
<td><strong>MIC 50</strong></td>
<td>0.5</td>
<td>0.125</td>
<td>4</td>
<td>1.5</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>0.0125</td>
<td>0.125</td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>0.25</td>
</tr>
<tr>
<td><strong>MIC 90</strong></td>
<td>4</td>
<td>1</td>
<td>8</td>
<td>16</td>
<td>128</td>
<td>128</td>
</tr>
<tr>
<td></td>
<td>0.4</td>
<td>1</td>
<td>8</td>
<td>16</td>
<td>128</td>
<td>128</td>
</tr>
<tr>
<td><strong>Resistant %</strong></td>
<td>21%</td>
<td>6%</td>
<td>28%</td>
<td>12%</td>
<td>36%</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td>18%</td>
<td>6%</td>
<td>28%</td>
<td>12%</td>
<td>36%</td>
<td>18%</td>
</tr>
<tr>
<td><strong>Sensitive %</strong></td>
<td>79%</td>
<td>94%</td>
<td>72%</td>
<td>68%</td>
<td>64%</td>
<td>82%</td>
</tr>
<tr>
<td></td>
<td>32%</td>
<td>94%</td>
<td>72%</td>
<td>68%</td>
<td>64%</td>
<td>82%</td>
</tr>
<tr>
<td><strong>EUCAST BP</strong></td>
<td>Ss 2, R=8</td>
<td>Ss 8, R=8</td>
<td>Ss 16, R=16</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Ss 8, R=8</td>
<td>Ss 8, R=8</td>
<td>Ss 16, R=16</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Ss 16, R=16</td>
<td>NA</td>
<td>NA</td>
<td>37%</td>
<td>53%</td>
<td>93%</td>
</tr>
<tr>
<td></td>
<td>Ss 3, R=16</td>
<td>NA</td>
<td>NA</td>
<td>37%</td>
<td>53%</td>
<td>93%</td>
</tr>
</tbody>
</table>

**P277**  
**PHYSIOLOGICAL RESPONSE TO EXERCISE IN AN ADULT CYSTIC FIBROSIS POPULATION: INVESTIGATING THE RELATIONSHIP BETWEEN HRR AT ANAEROBIC THRESHOLD AND FEV1% PREDICTED**

G Comber. Royal Wolverhampton NHS Trust, Wolverhampton, UK

10.1136/thoraxjnl-2015-207770.413

**Introduction**  
Cystic Fibrosis (CF) is an autosomal, recessive disease characterised by a mutation or dysfunction. Patients suffer a number of complications caused by poor sodium and chloride transport across cell membranes leading to viscous secretions. The disease is life limiting and around 85% of these early deaths are a result of respiratory failure with the most accurate prognosis marker being maximum volume of oxygen utilisation (VO2 max). This parameter is affected by a number of factors and can be increased or preserved through correct exercise prescription. For maximal benefits exercise should be targeted around anaerobic threshold however this is not easily identifiable during regular activities.

**Method**  
15 patients with CF underwent Cardiopulmonary exercise testing (CPET) to establish whether there was a significant correlation between Forced Expiratory Volume in one second percent predicted (FEV1%) and Heart Rate Reserve (HRR) at Anaerobic Threshold (AT) as a method of giving an easily monitored parameter (Heart Rate) as a target during exercise, for a given severity of lung disease, to gain maximal benefits from the activity.

**Results**  
The correlation between FEV1% and HRR at AT was found to be very weak, r (13) = 0.269, p > 0.05 however there was a strong correlation between FEV1% and Maximum volume of utilised oxygen percent Predicted (VO2 max%), r (13) = 0.601, p < 0.05.

**Discussion**  
This study shows that FEV1% cannot be used as a predictor of HRR at AT, however the lack of correlation does show a narrow window for HRR in which patients with CF should aim in order to exercise near AT and ultimately improve their fitness and prognosis. The strong correlation between FEV1% and VO2 max% serves a great purpose in the that prognosis and 5 year mortality risk can be estimated from a lung function test widely available and frequently performed as opposed to CPET which is only available in specialist centres.

**P278**  
**IS THERE A ROLE FOR TELEMEDICINE IN CYSTIC FIBROSIS? A SYSTEMATIC REVIEW**

1RC Curry, 2ZH Hon, 3R Archer, 4MI Wildman. 1Adult CF Centre, Northern General Hospital, Sheffield, UK; 2Scharr, University of Sheffield, Sheffield, UK

10.1136/thoraxjnl-2015-207770.414

**Background**  
As a result of new medical advances people with CF are now able to live longer but still require frequent specialist care input and support. To cope with an ever increasing complex condition and demand for care, CF centres are having to rethink the way they work. Telemedicine is an evolving field which has the advantage of remote monitoring and real time review and may provide a solution.

**Objectives**  
To determine whether telemedicine has a role in the management of CF in terms of: 1) Feasibility and acceptability, 2) Early pulmonary exacerbation detection, and 3) Self-management and improving adherence to prescribed therapies.

**Methods**  
A systematic search was undertaken to identify relevant studies. This involved seven electronic databases, the top four peer reviewed journals reporting on CF and telemedicine, and the three major conference proceedings in CF and telemedicine. Clinical trial registers were searched to find ongoing studies as supplementary evidence. A mixed methods synthesis was performed to combine results from quantitative and qualitative studies.

**Results**  
34 studies in total were included in the results synthesis. These consisted of mainly small pilot and feasibility studies. There were 7 RCTs largely reporting interim results rather than efficacy data. Rates of adherence to telemedicine varied between 10.16 to 59% but were generally poor with barriers including frequent measures being a burden, forgetting, and denial of results. There was a general consensus that pulmonary exacerbations can be detected early but no statistical tests of significance performed. There were also only 2 studies predominantly reporting qualitative evidence. After corroborating the results using thematic synthesis this led to 3 main themes (expectations, technical aspects, and impacts of telemedicine) linked to these were barriers and facilitators.
Conclusion The findings indicate that telemedicine in CF is feasible but the uptake amongst people with CF may be challenging. This is probably not surprising since adherence to treatment is often poor. Nevertheless telemedicine has the potential to play an important role in the early detection of pulmonary exacerbations and further studies are required.

**P279** THE FEMALE DISADVANTAGE IN UK CF REGISTRY DATA 2008–2013

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Introduction and objectives The UK Cystic Fibrosis (CF) registry has been in its current form since 2006 offering annual review data comprising of detailed demographic and clinical information on 99% of the UK CF population (>10,000 individuals). Whilst widely accepted that FEV1 and BMI are well-validated predictors of disease severity and outcome, the role of gender in CF remains debated. In some studies Pseudomonas aeruginosa infection occurred earlier in females with a resulting deterioration in FEV1. Here, we use CF registry data (2008–2013) to assess whether a female disadvantage in FEV1 or BMI exists in the UK population and whether PaS status differs by gender. This is the most complete UK CF registry gender-based analysis to date.

Methods and results Cross-sectional analysis of data from 2010 and 2013 supported decreased female survival (decreasing female prevalence with sequential age groups; 2013 p = 0.0001). It also highlighted lower BMI percentiles and more underweight (BMI <19) individuals amongst females (21.9%; males 13.6%; p = <0.0001), even when adjusted for lung function.

Females had worse lung function compared to males, particularly in adolescence; (females: mean FEV1 71.3% at 16–19 yrs (CI 69.2–73.4), males: 78.9% (CI 76.9–81.0); p < 0.0001).

Females had higher absolute rates (57.1% on any intravenous antibiotics; 44.8% males) and greater total duration of intravenous antibiotic use across all adult age groups (p <). Females had higher rates of CF-related diabetes from 16–29 years (females 28.2%, males 17.7%; p < 0.0005), itself independently associated with worse prognosis.

On full analysis from 2008–2013 the age at which chronic PaS was first reported occurred earlier in females (mean 15.5 yrs 95% CI 14.9–16.1) than males (16.7 yrs; 95% CI 16.1–17.3) p = 0.01.

Conclusions Disease severity appears worse in CF females compared to males on cross-sectional analysis of data from 2010 and 2013. Females have earlier PaS infection and lower BMI, both of which are individually associated with worse outcomes and increased intravenous antibiotic use. Females also have reduced lung function, and receive more treatment. These data suggest a persistent and measurable gender difference in the UK CF population which we aim to explore more closely in longitudinal analysis.

**P280** A SINGLE CENTRE EXPERIENCE OF SPONTANEOUS CLEARANCE OF MYCOBACTERIUM ABSCESSUS IN CYSTIC FIBROSIS PATIENTS

HD Green, PI Bany, R Bright-Thomas, AM Brennan, AK Webb, R Lord, A Horley, AM Jones, University Hospital of South Manchester, Manchester, UK

Introduction The Mycobacterium abscessus complex is an emerging group of pathogens, which pose significant management challenges in CF. Current guidelines specify treatment is indicated in patients with repeated sputum culture positivity alongside radiological or clinical deterioration. However, identifying NTM as the cause of deterioration in the polymicrobial CF lung is challenging. Additionally, M. abscessus complex isolates are usually multi-resistant, requiring lengthy and complex treatment regimens. Whether to treat patients based on culture results alone is contentious and approaches differ between centres. Here we analyse our experience of M. abscessus at a large UK adult CF centre.

Methods All patients with 1 or more positive sputum culture for M. abscessus since 2010, and minimum of 1 mycobacterial culture and 1 year of follow-up since first positivity were included. Anti-mycobacterial treatment and culture results following first positivity were recorded. M. abscessus eradication was defined as 4 consecutive negative cultures spanning at least 1 year.

Results 21 patients were included. Of these, 6 (29%) have received/are receiving, anti-mycobacterial therapy based on clinician diagnosis of M. abscessus pulmonary disease. All 6 currently remain culture positive. Of the 15 remaining patients, 6 are consistently culture positive (duration 12 months - 5 years), but do not have evidence of NTM pulmonary disease. Spontaneous clearance of M. abscessus from sputum has occurred in 7 patients (Table 1). Of these, 5 (71%) had ≥3 positive cultures including 1 patient with 5 positive samples spread over 2 years and 1 patient with 5 positive samples spread over 9 months. In 2 patients infection status cannot yet be confirmed as these patients have ≤4 mycobacterial culture results following their initial positive result.

Abstract P280 Table 1 Mycobacterium abscessus Sputum Culture and Treatment Status of Patients Attending Manchester Adult Cystic Fibrosis Centre

<table>
<thead>
<tr>
<th>Status of Treatment</th>
<th>Numbers (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistently culture positive with history of treatment</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>Persistently culture positive but never treated</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>Spontaneous clearance from sputum</td>
<td>7 (36.8)</td>
</tr>
<tr>
<td>Total number of patients</td>
<td>19</td>
</tr>
</tbody>
</table>

NB: 2 patients with <4 follow up sputum cultures were excluded from this table.

Conclusion Patients may spontaneously clear M. abscessus from their sputum, even with a history of multiple positive cultures over many months. If patients are treated on culture results alone there is a risk of initiating potentially unnecessary, lengthy and poorly tolerated treatment. Our results suggest that adhering to clinical guidelines of recognising clinical deterioration secondary to M. abscessus remains paramount before commencing treatment and assessment of treatment success without control data may be very misleading.
Poster sessions

**P281** THE EFFECTIVENESS OF ACUPUNCTURE IN MANAGING SYMPTOMS IN CF ADULTS

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10.1136/thoraxjnl-2015-207770.418

Introduction and objectives People with cystic fibrosis (CF) experience a wide spectrum of symptoms, both physical and psychological, which are often troublesome and can result in significantly impaired quality of life. Acupuncture has a strong evidence base in the treatment of a wide variety of symptoms, however there is currently very limited evidence for its role in the management of symptoms in people with CF. The objective of this pilot study was to provide preliminary evidence of the effectiveness and patient acceptance of this treatment in our large regional adult CF centre.

Methods In this observational prospective study, we offered acupuncture to CF inpatients attending our large regional adult CF centre if they were suffering from range of symptoms. Patients were asked to specify the symptoms being treated and its severity before and after treatment, as well as whether treatment achieved the desired outcome, whether they suffered any ill effects, whether it is a valuable service and whether they feel we should continue to offer acupuncture to patients. They were also offered the option of making free-text comments on their experience of the service.

Results 106 patients were included over a 12-month period. 50 patients were treated for pain (back/neck/shoulder pain, n = 28; unspecified location, n = 12; headache, n = 5; chest pain, n = 4, toe pain, n = 1) with pain significantly reducing after treatment (median severity 7 (IQR 6–8) vs. 4 (IQR 3–5), p < 0.001). 25 patients were treated for stress/anxiety with symptoms significantly reducing after treatment (median severity 8 (IQR 7–9) vs. 5 (IQR 3.6–6), p < 0.001). 10 patients were treated for breathlessness/tight chest with symptoms significantly reducing after treatment (median severity 7 (IQR 6–8) vs. 5 (IQR 4–6), p = 0.001). 21 patients were treated for a range of other symptoms including low energy levels, reduced appetite and constipation. 95 patients reported that treatment had achieved the desired result and 10 patients reported that it was too early to tell. 1 patient felt ‘a bit sick’ after treatment, but no other adverse effects were reported. All patients felt that acupuncture was a valuable service and should continue to be offered. 30 patients commented that the service should be available more frequently.

Conclusions Acupuncture was greatly appreciated by CF adults, with significant improvements in a wide variety of symptoms. A randomised controlled study is required to confirm these benefits.

**P282** THE DESIGN AND VALIDATION OF A NOVEL SEMIAUTOMATIC LUNG NAVIGATION PLATFORM

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Introduction In the era of lung cancer screening, tissue acquisition of peripheral lung lesions remains a challenge. We have developed a 3D electromagnetic navigation platform with airway segmentation and virtual bronchoscopy using a open source 3D slicer environment.

Methods The open source visualisation software (3D Slicer www.slicer.org) created a detailed airway segmentation and virtual bronchoscopy model from acquired CT images. A magnetic field emitter board provides tracking of a semiautomatic locatable sensor probe (SALP) in the working channel of the bronchoscope with always-on tip tracked sensor and can be steered both manually and automatically with joy stick, for accurate localization of peripheral lung lesion.

An extensive ex-vivo evaluation was performed in a breathing lung model that was developed using inflatable plasticized pig lungs in a negative-pressure. Following this, in-vivo real time navigation in a live porcine model using a selection of novel radioopaque fiducials placed endobronchially into distal airways.

Results After completion of a selection of experiments using the breathing pig lung model, fiducials were placed endobronchially in our live porcine model. Thereafter, CT images were used to create a virtual airway 3D segmentation model. After multiplaner re-construction, land mark based registration was performed to align the CT and anaesthetised porcine. Manual and automatic navigation with the bronchoscope containing the SALP was performed. The average navigation distance covered was 85.3 mm. The navigational system accurately determined 84% of the navigation points within the airways.

Conclusion Our navigational platform is inexpensive and open source and is the first to utilise SALP. In our model, there is good agreement between the position of the sensor probe during bronchoscopic navigation and as visualised in virtual bronchoscopy. Further work is being carried out to improve registration and accuracy of the navigational system before a pilot study in patients with peripheral lung nodules.

**P283** HYPERPOLARISED GAS MRI – A PATHWAY TO CLINICAL DIAGNOSTIC IMAGING

1JM Wild, 2G Collier, 1H Marshall, 1L Smith, 3G Norquay, 1AU Swift, 1FC Horn, 1F Chan, 1NJ Stewart, 1LC Hutchinson, 1M Rao, 1J Sabroe, 2RN Iven, 1A Horsley, 3S Siddiqui, 1K Ugomba, 1R Lawson. 1University of Sheffield, Sheffield, UK; 1North Western Lung Clinic, Manchester, UK; 2University of Leicester, UK; 3Sheffield Teaching Hospitals Trust

10.1136/thoraxjnl-2015-207770.419

Introduction Despite the excellent functional sensitivity of hyperpolarised gas MRI to early lung disease, clinical uptake of the technique has to date been hindered by patents, regulatory classification, availability of 51He and access to polariser technology. However, many of these constraints have been alleviated in recent years, and 129Xe MRI is now providing high quality lung images at relatively low cost. In January 2015 UK regulatory approval for the manufacture of hyperpolarised gases for routine clinical lung imaging was obtained in Sheffield. Here we present a case series as an overview of the clinical questions that this technology can help resolve in various respiratory indications.

Methods More than 20 patients (aged 13 to 74) have been clinically referred to date with HP gas MRI in Sheffield to date from NHS hospitals across the UK. Clinical histories include non-CF bronchiectasis (scanned before and after a 2 week course of IV antibiotics), COPD for consideration for LVRS/EB valves,
complex asthma (scanned before and after bronchodilator inhalation), CF, patients with poor gas transfer but well-preserved lung parenchyma on CT, IPF overlapping with emphysema.

Results
Figure 1 shows example images from a cross-section of patients scanned, details of the individual cases will be expanded upon. No adverse events related to imaging were reported. In terms of imaging workflow, scan time average was between 30 min and 1 h 30 min. Patients have been referred from clinics within a 100 km radius and we are also active in enabling novice sites further afield with the technology.

Conclusion
Hyperpolarised gas MR provides sensitive, regional images of lung function which can be used to aid in clinical decision making on an individual patient basis. With improvements in gas polarisation, MR hardware and image acquisition techniques routine clinical lung imaging with the cheaper gas isotope $^{129}$Xe is also now possible and large scale clinical evaluation of these methods in patient populations are now underway as part of clinical work up.

We recently presented a clinically appropriate dynamic oxygen-enhanced MRI (dOE-MRI) protocol. In this work, we interpret dOE-MRI data with a novel physiological model of gas exchange that maps the regional distribution of lung ventilation and perfusion, simulating results from a standard V/Q scan.

3D dOE-MRI data were acquired using a 1.5 T Philips scanner as in: a 5 min baseline $T_1$ acquisition, followed by a 15 min dynamic acquisition, during which the subject breathed 100% O$_2$ for the middle 5 min. Total scan time is under 30 min throughout which the subject breathes normally. The partial pressure of oxygen in the alveolar compartment was derived as proposed in and maps of regional alveolar ventilation and perfusion were produced using a novel two-compartmental model of gas exchange based on.

Figure 1 shows an example of whole-chest ventilation and perfusion maps from a healthy subject overlaid on a single volume of the acquired MRI (left column). The same maps are displayed as anterior/posterior and right/left anterior oblique projections (right column), equivalent to those achieved with V/Q scintigraphy.

Estimation of alveolar ventilation and perfusion distribution from 3D dynamic OE-MRI is feasible and can be obtained under clinically acceptable conditions using standard radiological equipment without ionising radiation risks. This approach opens the possibility for regional assessment of lung physiology using a single short scanning session.

REFERENCES
HELIUM MAGNETIC RESONANCE IMAGING IDENTIFIES REGIONAL VENTILATION, PERFUSION AND MICROSTRUCTURE ABNORMALITIES IN A CASE OF “HORSE-SHOE” LUNG

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10.1136/thoraxjnl-2015-207770.421

Introduction Helium magnetic resonance imaging (3He MRI) provides functional information on lung ventilation, perfusion and microstructure. We describe use of 3He MRI to assess lung function in a patient with “horse-shoe” lung.

Case presentation EB is a 46 year old female with congenital lung abnormalities diagnosed during infancy. Chest x-ray confirmed an abnormal right upper lobe (RUL). Pulmonary arteriography reported hypoplastic RUL vessels. Bronchoscopy confirmed tracheal stenosis, and cardiac catheterisation reported an abnormal pulmonary arterial pattern. A diagnosis of congenital lung anomalies along with asthma was made during her childhood. Throughout her life her condition has been characterised by recurrent severe respiratory tract infections requiring hospitalisation.

Recent CT chest confirmed right lung hypoplasia a deformed right main bronchus, moderate hypoplasia of the right main pulmonary artery and severe hypoplasia of RUL pulmonary vessels.

An isthmus joins the two lungs consistent with “horse-shoe lung”. Ventilation-perfusion scan reported 26% functioning right lung. Bronchoscopy confirmed tracheal and right main stem stenosis with left main stem bronchomalacia.

Surgical resection is an option for ‘horse-shoe’ lung characterised by recurrent infections. In this context, we proceeded to 3He MRI to obtain more detailed functional information.

Abstract P285 Figure 1

Results of 3He functional MRI

Communication between the right and left lungs was visualised (Figure 1). In the right lung, ventilation was reduced with increased heterogeneity (Figure 1a,
f). And perfusion notably reduced, in the RUL (Figure 1c. 3He apparent diffusion coefficient (ADC), which estimates acinar airway dimensions, was elevated and heterogeneous (Figure 1c), consistent with hypoplasia. The left lung was well ventilated and perfused with normal ADC values.

Conclusion 3He MRI shows promise in functional analysis of “horse-shoe” lung with hypoplasia. This can prove useful in surgical assessment of these patients and therefore improve their management.

REFERENCES
1 Dikensoy O, Kervancioglu R, Bayram NG, Eker M, Ekinci E. Horseshoe lung with scimitar syndrome and pleural lipoma. / Thorac Imaging 2006;21(1):73–5

P286 CORRELATIONS OF FUNCTIONAL MULTI-NUCLEAR MR IMAGING INDICES WITH PULMONARY FUNCTION TESTS IN THE ASSESSMENT OF IDIOPATHIC PULMONARY FIBROSIS

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Disease progression in idiopathic pulmonary fibrosis (IPF) is variable and unpredictable. Declining forced vital capacity (FVC) and transfer factor (TLCO) of 10% and 15% respectively are common markers of deterioration, but may be insufficiently sensitive to prognosticate and rely on serial measurements. Echocardiography provides screening for pulmonary artery hypertension (PAH), but is insensitive to pulmonary haemodynamic change before PAH is already apparent. Recently established Magnetic Resonance Imaging (MRI) techniques may provide insight into evaluating IPF. Greater septal thickness as measured by hyperpolarised xenon in patients with IPF compared with with healthy volunteers was previously demonstrated.1 Here, we investigate the correlation between MRI indices, including hyperpolarised gas ventilation and gadolinium-enhanced perfusion, with pulmonary function parameters in a pilot cohort of subjects with IPF.

Six subjects with IPF were recruited. T1 mapping was performed in all subjects. Imaging sequences following inhalation of hyperpolarised 3-Helium was used to calculate estimates for ventilated volume percentage (VV%) and coefficient of variation of ventilation (CoV). Dynamic contrast-enhanced lung perfusion MRI was performed for pulmonary haemodynamic assessment. All subjects underwent pulmonary function testing (PFTs).

VV% strongly correlated with transfer coefficient (KCO) with R = 0.955; p = 0.003, but also FEV (forced vital capacity)/FVC ratio. CoV is a measure of regional ventilation heterogeneity and trended to correlation with transfer factor TLCO (R = -0.775; p = 0.108). Time to peak (TTP) of the gadolinium perfusion signal showed negative correlation with FVC (R = -0.909 with p < 0.05) and trended to a negative correlation with TLCO (R = -0.766, p = 0.131). All p values two-tailed.

TTP correlation with PFT values suggests that changes in pulmonary haemodynamics may be detectable at an early stage of the disease process. VV% and helium mapping may provide information about regional airways ventilation in IPF.

MRI based assessments could prove useful in assessing different aspects of lung structure-function for use in future research and potentially in clinical assessment of patients with IPF. Sequential imaging with concurrent PFT and echocardiography would help to further assess the applicability of evolving MRI techniques.

P287 OFFLINE FRACTIONAL EXHALED NITRIC OXIDE AND BREATH FREQUENCY

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Introduction/objectives Fractional exhaled nitric oxide (FeNO) is a noninvasive method of assessing airway inflammation and recommended by NICE (2014) to aid asthma diagnosis and management. Offline measurement techniques demonstrate comparable results to online and are more practical in certain clinical settings, particularly in young children who struggle with online measurements. International guidelines (ATS/ERS 2005) recommend targets for pressure and flow but not for the number of breaths per sample. Young children may take multiple breaths to complete offline reservoir filling, but whether this influences results due to contamination of the sample with ambient gas from equipment deadspace has not been assessed. Our aims were to investigate the magnitude of such effects and form a predictive equation for how increasing breath number dilutes offline measurements.

Methods A prospective observational study was undertaken recruiting 20 volunteers aged 18–42 years (13 female). FeNO was measured online (Medisoft Exp’Air 2001) and offline following exhalation into a one-litre Tedlar bag using one, five or ten breaths to complete bag filling. Airway pressure was maintained above 5 cmH2O to ensure velum closure and expiratory flow at 50 (+/-5) ml/s.

Predicted percentages of offline FeNO relative to online were calculated by:

• 100 – ((equipment deadspace (53 mls) x no of breaths)/bag volume) x100
• Predicted offline values were compared to measured.

Results The median (IQR) online FeNO in parts per billion (ppb) was 24 (14–30) ppb. There was a significant reduction in offline FeNO with increasing breath number (p < 0.0001). Median (IQR) offline FeNO of 1-breath (22 (15–32) ppb) was
not significantly different to online FeNO (p = 0.51). Median (IQR) offline FeNO of 5-breaths was 16 (7–22) ppb and 10-breaths 13 (5–19) ppb, lower than online FeNO (p = 0.03 and p = 0.005 respectively).

The predicted offline values are compared with measured offline values, expressed as a percentage of online, in Table 1.

<table>
<thead>
<tr>
<th>Predicted FeNO as a percentage of online</th>
<th>Offline as a percentage of online FeNO (median)</th>
<th>Interquartile range</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 breath</td>
<td>94.7%</td>
<td>73.1–120.1%</td>
<td>0.81</td>
</tr>
<tr>
<td>5 breaths</td>
<td>73.5%</td>
<td>42.9–92.8%</td>
<td>0.58</td>
</tr>
<tr>
<td>10 breaths</td>
<td>42%</td>
<td>30.9–67.8%</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Conclusion One-breath offline collection methods had comparable results to online FeNO measurements, but higher breath number resulted in lower values likely due to sample contamination with ambient gas and dilution of nitric oxide. These results suggest that multiple breaths should not be used to obtain an offline FeNO result.

**P288 PREVALENCE OF NON-PULMONARY EMBOLISM DIAGNOSES ON CT PULMONARY ANGIOGRAPHY. ONE YEAR EXPERIENCE IN A DISTRICT GENERAL HOSPITAL**

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Introduction and objectives CT pulmonary angiography (CTPA) is recommended as the investigation of choice for suspected pulmonary embolism (PE). Even in appropriately risk-assessed groups, CTPA often proves negative for PE, but additional diagnostic information is still provided by technically adequate scans. We reviewed our CTPAs to assess technical quality and final diagnosis.

Methods Retrospective review of CTPAs performed in 2013 in a 588 bed district general hospital. All patients selected were considered either intermediate or high probability for PE based on Wells PE clinical risk scoring. Only imaging performed on patients presenting as acute admissions was reviewed. Patients under the age of 16 were excluded, but no upper age limit was applied in order to be fully representative of our patient population and clinical practice. Scans were assessed for their diagnostic and technical quality by the reporting radiologist.

Results 720 CTPAs were selected for review. Patient mean age 66.4 (range 17–103). PE was demonstrated in 135 studies (18.8%). 111 CTPAs (15%) excluded PE and were otherwise normal. 355 CTPA (49%) excluded PE but revealed an alternative diagnosis. Of these, cardiac failure (26%), emphysema (19%), pneumonia (16%), interstitial lung disease (10%), bronchiectasis (9%) and pleural disease (8%) were the most frequently reported clinically significant diagnoses. 119 CTPAs were considered technically inadequate to exclude PE based on insufficient contrast opacification, however an alternative explanatory diagnosis was seen in 76 (64%) of these. In the remaining 43 cases no diagnosis was reported, and only 2 patients had repeat CTPA performed during the same admission. Four patients from the non-diagnostic group represented within a 3 month follow up period and were subsequently proven to have PE on repeat CTPA.

Conclusions CTPA can provide an alternative diagnosis in the majority of cases even if PE is excluded. Of these, cardiac failure and emphysema were the most common diagnoses. Physicians must be vigilant for non-diagnostic scans and arrange further tests as appropriate, as in our series 4/43 patients with technically inadequate imaging on initial presentation subsequently represented with PE.
Introduction CT-guided lung biopsy is a widely used and established technique for the diagnosis of lung lesions, and several risks are well described. The most common complication is pneumothorax, occurring in approximately 20% of cases. We aimed to characterise the risk of post-procedure pneumothorax in our patient population, and determine whether lung function indices correlate with the incidence of pneumothorax.

Methods Patients undergoing CT-guided biopsy of intraparenchymal lesions from January 2014–2015 were retrospectively identified. Patients were stratified in to those with and without post-procedure pneumothorax. Spirometry and transfer factor for carbon monoxide (TLCO) were reviewed and compared using an unpaired t test.

Results 111 procedures were performed in 111 patients (53 men 58 women; mean age 70.4 years; range 40 to 88), all done for suspected malignancy. Pneumothorax was identified in 25 patients post biopsy (21%); age range 61 to 87; mean ± SD age, 73.4 ± 6.7), 12 female (48%) and 9 patients (36%) had emphysema.

Of the 25 patients with pneumothorax, FEV1 ranged from 32 to 115% predicted (80.5% ± 23.57%) and FVC ranged from 54 to 125% (91.9% ± 19.1%). TLCO was available for 14 patients, range 34 to 99% predicted (71.5% ± 19.2%). Of the 86 patients with no pneumothorax, FEV1 ranged from 27 to 126% predicted (73.9% ± 29.9%) and FVC ranged from 38 to 139% predicted (85% ± 21.9%). TLCO was available for 50 patients (58%), range 31 to 108% predicted (63.2% ± 18.9%).

There was no significant difference in FEV1 (p = 0.199), FVC (p = 0.109), FEV1/FVC ratio (0.99) or TLCO (0.176) between the two groups.

In patients developing pneumothorax, those requiring a chest drain (6/25, 24%) showed no significant difference in FEV1 or FVC (p = 0.76 and p = 0.41 respectively) to those managed conservatively. TLCO however was significantly lower in patients requiring chest drain insertion (79% ± 16.1% vs. 52.8% ± 12.8%, p = 0.002).

Conclusion From our patient group, spirometry data and TLCO showed no correlation with the frequency of pneumothorax. In those patients developing pneumothorax, a low TLCO may predict the need for invasive management.

Abstract P289 Table 1 Results of 135 patients undergoing EBUS-TBNA as a first line investigation for mediastinal and/or hilar lymphadenopathy

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients (n)</th>
<th>Patients with diagnostic test</th>
<th>Nodes sampled</th>
<th>Number of total passes</th>
<th>Inadequate samples (n)</th>
<th>Diagnostic samples (n)</th>
<th>Diagnosis of samples</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: IMHL</td>
<td>135</td>
<td>10 (97%)</td>
<td>102</td>
<td>110</td>
<td>3</td>
<td>103</td>
<td>Reactive: 15 (100%) Non-caseating granulomas: 1 (10%) Malignant: 1 (10%)</td>
</tr>
<tr>
<td>1a: IMHL with no radiological suggested diagnosis</td>
<td>12</td>
<td>12 (100%)</td>
<td>15</td>
<td>15</td>
<td>0</td>
<td>15</td>
<td>Reactive: 12 (100%) Non-caseating granulomas: 1 (10%) Malignant: 1 (10%)</td>
</tr>
<tr>
<td>1b: IMHL with radiologically suggested diagnosis</td>
<td>63</td>
<td>63 (98%)</td>
<td>279</td>
<td>300</td>
<td>7</td>
<td>293</td>
<td>Reactive: 63 (100%) Non-caseating granulomas: 1 (10%) Malignant: 4 (6%)</td>
</tr>
<tr>
<td>2: radiologically diagnosed likely lung cancer with mediastinal lymphadenopathy</td>
<td>10</td>
<td>10 (100%)</td>
<td>86</td>
<td>86</td>
<td>0</td>
<td>86</td>
<td>Reactive: 10 (100%) Non-caseating granulomas: 2 (20%) Malignant: 1 (10%)</td>
</tr>
<tr>
<td>3: other e.g. known/suspected malignancy (excluding lung), previous cancer diagnosis, post cancer treatment</td>
<td>32</td>
<td>32 (100%)</td>
<td>19</td>
<td>19</td>
<td>0</td>
<td>19</td>
<td>Reactive: 32 (100%) Non-caseating granulomas: 2 (20%) Malignant: 4 (6%)</td>
</tr>
</tbody>
</table>

P290 DO LUNG FUNCTION INDICES CORRELATE WITH RISK OF PNEUMOTHORAX FOLLOWING CT-GUIDED BIOPSY?
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Introduction and objectives The particle size distribution and the median mass aerodynamic diameter (MMAD) of an inhaled product are important characteristics which may influence the deposition of the drug in the lung and as a consequence may also affect its therapeutic index. We evaluated the relationship between in vitro MMAD and in vivo lung deposition (LD, expressed as fraction of the delivered dose) and the exhaled fraction (EF), using relevant literature from scintigraphic studies conducted in healthy volunteers and asthmatic patients. Moreover the relationship between the ratio of EF to LD and MMAD has been further assessed.

Methods Data from 21 studies in healthy volunteers (15 with pressurised metered dose inhalers (pMDI) and 6 with dry powder inhalers (DPI)) and 11 studies in asthmatic patients (8 pMDI and 3 DPI) have been evaluated. Asthmatic patients had a FEV1 >70% predicted, supporting pooling of the data with that of healthy volunteers.
Results
LD increased when MMAD decreased, so that when MMAD is about 1 μm the LD is more than 50% of the delivered dose and becomes markedly lower when MMAD approaches 4 μm. EF is low and did not change markedly. On the contrary, the ratio EF/LD is independent of the MMAD, suggesting that the EF is proportional to the LD and not affected by MMAD.

Conclusion
These data demonstrate that the EF/LD ratio is independent from the MMAD providing reassurance that a smaller particle size will not be associated with a higher exhaled fraction.

Difficult symptom control and breathlessness

M1 AN AUDIT OF ELECTRONIC OXYGEN PRESCRIBING AND OXYGEN SATURATION READINGS SHOWING A HIGH PREVALENCE OF RISK FACTORS FOR HYPERCAPNIA AND A HIGH INCIDENCE OF IATROGENIC HYPEROXAEMIA

P Whitemore, BR O’Driscoll. Salford Royal Foundation NHS Trust, Salford, UK

Background
BTS audits have shown that about 14% of UK hospital patients are on oxygen therapy at any given time but only half of these patients have a prescription or written order for oxygen use. Our 600 bed teaching hospital has electronic prescribing linked to an electronic bedside observations system (modified NEWS score). Hospital policy is to set a target oxygen saturation range for all in-patients. Patients score points if their oxygen saturation (SpO2) falls below their target range or if SpO2 rises above their target range on oxygen therapy.

Methods
We audited oxygen prescribing and SpO2 for all patients treated on medical and surgical wards during the month of December 2014. All data was contained within the electronic patient record.

Results
We audited 80,391 sets of observations for 6,800 patients (2239 medical, 4561 surgical).

- 99.8% of all patients had an oxygen target range prescribed electronically
- 12.7% of all patients (18.9% of medical patients and 9.6% of surgical patients) had risk factors for hypercapnia with a prescribed target range of 88–92% or less
- Overall 90.6% of oxygen saturation measurements were within target range (or above the target range breathing air).
- 59.9% of measurements on oxygen and 97.2% of observations on air were within the target range.
- 3.7% of oximetry measurements were below the target range (7.9% of those on oxygen)
- 5.8% of all oximetry measurements were above the target range due to use of oxygen (32.2% of measurements on oxygen were above target range)
- For patients using oxygen therapy with target range 94–98% or 88–92%, the percent of measurements within range, below range or above range is shown in the Table 1
- 53.2% of observations on patients using oxygen with target range 88–92% showed SpO2 above target range

Conclusions
An oxygen target range is prescribed for almost all inpatients at this hospital but hyperoxaemia (with associated risk of hypercapnia) remains prevalent amongst patients on oxygen therapy, especially those who have been identified as at increased risk of hypercapnia. This has led to a revised educational programme for nursing staff with an emphasis on keeping patients within their target range.

M2 USING A TRANSPORTABLE OXYGEN CONCENTRATOR (TPOC) TO FACILITATE PROMPT AND SAFE HOSPITAL DISCHARGE

F Hamilton, a G Ludford, a j Bott. b Dolby Vivisol, Gatwick, UK; cKSS AHSN, South East England, UK

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Abstract
Using a transportable oxygen concentrator (TPOC) to facilitate prompt and safe hospital discharge

1FH a Milton, 2G Luxford, 2JB Bott. 1Dolby Vivisol, Gatwick, UK; 2KSS AHSN, South East England, UK

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Introduction  Whilst current guidelines state that patients must be clinically stable prior to commencing home oxygen, respiratory patients can be discharged with a supply of oxygen. Multiple errors are often found on the Home Oxygen Order Forms (HOOFs) for hospital discharges and equipment requirements are often subsequently changed, generating wasteful activity and costs. The aim was to establish whether a TPOC could be provided to specialist respiratory teams within hospitals to promote efficient and safe discharge for those patients requiring home oxygen.

Method  Three hospitals with established Home Oxygen Assessment and Review Services (HOSAR) were issued with TPOCs. The Home Oxygen Supplier trained the HOSAR clinicians on use, and supplied written documentation on safety. The clinicians identified appropriate patients based on clinical assessments and issued them with a TPOC. A HOOF was then sent to the supplier with appropriate equipment for the patient’s long term needs. On installation of this, the supplier removed the TPOC and another was issued to the hospital to enable an ongoing supply.

Results  Of those discharged with a TPOC and a subsequent HOOF, only 3% (n = 6) of patients required a modality change or HOOF update within the following month, compared to 40% (n = 33296) of all other HOOFs received (Figure 1).

The largest group of patients issued with a TPOC on discharge were clinically coded as COPD (40%), followed by those coded as Palliative Care (28%).

---

Abstract M1 Table 1

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Medical n = 2239</th>
<th>Surgical n = 4561</th>
<th>Total n = 6800</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription for oxygen target range</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target 94-98%</td>
<td>1804 (80.6%)</td>
<td>4177 (90.3%)</td>
<td>5981 (87.1%)</td>
</tr>
<tr>
<td>Target 88-92%</td>
<td>387 (17.2%)</td>
<td>415 (8.9%)</td>
<td>802 (11.8%)</td>
</tr>
<tr>
<td>Other target range</td>
<td>37 (1.7%)</td>
<td>25 (0.5%)</td>
<td>62 (0.9%)</td>
</tr>
<tr>
<td>No prescription</td>
<td>11 (0.5%)</td>
<td>4 (0.1%)</td>
<td>15 (0.2%)</td>
</tr>
<tr>
<td>Satsuration of patients with target range 94-98% or 88-92%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In range or above range breathing air</td>
<td>90.9% of 41,960</td>
<td>90.4% of 35,605</td>
<td>90.6% of 77,565</td>
</tr>
<tr>
<td>Below target</td>
<td>4.9%</td>
<td>2.3%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Above target on O2</td>
<td>4.4%</td>
<td>7.4%</td>
<td>5.8%</td>
</tr>
<tr>
<td>Patients with target 94-98% using oxygen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In target range</td>
<td>78.2% of 5,556</td>
<td>51.8% of 4,725</td>
<td>66.1% of 10,281</td>
</tr>
<tr>
<td>Below target</td>
<td>11.9%</td>
<td>5.6%</td>
<td>9.0%</td>
</tr>
<tr>
<td>Above target on O2</td>
<td>9.6%</td>
<td>42.3%</td>
<td>24.6%</td>
</tr>
<tr>
<td>Patients with target 88-92% using oxygen</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In target range</td>
<td>47.5% of 2,767</td>
<td>25.8% of 877</td>
<td>42.1% of 3644</td>
</tr>
<tr>
<td>Below target</td>
<td>4.9%</td>
<td>4.1%</td>
<td>4.7%</td>
</tr>
<tr>
<td>Above target on O2</td>
<td>47.5</td>
<td>70.2%</td>
<td>53.2%</td>
</tr>
</tbody>
</table>

Abstract M2 Figure 1  Number of patients discharged from hospital with a TPOC

Conclusion  The results demonstrate the practical uses of a TPOC for hospital discharge in clinically appropriate patients and a greater degree of control over the accuracy of ordering. A precise cost saving cannot be demonstrated as it is unclear how many bed days were saved, but it is clear that a reduction in wasteful activity by more accurate ordering would have reduced costs.

Discussion  By using staff trained on equipment and accurately completing HOOFs, combined with equipment readily available, transition from hospital to home can be both clinically accurate, time efficient and cost effective.

REFERENCE

M3  ANXIETY AND DEPRESSION IN PATIENTS WITH BREATHING PATTERN DISORDERS OR CHRONIC RESPIRATORY DISEASE

Background  Patients that have chronic respiratory disease (CRD) and breathing pattern disorders (BPD) have a higher prevalence of anxiety and depression than the general population. These patients have worse respiratory health outcomes and in addition, their psychological problems are often left undiagnosed and untreated. Little is known about how anxiety and depression varies between CRD and BPD.

Methods  This prospective study involved screening patients attending secondary and tertiary respiratory clinics over an eight-week period. Patients were asked to complete the Hospital Anxiety and Depression Scale (HADS), Short Form-12 (SF-12) and St. George’s Respiratory Questionnaire (SGRQ). Demographic data and spirometry were also collected. Our primary outcome measure was the difference in these scores between patients with CRD (asthma, bronchiectasis and chronic obstructive pulmonary disease) compared to BPD (vocal cord dysfunction and dysfunctional breathing).

Thorax 2015;70(Suppl 3):A1–A254
**Results** 43 patients (21 with CRD and 22 with BPD) completed questionnaires; mean (SD) age 55 (17) yrs, 32 female. The overall prevalence of borderline anxiety was 17% and clinically significant anxiety 37%. The overall prevalence of borderline depression was 15% and clinically significant depression 29%. Of the patients with CRD, 29% had anxiety and 29% depression. In the BPD cohort, anxiety and depression were found in 45% and 30% of patients respectively. The difference between these groups was not statistically significant (anx: $P = 0.42$; dep: $P = 0.19$). Independent predictors for anxiety and depression were higher SGRQ (anx: $P = 0.001$; dep: $P < 0.0001$), lower SF-12 Mental (anx: $P < 0.0001$; dep: $P < 0.0001$) and Physical (anx: $P = 0.042$; dep: $P = 0.0027$) Health Composite Scores, and lower FEV$_1$% predicted (anx: $P = 0.0043$; dep: $P = 0.016$).

**Conclusions** Anxiety and depression are present in a significant numbers of individuals in both CRD and BPD, with no difference between these groups, so efforts should be made to screen for psychological problems in patients with both CRD and BPD. Worse respiratory function and more symptoms are important contributing factors to patients’ risk of anxiety and depression.

**M4** ASSOCIATION OF DESCRIPTORS OF BREATHLESSNESS WITH DIAGNOSIS, SELF-REPORTED SEVERITY OF BREATHLESSNESS AND SELF-REPORTED DISTRESS DUE TO BREATHLESSNESS IN PATIENTS WITH ADVANCED CHRONIC OBSTRUCTIVE PULMONARY DISEASE OR CANCER

S Chowienczyk, S Javadzadeh, S Booth, M Farquhar. University of Cambridge School of Clinical Medicine, Cambridge, UK

10.1136/thoraxjnl-2015-207770.431

**Introduction and objectives** Verbal descriptors are important in understanding patients’ experience of breathlessness. The selection of breathlessness descriptors may depend on the severity of breathlessness.\(^1\) Our objective was to examine the association between selection of the breathlessness descriptors devised by Simon et al., with diagnosis, self-reported severity of breathlessness and self-reported distress due to breathlessness.\(^2\)

**Methods** We studied 132 patients grouped according to their diagnosis advanced COPD (n = 69) or advanced cancer (n = 63), self-reported severity of breathlessness: mild breathlessness (Numerical rating scale (NRS) $\leq 3$, n = 53), moderate breathlessness (4$\leq$NRS$\leq 6$, n = 59) or severe breathlessness (NRS $> 7$, n = 20), and distress due to breathlessness: mild distress (NRS $\leq 3$, n = 31), moderate distress (4$\leq$NRS$\leq 6$, n = 44) or severe distress (NRS $> 7$, n = 57). Patients selected three breathlessness descriptors. The relationship between descriptors selected and patient groups was evaluated by cluster analysis.

**Results** Cluster analysis identified six clusters of descriptors: ‘breathing restrictions’, ‘enough air’, ‘out of breath’, ‘air hunger’, ‘effort’ and ‘chest tightness’. Different combinations of clusters were associated with each diagnostic group. The association of clusters with patient groups differed depending on their severity of breathlessness and their distress due to breathlessness. The ‘air hunger’ cluster was associated with patients with moderate or severe breathlessness, the ‘chest tightness’ cluster was associated with patients with mild breathlessness. The ‘air hunger’ cluster was associated with patients with severe distress due to breathlessness.

**Conclusions** The relationship between clusters and diagnosis is not robust enough to use the descriptors to identify the primary cause of breathlessness. Further work exploring how use of breathlessness descriptors reflects the severity of breathlessness and distress due to breathlessness could enable the descriptors to evaluate patient status and target interventions.

**Abstract M4 Table 1** Association of clusters with diagnosis, with severity of breathlessness and distress due to breathlessness\(^1\)

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Cluster 1</th>
<th>Cluster 2</th>
<th>Cluster 3</th>
<th>Cluster 4</th>
<th>Cluster 5</th>
<th>Cluster 6</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Breathing restrictions</td>
<td>Enough air</td>
<td>Out of breath</td>
<td>Air hunger</td>
<td>Effort</td>
<td>Chest tightness</td>
</tr>
<tr>
<td>Diagnosis of advanced:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>COPD</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Severity of breathlessness (NRS):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (NRS $\leq$3)</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Moderate (4$\leq$NRS$\leq 6$)</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Severe (NRS $&gt; 7$)</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Distress due to breathlessness (NRS):</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild (NRS$\leq$3)</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Moderate (4$\leq$NRS$\leq 6$)</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Severe (NRS $&gt; 7$)</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>*</td>
</tr>
</tbody>
</table>

\(^1\) * indicates that the cluster is associated with the patient group.

**REFERENCES**


**M5** COMPARISON OF RESPIRATORY HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH INTRACTABLE BREATHLESSNESS DUE TO ADVANCED CANCER OR ADVANCED COPD

\(^1\)S Javadzadeh, \(^2\)S Chowienczyk, \(^3\)S Booth, \(^4\)M Farquhar. \(^1\)Department of Public Health & Primary Care, Cambridge, UK; \(^2\)University of Cambridge, Cambridge, UK

10.1136/thoraxjnl-2015-207770.432

**Introduction and objectives** Breathlessness is common in patients with advanced cancer and almost universal in advanced chronic obstructive pulmonary disease (COPD), but studies suggest their experiences of breathlessness vary. Our objective was to seek quantitative evidence of differences in respiratory health-related quality of life (HRQoL) between these groups using the Chronic Respiratory Questionnaire (CRQ) and to contribute to the debate on the validity of CRQ in patients with cancer.

**Methods** The CRQ-Original was completed within baseline interviews for a randomised control trial of a palliative intervention for breathlessness. Independent-Samples Mann-Whitney U Tests were performed to identify significant differences in median scores for the four CRQ domains (mastery, dyspnoea, emotional function, fatigue) in patients with advanced COPD (n = 73) or advanced cancer (n = 67). The Minimally Clinically
Important Difference (MCID) of 0.5 was applied to determine clinical significance.

**Results** Patients with advanced COPD scored lower across all four CRQ domains. This was statistically significant for the dyspnoea, mastery, and emotional functioning scores (p < 0.05), and clinically significant for latter two, suggesting poorer respiratory HRQoL (Table 1).

**Conclusions** Patients with breathlessness due to advanced COPD had worse respiratory HRQoL than those due to advanced cancer. There are three potential explanations for this finding: (1) there may be a greater burden of breathlessness in COPD due to condition-longevity, (2) the burden of breathlessness may be less in cancer due to the episodic nature of the symptom in malignant conditions, and (3) it may reflect variance in palliative referral thresholds by disease group. Our results further suggest that greater access to palliative care is needed in advanced COPD and that formal psychometric testing of the CRQ may be warranted in cancer.

<table>
<thead>
<tr>
<th>Domain</th>
<th>Advanced COPD</th>
<th>Median</th>
<th>75th-25th Percentiles</th>
<th>Mean</th>
<th>Standard deviation</th>
<th>P value from Independent-Samples Mann-Whitney U Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastery</td>
<td>COPD</td>
<td>3.75</td>
<td>4.75-2.75</td>
<td>3.81</td>
<td>1.28</td>
<td>0.001*</td>
</tr>
<tr>
<td>Cancer</td>
<td>4.50</td>
<td>5.50-1.75</td>
<td>4.52</td>
<td>1.22</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnoea</td>
<td>COPD</td>
<td>3.00</td>
<td>3.60-2.40</td>
<td>3.02</td>
<td>0.93</td>
<td>0.038*</td>
</tr>
<tr>
<td>Cancer</td>
<td>3.50</td>
<td>4.00-2.60</td>
<td>3.47</td>
<td>0.98</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>COPD</td>
<td>2.88</td>
<td>3.75-2.00</td>
<td>2.97</td>
<td>1.13</td>
<td>0.126</td>
</tr>
<tr>
<td>Cancer</td>
<td>3.25</td>
<td>4.19-2.25</td>
<td>3.29</td>
<td>1.20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emotional</td>
<td>COPD</td>
<td>3.86</td>
<td>4.33-3.11</td>
<td>3.84</td>
<td>1.13</td>
<td>0.004*</td>
</tr>
<tr>
<td>Cancer</td>
<td>4.50</td>
<td>5.14-3.57</td>
<td>4.35</td>
<td>1.06</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p < 0.05.

**M7** LEADING FOR IMPROVEMENT – AN ESSENTIAL INGREDIENT IN QUALITY PATIENT CARE: A RESPIRATORY EXPERIENCE

S Kumar, M Gittus, A Cracknell, SDN Miller. Leeds Teaching Hospitals NHS Trust, Leeds, UK
10.1136/thoraxjnl-2015-207770.434

**Background and objectives** Many respiratory patients have deranged physiology and can deteriorate rapidly during acute episodes. Consequently, early decision-making is vital to improve outcomes and to ensure patient’s wishes are respected.

We aim to improve the care of inpatients who acutely deteriorate through clinical leadership, as part of a quality improvement (QI) collaboration, by improving early decision-making and clinical response.

As a pilot project we retrospectively (January 2012–September 2014) analysed all 2222 calls from three respiratory wards (84 beds). Fewer events occurred at the weekend (9.4% per day) compared to weekdays (16.2% per day). More events occurred between 0900–1700 (41.1%) compared to out of hours (58.9%). Decision-making was found to be poor with 12.2% patients having cardiopulmonary resuscitation (CPR) decisions in place.

**Methods** Following initial data analysis, one ward participated in a QI project to identify areas for improvement and target these through small tests of change. The interventions implemented by the ward team included a staff survey, “deteriorating patient stamp”, post-2222 call debriefing and “safety huddles”. The effectiveness of these interventions was measured through analysis of on-going arrest calls and documentation of decision-making in case-notes.

**Results** Reduction in number of 2222 calls on pilot ward between pre-intervention and post-intervention time periods (mean 1.44 vs. 0.56) as shown in Figure 1.

Total 2222 calls per bed reduced for the pilot ward (63.6% reduction) compared to non-pilot wards (9.68% increase) during the pre and post-intervention phases. Similar results were shown for cardiac arrests alone (62.5% reduction compared to 26.7% increase). Decision-making was improved through the

**M6** CAN CLINICAL PSYCHOLOGY INPUT IMPROVE CARE QUALITY AND REDUCE ADMISSIONS AMONG PATIENTS WITH RESPIRATORY DISEASE?

G Thew, J MacCallam, J Robinson, P Salkovskis, J Suntharalingam. Royal United Hospitals NHS Foundation Trust, Bath, UK
10.1136/thoraxjnl-2015-207770.433

**Introduction and objectives** Health outcomes for patients with respiratory conditions can be significantly affected by their psychological wellbeing; those experiencing psychological difficulties are less able to manage symptoms, have a poorer quality of life, and have more frequent hospital admissions. National guidance recommends the need for the assessment and treatment of psychological difficulties secondary to respiratory disease, but implementation of this across services is inconsistent. Here, we report the findings of a nine-month trial integrating clinical psychology into a specialist respiratory department, which aimed to identify the psychological needs within this patient group, provide interventions to address these needs, and to evaluate the impact of this across a range of outcome domains.

**Methods** Standardised measures were used at two timepoints to assess levels of common psychological difficulties among inpatients. Psychological assessment and intervention was implemented as clinically appropriate within the context of the wider multidisciplinary team. This addressed issues including breathlessness-related panic and anxiety, low mood, health concerns, self-management of illness, coping strategies, and supporting discharge. Data on hospital admissions were used to evaluate changes in healthcare use following intervention. Feedback was collected from both patients and staff to review the experience and acceptability of psychology provision.

**Results** Results showed that the rates of clinically significant symptoms of depression, anxiety, and health anxiety among inpatients were 71%, 40%, and 21% respectively. They highlighted that integrating clinical psychology into the multidisciplinary team was received well by patients and staff, leading to improved patient experiences and clinical outcomes, and a greater focus on holistic care. Of the 69 patients receiving psychology input with at least one month follow-up data, 77% showed a reduction in their admission frequency, and those readmitted showed an average reduction in length of stay of 1.7 days. The associated cost savings to the wider NHS more than covered the costs of providing psychology input.

**Conclusions** In light of existing literature, national guidance, and the present findings, we highlight the need for those commissioning and managing respiratory services to consider the varied benefits of integrating psychological provision for a patient group with high levels of psychological need.

**Abstract M5 Table 1** CRQ-Original scores by diagnostic group with associated p values

<table>
<thead>
<tr>
<th></th>
<th>Advanced COPD</th>
<th>Median</th>
<th>75th-25th Percentiles</th>
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<tr>
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<td>0.004*</td>
</tr>
<tr>
<td>Cancer</td>
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<td>5.14-3.57</td>
<td>4.35</td>
<td>1.06</td>
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<td></td>
</tr>
</tbody>
</table>
intervention phase with 75% of inpatients having DNACPR decisions and 46% escalation plans documented. Safety huddles helped improve ward culture and spread lessons learnt from debriefing of the last 3 events.

Conclusion Early results show there has been a reduction in total 2222 calls in the pilot ward compared to the other wards. We believe this is through improved decision making and empowering frontline staff. This could be scaled-up in other wards to have greater impact on patient care.

Abstract M7 Figure 1 Total number of 2222 calls on pilot ward. Interventions indicated by lettering (A): Staff survey, (B): Introduction of “deteriorating patient stamp “, (C): Debriefing following any arrests, (D): Introduction of “Safety huddle”. Mean of pre-intervention and intervention data, 1.44 and 0.56 respectively

M8 PREVALENCE OF RESPIRATORY DISEASE IN SEVERE MORBID OBESITY

Sjw Lipworth, T Thevanathan, Jw Copack, J Emmanuel. Barts and the London School of Medicine, London, UK

10.1136/thoraxjnl-2015-207770.435

Introduction It is well established that asthma and obstructive sleep apnoea (OSA) are significantly more prevalent in obese vs. non-obese populations. To date however there is limited data on whether this risk is increased with severity of obesity as most studies classify all patients >30 Kg/m2 simply as ‘obese’. In addition, many existing studies’ obese cohorts have fairly low BMI scores compared to patients attending specialist medical obesity services. Our study aims to examine the prevalence of these diseases in higher BMI groups, compare the relative risk of increasing obesity on prevalence of respiratory disease and investigate whether there is a synergistic effect of multiple demographic factors and severity of obesity.

Methods Data was collected from a total of 367 (of whom 159 had a BMI recorded) patient records attending a tier 4 obesity clinic over an 8 month period. Patients were divided into three groups according to severity of obesity, BMI 30–40, 40–50 and >50 Kg/m2. Index of multiple deprivation (IMD) scores (mapped to postcodes) were used as a proxy of socioeconomic status.

Results 43% of our total cohort had OSA, including 75.7% of those with a BMI >50 (Multivariate logistic regression OR 10.4 (95% CI 3.33 – 32.7, p < 0.001). In a chi-square analysis, this association was significant in both genders but stronger in males (Cramer’s V 0.481 vs 0.305) and was significantly associated with a worse IMD score, being white and increasing age. 11.6% of the cohort were asthma however there was no difference in prevalence between the groups OR 0.175 (95% CI 0.019 – 1.631, p = 0.126). There was however a significant co-effect of being male and increasing BMI in a multi-layer chi-square analysis p = 0.044.

Conclusions Our study highlights a very high prevalence of major respiratory diseases as co-morbidities in a severely obese population. Early data suggests a synergistic effect of Caucasian ethnicity, male gender and IMD score with increasing BMI on the risk of developing OSA (and Asthma for male gender). This is in contrast with our initial findings for Diabetes and Cardiovascular disease where the association is with Asian ethnicity.

M9 LUNG HEALTH OF OPIATE USERS (LHOP): A PILOT STUDY TO ASSESS THE RESPIRATORY HEALTH OF OPIATE MISUSERS ATTENDING A COMMUNITY SUBSTANCE MISUSE CLINIC

1A Pitt, 2C Mitchell, 2B Colwell, 3I Appelquist, 4A Ashby, 4C Lloyd, 5J Gilbody, 6J Lawson
1Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; 2Academic Unit of Primary Medical Care, The University of Sheffield, Sheffield, UK; 3South West Yorkshire NHS Trust/Phoenix Futures, Barnsley, UK; 4CLAHRC Mental Health and Co-Morbidities Stream, South Yorkshire, UK

10.1136/thoraxjnl-2015-207770.436

Introduction MDTs promote harm reduction in the care of opiate misusers (OMUs) through the prescription of opiate substitute medication and by encouraging smoking rather than injecting (to reduce the risk of blood-borne virus transmission and venous thromboembolism). The average life expectancy for a male OMU is 41 years and whilst evidence suggests that the current cohort of older OMUs are dying prematurely from non-drug related deaths, all-cause mortality studies rarely report the prevalence of chronic health problems. A recent case-controlled study reported a higher prevalence of asthma and COPD in OMUs after adjusting for tobacco consumption and other factors.

The study objective was to investigate the prevalence and illness burden of respiratory problems (asthma, COPD, symptomatic but undiagnosed lung disease) in patients with a history of current and/or past opiate misuse.

Methods Opportunistic clinic-based participant recruitment. Resting spirometry and researcher administered socio-demographic, inhaled drug use and validated respiratory patient reported outcome questionnaires: 1) prior diagnosis of asthma (ACT; mini-ARQoL) or COPD (CCQ); 2) respiratory health screening if no prior diagnosis (LFQ).

Results There were 36 participants (26 male; 10 female; aged 24–53). Only 8 had a diagnosis (all asthmatics); 35/36 smoked tobacco; 34/36 smoked heroin; 33/36 smoked cocaine; and 31/36 smoked cannabis. All asthmatics had poor control (<13) on the ACT (median score 8) and frequent beta-agonist use (none used inhaled corticosteroids). Of the others, 22/28 scored ≤18 on LFQ suggesting high symptom burden and three of these had obstructive resting spirometry increasing the possibility of COPD.

Conclusions Chronic respiratory health in drug users is an under-researched area with few screening or high quality intervention studies evident. We identified a significant respiratory symptom burden within this OMU cohort. Most smoked tobacco, heroin, cocaine and cannabis. Asthmatics reported poor
control and were potentially at risk of severe exacerbations, hospital admission and early progression to COPD.

Four further LHoP studies are planned: a pharmacy based intervention to improve asthma control/uptake of preventive interventions (smoking cessation; vaccinations); a case control study of GP asthma medication prescribing; prospective prognostic respiratory health cohort studies; and a qualitative study of asthmatic OMUs’ perspectives on respiratory health and inhaler use.

M10 THE DEVELOPMENT OF A VOCAL CORD DYSFUNCTION LARYNGOSCOPIC APPEARANCE SCALE

Haines, A Vyas, C Singer, I Howell, SJ Foxler. Lancashire Teaching Hospitals NHS Foundation Trust, Preston, UK; University of Central Lancashire, Preston, UK; Institute of Inflammation and Repair, University of Manchester, Manchester, UK

Introduction Vocal cord dysfunction (VCD) typically involves abnormal vocal cord movement during inspiration. The recognised gold standard for diagnosis is fibreoptic laryngoscopy (FOL) during a symptomatic attack. Despite this there are no reported VCD FOL assessment scales to facilitate agreement in presentation, disease severity and treatment monitoring. Our VCD tertiary airways clinic receives over 300 referrals a year. We run a weekly diagnostic FOL list and identified the need for a VCD FOL classification for optimal care.

Aims To gain consensus for a VCD FOL appearance scale and identify its interrater reliability.

Methods An expert consensus group was convened comprising two respiratory consultant physicians and two respiratory speech and language therapists (SLTs). All have significant experience in VCD FOL interpretation. The group met, discussed and agreed on the VCD FOL appearance scale (Table 1). Two assessment teams were identified, each comprising a respiratory physician and a respiratory SLT. Each team rated patients, referred for FOL with a clinical suspicion of VCD, in three consecutive diagnostic FOL lists. All procedures were recorded and then blindly re-rated during playback by the other assessment team.

<table>
<thead>
<tr>
<th>Scale</th>
<th>Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Normal vocal cord movements observed during respiration throughout assessment</td>
</tr>
<tr>
<td>1</td>
<td>Transient abnormal vocal cord movements observed during inspiration, with large proportions of normal vocal cord movements during respiration</td>
</tr>
<tr>
<td>2</td>
<td>Mild abnormal vocal cord movements observed during respiration (up to 50% vocal cord closure during inspiration)</td>
</tr>
<tr>
<td>3</td>
<td>Moderate abnormal vocal cord movements observed during inspiration (50% or more, but not total closure, i.e. gap still visible between the cords)</td>
</tr>
<tr>
<td>4</td>
<td>Total apposition of the vocal cords (i.e. 100% closure) observed during respiration</td>
</tr>
</tbody>
</table>

Results Eighteen patients received ratings; the mean (range) age was 51 (19–80) and 78% were female. The assessing teams agreed on the rating for seven patients. For nine patients there was disagreement but adjacent classifications. Interrater agreement was performed using a weighted kappa (1 = complete agreement in classification; 0.5 = disagreement but adjacent classifications; 0 = disagreement and non-adjacent classifications). There was moderate agreement between the teams; 0.44 with a 95% confidence interval of 0.18–0.70. There was no bias between the assessment teams, as each had mean ratings for all patients of 2.4.

Conclusions The VCD FOL appearance scale is a promising clinical assessment tool for the VCD population. We expected further interrater agreement; interestingly the majority of disagreement would not have changed management as classification still yielded a positive diagnosis. The differential may be attributed to whether ratings were performed live or in playback, and this should be investigated. With further development, standardisation of application and robust validation it will be a useful assessment to direct appropriate management and facilitate accurate and consistent diagnosis.

REFERENCES


THE UTILISATION OF HELIOX21 IN A TERTIARY VOCAL CORD DYSFUNCTION SERVICE

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Introduction Heliox21 reduces the work of breathing in patients with extra-thoracic airway obstruction, is not curative or intended to replace other treatments. In our specialist service we have significant numbers of patients whom have history of regular hospitalisations, relating to poorly controlled vocal cord dysfunction (VCD). The gold standard for treatment is respiratory speech and language therapy (rSLT). We increasingly value Heliox21 as an early adjunct to rSLT in severe patients who are establishing management strategies.

Aims To assess the impact of Heliox21 on patient admission rate and self-reported experience, for patients with severe VCD.

Methods We retrospectively reviewed the rSLT caseload from June–December 2014. All patients with endoscopically confirmed VCD, greater than five VCD related hospitalisations prior to the commencement of VCD treatment and who were prescribed Heliox21 for use in the community were included. We requested hospital admission data (from patient’s GP and secondary care physicians) between June 2013–June 2015, and reviewed medical and rSLT notes for demographic information/co-morbidity data/opinions of Heliox21.

Results Five patients met the inclusion criteria, three were available for analysis; one male and two female (aged 23,43,57 years). All had treated co-morbidities of asthma (BTS step 5) and reflux. One patient had treated nasal disease. Six-months prior to community Heliox21 administration the mean (range) number of hospital admissions was 11 (8–13); after instigation, during the same follow-up period, this reduced by 81% (2 admissions) and two patients had no hospitalisations. In all patients rSLT occurred simultaneously. Patient opinions included, ‘heliox gives me time to start my therapy and means I don’t ring 999 straight away,’ and, ‘heliox stops me from going to A&E all the time.’ Two patients, who had completed rSLT, had Heliox21 removed as it was no longer needed.

Conclusions Heliox21 has a positive impact on reducing VCD hospital admissions and is a low cost short-term solution (£160 set-up, £8.50 month). This retrospective review has limitations; the impact of rSLT alone on admission rates needs to be compared. Further investigation is needed to examine the worth of Heliox21 as an initial adjunct to rSLT, with consideration of how to prevent reliance.

Improving quality of care in COPD

SURGICAL INTERVENTIONS FOR EMPHYSEMA: THE EXPERIENCE OF A COMMUNITY BASED COPD SERVICE

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Methodology Surgical interventions for emphysema have become more accessible in the last few years.1 We have reviewed the referral rate and outcomes from our community based COPD service to a tertiary surgical centre. Our COPD service includes a respiratory consultant and nurse specialist and has access to secondary care respiratory investigations such as HRCT and pulmonary function testing.

Results During the period April 2013–March 2015 202 new referrals were made to the consultant led clinic of which 181 were subsequently diagnosed with COPD. 10 referrals for
consideration of surgical intervention were made, a referral rate of 6%. The referral rate from the same consultants secondary care clinic during this period was 8% (10 referrals from 126 new COPD patients).

Referred patients had a mean age of 60 years (range 45–72), mean COPD Assessment Test (CAT) score 19 (8–32), mean FEV1 38% predicted (22–64%) and mean RV 196% (163–246%).

All referred patients are discussed at a regional COPD MDT. 5 patients have subsequently received an intervention- 2 lung volume reduction surgery and 3 endobronchial valve placement. 2 patients declined further assessment following discussion with surgeons. 3 patients currently undergoing further investigation to assess operative risk. Outcomes from secondary care referrals were similar (3 had an intervention, 5 were declined and 2 awaiting further assessment).

Post operative CAT scores improved by an average of 9 points. Uncomplicated recovery is rare with complications ranging from wound infection to coughing up a valve. Patients felt the information given pre-operatively by the community and surgical services was at the right level, although it was noted by the community respiratory nurse that patients required significant psychological support before and after surgery.

Summary Management of complex emphysema is possible in a community setting, 6% of COPD patients were referred for assessment for surgical intervention for their emphysema. Objective and subjective patient reported outcome measures improved post operatively. Patients needed more intensive support from the community team in the peri- and post-operative periods.

REFERENCE

M15 USE OF E-CIGARETTES IN PATIENTS ACCESSING SECONDARY CARE IN CROYDON
R Siva. Croydon University Hospital, London, UK
10.1136/thoraxjnl-2015-207770.442

Background The introduction of electronic cigarettes on the market as a cheaper and allegedly healthier alternative to cigarettes, has led many people to use them. The aim of this study is to give us a better understanding of the increase in usage for people accessing stop smoking services in secondary care in Croydon.

Method Questionnaires were given to participants who were willing to take part. 50 participants were recruited during their hospital visit through the Croydon Respiratory Team (CRT) and the hospital based stop smoking service. Patient demographics were recorded and participants reported their behavioural changes, impact on health, reason for use, and intention of when to stop using e-cigarettes.

Results Participation were both male and female with the age range of 23–82 years. 17 participants (35%) reported a diagnosis of COPD (Chronic Obstructive Pulmonary Disease). 34 participants were single users (only used e-cigarettes) and 16 were dual users (use e-cigarettes and other NRT products). Results revealed that e-cigarettes are popular, well tolerated and various brands used. The most popular brand was Vapour Zone cigarettes with 14 users followed by V2 Cig with 8 users. The findings also showed that some patients are using 2 types of e-cigarettes: 2 participants in this study were using more than one brand at the same time. Duration of using e-cigarettes was from one week to over 18 months with 50% of patients having used e-cigarettes for at least 3 months. 26 patients (52%) reported improvement in breathing and 9 patients (18%) reported a reduction in symptoms. 21 patients (42%) had reduced their cigarette use and 19 (38%) had quit smoking. Out of these 25 patients who were using e-cigarettes for at least 3 months; 12 had quit smoking. 22 participants reported hearing about e-cigarettes through the media, 14 through friends, 3 from health professionals, 3 from relatives and 3 through media and friends. It was interesting to note that despite all participants wanting to stop smoking, 33 participants were not sure when they intended to stop using e-cigarettes.

Conclusions The use of e-cigarettes is common in patients accessing secondary care in Croydon. Many patients either quit or reduced smoking and many reported improvement in symptoms. Duration of use of e-cigarettes is variable but half of patients surveyed had used them for at least 3 months. Whilst this study provides some local data, further research is required to help shape future respiratory and smoking cessation services and policies.

M16 ARE WE SHOUTING LOUD ENOUGH? – A COMPARISON OF PRIMARY VERSUS SECONDARY CARE SPIROMETRY
EJA Harris, S Grant, S Yarde, G O’Connell-Ramsay, S Sturney, J Suntharalingam. Royal United Hospitals, Bath, UK
10.1136/thoraxjnl-2015-207770.443

Background Abnormal spirometry results are a leading cause of referral to secondary care in the UK. Spirometry performed in GP practices is often supervised by nursing staff and in secondary care by dedicated respiratory physiologists. We felt that patients who performed spirometry in secondary care would be encouraged to exhale to their full capacity and achieve higher spirometric values.

Methods We collected patient spirometry values from 87 GP referral letters and compared them with the values obtained at our lung function laboratory at a district general hospital. We used a paired t-test to compare the two sets of spirometry results.

Results We found that there were significant differences between the lab FEV1 (p = 0.034), FVC (p < 0.0001) and FEV1/FVC ratio (p = 0.0001) compared to primary care values. There was a 77 ml average increase in FEV1 and a 241 ml average increase in FVC when spirometry was performed in our lung function lab.

Importantly, when we looked at the individual results, 18 patients (21%) originally deemed to have restrictive spirometry had obstructive spirometry when performed in our lab. Six patients (7%) originally had obstructive spirometry which proved to be normal or restrictive in our lab.

Conclusions A significant difference was identified between GP and secondary care spirometry. The most important aspect of this is the understanding that spirometry is effort based. Most patients require significant encouragement to perform to their limit. If a less than maximal effort is made, the FVC value is most affected. This may cause truly obstructive spirometry to appear restrictive.

Primary care spirometry gave a misleading picture in 28% of cases in this cohort, resulting in instances where referrals, investigations and treatments might have been avoided and possibly
managed in primary care. Effective spirometry enables more accurate diagnosis, therefore reducing the chance of under or over treatment.

M17 IMPROVE ACCURACY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) DIAGNOSIS BY OFFERING QUALITY ASSURED SPIROMETRY

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Background and objective Spirometry is a commonly performed diagnostic test in the primary care with variable quality. Around a quarter of the spirometry done in the community is inaccurate and in up to one half of the cases referred to secondary care, diagnosis is changed when spirometry is repeated. We conducted this study to look at the impact of educational intervention in improving the accuracy of COPD.

Methods Seventeen practices across 2 regions in East of England participated in the study. Nurses from these practices underwent educational intervention in the form of attending a structured training to perform Spirometry. Spirometry data and confidence scores in performing and interpreting procedure were collected pre and post training.

Results Clinician’s confidence in performing spirometry improved from 5.1 to 7.6 (p = 0.001) on a visual analogue scale post intervention. Confidence to interpret Spirometry improved from 4.3 to 6.5 (p = 0.001). Following intervention tracing improved in thirty nine percent of patients who had poor quality of tracing pre-intervention. Twenty two percent of patients had a change in diagnosis post intervention with medication changes in 33% of the patients.

Conclusions Educational intervention with a structured spirometry course improves the quality and accuracy of spirometry in the primary care. Study support quality assured spirometry for all healthcare providers who are involved in doing the procedure in primary care.

M18 KNOWLEDGE AND ATTITUDES OF SECONDARY CARE STAFF TOWARD GIVING ADVICE ON SMOKING, WEIGHT MANAGEMENT, ALCOHOL AND PHYSICAL ACTIVITY

S Mendes, B Menezes, B Mallia, H Abusriwil. Sandwell and West Birmingham NHS Trust, Birmingham, UK.

Introduction It is well recognised that adopting a healthier lifestyle leads to better health, improved survival and reduced NHS costs. There are numerous missed opportunities within secondary care to identify high-risk patients and intervene early to prevent illness. The aim of this study was to examine knowledge, attitude and perceived barriers of members of staff to provide healthy lifestyle advise such as Smoking cessation, Weight management, Alcohol consumption and Physical activity (SWAP) and referral to appropriate services.

Methods A questionnaire was distributed to all members of staff working at Sandwell and West Birmingham Hospitals NHS trust electronically and via paper copies.

Results A total of 558 responses were secured from a wide breadth of staff (doctors (23%), Nurses/midwives (36.2%), allied health professionals (11.3%), Pharmacists (1.8%), Admin (8.1%), Domestic/porters (4.1%), clinical support staff (13.8%). Most respondents saw it as their role to encourage people to adopt a healthy lifestyle. Staff had limited knowledge of local resources, however significantly higher knowledge scores were seen for stopping smoking versus weight management (P < 0.001) and physical activity (P < 0.001). Most respondents knew how to refer patients for smoking cessation (66%) and alcohol services (63%), which was significantly higher compared to weight management (39%) and physical activity (36%) services (P < 0.001). 56% participants had not given any life style advice within the previous week, 43% to at least 5 people and 3% to more than 10. 72% participants had not referred anyone to services. The top barriers identified included patient un-readiness to change, unclear referral pathways, lack of time and need for additional training. 82% of staff had no formal training.

M19 THE COST OF HIGH DOSE CORTICOSTEROID PRESCRIBING IN LONDON – HOW MUCH IS TOO MUCH?

V Mak, 1C D’Ancona, 2B Rampersad, 3J Khambh. 1Imperial College Healthcare Trust, London, UK; 2Guys and St Thomas’ Foundation Trust, London, UK; 3NHSE London Procurement Partnership, London, UK.

Introduction A high dose ICS (HDICS) is defined as daily dose ≥1000 micrograms beclometasone dipropionate equivalent and is associated with an increased risk of side effects over their lower dose alternatives, but minimal increase in efficacy. In asthma, HDICS are reserved for severe disease, while in COPD, ICS are beneficial only in those with an FEV1 <50% and frequent exacerbations, but there is evidence for overuse (White P et al. PLoS One 2013 8:e75221). Currently, HDICS (as combination inhalers), comprise 2 of the top 4 highest spend medicines in the NHS (NHSSBSA Mar 2015), so the aim of this study was to...
investigate trends in ICS prescribing across the London Clinical Commissioning Groups (CCGs) and reasons for variation.

Methods The NHS London Procurement Partnership monitors prescribing across London. It has designed a dashboard of primary care prescribing initiatives in collaboration with London CCGs, one of which attempts to support optimised ICS prescribing. The prescribing data for the financial year 2014/15 was compared with 2013/14 for the 32 London CCGs and London as a whole.

Results All but 2 London CCGs increased their total ICS spend between 2014/15 and 2013/14. Altogether, this was an increase of 3% to £67.6 million. In 2014/15, HDICS accounted for 20% of all ICS items prescribed (range 11–27%), or £23.5 million (36%) of total ICS spend (range 23–50%). 732 CCGs reduced expenditure on HDICS by >1% compared with 2013/14, with one achieving a 16% reduction. Reduction in HDICS prescribing occurred mostly in CCGs with respiratory integrated care teams.

Conclusion In light of the National Review of Asthma Deaths, the increase in total spend on ICS may be appropriate. However, 20% of all ICS prescribed in London are for HDICS preparations accounting for 36% of the total spend on ICS. With more than two fold variation across CCGs, some HDICS prescribing may be inappropriate and reduction may be associated with the presence of integrated care teams. If all CCGs in London could manage a 10% reduction in inappropriate HDICS prescribing, this could reduce the risk of side effects to patients and save over £2 million per annum.

M20 A FIVE-YEAR ANALYSIS OF AN INTEGRATED COPD SERVICE IN HACKNEY, LONDON – IS THIS THE RIGHT DIRECTION?

1A Garnee, 2M Hodson, 3G Ketetsis, 2A Bhownik, 1City and Hackney Clinical Commissioning Group, London, UK; 2ACERS, Respiratory Department, Homerton University Hospital, London, UK; 3North East London Commissioning Support Unit, London, UK

In response to high mortality rates, high numbers of COPD admissions, poor quality of care and a lack of integration of services for people with COPD, City and Hackney Primary Care Trust tendered the provision of an acute- and community-based COPD service from Homerton University Hospital in 2009 (the Acute COPD Early Response Service: ACERS).

We studied the impact of ACERS on outcomes for COPD patients in City and Hackney including patient CAT scores, healthcare usage (admissions, length of stay and bed days) and place of death, from 2010 to 2015.

We found a decrease in COPD admissions (from 1.38 admissions per 1000 population to 1.24 per 1000 population) following the establishment of the ACERS service (compared to an increase seen nationally over this time) and a significant reduction in the number of bed days for COPD patients – from 1,817 per year to 1,200 per year (Mann Whitney U test Z-Score 3.6607, p < 0.05). This was alongside a significant increase in patients staying less than 2 days in hospital – from 27% to 34% (significant at p < 0.0001) reflecting the effect of the service on early discharge. We also found a significant increase in the number of patients dying outside of hospital (a proxy for quality of end of life care as most patients express wishes to be cared for and die in their own home or a hospice). The percentage of City and Hackney COPD patients dying outside of hospital increased from 24% to 42% following introduction of ACERS (p = 0.00015). Patient satisfaction with the service was high and patients saw a clinically significant improvement in CAT scores (from 24 to 20, n = 69) following intervention by the ACERS team.

This data was used in a locally developed economic model to determine the economic benefits of the ACERS team and whether therefore, when comparing to the cost of the service, this service was cost-saving overall. The model found that the impact on place of death and healthcare usage meant that ACERS had net monetary benefits to commissioners.

We conclude that an exemplar integrated COPD service can provide financial and other benefits to commissioners which equate to a cost saving service with high return on initial investment. ACERS has been expanded from its original remit to now include management of patients with asthma and bronchiectasis.

M21 COMPARISON OF THE EFFECT OF A VENTILATION MULTIDISCIPLINARY MEETING ON UTILISATION OF CRITICAL CARE RESOURCES

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10.1136/thoraxjnl-2015-207770.448

Introduction and objectives Optimal utilisation of critical care resources requires timely discharge of patients from critical care to appropriate wards. This represents a challenging and high risk transition. Local audits revealed that a few multimorbid patients with difficult respiratory weans accounted for 30% of critical care bed days. A weekly ventilation multidisciplinary team (VMDT) meeting combining respiratory and critical care expertise was established at a 692-bed hospital to improve management and resource use for this patient group. The effect was compared to a 2nd hospital within the same trust without VMDT.

Method A retrospective comparison of 6 month periods before (period 1: 1/10/07–31/3/08) and after (period 2: 1/10/12–31/3/13) introducing VMDT was carried out using data collected for Intensive Care National Audit and Research Centre. The same data was collected for a sister hospital, belonging to the same trust, without VMDT. The numbers of discharges to a respiratory ward with non-invasive ventilation (NIV) facilities were compared with Chi-Square test. The numbers of level 1 critical care bed days were compared with T test.

Results In period 1, hospital 1 discharged 458 patients from critical care and hospital 2 discharged 456. In period 2 these figures were 494 (p = 0.30) and 495 (p = 0.84) respectively. There was no change to background parameters. The number of discharges to respiratory ward with NIV facilities increased significantly in hospital 1 (36 to 65, p = 0.011) after VMDT. Whilst the number of patients discharged to respiratory ward increased in hospital 2 this was not significant (9 to 19, p = 0.13). The number of level 1 bed days fell significantly (208 to 18, p < 0.00000000001) in hospital 1. Hospital 2 saw an increase in level 1 days over the same period.

Conclusion Introduction of VMDT increased the proportion of respiratory patients discharged to a respiratory ward from critical care and reduced level one bed days in hospital 1 by expediting the discharge of complex respiratory wean patients thereby increasing patient flow and liberating critical care resources. The same reduction was not observed in the hospital 2 suggesting this effect was not due to trust wide changes in critical care practice.
**M22** DOES A NURSE-LED NON INVASIVE VENTILATION (NIV) SERVICE IMPROVE PATIENT OUTCOMES?

H Mainman, S Chambers, HJ Curtis. Queen Elizabeth Hospital, Gateshead, UK

10.1136/thoraxjnl-2015-207770.449

**Introduction and objectives**
Non-invasive ventilation (NIV) has been shown to reduce in-patient mortality in AECOPD from 20 to 10%. In 2011 national data revealed that there were multifactorial failures in effective NIV service provision, with a 26% inpatient mortality rate.

Local audit data in 2012 showed our in-patient mortality was 40% for all patients treated with NIV compared to a national rate of 30%. There was evidence of missed patients and delays to treatments. Could a nurse-led NIV service improve upon this?

**Methods**
We set up a dedicated 24/7 nurse-led service with portable NIV machines and allocated respiratory ward beds in December 2013. The nurse would aim to be involved in all AECOPD admissions from the outset, with support from acute medical team. All aspects of clinical care were prospectively collected including nursing workload.

**Results**
More patients received NIV with an improved success rate and reduced in-patient mortality rate. Mortality fell to 12% by summer 2014, and was 0% in patients with pH 7.25–7.35. Quality indicators also improved e.g. failure planning, input from respiratory team and consultants (See Table 1).

**Abstract M22 Table 1**

<table>
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<tr>
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<tbody>
<tr>
<td>Patients/month</td>
<td>7–8</td>
<td>15</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>NIV Success</td>
<td>66%</td>
<td>76%</td>
<td>72%</td>
<td>66%</td>
</tr>
<tr>
<td>Mortality – all patients</td>
<td>40%</td>
<td>33%</td>
<td>11%</td>
<td>20%</td>
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<tr>
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<td>13%</td>
<td>0%</td>
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<td>Speed of access to NIV</td>
<td>300 mins mean</td>
<td>100% within 1hr</td>
<td>64%</td>
<td>62%</td>
</tr>
<tr>
<td></td>
<td>time to NIV from decision</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>of decision</td>
<td>within</td>
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<tr>
<td></td>
<td>NIV</td>
<td>1hr</td>
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<tr>
<td></td>
<td>within</td>
<td></td>
<td></td>
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<tr>
<td>Oxygen Toxicity</td>
<td>26%</td>
<td>3%</td>
<td>16%</td>
<td>21%</td>
</tr>
<tr>
<td>Failure plans in place</td>
<td>93%</td>
<td>100%</td>
<td>80%</td>
<td>83%</td>
</tr>
<tr>
<td>Consultant-led decisions</td>
<td>53%</td>
<td>51%</td>
<td>30%</td>
<td>32%</td>
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<tr>
<td>Respiratory team involvement</td>
<td>45%</td>
<td>59%</td>
<td>43%</td>
<td>44%</td>
</tr>
<tr>
<td>(in addition to acute medicine)</td>
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<td></td>
<td></td>
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<tr>
<td>LOS (Mean) days</td>
<td>12</td>
<td>11</td>
<td>6.5</td>
<td>8.8</td>
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<tr>
<td>Oxygen alert</td>
<td>No data</td>
<td>70%</td>
<td>95%</td>
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</tbody>
</table>

**Conclusions**
Although survival rates were maintained over winter 2014/15, quality indicators slipped, due to nursing pressures across our trust, which compromised the service. During this period the NIV-nurse had extra or alternative duties on 28% of the shifts. As a consequence 6 patients were treated on Intensive care and 3 operations were cancelled.

**M23** THE USE OF WEARABLES FOR COPD PATIENTS: A QUALITATIVE STUDY

S Nabhani, R Siva, R Kayali, C Yagambrun, P Robinson, M Spruit, A Vaes, Ji Wacken, L Caldoni, R Paradiso, JI Chang, Kingston University, London, UK; Croydon University Hospital, London, UK; CIRO, Holland; CSSEM, Switzerland; Smartex, Italy

10.1136/thoraxjnl-2015-207770.450

There have been significant advances in Technology enabled care (TEC) including wearable technology. However, to our knowledge, there is a paucity of literature related to patient perceptions of smart wearable sensors.

The WELCOME platform (FP-7 funded project) is an innovative integrated system using wearable sensors and smart computing for COPD patients with co-morbidities. The aim of this platform is the early diagnosis of exacerbations and disease deterioration allowing for early intervention.

The wearable sensors in this project have been integrated into a vest (Figure 1) and several prototypes with mock sensors were developed. A structured interview was designed to explore COPD patient perceptions pertaining to vest comfort, ease of wear and handling, willingness to use and concerns. Interviews were designed to take place at the clinic (England and Netherlands) where patients are provided with a suitably sized vest to try on followed by the structured interviews.

Via our robust data collection and rolling analysis, we have been able to influence decision makers into not “pulling” the NIV nurse to alternative duties and compromising our successful service.

**Abstract M23 Figure 1**

Via our robust data collection and rolling analysis, we have been able to influence decision makers into not “pulling” the NIV nurse to alternative duties and compromising our successful service.
To date, 15 interviews have been completed at Croydon Healthcare services Trust, and the Dutch interviews are underway.

Results The interview transcripts were thematically analysed using mostly framework analysis. Analysis was conducted using NVivo 10. The following themes emerged from the data: 1) Acceptance of vest 2) Willingness to wear the vest during daytime 3) Discomfort with sensor size and shape prohibiting night wear 4) Demonstrated capability of donning the vest and handling of the sensors 5) Safety concerns emphasising importance of patient education before use 6) Gender related concerns regarding vest design.

Conclusion The vests were well received by patients however the above results illustrate the importance of involving the end users in the design and development of any smart intervention. These results will be used for the final design and development of the vest.

REFERENCE

M24 PREVALENCE OF ANXIETY AND PATIENT CHARACTERISTICS FROM A RANDOMISED CONTROLLED TRIAL (RCT) TO IDENTIFY IF COGNITIVE BEHAVIOURAL THERAPY (CBT) BY RESPIRATORY NURSES REDUCES ANXIETY IN COPD

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10.1136/thoraxjnl-2015-207770.451

Introduction Anxiety and depression are common co-morbidities in COPD. Anxiety is associated with increased breathlessness, lower levels of self-efficacy, impaired health status, poorer treatment outcomes and reduced survival, increased risk of hospitalisation, longer in-patient stay, readmissions and unhealthy behaviours such as smoking and lack of exercise. The aim of this abstract is to present prevalence data, engagement and baseline patient characteristics from the largest RCT on CBT in COPD.

Study design A multicentre RCT with follow up at 3, 6 and 12 months (ISRCTN55206395). Outcome measures include mean HADS-A (anxiety) and HADS-D (depression) score,1 EuroQol 5D Questionnaire,2 COPD Clinical Assessment Tool3 and admission prevention at three, six and 12 months post intervention.

Approach 1,518 patients were screened for symptoms of anxiety using the Hospital Anxiety and Depression Scale (HADS). Two thirds, 705 (59%) patients scored ≥8 for anxiety and were approached.

Intervention Up to 6 CBT sessions provided by one of four respiratory nurses were offered. Self-help leaflets on anxiety and depression were provided as standard care.

Usual care Self-help leaflets only.

Results 42% of eligible patients consented to take part. Groups were well matched at baseline (Table 1) with no correlation between FEV1 and anxiety. A median of 4 CBT sessions (range 2–6) was delivered. Retention was high: 85% at 3 months and 72% at 6 months.

CONCLUSION The prevalence of anxiety and depression is high in patients with COPD and screening is therefore recommended. Affected patients were willing to engage in CBT in this large study. Results from 3, 6 and 12 months data will be available in November 2015 and will be reported. Results will include the cost effectiveness of CBT in COPD delivered by respiratory nurses.

Funding NIHR fellowship.

REFERENCES

Abstract M24 Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>CBT Group (n = 139)</th>
<th>Control Group (n = 140)</th>
<th>p-value (95% CI)</th>
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<tbody>
<tr>
<td><strong>Age</strong></td>
<td>66</td>
<td>67</td>
<td>66.5</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>61 (44)</td>
<td>67 (48)</td>
<td>128 (46)</td>
</tr>
<tr>
<td>Female</td>
<td>78 (56)</td>
<td>73 (52)</td>
<td>151 (54)</td>
</tr>
<tr>
<td><strong>Severity of COPD</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>16 (11)</td>
<td>13 (9)</td>
<td>29 (10)</td>
</tr>
<tr>
<td>Moderate</td>
<td>44 (32)</td>
<td>47 (34)</td>
<td>91 (33)</td>
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<tr>
<td>Severe</td>
<td>50 (36)</td>
<td>49 (35)</td>
<td>98 (35)</td>
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<tr>
<td>Very Severe</td>
<td>29 (21)</td>
<td>31 (22)</td>
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<tr>
<td><strong>Educational Level</strong></td>
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<tr>
<td>No educational qualifications</td>
<td>100 (75)</td>
<td>103 (77)</td>
<td>203 (73)</td>
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<tr>
<td><strong>HADS-Axisy Score</strong></td>
<td>12.3 (3.19)</td>
<td>12.0 (2.94)</td>
<td>0.47 (-0.456–0.988)</td>
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<tr>
<td><strong>HADS-Depression Score</strong></td>
<td>9.4 (4.01)</td>
<td>9.0 (3.68)</td>
<td>0.34 (-0.470–1.347)</td>
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<td><strong>CAT (Health Status)</strong></td>
<td>28.2 (6.45)</td>
<td>28.7 (5.99)</td>
<td>0.52 (-1.944–0.990)</td>
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<td><strong>EQ5D</strong></td>
<td>0.41 (0.29)</td>
<td>0.41 (0.30)</td>
<td>0.95 (-0.07–0.07)</td>
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<td><strong>Married or Co-habiting</strong></td>
<td>68 (49)</td>
<td>63p (45)</td>
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<td><strong>Current smoker</strong></td>
<td>39 (28)</td>
<td>40 (29)</td>
<td>79 (28)</td>
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<td><strong>Mean pack years</strong></td>
<td>46</td>
<td>49</td>
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<tr>
<td><strong>BMI</strong></td>
<td>26</td>
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Conclusion The prevalence of anxiety and depression is high in patients with COPD and screening is therefore recommended. Affected patients were willing to engage in CBT in this large study. Results from 3, 6 and 12 months data will be available in November 2015 and will be reported. Results will include the cost effectiveness of CBT in COPD delivered by respiratory nurses.

Funding NIHR fellowship.

Education and training: from simulation to social media

M25 OXYGEN: TOO MUCH OF A GOOD THING? CAN SIMULATION IMPROVE EDUCATION?

JL Parkin, E Lloyd. University of Bristol, Bristol, UK

10.1136/thoraxjnl-2015-207770.452

A cohort of chronic obstructive pulmonary disease patients experience acute exacerbations (AECOPD) presenting with worsening sputum production, cough and breathlessness. The recommended treatment for AECOPD involves using a 28% Venturi mask to achieve an arterial oxygen saturation of 88–92%. These guidelines have been poorly adhered to with many health professionals still administering high flow oxygen. An AECOPD model, created on the human patient simulator, was administered with 28% or 100% oxygen. 28% oxygen relieved hypoxia
TWEETING IS TEACHING - #RESPED: FREE, OPEN ACCESS TWITTER EDUCATIONAL RESOURCE FOR TRAINEES AND SPECIALISTS IN RESPIRATORY MEDICINE

1RW Lee, 1Li Smith, 1Hillman. 2Division of Asthma, Allergy and Lung Biology, Guy’s Hospital, King’s Health Partners, London, UK; 2University College London Hospitals NHS Foundation Trust, London, UK.

Abstract M25 Figure 1

(PaO₂ = 84.9 mmHg), caused mild hypercapnia (PaCO₂ = 49.6 mmHg) and the blood pH was normal (pH = 7.37). 100% oxygen enabled better arterial oxygenation (PaO₂ = 129.3 mmHg) but caused severe hypercapnia (PaCO₂ = 100.9 mmHg) and acidosis (pH = 6.98). Preclinical medical students were randomly allocated to simulation or lecture-based learning (the study has a crossover design) and were taught the correct use of oxygen administration. A greater proportion of students rated them an excellent understanding of the key learning points after simulation (100%) compared to the lecture-based learning (33%) and it was sufficient to significantly improve test scores (p = 0.0135). Simulation could be used to educate future health professionals in using 28% oxygen to reduce the risk of hypercapnic respiratory acidosis in AECOPD.

REFERENCES

WHEEZES, COUGHS AND SPLUTTERS: HOW DO PAEDIATRIC TRAINEES MANAGE THEM?

1M Ramphul, 1U Thanikkel, 2R Ross Russell. 1East of England Deanery, Cambridge, UK; 2Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK.

Introduction and objectives Wheezy pre-school children frequently present to paediatric departments. There is a wide variation in how paediatric trainees investigate and manage these children, which can be associated with unnecessary costs to the NHS. Our aim was to assess this diversity in management options initiated by paediatric trainees.

Methods Web-based survey on how paediatric trainees approach scenarios of wheezy pre-school children. Trainees across the UK were asked to fill in a questionnaire consisting of four case scenarios involving wheezy children under the age of 5.

Results 194 trainees responded to the survey. There was a good representation amongst different training grades across UK deaneries. In the bronchiolitis scenario, 13% requested blood tests or
RESPIRATORY CLINICIANS’ EXPERIENCES OF END-OF-LIFE CARE IN IDIOPATHIC PULMONARY FIBROSIS

B Turnpenny, K Shepherd, Z Borrill. Pennine Acute NHS Trust, Manchester, UK

Introduction Referral rates to Specialist Palliative Care are low in Idiopathic Pulmonary Fibrosis (IPF) despite mean survival of 3 years, and a high symptom burden in the final year, in particular dyspnoea, chest pain, anxiety and depression, and fatigue. This study aimed to explore chest clinicians’ experiences across the UK for paediatric trainees, and reduce the financial burden on the NHS.

Methods Questionnaires were distributed at a regional Respiratory meeting, focussing on initiating End-of-Life discussions, predicting prognosis, training, and reasons for low palliative care referrals. 57 completed questionnaires - 17 chest consultants, 28 chest registrars, 11 physiotherapists, and 1 nurse clinician. 23 (40%) initiated End-of-Life discussions in severe IPF frequently or very frequently, and 47 (84%) felt it was a very important or important part of their role, but 42% felt predicting prognosis in advanced IPF was difficult or very difficult. More consultants felt End-of-Life discussions were an important part of their role than registrars.

Several aspects of End-of-Life care were felt to be harder in severe IPF than advanced malignancy (Figure 1), although similar to advanced COPD. 22 (42%) referred patients with severe IPF to hospital palliative care services very frequently or frequently, and 19 (37%) to community palliative care very frequently or frequently. Less than 10% of all respondents felt they had significant training in initiating End-of-Life discussions, palliating symptoms, or services available.

The three symptoms perceived to be experienced most in patients dying with IPF were breathlessness, anxiety and fatigue (cohort data supports this). The three commonest reasons for low palliative care referrals were healthcare team perceptions that palliative care services focussed on cancer, patient’s lack of awareness of prognosis, and difficulty clinicians have in predicting prognosis.

Conclusion Chest clinicians find predicting prognosis in ILD difficult, and this contributes to low palliative care referrals. They have minimal training in End-of-Life issues in IPF and there is a lack of local services for such patients. Respiratory training, and commissioning groups, are challenged to develop better End-of-Life services for a condition carrying a high symptom burden and often distressing death.

REFERENCES
2 Bajwah S, Higginson IJ, Ross JR. et al. Specialist palliative care is more than drugs: a retrospective study of ILD patients. Lung. 2012;190:215–20

TRIETING TO CAUSE LESS PAIN FOR OUR PATIENTS! USING LOCAL ANAESTHESIA FOR ARTERIAL BLOOD GAS SAMPLING

N Maningo, S Chaudhry, A Parwaiz, B Suwal, RA Evans, RH Green, I Valero-Sanchez. University Hospitals of Leicester NHS Trust, Leicester, UK

Background Direct radial artery puncture (DRAP) is considered the gold standard procedure for arterial blood gas (ABG) sampling, but it is associated with significant pain. The current ‘BTS guidelines for oxygen use in adult patients’ recommend using local anaesthesia (LA) for all ABG sampling except in emergency situations. LA can be administered subcutaneously or topically.

Aims
1. To assess the attitudes towards LA for ABG sampling in a population of medical junior doctors (JD).
2. To assess the effectiveness of topical lidocaine cream for ABG sampling by DRAP for respiratory inpatients.
Methods
1. Firstly, we surveyed a population of JD working in our Hospital using an electronic survey platform (SurveyMonkey®).
2. Secondly, a group of inpatients requiring ABG sampling were surveyed over two months whereby half received topical LA and half did not. The LA used was Denela® 5% cream (Lidocaine 2.5% + Prilocaine 2.5%) applied 10 to 15 min prior to DRAP. Pain associated with DRAP was assessed using a combination of the Wong-Baker FACES pain rating visual scale¹ and a visual analogue pain scale, both scoring the pain from 1 (“no pain”) to 6 (“worst pain”).

Results
1. 68 JD were contacted and 26 responses were received (shown in Table 1).
2. 56 DRAP were performed for ABG sampling, 50% received topical LA. The median (inter-quartile range) pain score was reduced with LA prior to DRAP (2.0 [1.8] “moderate pain”) compared to performing DRAP without LA (3.0 [4.0] “severe pain”), p < 0.008. The doctors reported insignificant interruption to their ward duties by using topical LA.

Abstract M29 Table 1 Results of electronic survey: Use of local anaesthesia in arterial blood gas sampling

<table>
<thead>
<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
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<tr>
<td>Do you take arterial blood sampling regularly?</td>
<td>100%</td>
<td>0%</td>
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<tr>
<td>If answered “yes” to Q1, how often do you estimate you perform ABG sampling?</td>
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<tr>
<td>Practically every day: 34.6%</td>
<td></td>
<td></td>
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<tr>
<td>At least once weekly: 15.4%</td>
<td></td>
<td></td>
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<tr>
<td>Less than once weekly: 50.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have you ever used local anaesthesia for radial arterial blood sampling?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(excluding arterial lines)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes: 26.9%</td>
<td>73.1%</td>
<td></td>
</tr>
<tr>
<td>If answered “no” to Q3, what’s the reason for it?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I have never heard about this practice before.</td>
<td>31.6%</td>
<td></td>
</tr>
<tr>
<td>I have not been taught how to do it.</td>
<td>47.4%</td>
<td></td>
</tr>
<tr>
<td>I usually don’t have time to do it.</td>
<td>31.6%</td>
<td></td>
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<tr>
<td>I do not think it would reduce the pain associated with the procedure significantly</td>
<td>26.3%</td>
<td></td>
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</table>

Conclusions Currently, LA is not used routinely as part of the ABG sampling by DRAP in our centre. Pain was significantly reduced with the use of LA when performing DRAP.

These data will help inform quality improvement projects designed to implement the usage of LA for ABG sampling using DRAP as per BTS recommendations.

REFERENCE
1 Baker C. Orthopaedic Nursing 1987;6(1):11–2

Abstract M30 Figure 1

Conclusion Although this study was small, the results are positive. There are however, implications to running further courses due to the willingness of faculty to facilitate sessions in their own time. This research does show that medical trainees do not feel confident in performing procedural skills, highlighting the need for more sustainable teaching in these areas to improve confidence and thus inspire trainees in medical careers.

REFERENCES
One Respiratory Physician trained to perform EBUS in a teaching Hospital in the UK and had supervised experience for approximately 50 cases over a period of 1 year.

This learnt skill was taken abroad to another respiratory department with no prior experience in EBUS. One other colleague was nominated to take part and be trained over the introductory period of 9 months.

Typically 2 endoscopy nurses were present, and rotation of staff was controlled to maintain expertise throughout this period. On site Consultant Pathologists and a cytopathology technician were present for each procedure.

Patients underwent standard bronchoscopy then proceeded immediately to EBUS. Moderate conscious sedation was used. A total of 50 patients went forward for EBUS-TBNA in this period. 25 were female and 25 were men with a mean age of 64.3 and 58 respectively with a range of 20 to 87 years. A total of 56 nodes were performed and the most commonly biopsied nodal stations were 7 (43%) and 4R (42%). Nodal stations biopsied included 2R, 4R, 4L, 7, 10R, and 11R.

The overall accuracy, sensitivity and specificity was 92%, 90% and 100% respectively. The accuracy, sensitivity and specificity for lung cancer diagnosis was 89%, 87% and 100% respectively. The sensitivity and accuracy for sarcoidosis was 100%.

One complication of minor bleeding was noted.

We conclude that a safe and reliable EBUS service can be started in a department where a physician has been involved with 50 cases. We postulate it takes a further 50 cases per consultant to achieve competency and in our department about 9 months at present. We think it is important to control the number of staff performing the procedures initially and this approach is associated with minimal complication and good results for our first cases.

Abstract M31 Figure 1

**Overall statistics for all diagnosis**

- **Accuracy**: 100, 95, 90, 85
- **Sensitivity**: 100, 95, 90, 85
- **Specificity**: 100, 95, 90, 85

**Abstract M32**

**DESIGN AND DEVELOPMENT OF A NEW PMDI TRAINING AID**

1MJ Sanders, 1A Brun, 2C Tran. 1Clement Clarke International Ltd., Harlow, UK;
2I2c Pharmaceutical Services, Cardiff, UK

10.1136/thoraxjnl-2015-207770.459

**Introduction and objectives** Despite differences in actuator resistance between pressurised metered dose inhalers (pMDIs), ‘inhale deeply and slowly’ remains universally recommended for drug delivery. Training aids to tutor inspiratory flow rate are vulnerable to resistance effects and can lead to patient error under a misconception of corrected technique. Actuator mouthpiece design can also limit availability of suitable training devices. Using the Flutiform low-resistance pMDI (Napp Laboratories Ltd), we describe here the development and testing of a suitable training aid based on the audible tone Flo-Tone trainer (Clement Clarke).

**Methods** Flutiform 5 µg formoterol fumarate/125 µg fluticasone propionate (4.5/115 µg ex-actuator respectively) was assessed via the Next Generation Impactor (NGI) operated at 30 L/min, alone, and together with machined (Ma) or moulded (Mo) mouthpiece adaptors attached to the commercially available Flo-Tone (FTc), anti-static plastic Flo-Tone (FTas), or an abbreviated version (FTab). All least three replicates of each were completed.

Drug recovery (µg) from the actuator, adaptor, Flo-Tone, induction port and NGI was determined. The key aerosol performance parameters Fine Particle Fraction (FPF, % <5 µm) and Fine Particle Dose (FPD, µg < 5 µm) were determined.

**Results** Formoterol and fluticasone drug delivery data trends were the same. Here we report the fluticasone data. Drug mass recovery (Figure 1) indicated that the moulded mouthpiece adaptor with abbreviated Flo-Tone (Mo-FTab) approximated most closely to Flutiform drug delivery without a training aid. All prototypes showed reduced throat (induction port) deposition. FPF% and FPD µg data for all prototypes, respectively, were: Flutiform alone, 44.8, 46.9; Ma1-FTc, 36.7, 34.5; Mo-FTc, 34.1, 34.5; Mo-FTas, 34.4, 36.9; and Mo-FTab, 44.6, 46.4.

**Conclusions** This process has shown that it is possible to tailor an existing audible training aid to a specific pMDI, enabling an audible training tone at an appropriate inspiratory flow rate without drug delivery compromise. We are currently extending this design-development research to create a standardised device suitable for a range of pMDIs in popular use and that vary in actuator resistance.
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Dr James Chalmers  Professor Simon Johnson  Dr Tom Wilkinson
Professor Jane Davies  Dr Ricardo Jose  Dr Tom Wilkinson
Professor Louise Donnelly  Professor Nick Maskell  Dr Duncan Wilson
Dr Neil Greening  Dr Justin Pepperell

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Professor Jane Davies  Professor Simon Johnson  Dr Robert Rintoul
Professor Louise Donnelly  Dr Ricardo Jose  Dr Tom Wilkinson
Dr Neil Greening  Professor Nick Maskell  Dr Duncan Wilson
Dr Simon Hart

The BTS/BLF/BALR Early Career Investigators and Medical Student Award abstracts were judged by:

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The refereeing of the abstracts was performed by:

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Professor Andrew Bush  Dr Ian Forrest  Dr Christopher Johnson
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Professor Sam Janes, Chairman, BTS Science and Research Committee
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(FEV₁ < 50% predicted)

**Fostair**

**Beclometasone + formoterol**

**Prescribing information**

**Presentation** Each metered dose contains 100 micrograms (mcg) of beclometasone dipropionate (BDP) and 6mcg of formoterol fumarate dihydrate. **Indications** Asthma: Regular treatment of asthma in patients who are not adequately controlled on an inhaled corticosteroid (ICS) and ‘as needed’ rapid acting beta₂-agonist or patients who are adequately controlled on both ICS and long-acting beta₂-agonists (LABA), where the use of an ICS/LABA combination is appropriate. COPD: Symptomatic treatment of patients with severe COPD (FEV₁ < 50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators.

**Dosage and administration** For inhalation in adult patients (≥18 years). BDP in Fostair is characterised by an extrafine particle size distribution which results in a more potent effect than formulations of BDP with a non-extrafine particle size distribution (100mcg of BDP extrafine in Fostair are equivalent to 250mcg of BDP in a non-extrafine formulation).

Asthma: Fostair may be used as a maintenance therapy (with a separate rapid-acting bronchodilator as needed) or as a maintenance and reliever therapy (taken as a regular maintenance treatment and as needed in response to asthma symptoms). Maintenance therapy 1-2 inhalations twice daily. The maximum daily dose is 4 inhalations. Patients should receive the lowest dose that effectively controls their symptoms. Maintenance and reliever therapy: 1 inhalation twice daily plus 1 additional inhalation as needed in response to symptoms. If symptoms persist after a few minutes, an additional inhalation is recommended. The maximum daily dose is 8 inhalations. COPD: 2 inhalations twice daily. Can be used with the AeroChamber Plus® spacer device.

**Contraindications** Hypersensitivity to the active substances or to any of the excipients (HFA-134a, ethanol anhydrous, hydrochloric acid).

**Warnings and precautions** Use with caution in patients with cardiac disease, occlusive vascular diseases, arterial hypertension, angina, myocardial infarction, severe heart disease, occlusive vascular diseases, arterial hypertension, angina, myocardial infarction, severe heart disease, and other conditions that may be exacerbated by effects of sympathomimetics.

**Side effects** Common: pharyngitis, oral candidiasis, headache, dizziness, oto-toxicity, palpitations, prolongation of QTc interval, electrocardiogram changes, tachycardia, tachyarrhythmia, atrial fibrillation, hyperaemia, flushing, cough, productive cough, throat irritation, asthmatic crisis, diaphoresis, dry mouth, dyspepsia, dysphagia, burning sensation of the lips, nausea, diaphoresis, pruritus, rash, hyperhidrosis, urticaria, muscle spasm, myalgia. Rare: Creatine protein increased, platelet count increased, free fatty acids increased, blood insulin increased, blood ketone body increased, blood cortisol decrease. Rare: Ventricular extrasystoles, angina pectoris, paradoxic bronchospasm, angioedema, nephritis, blood pressure increased, blood pressure decreased. Very rare: Thrombocytopenia, hypersensitivity reactions, including rashes, lipo, face, eyes and pharyngeal oedema, adrenal suppression, glaucoma, cataract, dyspnoea, exacerbation of asthma, growth retardation in children and adolescents, peripheral oedema, bone density decreased. Unknown frequency: Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (predominantly in children). Refer to SmPC for full list of side effects.

**Legal category** POM. **Pack and price** £29.32. **Pack size** 1x120 actuations. **Marketing authorisation holder** Chiesi Limited, 333 St Sow Road, Manchester, M22 5LG. **Date of preparation** June 2015.

**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 Chiesi Limited. (address as above) Tel: 0161 488 5555.**


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