British Thoracic Society
Winter Meeting 2014

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

3 to 5 December 2014
Programme and Abstracts

Approved by the Federation of the Royal Colleges of Physicians of the UK for 18 category 1 (external) credits.
Code: 92364
Map to QEII Conference Centre

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 cafe facilities will be open in the Pickwick Suite on the 1st floor from 8.00am to 4.00pm on Wednesday 3 and Thursday 4 December and from 8.00am to 2.30pm on Friday 5 December. Snack bars, serving hot and cold drinks, sandwiches and confectionery only, will be open at the same times in the Whittle & Fleming Rooms on the 3rd floor.
Full cafe facilities will be open in the Pickwick Suite on the 1st floor from 8.00am to 4.00pm on Wednesday 3 and Thursday 4 December and from 8.00am to 2.30pm on Friday 5 December. Snack bars, serving hot and cold drinks, sandwiches and confectionery only, will be open at the same times in the Whittle & Fleming Rooms on the 3rd floor.
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## Daily Programme

### Wednesday 3 December 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
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</thead>
<tbody>
<tr>
<td>8.00am – 9.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming Rooms/3&lt;sup&gt;rd&lt;/sup&gt;</td>
</tr>
<tr>
<td>8.45am – 4.00pm</td>
<td>Poster viewing P1-P13/P14-P26 P27-P34 P44-P57 P58-P68 P69-P78 P79-P87 P88-P95 P96-P106</td>
<td>Whittle &amp; Fleming Rooms/3&lt;sup&gt;rd&lt;/sup&gt;</td>
</tr>
<tr>
<td>8.00am – 4.30am</td>
<td>BTS Journal Club</td>
<td>Albert Suite/2&lt;sup&gt;nd&lt;/sup&gt;</td>
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<tr>
<td>8.30am – 10.15am</td>
<td>Symposium</td>
<td>Churchill Auditorium/Ground</td>
</tr>
<tr>
<td>8.30am – 10.15am</td>
<td>Spoken session S1-S6 S7-S12</td>
<td>St James’s Suite/4&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
<tr>
<td>8.30am – 10.30am</td>
<td>Joint BTS/BALR symposium (part I)</td>
<td>Westminster Suite/4&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
<tr>
<td>8.45am – 10.15am</td>
<td>Spoken session S13-S17</td>
<td>Abbey Room/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>9.00am – 10.30am</td>
<td>Open meeting</td>
<td>Victoria Suite/2&lt;sup&gt;nd&lt;/sup&gt;</td>
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<tr>
<td>10.00am – 11.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming Rooms and Benjamin Britten Lounge/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<tr>
<td>10.00am – 12.00pm</td>
<td>Symposium</td>
<td>Mountbatten Room/6&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>10.00am – 12.00pm</td>
<td>Spoken session S18-S22</td>
<td>St James’s Suite/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>10.30am – 12.15pm</td>
<td>Spoken session S23-S28</td>
<td>Elizabeth Windsor Room/5&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>10.30am – 12.30pm</td>
<td>Symposium</td>
<td>Westminster Suite/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>10.45am – 11.45am</td>
<td>Open meeting</td>
<td>Albert Suite/2&lt;sup&gt;nd&lt;/sup&gt;</td>
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<tr>
<td>11.00am – 12.00pm</td>
<td>Open meeting</td>
<td>Victoria Suite/2&lt;sup&gt;nd&lt;/sup&gt;</td>
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<tr>
<td>11.00am – 12.00pm</td>
<td>Open meeting</td>
<td>Rutherford Room/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>11.00am – 1.00pm</td>
<td>Joint BTS/BALR symposium (part 2)</td>
<td>Westminster Suite/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>12.00pm – 2.00pm</td>
<td>LUNCH Cash catering only</td>
<td>Pickwick Suite/1&lt;sup&gt;st&lt;/sup&gt; and Whittle &amp; Fleming Rooms/3&lt;sup&gt;rd&lt;/sup&gt;</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>Open meeting</td>
<td>Nurse Advisory Group</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>Open meeting</td>
<td>NICE Pneumonia Guideline 2014</td>
</tr>
</tbody>
</table>

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

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

**THURSDAY 4 DECEMBER 2014**

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
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</thead>
<tbody>
<tr>
<td>8.00am – 9.00am</td>
<td><strong>COFFEE/TEA</strong></td>
<td>Whittle &amp; Fleming Rooms/3rd</td>
</tr>
<tr>
<td>8.45am – 4.00pm</td>
<td>Poster viewing</td>
<td>P107-P114</td>
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<td></td>
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<td>P115-P125</td>
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<tr>
<td>Authors present</td>
<td>Integrated knowledge in practice</td>
<td>Whittle &amp; Fleming Rooms/3rd</td>
</tr>
<tr>
<td>10.00am – 11.00am</td>
<td>Clinical delivery of pulmonary rehabilitation</td>
<td>Whittle &amp; Fleming Rooms/3rd</td>
</tr>
<tr>
<td>8.45am – 4.00pm</td>
<td>Moderated poster viewing</td>
<td>M137-M148</td>
</tr>
<tr>
<td>8.00am – 8.30am</td>
<td><strong>BTS Journal Club</strong></td>
<td>Physiology</td>
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<tr>
<td>8.30am – 10.00am</td>
<td>Joint BTS/BTOG symposium</td>
<td>Lung cancer</td>
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<tr>
<td>8.30am – 10.15am</td>
<td>Joint BTS/BPRS symposium</td>
<td>Wheezing phenotypes</td>
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<tr>
<td>8.30am – 10.15am</td>
<td>Spoken session</td>
<td>S40-S45</td>
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<tr>
<td>8.30am – 10.15am</td>
<td>Spoken session</td>
<td>S46-S51</td>
</tr>
<tr>
<td>8.30am – 10.15am</td>
<td>Spoken session</td>
<td>S52-S57</td>
</tr>
<tr>
<td>8.45am – 10.15am</td>
<td>Symposia</td>
<td>COPD: co-morbidities, deficiencies and interventions</td>
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<tr>
<td>8.45am – 10.15am</td>
<td>Symposium</td>
<td>Work and workplaces for occupational lung disease</td>
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<tr>
<td>8.45am – 10.30am</td>
<td>Spoken session</td>
<td>S58-S63</td>
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<td>9.00am – 10.00am</td>
<td>Open meeting</td>
<td>COPD SAG</td>
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<tr>
<td>9.00am – 10.00am</td>
<td>Open meeting</td>
<td>Cystic Fibrosis SAG</td>
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<tr>
<td>10.00am – 10.15am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming Rooms and Benjamin Britten Lounge/1st</td>
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<tr>
<td>10.00am – 10.15am</td>
<td>Spoken session</td>
<td>S64-S68</td>
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<tr>
<td>10.00am – 10.15am</td>
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<td>Plenary scientific symposium</td>
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<td>LUNCH</td>
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<td>12.00pm – 2.00pm</td>
<td>Cash catering only</td>
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<tr>
<td>12.15pm – 1.15pm</td>
<td>Open meeting</td>
<td>Lung Cancer and Mesothelioma SAG</td>
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<tr>
<td>12.15pm – 1.45pm</td>
<td>Open session</td>
<td>UKRRC session</td>
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### DAILY PROGRAMME (cont.)

**THURSDAY 4 DECEMBER 2014**

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
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<tr>
<td>12.30pm – 1.15pm</td>
<td>The Snell Memorial Lecture</td>
<td>Churchill Auditorium/Ground</td>
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<tr>
<td></td>
<td>Mycobacterium TB: where did it come from and where is it going?</td>
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<tr>
<td>12.30pm – 1.30pm</td>
<td>Open meeting</td>
<td>Abbey Room/4th</td>
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<tr>
<td></td>
<td>Pulmonary Vascular Disease SAG</td>
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<tr>
<td>12.45pm – 1.45pm</td>
<td>Open meeting</td>
<td>Rutherford Room/4th</td>
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<tr>
<td></td>
<td>Occupational and Environmental Lung Disease SAG</td>
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<tr>
<td>1.30pm – 2.30pm</td>
<td>Poster discussion P107-P114</td>
<td>Henry Moore Room/4th</td>
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<td></td>
<td>Integrated knowledge in practice</td>
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<tr>
<td>1.45pm – 3.30pm</td>
<td>Spoken session S69-S74</td>
<td>St James’s Suite/4th</td>
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<td>Lung cancer: how are we doing and what’s next?</td>
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<tr>
<td>1.45pm – 3.30pm</td>
<td>Spoken session S75-S80</td>
<td>Abbey Room/4th</td>
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<td></td>
<td>Clinical TB</td>
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<tr>
<td>1.45pm – 3.45pm</td>
<td>Symposium</td>
<td>Mountbatten Room/6th</td>
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<td>Poor asthma outcomes – can we do better?</td>
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<td>2.00pm – 3.25pm</td>
<td>Poster discussion P115-P125</td>
<td>Elizabeth Windsor Room/5th</td>
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<td></td>
<td>Clinical delivery of pulmonary rehabilitation</td>
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<td>2.00pm – 3.25pm</td>
<td>Poster discussion P126-P136</td>
<td>Rutherford Room/4th</td>
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<td>The lungs at work: occupational lung disease</td>
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<td>2.00pm – 3.30pm</td>
<td>Symposium</td>
<td>Churchill Auditorium/Ground</td>
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<td>“Hot topics”</td>
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<tr>
<td>2.00pm – 3.30pm</td>
<td>Moderated poster discussion M137-M148</td>
<td>Mountbatten Lounge/5th</td>
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<td></td>
<td>COPD: co-morbidities, deficiencies and interventions</td>
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<tr>
<td>2.00pm – 3.30pm</td>
<td>Open session</td>
<td>Albert Suite/2nd</td>
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<td>BLF research highlights</td>
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<td>2.00pm – 3.30pm</td>
<td>Spoken session S81-S85</td>
<td>Westminster Suite/4th</td>
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<td>Predicting and preventing re-admissions in COPD: what is the real cost?</td>
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<td>3.00pm – 4.30pm</td>
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<td>Whittle &amp; Fleming Rooms, Benjamin Britten Lounge/3rd</td>
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<td>3.15pm – 4.15pm</td>
<td>Open meeting</td>
<td>Victoria Suite/2nd</td>
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<td>3.45pm – 5.15pm</td>
<td>Spoken session S86-S90</td>
<td>Henry Moore Room/4th</td>
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<td>Pulmonary infection: discovery science</td>
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<td>3.45pm – 5.15pm</td>
<td>Poster discussion P149-P159</td>
<td>Elizabeth Windsor Room/5th</td>
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<td>Predicting clinical outcomes in acute respiratory illness</td>
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<td>3.45pm – 5.20pm</td>
<td>Poster discussion P160-P172</td>
<td>Abbey Room/4th</td>
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<td>Pulmonary arterial hypertension: diagnosis, management and outcomes</td>
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<td>3.45pm – 5.30pm</td>
<td>Spoken session S91-S96</td>
<td>St James’s Suite/4th</td>
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<td>New asthma treatments</td>
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<td>3.45pm – 5.30pm</td>
<td>Spoken session S97-S102</td>
<td>Albert Suite/2nd</td>
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<td>Mechanistic insights in acute lung injury</td>
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<td>3.45pm – 5.45pm</td>
<td>Symposium</td>
<td>Churchill Auditorium/Ground</td>
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<td>COPD – placing the new inhalers in context</td>
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<td>4.00pm – 5.15pm</td>
<td>Poster discussion P173-P182</td>
<td>Mountbatten Room/6th</td>
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<td>In the pleural zone</td>
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<td>4.00pm – 5.15pm</td>
<td>Poster discussion P183-P192</td>
<td>Westminster Suite/4th</td>
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<td>TB: non pulmonary and hepatotoxicity</td>
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<td>4.00pm – 5.30pm</td>
<td>Poster discussion P193-P204</td>
<td>Rutherford Room/4th</td>
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<td>Cystic fibrosis</td>
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<tr>
<td>5.30pm – 7.15pm</td>
<td>The President’s Reception – All welcome!</td>
<td>Benjamin Britten Lounge/3rd</td>
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</tbody>
</table>

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### DAILY PROGRAMME

**FRIDAY 5 DECEMBER 2014**

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
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<tbody>
<tr>
<td>8.00am – 9.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming Rooms/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<tr>
<td>8.45am – 2.00pm</td>
<td>Poster viewing</td>
<td>P205-P214 Lung function testing: new approaches</td>
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<td>Authors present</td>
<td>P215-P226 Diagnostic and therapeutic intervention</td>
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<td>10.00am – 11.00am</td>
<td>P227-P241 Asthma treatments</td>
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<td>P242-P247 Transplantation advances</td>
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<td>P248-P262 Improving patient therapies in COPD</td>
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<td>P273-P280 ILD: diagnosis, co-morbidities and</td>
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<td>P281-P289 Smoking detection and cessation and</td>
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<td>P290-P296 Screening and treating sleep apnoea</td>
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<td>P297-P304 From hospital to home: NIV in clinical</td>
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<td>8.45am – 2.30pm</td>
<td>Moderated poster viewing</td>
<td>M263-M272 IPF: education, information and health</td>
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<tr>
<td>8.00am – 8.30am</td>
<td>BTS Journal Club</td>
<td>COPD</td>
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<tr>
<td>8.30am – 10.00am</td>
<td>Symposium</td>
<td>Respiratory nerves: getting on your patients’ nerves</td>
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<td>Mountbatten Room/6&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>8.30am – 10.00am</td>
<td>Spoken session</td>
<td>COPD outcomes</td>
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<td>St James’s Suite/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>8.30am – 10.00am</td>
<td>Spoken session</td>
<td>Scientific advances in lung cancer</td>
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<td>Henry Moore Room/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>8.30am – 10.00am</td>
<td>Spoken session</td>
<td>Infection of the pleural space in disease and on</td>
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<td>Abbey Room/4&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>8.30am – 10.15am</td>
<td>Symposium</td>
<td>New developments in bronchiectasis</td>
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<td>Churchill Auditorium/Ground</td>
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<tr>
<td>8.30am – 10.15am</td>
<td>Symposium</td>
<td>Autophagy – an important mechanism in the treatment</td>
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<td>of respiratory disease</td>
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<td>Elizabeth Windsor Room/5&lt;sup&gt;th&lt;/sup&gt;</td>
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<tr>
<td>9.00am – 10.00am</td>
<td>Open meeting</td>
<td>Asthma SAG</td>
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<tr>
<td>9.00am – 10.00am</td>
<td>Open meeting</td>
<td>Sleep Apnoea SAG</td>
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<tr>
<td>10.00am – 11.00am</td>
<td>COFFEE/TEA</td>
<td>Whittle &amp; Fleming Rooms and Benjamin Britten</td>
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<td>Lounge/3&lt;sup&gt;rd&lt;/sup&gt;</td>
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<tr>
<td>10.30am – 11.30am</td>
<td>Open meeting</td>
<td>Tobacco SAG</td>
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<tr>
<td>10.30am – 12.00pm</td>
<td>Symposium</td>
<td>Measurement and treatment of breathlessness</td>
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<td></td>
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<td>Churchill Auditorium/Ground</td>
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<tr>
<td>10.30am – 12.00pm</td>
<td>Symposium</td>
<td>Controversies in respiratory infection and</td>
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<td></td>
<td>vaccination</td>
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<td>Elizabeth Windsor Room/5&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
<tr>
<td>10.30am – 12.00pm</td>
<td>Spoken session</td>
<td>Clinical investigations and outcomes in pulmonary</td>
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<td>vascular disease</td>
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<td></td>
<td>St James’s Suite/4&lt;sup&gt;th&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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

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<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
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</thead>
<tbody>
<tr>
<td>10.30am – 12.00pm</td>
<td>Spoken session</td>
<td>S123-S127</td>
</tr>
<tr>
<td>10.30am – 12.15pm</td>
<td>Spoken session</td>
<td>S128-S133</td>
</tr>
<tr>
<td>10.30am – 12.30pm</td>
<td>Symposium</td>
<td>Drug development for acute lung injury</td>
</tr>
<tr>
<td>12.00pm – 2.00pm</td>
<td>LUNCH</td>
<td>Pickwick Suite/1&lt;sup&gt;st&lt;/sup&gt; and Whittle &amp; Fleming Rooms/3&lt;sup&gt;rd&lt;/sup&gt;</td>
</tr>
<tr>
<td>12.30pm – 1.15pm</td>
<td>The Morriston Davies Lecture</td>
<td>Communicating risk and uncertainty to the public and policy makers</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>Open meeting</td>
<td>Critical Care SAG</td>
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<tr>
<td>1.30pm – 2.45pm</td>
<td>Poster discussion</td>
<td>P205-P214</td>
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<tr>
<td>1.30pm – 3.00pm</td>
<td>Poster discussion</td>
<td>P215-P226</td>
</tr>
<tr>
<td>1.30pm – 3.10pm</td>
<td>Spoken session and update</td>
<td>S134-S138</td>
</tr>
<tr>
<td>1.30pm – 3.15pm</td>
<td>Symposium</td>
<td>Clinical audit and quality improvement</td>
</tr>
<tr>
<td>1.30pm – 3.15pm</td>
<td>Spoken session</td>
<td>S139-S144</td>
</tr>
<tr>
<td>1.30pm – 3.20pm</td>
<td>Poster discussion</td>
<td>P227-P241</td>
</tr>
<tr>
<td>1.30pm – 3.30pm</td>
<td>Symposium</td>
<td>25 years of sleep research: where are we now?</td>
</tr>
<tr>
<td>2.00pm – 3.00pm</td>
<td>Poster discussion</td>
<td>P242-P247</td>
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<tr>
<td>2.30pm – 4.20pm</td>
<td>Poster discussion</td>
<td>P248-P262</td>
</tr>
<tr>
<td>3.00pm – 4.15pm</td>
<td>Moderated poster discussion</td>
<td>M263-M272</td>
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<tr>
<td>3.15pm – 4.15pm</td>
<td>Poster discussion</td>
<td>P273-P280</td>
</tr>
<tr>
<td>3.15pm – 4.15pm</td>
<td>Open meeting</td>
<td>Interventional Procedures SAG</td>
</tr>
<tr>
<td>3.15pm – 4.30pm</td>
<td>Poster discussion</td>
<td>P281-P289</td>
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<tr>
<td>3.30pm – 4.30pm</td>
<td>Poster discussion</td>
<td>P290-P296</td>
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<tr>
<td>3.30pm – 4.30pm</td>
<td>Poster discussion</td>
<td>P297-P304</td>
</tr>
<tr>
<td>3.00pm – 4.45pm</td>
<td>COFFEE/TEA</td>
<td>Benjamin Britten Lounge/3&lt;sup&gt;rd&lt;/sup&gt;</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 3 DECEMBER 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
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</tr>
</thead>
<tbody>
<tr>
<td>9.30am – 10.30am</td>
<td>Lung Physiology SAG</td>
<td>Victoria Suite/2nd</td>
</tr>
<tr>
<td>10.45am – 11.45am</td>
<td>Interstitial and Rare Lung Disease SAG</td>
<td>Albert Suite/2nd</td>
</tr>
<tr>
<td>11.00am – 12.00pm</td>
<td>Lung Infection SAG</td>
<td>Victoria Suite/2nd</td>
</tr>
<tr>
<td>11.00am – 12.00pm</td>
<td>Tuberculosis SAG</td>
<td>Rutherford Room/4th</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>Nurse Advisory Group</td>
<td>Victoria Suite/2nd</td>
</tr>
<tr>
<td>3.15pm – 3.45pm</td>
<td>Clinical Data SAG</td>
<td>Victoria Suite/2nd</td>
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THURSDAY 4 DECEMBER 2014

<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>COPD SAG</td>
<td>Victoria Suite/2nd</td>
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<tr>
<td>9.00am – 10.00am</td>
<td>Cystic Fibrosis SAG</td>
<td>Rutherford Room/4th</td>
</tr>
<tr>
<td>12.15pm – 1.15pm</td>
<td>Lung Cancer and Mesothelioma SAG</td>
<td>Victoria Suite/2nd</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>Pulmonary Vascular Disease SAG</td>
<td>Abbey Room/4th</td>
</tr>
<tr>
<td>12.45pm – 1.45pm</td>
<td>Occupational and Environmental Lung Disease SAG</td>
<td>Rutherford Room/4th</td>
</tr>
<tr>
<td>3.15pm – 4.15pm</td>
<td>Specialist Trainees Advisory Group</td>
<td>Victoria Suite/2nd</td>
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</tbody>
</table>

FRIDAY 5 DECEMBER 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Details</th>
<th>Location/Floor</th>
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</thead>
<tbody>
<tr>
<td>9.00am – 10.00am</td>
<td>Asthma SAG</td>
<td>Victoria Suite/2nd</td>
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<tr>
<td>9.00am – 10.00am</td>
<td>Sleep Apnoea SAG</td>
<td>Rutherford Room/4th</td>
</tr>
<tr>
<td>10.30am – 11.30am</td>
<td>Tobacco SAG</td>
<td>Rutherford Room/4th</td>
</tr>
<tr>
<td>12.30pm – 1.30pm</td>
<td>Critical Care SAG</td>
<td>Victoria Suite/2nd</td>
</tr>
<tr>
<td>3.15pm – 4.15pm</td>
<td>Interventional Procedures SAG</td>
<td>Victoria Suite/2nd</td>
</tr>
</tbody>
</table>

BTS MEDAL AND AWARD PRESENTATIONS

Wednesday 3 December 2014 at 4.15pm in the Churchill Auditorium, 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 Address from the President of the American Thoracic Society. Please come along to this session to congratulate the winners.

THE BTS PRESIDENT’S RECEPTION

Thursday 4 December 2014, 5.30pm to 7.15pm in the Benjamin Britten Lounge, 3rd floor

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

**Benjamin Britten Lounge, 3rd floor**

- 61 Association for Respiratory Technology and Physiology (ARTP)
- 60 Association of Chartered Physiotherapists in Respiratory Care (ACPRC)
- 59 Association of Respiratory Nurse Specialists (ARNS)
- 55 BMJ Group
- 62 British Association for Lung Research (BALR)
- 66 British Lung Foundation
- 50 British Thoracic Society
- 56 BTS Nurse Advisory Group
- 63 Education for Health
- 57 European Respiratory Society
- 51 National COPD Audit Programme, led by the Royal College of Physicians
- 58 Primary Care Respiratory Society UK
- 64 Primary Ciliary Dyskinesia (PCD) Family Support Group UK
- 52 Royal College of Physicians NRAD

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**Exhibitors and stand numbers**

**Whittle & Fleming Rooms, 3rd floor**

- 16, 17 & 18 Almirall
- 29 Aquilant Endoscopy
- 21, 22 & 28 AstraZeneca Ltd
- 1 Bayer
- 33, 34 & 35 Boehringer Ingelheim
- 36 Boston Scientific
- 2 Chiesi Ltd
- 15 Clement Clarke International
- 31 & 32 Forest Laboratories UK Ltd, a subsidiary of Actavis PLC
- 4 & 10 GlaxoSmithKline
- 8 Hitachi Medical Systems & Pentax Medical
- 23, 24, 25 & 26 Intermune
- 11 Napp Respiratory
- 9 Novartis
- 6 & 7 Olympus
- 13 Otsuka
- 27 Oxford Diagnostic Laboratories
- 5 PneumRx
- 12 Pulmonx
- 19 & 20 Rocket Medical plc
- 3 Teva UK Ltd
- 30 Vertex
- 14 Vitalograph

**Benjamin Britten Lounge, 3rd floor**

- 40 Actegy Ltd
- 45 Actelion Pharmaceuticals Ltd
- 41 Dolby Vivisol
- 37 Medela
- 39 Nutricia Advanced Medical Nutrition
- 47 Pfizer UK
- 44 Pharmaxis
- 48 R Cegla Ltd
- 49 Wise press Medical Bookshop
Wednesday 3 December 2014

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

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

P1-P13
Cough: mechanisms and therapies
Discussion of abstracts will take place from 1.00pm to 2.35pm in the Henry Moore Room, 4th floor

P14-P26
Basic mechanisms of acute lung injury, ILD and PAH
Discussion of abstracts will take place from 1.15pm to 2.50pm in the Abbey Room, 4th floor

P27-P34
Keeping your distance: telemonitoring and telehealth
Discussion of abstracts will take place from 2.00pm to 3.00pm in the Albert Suite, 2nd floor

P44-P57
Asthma: investigation and organisation of care
Discussion of abstracts will take place from 2.00pm to 3.45pm in the Elizabeth Windsor Room, 5th floor

P58-P68
COPD phenotyping
Discussion of abstracts will take place from 2.30pm to 4.00pm in the St James’s Suite, 4th floor

P69-P78
Improving lung cancer outcomes
Discussion of abstracts will take place from 2.45pm to 4.00pm in the Henry Moore Room, 4th floor

P79-P87
Clinical management of pulmonary infection
Discussion of abstracts will take place from 3.00pm to 4.10pm in the Abbey Room, 4th floor

P88-P95
Smoothing the process: clinical management of COPD and bronchiectasis
Discussion of abstracts will take place from 3.05pm to 4.05pm in the Albert Suite, 2nd floor

P95-P106
Getting to grips with paediatric lung disease
Discussion of abstracts will take place from 3.30pm to 5.00pm in the Mountbatten Room, 6th floor

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SCIENTIFIC PROGRAMME

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

M35-M43
Tackling TB
Discussion of abstracts will take place from 2.00pm to 3.10pm in the Mountbatten Lounge, 5th floor

8.00am – 8.30am
Albert Suite, 2nd Floor
BTS JOURNAL CLUB
LUNG TRANSPLANTATION
Professor Paul Corris (Newcastle upon Tyne)

8.30am – 10.15am
Churchill Auditorium, Ground Floor
SYMPOSIUM
COPD EXACERBATIONS – IMPROVING THE OUTCOME
Chaired by: Dr Gillian Lowrey (Derby) and Dr Elin Roddy (Shrewsbury)

8.30am  Predicting survival in COPD exacerbations
Dr Jennifer Quint (London)

8.55am  PR during and after exacerbations
Dr Neil Greening (Leicester)

9.20am  Technology post admission
Dr Hilary Pinnock (Whitstable & Edinburgh)

9.45am  Care bundles
Dr James Calvert (Bristol)

The optimal management of COPD exacerbations is an important area in respiratory medicine. This session addresses the factors that predict poor prognosis in AECOPD and reviews the evidence for interventions that have been proposed to improve outcomes; pulmonary rehabilitation, telehealth and care bundles.

8.30am – 10.15am
St James’s Suite, 4th Floor
SPOKEN SESSION: S1 – S6
Occupational lung disease
Chaired by: Professor Paul Cullinan (London) and Dr Johanna Feary (London)
SCIENTIFIC PROGRAMME

8.35am S1
A new, efficient web-based tool to collect and code lifetime job histories in large population-based studies: the COPD project in the UK Biobank cohort
S De Matteis, D Jarvis, M Wheatley, H Azhar, A Young, H Young, L Rushton, P Cullinan

8.50am S2
Development of a job exposure matrix for SOC 2000 listings to identify occupational causes of COPD
S Sadhra, D Fishwick, OP Kurmi, H Chambers, KBH Lam, S Hutchings, D Jarvis, S De Matteis, L Rushton, JG Ayres, P Cullinan

9.05am S3
Idiopathic pulmonary fibrosis, mesothelioma, and asbestosis mortality trends for England and Wales: is asbestos exposure associated with IPF?
C Reynolds, C Barber, P Cullinan

9.20am S4
Relationship between historic UK asbestos imports and annual mortality due to mesothelioma, asbestosis and idiopathic pulmonary fibrosis.
CM Barber, RE Wiggans, D Fishwick

9.35am S5
Prevalence of IgE sensitisation to ‘improver mix’ enzymes among symptomatic bakers working in UK scratch bakeries
M Jones, J Welch, J Turvey, J Cannon, B Fitzgerald, J Szram, P Cullinan

9.50am S6
The role of individually ventilated cages in prevention of laboratory animal allergy: a proof of concept study
JR Feary, Z Lightfoot, B Fitzgerald, S Schofield, M Jones, P Cullinan

Wednesday 3 December 2014

8.30am – 10.15am
Mountbatten Room, 6th Floor
SPOKEN SESSION: S7 – S12
Novel approaches to the management of ILD
Chaired by: Dr Nick Hirani (Edinburgh) and Professor Luca Richeldi (Southampton)

8.35am S7
Nitrofurantoin lung toxicity – are steroids useful?
ADL Marshall, HK Bayes, OJ Dempsey

8.50am S8
Rituximab therapy for refractory myositis related interstitial lung disease unresponsive to conventional immunosuppression: the Bristol Interstitial Lung Disease Service experience
C Sharp, N Dodds, A Edey, H Adamali, H Gunawardena, A Millar

9.05am S9
Acute inflammatory presentation associates with survival in interstitial lung disease and extracorporeal membrane oxygenation-requiring severe respiratory failure: a single centre case series
L Starsmore, B Lams, S Agarwal, A Nair, R Preston, N Barrett, G Glover, N Ioannou, C Langrish, D Wyncoll, CIS Meadows

9.20am S10
Cost burden of N-acetylcysteine (NAC) in adult patients with idiopathic pulmonary fibrosis
R Nasr, I Kausar, N Chaudhuri

9.35am S11
Pirfenidone post-authorization safety registry (PASSPORT) – interim analysis of IPF treatment
TM Maher, V Cottin, M Skoeld, S Tomassetti, A Azuma, C Giot, D Yocum, S Hamza, D Koschel

9.50am S12
Effect of baseline FVC on decline in lung function with nintedanib: results from the INPULSIS™ trials
U Costabel, Y Inoue, L Richeldi, HR Collard, S Stowasser, IT Schoepfe, A Azuma
Wednesday 3 December 2014

8.30am – 10.30am
Westminster Suite, 4th Floor
JOINT BTS/BALR SYMPOSIUM (part 1)
MODELLING RESPIRATORY DISEASE: CURRENT CONCEPTS FOR DRUG DISCOVERY
Chaired by: Dr Paul Mercer (London) and Professor Terry Tetley (London)

8.30am
Testing, testing, 123: using in vivo models to identify new drugs for respiratory disease
Professor Clive Page (London)

9.10am
Seeing is believing! Imaging in vivo models of lung disease
Dr Chris Scotton (Exeter)

9.50am
Who needs lungs to study lung disease?
Using zebrafish to study inflammation
Professor Stephen Renshaw (Sheffield)

This session will discuss the use of existing animal models in the context of investigating the pharmacology of pulmonary inflammation; highlight the use of micro-CT as a viable system for imaging lung fibrosis in mice in the bleomycin model of lung fibrosis; and demonstrate how pulmonary neutrophilic inflammation can be modelled and visualised in vivo using a transgenic zebrafish model.

8.45am – 10.15am
Abbey Room, 4th Floor
SPOKEN SESSION: S13 – S17
Clinical management of lung infection
Chaired by: Dr Adam Hill (Edinburgh) and Dr Michael Loebinger (London)

8.50am
S13
Incidence and risk factors for the development of hospital acquired pneumonia in older hospitalised patients
LA Burton, RJG Price, KE Barr, SM McAuley, JB Allen, A Clinton, G Phillips, CA Marwick, MET McMurdo, MD Witham

9.05am
S14
Time trends and risk factors for hospitalisation after community-acquired pneumonia in older adults in England

9.20am
S15
Clinical characteristics of hospitalised patients misdiagnosed with community-acquired pneumonia
H Pick, J Lacey, D Hodgson, E MacDonald, A Turvey, T Bewick

9.35am
S16
A randomised controlled trial of Atorvastatin as a stable treatment in bronchiectasis
P Mandal, J Chalmers, M Sidhu, D Davidson, A Rossi, A Hill

9.50am
S17
Cardiovascular risk factors in people with bronchiectasis: a cross sectional study
V Navaratnam, E Millett, JR Hurst, SL Thomas, L Smeeth, RB Hubbard, J Brown, JK Quint

9.30am – 10.30am
Victoria Suite, 2nd Floor
OPEN MEETING

BTS Lung Physiology Specialist Advisory Group

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

10.30am – 12.00pm
Mountbatten Room, 6th Floor
SYMPOSIUM
CYSTIC FIBROSIS: CURRENT ISSUES
Chaired by: Dr Ian Balfour Lynn (London) and Dr Stephen Bourke (Newcastle upon Tyne)

10.30am
Inhaled treatment regimens: burden and benefit
Professor Diana Bilton (London)

11.00am
Segregation for infection control: evidence and effectiveness
Dr Andrew Jones (Manchester)

11.30am
Gene therapy
Professor Eric Alton (London)
The objectives of this session are to: evaluate the evidence for inhaled antibiotic therapies in cystic fibrosis and the relative impact of regimes on patients and their adherence; review the evidence for transmission of bacterial pathogens in cystic fibrosis and the impact and importance of segregation to prevent transmission; discuss the latest developments in gene therapy and its role in relation to other emerging treatments in cystic fibrosis.

10.30am – 12.00pm
St James’s Suite, 4th Floor
SPOKEN SESSION: S18 – S22
COPD investigations
Chaired by: Dr John Hurst (London) and Dr David Parr (Coventry)

10.35am  S18
Rate of decline in lung density may predict long-term outcome in patients with alpha 1 antitrypsin deficiency (AATD)
CE Green, D Parr, RA Stockley, AM Turner

10.50am  S19
Imaging derived regional lung function using hyperpolarised xenon MRI (Xe-MRI) and quantitative computed tomography (QCT) in chronic obstructive pulmonary disease (COPD)
TN Matin, X Xu, T Doel, V Grau, N Rahman, A Nickol, FV Gleeson

11.05am  S20
18F-Fluorodeoxyglucose (18FDG) PET pulmonary imaging: comparative methodology in COPD patients
G Choudhury, A Fletcher, M Connell, B Whitcher, S Fergusson, T Clark, BVennart, I Kilty, E VanBeek, W MacNee

11.20am  S21
Culture independent identification of bacterial communities in the respiratory tract of patients with COPD, healthy non-smokers and healthy smokers
GG Einarsson, A Walker, MM Tunney, JS Elborn

11.35am  S22
The effect of cigarette smoke on important pathogens in COPD lung infection
K McGown, MM Tunney, SJ McGrath, JS Elborn, DF Gilpin

10.30am – 12.15pm
Elizabeth Windsor Room, 5th Floor
SPOKEN SESSION: S23 – S28
Sleep disordered breathing: assessment and treatment
Chaired by: Dr Melissa Hack (Newport) and Dr Justin Pepperell (Taunton)

10.35am  S23
Results of a national survey of pre-operative screening for obstructive sleep apnoea
R Sharrock, S Baudouin, S West

10.50am  S24
Repeatability and effect of incentives on an office based advanced driving simulator (MiniUoLDS) to assess driving performance in obstructive sleep apnoea syndrome (OSAS)
A Dwarakanath, SL Jamson, PD Baxter, MW Elliott

11.05am  S25
Sleepy snorers with “flow limitation syndrome”: a missed opportunity for CPAP?
R Yadavilli, B Chakrabarti, S McDougall, L Horne, S Emegbo, S Craig, N Duffy, R Parker, J O’Reilly

11.20am  S26
What are the predictors of developing hypoventilation in obesity?
A Manuel, N Hart, J Stradling

11.35am  S27
Venous bicarbonate as a clinical tool for identifying obesity hypoventilation syndrome in the sleep clinic
B Prudon, SD West
Wednesday 3 December 2014

11.50am  S28  
Liraglutide 3.0 mg reduces severity of obstructive sleep apnoea and body weight in obese individuals with moderate or severe disease: SCALE sleep apnoea trial  
A Collier, A Blackman, G Foster, G Zammit, R Rosenberg, T Wadden, L Aronne, B Claudius, T Jensen, E Mignot

10.30am – 12.30pm  
Churchill Auditorium, Ground Floor  
SYMPOSIUM  
PLEURAL DISEASE – WHAT IS CURRENT BEST PRACTICE?  
Chaired by: Dr Nick Maskell (Bristol) and Dr Najib Rahman (Oxford)

10.30am  
Primary spontaneous pneumothorax management – don’t follow the BTS guidelines!  
Pro – Dr John Harvey (Bristol)  
Con – Dr Andrew MacDuff (Wolverhampton)

11.00am  
Indwelling pleural catheters should be first line management for all non-trapped symptomatic malignant pleural effusions  
Pro – Dr Mark Slade (Cambridge)  
Con – Dr Mohammed Munawvar (Preston)

11.50am  
All patients with pleural infection should undergo VATS surgery if not responding to initial tube drainage and antibiotics  
Pro – Mr John Edwards (Sheffield)  
Con – Dr Alex West (London)

This session will highlight that conservative/ambulatory management of PSP might be appropriate; allow discussion of the correct place of IPCs in the management of MPE; debate whether VATS should be first line for all cases of CPE/empyema; and if there is a role for tPA /DNase.

10.45am – 11.45am  
Albert Suite, 2nd Floor  
OPEN MEETING  
BTS Interstitial and Rare Lung Disease Specialist Advisory Group

SCIENTIFIC PROGRAMME

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

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

11.00am – 1.00pm  
Westminster Suite, 4th Floor  
JOINT BTS/BALR SYMPOSIUM (part 2)  
MODELLING RESPIRATORY DISEASE: CURRENT CONCEPTS FOR DRUG DISCOVERY  
Chaired by: Professor Rachel Chambers (London) and Dr Amanda Tatler (Nottingham)

11.00am  
The next dimension: 3D in vitro modelling of fibrotic lung disease  
Professor Eric White (Michigan)

11.40am  
Lung-on-a-chip: engineering asthmatic airways in vitro  
Professor Donna Davies (Southampton)

12.20pm  
Screen-ovation: novel in vitro platforms for anti-fibrotic drug development  
Dr Carmel Nanthakumar (GlaxoSmithKline)

Part 2 will present data showing that de-cellularised human lung matrix can be used as an ex vivo model of lung fibrosis. Development of “lung on a chip” will be discussed and its use in the context of severe/refractory asthma. Recent work using primary fibroblasts to model fibrogenesis in vitro will also be highlighted.

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

12.15pm – 1.15pm
Victoria Suite, 2nd Floor
OPEN MEETING
BTS Nurse Advisory Group

12.30pm – 1.30pm
Rutherford Room, 4th Floor
OPEN MEETING
NICE Pneumonia Guideline 2014
Chaired by: Professor Mark Woodhead (Manchester)
Speakers to be confirmed

12.45pm – 1.30pm
Churchill Auditorium, Ground Floor
THE BTS LECTURE
Asthma phenotypes: evolution from clinical to molecular
Professor Sally Wenzel (Pittsburgh)
Introduced by: Professor Ashley Woodcock (Manchester)

1.00pm – 2.30pm
St James’s Suite, 4th Floor
SPOKEN SESSION: S29 – S33
‘Blood and spit’ – What to measure in AECOPD
Chaired by: Dr Stephen Bourke (North Tyneside) and Professor Peter Calverley (Liverpool)

1.05pm  S29
Prognostic value of platelet count in patients admitted with an acute exacerbation of COPD (AECOPD)
C Echevarria, J Steer, GJ Gibson, SC Bourke

1.20pm  S30
Red cell distribution width as a predictor of hospital mortality in acute exacerbations of COPD (AECOPD)
C Echevarria, J Steer, GJ Gibson, SC Bourke

1.35pm  S31
Predicting death or deterioration in patients admitted with acute exacerbation of COPD using physiological and blood parameters

Wednesday 3 December 2014

1.50pm  S32
The relationship between exercise capacity and inflammatory markers at COPD exacerbation
AD Alahmari, BS Kowlessar, ARC Patel, AJ Mackay, SE Brill, JP Allinson, R Singh, JA Wedzicha, GC Donaldson

2.05pm  S33
Sputum colour in the light of the health related quality of life, airways and systemic biomarkers in exacerbations of COPD
V Kim, N Williams, K Ostridge, A Barton, MM Wojtas, E Aris, M Peeters, JM Devaster, S Bourne, T Wilkinson

1.00pm – 2.35pm
Henry Moore Room, 4th Floor
POSTER DISCUSSION: P1 – P13
Cough: mechanisms and therapies
Chaired by: Professor Maria Belvisi (London) and Professor Jacky Smith (Manchester)

P1 A novel capsaicin cough challenge in healthy adults; beyond the C5
K Holt, C Gibbard, K Ahern, JA Smith

P2 Characterisation of Aδ- and c-fibres innervating guinea-pig airways
JJ Adcock, MA Birrell, SA Maher, SJ Bonvini, ED Dubuis, MA Wortley, KE Baker, MG Belvisi

P3 Efficacy of a physiotherapy, speech and language therapy intervention (PSALTI) on health related quality of life (HRQoL) for patients with refractory chronic cough: a randomised control trial
SAF Chamberlain, SS Birring, L Clarke, A Douiri, SM Parker, SJ Fowler, J Hull, KF Chung, A Pandyan, R Garrod

P4 Establishing a role for TRPV1 on sensory nerves in COPD associated chronic cough
MA Wortley, SA Maher, SJ Bonvini, ED Dubuis, J Nasra, K Holt, R Dockry, S Sen, D Singh, JA Smith, P Round, S Gilbert, V Marchant, J Ford, MA Birrell, MG Belvisi
Wednesday 3 December 2014

P5  Lipid-laden macrophages in bronchoalveolar lavage fluid are not diagnostic of airway reflux
YA Hayman, L Sadofsky, S Faruqi, SP Hart, AH Morice

P6  Menthol has beneficial effects in the airways through a TRPM8-independent mechanism
SA Maher, MA Birrell, SJ Bonvini, MA Wortley, ED Dubuis, F Shala, VC Jones, P Flajolet, Y Negreskul, Z Britton, L Hebib, MG Belvisi

P7  Neuronal dysfunction in asthma; insights from the study of the cough reflex
I Satia, K Holt, H Badri, M Woodhead, P O’Byrne, P O’Byrne, SJ Fowler, JA Smith

P8  Objective cough frequency monitoring in bronchiectasis
A Spinou, R Garrod, KK Lee, C Elston, MR Loebinger, KF Chung, R Wilson, SS Birring

P9  Cough is prevalent in higher proportion of older patients with both idiopathic pulmonary fibrosis and non-specific interstitial lung disease
G Saini, T McKeever, R Braybrooke, R Hubbard, G Jenkins, RM Marshall, PL Lukey, JS Simpson

P10  The effect of naltrexone, an opioid receptor antagonist, on capsaicin evoked cough, in healthy male subjects
I Satia, K Holt, E Hilton, AA Woodcock, J Smith

P11  The role of GABAB receptor mechanisms in the human cough reflex

P12  The usefulness of heartburn as a marker of the success of acid suppression therapy in chronic cough
H Badri, I Satia, A Woodcock, JA Smith

P13  The overlapping prevalence of chronic mucus hypersecretion (CMH) and chronic cough (CC)
JPA Allinson, RH Hardy, GCD Donaldson, SOS Shaheen, DK Kuh, JAW Wedzicha

SCIENTIFIC PROGRAMME

1.15pm – 2.50pm
Abbey Room, 4th Floor
POSTER DISCUSSION: P14 – P26

Basic mechanisms of acute lung injury, interstitial lung disease and pulmonary arterial hypertension

Chaired by: Professor Louise Donnelly (London) and Dr Mark Griffiths (London)

P14  Very high quality next-generation DNA sequencing data from human genomic DNA samples stored, and intermittently defrosted over two decades
CL Shovlin, FS Govani, IG Mollet, E Thomas, MD Jones, A Giess, L Game

P15  Directional next generation whole transcriptome sequencing of primary human pulmonary microvascular endothelial cells
CL Shovlin, D Patel, FS Govani, A Giess, MD Jones, L Game, IG Mollet

P16  A systematic characterization of inflammation in chronic thromboembolic pulmonary hypertension
C Hadinnapola, M Southwood, D Jenkins, K Sheares, M Toshner, J Pepke-Zaba

P17  Molecular complexities identified through targeted genomic sequencing of the HHT3 locus on chromosome 5
CL Shovlin, IG Mollet, A Giess, E Thomas, MD Jones, L Game, FS Govani

P18  Robo1/4-Slit2 expression in pulmonary vascular cells: implications for PAH?
J Chowdhury, L Ramakrishnan, T Svermova, S Mumby, D Shao, SJ Wort, A Burke-Gaffney

P19  The role of differential TNFR signalling in maintenance of alveolar epithelial homeostasis
FR Millar, AG Proudfoot, D Salman, C Summers, P Morley, J Cordy, A Bayliffe, C Dean, MJ Griffiths

P20  Delineating the contribution of formylated peptides and formyl peptide receptor 1 to the pathogenesis of acute lung injury
DA Dorward, CD Lucas, MK Doherty, GB Chapman, E Scholefield, A Conway-Morris, T Kipari, CT Robb, JM Felton, PD Whitfield, C Haslett, K Dhaliwal, AG Rossi
**SCIENTIFIC PROGRAMME**

**P21** Hypoxia-induced neutrophil survival is dependent on phosphoinositide 3-kinase (PI3-K)-mediated signalling  
S Palazzo, L Porter, JK Juss, E Hessel, A Amour, D House, M Begg, ER Chilvers

**P22** Endoplasmic reticulum stress markers correlate with fibrosis in idiopathic pulmonary fibrosis and non-specific interstitial pneumonia  
H Parfrey, B Beardsley, J Knight, SJ Marciniak, D Rassl

**P23** Target and biomarker discovery for Hedgehog pathway activity in idiopathic pulmonary fibrosis in support of a phase 2 randomized, double-blind, placebo-controlled study to assess efficacy and safety of vismodegib in IPF (ISLAND)  

**P24** Vitamin D levels are low in sarcoidosis and contribute to abnormal monocyte activity  
AP Crawshaw, YR Kendrik, E Martinez Estrada, L-P Ho

**P25** Distinct pro-inflammatory gene expression profile in monocytes from sarcoidosis patients with active disease  
AP Crawshaw, YR Kendrik, E Repapi, S Taylor, L-P Ho

**P26** P38 MAPK inhibition enhances corticosteroid effects in human epithelial cells via increased GR nuclear localisation  
S Lea, K Gaffey, J Plumb, R Gaskell, D Singh

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**Wednesday 3 December 2014**

**2.15pm** The microbiome in asthma and COPD  
*Professor William Cookson (London)*

**2.45pm** The microbiome in cystic fibrosis  
*Professor Stuart Elborn (Belfast)*

Over recent years, molecular tools have transformed the way we regard the microbiology of the airway, demonstrating significantly more species than was suspected with conventional culture techniques. What exactly these findings mean is less clear. In this session we will have state of the art reviews by experts in three fields to begin to address this knowledge gap.

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**2.00pm – 3.00pm**  
Albert Suite, 2nd Floor  
**POSTER DISCUSSION: P27 – P34**

**Keeping your distance: telemonitoring and telehealth**

*Chaired by: Dr Martin Allen (Stoke-on-Trent) and Dr Jo Congleton (Worthing)*

**P27** The use of telemonitoring to assist in the early supported discharge for patients admitted with an exacerbation of COPD  
G Dawson, M Collinge, JA Roberts, N Diar Bakerly

**P28** The use of smartphone application (COPD Assist) to support the implementation of local primary care guidelines on the management of patients with COPD  
N Diar Bakerly, S McCorkindale, G Patel

**P29** Impact of respiratory virtual clinics in primary care on responsible respiratory prescribing and inhaled corticosteroid withdrawal in patients with COPD: a feasibility study  

**P30** Use of a regional COPD dashboard to effect large scale change  
J Congleton, J Wookey, J Bott, KSS AHSN Respiratory Programme

**P31** Intelligence based information system (IBIS) reduces respiratory patients’ use of secondary health care resources  
SKM Harlow, J Tollit, MJ Irvin-Sellers
**Wednesday 3 December 2014**

**P32** A novel automated referral system using the electronic prescription of prednisolone >=30mg and nebulised bronchodilators to the respiratory specialist team is robust and effective
RC Colclough, T Avent, K Breese, C Craddock, D Curry, K Swindells, S Gompertz

**P33** ‘Light touch’ telemonitoring for people with COPD in Lothian: a pilot evaluation with nested qualitative study
HJ Pinnock, M MacNab, S Lee, L McCloughan, J Hanley, A Lindsay, B McKinstry

**P34** What is integrated care and what is the value of an integrated respiratory specialist?
NJ Roberts, M Ward, IS Patel, J Yorke, J Williams, R Walters, M McKeivitt, S Edwards

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**2.00pm – 3.10pm**
Mountbatten Lounge, 5th Floor
**MODERATED POSTER DISCUSSION:**
**M35 – M43**

**Tackling tuberculosis**
Chaired by: Dr Marc Lipman (London) and Dr Anna Rich (Nottingham)

**M35** Adverse effects of latent tuberculosis treatment in migrants
EK Denny, VM Macavei, S Rolls, C Ma, NP Jayasekera, TC O’Shaughnessy, VLC Potter, VLC White, H Kunst

**M36** Evaluating aerosol administration of a candidate TB vaccine MVA85A
Z Manjaly Thomas, I Satti, S Harris, J Meyer, S Sheehan, H Bettinson, H McShane

**M37** Does the tuberculin skin test increase the detection of TB infection when screening HIV positive patients? Three years’ experience in a District General Hospital
A Bennett, J Ashby, M Curtiss, N Pal, T Wambaa, S Menzies

**M38** Health professionals’ views of tuberculosis cohort audit in North West England
S Wallis, K Jehan, M Woodhead, P Cleary, K Dee, S Farrow, P McMaster, C Wake, J Walker, SB Squire

**M39** Screening for tuberculomas in patients with miliary tuberculosis – what modality of imaging should we be using?
R Ghani, H Durkan, L John, R Davidson, J Buckley

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**M40** Tackling poor attendance to tuberculosis clinic – who, why and what can be done
EK Denny, SE Black, Y Bogle, VM Macavei, TC O’Shaughnessy, VLC White, H Kunst, NP Jayasekera

**M41** Recurrent tuberculosis and its risk factors in the UK’s largest TB centre
K Avery, R Ghani, J Buckley, L John, RN Davidson

**M42** Increasing complexity of treating TB in older patients
J Barrett, GA O’Hara, A Nundoll, N Price, H Milburn, RAM Breen

**M43** The accuracy of clinical TB diagnoses in culture negative patients
L Maynard Smith, NP Jayasekera, VM Macavei, TC O’Shaughnessy

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**2.00pm – 3.30pm**
Westminster Suite, 4th Floor
**SYMPOSIUM T1 – T6**

**BTS/BLF/BALR Early Career Investigator Symposium**
Chaired by: Professor Edwin Chilvers (Cambridge) and Professor Moira Whyte (Sheffield)
Judged by: Professor Sam Janes (London), Professor Ann Millar (Bristol) and Professor Terry Tetley (London)

**T1** Aspirin reduces pulmonary inflammation in an inhaled lipopolysaccharide model of acute respiratory distress syndrome (ARDS) in healthy volunteers and in a human ex vivo lung perfusion model of ARDS
UIH Imran Hamid, JC Conlon, SP Spence, AB Boyle, MF Fitzgerald, MS Shyamsunder, AK Krasnodembskaya, AK Kissenpfennig, RV Verghis, CS Scott, DFM McAuley, CO O’Kane

**T2** Vitamin D enhances bronchial epithelial cell antioxidant responses and reduces their pro-inflammatory cytokine response to stimulation by urban particulate matter
PE Pfeffer, FJ Kelly, CM Hawrylowicz

**T3** The effect of electronic cigarette exposure on innate immune cells
L Maynard Smith, NP Jayasekera, VM Macavei, TC O’Shaughnessy
SCIENTIFIC PROGRAMME

AJ Higham, NJW Rattray, JA Dewhurst, D Singh

T4 Pneumococcal conjugate vaccine reduces rate, density and duration of experimental human pneumococcal colonisation: first human challenge testing of a pneumococcal vaccine
AM Collins, AD Wright, E Mitsi, JF Gritzfeld, C Hancock, D Shaw, SH Pennington, B Morton, DM Ferreira, SB Gordon

T5 OPG regulates pulmonary arterial smooth muscle cell proliferation and the expression of PAH-associated genes via FAS
S Dawson, J Pickworth, AMK Rothman, J Iremonger, N Arnold, S Francis, A Lawrie

T6 Impact of environmental differences in the prevalence of airway dysfunction in elite athletes: GB boxing versus GB swimming
IK Levai, JW Dickinson, M Loosemore, J Greenwell, JH Hull, G Whyte

This symposium will showcase the very best original research submitted to the Winter Meeting by UK scientists and clinicians in the early part of their research career, as they compete for prestigious prizes from the BTS, BLF and BALR.

2.00pm – 3.45pm
Rutherford Room, 4th Floor
SPOKEN SESSION: S34 – S39
Pulmonary arterial hypertension: scientific advances
Chaired by: Dr Luke Howard (London) and Dr Mark Toshner (Cambridge)

2.05pm S34
BMPR-II deficiency leads to an increase in lung egg deposition, pulmonary vascular remodelling and an abnormal liver vasculature in mice chronically infected with S. mansoni
A Crosby, E Soon, F Jones, M Southwood, L Haghighat, M Toshner, T Raine, I Horan, P Yang, A Davenport, S Moore, PWright, D Dunne, N Morrell

Wednesday 3 December 2014

2.20pm S35
BMP9 and BMP10 mediate connexin expression in endothelial cells: implications for PAH and HHT
PD Upton, JM Wilkinson, KA Wiggins, NW Morrell

2.35pm S36
Ferroportin is expressed in human pulmonary artery smooth muscle cells: implications for pulmonary arterial hypertension
L Ramakrishnan, S Mumby, JS Wort, G Quinlan

2.50pm S37
Vascular endothelial cell growth factor-A (VEGF-A) signalling and neovascularisation of pulmonary endarterectomy material in chronic thromboembolic pulmonary hypertension (CTEPH)
M Southwood, C Hadinnapola, E Moseley, D Jenkins, M Goddard, K Sheares, M Toshner, J Pepke-Zaba

3.05pm S38
The Brd4 inhibitor, JQ1 decreases proliferation and arrests the cell cycle of pulmonary vascular cells: implications for pulmonary arterial hypertension
S Mumby, N Gambaryan, I Adcock, SJ Wort

3.20pm S39
The role of soluble guanylate cyclase stimulator Bay 41-2272 on remodelling processes relevant to the pathogenesis of pulmonary arterial hypertension
D Shao, SJ Wort

2.00pm – 3.45pm
Elizabeth Windsor Room, 5th Floor
POSTER DISCUSSION: P44 – P57
Asthma: investigation and organisation of care
Chaired by: Dr Philip Ind (London) and Dr Adel Mansur (Birmingham)
Assessment of spirometry and impulse oscillometry in relation to asthma control
A Manoharan, WJ Anderson, J Lipworth, BJ Lipworth

Sputum and nasal markers of inflammation in severe asthma – a pilot study
G Tavernier, R Niven

The influence of age and gender on allergy test results: implications for the use as biomarkers in childhood asthma
HRM Mohammad, DB Belgrave, KKH Harding, AS Simpson, AC Custovic

Continuous laryngoscopy during exercise (CLE): a practical and valuable test in a respiratory service?
B Panchasara, GS Haji, S Ward, A Menzies-Gow, JH Hull

Prevalence and determinants of vitamin D deficiency in asthma patients
DA Jolliffe, AR Martineau, BM Maclachlin, KK Kiplin, P Timms, CAM Mein, RW Walton, CJG Griffiths

Can the asthma control questionnaire (ACQ) and/or the blood eosinophil count accurately detect sputum eosinophilia?
JR Anderson, DB Hodgson, EE Wilson, TW Harrison, DE Shaw

Difficult asthma clinics: are they effective?
I Macpherson, S Fielding, JG Douglas

Barriers and facilitators to effective self-management of asthma – a systematic review and thematic synthesis
SE Kirby, C Miles, E Arden-Close, L Yardley, A Bruton, M Hankins, DM Thomas

PRISMS: a systematic review of the MRC ‘Phase IV’ evidence on implementing asthma self-management
H Pinnock, E Epiphaniou, HL Parke, G Pearce, SJ C Taylor

Manchester desert island question
KE George, HGT Brice, SJ Fowler, LJ Holmes, R Daly, RM Niven

Which secondary care asthma patients are most likely to over-estimate their control? A cross-sectional study
L Patel, J Blakey, K Mortimer

Is prescription uptake and medication adherence rating scale (MARS) a useful tool in assessing asthma control in children with problematic severe asthma (PSA) ?
P Nagakumar, P Hall, M Bracken, S Saglani, A Bush, L Fleming

Impact of pharmacist-led asthma and COPD reviews in general practice
H Khachi

Factors influencing length of hospital stay in asthma exacerbations: results of a service improvement project
AJ Hanson, Y Vali, JRA Fisher-Black, G Woltmann, M Richardson, AJ Wardlaw, S Siddiqui

2.00pm – 4.00pm
Churchill Auditorium, Ground Floor
SYMPOSIUM
TREATING IDIOPATHIC PULMONARY FIBROSIS: THE DAWN OF A NEW ERA
Chairs: Dr Gisli Jenkins (Nottingham) and Dr Toby Maher (London)

2.00pm IPF therapy: exploring the cancer paradigm
Dr Martin Kolb (Hamilton, Ontario)

2.30pm Novel imaging in IPF
Dr Joanna Porter (London)

3.00pm Modifying the microbiome: antibiotics for IPF
Dr Andrew Wilson (Norwich)

3.30pm Pirfenidone: Capacity to Ascend?
Dr Nik Hirani (Edinburgh)

2014 saw further major breakthroughs in our understanding of idiopathic pulmonary fibrosis. This session will explore some of these recent highlights in the emerging management concepts and novel therapies for IPF.

2.30pm – 4.00pm
St James’s Suite, 4th Floor
POSTER DISCUSSION: P58 – P68
COPD phenotyping
Chaired by: Dr Charlotte Bolton (Nottingham) and Dr David Parr (Coventry)
A comparison between the clinical features of PiSZ and PiZZ patients with alpha-1 antitrypsin deficiency
S Vayalapra, RG Edgar, D Griffiths, RA Stockley, AM Turner

Utility of FIB4 score and liver disease in alpha-1 antitrypsin deficiency (A1ATD)
D Bruce-Hickman, A D Saleh, B Gooptu, DA Lomas, D Thorburn, J R Hurst

Cannabis lung causing debilitating emphysema: are we on the verge of an epidemic?
NB Chinnappa, K Zalewska, D McKeon

The prevalence of hypercapnia in patients with alpha-1-anti-trypsin deficiency (AATD)
C Dave, A Turner, T Spruell

Correlation of quantitative chest CT measures with lung function and functional parameters in a cohort of moderate to very severe COPD patients
K Ostridge, N Williams, V Kim, A Barton, MM Wojtas, S Harden, E Aris, M Peeters, JM Devaster, S Bourne, T Wilkinson

Assessment of regional variability in matrix metalloproteinase concentrations by CT informed bronchoalveolar lavage in patients with COPD
K Ostridge, S Harden, P Elkington, KJ Staples, T Wilkinson

Evaluation of saliva biomarkers as indicators of health status and exacerbations in COPD
N Patel, P Jones, V Adamson, G Thorpe, J Belcher, M Spiteri

Static balance deficit in chronic obstructive pulmonary disease: prevalence, clinical characteristics and risk of significant falls
JL Canavan, SSC Kon, CM Nolan, SE Jones, MJ Polkey, WD-C Man

Sarcopenia in COPD: prevalence, clinical correlates and response to pulmonary rehabilitation
SE Jones, M Maddocks, SSC Kon, JL Canavan, CM Nolan, AL Clark, MI Polkey, WD-C Man

Laryngeal narrowing in chronic obstructive pulmonary disease (COPD): a mechanism for generating intrinsic PEEP?

Time-course of human rhinovirus infection and upper respiratory tract symptoms during COPD exacerbations
SN George, SE Brill, JP Allinson, R Singh, B Kowlessar, RJ Sapsford, GC Donaldson, JA Wedzicha

A study of the effect of the 2013 ‘Be clear on lung cancer’ campaign on 2 week wait referrals to an inner North West London cancer centre
HJ Ramsey, YFG Chan, S Obaidee, EF Bowen, SL Elkin

Improved lung cancer referral rates and early diagnosis in a district general hospital
MS Sidhu, AG Gulati, PH Hawkins, SC Cooper

Population based epidemiology, treatment and prognosis of malignant mesothelioma in Leeds, UK – a matched historical comparison
RS Raju, MEJ Callister

Incidental detection of early stage non-small cell lung cancer – time to implement screening?
RM Thakrar, JM Brown, SV Brazil, M Nankivell, DR Lawrence, PJ George, SM Janes, N Navani

The rate of incidental synchronous pathology on PET-CT scans performed for thoracic malignancy and subsequent impact on lung cancer pathways
TRE Jones, HJ Curtis

Follow-up of lung cancer patients post surgery
R Aslam, AR Biswas, P Blaxill

Prognostic implications of the modified Glasgow prognostic score in early stage non-small cell lung cancer
AM MacKenzie, E Johnson, STsim, KG Blyth
Wednesday 3 December 2014

**P76** When is it safe to discharge resected stage 1A/1B NSCLC from the clinic?
G Kamalatharan, CS Moorcroft, R Shah, SCO Taggart

**P77** Carcinoma in-situ at the bronchial resection margin – a case for routine surveillance with autofluorescence bronchoscopy
RM Thakrar, JM Brown, H Apperley, M Falzon, DR Lawrence, PJ George, N Navani, SM Janes

**P78** Can PET standard uptake variable (SUV) predict disease progression in early-stage non-small cell lung cancer (NSCLC)?
FJ Frost, GH Jones, J Greenwood, M Ledson, MJ Walshaw

3.00pm – 4.10pm
Abbey Room, 4th Floor
**POSTER DISCUSSION: P79 – P87**
Clinical management of pulmonary infection
Chaired by: Dr Mathew Berry (London) and Professor Stephen Gordon (Liverpool)

**P79** Bronchiectasis severity in primary immuno-deficiency – a two centre study
AD Saleh, JR Hurst, J Davison, C Stroud, D Lowe, A De Soyza

**P80** Characterisation of the EQ-5D-5L and exercise performance in bronchiectasis
SJ Greenwood, T Pemberton, LJ Grillo

**P81** The increasing secondary care burden of bronchiectasis in England
V Navaratnam, E Millett, JR Hurst, SL Thomas, L Smeeth, RB Hubbard, J Brown, JK Quint

**P82** Effect of a standardised chest clearance pathway on quality of life and hospital admissions in patients with non cystic fibrosis bronchiectasis
LT Yeo, K Bentley, ZL Borrill

**P83** Non-tuberculous mycobacteria in patients with COPD – frequently poor outcomes despite treatment
AM Malhotra, H Milburn, R Breen

**P84** Is the CURB-65 score a reliable tool for guiding initial antibiotic therapy in acutely unwell patients with community acquired pneumonia?

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**SCIENTIFIC PROGRAMME**

A Hadjimichalis, C Coulter, D Jeyaratnam

**P85** HIV-related acute respiratory admissions – good outcomes and an opportunity for testing
P Howlett, D Lux, R Kulasegaram, RAM Breen

**P86** Do we need a specific guideline for the management of aspiration pneumonia (AP)?
S Cormack

**P87** Klebsiella pneumoniae survival on plastic valved holding chamber bodies
MJ Sanders, R Bruin

3.00pm – 4.30pm
**COFFEE/TEA** will be served in the Whittle & Fleming Rooms and Benjamin Britten Lounge, 3rd floor and the Mountbatten Lounge, 5th floor (3.15pm – 3.30pm only)

3.05pm – 4.05pm
Albert Suite, 2nd Floor
**POSTER DISCUSSION: P88 – P95**
Smoothing the process: clinical management of COPD and bronchiectasis
Chaired by: Dr Colin Gelder (Coventry) and Mrs Jane Scullion (Leicester)

**P88** An evaluation of the patients pathway to accident and emergency (A&E) or inpatient admission following an exacerbation of asthma or chronic obstructive pulmonary disease (COPD) in a large teaching hospital
M Naqvi, H Khachi

**P89** Attendance of secondary care respiratory outpatient appointments in illicit drug users with recurrent hospital admissions with ‘COPD’ at a city centre teaching hospital
R Huang, AM Collins, N Williams, N Garner, T Perry, H Burhan

**P90** CATCH – community access to CT chest
CS Moorcroft, G Kamalatharen, S Elliot, A Walsham, A Sharman, SCO Taggart

**P91** Development and implementation of a structured, annual ‘Comprehensive respiratory assessment’ for individuals with advanced COPD
N Toms, NJ Greening, R Free, JE Williams, RA Evans, MC Steiner
### SCIENTIFIC PROGRAMME

| P92 | Improving diagnosis and management of patients with COPD in the acute medical admission unit: a “right care” approach |
|     | Z Rutter-Locher, V Patel, K Taylor, P Kelly, I Patel |
| P93 | Supporting patient involvement in service development: eliciting patient-centred information to inform commissioning of COPD services |
|     | F Early, T Watts, K Homan, A Green, M Brookes, J Fuld |
| P94 | Patient agenda setting and clinic efficiency in outpatients: an individual randomized controlled trial |
|     | A Everden, F Early, K Homan, J Fuld |
| P95 | Non CF bronchiectasis |
|     | CJ Baggott, E Harris, J Suntharalingam, AS Malin |

#### Wednesday 3 December 2014

| P99 | Comparison of multiple breath washout using a commercial device and a mass spectrometer in school age children with cystic fibrosis |
|     | JA Duncan, E Raywood, A Bush, J Stocks, P Aurora |
| P100 | The feasibility of using commercial multiple breath nitrogen washout devices in school-aged children |
|     | E Raywood, J Duncan, S Legg, P Aurora, J Stocks |
| P101 | Effects of using a mask vs. mouthpiece on the multiple breath inert gas washout technique |
|     | S Lum, J Stocks, W Kozlowska, P Aurora |
| P102 | Recovery of baseline lung function after a pulmonary exacerbation in children with primary ciliary dyskinesia (PCD) |
|     | M Sunther, S Carr, C Hogg, A Bush |
| P103 | Do children with primary ciliary dyskinesia harbour the same pathogens in the upper and lower airway? |
|     | GS Marsh, NL Collins, A Bush, C Hogg, SB Carr |
| P104 | Comparison of the upper and lower airway microbiota in children |
|     | B Ahmed, MJ Cox, WOC Cookson, JC Davies, MF Moffatt, A Bush |
| P105 | Safety, feasibility and quality of sputum induction in preschool children with obstructive airways disease |
| P106 | Sputum induction reduces the need for bronchoscopy in school-aged children with cystic fibrosis |
|     | N Collins, K Robson, P Nagakumar, S Saglani, NWG Voase, JC Davies |

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**3.15pm – 3.45pm**  
**Victoria Suite, 2nd Floor**  
**OPEN MEETING**  
**BTS Clinical Data Specialist Advisory Group**

**3.30pm – 5.00pm**  
**Mountbatten Room, 6th Floor**  
**POSTER DISCUSSION: P96 – P106**  
**Getting to grips with paediatric lung disease**  
*Chaired by: Dr Paul Aurora (London) and Professor Jane Davies (London)*

| P96 | A new interactive game device may improve compliance with spacer devices in very young children |
|     | CS Murray, S Shakir, T Aslam |
| P97 | Diverging trends in prevalences of asthma, eczema and hayfever in children aged 9-12 years |
|     | M Barnish, N Tagiyeva, L Aucott, G Devereux, S Turner |
| P98 | A questionnaire survey of parent experiences and perspectives in children diagnosed with interstitial lung disease (ILD) |
|     | C Gilbert, A Bush, S Cunningham |
**Wednesday 3 December 2014**

4.15pm – 4.40pm  
Churchill Auditorium, 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 – 5.15pm  
Churchill Auditorium, Ground Floor  
**THE AMERICAN THORACIC SOCIETY PRESIDENT’S ADDRESS**  
The future of pulmonary science: a paediatrician’s perspective  
Professor Thomas Ferkol  
Introduced by: Professor Ann Millar

5.15pm – 5.45pm  
Churchill Auditorium, Ground floor  
**BTS ANNUAL GENERAL MEETING**  
(BTS members only)

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**Thursday 4 December 2014**

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

8.45am – 4.00pm  
Whittle & Fleming Rooms, 3rd Floor  
**POSTER VIEWING**  
Authors present: 10.00am – 11.00am  
P107-P114  
**Integrated knowledge in practice**  
Discussion of abstracts will take place from 1.30pm to 2.30pm in the Henry Moore Room, 4th floor  
P115-P125  
**Clinical delivery of pulmonary rehabilitation**  
Discussion of abstracts will take place from 2.00pm to 3.25pm in the Elizabeth Windsor Room, 5th floor  
P126-P136  
**The lungs at work: occupational lung disease**  
Discussion of abstracts will take place from 2.00pm to 3.25pm in the Rutherford Room, 4th floor  
P149-P159  
**Predicting clinical outcomes in acute respiratory illness**  
Discussion of abstracts will take place from 3.45pm to 5.15pm in the Elizabeth Windsor Room, 5th floor

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**SCIENTIFIC PROGRAMME**

**P160-P172**  
Pulmonary arterial hypertension: diagnosis, management and outcomes  
Discussion of abstracts will take place from 3.45pm to 5.20pm in the Abbey Room, 4th floor

**P173-P182**  
In the pleural zone  
Discussion of abstracts will take place from 4.00pm to 5.15pm in the Mountbatten Room, 6th floor

**P183-P192**  
TB: non pulmonary and hepatotoxicity  
Discussion of abstracts will take place from 4.00pm to 5.15pm in the Westminster Suite, 4th floor

**P193-P204**  
Cystic fibrosis  
Discussion of abstracts will take place from 4.00pm to 5.30pm in the Rutherford Room, 4th floor

8.45am – 4.00pm  
Mountbatten Lounge, 5th floor  
**MODERATED POSTER VIEWING**  
M137-M148  
**COPD: co-morbidities, deficiencies and interventions**  
Discussion of abstracts will take place from 2.00pm to 3.30pm in the Mountbatten Lounge, 5th floor

8.00am – 8.30am  
Albert Suite, 2nd Floor  
**BTS JOURNAL CLUB**  
**PHYSIOLOGY**  
Professor John Moxham (London)

8.30am – 10.00am  
Churchill Auditorium, Ground Floor  
**JOINT BTS/BTOG SYMPOSIUM**  
**LUNG CANCER**  
Chaired by: Professor David Baldwin (Nottingham) and Dr Sanjay Popat (London)

**8.30am**  
Latest ablative radiotherapy techniques  
Professor Suresh Senan (Amsterdam)

**9.00am**  
Latest surgery techniques/limited resection  
Professor Frank Detterbeck (New Haven, Connecticut)

**9.30am**  
Lumps, bumps, spots and shadows: the scary world of the pulmonary nodule  
Professor Gerard Silvestri (South Carolina)
This session will examine what is the evidence behind our management of lung nodules and their follow up and explore tissue sparing surgery and novel radiotherapy techniques for lung cancer treatment. What should we be doing in 2015?

8.30am – 10.15am
Mountbatten Room, 6th Floor
JOINT BTS/BPRS SYMPOSIUM
WHEEZING PHENOTYPES IN ADULTS AND CHILDREN
Chaired by: Dr Iolo Doull (Cardiff) and Professor Liam Heaney (Belfast)

8.30am  Pre-school wheezing phenotypes
  Professor Andrew Bush (London)

8.55am  Wheezing phenotypes in older children and longitudinal changes
  Professor John Henderson (Bristol)

9.20am  Wheezing phenotypes in adults
  Professor Ian Pavord (Oxford)

9.45am  Longitudinal changes in wheezing phenotypes in adults
  Professor Debbie Jarvis (London)

The objective of this session is to explore phenotypes of wheezing patients at different ages, understand how they differ and the implications this has for prognosis and clinical treatments, as well as the design of interventional clinical trials.

8.30am – 10.15am
St James’s Suite, 4th Floor
SPOKEN SESSION: S40 – S45
Images in pleural disease
Chaired by: Dr Justin Pepperell (Taunton) and Dr Najib Rahman (Oxford)

8.35am  S40
  Improving the patient journey: thoracic ultrasonography as an adjunct to decision making and diagnostic pathways in pleural disease
  JP Corcoran, RJ Halifax, I Psallidas, A Talwar, A Sykes, NM Rahman

8.50am  S41
  Looking beyond the pleura – a systematic review of thoracic ultrasonography to diagnose lung consolidation in respiratory failure

8.30am – 10.15am
Abbey Room, 4th Floor
SPOKEN SESSION: S46 – S51
Basic mechanisms in COPD pathogenesis
Chaired by: Professor Louise Donnelly (London) and Dr Tom Wilkinson (Southampton)

8.35am  S46
  Phagocytosis by blood neutrophils is not attenuated in patients with chronic obstructive pulmonary disease
  GM Walton, T Purvis, C Chadwick, RA Stockley, E Sapey

8.50am  S47
  Enhanced IL-6/CCL3 signaling in the plasma of patients with COPD
  AK Ravi, S Khurana, A Banyard, J Plumb, G Booth, M Catley, L Healy, E Smith, J Vestbo, D Singh
Thursday 4 December 2014

9.05am  S48
Air pollution particulate matter promotes DC maturation and enhances their stimulation of CD8 lymphocyte responses
TR Ho, PE Pfeffer, E Mann, FJ Kelly, NC Matthews, CM Hawrylowicz

9.20am  S49
Telomere attrition in circulating white blood cells in COPD relates to lung function and outcomes
RA Rabinovich, G Choudhury, R Lahkdar, EM Drost, L McGlynn, J Bai, PG Shiels, BE Miller, R Tal-Singer, A Agusti, W MacNee

9.35am  S50
Airway smooth muscle inflammation is controlled by microRNA-145 targeting of SMAD3 in COPD
L O’Leary, B Tildy, E Papazoglou, IM Adcock, KF Chung, MM Perry

9.50am  S51
Circulating desmosine relates to cardiovascular comorbidity, coronary artery calcification score (CACS), systemic inflammation and mortality in patients with COPD

8.30am – 10.15am
Westminster Suite, 4th Floor
SPOKEN SESSION: S52 – S57
How does clinical respiratory physiology help the clinician?
Chaired by: Dr Nicholas Hart (London) and Dr Annabel Nickol (Oxford)

8.35am  S52
Is a raised bicarbonate, without hypercapnia, part of the physiological spectrum of obesity-related hypoventilation?
A Manuel, N Hart, J Stradling

8.50am  S53
Neural respiratory drive and symptoms limiting exercise capacity in chronic obstructive pulmonary disease
CJ Jolley, YM Luo, J Steier, K Sylvester, WV Man, G Rafferty, MI Polkey, J Moxham

9.05am  S54
Neural respiratory drive measured using parasternal intercostal muscle electromyography in patients with interstitial lung disease
A Kaaba, C Jolley, V MacBean, C Reilly, S Birring, J Moxham, G Rafferty

9.20am  S55
Neural respiratory drive using parasternal electromyography in clinically stable cystic fibrosis patients: a physiological marker of lung disease severity and exercise capacity
L Smith, CC Reilly, V MacBean, CJ Jolley, C Elston, J Moxham, GF Rafferty

9.35am  S56
Differences in forced oscillation technique between healthy individuals, obstructive sleep apnoea and obesity hypoventilation syndrome
S Mandal, A Vaughan-France, T Dhir, ES Suh, P Pompilio, R Dellaca, N Hart

9.50am  S57
Aerobic training and detraining in COPD and healthy controls
B Popat, L Latimer, L Houchen-Wolloff, C Bolton, M Steiner

8.45am – 10.15am
Elizabeth Windsor Room, 5th Floor
SYMPOSIUM
WORK AND WORKPLACES FOR RESPIRATORY PATIENTS ARE CHANGING
Chaired by: Professor Dame Carol Black (London) and Professor Andrew Curran (Buxton)

8.45am  New and future inhaled hazards and risks: nano particles and beyond
Professor Terry Tetley (London)
**SCIENTIFIC PROGRAMME**

**9.15am** The changing nature of work and workers: demographics, work and respiratory disease  
*Professor Dame Carol Black (London)*

**9.45am** The changing nature of the workplace: what this means for respiratory patients  
*Professor David Fishwick (Sheffield)*

_This session will highlight how changing population demographics will interface with the world of work, with particular relevance to those with breathing problems; will highlight what is known, and what is needed to be known, about how workers and workplaces need to adapt to the needs of respiratory patients._

**8.45am – 10.30am**  
**Henry Moore Room, 4th Floor**  
**SPOKEN SESSION: S58 – S63**  
**Latent TB and biomarkers**  
*Chaired by: Dr Brian Choo-Kang (Glasgow) and Dr Heinke Kunst (London)*

**8.50am**  
*S58*  
Prospective health economic evaluation of different recommended strategies for TB testing in a contemporary HIV positive cohort  
SJ Capocci, J Sewell, C Smith, I Cropley, S Bhagani, S Morris, M Johnson, MCI Lipman

**9.05am**  
*S59*  
Evaluating the clinical utility of Xpert® MTB/RIF for the diagnosis and management of tuberculosis in a high burden region of the UK  
J Kim, B O’Connor, H Patel, N Perera, M Wiselka, G Woltmann, P Haldar

**9.20am**  
*S60*  
C-reactive protein reflects mycobacterial load in active tuberculosis but cannot be used as a rule-out diagnostic test  
KEN Clark, J Brown, JM Hopwood, O Lynard, D Creer, RD Barker, C Smith, R Breen, I Cropley, M Lipman

**Thursday 4 December 2014**

**9.35am**  
*S61*  
High levels of latent TB infection, blood borne viruses, poor treatment outcomes and unmet need among hard to reach groups in London: the TB Reach study  
GFernando, SHemming, SYates, LPosas, EGarber, VGant, RAldridge, AMGeretti, JHarvey, AHayward, MLipman, TDMcHugh, AStory

**9.50am**  
*S62*  
Risk factors for IGRA positivity in contacts of active tuberculosis in a UK high-prevalence setting  
AC Repossi, RD Turner, GH Bothamley

**10.05am**  
*S63*  
Investigation of serum biomarkers in tuberculosis diagnosis  
CD Tweed, GH Bothamley

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

**9.00am – 10.00am**  
**Rutherford Room, 4th Floor**  
**OPEN MEETING**  
**BTS Cystic Fibrosis Specialist Advisory Group**

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

**10.30am – 12.00pm**  
**St James’s Suite, 4th Floor**  
**SPOKEN SESSION: S64 – S68**  
**Clinical trials and outcome measures in paediatric lung disease**  
*Chaired by: Dr Jeremy Hull (Oxford) and Dr Sejal Saglani (London)*
### Thursday 4 December 2014

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<th>Time</th>
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<tbody>
<tr>
<td>10.35am</td>
<td>S64</td>
<td>Eosinophil cationic protein and cytokine analysis in exhaled breath condensate in paediatric asthma</td>
<td>A Whitehouse, R Brugha, N Mushtaq, I Dundas, J Grigg</td>
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<tr>
<td>10.50am</td>
<td>S65</td>
<td>Urinary prostaglandins as inflammatory markers for childhood asthma exacerbations</td>
<td>R Brugha, N Mushtaq, I Dundas, M Sanak, J Grigg</td>
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<tr>
<td>11.05am</td>
<td>S66</td>
<td>The GLI spirometry reference equations influence the apparent rate of decline in FEV1 among children and adolescents with cystic fibrosis</td>
<td>G Davies, P Aurora, A McDonald, A Prasad, D Bilton, J Stocks, S Stanojevic</td>
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<tr>
<td>11.20am</td>
<td>S67</td>
<td>Lung clearance index (LCI) is a sensitive predictor of high resolution computed tomography (HRCT) scores in children with non-CF bronchiectasis</td>
<td>S J Irving, A Nair, J C Davies, D Hansell, C Hogg, A Bush</td>
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<td>11.35am</td>
<td>S68</td>
<td>The Hi-flo study: a prospective open randomised controlled trial of high flow nasal cannula oxygen therapy against standard care in bronchiolitis</td>
<td>C Hathorn, G Ernst, S Hasan, D Wong, M Seear</td>
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### SCIENTIFIC PROGRAMME

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<tr>
<td>11.20am</td>
<td></td>
<td>Molecular genetics meets respiratory immunology and respiratory infection</td>
<td>Dr Alison Condliffe (Cambridge)</td>
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<tr>
<td>11.45am</td>
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<td>IPF: early diagnosis for early treatment</td>
<td>Professor Luca Richeldi (Southampton)</td>
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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.

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<tr>
<td>10.30am</td>
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<td>MDR TB – an emerging Eastern European problem for Western Europe</td>
<td>Dr Christoph Lange (Germany)</td>
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<tr>
<td>11.00am</td>
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<td>New therapies – REMox trial</td>
<td>Professor Stephen Gillespie (Fife)</td>
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<tr>
<td>11.30am</td>
<td></td>
<td>Challenges in paediatric TB</td>
<td>Professor Beate Kampmann (London)</td>
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The objectives of this session are to: understand the increasing issue of MDR TB emerging from Eastern Europe and the clinical and practical difficulties in managing this pattern of disease; provide an update on the novel therapies and combinations emerging in clinical trials, and with a focus on the recently completed REMox study; and review the current challenges in paediatric TB with an update on the optimum drug regimes and diagnostic approaches for active and latent paediatric TB.

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<td>12.00pm</td>
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<td>LUNCH will be available to purchase in the Cafe in the Pickwick Suite, 1st floor, and the Snack Bar in the Whittle &amp; Fleming Rooms, 3rd floor</td>
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<tr>
<td>12.15pm</td>
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<td>BTS Lung Cancer and Mesothelioma Specialist Advisory Group</td>
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### PLENOARY SCIENTIFIC

**Chairled by: Professor Sam Janes (London)**

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<tr>
<td>10.30am</td>
<td></td>
<td>Pneumococcal carriage and pulmonary immunity</td>
<td>Professor Stephen Gordon (Liverpool)</td>
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<tr>
<td>10.55am</td>
<td></td>
<td>A walk around the pleural space</td>
<td>Dr Nick Maskell (Bristol)</td>
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OPEN SESSION – UKRRC
Getting your respiratory research funded; what’s out there and how to access it
Chair by: Professor David Lomas (Dean, UCL Faculty of Medical Sciences)
Speakers: Dr Clare McVicker (Wellcome Trust)
Professor Ian Hall (Medical Research Council)
Mr Ian Jarrold British (Lung Foundation)
Dr David King (National Institute of Health Research)
Dr Samantha Walker (Asthma UK)

This session, organised by the UK Respiratory Research Collaborative (UKRRC), will comprise short presentations from the major funders of respiratory research in the UK 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. Lunch will be provided.

SNELL MEMORIAL LECTURE
Mycobacterium tuberculosis: where did it come from and where is it going?
Professor Douglas Young (London)
Introduced by: Professor Ann Millar (Bristol)

OPEN MEETING
BTS Pulmonary Vascular Disease Specialist Advisory Group

OPEN MEETING
BTS Occupational and Environmental Lung Disease Specialist Advisory Group

POSTER DISCUSSION: P107 – P114
Integrated knowledge in practice
Chair by: Mrs Samantha Prigmore (London) and Dr Paul Walker (Liverpool)
P107 Knowledge of non invasive ventilation in a district general hospital – a cause for concern?
RC Jones, A Stanton, M Juniper

P108 Acute NIV practices at a district general hospital and the impact of regular electronic feedback on patient outcome
TJC Ward, VW Sandoo, SF Hussain

P109 Can a theory-informed interactive animation increase intentions to engage in physical activity in young people with asthma?
G Hoskins, B Williams, J Murray, S Skar, J McGhee, D Gauld, G Brown, S Treweek,
F Sniehotta, L Cameron, A Sheikh, S Hagen

P110 Exposure to community COPD during specialty training
GH Jones, A Collins, S Sibley, D Wat, MJ Walshaw

P111 Procedural experience, training opportunities and attitudes towards intercostal chest drain insertion: variations between consultants, trainees and medical sub-specialties
JP Corcoran, RJ Hallifax, A Talwar, I Psallidas, A Sykes, NM Rahman

P112 Speech and language therapy by Skype™ for vocal cord dysfunction and chronic cough
SF Lillie, J Haines, A Vyas, SJ Fowler

P113 The use of local anaesthesia in improving the patient experience of arterial blood gases: Students and trainers are still not getting the message
Z Mangera, C Gunasekera, J Kinley, J King, B Walker, O Cohen, P Dilworth

P114 What skills, experience and training are need to work in integrated respiratory specialist roles and how can we roll these posts out in the UK?
NJ Roberts, M Ward, IS Patel, J Yorke, J Williams, R Walters, M McKevitt, S Edwards
Thursday 4 December 2014

1.45pm – 3.30pm
St James’ s Suite, 4th Floor
SPOKEN SESSION: S69 – S74
Lung cancer: how are we doing and what’s next?
Chaired by: Dr Robert Milroy (Glasgow) and Dr Mick Peake (Leicester)

1.50pm  S69
Rising standards of care continue in year 9 of the National Lung Cancer Audit
P Beckett, A Yelland, I Woolhouse, MD Peake

2.05pm  S70
Results from the first National Lung Cancer Organisational Audit
IS Woolhouse, C Meace, K Greenaway, P Beckett, MD Peake

2.20pm  S71
Are quality standards and accredited centres for mediastinal staging with EBUS needed? A report from the Manchester Cancer EBUS Group
M Evison, P Crosbie, J Morris, J Martin, R Shah, H Doran, J Hoyle, S Bailey, D Rana, R Sundar, R Booton

2.35pm  S72
Clinical prediction models for malignancy in solitary pulmonary nodules – a validation study in a UK population
A Al-Ameri, P Malhotra, H Thygesen, S Vaidyanathan, P Plant, S Karthik, A Scarsbrook, M Callister

2.50pm  S73
Infrared spectroscopy for the detection of extended field carcinogenesis: a new paradigm for lung cancer screening?
JM Brown, L Foreman, K Oliver, R Thakrar, A Maréchal, P Rich, SM Janes

3.05pm  S74
Circulating tumor cells in peripheral and pulmonary venous blood predict poor long-term survival in surgically resected non-small cell lung cancer patients
ZD Liu, SF Xu, RD Zhang, YS Li, Y Han, CY Su, Z Chen, H Wang, SK Liu, QY Zhao, SJ Zhou, DZ Zhen, DP Yu, N Xiao, XY Song, M Qin

1.45pm – 3.30pm
Abbey Room, 4th Floor
SPOKEN SESSION: S75 – S80
Clinical TB
Chaired by: Professor Graham Bothamley (London) and Dr Martin Dedicoat (Birmingham)

1.50pm  S75
Risk factors and therapeutic implications of Vitamin D deficiency in Malawian adults with pulmonary tuberculosis
DJ Sloan, C Guwende, G Banda, D Shani, M Kamdolozi, B Chisale, J Dutton, RS Heyderman, AE Butterworth, EL Corbett, HC Mwandumba, SH Khoo, TJ Allain, GR Davies

2.05pm  S76
TB infection in the Nepali population in South-East London displays different characteristics compared to the TB population in Nepal
N Dearnley, R Eyres, T Simpson, E Stephenson, M Belton, P Palchaudhuri

2.20pm  S77
Pre-treatment chest x-ray severity and its relation to bacterial burden in pulmonary tuberculosis
SE Murthy, F Chatterjee, PPJ Phillips, SR Murray, TD McHugh, SH Gillespie
2.35pm  S78
Do tuberculosis cases managed by clinicians with average annual caseloads below 10 have poorer treatment outcomes?
HR Stagg, HL Thomas, D Pedrazzoli, LF Anderson, I Abubakar, CS Merle

2.50pm  S79
Cough prevalence and frequency in pulmonary tuberculosis
RD Turner, AC Repossi, S Matos, SS Birring, GH Bothamley

3.05pm  S80
Impact of peer educators on uptake of mobile x-ray tuberculosis screening at homeless hostels: a cluster randomised controlled trial
R Aldridge, S Yates, S Hemming, L Possas, G Ferenando, E Garber, A Hayward, T McHugh, M Lipman, A Story

1.45pm – 3.45pm
Mountbatten Room, 6th Floor
SYMPOSIUM
POOR ASTHMA OUTCOMES – CAN WE DO BETTER?
Chaired by: Professor Liam Heaney (Belfast) and Dr Bernard Higgins (Newcastle upon Tyne)

1.45pm  National Review of Asthma Deaths – what have we learnt?
Dr Mark Levy (London)

2.15pm  How to Finnish asthma
Professor Tari Haahela (Helsinki)

2.45pm  Organising asthma care – what can we do better?
Dr Hilary Pinnock (Whitstable and Edinburgh)

3.15pm  Healthcare systems and provision – the role of the patient!
Dr Tom Walker (Belfast)

This session will review the recent information from the National Review of Asthma Deaths and will then examine how we can address these issues. The session will review healthcare systems and outcomes from Finland, which has had success in improving asthma outcomes and will then explore how the UK can try and improve outcomes. The session will also examine the duties and responsibilities of healthcare providers and patients in improving outcomes.

2.00pm – 3.25pm
Elizabeth Windsor Room, 5th Floor
POSTER DISCUSSION: P115 – P125
Clinical delivery of pulmonary rehabilitation
Chaired by: Dr Neil Greening (Leicester) and Professor Sally Singh (Leicester)

P115  Evidence of post-code lottery in the availability of pulmonary rehabilitation (PR) in the East of England (EoE)
L Jongepier, R Barlow

P116  Differences in patient outcomes between a 6, 7 and 8 week pulmonary rehabilitation programme
R Barlow, I Easton, L Andrews

P117  Pulmonary rehabilitation in the East of England – 2.5-fold variation in completion rates
L Jongepier, R Barlow

P118  Quantity and quality of referrals to pulmonary rehabilitation from primary care following inclusion in the quality and outcomes framework (QOF) in Wales
J Ayling-Smith, M Owen, J Byers, D Menzies

P119  Is a practice incremental shuttle walk test needed for patients with chronic obstructive pulmonary disease admitted to hospital for an acute exacerbation?
V Johnson-Warrington, K Mitchell, S Singh

P120  Shared decision making in a pulmonary rehabilitation setting for COPD patients
CL Madsen, J Tomkinson

P121  Speech and language therapy in pulmonary rehabilitation: the implication of education sessions on dysphagia management
SF Lillie, J Haines, A Vyas, SJ Fowler

P122  A survey of pulmonary rehabilitation (PR) services in Kent, Surrey, Sussex (KSS)
J-P Crofton-Biwer, E Lazar, J Bott
Thursday 4 December 2014

P123  The benefits of pulmonary rehabilitation (PR) in interstitial lung disease (ILD): observations from Oxfordshire's mixed respiratory disease, community based PR programme
R Lardner, S Bolton, R Hoyles

P124  Do we need a practice incremental shuttle walk test for patients with interstitial lung disease referred for pulmonary rehabilitation?
V Johnson-Warrington, L Sewell, M Steiner, M Morgan, S Singh

P125  The Irish Lung Fibrosis Association's 2000 steps a day challenge: a pilot study to evaluate a novel home exercise programme for lung fibrosis patients
N Cassidy, IA Byrne, D Danaher, JJ Egan

2.00pm – 3.25pm
Rutherford Room, 4th Floor
POSTER DISCUSSION: P126 – P136
The lungs at work: occupational lung disease
Chaired by: Professor David Fishwick (Sheffield) and Dr Jo Szram (London)

P126  Breathlessness and lung function predicts future work disability in older workers: detection, intervention, retention?
J Szram, SJ Schofield, APM Woods, P Cullinan

P127  COPD and the workplace; attitudes of those with and without the condition in a population based study
D Fishwick, L Lewis, A Darby, JC Waterhouse, R Wiggans, LM Bradshaw

P128  A new, efficient spirometry-based algorithm to predict restrictive lung disease in workplace respiratory surveillance
S De Matteis, AA Iridoy, P Cullinan

P129  Systematic review and meta-analysis of cross-sectional studies on arc welding fume effects and obstructive lung disease
A Marongiu, C Minelli, C Canova, S Schofield, J Szram, P Cullinan

2.00pm – 3.30pm
Churchill Auditorium, Ground Floor
SYMPOSIUM
“HOT TOPICS”
Chaired by: Dr Martin Allen (Stoke-on-Trent) and Dr Sanjay Agrawal (Leicester)

2.00pm  Presentation from Professor Mike Morgan, NHS England National Clinical Director for Respiratory: looking forward to the future

2.45pm  Pro-con debate on the use of e-cigarettes
Pro: Professor John Britton (Nottingham)
Con: Dr Andrew Furber (Wakefield)
SCIENTIFIC PROGRAMME

2.00pm – 3.30pm
Mountbatten Lounge, 5th Floor

MODERATED POSTER DISCUSSION:
M137 – M148
COPD: co-morbidities, deficiencies and interventions
Chaired by: Dr Jennifer Quint (London) and Dr Louise Restrick (London)

M137 Can steroid insensitivity in COPD patients be restored using vitamin D?
D Mukherjee, D Parekh, R Dancer, M Ungurs, H Khiroya, AM Turner

M138 Do standard cardiovascular risk scores identify risk in patients with COPD?
ME John, S Hussain, M Al Haddad, CE Bolton

M139 Frailty and premature cardiovascular ageing in COPD
AM Albarrati, NS Gale, S Enright, M Munnery, I Munnery, S Saikia, JR Cockcroft, DJ Shale

M140 Effect of beta-blockade on lung function in a population with arterial vascular disease with and without COPD
A Key, M West, M Parry, F Torella, S Jack, N Duffy, PP Walker

M141 Impact of beta-blockade on exercise capacity and dynamic hyperinflation in people with and without COPD awaiting vascular surgery
A Key, M Parry, M West, S Jack, F Torella, N Duffy, PP Walker

M142 The association between exacerbation frequency and stroke risk, in patients with COPD: a matched case-control study
CL Windsor, E Herrett, L Smeeth, J Quint

M143 Progression of central arterial stiffness in COPD after 2 years of observation
NS Gale, AM Albarrati, MM Munnery, IC Munnery, RM Tal-Singer, JR Cockcroft, DJ Shale

Thursday 4 December 2014

M144 Acute dietary nitrate supplementation reduces the oxygen cost of submaximal exercise in COPD
KJ Curtis, R Tanner, K O’Brien, MI Polkey, LM Edwards, NS Hopkinson

M145 Prevalence and determinants of vitamin D deficiency in patients with chronic obstructive pulmonary disease
DA Jolliffe, AR Martineau, WYJ James, KI Islam, CAM Mein, PMT Timms, RW Walton, CJG Griffiths

M146 Validation of five non-invasive respiratory rate monitors in patients with COPD in a laboratory setting
N Rubio, B McKinstry, R Parker, H Pinnock, C Weir, J Hanley, C Yerramasu, L Cruz-Mantoani, W MacNee, RA Rabinovich

M147 Feasibility of delivering an occupational health intervention aimed at improving work productivity, among working COPD patients
K Kalirai, P Adab, R Jordan, JG Ayres, S Sadhra

M148 Investigating the feasibility of an online health resource with nurse coaching to support self-management in COPD
J Young, F Early, S Wisbauer, K Homan, J Fuld, L Tojo

2.00pm – 3.30pm
Albert Suite, 2nd Floor

OPEN SESSION

BLF research highlights
Chaired by: Dr Noel Snell (Director of Research, BLF)

2.00pm Genetically modified cell therapy for the treatment of malignant pleural mesothelioma
Dr Beth Sage (London)

2.30pm PAR1, thrombin and exacerbation frequency in COPD
Dr John Hurst (London)

3.00pm Asthma in RAF personnel: measuring its severity and its impact on service careers
Professor Paul Cullinan (London) and Dr Joanna Szram (London)
Thursday 4 December 2014

2.00pm – 3.30pm
Westminster Suite, 4th Floor
SPOKEN SESSION: S81 – S85
Predicting and preventing re-admission in COPD – what is the real cost?
Chaired by: Professor John Moxham (London) and Dr Richard Russell (London)

2.05pm  S81
Gait speed is a predictor of mortality following hospitalisation for acute exacerbations of COPD
SSC Kon, SE Jones, SJ Schofield, JL Canavan, CM Nolan, MJ Dickson, BM Haselden, MI Polkey, P Cullinan, WD-C Man

2.00pm – 4.30pm
COFFEE/TEA will be served in the Whittle & Fleming Rooms and Benjamin Britten Lounge, 3rd floor

3.05pm  S85
Effects of post exacerbation pulmonary rehabilitation (PEPR) on exercise tolerance, quality of life (QoL) and health care utilisation
SKM Harlow, A Lewko, H Black, S Blandford, MJ Irvin-Sellers
4.50pm  S90
Role for IL-1alpha in viral-induced inflammatory responses in a coculture model of the airway mucosa
A Hill, L Tezera, C Blume, C Grainge, DE Davies, EJ Swindle

3.45pm – 5.15pm
Elizabeth Windsor Room, 5th Floor
POSTER DISCUSSION: P149 – P159
Predicting clinical outcomes in acute respiratory illness
Chaired by: Dr Emma Browne (Newcastle upon Tyne) and Dr Matthew Wise (Cardiff)
P149 Characteristic and prognosis of patients with COPD and type 2 respiratory failure
T Spruell, C Dave, R Mukherjee, AM Turner
P150 Hospital re-admissions with exacerbation of obstructive pulmonary disease in illicit drug smokers
R Yadavilli, R Huang, AM Collins, W Yew Ding, N Garner, J Williams, H Burhan
P151 Can the DECAF score be used to guide prognosis after an acute admission for COPD exacerbation?
B Rabbani, P Brammer
P152 The relationship between educational qualifications, access to information technologies and clinical outcomes in patients with acute exacerbation of COPD (AECOPD)
R Wijayarathna, ES Suh, S Mandal, N Hart
P153 Stratifying pneumonic episodes and acute exacerbations in COPD patients – a continuum or discrete phenomena?
NW Williams, KO Ostridge, VK Kim, AB Barton, MMW Wojtas, SH Harden, EA Aris, MP Peeters, JMD Devaster, SB Bourne, TW Wilkinson
P154 The impact of a discharge care bundle on the 30-day readmission rate following hospitalisation for acute COPD exacerbation
JM Seymour, D Nedelcu

Thursday 4 December 2014
P155 Compliance with guidelines for the management of theophylline in patients with acute exacerbations of COPD
M Ullah, D Anshur, S Lugg, S Gompertz
P156 Can specialist nurses predict which patients will readmit following delivery of a COPD care bundle?
L Sewell, C Mitchell-Issitt, K Barley, C Chebbout, S Msimanga, L Clinch, S Boyce, MCS Steiner, SJ Singh
P157 Cancer patients with severe community acquired pneumonia have poorer outcomes due to increased illness severity and septic shock at admission to intensive care
RJ José, AO Mohammad, JP Goldring, RC Chambers, JS Brown, B Agarwal
P158 Evaluation of vital capacity changes in spinal injured patients during episode of sepsis
M Nasher, AC Pocock, T Ward, T Bongers
P159 Weaning and long term ventilation outcomes in spinal injury patients after referral to a regional spinal injury centre
AC Pocock, M Nasher, T Ward, T Bongers

3.45pm – 5.20pm
Abbey Room, 4th Floor
POSTER DISCUSSION: P160 – P172
Pulmonary arterial hypertension: diagnosis, management and outcomes
Chaired by: Dr Joanna Pepke Zaba (Cambridge) and Dr John Wort (London)
P160 The role of specialist palliative care services in the management of patients with pulmonary arterial hypertension; a review of current practice
P161 Assessment of age-adjusted D-dimer cut-off values in investigating venous thromboembolism in older patients: a retrospective analysis
SSM Lau, GEJ Murphy
P162 A two month prospective study: are CTPAs requested appropriately and if not do they diagnose alternative pathologies?
Thursday 4 December 2014

S Antoniou, HT Tung, S Srivastava

P163 Accuracy of inflammatory markers to distinguish between pneumonia and pulmonary embolism in acute settings
L Chishimba, F Iqbal, A Kasule, A Joyson, J Williams, S Argawal, I Hussain

P164 \(\Delta NTproBNP\) predicts survival and more accurately reflects changing right ventricular structure and function than 6MWD in pulmonary hypertension
Mj Brewis, MK Johnson, AJ Peacock

P165 Ambulatory management of suspected pulmonary embolism at a district general hospital. A 2 year review
A Griffiths

P166 Patients with confirmed and suspected pulmonary emboli have the same two-year mortality
AP Williams, C Burford, R Poyner, HSV Nair, D Menzies

P167 Outcomes and predictors of mortality in cancer patients with incidental pulmonary embolism
D Grant, J Franklin, L Watts, N Rahman, FV Gleeson

P168 Reduced gas transfer (TLCO) predicts poor outcome in patients with pulmonary hypertension and heart failure with preserved ejection fraction
N Hussain, S Ramjug, C Billings, J Hurdman, CA Elliot, R Condliffe, DG Kiely

P169 Rates of recovery of oxygen consumption and heart rate after cardiopulmonary exercise testing predict survival in patients with precapillary pulmonary hypertension
SD Thomson, AJ Peacock, MK Johnson

P170 Heart rate recovery at one minute following incremental shuttle walk test predicts outcome in pulmonary hypertension
CG Billings, J Hurdman, M Austin, I Armstrong, CA Elliot, RA Condliffe, DG Kiely

P171 Implications of a non-constant resistance-compliance product in pulmonary arterial hypertension
C Hadinnapola, J Pepke-Zaba, M Toshner

SCIENTIFIC PROGRAMME

P172 Pulmonary hypertension in IPF: utility of HRCT
G Bettini, MA Mazzei, D Castoria, E Kacerja, RM Refini, F De Negri, N Cioffi Squitieri, S Guerrini, FG Mazzei, P Rottoli, L Volterrani

3.45pm – 5.30pm
St James’s Suite, 4th Floor
SPOKEN SESSION: S91 – S96

New asthma treatments
Chaired by: Dr Andrew Menzies-Gow (London) and Professor Michael Shields (Belfast)

3.50pm S91
Once-daily tiotropium Respimat\textregistered add-on to ICS + LABA improves symptom control and reduces exacerbations in patients with symptomatic asthma
D Price, M Engel, P Moroni-Zentgraf, H Schmidt, R Dahl, P Paggiaro, M Vandewalker, HAM Kerstjens, A Kaplan

4.05pm S92
Efficacy of once-daily tiotropium Respimat\textregistered 5 \(\mu\)g from five Phase III trials in adults with symptomatic asthma
D Price, E D Bateman, P Paggiaro, A Kaplan, M Engel, H Schmidt, P Moroni-Zentgraf, HAM Kerstjens

4.20pm S93
A prospective study investigating exacerbations, healthcare utilisation and health economic indicators in omalizumab treated severe allergic asthma patients – results from an interim analysis of the APEX II study
M Masoli, A Menzies-Gow, L Dobson, JB Morjaria, R Allcock, R Niven

4.35pm S94
A prospective study investigating oral corticosteroid (OCS) use and quality of life in omalizumab treated severe allergic asthma patients – results from an interim analysis of the APEX II study
R Chaudhuri, A Menzies-Gow, H Khachi, S Hand, R Gore, R Niven
SCIENTIFIC PROGRAMME

Thursday 4 December 2014

4.20pm  S99
Effects of differential TNF receptor signalling in modulating neutrophil-endothelial interactions in the pulmonary microvasculature
AG Proudfoot, J Juss, S Appleby, P Morley, J Cordy, A Bayliffe, M Hind, ER Chivers, M Griffiths, C Summers

4.35pm  S100
Proteinase-activated receptor 1 signalling contributes to neutrophilic inflammation and alveolar barrier disruption in Streptococcus pneumoniae pneumonia
RJ José, AE Williams, MG Sulikowski, DA Brealey, JS Brown, RC Chambers

5.05pm  S102
Lipoxin A4 improves efferocytosis via inhibition of the HMGB1 in human alveolar macrophages
Q Wang, D Parekh, VK D'Souza, R Dancer, JM Patel, D Bartis, F Gao, Q Lian, S Jin, DR Thickett

SCIENTIFIC PROGRAMME

4.50pm  S95
Double-blind multi-centre randomised controlled trial of vitamin D3 supplementation in adults with inhaled corticosteroid-treated asthma (ViDiAs)
AR Martineau, BD MacLaughlin, RL Hooper, NC Barnes, DA Jolliffe, AB Choudhury, RK Rajakulasingam, A Bhowmik, DE Simcock, J Grigg, CJ Corrigan, CM Hawrylowicz, CJ Griffiths

5.05pm  S96
Bronchial thermoplasty reduces peripheral blood eosinophils in severe asthma demonstrating systemic effects of a localised therapy
DM Ryan, LJ Holmes, G McCumesky, RD Daly, K Hince, G Tavernier, S Fowler, RM Niven

3.45pm – 5.30pm
Albert Suite, 2nd Floor

SPOKEN SESSION: S97 – S102
Mechanistic insights in acute lung injury
Chaired by: Dr Chris Scotton (Exeter) and Professor Terry Tetley (London)

3.50pm  S97
Long term survival in patients who undergo oesophagectomy is lower in patients who develop post-operative acute respiratory distress syndrome
RCA Dancer, D Parekh, GD Perkins, DR Thickett

4.05pm  S98
A novel human model to study alveolar injury and repair
J Alçada, JP Ng-Blichfeldt, AG Proudfoot, MJD Griffiths, CH Dean, M Hind

3.45pm – 5.45pm
Churchill Auditorium, Ground Floor

SYMPOSIUM
COPD – PLACING THE NEW INHALERS IN CONTEXT
Chaired by: Professor Emma Baker (London) and Dr Louise Restrick (London)

3.45pm  How will we know if new inhalers for COPD are good news for patients?
Dr Nick Hopkinson (London)

4.15pm  Do the new inhaled molecules offer significant benefit to patients with COPD?
Professor Dave Singh (Manchester)
Thursday 4 December 2014

4.45pm  Do new inhaler devices offer significant benefits to patients with COPD?
Professor Federico Lavorini (Florence)

5.15pm  Adding value and reducing waste in healthcare research
Professor Sir Muir Gray (Oxford)

The last couple of years have seen a proliferation of new inhalers. This session addresses the question of whether new drugs and new devices will benefit patients, what constitutes value in healthcare and how the respiratory health care community should respond.

4.00pm – 5.15pm
Mountbatten Room, 6th Floor
POSTER DISCUSSION: P173 – P182
In the pleural zone
Chaired by: Dr George Antunes (Middlesbrough) and Dr Alex West (London)

P173  Ambulatory management of spontaneous pneumothorax
K Thomas, M Naeem, RV Reddy

P174  Utility of needle aspiration in patients with primary spontaneous pneumothorax with complete lung collapse: a retrospective 5-year study
MB Ganaie, S Bikmalla, MA Afridi, MA Khalil, IR Hussain, M Haris

P175  Measurement of air leak post-thoracic surgery: implications for medical management of pneumothorax
RJ Hallifax, J Mitchell, JP Corcoran, I Psallidas, NM Rahman, E Belcher

P176  Iatrogenic pneumothorax post CT-guided lung biopsy – how do we manage it?
AM Lewis, AA Ionescu

P177  Patient-related outcome measurements in pleural effusions
I Psallidas, JP Corcoran, EK Mishra, RJ Hallifax, NM Rahman

P178  Clinician and patient experience in the delivery of a day-case local anaesthetic thoracoscopy service at a specialist pleural unit
I Psallidas, JP Corcoran, RJ Hallifax, A Talwar, A Sykes, NM Rahman

4.00pm – 5.15pm
Westminster Suite, 4th Floor
POSTER DISCUSSION: P183 – P192
TB: non pulmonary and hepatotoxicity
Chaired by: Dr Jack Barker (London) and Professor Onn Min Kon (London)

P183  Endobronchial ultrasound and tuberculosis: beware the non-caseating granuloma
J Murray, AC Repossi, S Ismail, A Bhowmik, GH Bothamley

P184  Female genital tuberculosis: the long road to diagnosis
JL Potter, SG Leddy, H Kunst, VLC White

P185  Improving the accuracy of microbiological diagnosis of TB lymphadenitis – is a multidisciplinary approach necessary?
A Saigal, H S Kalsi, R Sands, A Jayaratnam

P186  Intrathoracic lymph node tuberculosis – a comprehensive clinical description
KJH Kow, DW Connell, A Singanayagam, D Ap Dafydd, H Jarvis, M O’Donoghue, MI Wickremasinghe, A Lalvani, OM Kon

P187  The use of moxifloxacin for the treatment of ophthalmic tuberculosis
JL Potter, R Agrawal, C Barraclough, F Rahman, H Kunst, M Westcott
Increased pulmonary M. avium-intracellulare isolates account for much of the national rise in non-tuberculous mycobacteria incidence, 2007-2012
NM Shah, J Davidson, L Anderson, HL Thomas, M Lipman, I Abubakar

Should screening for chronic viral hepatitis in patients with tuberculosis be introduced to NICE guidelines?
JL Potter, C Hyams, M Shaukat, ZO Babiker, VM Macavei, N Jayasekera, H Kunst, GR Foster, VLC White

Drug induced liver injury in the treatment of tuberculosis in a busy UK centre
S Chitty, R Ghani, JK Roe, H Davidson, M Routledge, T Edwards, C Hafeley, S Collin, A Ritchie, J Dzvova, J Buckley, RN Davidson, L John

With a low incidence of drug-induced hepatitis, should we be offering latent TB treatment to more patients over the age of 35?
P Howlett, N Lungu, W Owen, R Breen, L Baker

Aside from age, do other factors increase the risk of hepatotoxicity in patients treated for latent TB infection?
CY Ma, JL Potter, H Kunst, VLC White

Longitudinal associations between FEV1 and HbA1c in a UK cohort of young people with cystic fibrosis
L Selby, T Rootsey, R Williams, K Ong, D McShane

Prevalence of undiagnosed pre-diabetes and diabetes in a UK cohort of young people with cystic fibrosis
L Selby, T Rootsey, R Williams, K Ong, D McShane

Prospective examination of the effects of ivacaftor on glycaemic health
A Banerjee, AL Brennan, AR Horsley, PJ Barry

The effect of Ivacaftor therapy on the microbial diversity of cystic fibrosis lung infection
HD Green, PJ Barry, C Paisey, A Smith, WG Flight, J Marchesi, AM Jones, A Horsley, E Mahenthiralingam

The incidence of new Pseudomonas aeruginosa infection in children with cystic fibrosis
FJ Gilchrist, J Belcher, AM Jones, D Smith, Ar Smyth, KW Southern, P Spanel, AK Webb, W Lenney

New approaches to the culture of Mycobacterium abscessus complex from patients with cystic fibrosis
JE Foweraker, S Jalili, V Athithan, D Grogono, MC Curran, RA Floto

Molecular analysis demonstrates shared strains of Mycobacterium abscessus isolates in cystic fibrosis patients attending a single centre
HD Green, Rowland Bright-Thomas, PJ Barry, N Woodford, B Isalska, A Horsley, D Kenna, AM Jones

Preliminary evaluation of the fungal airway microbiome in adult cystic fibrosis by next-generation sequencing, culture and staining techniques

Pneumocystis jirovecii prevalence in a large UK adult cystic fibrosis centre
HD Green, R Bright-Thomas, PJ Barry, A Horsley, K Mutton, AM Jones

Studying the relationship between matrix metalloproteinases and lung tissue damage during a clinical exacerbation of cystic fibrosis
HAP Passman, TD Daniels, PE Elkington

Development of an optimal F/HN pseudotyped SIV vector for CF gene therapy
A Banerjee, AL Brennan, AR Horsley, PJ Barry
Thursday 4 December 2014

SC Hyde, EWFW Alton, AC Boyd,
MM Connolly, M Chan, JC Davies,
LA Davies, S Gea-Sorli, U Griesenbach,
M Hasegawa, JA Innes, M Inoue, G McLachlan,
C Meng, IA Pringle, SG Sumner-Jones,
SG Tsugumine, DR Gill

P204 Immune responses to single and repeated administration of PGM169/GL67A: the UK CF gene therapy consortium clinical trials

U Griesenbach, AC Boyd, R Calcedo,
S Cheng, S Cunningham, JC Davies,
M Dewar, DR Gill, A Doherty, T Higgins,
SC Hyde, M Manvell, C Meng, JA Innes,
MP Limberis, E Punch, R Scheule, N Soussi,
S Soussi, JM Wilson, EWFW Alton

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

Friday 5 December 2014

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

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

P205-P214
Lung function testing: new approaches
Discussion of abstracts will take place from
1.30pm to 2.45pm in the Rutherford Room,
4th floor

P215-P226
Diagnostic and therapeutic interventional procedures
Discussion of abstracts will take place from
1.30pm to 3.00pm in the Westminster Suite,
4th floor

P227-P241
Asthma treatments
Discussion of abstracts will take place from
1.30pm to 3.20pm in the St James’s Suite, 4th floor

SCIENTIFIC PROGRAMME

P242-P247
Transplantation advances
Discussion of abstracts will take place from
2.00pm to 3.00pm in the Henry Moore Room,
4th floor

P248-P262
Improving patient therapies in COPD
Discussion of abstracts will take place from
2.30pm to 4.20pm in the Albert Suite, 2nd floor

P273-P280
ILD: diagnosis, co-morbidities and treatment
Discussion of abstracts will take place from
3.15pm to 4.15pm in the Henry Moore Room, 4th floor

P281-P289
Smoking detection and cessation and non-tobacco products
Discussion of abstracts will take place from
3.15pm to 4.30pm in the Abbey Room, 4th floor

P290-P296
Screening and treating sleep apnoea
Discussion of abstracts will take place from
3.15pm to 4.30pm in the Elizabeth Windsor Room,
5th floor

P297-P304
From hospital to home: NIV in clinical practice
Discussion of abstracts will take place from
3.30pm to 4.30pm in the St James’s Suite, 4th floor

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

M263-M272
IPF: education, information and health status
Discussion of abstracts will take place from
3.00pm to 4.15pm in the Mountbatten Lounge, 5th floor

8.00am – 8.30am
Albert Suite, 2nd Floor
BTS JOURNAL CLUB
COPD
Professor Wisia Wedzicha (London)
**SYMPOSIUM**

**RESPIRATORY NERVES: GETTING ON YOUR PATIENTS’ NERVES?**

*Chaired by: Professor Clive Page (London) and Professor Ashley Woodcock (Manchester)*

8.30am What do we know about innervation of the airways?
*Dr Brendan Canning (Baltimore)*

9.00am Nerves as therapeutic targets in respiratory disease
*Professor Maria Belvisi (London)*

9.30am Emerging therapies for cough
*Professor Jacky Smith (Manchester)*

This session will: explain the sensory innervation of the airways and how activation of these fibres leads to respiratory symptoms such as cough, wheeze and breathlessness; describe models of neuronal dysfunction in respiratory disease; understand how pharmacology provides insights into the underlying mechanisms and identifies targets for future treatment; and appreciate novel therapies for cough and the evidence for their use.

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**SPOKEN SESSION: S103 – S107**

**COPD outcomes**

*Chaired by: Dr William Elston (Derby) and Dr Colin Gelder (Coventry)*

8.35am S103
No loss in efficacy following switch from salmeterol/fluticasone combination to indacaterol monotherapy in patients with moderate COPD: the INSTEAD study
*A Rossi, T van der Molen, R Del Olmo, A Papi, L Webhe, M Quinn, C Lu, D Young, R Cameron, E Bucchiioni, P Altman*

8.50am S104
Double-blind multi-centre randomised controlled trial of vitamin D3 supplementation in COPD (ViDiCO)

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**SPOKEN SESSION: S108 – S112**

**Scientific advances in lung cancer**

*Chaired by: Dr Adam Giangreco (London) and Dr Frank McCaughan (London)*

8.35am S108
MIF as the key regulator for mesenchymal stem cells homing to tumours by 3D and in vivo lung metastasis models
*S Lourenco, VH Teixeira, T Kalber, R Thakrar, A Floto, SM Janes*
Friday 5 December 2014

8.50am  **S109**
Mesenchymal stem cells expressing full length TRAIL – a promising therapy for cancer
ZQ Yuan, KK Kolluri, SM Janes

9.05am  **S110**
Dysregulated iron metabolism mediated by IRP2 may influence lung cancer progression, particularly in the context of cigarette smoke exposure
NA Ahmad, JSM Moore, KW Woolnough, II Ismail, MB Bedford, UBN Naidu, CT Tselepis, AMT Turner

9.20am  **S111**
Methods to isolate basal cells from the respiratory epithelium
L Succony, KHC Gowers, RE Hynds, M Hayward, DR Lawrence, A Giangreco, SM Janes

9.35am  **S112**
MMP12 and LMO7 are key genes involved in the early pathogenesis of squamous cell carcinoma of the lung
VH Teixeira, S Lourenco, M Falzon, A Capitanio, S Bottoms, B Carroll, J Brown, JP George, SM Janes

8.30am – 10.00am
Abbey Room, 4th Floor
**SPOKEN SESSION: S113 – S117**

**Infection of the pleural space in disease and on purpose**
*Chaired by: Dr Rhian Finn (Swansea) and Dr Nicholas Maskell (Bristol)*

8.35am  **S113**
Predictors of bacterial ‘load’ in pleural infection
JM Wrightson, JA Wray, TL Street, SJ Chapman, DWM Crook, NM Rahman

8.50am  **S114**
Previously unrecognised oral anaerobes in pleural infection
JM Wrightson, JA Wray, TL Street, SJ Chapman, DWM Crook, NM Rahman

8.30am – 10.15am
Churchill Auditorium, Ground Floor
**SYMPOSIUM**

**NEW DEVELOPMENTS IN BRONCHIECTASIS**
*Chaired by: Professor Tobias Welte (Hannover) and Professor Robert Wilson (London)*

8.30am  Networks and pipelines – the future of bronchiectasis research and development
*Dr Anthony De Soyza (Newcastle upon Tyne)*

8.55am  Pseudomonas aeruginosa: implications and management
*Dr Charles Haworth (Cambridge)*

9.20am  Non tuberculous mycobacteria
*Dr Michael Loebinger (London)*

9.45am  Benefits and risks of macrolide treatment
*Dr Adam Hill (Edinburgh)*
The objectives of this session are to: hear about the latest developments, including emerging therapies, and new UK and international networks driving forward clinical research in bronchiectasis; review the latest evidence linking Pseudomonas aeruginosa with poor outcome in bronchiectasis, and new clinical trial data on long term antibiotic management for P.aeruginosa; review the importance of NTM as a cause and consequence of bronchiectasis; review recent trial evidence on the benefits and risks of macrolides in bronchiectasis in light of concerns about antibiotic resistance and additional adverse effects.

8.30am – 10.15am
Elizabeth Windsor Room, 5th Floor
SYMPOSIUM
AUTOPHAGY – AN IMPORTANT MECHANISM IN THE TREATMENT OF RESPIRATORY DISEASE
Chaired by: Professor Louise Donnelly (London) and Dr Nicholas Hart (London)

8.30am
A clinical introduction to autophagy
Professor David Rubinsztein (Cambridge)

9.00am
The role of autophagy in lung inflammation and infection
Professor Andres Floto (Cambridge)

9.30am
Autophagy mechanisms in skeletal muscle wasting during critical illness
Dr Ilse Vanhorebeek (Leuven)

The objectives of this session are to understand: the biological processes involved in autophagy and their potential relevance to lung pathophysiology, development and aging; the role of autophagy in regulating inflammation, inflammatory lung damage and tissue repair; and the impact of autophagy on muscle wasting.

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

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

10.30am – 11.30am
Rutherford Room, 4th Floor
OPEN MEETING
BTS Tobacco Specialist Advisory Group

10.30am – 12.00pm
Churchill Auditorium, Ground Floor
SYMPOSIUM
MEASUREMENT AND TREATMENT OF BREATHLESSNESS
Chaired by: Professor Mary Marrell (London) and Dr Annabel Nickol (Oxford)

10.30am
Assessment of cardiopulmonary dyspnoea
Dr Luke Howard (London)

11.00am
Novel neural mechanisms for breathlessness to develop new treatments
Dr Kyle Pattinson (Oxford)

11.30am
Management of refractory breathlessness
Professor Miriam Johnson (Hull)

Breathlessness is the most common feature of chronic cardio-respiratory disease. The objectives of this session are to: (1) clearly define a comprehensive clinical approach to determine the factors contributing to cardio-respiratory dyspnoea; (2) provide a ‘state of the art’ update of our current understanding of breathlessness and propose novel treatment strategies; (3) discuss the multidisciplinary approach to the management of difficult to control dyspnoea.

10.30am – 12.00pm
Elizabeth Windsor Room, 5th Floor
SYMPOSIUM
CONTROVERSIES IN RESPIRATORY INFECTION AND VACCINATION
Chaired by: Dr Michael Loebinger (London) and Dr Tom Wilkinson (Southampton)
Friday 5 December 2014

10.30am  Inhaled corticosteroids and risk of pneumonia in COPD
Professor Samy Suissa (Montreal)

11.00am  Future directions in pneumococcal vaccination
Professor Jeremy Brown (London)

11.30am  Controversies with community acquired pneumonia
Professor Tobias Welte (Hannover)

The first presentation will look at the evolving field of pneumococcal vaccination and will provide both basic science and clinical updates for the audience, in addition to a look to the recent data from large trials. The second presentation will address the emerging evidence for pneumonia risk associated with inhaled corticosteroid use in COPD and revisit analysis of risk and benefit. Finally, capturing developments in the area of treatment for community acquired pneumonia, and hence the talk will be able to review the present state with respect to current and new treatment paradigms including the use of corticosteroids.

10.30am – 12.00pm
St James’s Suite, 4th Floor

SPOKEN SESSION: S118 – S122

Clinical investigations and outcomes in pulmonary vascular disease
Chaired by: Dr Karen Sheares (Cambridge) and Dr Claire Shovlin (London)

10.35am  S118
Incidence and severity of chronic thromboembolic pulmonary hypertension following the introduction of a one-stop clinic for acute pulmonary embolism
D De Foneska, R Condliffe, CA Elliot, R Hughes, J Hurdman, S Ghafur, M Schofield, JJ van Veen, R Maclean, DG Kiely

10.50am  S119
Left ventricular dysfunction influences survival in connective tissue disease associated pulmonary arterial hypertension but not idiopathic pulmonary arterial hypertension
SF Crawley, KG Blyth, LE McLure, HJ Dargie, AJ Peacock

11.05am  S120
Right ventricular dysfunction in pulmonary hypertension with combined pulmonary fibrosis and emphysema syndrome
AJ Swift, S Rajaram, D Capener, C Elliot, R Condliffe, J Hurdman, DG Kiely, JM Wild

11.20am  S121
The utility of the incremental shuttle walking test in pulmonary hypertension: results from the ASPIRE registry
CG Billings, J Hurdman, R Condliffe, I Armstrong, I Smith, CA Elliot, DG Kiely

11.35am  S122
Outcome after pulmonary endarterectomy (PEA): long term follow-up of the UK national cohort
J Cannon, L Su, K Page, A Ponnaberanam, M Toshner, D Taboada, K Sheares, C Ng, J Dunning, STsui, D Jenkins, J Pepke-Zaba

10.30am – 12.00pm
Abbey Room, 4th Floor

SPOKEN SESSION: S123 – S127

Novel approaches to rehabilitation and exercise therapy in COPD
Chaired by: Dr Charlotte Bolton (Nottingham) and Dr Bronwen Connolly (London)

10.35am  S123
Does exercising with domiciliary non-invasive ventilation (NIV) improve quality of life (QoL) in patients with severe chronic obstructive pulmonary disease (COPD)?
KAM Buchan, K Badlan, M Fletcher, AH Kendrick

10.50am  S124
Effects of two adapted physical activity training programs on pulmonary functionality and exercise capacity in patients affected by chronic obstructive pulmonary disease

SCIENTIFIC PROGRAMME

AS Delussu, A Laudisio, C Pedone, L Costanzo, F Di Meo, C Pizzoli, S Lubich, L Polidori, F Paradisi M Traballesi, C Pisicchio, R Antonelli Incalzi

11.05am  S125
A comparison between weight supported and unsupported exercise on energy expenditure and cardiorespiratory response during exercise in obese adults with treated obstructive sleep apnoea
RA Evans, TE Dolmage, PG Robles, D Brooks, RS Goldstein

11.20am  S126
Developing healthy lifestyle interventions for overweight patients with obstructive sleep apnoea (OSA): a survey of patient attitudes and current practice
I Valero Sanchez, S Wimpress, C Brough, SJ Singh, RA Evans

11.35am  S127
Clinical implementation of exercise therapy during critical illness: a longitudinal observational cohort study
KT Roberts, B Connolly, A Curtis, C Whiteley, N Hart

10.30am – 12.15pm
Westminster Suite, 4th Floor
SPOKEN SESSION: S128 – S133

Asthma: basic mechanisms
Chaired by: Professor Alan Knox (Nottingham) and Professor Ian Sabroe (Sheffield)

10.35am  S128
Does the time of day of allergen challenge affect the degree of inflammatory response in the murine lung?
HJ Durrington, SN Farrow, DW Ray

Friday 5 December 2014

10.50am  S129
Inflammatory cytokines influence respiratory epithelial anti-viral immune responses via inducible epigenetic control of RIG1 expression: a model of early life origins of asthma?
CM Spalluto, A Singhania, CH Woelk, T Sanchez-Elsner, KJ Staples, TMA Wilkinson

11.05am  S130
TNFα driven CAR phosphorylation promotes trans epithelial migration of leukocytes
AP Hicks, P Morton, A Noble, E Raynor, M Parsons, G Santis

11.20am  S131
Peripheral blood mononuclear cells from children with severe asthma exhibit an impaired corticosteroid sensitivity, which also correlates with increasing body mass index
N Yemula, E Gaillard, Y Amrani

11.35am  S132
Sputum and bronchial biopsy expression of 8-oxo-7,8-dihydro-2’-deoxyguanosine (8-oxodG) in asthma is related to neutrophilic inflammation and poor asthma control
DJE Goold, V Mistry, A Singapuri, M Cooke, R Berair, CE Brightling

11.50am  S133
β2-adrenergic receptor Gly16Arg polymorphism is not associated with impaired asthma control in corticosteroid treated adult asthmatics
B Griffin, A Manoharan, WJ Anderson, J Lipworth, BJ Lipworth
**Friday 5 December 2014**

**10.30am – 12.30pm**
Mountbatten Room, 6th Floor
**SYMPOSIUM**
**DRUG DEVELOPMENT FOR ACUTE LUNG INJURY**
Chaired by: Dr Mark Griffiths (London) and Professor Ann Millar (Bristol)

10.30am  The mechanisms of acute lung injury
Professor Rachel Chambers (London)

11.00am  An approach to investigator led studies: HARPing on about the statin story
Professor Danny McAuley (Belfast)

11.30am  Prevention of ARDS
Dr Daniel Talmor (Boston)

12.00pm  ACEing ARDS: recombinant human angiotensin converting enzyme 2 treatment for ARDS
Dr Andrew Bayliffe (GlaxoSmithKline)

Acute lung injury is a major cause of morbidity and mortality despite improvements in management. Central to continued progress in this field is improved understanding of basic mechanisms that can be translated into multi-centre clinical trials. This session will describe some of the recent developments in all these areas.

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

**12.30pm – 1.15pm**
Churchill Auditorium, Ground Floor
**THE MORRISTON DAVIES LECTURE**
Communicating risk and uncertainty to the public and policy makers
Professor Sir David Spiegelhalter (Cambridge)
Introduced by Dr Ian Campbell (Cardiff)

**12.30pm – 1.30pm**
Victoria Suite, 2nd Floor
**OPEN MEETING**
**BTS Critical Care Specialist Advisory Group**

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**SCIENTIFIC PROGRAMME**

**1.30pm – 2.45pm**
Rutherford Room, 4th Floor
**POSTER DISCUSSION: P205 – P214**
Lung function testing: new approaches
Chaired by: Professor Mike Hughes (London) and Dr Karl Sylvester (Cambridge)

**P205**  Multiple breath washouts in children can be significantly shortened without compromising measurement quality
FA Ahmad, SI Irving, AB Bush, LF Fleming, SS Saglani

**P206**  Changes in indices derived from multibreath washout (MBW) following treatment with Ivacaftor in patients with cystic fibrosis
KML Harman, SJ Irving, K Bayfield, C Saunders, EJ Spearing, JC Davies

**P207**  Reliability of measurements using Innocor breath by breath analyser during a maximal exercise test in cystic fibrosis patients
KJ Bayfield, M McGovern, AJ Simpson, M Embley, S Cunningham, JC Davies, EWFW Alton, JA Innes

**P208**  Assessment of Curvilinearity (Curv) and phase III analysis of multiple breath washout (MBW)
SJ Irving, A Bush

**P209**  Standardisation of lung clearance index in a multicentre clinical trial
DK Armstrong, KJ Bayfield, EWFW Alton, AC Boyd, S Cunningham, HI Elgmati, DR Gill, U Griesenbach, TE Higgins, SC Hyde, JA Innes, CJ Saunders, EJ Spearing, JC Davies

**P210**  Airways resistance in bronchial challenge testing
MAJ Baxter, D Coates, AM Wilson

**P211**  FEV1/FIV1 index in amyotrophic lateral sclerosis patients
G Kaltsakas, M Rentzos, T Alexakis, V Zouvelou, I Evdokimidis, NG Koulouris, SAG Gennimata, AFP Palamidas

**P212**  Parasternal intercostal electromyography to assess neural respiratory drive in healthy adult subjects
V MacBean, C Hughes, G Nicol, CC Reilly, GF Rafferty
**SCIENTIFIC PROGRAMME**

**P213** The impact of sleep disordered breathing on peripheral muscle  
S Mandal, T Dhir, A Vaughan-France, ES Suh, N Hart

**P214** Utilisation of cardio-pulmonary exercise testing (CPET) at an English acute hospital  
E Parkes, VC Moore, D Comer, F Rauf, N Santana-Vaz, R Mukherjee

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**Friday 5 December 2014**

**P221** The use of cytological specimens to determine epidermal growth factor receptor (EGFR) mutation status in non-small cell lung cancers (NSCLC)  
GH Jones, FJ Frost, A Lakhanpal, C Smyth, M Ledson, MJ Walshaw

**P222** Short and long-term consequences of pneumothorax following CT-guided lung biopsy for lung malignancy  
E Johnson, A MacKenzie, S Tsim, KG Blyth

**P223** Consent for medical thoracoscopy: the truth, the whole truth and nothing but the truth?  
SJ Jafri, K Ramsay, PA Beckett, RJ Berg

**P224** Lymph node assessment in surgical resection of non-small cell lung cancer (NSCLC): are we hitting the target?  
AC McKay, H Ewan, G Beattie, AJB Kirk, M Asif

**P225** Revised BTS guidelines for securing cancer diagnosis at bronchoscopy – a higher recommended yield is realistic and achievable  
AE Stanton, CI Mackinlay

**P226** Abstract withdrawn

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**1.30pm – 3.00pm**  
**Westminster Suite, 4th Floor**  
**POSTER DISCUSSION: P215 – P226**  
**Diagnostic and therapeutic interventional procedures**  
*Chaired by: Dr Richard Booton (Manchester) and Dr Neal Navani (London)*

**P215** Referral patterns for mediastinal staging with EBUS across a lung cancer network. A report from the Manchester Cancer EBUS sub-group  
M Evison, P Crosbie, J Morris, J Martin, R Shah, H Doran, J Hoyle, S Bailey, D Rana, R Sundar, R Booton

**P216** Local endobronchial ultrasound (EBUS) service reduces waiting time for test results  
JL Dickson, M Lawson

**P217** The negative predictive value of endosonography for mediastinal staging of non-small cell lung cancer  
K Sayal, M Scarci, N Carroll, B Dougherty

**P218** Nodal staging in lung cancer: a risk stratification model for lymph nodes classified as negative by EBUS-TBNA  
M Evison, P Crosbie, J Morris, J Martin, R Shah, P Barber, R Booton

**P219** A retrospective analysis of the relationship between EBUS-TBNA diagnostic utility and lung cancer stage  
CL Marchand, ARL Medford

**P220** Role of EBUS-TBNA in the diagnosis of primary and relapsing haematological malignancy  
RM Thakrar, G Hardavella, JM Brown, L Succony, M Falzon, E Borg, V Jeebun, M Munnavar, SM Janes, N Navani

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**SPOKEN SESSION: S134 – S138**  
**Basic mechanisms of IPF**  
**And an update on the BTS Interstitial Lung Disease Registry Programme**  
*Chaired by: Professor Rachel Chambers (London) and Professor Monica Spiteri (Stoke-on-Trent)*

**1.35pm**  
**S134** Kinase selectivity profiles of nintedanib and imatinib  
R Rajagopalan, J Nicholas, S Misialek, S Buckman, S Seiwart

**1.50pm**  
**S135** Does CD248 have a role in IPF?  
LE Crowley, D Bartis, L Borthwick, A Fisher, DR Thickett
2.05pm **S136**
mTOR signalling is an essential pathway for TGF-β1 induced αSMA and collagen gene expression
HV Woodcock, S Peace, CB Nanthakumar, TM Maher, PF Mercer, RC Chambers

2.20pm **S137**
Vascular endothelial growth factor (VEGF) expression in the IPF lung – a role for anti-angiogenic isoforms?
SL Barratt, T Blythe, C Jarrett, GI Welsh, K Ourradi, C Scotton, DO Bates, AB Millar

2.35pm **S138**
Nanodiamond delivery of vascular endothelial growth factor promotes fetal lung development in a rat model of congenital diaphragmatic hernia
N Al-Juffali, S Loukogeorgakis, J Jimenez, P Mghsoudliou, J Toolen, P Carmeliet, J Deprest, P De Coppi, S Janes

*BTS Medical Student Award Winners*

2.50pm
**Update on the BTS Interstitial Lung Disease Registry Programme**
Professor Monica Spiteri (Stoke-on-Trent)

1.30pm – 3.15pm
Mountbatten Room, 6th Floor
**SYMPOSIUM**
**CLINICAL AUDIT AND QUALITY IMPROVEMENT**
*Chaired by: Dr James Calvert (Bristol)*

1.30pm
Introduction

1.35pm
National COPD Audit Programme
*Professor Mike Roberts (London)*

1.50pm
National Secondary Care COPD Audit
*Dr Robert Stone (Taunton)*

1.30pm – 3.15pm
Elizabeth Windsor Room, 5th Floor
**SPOKEN SESSION: S139 – S144**
**New insights in skeletal muscle wasting and weakness**
*Chaired by: Dr Nicholas Hart (London) and Dr Samantha Sathyapala (London)*

1.35pm **S139**
A paradoxical rise in rectus femoris myostatin (GDF-8) and GDF-15 in response to neuromuscular electrical stimulation in critical care
SAA Bloch, T Syburrah, U Rosendahl, PR Kemp, MJD Griffiths, MI Polkey

1.50pm **S140**
GDF-15 down-regulation of muscle microRNA drives increased sensitivity to TGF-β signalling; a novel mechanism in intensive care unit acquired weakness
SAA Bloch, JY Lee, T Syburrah, U Rosendahl, PR Kemp, MJD Griffiths, MI Polkey

2.05pm **S141**
Tumour necrosis factor receptor I shedding is related to acute skeletal muscle wasting in critical illness
ZA Puthucheary, J Rawal, MJW McPhail, T Dew, R Phadke, A Rowlerson, SDR Harridge, HE Montgomery, N Hart

2.20pm **S142**
Vastus lateralis proteomic analysis in muscle wasted patients with COPD using two-dimensional fluorescent electrophoresis
RA Rabinovich, Ri Lahkdar, EM Drost, R Bastos, W MacNee
Once-daily tiotropium Respimat®: safety and tolerability results from five Phase III trials in adults with symptomatic asthma
J Haughney, M Vandewalker, E Meltzer, P Paggiaro, M Engel, A Unseld, P Moroni-Zentgraf, HAM Kerstjens

Treatment of allergic rhinitis with theophylline: a double-blind, randomised, crossover study
P Sankaran, C Brockwell, A Clark, AM Wilson

Long-term impact of inhaled corticosteroids on bone mineral density and fracture risk in patients with asthma: systematic review and meta-analysis
YK Loke, D Gilbert, M Thavarajah, P Blanco, AM Wilson

Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis
YK Loke, M Thavarajah, P Blanco, AM Wilson

Prednisolone/cortisol spot test of non-adherence in corticosteroid-dependent asthma
A Mansur

Relationship between bone mineral density and bone turnover markers in severe asthma patients on systemic corticosteroids
HGT Brice, JP Farrant, SJ Fowler, LJ Holmes, J Tang, C Washbourne, I Piec, W Fraser, J Sweeney, LG Heaney, RM Niven

A review of the steroid sparing impact of Mycophenolate mofetil in the severe asthma population at the North West Lung Centre, University Hospital South Manchester
KE George, HGT Brice, SJ Fowler, LJ Holmes, R Daly, RM Niven

The effect of inhalation duration on lung deposition with a pressurized metered-dose inhaler (pMDI)
C Van Holsbeke, J Marshall, J De Backer, W Vos

Effect of inhaled corticosteroid (ICS) particle size on asthma efficacy and safety outcomes: a systematic literature review

P230 Once-daily tiotropium Respimat® improves lung function in patients with severe symptomatic asthma independent of leukotriene modifier use
R Dahl, DE Doherty, J Corren, J Karpel, HAM Kerstjens, M Engel, P Moroni-Zentgraf, H Schmidt, S Hashimoto

P231 Once-daily tiotropium Respimat®: safety and tolerability results from five Phase III trials in adults with symptomatic asthma
J Haughney, M Vandewalker, E Meltzer, P Paggiaro, M Engel, A Unseld, P Moroni-Zentgraf, HAM Kerstjens

P232 Treatment of allergic rhinitis with theophylline: a double-blind, randomised, crossover study
P Sankaran, C Brockwell, A Clark, AM Wilson

P233 Long-term impact of inhaled corticosteroids on bone mineral density and fracture risk in patients with asthma: systematic review and meta-analysis
YK Loke, D Gilbert, M Thavarajah, P Blanco, AM Wilson

P234 Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis
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P235 Prednisolone/cortisol spot test of non-adherence in corticosteroid-dependent asthma
A Mansur

P236 Relationship between bone mineral density and bone turnover markers in severe asthma patients on systemic corticosteroids
HGT Brice, JP Farrant, SJ Fowler, LJ Holmes, J Tang, C Washbourne, I Piec, W Fraser, J Sweeney, LG Heaney, RM Niven

P237 A review of the steroid sparing impact of Mycophenolate mofetil in the severe asthma population at the North West Lung Centre, University Hospital South Manchester
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C Van Holsbeke, J Marshall, J De Backer, W Vos

P239 Effect of inhaled corticosteroid (ICS) particle size on asthma efficacy and safety outcomes: a systematic literature review
Friday 5 December 2014

E Suarez, S Fang, J Abraham, RL DiSantostefano, DA Stempel, L Frith, NC Barnes

P240 Smartinhalers – a new approach to assessing adherence in difficult asthma
P Hall, M Bracken, D Winch, P Nagakumar, A Bush, S Saglani, L Fleming

P241 Anti-reflux surgery conveys a long term improvement in respiratory symptoms in asthma and chronic cough
KE Cusworth, CA Lynch, S Ejiofor, R Sathyamurthy, P Super, C Noble, AH Mansur

1.30pm – 3.30pm
Churchill Auditorium, Ground Floor

SYMPOSIUM

25 YEARS OF SLEEP RESEARCH: WHERE ARE WE NOW?
Chaired by: Dr Alison McMillan (London) and Dr Sophie West (Newcastle upon Tyne)

1.30pm  Cellular effects of intermittent hypoxia and lessons for sleep apnoea
Dr Silke Ryan (Dublin)

2.00pm  What have we learnt from the CPAP withdrawal model in OSA?
Professor John Stradling (Oxford)

2.30pm  Nerve stimulation treatment and novel treatments for OSA
Professor Pat Strollo (Pittsburgh)

3.00pm  Mad studies for sleep apnoea
Dr Tim Quinnell (Cambridge)

At the end of this exciting session participants should understand the effects of intermittent hypoxia on cellular systems in the pathophysiology of sleep apnoea and its interactions with endothelial function and cardiovascular disease. These may inform and stimulate the ongoing research into interactions of COPD and cardiovascular disease in our patient population. Participants will share hot off the press recent research into effects of sleep apnoea on the genome and get a good working knowledge of alternative treatments for sleep apnoea in CPAP intolerant patients.

2.30pm – 4.20pm
Albert Suite, 2nd Floor

POSTER DISCUSSION: P242 – P247

Transplantation advances
Chaired by: Professor Andrew Fisher (Newcastle upon Tyne) and Dr Jasvir Parmar (Cambridge)

P242 Pirfenidone as a bridge to lung transplantation in patients with progressive IPF
P Riddell, P Minnis, P Ging, JJ Egan

P243 A retrospective observational study of 20 year lung transplant survivors - a single centre experience

P244 Characteristics and outcomes in lung transplant recipients aged 65 and over
S Isse, R Hackett, D Thomas, P Catarino, S Tsui, JS Parmar

P245 Evaluation of outcomes of oral Ribavirin in the treatment of viral lower respiratory tract infection in lung transplant patients
RJ Hackett, S Isse, J Parmar, D Thomas

P246 Lung transplantation for patients with idiopathic pulmonary fibrosis and asymptomatic coronary artery disease
P Riddell, K Redmond, D Eaton, L Nolke, SH Javadpour, D Healy, J McCarthy, JJ Egan

P247 Management of airway stenosis and bronchomalacia with biodegradable stents after lung transplantation. Single institution experience
S Gelvez-Zapata, A Wilkinson, D Thomas, M Pittman, J Parmar

2.00pm – 3.00pm
Henry Moore Room, 4th Floor

POSTER DISCUSSION: P248 – P262

Improving patient therapies in COPD
Chaired by: Dr Nick Hopkinson (London) and Dr John Hurst (London)

P248 Current COPD disease burden associated with maintenance monotherapy in the UK
SC Edwards, SE Fairbrother, A Scowcroft, L White, BJ Lipworth
**SCIENTIFIC PROGRAMME**

**P249** Effect size of open-label versus double-blind administration of tiotropium in trials investigating health-related quality of life in COPD  
H Schmidt, H Köglé, S Geier, T Glaab, I Leimer

**P250** Effects of 12 weeks of once-daily tiotropium and olodaterol fixed-dose combination on exercise endurance in patients with COPD  
F Maltais, J.B Galdiz Iturri, A Kirsten, D Singh, A Hamilton, K Tetzlaff, Y Zhao, R Casaburi

**P251** Efficacy and safety of once-daily indacaterol/ mometasone compared with twice-daily salmeterol/fluticasone in patients with moderate to very severe COPD  
A-M Kirsten, A Richard, A-M Tanase, C Weihua, M Hosoe, B Hederer

**P252** GOLD category and optimal management: a Canadian perspective  
K Safka, L McIvor, A McIvor

**P253** Meta-analysis on statins in chronic obstructive pulmonary disease  
GPLC Ambrocio, IA Roque, MPPC Jorge, IL

**P254** Once-daily tiotropium and olodaterol fixed-dose combination via the Respimat® improves outcomes versus mono-components in COPD in two 1-year studies  

**P255** Once-daily tiotropium Respimat® add-on to at least ICS maintenance therapy reduces exacerbation risk in patients with uncontrolled symptomatic asthma  
DMG Halpin, P Paggiaro, E Bleecker, M Engel, P Moroni-Zentgraf, H Schmidt, HAM Kerstjens

**P256** Safety of once-daily tiotropium and olodaterol fixed-dose combination via the Respimat in chronic obstructive pulmonary disease in two 1-year studies  

**P257** Sub-optimal inhaler technique in patients aged over 75 years  
S Vandermolen, J Berner, M Almond, F Huwez

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**Friday 5 December 2014**

**P258** The 24-hour lung function profile of once-daily tiotropium and olodaterol fixed-dose combination compared with placebo and monotherapies in chronic obstructive pulmonary disease  
E Derom, J Westerman, L Grönke, A Hamilton, C Li, KM Beeh

**P259** Tiotropium HandiHaler® and Respimat® in COPD: a safety analysis on pooled data  
DMG Halpin, R Dahl, C Hallmann, I Leimer, A Mueller, DP Tashkin

**P260** Tiotropium Respimat® add-on to inhaled corticosteroids improves lung function in patients with symptomatic mild asthma: results from a Phase III trial  
P Paggiaro, DMG Halpin, R Buhl, M Engel, VB Zubek, Z Blahova, P Moroni-Zentgraf, E Pizzichini

**P261** Tiotropium safety and performance in Respimat® (TIOSPIR™): safety and efficacy in patients naive to treatment with anticholinergics  
R Wise, P Calverley, R Dahl, D Dusser, N Metzdorf, A Mueller, A Fowler, A Anzueto

**P262** Tiotropium safety and performance in Respimat® (TIOSPIR™): safety and efficacy in patients with tiotropium HandiHaler® use at baseline  
P Calverley, A Anzueto, R Dahl, A Mueller, A Fowler, N Metzdorf, R Wise, D Dusser

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**3.00pm – 4.15pm**  
Mountbatten Lounge, 5th Floor

**MODERATED POSTER DISCUSSION:**  
**M263 – M272**

**IPF: education, information and health status**

**Chaired by: Mrs Annette Duck (Manchester) and Dr Helen Parfrey (Cambridge)**

**M263** A quarter of IPF patients not eligible for pirfenidone treatment due to the NICE criteria significantly decline over time  
N Chaudhuri, CT Leonard

**M264** Health and economic impact of prescribing pirfenidone  
N Chaudhuri, CT Leonard
Friday 5 December 2014

M265 Daily activity monitoring in idiopathic pulmonary fibrosis
MG Crooks, SP Hart

M266 Development of an idiopathic pulmonary fibrosis (IPF) patient reported outcome measure (PRoM): an iterative approach to item generation
AM Russell, T Sanderson, S Fleming, AU Wells, TMM Maher, TP Cullinan

M267 Health status and quality of life in idiopathic pulmonary fibrosis and sarcoidosis: effect of fatigue
CP Atkins, D Gilbert, C Brockwell, S Robinson, AM Wilson

M268 The IPF diagnosis – communicating a life sentence
S Wibberley, Y Ochiai, R Pitt, N Mathieson

M269 The emotional turmoil of IPF
S Wibberley, Y Ochiai, R Pitt, N Mathieson

M270 Obtaining information when you have a rare disease – the potential for IPF support groups
S Wibberley, Y Ochiai, R Pitt, N Mathieson

M271 A survey of trainee experiences in interstitial lung disease
C Sharp, M Gibbons

M272 Estimated cost and payment by results (PBR) tariff reimbursement for idiopathic pulmonary fibrosis services across 14 specialist providers in England

3.15pm – 4.15pm
Victoria Suite, 2nd Floor
OPEN MEETING
BTS Interventional Procedures Specialist Advisory Group

3.15pm – 4.15pm
Henry Moore Room, 4th Floor
POSTER DISCUSSION: P273 – P280
ILD: diagnosis, co-morbidities and treatment
Chaired by: Dr Joanna Porter (London) and Dr Lisa Spencer (Liverpool)

SCIENTIFIC PROGRAMME

P273 Assessment of lung microstructure in interstitial lung disease with hyperpolarised gas MRI
NJ Steward, G Norquay, J Parra-Robles, H Marshall, G Leung, PS Murphy, RF Schulte, CA Elliot, R Condliffe, CG Billings, I Smith, PD Griffiths, J Wolber, MKB Whyte, DG Kiely, JM Wild

P274 Anti-synthetase syndrome: validity of ANA as a screening tool – the Oxford ILD Service experience
TW Nicholson, A Woods, J David, R Hoyles

P275 EBUS or EUS in the diagnosis of sarcoidosis?
ADL Marshall, I MacPherson, GP Currie, GW Chalmers

P276 Characterisation of reflux and aspiration in idiopathic pulmonary fibrosis; an integrated approach

P277 The incidence of lung cancer in people with idiopathic pulmonary fibrosis and connective tissue disease associated pulmonary fibrosis in the UK: a population based study
W Dalleywater, HA Powell, G Jones, RB Hubbard, V Navaratnam

P278 Extra-corporeal membrane oxygenation and diffuse alveolar haemorrhage – a single centre case series and analysis of the ELSO database
TRG Simpson, CY Ling, G Glover, N Barrett, N Ioannou, B Lams, C Langrish, C Meadows, N Agarwal, D D’Cruz

P279 Reduction in disease progression with nintedanib in the INPULSIS™ trials
V Cottin, H Taniguchi, HR Collard, L Richeldi, S Stowasser, I Tschoepe, R Schlenker-Herceg, G Raghu

P280 Extended clinical experience with pirfenidone during a named patient programme for idiopathic pulmonary fibrosis (IPF): interim results
H Parfrey, N Chaudhuri, MA Gibbons, L Anning, M Balkin, S Cooper, R Dew, TM Maher
SCIENTIFIC PROGRAMME

3.15pm – 4.30pm
Abby Room, 4th Floor

POSTER DISCUSSION: P281 – P289
Smoking detection and cessation and non tobacco products

Chaired by: Dr Sarah Foster (Taunton) and Dr Henry Steer (Gloucester)

P281 Smoking prevalence and stop smoking interventions for patients admitted to an emergency department (ED) in a busy, inner city hospital
R Thomas, F Warden, M Stern

P282 A prospective study to determine the accuracy of self-reported smoking habits in patients with tuberculosis
AL Carver, R Whitfield, MR Soobratty, GV O’Donovan, G Grove, GF Cope, HJ Milburn

P283 Chronic obstructive pulmonary disease (COPD) case-finding and tobacco dependence on long stay psychiatric wards
D Hughes, M Jeanneret, F Johansson, K Sherring, L Restrick

P284 A questionnaire study of electronic cigarette usage in patients attending respiratory clinics in a district general hospital
AD Macfoy, E Crawford, K Srinivasan, H Moudgil

P285 Assessing the impact of varenicline initiation during acute hospital admission for current smokers with respiratory diseases: 18-month experience from an inner city district teaching hospital
A Ainley, E Pang, B Coleman, M Stern, LJ Restrick

P286 Recommendations for smoking cessation service provision for smokers with COPD with multiple complex needs: findings from a pilot study
SY Yap, E Pang, S Lunn, C Croft, M Stern

P287 Measuring the acute cardiovascular effects of shisha smoking: a cross-sectional study
MK Kadhum, AEJ Jaffery, AH Haq, JB Bacon, BM Madden

Friday 5 December 2014

P288 The desensitisation effect of graphic health warning labels and cross-cultural differences in the awareness of smoking related consequences: comparing a London and Singapore cohort
C Ratneswaran, B Chisnall, A Douiri, MY Li, STan, S Tan, C Chang, D Anantham, J Steier

P289 Carboxyhaemoglobin levels in emergency department patients: an important tool in validating smoking history and detecting "missed smokers"
RW Fowler

3.30pm – 4.30pm
Elizabeth Windsor Room, 5th Floor

POSTER DISCUSSION: P290 – P296
Screening and treating sleep apnoea

Chaired by: Dr Rebecca Mason (Bath) and Dr Sophie West (Newcastle upon Tyne)

P290 Validation of preoperative screening algorithm for obstructive sleep apnoea
VM Macavei, J Mitic, M Berger, OE Mohr, TC O’Shaughnessy

P291 Obstructive sleep apnoea screening for patients undergoing bronchoscopy – is it required?
V Palissery, D Ghosh, MW Elliott

P292 Validation of the STOP-BANG questionnaire as a screening tool for sleep apnoea in patients undergoing ablation for paroxysmal atrial fibrillation
MA Pittman, M Mason, D Packer, R Chadwick, A Clutterbuck-James, S Fynn, TG Quinell

P293 Is obstructive sleep apnoea a risk factor for chronic kidney disease?
F Rauf, J Kerks, D Comer, I Dasgupta, M Daniels, R Mukherjee, S Wharton

P294 Factors affecting CPAP compliance
JA Stockley, S Huq, S Madathil, JA Hunt, BG Cooper

P295 Patients’ preference of established and emerging treatments for obstructive sleep apnoea
T Campbell, MF Pengo, R Brown, A Birdseye, K Bacon, J Steier
P296 Effectiveness of adaptive servo ventilation in the treatment of central sleep apnoea
A Al-Ameri, M Latham, J Pateraki, M Elliott

3.30pm – 4.30pm
St James’s Suite, 4th Floor
POSTER DISCUSSION: P297 – P304
From hospital to home: NIV in clinical practice
Chaired by: Dr Mike Davies (Papworth) and Dr Mark Elliott (Leeds)

P297 Effect of BTS-recommended medical leadership on the “door-to-mask” time of acute non-invasive ventilation (NIV) setups
H Boryslawskyj, F Rauf, B Beauchamp, A Oakes, N Santana-Vaz, B Chakraborty, R Mukherjee

P298 Referral patterns and mortality in a non-invasive ventilation (NIV) unit in a tertiary university hospital in the UK
K Aldridge, S Bikmalla, A Thomas

P299 The role of a multidisciplinary respiratory hub in improving post-discharge follow up of patients receiving acute non-invasive ventilation (NIV)
F Rauf, A Oakes, Y Khan, T Stuart, B Chakraborty, AM Turner, R Mukherjee

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

**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.

**Professor Emma Baker** is a Professor of Clinical Pharmacology at St George’s, University of London. She has clinical and research interests in advanced COPD, particularly in co-morbidities and new treatments. Her research is funded by the Medical Research Council and British Lung Foundation. As a clinical pharmacologist she conducts investigator-led clinical trials and leads on medicines management. She is Respiratory Specialist Lead for the South London CRN.

**Professor David Baldwin** works as a Consultant Respiratory Physician, Interventional Bronchoscopist, and Group 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. 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 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 at the Royal Brompton Hospital and specialises in all aspects of paediatric respiratory medicine. He is the Director of Paediatric Cystic Fibrosis at the Brompton Hospital, one of the largest paediatric CF clinics in the UK. He is on the National CF Clinical Reference Group and is also Chair of the CF Group of the ERS.

**Dr Andrew Bayliffe** PhD leads the Acute Respiratory Distress Syndrome (ARDS) Medicine Development Team within the Respiratory Therapy Area Unit at GlaxoSmithKline R&D. He holds a PhD in molecular pharmacology from Leeds University and has 15 years research and development experience at GSK, predominantly in infectious diseases, immune-inflammatory, and critical care conditions. For the last five years, he has been focussed on the evaluation of experimental therapies for ARDS, and in collaboration with leading clinical experts around the world, has initiated a number of experimental trials in acute inflammatory conditions including ARDS.

**Professor Maria Belvisi** is Head of the Respiratory Pharmacology Group at the National Heart and Lung Institute at Imperial College. She obtained a BSc in pharmacology in 1986 at King’s College London and a PhD at 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. She is involved in multidisciplinary translational research which integrates basic science with clinical studies, thereby providing novel insights into common airway diseases. She also worked for a period in the pharmaceutical industry leading a team in the Respiratory Therapeutic area at Aventis Pharma. Her achievements in industry included running the pre-clinical pharmacology effort in support of an inhaled corticosteroid with an improved therapeutic ratio (ciclesonide/Alvesco), which is now approved for use in man in several countries. She was elected as a Fellow of the British Pharmacological Society in 2005. Professor Belvisi has an extensive publication record in peer review journals and serves on the Editorial Board of several journals. She has also received several prizes and awards including the Pfizer Award for Science in the UK (1994) and the Trabbuchi Award (1996) and the Woman in Inflammation Science (2009, awarded by the World Inflammation Society), AstraZeneca prize for Women in Pharmacology (2011; awarded by the British Pharmacological Society).

**Professor Diana Bilton** directs the Adult CF Unit at the Royal Brompton Hospital and is Adjunct Professor at Imperial College. She is also an Associate Editor for the Journal of Cystic Fibrosis and Chairs the UK CF Registry. Professor Bilton is Chair of the Cystic Fibrosis Clinical Reference Group for UK Specialist Commissioning. She was a co-author on the BTS Bronchiectasis Guidelines and continues to work on developing new treatments for bronchiectasis as the chief investigator on a number of trials.

**Dr Hans Bisgaard** MD, DMS is a Specialist in Paediatric Pulmonology and Allergology, and has devoted his research to unravelling the origins of asthma, for which he established the two
comprehensive Copenhagen Prospective Studies on Asthma in Childhood (COPSAC) birth cohorts, combining extensive clinical data with cutting-edge interdisciplinary basic research.

**Professor Dame Carol Black** DBE, MD, FRCP, MACP, FMedSci is Principal of Newnham College Cambridge, Expert Adviser on Health and Work to the Department of Health, England, Chair of the Nuffield Trust, and Chair of the Governance Board of the Centre for Workforce Intelligence. In November 2011 she completed as Co-Chair an independent review for the UK Government of sickness absence in Britain, to which the Government has recently responded.

Professor Black is a past-President of the Royal College of Physicians, of the Academy of Medical Royal Colleges, and of the British Lung Foundation. The Centre she established at the Royal Free Hospital in London is internationally renowned for research and treatment of connective tissue diseases such as scleroderma.

**Professor Graham Bothamley** is a Respiratory Physician at the Homerton University Hospital, London. He is Chair of the European Respiratory Society Tuberculosis Group and TBNET (http://www.tb-net.org/). He is engaged in translational research in tuberculosis and has published >100 papers, with a special interest in early diagnosis and biomarkers.

**Dr Stephen J Bourke** is a Consultant Physician in Respiratory Medicine at the Royal Victoria Infirmary, Newcastle upon Tyne. He is Lead Physician for the Newcastle Adult Cystic Fibrosis Centre and is Chair of the BTS Cystic Fibrosis Specialist Advisory Group. He has research interests in clinical aspects of cystic fibrosis.

**Professor Jeremy Brown** is an Academic Respiratory Consultant with a subspecialty interest in lung infection. He did his clinical training in London alternating with Wellcome funded laboratory research at Imperial College into respiratory pathogens. Since 2003 he has run his own laboratory at UCL and been a Consultant at UCLH. His clinical practice is mainly caring for patients with a range of clinical respiratory infection problems, including bronchiectasis, aspergillosis, pneumonia in immunocompetent and immunocompromised patients, and empyema. Professor Brown’s laboratory investigates mechanisms of immunity to *Streptococcus pneumoniae* and potential new vaccine candidates, funded mainly by research charities and the Medical Research Council. He was previously an assistant editor for Thorax for four years and chaired the British Thoracic Society Specialist Advisory Group for Respiratory Infections.

**Professor Andrew Bush** is Professor of Paediatrics at Imperial College, Professor of Paediatric Respirology at the National Heart and Lung Institute and Consultant Paediatric Chest Physician, Royal Brompton Hospital. He has written a lot of papers, that no-one reads, and given a lot of talks, which are instantly forgettable. His chief enjoyments are researching clinical physiology and airway inflammation; clinical paediatrics, which means having fun playing with little kids who do more good for him than ever he did for them; unsuccessfully trying to penetrate the opacity which surrounds the world of adult chest medicine, whose occupants cannot understand that they are obsolete because all adult diseases are determined in childhood; and above all, his family, which includes two fabulous grandsons who happily for them do not resemble their grandfather in any way whatsoever.

**Dr James Calvert** is a Chest Physician and Deputy Medical Director at North Bristol Trust. He leads the COPD and TB services. He has a longstanding interest in patient safety which he has pursued through roles at the Southwest SHA and NHS England. He Chairs the BTS Professional and Organisational Standards Committee.

**Dr James Chalmers** is Wellcome Trust Postdoctoral Fellow at the University of Dundee and a lecturer in Respiratory Medicine. His research and clinical interests are in respiratory infections, particularly bronchiectasis, community-acquired pneumonia, and COPD. He leads a research group investigating the mechanisms and consequences of bacterial infection in chronic lung disease, supported by grants from the Wellcome Trust, Medical Research Council, Scottish Government, and charities. He is a current member of the British Thoracic Society Science and Research Committee, the European Respiratory Society Long-Range Planning Committee, and the American Thoracic Society Microbiology, Tuberculosis and Pulmonary Infections Programme Committee. He is a member of the International Advisory Board of the Lancet Respiratory Medicine, is Associate Editor of Plos One and was Guest Editor of the recent European Respiratory Monograph on Community Acquired Pneumonia. He is Chair of the European Bronchiectasis Network and Registry (EMBARC).
SPEAKERS’ BIOGRAPHICAL DETAILS

Dr Alison Condliffe is a University Lecturer at the University of Cambridge and an Honorary Consultant in Respiratory Medicine at Addenbrooke’s and Papworth Hospitals. Her main academic interest is in cell signalling in innate and adaptive immunity; her clinical remit is respiratory infection, with a subspecialist interest in infections in immunodeficiency disorders.

Professor Paul A Corris is Professor of Thoracic Medicine at Newcastle University. He directs the National Pulmonary Vascular Service (Newcastle) and is Deputy Director of the Transplant Institute within the Institute of Cellular Medicine at Newcastle University. He is Past-President of both the British Thoracic Society and the International Society for Heart and Lung Transplantation. In 2014, Professor Corris was elected President Elect of the International Pulmonary Vascular Research Institute and is currently Chairman of NHS England Clinical Reference Group for Pulmonary Hypertension. He sits on the editorial boards of "Transplantation" and the "Journal of Heart and Lung Transplantation," and was a previous Associate Editor of "Thorax."

Professor Andrew Curran joined the Health and Safety Laboratory (HSL) in 1991 and has worked his way up through the organisation to his current position as Director of Science and Delivery. He has a BSc (Hons) degree in Biological Sciences from Birmingham University and a PhD in Cancer Research from Nottingham University. Whilst at HSL he developed a research interest in occupational respiratory disease and he has published and lectured extensively in this area. He was instrumental in the establishment of the Centre for Workplace Health. The Centre is a collaborative venture between HSL, the University of Sheffield and the Sheffield Teaching Hospitals Foundation Trust and is an active and well-respected organisation in the field of workplace well-being. Andrew is the Centre’s Scientific Director. He is an Honorary Professor at the University of Sheffield and Fellow of the Society of Biology, a Fellow of the Chartered Management Institute and an honorary Fellow of the Faculty of Occupational Medicine. He is also a Board Member of the International Commission on Occupational Health. His role in HSL has expanded in recent years and he has assumed various operational management roles. He has been effective in managing change in the Laboratory, as it has commercialised its approach to deliver work for public and private sector organisations external to HSE. Professor Curran brings his long-standing knowledge of the HSL and its culture, essential to the successful delivery of the change processes underway in the Laboratory. He is well respected in the scientific community and has wide experience of the development and delivery of scientific strategies and programmes. He is an experienced leader of staff in scientific environments.

Professor Donna Davies is Professor of Respiratory Cell and Molecular Biology in the Faculty of Medicine at the University of Southampton. She has pioneered the use of in vitro models and tissue engineering as alternatives to using animal models of asthma, COPD and IPF. Her work on viral infection resulted in establishment of the University spin-out company, Synairgen, which has developed inhaled interferon-beta (SNG001) as a novel treatment for asthma exacerbations. SNG001 was out-licensed to AstraZeneca in July 2014.

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 areas, 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 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.

Professor Louise Donnelly is a Professor of Respiratory Cell Biology, in the section of Airway Disease, at the National Heart and Lung Institute, Imperial College London. Her research interests are primarily focused on the cellular profile of inflammatory lung diseases including asthma and COPD. In particular, her work investigates how inflammatory cells are altered in the disease state and how these changes can be exploited in the development of novel therapeutic strategies. To this end, Professor Donnelly’s group have established a
number of human primary cell systems to investigate mechanisms of aberrant inflammation.

**Professor Andres Floto** is Professor of Respiratory Biology at the University of Cambridge, a Wellcome Trust Senior Clinical Fellow at the Cambridge Institute for Medical Research, and Research Director of the Cambridge Centre for Lung Infection at Papworth Hospital, Cambridge. His research is focused on understanding how immune cells interact with bacteria, how intracellular killing and inflammation are regulated and sometimes subverted during infection, and how therapeutic enhancement of cell-autonomous immunity may provide a novel strategy to treat multi drug resistant pathogens.

**Professor Stephen H Gillespie** MB BCh MD DSc FRCP(Edin) FRCPath was brought up in Belfast and educated at the Royal Belfast Academical Institution and the Queen’s University Belfast where he graduated in Medicine. He trained in Internal Medicine and Clinical Microbiology at the Royal Victoria Hospital Belfast before being appointed as the Merchers’ Lecturer in Clinical Tropical Medicine at the London School of Hygiene and Tropical Medicine. After field research in Kenya and Tanzania Professor Gillespie was appointed as Senior Lecturer in Clinical Microbiology at the Royal Free Hospital School of Medicine and subsequently Professor after its merger with University College London. Professor Gillespie has worked clinically as a Consultant Clinical Microbiologist leading the department until 2005. He was then appointed as Regional Microbiologist for London where he led the London laboratory response to the 2009 influenza pandemic. In 2010 he was appointed as the Foundation Sir James Black Chair of Medicine at the University of St Andrews.

He is currently the Chief Investigator of the REMoxTB project, the first regulatory pivotal trial that is investigating two treatment-shortening regimens. Professor Gillespie is also one of the three Chief Investigators for the PanACEA consortium that is the main European-African clinical trials network. Whilst continuing his clinical trial work, his current work in St Andrews is to develop new and more comprehensive mathematical models of tuberculosis treatment and novel approaches to identify differing tuberculosis cell cycle by non-invasive methodology.

**Professor Stephen Gordon** joined the Liverpool School of Tropical Medicine in 2005 and holds an Honorary Consultant contract in General Medicine in the Royal Liverpool Hospital and University Hospital Aintree. He combines respiratory and general medicine with research and teaching. His main interests include pulmonary factors contributing to susceptibility to infection, including air pollution, the pathogenesis of pneumococcal infection and inhaled vaccines against pneumonia.

**Dr Neil Greening** is a NIHR Clinical Lecturer and Specialist Registrar in Leicester. He qualified from Newcastle upon Tyne and moved to Leicester for respiratory specialist training in 2007. His interests are in COPD, particularly its systemic effects and impact of exacerbations. He has contributed to the BTS Pulmonary Rehabilitation Guidelines and Quality Standards.

**Dr Mark Griffiths** is a Consultant Physician in the Adult Intensive Care Unit, Royal Brompton Hospital and Honorary Reader in Critical Care, Imperial College London. He trained in London becoming accredited in Respiratory and General Internal Medicine before specialising in Critical Care. He is the Chair of the British Thoracic Society Specialist Advisory Group in Respiratory Critical Care (2012-5) and the Intensive Care Society’s Guideline Development Group for the Management of ARDS, reflecting his clinical interests. He is the Education Director of the NIHR Respiratory Biomedical Research Unit (rBRU) partnership between the Trust and Imperial College London.

**Dr Nicholas Hart** is the Clinical and Academic Director of the Lane Fox Respiratory Unit at St Thomas’ Hospital, Reader in Respiratory and Critical Care Medicine at Kings College London and Directorate Research and Development Lead for Peri-Operative Medicine, Critical Care and Pain at Guys and St Thomas’ NHS Foundation Trust. The Lane Fox Respiratory Unit is a national weaning, rehabilitation and complex home ventilation unit specialising in provision of long-term ventilatory support. He has developed the Lane Fox Clinical Respiratory Physiology Centre which focuses on (1) advanced physiological monitoring and ventilatory strategies in chronic respiratory failure and (2) muscle wasting, weakness and rehabilitation. He is currently chief investigator of the three UKCRN portfolio trials.

**Dr John Harvey** has been a Consultant Respiratory Physician at The North Bristol Lung Centre for 29 years. He has been interested in pleural disease ever since designing and co-ordinating the 1994 BTS trial.
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comparing simple aspiration with chest drain insertion in the management of pneumothorax and subsequently helping to write guidelines on the management of pneumothorax for the BTS and ATS. On reflection, as his presentation will show, he now appreciates how misguided his advice has been. He is currently working for Brighton and Sussex Medical School and also teaches respiratory medicine in Africa and India in a voluntary capacity and as part of the RCP Overseas Initiative.

Dr Charles Haworth is Clinical Director of Thoracic Services and Director of the Cambridge Centre for Lung Infection at Papworth Hospital. He is Co-chair of the Cystic Fibrosis Foundation/European CF Society NTM Guidelines Group and the BTS NTM guidelines group. He is also a member of the BTS Bronchiectasis Guideline Group.

Professor John Henderson is Professor of Paediatric Respiratory Medicine at the University of Bristol and Bristol Children’s Hospital. His interests are in asthma epidemiology, with a focus on genetic and early life influences on asthma in children. He is Co-Director of the Avon Longitudinal Study of Parents and Children (ALSPAC).

Dr Bernard Higgins is a Consultant Respiratory Physician in Newcastle, having previously trained in Manchester, Edinburgh and Nottingham. He has a particular interest in asthma, and chaired the British Asthma Guideline Steering Group and the BTS Specialist Advisory Group for Asthma over recent years. He took over as Chair of the BTS Executive Committee at the end of 2012.

Dr Adam Hill is a Consultant Chest Physician and Honorary Reader at the Royal Infirmary and University of Edinburgh. He is the Respiratory Infection Lead and has a special interest in bronchiectasis, community acquired pneumonia and tuberculosis. He is actively involved in clinical and translational research in respiratory infection. He leads the BTS National Bronchiectasis Audit, chaired a group setting BTS Quality Standards for Bronchiectasis and is Chairing the new Bronchiectasis Guidelines.

Dr Nik Hirani qualified from Nottingham University in 1990 and continued general medical and respiratory training in the South West, Nottingham and finally Edinburgh. In 1996 he took up a Wellcome Clinical Training Fellowship studying the pathogenesis of acute respiratory distress syndrome (ARDS). He was subsequently a Clinical Lecturer in Respiratory Medicine and since 2002 has held a GSK Clinician Scientist Fellowship. He is currently a Senior Lecturer in Respiratory Medicine and Honorary Consultant and PI in the MRC Centre for Inflammation Research in Edinburgh. His research interests include the role of hypoxic signalling and macrophage biology in lung inflammation and repair and he leads a specialist interstitial lung disease service. He has previously chaired the BTS ILD Guideline Committee, the Specialist Advisory Group for ILD and NICE Working Group for Idiopathic Pulmonary Fibrosis.

Dr Nicholas Hopkinson is a Clinical Senior Lecturer at the National Heart and Lung Institute of Imperial College and the Royal Brompton and Harefield NHS Foundation Trust. His research interests are in pulmonary physiology, skeletal muscle impairment and exercise limitation in COPD and other respiratory conditions. His work has been funded by the MRC, the British Lung Foundation and the Wellcome Trust. @ COPDdoc

Dr Luke Howard is a Consultant Respiratory Physician at Hammersmith Hospital, specialising in the pulmonary circulation and exercise physiology. He is the Clinical Lead for the Exercise Service, which undertakes over 600 diagnostic tests per annum including exercise haemodynamics and echocardiography.

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. He works as a Consultant for the NHS in Respiratory Medicine with a particular interest in lung cancer, mesothelioma, interventional and diagnostic bronchoscopy and early lung cancer detection. He won the European Thoracic Oncology Investigator of the Year Prize in 2010. He is Director of the Lung Cancer Board for London Cancer, Vice-chair of the Lung Cancer CRG and leads an ERS Working Group on Lung Cancer. He is Chair of the BTS Winter Meetings 2013-2015.
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**Professor Miriam Johnson** MD, FRCP, MRCP is Professor of Palliative Medicine at Hull York Medical School, University of Hull. Her research interests include the mechanisms and management of chronic refractory breathlessness in advanced disease. She is the Co-director of the Supportive Care, Early Diagnosis and Advanced Disease (SEDA) Research Group at the University of Hull, and a member of the NCRI Supportive and Palliative Care Clinical Studies Group.

**Dr Andrew Jones** is a Consultant Physician and Honorary Reader at the Manchester Adult Cystic Fibrosis Centre. He has published over 80 papers and has an interest in CF microbiology and infection control. Dr Jones Chaired the UK Cystic Fibrosis Trust Infection Control Group that developed national guidelines for control of *B. cepacia* complex, *P. aeruginosa*, MRSA and *M. abscessus*. He is a member of the UK Cystic Fibrosis Trust Microbiology Standards Working Group, and an Associate Editor for Thorax.

**Professor Beate Kampmann** holds a Chair in Paediatric Infection and Immunity at Imperial College, London and was appointed as the Scientific Director for Vaccinology Research at the MRC Unit-The Gambia in July 2010. She directs a comprehensive tuberculosis research programme both in the UK and Sub-Saharan Africa. She set up and Chairs the ptbnet, a collaborative European network of paediatricians and scientists involved in diagnosis and management of childhood TB in 18 countries in Europe.

**Dr Martin Kolb** practices in Hamilton, ON, Canada with a focus on Interstitial Lung Diseases. He has a PhD in Experimental Medicine and is Director of the Division of Respiratory at McMaster University and Research Director of the Firestone Institute for Respiratory Health. Dr. Kolb’s major basic science interests are mechanisms of lung injury, repair and fibrosis, particularly in IPF. His clinical research includes biomarkers and clinical trials in IPF.

**Professor Christoph Lange** is Head, Centre of Infectious Diseases Borstel/Lübeck (DGI); Professor at the Medical University Lübeck; Vice Chair, Centre of Infection and Inflammation University of Lübeck; Associate Professor; USMF; Chisinau, Republic of Moldova; Associate Professor; UNAM, School of Medicine, Windhoek, Namibia; and Head, Clinical TB Unit, German Centre for Infection Research. Professor Lange is Chair of the Mycobacteriology Section of the German Society of Infectious Diseases (DGI); Chair of the Infectious Diseases Assembly, European Respiratory Society (ERS); Associate Editor International Journal of Tuberculosis and Lung Diseases (IJTLD); Respirology Steering Committee member of the ESCMID Mycobacteria Study Group (ESGMYC); Co-editor European Respiratory Monograph on Tuberculosis; Steering Committee member of RESIST-TB; and Doctor honoris causa, USMF, Chisinau, Republic of Moldova.

**Dr Mark L Levy** is a GP in London and has co-authored six asthma books and published over 150 papers on respiratory subjects. Dr Levy was one of the six founders of the PCRS-UK (formerly the GPIAG). He is a member of the GINA Board and was Clinical Lead for NRAD. His CV is detailed at www.consultmarklevy.com

**Dr Michael Loebinger** is a Consultant Physician at the Royal Brompton Hospital and Honorary Senior Lecturer at Imperial College. He has particular interest in bronchiectasis, and infections caused by gram negative bacteria, non-tuberculosis mycobacteria and fungi. He chairs the Infection Specialist Advisory Group for the British Thoracic Society and is co-writing both the National Bronchiectasis and Non-tuberculous Mycobacteria Guidelines. He is a founding member of European and UK clinical and research bronchiectasis networks.

**Dr Gill Lowrey** works as a Respiratory Consultant for the Royal Derby NHS Foundation Trust. She has a special interest in COPD. Locally she works as part of an integrated COPD team and has helped to develop the use of both admission and discharge bundles for exacerbations of COPD. The service also provides a specialist COPD clinic for complex COPD patients. She leads the Trust’s oxygen group and has developed a respiratory quality dashboard aimed at improving safety and quality of care within the department. She is a member of the BTS Specialist Advisory Group on COPD and sits on the Secondary Care Steering Group for the National COPD audit.

**Dr Andrew MacDuff** is a Consultant in Respiratory and Critical Care Medicine at New Cross Hospital, West Midlands. He trained in respiratory medicine in the West Midlands and South-East Scotland. He completed a PhD in acute lung injury and undertook advanced training in ICM in Edinburgh. He was a member of the Pneumothorax Sub-group of the BTS Pleural Guidelines Committee.
**SPEAKERS’ BIOGRAPHICAL DETAILS**

**Dr Toby Maher** is an NIHR Clinician Scientist. He is a Senior Lecturer at Imperial College, London and Consultant Physician working on the Interstitial Lung Disease Unit at the Royal Brompton Hospital. His clinical interests are idiopathic pulmonary fibrosis, connective tissue disease associated interstitial lung disease and sarcoidosis. His specific research interests include; biomarker discovery, clinical trials in ILD and study of the role of the microbiome, apoptosis and senescence in the pathogenesis of IPF.

**Dr Nick Maskell** is a Reader in Respiratory Medicine at the University of Bristol and Honorary Consultant, North Bristol NHS Trust. He undertook his DM thesis on pleural diseases in Oxford prior to taking up a consultant post at North Bristol NHS Trust in 2003. His research interests include clinical trials in pleural disease, mesothelioma and patient safety during pleural procedures. He Leads the Pleural Service at North Bristol NHS Trust and the Bristol Pleural Clinical Trials Unit. He Chaired the last BTS Pleural Disease Guideline Group, and is Co-chair of the 2014 BTS Mesothelioma Guideline Group.

**Professor Danny McAuley** is a Consultant and Professor in Intensive Care Medicine at the Regional Intensive Care Unit at the Royal Victoria Hospital and Queen’s University of Belfast. He undertook his training in Belfast, Birmingham, London and San Francisco. He is Co-Director of Research for the UK Intensive Care Society and Chair of the Irish Critical Care Trials Group. He has two main research interests; acute respiratory distress syndrome and clinical trials.

**Professor Ann Millar** is 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 Mary Morrell** is Professor of Sleep and Respiratory Physiology, Imperial College London, Royal Brompton Hospital. Her research investigates the causes and consequences of sleep disordered breathing; translating findings into improvements in patient care. Recent studies have focused on the neurological impact of sleep apnoea; particularly in older people. Professor Morrell is committed to education and is Head of Years 1 & 2 MBBS/BSc Medicine, Imperial College.

**Professor John Moxham** is Professor of Respiratory Medicine at King’s College, London. After training at University College Hospital and the Brompton he was appointed as a Consultant Physician at King’s College Hospital in 1982. His main research interests have been in respiratory physiology. He is Chair of Action on Smoking and Health (ASH). Currently he is Director of Clinical Strategy for the King’s Health Partners Academic Health Sciences Centre.

**Dr Mohammed Munavvar** has been a Consultant Chest Physician at Lancashire Teaching Hospitals, Preston for about 15 years. He is also Director of R & D for the Trust and Regional Advisor to the Royal College of Physicians of Edinburgh. He has been the founder/organiser of the Preston Basic Bronchoscopy Course and BTS Interventional Bronchoscopy/Thoracoscopy Course for several years. He has been a faculty member at the Lille Interventional Bronchoscopy and Thoracoscopy courses, European Association of Bronchology’s courses, besides workshops arranged by the Gulf Thoracic Society, Saudi Thoracic Society and Indian Association of Bronchology. Dr Munavvar Chaired the BTS Basic Bronchoscopy Guideline Development Committee, is a Specialist Adviser to NICE Interventional Procedures Committee and has been a member of the BTS SAG for Interventional Pulmonology and BTS Education and Training Committee. He is actively involved in the evaluation of innovative techniques and tools in thoracoscopy and bronchoscopy, and has a special interest in the overall management of lung cancer, pleural pathologies and TB.

**Dr Carmel B Nanthakumar** is a Senior Scientific Investigator leading a research team in the Fibrosis Discovery Performance Unit at GlaxoSmithKline. She received her undergraduate degree from Queen Mary and Westfield College London and completed her PhD within the Division of Medicine at UCL, prior to joining Respiratory R&D at AstraZeneca. She has since led research teams at Merck and Cancer Research Technology before joining GSK in 2007. In her current role, Dr Nanthakukmar divides her time between GSK and the Centre for Inflammation and Tissue Repair (CITR) at UCL as part of the CRAFT Consortium, pursuing research into novel therapies for fibrotic conditions using human relevant systems.

**Dr Kyle Pattinson** is a Senior Clinical Research Fellow at the University of Oxford and Honorary Consultant Anaesthetist at Oxford University Hospitals NHS Trust. His research investigates the brain...
mechanisms of respiratory control in humans using functional magnetic resonance imaging with a particular focus on understanding brain processes underlying breathlessness.

**Professor Ian D Pavord**, MA DM FRCP is Professor of Respiratory Medicine at the University of Oxford and Honorary Consultant Physician at the Oxford University Hospitals. He is a Fellow of St Edmund Hall. He was a Consultant Physician from 1995 and Honorary Professor of Medicine from 2005 to 2013 at the Institute for Lung Health, Glenfield Hospital, University Hospitals of Leicester NHS Trust. He is an NIHR Senior Investigator. Professor Pavord has a research interest in the clinical aspects of inflammatory airway diseases and he has pioneered the clinical use of non-invasive measures of airway inflammation in these conditions. He has identified a number of clinically important phenotypes of inflammatory airway disease and has played a lead role in the clinical development of three of the most promising new treatments for severe airway disease.

Professor Pavord is co-editor of Thorax, joint Chief Medical Officer of Asthma UK and a former Associate Editor of the American Journal of Respiratory and Critical Care Medicine. He is the author of more than 280 publications including 6 in the New England Journal of Medicine and 11 in the Lancet. He gave the Cournand Lecture at the 2004 European Respiratory Society Meeting, the second UK based researcher to have been given this honour.

**Dr Hilary Pinnock** is a Reader with the University of Edinburgh, and a GP in Whitstable, Kent. Her research interests focus on delivery of care including implementing self-management for asthma, telehealthcare for monitoring respiratory disease, and supportive care for people with severe COPD. She is actively involved with the Primary Care Respiratory Society UK, the International Primary Care Respiratory Group and the European Respiratory Society. She Chairs the Self-Management Evidence Review Group of the BTS/SIGN Asthma Guideline.

**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** is a Consultant in Respiratory and General Medicine at UCLH and a Reader in the Department of Medicine at UCL. Her clinical interest is in interstitial lung disease (ILD), in particular ILD in the context of autoimmune disorders. She is the Clinical Lead for ILD at UCLH and Medical Director of the UCL partners ILD Consortium, and the Medical Director of the Breathing Matters Charity. Dr Porter studied Medicine and Pharmacology at Cambridge University followed by clinical studies at Oxford University Medical School. She went on to train in respiratory and intensive care medicine at the Brompton, St George’s, and St Thomas’ Hospitals, before completing her respiratory training at UCLH. Dr Porter was awarded a PhD for her work in inflammation at UCL as an MRC Clinical Fellow and went on to be awarded a Wellcome Postdoctoral Clinical Fellowship at UCL. Her research is in the area of inflammatory lung disease; she heads the Leukocyte Trafficking Laboratory at UCL in the Centre for Inflammation and Tissue Repair (CITR) and has a translational research interest in novel imaging techniques, biomarkers and therapies in ILD and other inflammatory lung diseases.

**Dr Tim Quinnell** works in the Respiratory Support and Sleep Centre, Papworth Hospital, Cambridge, and is Lead Consultant for the Sleep Laboratory. He specialises in respiratory and non-respiratory sleep disorders, domiciliary NIV and weaning from invasive ventilation. He is Chief Investigator for the NIHR Trial of Mandibular Advancement Devices in Obstructive Sleep Apnoea (TOMADO). He sits on the British Sleep Society Executive Committee.

**Dr Jennifer Quint** is a Senior Lecturer in Epidemiology at the London School of Hygiene and Tropical Medicine and an Honorary Consultant in Thoracic Medicine at University College London Hospitals NHS Trust. Her clinical and research interests focus mainly on COPD and the relationship with cardiovascular disease and exacerbations. She is currently funded on a Medical Research Council Population Health Scientist Fellowship to investigate the causal roles of environmental factors and infections on exacerbations of COPD. As well as her research she teaches and tutors on the MSc Epidemiology course at LSHTM and as part of her clinical commitment is involved in the COPD service both at UCLH and the local Integrated Community Service.
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Dr Najib Rahman, is a Consultant and Senior Lecturer at the University of Oxford and Oxford Centre for Respiratory Medicine, Churchill Hospital, Oxford. Dr Rahman runs the Oxford Pleural Unit, and conducts clinical research in pleural disease at the Oxford Centre for Respiratory Medicine. He directs the Oxford Respiratory Trials Unit. He is currently involved in randomized and observational studies in pleural infection and malignant pleural effusion intervention. He is trained in Thoracoscopy, Thoracic Ultrasound (RCR Level II) and Clinical Trials methodology. He has published in the fields of pleural disease and thoracic ultrasound.

Professor Stephen Renshaw is Professor of Respiratory Medicine in Sheffield, combining clinical work in respiratory medicine with research into the molecular controls of inflammation resolution. Professor Renshaw’s work encompasses work on primary human neutrophils, but increasingly uses the zebrafish to model neutrophil function in vivo. He studied medical sciences at Cambridge before moving to Oxford, where he qualified as a doctor in 1994. After a clinical rotation in Nottingham, Professor Renshaw moved to Sheffield to take up a Wellcome Trust Clinical Training Fellowship, to work on the role of death receptor signalling in the regulation of neutrophil lifespan in inflammation with Professor Moira Whyte. He was awarded his PhD in 2001, and became Clinical Lecturer in Respiratory Medicine. In 2004, he was awarded an MRC Clinician Scientist Fellowship, to develop a zebrafish model of inflammation, and was appointed Honorary Consultant at the same time. He has been able to develop a unique neutrophil-specific transgenic zebrafish which has allowed several novel advances, and has developed the zebrafish as a model for inflammatory diseases. In 2008, he was awarded a Senior Clinical Fellowship to continue these studies. He has a range of unique transgenic models in development, and has performed unbiased genetic and “chemical genetic” screens to help understand inflammation in vivo.

Dr Louise Restrick is an Integrated Respiratory Physician at Whittington Health, North London, a member of IMPRESS and Leads the London Respiratory Network (www.networks.nhs.uk/nhs-networks/london-lungs/).

Dr Elin Roddy is a Consultant Respiratory and General Physician at Shrewsbury and Telford Hospital NHS Trust. As well as being Lead Clinician for Lung Cancer and End of Life Care within her Trust, she also has an interest in early supported discharge for COPD and smoking cessation.

Professor David Rubinsztein is a Wellcome Trust Principal Research Fellow and Professor of Molecular Neurogenetics at the University of Cambridge, where he is Deputy Director of the Cambridge Institute for Medical Research. He was awarded the Graham Bull Prize for Clinical Science by the Royal College of Physicians in 2007. Professor Rubinsztein is a Fellow of the Academy of Medical Sciences and a member of EMBO.

Dr Gary Ruiz BSc FRCP FRCPCH was appointed Consultant Respiratory Paediatrician in 1994 at King’s where he created the paediatric TB clinic and paediatric bronchoscopy and empyema services. He became Head of Paediatric Respiratory Medicine in 2010. He has wide interests in all aspects of respiratory disease in children, but particularly lung infection, including tuberculosis and mycobacterial disease in cystic fibrosis. He has been the BPRS representative on the BTS Tuberculosis SAG since December 2012. He is also a member of the ERS and ECFS and was a Trustee of the BLF.

Dr Silke Ryan, MD PhD graduated in medicine from the University of Jena, Germany in 1998, and received her MD thesis in 1999. In 2003, she entered a three year research fellowship at University College Dublin, Ireland, resulting in the award of her PhD. She completed the Irish Specialist Registrar Training Programme in Internal and Respiratory Medicine in October 2010, received the European Diploma in Respiratory Medicine in 2010 and Membership of the Royal College of Physicians of Ireland in 2003. She is currently a Consultant in Respiratory and Sleep Medicine at St Vincent’s University Hospital in Dublin and since December 2011, she has also been appointed as Research Fellow at University College Dublin.

Dr Ryan has focused her research on molecular responses to intermittent hypoxia (IH) and the importance of these events in the development of cardiovascular complications in obstructive sleep apnea syndrome (OSAS). Her work has significantly advanced our understanding of the role of IH in generating systemic inflammation. Using a translational approach, ranging from in vitro experiments utilizing a cell culture model of IH to carefully defined patient cohort studies, she has demonstrated a preferential activation of pro-inflammatory pathways by IH mediated by the transcription factor nuclear factor kappa B (NF-κB).
over adaptive, hypoxia-inducible factor 1 (HIF-1)-dependent pathways, which contrasts with sustained hypoxia where activation of adaptive and protective pathways predominate. In a well-controlled population of male OSAS patients and matched controls, she identified a strong association between IH severity and circulating NF-κB-dependent genes, namely tumour necrosis factor alpha (TNF-α) and interleukin (IL)-8, which are important in the pathogenesis of atherosclerosis, and also, a significant fall of these levels with continuous positive airway pressure (CPAP) therapy. Furthermore, her work has contributed to our understanding of the signalling mechanisms of IH-induced NF-κB-activation by identifying a key role of the p38 mitogen-activated protein kinase (MAPK) in this process. Dr Ryan has published multiple high impact papers, and her original publication in Circulation (2005) is already recognized as a seminal paper on this topic with more than 200 citations. Dr Ryan has recently been awarded a four year independent research grant from the Health Research Board of Ireland which will allow her to continue her work into the basic mechanisms of cardiovascular disease in OSAS with an emphasis on the impact of intermittent hypoxia on adipose tissue. Dr Ryan states that receiving this award is a tremendous honour and further motivation to continue research in this exciting field. She wishes to thank her mentors and collaborators and she looks forward to presenting her research at future meetings.

**Dr Chris Scotton** is a Senior Lecturer in Lung Pathobiology at the University of Exeter (where he co-ordinates the Respiratory Medicine Group) and an Honorary Senior Research Fellow at UCL. His current research focuses on interstitial lung disease and resolution of injury. Through close links with the clinic and external collaborators, Dr Scotton is investigating novel therapeutic opportunities for ILD. He is also an active member of the British Association for Lung Research, having served on the committee since 2010.

**Professor Suresh Senan** is Professor of Clinical Experimental Radiotherapy at the VU University Medical Center in Amsterdam. He qualified at the National University of Singapore, before training in general internal medicine, and later radiotherapy and oncology at the Beatson Oncology Center, Glasgow. He has been working in The Netherlands since 1994.

**Professor Dave Singh** is a Chair of Clinical Pharmacology and Respiratory Medicine at the University of Manchester. His research interests are the pharmacotherapy of asthma and COPD, including the basic pharmacology and clinical trials of novel drugs. He is a member of the GOLD science committee, and has >100 publications.

**Dr Mark Slade** is Consultant Respiratory Physician and Medical Director at Papworth Hospital NHS Foundation Trust. He has a particular interest in lung cancer and interventional pulmonology. He is Chair of the BTS Lung Cancer and Mesothelioma Specialist Advisory Group, has led a project to improve the diagnostic pathway for lung cancer for the Anglia Cancer Network, and has served on guideline committees for the BTS and the ACCP.

**Sir David Spiegelhalter** FRS OBE is Winton Professor for the Public Understanding of Risk and Professor of Biostatistics at Cambridge University. He leads a small team (UnderstandingUncertainty.org) that attempts to improve the way in which risk and uncertainty are taught and discussed in society. In 2012 he presented the BBC4 documentary ‘Tails you Win: the Science of Chance’, and in 2011 came 7th in an edition of Winter Wipeout.

**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 the association between 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, and an Honorary Doctorate from Grenoble University.

**Dr Patrick J Strollo, Jr, MD** is Professor of Medicine and Clinical and Translational Science at the University of Pittsburgh School of Medicine in the Division of Pulmonary Allergy and Critical Care Medicine. He is the Director of the UPMC Sleep Medicine Centre. His research has involved team science with an emphasis on translational investigations. His work along with his collaborators has focused on three broad areas of investigation: 1) New strategies/tools for the diagnosis of sleep disordered breathing; 2) Management of sleep disordered breathing with positive pressure therapy and other novel treatments and; 3) The impact of sleep disordered breathing on cardiovascular function.

**Professor Samy Suissa**, PhD is Director, Centre of Clinical Epidemiology, Jewish General Hospital, James McGill Professor of Epidemiology and Biostatistics, and
SPEAKERS’ BIOGRAPHICAL DETAILS

Professor Suissa, who heads the Canadian Network for Observational Drug Effect Studies (CNODES), received the Distinguished Investigator Award from the Canadian Institute of Health Research (CIHR). He has conducted epidemiological studies on the effects of various chronic disease medications and authored over 370 peer-reviewed papers. He serves on the editorial boards of various scientific journals including the European Respiratory Journal, Lancet Respiratory Medicine, COPD, and is Section Head Editor for F-1000 Medicine.

Dr Daniel Talmor is Professor of Anaesthesia at Harvard Medical School and interim Chair of the Department of Anesthesia, Critical Care and Pain Medicine at Beth Israel Deaconess Medical Center in Boston. Dr Talmor attends clinically both in the operating room and the surgical ICU. His research group focuses on the early identification, prevention and treatment of critical illness. Among these treatments, he has developed novel methods for delivery of mechanical ventilation using esophageal pressure measurements. This work has been supported by grants from the National Institutes of Health, the Centers for Medicare and Medicaid Services and the Gordon and Betty Moore Foundation.

Dr Ilse Vanhorebeek is an Engineer in Applied Biological Sciences (KU Leuven, 1997) with a PhD degree in Pharmaceutical Sciences (KU Leuven, 2002). In 2003, she joined the Laboratory of Intensive Care Medicine at KU Leuven, where she obtained a Research Professorship in 2009. Her research mainly focuses on the central theme of mitochondrial disturbances and autophagy during critical illness and impact of critical care interventions.

Dr Tom Walker is Senior Lecturer in Ethics and Director of the Centre for Ethics at Queen’s University Belfast. His main research interests are in the ethics of treatment for chronic conditions, and obligations to disclose information. In both cases he has a particular interest in the responsibilities of patients.

Professor Tobias Welte, MD is Professor of Medicine and Department Head, Department of Respiratory Medicine, Medizinische Hochschule, Hannover, Germany. Since 2004, Professor Welte has been Professor of Pulmonary Medicine at Hannover Medical School in Hannover, Germany. Prior to this, he was Head of the Division of Pneumology and Intensive Care at the University of Magdeburg in Magdeburg, Germany. He completed his Fellowship in Pneumology at Medizinische Hochschule in Hannover, Germany, and two residencies at County Hospital in Lehrte, Germany.

Professor Welte is both the President of the German Society of Pneumology (DGP) and the President of the German Sepsis Society. He is also the spokesman of the Inflammation Section of the German Research Council (DFG). He serves on the Board of the German Association of Intensive Care Medicine (DIVI) and is the Chairman of the German Network for Community-acquired Pneumonia (CAPNETZ) Foundation and a board member of the German Centre of Lung Research. Additionally, Professor Welte is the Chief Editor of the European Respiratory Monograph, and member of the Editorial Board of the European Respiratory Journal and of Respiratory Medicine.

Professor Welte’s current interests lie in epidemiology, prevention, diagnosis and management of respiratory infections and sepsis and in pathophysiology and treatment of obstructive airway disease including asthma, COPD, and bronchiectasis. Animal models either of pneumococcal and mycobacterial infections and of asthma and COPS are established in his laboratory. The major focus of basic research is on macrophage trafficking into the lung and activation in the lung and neurogenic inflammation on the one hand, and on the role of proteases, mainly cathepsines for the host immunological response on the other hand. He has had more than 500 peer-reviewed articles published and has written numerous chapters for a wide range of books in the field of pneumology and intensive care medicine.

Dr Sally Wenzel’s career began at the University of Florida Medical School, followed by Internal Medicine studies at Wake Forest University and Pulmonary/Critical Care Fellowship at Virginia Commonwealth University. In 1986, Dr Wenzel took a position at University of Colorado/National Jewish Health, rising to Professor of Medicine with an endowed chair. She served on the Pulmonary—Allergy Advisory Committee to the FDA, was Assembly Chair for the American Thoracic Society Section on Allergy, Immunology and Inflammation, Chairing the ATS International Conference Committee. She received the Elizabeth Rich Award for promoting women in science. Dr Wenzel served as Deputy Editor for the American Journal of Respiratory and Critical Care Medicine and served on the LCMI Study Section for NIH grant reviews.
In 2006, the University of Pittsburgh recruited Dr Wenzel to establish the Asthma Institute to further the understanding of asthma and related airway diseases. She is currently a tenured professor, holding the UPMC endowed Chair in Translational Airway Biology, as well as Director of the Asthma Institute. She leads the Pulmonary, Allergy and Critical Care Medicine Division’s Allergy Programme. The Asthma Institute has a strong growth record for governmental and industry support and maintains active community outreach/educational programs. Dr Wenzel trains and mentors the next generation of scientists in allergy/asthma and delivers state-of-the-art airway disease evaluation and care to both national and international patients utilizing phenotype-targeted, personalized medicine approaches. Dr Wenzel was named Top Doctors in America from 2001 to present and in 2014 she was inducted into the American Association of Physicians.

**Dr Alex West** is a Consultant Chest Physician at Guy’s and St Thomas’ Hospital, London. He has a particular interest in the management of pleural diseases both from an interventional and clinical perspective, and maintains an active research interest in this area also.

**Dr Sophie West** has been the Lead of the Newcastle Regional Sleep Service based at the Freeman Hospital since 2009. She qualified in Leicester, and worked in Leicester, Peterborough, London and Oxford before moving North. Her research interests include OSA, type 2 diabetes and the role of CPAP in treating diabetic retinopathy.

**Dr Eric White** is Associate Professor of Medicine, Pulmonary and Critical Care Medicine, Graduate Programme in Cellular and Molecular Biology at the University of Michigan Medical School and Graduate Programme in Biomedical Sciences. His research focuses on the contribution of extracellular matrix to both fibroblast and epithelial cell behaviors in idiopathic pulmonary fibrosis. He has pioneered methods to decellularize human lung tissue for use in *in vitro* experimentation; his laboratory has made important observations regarding the role of fibronectin in idiopathic pulmonary fibrosis.

**Dr Tom Wilkinson** is Reader in 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 Co-lead of the Southampton COPD Group, Respiratory Lead for the Wessex CLAHRC and his research group focuses on improving understanding of the susceptibility of patients with airways disease to bacterial and viral infection and the development of novel approaches to vaccination and targeted anti-infective therapy.

**Dr Andrew Wilson** is a Clinical Senior Lecturer at Norwich Medical School and an Honorary Consultant Chest Physician at Norfolk and Norwich University Hospital. His research interests include the evaluation of therapeutic interventions by clinical trials and he is the chief investigator for a national study of co-trimoxazole therapy in patients with idiopathic pulmonary fibrosis.

**Professor Douglas Young** is the Fleming Professor of Medical Microbiology at Imperial College London and Head of the Division of Mycobacterial Research at the MRC National Institute for Medical Research. He works on the fundamental biology of mycobacterial infection and on the discovery of vaccines and drugs for improved disease control.
**Actegy Ltd**  
Stand number 40

Actegy Ltd develop and market innovative electrical healthcare products. Products are developed in partnership with leading UK universities and hospitals, with ongoing clinical trials.

**Aerosure Medic:**
A new handheld device designed to reduce breathlessness and improve mucus clearance via High Frequency Airways Oscillation (HFAO). Combines the two well-established techniques of inspiratory muscle training (IMT) and oscillatory positive expiratory pressure (OPEP). Aerosure is electrically driven and is not dependent on pressure generation by user for optimal performance.

**Revitive IX (Circulation Booster):**
A footplate system to deliver neuromuscular electrical stimulation (NMES) to the feet and lower legs. Shown to increase blood flow, reduce oedema and alleviate pain. Over 1 million Revitive’s sold worldwide.

**Tel:** 01344 636 940  
**Email:** info@actegy.com  
**Websites:** www.actegy.co.uk / www.aerosure-medic.com / www.revitive.com

**Actelion Pharmaceuticals Ltd**  
Stand number 45

Actelion Pharmaceuticals Ltd is a biopharmaceutical company focused on the discovery, development and commercialisation of innovative treatments for diseases with significant unmet medical needs and is a leader in the field of Pulmonary Arterial Hypertension (PAH).

For further information please contact Actelion:  
**Tel:** 0208 987 3333  
**Website:** www.actelion.co.uk

**Almirall**  
Stand numbers 16, 17 & 18

Almirall is an international pharmaceutical company based on innovation and committed to health. Headquartered in Barcelona, it researches, develops, manufactures and commercialises its own R&D and licensed drugs with the aim of improving people’s health and wellbeing. Almirall focuses its research resources on respiratory, gastrointestinal, dermatology and pain. Almirall’s products are currently present in over 70 countries in the five continents. It has direct presence in Europe and Mexico through 12 affiliates.

**Tel:** 0207 160 2500  
**Email:** priya.mudgil@almirall.com  
**Website:** www.almirall.com

**Aquilant Endoscopy**  
Stand number 29

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 of Chartered Physiotherapists in Respiratory Care**  
Stand number 60

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.

**Tel:** 0774 011 7902  
**Email:** secretary@acprc.org.uk  
**Website:** www.acprc.org.uk

**Association of Respiratory Nurse Specialists**  
Stand number 59

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 1,150 members across the UK.
EXHIBITORS’ INFORMATION

To find out more about the journal come visit us at stand 55
Tel: 020 7387 4499
Email: support@bmj.com
Website: www.thorax.bmj.com

Boehringer Ingelheim
Stand numbers 33, 34 & 35
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.

Taking social responsibility is an important element of the corporate culture at Boehringer Ingelheim. This includes worldwide involvement in social projects, such as the initiative “Making more Health” and caring for the employees. Respect, equal opportunities and reconciling career and family form the foundation of the mutual co-operation. In everything it does, the company focuses on environmental protection and sustainability.

In 2013, Boehringer Ingelheim achieved net sales of about 14.1 billion Euros. R&D expenditure corresponds to 19.5% of its net sales.
Tel: 01344 424 600
Email: communicationsukireland@boehringer-ingelheim.com
Website: www.boehringer-ingelheim.com

Boston Scientific
Stand number 36
Boston Scientific (NYSE: BSX) is a worldwide developer, manufacturer and marketer of medical devices with approximately 25,000 employees and revenue of $7.806 billion in 2010. For more than 30 years, Boston Scientific has advanced the practice of less-invasive medicine by providing a broad and deep portfolio of innovative products, technologies and services across a wide range of medical specialties. The Company’s products help physicians and other medical professionals improve their patients’ quality of life by providing alternatives to surgery.

For enquiries relating to Bronchial Thermoplasty please call Tom Martin on:
Tel: 07717 516 358
Email: tom.martin@bsci.com
Website: www.btforasthma.com

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
Twitter: @ARNS_UK
You can also find us on Facebook

AstraZeneca Ltd
Stand numbers 21, 22 & 28
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 number 1
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

BMJ Journals
Thorax
Stand number 55
Thorax is one of the world’s leading respiratory medicine journals, publishing clinical and experimental research articles on respiratory medicine, paediatrics, immunology, pharmacology, pathology, and surgery. Published monthly, each issue covers topics such as COPD, asthma, smoking, respiratory infection and lung cancer.
Visit thorax.bmj.com online for free editor’s choice articles, online archive, email alerts and podcasts.
EXHIBITORS’ INFORMATION

British Association for Lung Research  Stand number 62
The BALR has provided a focus for exchange of ideas between all respiratory researchers, basic scientist and clinician 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

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 further information, please visit www.blf.org.uk. 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. Follow us on Twitter at http://twitter.com/lunguk or join us on Facebook at http://www.facebook.com/britishlungfoundation

Website:  www.blf.org.uk

BTS Nurse Advisory Group  Stand number 56
The British Thoracic Society Nurse Advisory Group (BTS NAG) provides nursing expertise to the British Thoracic Society, with the majority of the BTS 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 competencies. 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 56 in the Benjamin Britten Lounge.

Website:  www.brit-thoracic.org.uk

Chiesi Limited  Stand number 2
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  Stand number 15
Respiratory specialists, Clement Clarke International, have a series of innovations to showcase at the BTS Meeting. Among the list; new training tools aimed at pMDI technique including Trainhaler, a new placebo-like pMDI simulator for patient coaching together with Flo-Tone (now on FP10), a flow and co-ordination tool. Also, the In-Check M, for measuring inspiratory flow rate for pMDI education. Other products include the new and improved Able Spacer (now on FP10); a transparent, anti-microbial spacer, which inhibits microbial growth.

Tel:  01279 414 969
Email:  resp@clement-clarke.com
Website:  www.clement-clarke.com

Dolby Vivisol  Stand number 41
Dolby Vivisol supports over 110,000 patients across Europe providing a range of therapies including oxygen therapy, treatment of OSAS and ventilation therapy. Our mission is to allow patients to stay at home by bringing the therapy to them with the same or better level of care than the hospital.

“Working Together to Improve Lives by Inspiring Excellence in Home Healthcare” is at the core of what we do. The company focuses on continually improving its services, aiming to offer the NHS efficient, sustainable solutions.
By bringing our vision to life we seek to help create the most beneficial care environment within the patient’s home, enabling them to follow their prescribed treatment, achieve the best possible outcome and improve their quality of life.

Tel: 0330 123 0305  
Email: enquiries@dolbyvivisol.com  
Website: www.dolbyvivisol.com

**EXHIBITORS’ INFORMATION**

**Education for Health Stand number 63**

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 Stand number 57**

Founded in 1990, the European Respiratory Society (ERS) is a not-for-profit, international medical organisation. It is the largest society in Europe in its field, with more than 10,000 members in over 100 countries.

The ERS aims to alleviate suffering from respiratory disease and to promote lung health through research, clinical education, advocacy and public awareness. The ERS is dedicated to raising awareness of lung health and improving prevention, management and treatment of lung disease.

Tel: +41 21 213 01 01  
Email: info@ersnet.org  
Website: www.ersnet.org

**Forest Laboratories UK Ltd (a subsidiary of Actavis PLC) Stand numbers 31 & 32**

Forest Laboratories UK Ltd, (a subsidiary of Actavis PLC) is committed to the continual educational support of multi-disciplinary healthcare professionals involved in the treatment of cystic fibrosis. Forest has been creating cutting-edge pharmaceutical products for over 70 years. From our facilities and offices across Europe we develop, manufacture and market high-quality prescription and healthcare brands that help people across the world lead healthier, happier lives. As the European arm of US-based Forest Laboratories Inc, we are driven to build on its success, and become one of Europe’s leading pharmaceutical businesses.

Tel: 01322 421 800  
Website: www.frxeurope.eu

**GlaxoSmithKline Stand numbers 4 & 10**

GSK is a UK-based science-led global healthcare company that makes innovative medicines, vaccines and consumer health products, used by millions of people worldwide. In pursuing our mission to eradicate the patient impact of COPD and asthma, we are taking a patient-centred approach to the development of medicines and devices. GSK has been investing more in respiratory research than any other healthcare company over the past 40 years. Last year GSK announced support for the AllTrials campaign, becoming the first pharmaceutical company to commit to publishing detailed clinical study reports for all our medicines. For further company information visit:

Website: www.gsk.com

**Hitachi Medical Systems | PENTAX Medical for Endobronchial Ultrasound Technology Stand number 8**

PENTAX Medical and Hitachi Medical Systems profile their collaborative partnership at BTS 2014 showcasing innovative high resolution ultrasound with high definition video endoscopy imaging, together delivering clinical solutions and driving quality patient care. Forming one of the world’s most trusted white light endoscopy and EBUS/EUS alliances, their combined innovation ensures diagnostic accuracy and safety for complete mediastinal staging and clinical diagnosis.

PENTAX Medical  
Tel: 01753 792 733  
Website: www.pentaxmedical.co.uk  
Hitachi Medical Systems UK Ltd  
Tel: 0844 800 4294  
Website: www.hitachi-medical-systems.co.uk

**InterMune Stand numbers 23-26**

InterMune is focused on therapies for the treatment of idiopathic pulmonary fibrosis (IPF), a progressive and fatal lung disease. Pirfenidone, the only medicine approved for IPF anywhere in the world, is approved for marketing by InterMune in the EU and Canada.
EXHIBITORS’ INFORMATION

Tel: 0203 744 9900
Email: med-info@intermune.co.uk
Website: www.intermune.co.uk

**Medela**  Stand number 37
Over the past 50 years, Medela has developed from a small family owned company in Switzerland to a global producer of innovative Medical Vacuum Technology. Throughout our company history, we have questioned conventional solutions in order to manufacture Swiss quality products that are based on sound and thorough research. In close collaboration with medical experts, we strive to set new standards in thoracic drainage therapy. Our aim is to provide advanced treatment with easy to use systems that improve and simplify patient management whilst being cost efficient.
Tel: 0161 776 0400
Email: info@medela.co.uk
Website: www.medela.co.uk

**Napp Respiratory**  Stand number 11
Napp Pharmaceuticals Limited is a UK company, providing medicines in the fields of respiratory care, pain management and oncology. With a strong heritage in delivering products that make a positive difference to patients’ lives, Napp is committed to becoming a long-term partner to the NHS, offering value through the medicines and services we provide. The Napp Respiratory franchise supports a wide range of initiatives, delivering real world evidence and high quality educational services that are aligned to the evolving needs of the NHS commissioning and provider environments.
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 51
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. We provide physicians in 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, we advise and work 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
Twitter: #COPDaudit

**Novartis**  Stand number 9
Novartis, created through the merger of Ciba–Geigy and Sandoz in 1996, is one of the largest and most widely respected healthcare companies in the world. Headquartered in Basel, Switzerland, Novartis is a world leader in the research and development of products that protect and improve health and well-being. Novartis employs over 135,000 people worldwide in 140 countries. In 2013, Novartis medicines and vaccines were used to treat and protect more than 1.2 billion people globally.
Tel: 01276 692 255
Website: www.novartis.co.uk

**Olympus**  Stand numbers 6 & 7
Olympus is proud to be celebrating the 10th Anniversary of EBUS-TBNA in the UK. Visit our stand to celebrate with us and collect a free copy of Bronchoscopy Today featuring our exclusive “10 Years of EBUS” interviews.
Since Olympus was founded in Japan in 1919, it has become a leading manufacturer of innovative optical and digital equipment for the healthcare sector. For over 90 years we have led the way in designing endoscopy and microscopy products, medical and industrial equipment, cameras and voice recorders.
At Olympus we try to make the world a little better every day, and a healthier, safer and more fulfilling place for us all to live in. We are committed to developing new technologies, products and services that comply...
EXHIBITORS’ INFORMATION

Pharmaxis Stand number 44
“Focused innovation in respiratory medicine”
Pharmaxis is a specialist pharmaceutical company committed to the research, development and commercialisation of products that address chronic respiratory and autoimmune diseases.
Our R&D activity has resulted in the successful development of mannitol as a diagnostic test for bronchial hyperresponsiveness (Aridol® or Osmohale®), and more recently as an osmotic mucolytic treatment for Cystic Fibrosis (Bronchitol®).
There is on-going research into further applications for mannitol.
Tel: 01628 902 121
Email: eu.info@pharmaxis.com
Website: www.pharmaxis.com.au

PneumRx Stand number 5
PneumRx develops, manufactures, and sells innovative medical devices to treat pulmonary disease. The RePneu® Endobronchial Coil is a minimally invasive implantable device for treatment of emphysema.
RePneu is CE Marked and available in Europe. RePneu is approved for investigational use only in US.
Tel: + 31 73 30 30 599
Email: Info-EU@pneumrx.com
Website: www.pneumrx.com

Pulmonx Stand number 12
Pulmonx, based in Neuchâtel, Switzerland and Redwood City, California, is focused on developing and marketing minimally-invasive medical devices and technologies for the diagnosis and treatment of pulmonary disorders.
Pulmonx takes a unique approach to treating emphysema by providing an assessment tool to plan and optimize EBV treatment. The Chartis Pulmonary Assessment System is composed of a balloon catheter and a simple, easy-to-use console which characterises airflow within lung regions. The goal is to understand the patient’s specific lung anatomy in order to plan for optimal treatment.
The company has CE mark for the Zephyr EBV and the Chartis System, and Pulmonx products are sold in Europe, Asia, and in other countries worldwide. The company does not yet market or sell its products in the United States.
Tel: +41 32 475 2070
Email: info@pulmonx.com
Website: www.pulmonx.com

Otsuka Stand number 13
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Website: www.pulmonx.com

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Mobile: 07944 623 237  
Email: info@cegla.com or simon.williamson@cegla-ltd.com  
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Early career investigator symposium

T1 ASPIRIN REDUCES PULMONARY INFLAMMATION IN AN INHALED LIPOPOLYSACCHARIDE MODEL OF ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS) IN HEALTHY VOLUNTEERS AND IN A HUMAN EX VIVO LUNG PERFUSION MODEL OF ARDS

UH Imran Hamid, JC Corlton, SP Spence, AB Boyle, MF Fitzgerald, MS Shyamsundar, AK Krasnodembskaya, AK Kissenpfennig, RV Verghis, CS Scott, DFM McAuley, CO O’Kane. Queens University of Belfast, Belfast, UK

10.1136/thoraxjnl-2014-206260.1

Introduction Platelet activation may play a role in the pathogenesis of ARDS. Animal studies have shown that aspirin therapy reduces pulmonary oedema and development of lung injury. Our recent observational study has shown patients with ARDS on aspirin had a reduced risk of death.

Objective To test the hypothesis that aspirin reduces pulmonary inflammation in clinically relevant models of ARDS induced by inhaled lipopolysaccharide (LPS).

Methods Healthy subjects were enrolled in a double-blind, placebo-controlled, allocation concealed study and were randomised to receive aspirin 75 mg or aspirin 1200 mg or placebo (1:1:1) for seven days prior to LPS inhalation. Measurements were performed in bronchoalveolar lavage (BAL) fluid obtained at 6 h after inhaling 50 micrograms of LPS. Parallel experiments were run in an ex vivo lung perfusion model (EVLP) using human lungs to determine the effects of aspirin on inflammatory cytokine production and BAL neutrophilia in response to intra-bronchial administration of LPS (6 mg).

Results 33 healthy volunteers were enrolled. There was no significant difference between aspirin 75 mg and aspirin 1200 mg. Data for both aspirin groups were combined as per the a priori analysis plan. Aspirin pre-treatment reduced LPS-induced BAL neutrophilia (Figure 1a), MMP-9 (33 ng/ml vs 48 ng/ml, p = 0.03), the neutrophil-specific protease MMP-8 (3 ng/ml vs 6 ng/ml, p = 0.03) and the pro-inflammatory cytokine TNF-α (80 pg/ml vs 106 pg/ml, p = 0.02). There was also a non-significant trend towards reduction in a range of inflammatory cytokines (IL-1β, IL-8 and IL-6).

Pre-treatment with aspirin in the EVLP model also showed a similar reduction in BAL neutrophilia (Figure 1b), along with a trend towards reduction in pro-inflammatory cytokines (IL-8, IL-6, TNF-α, MCP-1).

Conclusion This is the first data to find that aspirin can reduce neutrophilic inflammation in both these models of ARDS. Further clinical studies are planned to assess the role of aspirin in ARDS.

REFERENCES

Abstract T1 Figure 1 Aspirin reduces BAL neutrophilia in models of ARDS

T2 VITAMIN D ENHANCES BRONCHIAL EPITHELIAL CELL ANTIOXIDANT RESPONSES AND REDUCES THEIR PRO-INFLAMMATORY CYTOKINE RESPONSE TO STIMULATION BY URBAN PARTICULATE MATTER

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10.1136/thoraxjnl-2014-206260.2

Background Particulate matter (PM) air pollution and vitamin D deficiency are environmental factors associated with asthma exacerbations and severe asthma. PM stimulates cellular inflammatory pathways through oxidative stress and vitamin D has been shown in other organ systems to protect against oxidative stress. We therefore investigated whether vitamin D might protect against PM-induced pro-inflammatory responses.

Methods Primary human bronchial epithelial cells (HBECs) were cultured with ambient PM and/or physiological concentrations of vitamin D. Production of pro-inflammatory cytokines was measured by multiplex bead array, gene transcription by microarray and oxidative stress with appropriate assays.

Results Addition of vitamin D significantly decreed production of IL-6 by PM-stimulated HBECs (p = 0.011), however, the reduction was greater in HBECs from healthy (n = 8) than from asthmatic (n = 7) donors (48.7% vs 28.0% reduction, p = 0.048).

Gene transcription microarray identified a subset of pro-inflammatory cytokine genes all down-regulated by vitamin D including IL6, IL24, CXCL10 and CCL20. Microarray also identified effects of vitamin D on antioxidant genes including G6PD (3.1 fold-increase with 1,25(OH)D3, p < 0.001). G6PD encodes glucose-6 phosphate dehydrogenase, which is vital for production of reducing equivalents for antioxidant responses.

Vitamin D significantly increased the cellular ratio of reduced to oxidised glutathione (1.6 fold-increase with 25(OH)D3, p = 0.042), enhancing the ability of cellular antioxidant pathways to protectively respond to oxidative stress. Furthermore, addition of vitamin D reduced levels of PM-stimulated 8-isoprostane (19.8% reduction, p = 0.045), a marker of oxidative stress damage. Inhibition of G6PD reduced the beneficial effect of vitamin D on PM-stimulated HBEC responses.

Conclusion Vitamin D beneficially modulates the response of human bronchial epithelial cells to pathological stimulation by PM, in part through enhancing antioxidant pathway responses. A reduction in PM-stimulated IL-6 is likely important given the association between PM, systemic inflammation and an IL-6 dependent coagulopathy in animal models. Furthermore, many of the vitamin D regulated mediators in the array have profound actions on the adaptive immune system. However, our research has also revealed the novel finding that cells from healthy and asthmatic individuals may respond differently to vitamin D.

T3 THE EFFECT OF ELECTRONIC CIGARETTE EXPOSURE ON INNATE IMMUNE CELLS

AJ Hight, NW Rattay, JA Dewhurst, D Singh. University of Manchester, Manchester, UK

10.1136/thoraxjnl-2014-206260.3

Introduction Are electronic cigarettes (e-cigs) safe? The long-term effects of e-cigs are unknown. E-cigs contain a variety of substances that may be harmful to the lungs. We hypothesised that e-cigs have the potential to cause pulmonary inflammation.
We have investigated the effects of e-cigs on human innate immune cells in vitro.

**Methods** Blood neutrophils from six healthy non-smokers were exposed to e-cig vapour extract (ECVE) for 6 hr. MMP-9 and CXCL8 release were measured by ELISA and MMP-9 activity was measured by zymography. p38 MAPK activation was also measured, along with neutrophil shape change and CD11b and CD66b expression by flow cytometry. Finally, we measured CXCL8 release from alveolar macrophages isolated from resected lung tissue from three ex-tobacco smokers exposed to ECVE for 24 hr.

**Results** Exposure of neutrophils to ECVE increased MMP-9 and CXCL8 release with the maximal effect observed at an optical density (OD) of 0.003 (Table 1). This was observed along with an increase in MMP-9 gelatinase activity and increased p38 MAPK activation.

Furthermore, neutrophil shape change, and dual CD11b and CD66b expression increased in response to ECVE treatment compared to untreated cells.

Following a similar trend, 0.003 (OD) ECVE caused an increase in CXCL8 release from alveolar macrophages.

**Discussion** We have shown that e-cig exposure causes an inflammatory response from neutrophils and macrophages. The effects discussed here are similar to those caused by tobacco cigarettes. Based on these findings, the use of e-cigs may pose a risk to public health.
Introduction and objectives Pulmonary arterial hypertension (PAH) is a fatal lung disease characterised by progressive pulmonary vascular remodelling, a key component of which is the proliferation and migration of pulmonary arterial smooth muscle cells (PA-SMCs). Although current therapies are good at alleviating symptoms, they do not reverse the underlying pulmonary vascular remodelling. We have previously demonstrated that the secreted glycoprotein, osteoprotegerin (OPG, TNFRSF11B), is elevated within pulmonary vascular lesions and serum from idiopathic PAH (IPAH) patients and induces PA-SMC proliferation and migration in vitro. Furthermore, genetic deletion or antibody blockade of OPG can prevent and reverse disease in preclinical animal models. However, how OPG signals to mediate PA-SMC phenotype remains unclear. We therefore aimed to characterise the OPG signalling cascade in PA-SMCs, and identify the receptor through which this is mediated.

Methods PA-SMCs were stimulated with 0.2% FCS and OPG (50 ng/ml) for 10 and 60 min. Phosphorylation targets were identified by Kinex antibody microarray (Kinexus, Canada). An RNA expression microarray (Agilent) was performed on PA-SMCs following 6-hour OPG stimulation. OPG binding partners were identified following reverse transfection of HEK293 cells with 2054 human membrane proteins (Retrogenix, Sheffield, UK). Interactions were confirmed in PA-SMCs by co-immunoprecipitation. PA-SMCs were pre-treated with Fas neutralising antibody (1500 ng/ml), TRAIL antibody (1500 ng/ml) or both antibodies, 30 min before OPG stimulation. Proliferation was assessed after 72 h.

Results OPG induced significant activation of CDK4 and CDK5, HSP27 and ERK1/2, and significant decrease in phospho-mTOR. OPG significantly altered the expression of 57 PAH-associated genes, including TRAIL. Four novel OPG interactions with IL1RACP, Fas, TMPRSS11D and GAP43 were identified and we confirmed OPG interaction with IL1RACP and Fas in PA-SMC. Fas RNA expression was elevated in IPAH PA-SMCs and protein expression was elevated in the right ventricle and pulmonary artery from IPAH patients. Fas blockade reduced OPG-induced proliferation by ~40%, which was further reduced by simultaneous TRAIL blockade. Fas blockade also prevented OPG-induced PDGFRα and TNC RNA expression.

Conclusions These studies begin to reveal the intracellular signalling mechanisms and receptor through which OPG induces PA-SMC proliferation, further highlighting the therapeutic potential of targeting OPG in PAH.

**IMPACT OF ENVIRONMENTAL DIFFERENCES IN THE PREVALENCE OF AIRWAY DYSFUNCTION IN ELITE ATHLETES: GB BOXING VS. GB SWIMMING**


Objectives Exercising in a provocative environment (e.g. indoor swimming pool) at sustained high minute ventilation rates may increase the prevalence of airway dysfunction in athletic populations. The purpose of the study was to evaluate the impact of environmental differences in the prevalence of airway dysfunction in two cohorts of elite GB athletes.

Methods Airway dysfunction was evaluated in the GB boxing (n = 39, Mean (SD) age: 22.0 (3.2) yrs.) and swimming squads (n = 33, Mean (SD) age: 21.0 (3.0) yrs.). All participants completed a Eucapnic Voluntary Hyperpnoea (EVH) challenge test, an indirect bronchoprovocation test, to characterise airway dysfunction (defined as abnormal if >10% fall in FEV1, post-challenge). Fraction of exhaled Nitric Oxide (FeNO) was measured and participants completed a symptom and medication questionnaire.

Results The prevalence of airway dysfunction was greater in elite swimmers (70%) than boxers (8%) (p < 0.001) (Figure 1). The EVH assessment process revealed missed and incorrect diagnosis of airway dysfunction; specifically 63% (17 of 26) of those with airway dysfunction had no prior diagnosis of asthma or exercise induced bronchoconstriction. Moreover, a prior diagnosis of asthma was not supported by testing in 9% (4 of 46) of the athletes. These athletes were prescribed one or a combination of short-acting β2-agonists, long-acting β2-agonists and inhaled corticosteroids. Neither symptoms nor baseline lung function were predictive of a positive EVH-challenge in swimmers. No correlation between change in lung function or airway dysfunction and FeNO value.

Conclusions The prevalence of airway dysfunction was nine fold greater in elite swimmers when compared with boxers. This finding emphasises the high proportion of EVH-positive elite swimmers and the importance of strategies needed to ensure their respiratory health is optimised. These results also suggest that airway dysfunction is not only related to intensity and frequency of exertional hyperpnoea but also environmental conditions.
Occupational lung disease

A NEW, EFFICIENT WEB-BASED TOOL TO COLLECT AND CODE LIFETIME JOB HISTORIES IN LARGE POPULATION-BASED STUDIES: THE COPD PROJECT IN THE UK BIOBANK COHORT

1S De Matteis, 1D Janis, 1M Wheatley, 1H Ashar, 2A Young, 2H Young, 1L Ruchton, 3P Cullinan. 1Imperial College London, London, London, UK; 2Oxford University, Oxford, UK

Introduction and objectives The manual collection and coding of job histories is the standard method for assessing occupational exposure, but may be infeasible for large population-based studies such as the UK Biobank cohort.

Our aim was to develop a new web-based tool to automatically collect and code individual lifetime job histories in the UK Biobank cohort for investigating the causes and burden of work-related COPD in the UK.

Methods UK Biobank is a population-based cohort of 502,682 subjects, aged 40–69 years, recruited in 2006–2010. Baseline spirometry data, current employment and smoking histories were collected. We developed a job questionnaire based on the hierarchical structure of the standard occupational classification (SOC) 2000 to allow participants to automatically self-collect and code their lifetime job histories. The web-based prototype (www.imperial.ac.uk/biobank/questionnaire) was pre-piloted in May–August 2013 among key job sectors using snowball sampling together with a feedback survey.

Results 171 subjects participated in both the pre-piloting and feedback survey. 91% completed the questionnaire in <20 min; 85% considered the instructions clear, and 80% found their job categories/titles easy. Overall, 96% judged the questionnaire to be clear and easy. A revised questionnaire has now been designed and will be accessible from different media including PCs/laptops, tablets and smart phones to encourage high response. A demonstration version will be made available to conference participants.

Conclusions Our web-based job questionnaire is an efficient new standard tool for collecting and automatically coding lifetime job histories in large population-based studies and is adaptable for use in many occupational and environmental health research projects.

DEVELOPMENT OF A JOB EXPOSURE MATRIX FOR SOC 2000 LISTINGS TO IDENTIFY OCCUPATIONAL CAUSES OF COPD

1S Sadhra, 1D Fishwick, 1OP Kurmi, 1H Chambers, 1KH Lam, 1S Hutchings, 1D Janis, 3S De Matteis, 1L Ruchton, 1JG Ayres, 3P Cullinan. 1University of Birmingham, Birmingham, UK; 2Health and Safety Laboratory, Buxton, UK; 3University of Oxford, Oxford, UK; 4Imperial College London, London, UK

Introduction Occupational exposures are associated with the presence of a significant proportion of chronic obstructive pulmonary disease (COPD). The majority of the previous population studies have relied on self-reported exposures to vapours, gases, dusts and fumes (VGDF), which could lead to substantial misclassification. We aim to develop an occupational inhalation job exposure matrix (JEM) developed for use specifically with SOC 2000 occupational codes covering a wider range of occupational airborne pollutant types.

Methods The development of airborne chemical exposure JEM (ACE-JEM) involved a four-stage approach; first, exposure (yes/no) to each of the six different airborne pollutants types (vapours, gases, dusts, fumes, fibres and mists; VGDFMF) was assessed for each of the 353 SOC codes, then three levels of exposure estimates (low, medium and high) (L-JEM1) and four levels of proportion exposed (0–4%, 5–9%, 20–49% and >=50%) (P-JEM2) were assigned to the exposed codes and for each pollutant type. The two P and L JEMs were then combined to produce the final ACE-JEM. The estimated exposure of the 6 pollutant types was expanded to include biological dusts, mineral dusts, metals, diesel fumes and ashamgers.

Results For L-JEM1 186 (53%) of the codes were assigned as exposed to at least one type of VGDFMF. The most common exposure was dust (40% of all SOC codes) followed by fumes (26%). Over 68% of all codes were assigned as not being exposed to fibres, gases or mists. The pollutant with the highest proportion in the high exposure group was dusts (13%), and 33% of the codes were assigned as exposed to ashamgers. Overall, 53% of the codes were assigned as exposed to CGDF, with 22% assigned as having medium or high exposure to VGDF.

Discussion An expert assessment derived JEM has been developed, using a strict set of a priori defined rules. This JEM will assist attribution of possible harmful workplace exposures in future epidemiological studies. The ACE-JEM could also be applied to studies to assess risks of other respiratory diseases, including asthma and extrinsic allergic alveolitis.
**Abstract S3 Figure 1**

**Conclusions** New antifibrotic treatments for IPF throw into sharp focus the question of whether or not a proportion of IPF is due to occult asbestos exposure; patients known to have asbestos exposure are currently not considered to be candidates for antifibrotic treatments. Our data are consistent with a proportion of IPF being attributable to asbestos exposure but are not conclusive and further research is needed.

**Background** Previous studies from a number of countries have demonstrated that the rising mortality due to mesothelioma and asbestosis can be predicted from their historic asbestos usage. Mortality due to idiopathic pulmonary fibrosis (IPF) is also rising in the UK, without any identified explanation. This analysis compared annual male and female mortality due to IPF, asbestosis and mesothelioma, and examined the relationship between mortality and national asbestos import data.

**Methods** Mortality data for IPF and asbestosis in England and Wales were available from the Office for National Statistics (ONS). Data for mesothelioma deaths in England and Wales and historic UK asbestos import data were available from the Health and Safety Executive (HSE). The numbers of annual deaths due to each condition were plotted separately by gender, against UK asbestos import data, 48 years earlier. Pearson correlation co-efficients were then calculated.

**Results** Correlation co-efficients for each condition are shown in Table 1. The annual number of deaths due to mesothelioma and IPF were significantly correlated with historical asbestos imports for both genders. For asbestosis mortality, a similar relationship was found for male but not female deaths.

**Conclusion** The strength of the association between IPF and historical asbestos imports was similar to that seen for mesothelioma mortality. This finding suggests that the role of occupational and environmental asbestos exposure in the aetiology of IPF requires further consideration.

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**Abstract S4 Table 1** Correlation co-efficients for historic national asbestos import data, plotted against annual mortality due to mesothelioma, asbestosis, and idiopathic pulmonary fibrosis (IPF)

<table>
<thead>
<tr>
<th></th>
<th>Mesothelioma</th>
<th>Asbestosis</th>
<th>IPF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>0.96 (p &lt; 0.001)</td>
<td>0.87 (p &lt; 0.001)</td>
<td>0.96 (p &lt; 0.001)</td>
</tr>
<tr>
<td>Female</td>
<td>0.94 (p &lt; 0.001)</td>
<td>-0.15 (p = 0.32)</td>
<td>0.97 (p &lt; 0.001)</td>
</tr>
</tbody>
</table>

**Abstract S5 Table 1** Sensitisation to ‘improver mix’ enzyme in bakers stratified by sensitisation to either flour and/or alpha amylase

<table>
<thead>
<tr>
<th></th>
<th>Quantity of enzyme used in ‘improver mix’</th>
<th>Sensitisation to ‘improver mix’ enzyme</th>
<th>Bakers co-sensitised to flour and/or alpha amylase</th>
<th>Bakers not-sensitised to flour and/or alpha amylase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improver enzyme used in bakery</td>
<td>ppm</td>
<td>All bakers</td>
<td>Bakers</td>
<td>Bakers</td>
</tr>
<tr>
<td>Maltogenic amylase</td>
<td>40-50</td>
<td>5%</td>
<td>12/260</td>
<td>10/84</td>
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<tr>
<td>Fungal Xylanase</td>
<td>20</td>
<td>15%</td>
<td>11/119</td>
<td>8/26</td>
</tr>
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<td>Cellulase</td>
<td>25</td>
<td>9%</td>
<td>11/119</td>
<td>8/26</td>
</tr>
<tr>
<td>Lipase</td>
<td>20</td>
<td>10%</td>
<td>11/119</td>
<td>8/26</td>
</tr>
<tr>
<td>Bacterial Xylanase</td>
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<td>Fungal α-amylase</td>
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<tr>
<td>Glucose Oxidase</td>
<td>5–10</td>
<td>11%</td>
<td>11/119</td>
<td>8/26</td>
</tr>
</tbody>
</table>
Methods We assayed specific IgE sensitisation in 300 bakers employed by one of two large UK supermarkets who, at routine health surveillance, had declared work related upper or lower respiratory symptoms. Sensitisation was determined using radioallergosorbent assay to enzymes contained within the specific ‘improver’ mix used by the employing supermarket; each mix contained eight individual enzymes which were not necessarily common to both supermarkets.

Results Bakers were sensitised to each of the individual ‘improver’ enzymes with a prevalence ranging from 1.8% to 23.9%; the frequency did not appear to be associated with the quantity of enzyme incorporated in the mix. Sensitisation was far more likely if a baker was sensitised also to either flour or fungal alpha amylase; but a small proportion (5%) of bakers who were sensitised to neither flour nor fungal alpha amylase had specific IgE to one or more of the ‘improver mix’ enzymes.

Conclusions Bakers working in UK supermarket bakeries can become sensitised to improver enzymes other than fungal alpha amylase. The clinical significance of this remains unclear but the message is important both in the diagnosis of bakers with work-related respiratory symptoms and in any programme of immunological surveillance.

Abstract S6 Table 1 Baseline characteristics SPIRAL study participants to date and preliminary results

<table>
<thead>
<tr>
<th>Sex</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>53 (59%)</td>
</tr>
<tr>
<td>Female</td>
<td>83 (61%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Job Title</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scientist</td>
<td>81 (60%)</td>
</tr>
<tr>
<td>Animal Technicians</td>
<td>40 (29%)</td>
</tr>
<tr>
<td>Other</td>
<td>15 (10%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Type of facility</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVC only</td>
<td>29 (12%)</td>
</tr>
<tr>
<td>Open cages</td>
<td>84 (37%)</td>
</tr>
<tr>
<td>Mixed facilities (IVC and open cages)</td>
<td>57 (43%)</td>
</tr>
<tr>
<td>Participant unsure</td>
<td>6 (4%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Reported work related symptoms</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic rhinitis</td>
<td>21 (10%)</td>
</tr>
<tr>
<td>Allergic conjunctivitis</td>
<td>16 (10%)</td>
</tr>
<tr>
<td>Asthma</td>
<td>11 (6%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sensitisation to mouse epithelium on skin-prick testing</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>15 (11%)</td>
</tr>
<tr>
<td>Negative</td>
<td>122 (89%)</td>
</tr>
</tbody>
</table>

*percentages may not equal 100 due to rounding
lung function (available in 9 patients) demonstrated a mean improvement in % predicted FVC and FEV1 of +3.3 (p = 0.009) and +3.7 (p = 0.006), respectively, following cessation of nitrofurantoin. 44% of patients were also prescribed oral prednisolone. Comparing these two groups (cessation + steroid vs cessation alone) showed no significant difference in % predicted FVC (p = 0.47) or FEV1 (p = 0.87), gender, age or imaging at diagnosis. Following treatment, there was no significant difference in % predicted FVC (p = 0.87) or FEV1 (p = 0.93) between groups. The mean % predicted FVC improvement was 31% in the steroid group and 34% in the cessation only group, showing no significant difference between groups (p = 0.86).

Conclusions With increased nitrofurantoin prescribing, the prevalence of NL will continue to rise throughout the UK and heightened awareness of the condition will be required in primary and secondary care. Our data demonstrates that significant improvements in lung function occur on cessation of nitrofurantoin and suggests no benefit is conferred by additional use of corticosteroid in patients with chronic NL.

REFERENCES

S8 RITUXIMAB THERAPY FOR REFRACTORY MYOSITIS RELATED INTERSTITIAL LUNG DISEASE UNRESPONSIVE TO CONVENTIONAL IMMUNOSUPPRESSION: THE BRISTOL INTERSTITIAL LUNG DISEASE SERVICE EXPERIENCE
C Sharp, N Dodds, A Edey, H Adamali, H Gunawardena, A Millar. North Bristol NHS Trust, Bristol, UK
10.1136/thoraxjnl-2014-206260.14

Introduction Rituximab is a chimeric monoclonal antibody against CD20 that depletes B-lymphocytes. There is increasing evidence for its use in Scleroderma ILD.1 Recently it has been reported as rescue therapy in patients with connective tissue disease related severe fibrotic lung disease who have failed conventional immunosuppression.2 It remains unclear which patients are most likely to benefit from this potent immunosuppressive treatment. We review here the experience of the Bristol Interstitial Lung Disease service in use of Rituximab in a subset of patients with myositis (Anti-synthetase syndrome and Dermatomyositis).

Methods We retrospectively reviewed the case notes of 10 patients with severe and progressive ILD despite immunosuppression with Cyclophosphamide and Mycophenolate Mofetil, who had received salvage treatment with Rituximab. Serial pulmonary function tests, 6 min walk distances and HRCT appearances (as assessed by a Thoracic radiologist) were compared in the year before and after Rixtuximab therapy. Changes in physiological variables compared to nadir at treatment were compared with paired-samples T-Test.

Results The average age of the patients was 49.8 (range 26.9–72.99), with 7/10 female. 4 patients had dermatomyositis, while 6 had Anti-Synthetase Syndrome (2 Anti-Jo1, 2 Anti-PL12, 1 Anti-PL7, 1 Anti-PM-Scl). There were complete lung function data available for 9 patients and 6MWD data for 6 patients.

CT appearances stabilised in all 9 patients with follow-up scans available, with significant improvement in 2 (1 after a second pulse of Rituximab).

FVC improved after treatment by an average of 9.2% (p = 0.023, 95% CI 1.67–16.76), with TLCO improving by an average of 6.1% (NS). Figure shows % change in FVC and TLCO leading to and after therapy, 6MWD remained stable.

There were no adverse events reported.

Summary Our experience adds to the growing evidence to support the use of Rituximab in severe CTD-ILD, and suggests that a subset of patients with myositis may show good therapeutic response.

REFERENCES
1 Daoussis et al. Rheumatology. 2010;49;271–80
2 Keir et al. Respirology. 2013;19;333–9

S9 ACUTE INFLAMMATORY PRESENTATION ASSOCIATES WITH SURVIVAL IN INTERSTITIAL LUNG DISEASE AND EXTRACORPOREAL MEMBRANE OXYGENATION-REQUIRING SEVERE RESPIRATORY FAILURE: A SINGLE CENTRE CASE SERIES
L Starsmore, B Lams, S Agarwal, A Nair, R Preston, N Barrett, G Glover, N Ioannou, C Langrish, D Wyncoll, CIS Meadows. Guy’s and St Thomas’ NHS Foundation Trust, London, UK
10.1136/thoraxjnl-2014-206260.15

Introduction Patients with interstitial lung disease (ILD) and severe respiratory failure (SRF) requiring mechanical ventilation are widely perceived to have poor outcomes. A therapeutic strategy incorporating extracorporeal membrane oxygenation (ECMO) improves all cause SRF survival. There exist no data on the use of ECMO in severe ILD. ECMO may offer lung rest, reduce the inflammatory burden associated with mechanical ventilation and allow time for effective immunosuppression. We hypothesised that the use of ECMO and early immunosuppression increases survival in patients with ILD in whom mechanical ventilation was failing.

Methods Retrospective interrogation of a single centre ECMO database for patients with ILD between 2011 and 2014. Variables collected included diagnosis; immunosuppression regimen; duration of symptoms prior to ECMO initiation; serum biochemistry; clinical severity score (SOFA) and survival to ECMO decannulation, ICU discharge and at 6 months. ECMO centre admission computed tomography (CT) thorax scans were independently analysed for pattern and degree of abnormality by two radiologists. Variables were compared between responders (those who survived without lung transplant) and non responders (composite group of those who died and one patient who survived with lung transplantation). Two-tailed t-tests were used for all comparisons.

Results 12 patients with an ILD diagnosis who received ECMO were identified. ECMO and ICU survival was 58.3%, The group of responders had a shorter duration of symptoms prior to ECMO (p = 0.04), a higher CRP (p = 0.046), a higher SOFA
score \( p = 0.01 \) and a lower preponderance of diffuse alveolar damage (DAD) on CT \( p = 0.19 \) although there was no difference in overall extent of CT abnormality. (Table 1).

**Conclusions** The use of ECMO and early immunosuppression led to a 58.3% survival in a group of ILD associated SRF who would otherwise have been highly likely to die. The responders were characterised by a more acute and more inflammatory presentation. We suggest that ECMO and immunosuppression should be considered in patients with ILD and SRF who are failing mechanical ventilation.

**References**
1. Raghu G et al
2. Kausar et al

**S11 PIRFENIDONE POST-AUTHORISATION SAFETY REGISTRY (PASSPORT)—INTERIM ANALYSIS OF IPF TREATMENT**

Introduction Pirfenidone (Esbriet®) is approved for mild/moderate idiopathic pulmonary fibrosis (IPF). PASSPORT is a post-authorisation safety registry required by the European Medicine Agency.

**Objective** To present interim data from PASSPORT.
Method Up to 140 EU sites will enrol 1000 patients. Safety data are recorded at routine clinic visits for 2 years. Adverse drug reactions (ADR: a noxious, unintended drug response at therapeutic doses) and serious ADRs (SADR: ADrs that are life-threatening; cause death, disability, congenital anomaly; require hospitalisation or an intervention to prevent permanent impairment) are collected.

Results Data from 530 patients enrolled by 68 sites in 7 countries are included. Age was 69 ± 8.8 years (mean ± SD); IPF diagnosis duration was 1.8 ± 3.51 years; 81% were men. Median time in study was 5.5 months; total exposure was 284 person-years.

Of 311 patients with ADRs, 85 discontinued due to ADR and 41 discontinued for other reasons. Approximately 1/3 of patients with ADRs had their dose adjusted.

For patients who experienced an ADR:

- 55% of patients without a dose adjustment were able to continue treatment, while 69% of those with a dose adjustment were able to continue treatment.
- 20% discontinued due to the ADR after having a dose adjustment, but 31% discontinued due to the ADR without a dose adjustment.

When ADRs were managed by dose adjustment, dose adjustment was associated with continuing treatment.

Conclusion PASSPORT ADRs are comparable to those in clinical trials of pirfenidone in IPF. No new safety issues emerged. Dose adjustment may influence long-term tolerability of pirfenidone.
knock on effects on antibiotic use and length of hospital stay, ways of preventing HAP would be of potential importance to health services.

**S14** TIME TRENDS AND RISK FACTORS FOR HOSPITALISATION AFTER COMMUNITY-ACQUIRED PNEUMONIA IN OLDER ADULTS IN ENGLAND

ERC Millett, Bl. De Stavola, JK. Quint, L. Smeeth, SL Thomas. London School of Hygiene and Tropical Medicine, London, UK

10.1136/thoraxjnl-2014-206260.20

**Introduction and objectives** Hospitalisation rates for community-acquired pneumonia (CAP) among older individuals have increased in Europe, but the reasons for this remain unclear. It may be due to increasing incidence of CAP in older adults, or an increasing tendency to hospitalise – either due to worsening co-morbidities, and/or changes in service provision. We used English linked electronic health records to investigate trends in hospitalisation after a CAP diagnosis independent of CAP incidence, and determinants of any increasing trend.

**Methods** General practice records from the Clinical Practice Research Datalink (1998–2011) were linked to hospital admission records and mortality data, and CAP episodes among patients aged ≥65 years were identified. Episodes resulting in hospitalisation within 28 days of CAP diagnosis were compared to non-hospitalised CAP episodes, and multilevel logistic regression models built to estimate odds ratios for co-morbidities, frailty, and other factors, and to predict the probability of hospitalisation over time. Indicators of CAP severity (including mortality in the 28 days post-CAP) and pathways of care were also examined as explanations for hospitalisation trends.

**Results** Hospitalisation after CAP increased markedly over the study period; after controlling for a wide range of comorbidities and other factors, the predicted probability of hospitalisation rose from 57% (1998–2000) to 86% (2009–2010). Factors associated with hospitalisation included 14 co-morbidities, five frailty factors, and four medications/vaccinations. In the fully adjusted model most of these factors were associated with increased odds of hospitalisation, but some (including dementia and terminal illness) lowered the odds of hospitalisation. Over the study period, a growing proportion of CAP patients were admitted to hospital via A&E and the proportion referred by general practitioners increased. Over the study period, increasing CAP hospitalisations. If the incidence of CAP in this age group also continues to increase, these combined trends will place an expanding burden on the health service.

**S15** CLINICAL CHARACTERISTICS OF HOSPITALISED PATIENTS MISDIAGNOSED WITH COMMUNITY-ACQUIRED PNEUMONIA

H. Pick, J Lacey, D Hodgson, E MacDonald, A Turvey, T Bewick. Derby Hospitals NHS Foundation Trust, Derby, UK

10.1136/thoraxjnl-2014-206260.21

**Background** The diagnosis and treatment of patients hospitalised with community-acquired pneumonia (CAP) is predicated on an acutely abnormal chest radiograph. Little is known about patients who present with infective respiratory symptoms with no consolidation, who have clinically significant non-pneumonic lower respiratory tract infection (LRTI).

**Methods** A prospective observational cohort study of consecutive patients admitted to hospital with infective respiratory symptoms and treated for suspected CAP over winter 2013/14. Management was at the discretion of the admitting team.

**Results** Of 628 patients admitted to hospital during the study, 304 (48.4%) did not have acute consolidation on chest radiograph; 166 were reported as clear, and 138 as either longstanding abnormality or not acute infection. Patients with LRTI had lower admission C-reactive protein levels (median 49 mg/l vs. 85 mg/l; p < 0.01), were older (median 80.0 years vs. 76.3 years; p = 0.005), and were more likely to be managed on a non-respiratory ward (174/304 (57.2%) vs. 127/324 (39.1%); p < 0.001). A higher proportion of patients with LRTI were care home residents, although this did not reach statistical significance (56/304 (18.4%) vs. 45/324 (13.9%); p = 0.12). A microbiological diagnosis was made in only 9/304 (3.0%) patients with LRTI compared with 45/324 (13.9%) with CAP (p < 0.0001). CAP patients had a discharge clinical code of CAP (J12–18) in 247/324 (76.2%) cases; 121/304 (39.8%) patients with LRTI were miscoded as CAP. Thirty-day mortality was similar in both groups (48/324 (14.8%) vs. 43/304 (14.1%) p = 0.82), but median length of hospital stay was longer for patients with CAP (7.0 days vs. 5.6 days; p = 0.002).

**Conclusion** Almost half patients treated for CAP were misdiagnosed and over-treated with broad spectrum antibiotics. Patients with non-pneumonic LRTI were older, with lower C-reactive protein levels, but similar 30-day mortality. Acute respiratory illness in this group may therefore be driven by decompenesed comorbidity rather than an underlying inflammatory condition; broad spectrum antibiotics may not be useful. No national guidance currently exists on the optimal management of this group, and further study is required.

**REFERENCE**

**S16** A RANDOMISED CONTROLLED TRIAL OF ATORVASTATIN AS A STABLE TREATMENT IN BRONCHIECTASIS

1P Mandal, 1J Chalmers, 1M Sidhu, 1D Davidson, 1A Rossi, 3AH i l l. 1Lim WS. 1BTS guidelines for the management of community acquired pneumonia in adults: update 2009. Thorax 2009;64 Suppl 3,iii1-ii55.

**Background** Bronchiectasis is characterised by chronic cough, sputum production, and recurrent chest infections. Pathogenesis is poorly understood, but excess neutrophilic airway inflammation is seen. Evidence suggests that statins have pleiotropic effects; therefore these drugs could be a potential anti-inflammatory treatment for patients with bronchiectasis. We did a proof-of-concept randomised controlled trial to establish if atorvastatin could reduce cough in patients with bronchiectasis. In addition, we wanted to establish the anti-inflammatory mechanisms of statins contributing to this.

**Methods** Patients aged 18–79 years were recruited from the Royal Infirmary of Edinburgh. Participants had clinically significant bronchiectasis confirmed by chest CT and two or more chest infections in the preceding year. Individuals were randomly...
allocated to receive either atorvastatin (80 mg) or a placebo, orally once a day for 6 months. Primary endpoint was reduction in cough from baseline to 6 months, measured by the Leicester Cough Questionnaire (LCQ) score (range 3–21; 3 severe cough; minimum clinically important difference, 1.3 units).

Findings

(i) RCT

30 individuals were assigned atorvastatin and 30 were allocated placebo. There was evidence of a difference in baseline to 6-month change in LCQ between the treatment groups, with a significant improvement in the statin treated group, with a mean difference 2.2, 95% CI for difference (0.5, 3.9) p = 0.01.

When analysed as proportion of improvement in LCQ, in the statin treated group 40% patients had a 1.3 Units or more improvement in the LCQ compared with 17% in the placebo group; difference in proportion 23% (95% CI for difference 1%, 45%), p = 0.04.

There was significantly increased number of apoptotic airway neutrophils [mean difference of 8.9 (11.7); p = 0.04] with a trend towards a decreased total number of neutrophils in the sputum; p = 0.09; in statin treated group.

(ii) In vitro studies

Statins enhance apoptosis of neutrophils in vitro due to a reduction in stimuli induced increase in calcium flux.

Interpretation

6 months of atorvastatin improved cough on a quality-of-life scale in patients with bronchiectasis. Multicentre studies are now needed to assess whether long-term statin treatment can reduce exacerbations. Further studies are needed to establish if statins regulate Ca\(^{2+}\) flux by altering the intracellular or extracellular pathways.

### Cardiovascular Risk Factors in People with Bronchiectasis: A Cross Sectional Study

<table>
<thead>
<tr>
<th>Cardiovascular risk factor or prescription of cardiovascular medication</th>
<th>Number of people (%) (n=3,895,800)</th>
<th>Number without bronchiectasis (%) (n=3,884,858)</th>
<th>Number with bronchiectasis (%) (n=10,942)</th>
<th>Adjusted odds ratio* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never smoker</td>
<td>773,094 (19.8)</td>
<td>768,975 (19.8)</td>
<td>4119 (37.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>Ex-smoker</td>
<td>296,223 (7.6)</td>
<td>293,072 (7.5)</td>
<td>3151 (28.8)</td>
<td>1.30 (1.23–1.36)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>605,205 (15.5)</td>
<td>601,533 (15.5)</td>
<td>3672 (33.6)</td>
<td>0.88 (0.84–0.92)</td>
</tr>
<tr>
<td>Missing data</td>
<td>2,221,278 (57.0)</td>
<td>2,221,278 (57.2)</td>
<td>0</td>
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</tr>
<tr>
<td>Hypertension</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>695,340 (17.9)</td>
<td>691,569 (17.8)</td>
<td>3771 (34.5)</td>
<td>0.94 (0.90–0.98)</td>
</tr>
<tr>
<td>No</td>
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<td>3,193,289 (82.2)</td>
<td>7171 (65.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>3,643,743 (93.5)</td>
<td>3,634,097 (93.5)</td>
<td>9646 (88.2)</td>
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<td>250,761 (6.5)</td>
<td>1296 (11.8)</td>
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<td>Diabetes</td>
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<tr>
<td>Yes</td>
<td>3,708,873 (95.2)</td>
<td>3,698,882 (95.2)</td>
<td>9991 (91.3)</td>
<td>1.00</td>
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<td>No</td>
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<td>186,300 (4.8)</td>
<td>951 (8.7)</td>
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<td>Family history of cardiovascular disease</td>
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<tr>
<td>Yes</td>
<td>3,104,934 (79.7)</td>
<td>3,096,973 (79.7)</td>
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<td>790,866 (20.3)</td>
<td>787,885 (20.3)</td>
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<td>1.14 (1.07–1.19)</td>
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<td>β blockers</td>
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<td></td>
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<td>Yes</td>
<td>3,350,205 (86.0)</td>
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<td>545,555 (14.0)</td>
<td>40 (0.4)</td>
<td>0.02 (0.01–0.03)</td>
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<td>Angiotensin converting enzyme (ACE) inhibitor or Angiotensin II receptor blocker</td>
<td></td>
<td></td>
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<tr>
<td>Yes</td>
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<td>447,697 (11.5)</td>
<td>82 (0.8)</td>
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<td>Nitrates</td>
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<td>1169 (10.7)</td>
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<td>Calcium channel blockers</td>
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<td>1934 (17.7)</td>
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<td>Anti-platelets</td>
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<td>Yes</td>
<td>3,446,225 (88.5)</td>
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<td>449,008 (11.6)</td>
<td>567 (5.2)</td>
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<td>Lipid lowering drugs</td>
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<td>472,062 (12.1)</td>
<td>471,649 (12.1)</td>
<td>413 (3.8)</td>
<td>0.11 (0.10–0.12)</td>
</tr>
</tbody>
</table>

*Odds ratios adjusted for age and sex
Background We have previously demonstrated that individuals with bronchiectasis have a higher prevalence of cardiovascular disease compared to the general population. It is unclear if this is due to higher prevalence of cardiovascular risk factors amongst people with bronchiectasis or through other mechanisms.

Methods We conducted a cross-sectional study using electronic primary care data from the Clinical Practice Research Database (CPRD-GOLD) to estimate the prevalence of cardiovascular risk factors (smoking habit, diabetes, hypertension, hyperlipidaemia, family history of cardiovascular disease) and medication commonly prescribed to manage cardiovascular disease amongst people with and without bronchiectasis. Logistic regression was used to generate odds ratios for each risk factor or cardiovascular drug, adjusting for age and sex.

Results Approximately 3.9 million individuals were included in our study, 10,942 (0.3%) of which had a record of bronchiectasis. Individuals with bronchiectasis were predominantly female (60.4%) and the median age at time of diagnosis was 56.2 (Inter-quartile range: 40.6–67.5) years. The prevalence of hypertension, diabetes and hypercholesterolaemia was slightly lower in individuals with bronchiectasis. We also found that people with bronchiectasis were less likely to have prescriptions for beta blockers, angiotensin converting enzyme inhibitors or angiotensin II receptor blockers, anti-platelets and lipid lowering drugs (see Table 1).

Conclusions Patients with bronchiectasis have a lower prevalence of cardiovascular risk factors compared to the general population. This raises the possibility that other factors associated with bronchiectasis could be contributing to the increase risk in cardiovascular disease.

REFERENCE

COPD investigations

**S18** RATE OF DECLINE IN LUNG DENSITY MAY PREDICT LONG-TERM OUTCOME IN PATIENTS WITH ALPHA 1 ANTITRYPSIN DEFICIENCY (AATD)

CE Green, DP a r r , RA Stockley, AM Turner. University of Birmingham, Birmingham, UK; University Hospitals Coventry and Warwickshire NHS Trust, Coventry, UK

Introduction and objectives Alpha-1-Antitrypsin Deficiency (A1ATD) is a genetically determined anti-protease deficiency which predisposes to emphysema. Factors predicting mortality in untreated A1ATD patients include poor FEV1, gas transfer and low lung density. Indeed the latter has been shown to be the most sensitive measure of progression and hence has become the primary outcome in recent studies of augmentation therapy. We hypothesised that patients with the most rapid decline in lung density would be those most at risk of death and most in need of transplantation as the only viable rescue option.

Methods Augmentation naïve patients with 2 quantitative CT scans were selected from the UK A1ATD registry. The annual decline in lung density was determined using the difference between the 2 scans and patients were divided into those with no decline, a slow decline (0–2 g/l/year) or a rapid decline (> 2). Subsequent death or lung transplant was noted.

**S19** IMAGING DERIVED REGIONAL LUNG FUNCTION USING HYPERPOLARISED XENON MRI (XE-MRI) AND QUANTITATIVE COMPUTED TOMOGRAPHY (QCT) IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)


Introduction and objectives To derive quantitative regional imaging lung function parameters using hyperpolarised xenon MRI (XE-MRI) and computed tomography (QCT), and compare these to pulmonary function tests (PFTs) in subjects with chronic pulmonary obstructive disease (COPD).

Methods Twenty patients with COPD (stage II – IV GOLD criteria classification) underwent XE-MRI at 1.5T, QCT, and PFTs. Whole lung and lobar percentage ventilated volumes were obtained using automated segmentation of multi-slice Xe-MRI ventilation images acquired at a breath hold of FRC + 1L using in-house software. Average whole lung apparent diffusion coefficients (ADCs) were calculated from multi-slice Xe-MRI
**Introduction**  
18FDG PET/CT imaging may be a useful tool to study COPD and lung inflammation; however the optimal protocol for this imaging biomarker has yet to be established.

**Method** We aimed to develop a combined 18FDG-PET/CT imaging protocol optimised to quantify lung inflammation. Six patients with moderate-to-severe COPD underwent dynamic 18FDG-PET imaging combined with blood sampling (both arterial and venous over 60 min) to determine the localised plasma activity time curve. High resolution CT (HRCT) was utilised to segmentate the lung and determine areas of emphysema. 3 sets of comparative input functions were analysed (arterial, venous and image derived arterial input functions). 18FDG kinetics was fitted using the Patlak method.

**Results** Similar results were obtained using time activity curves from all three input functions. The arterial input was always found to be slightly higher than the others (Figure 1). Patlak analysis of the time-activity curves for each of the CT derived lung lobes allowed generation of images of slope (1st row), intercept (2nd row) and CT (3rd row). The acquisition of HRCT co-registered to FDG-PET allows more accurate demarcation and quantification of FDG in emphysematous areas of the lung. Attempt to improve the signal by excluding voxels without COPD tissue (-935 to -300 HU) has been undertaken as well. The reproducibility of this technique is currently being studied where 20 patients are being scanned twice 4 weeks apart and compared to a baseline scan from 5 healthy controls.

**Conclusion** 18FDG PET/CT imaging has the potential to be a non-invasive biomarker of lung inflammation in COPD.

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**Abstract S20 Figure 1** Shows an example of time activity curves from arterial, venous and image derived techniques (on left) and (on right) a Patlak image from venous plasma slope (1st row), intercept (2nd row) and CT (3rd row)

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**Abstract S21**  
**18F-FLUORODEOXYGLUCOSE (18FDG) PET PULMONARY IMAGING: COMPARATIVE METHODOLOGY IN COPD PATIENTS**

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*A Fletcher,*  
*M Connell,*  
*B Whitcher,*  
*S Ferguson,*  
*T Clark,*  
*B Vennart,*  
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*Queens Medical Research Institute, Edinburgh, UK;*  
*Pfizer Inc, USA*

Introduction and aims The role bacteria play in the development and progression of Chronic Obstructive Pulmonary Disease (COPD) is unclear. We used culture-independent methods to describe differences and/or similarities in microbial communities...
Method CSE was prepared as described previously. Briefly, smoke from one, two, three or four cigarettes was bubbled through 100 ml growth medium. Bacterial type strains (*Pseudomonas aeruginosa, Moraxella catarrhalis, Streptococcus pneumoniae, Prevotella spp and Haemophilus influenzae*) were inoculated into growth medium +/- CSE and incubated either aerobically or anaerobically (*Prevotella* spp). Total viable counts (TVC cfu/ml) were estimated from 0–48 hrs (aerobes) and 0–72 hrs (*Prevotella* spp). Changes in minimum inhibitory concentration (MIC) of antibiotics used in the treatment of respiratory infections were determined by E-Test®, in bacterial cultures exposed daily to CSE over 12 days. Results The growth of *P. aeruginosa, S. pneumoniae* and *H. influenzae* were not completely inhibited by any concentration of CSE; however a reduction in growth rate at higher concentrations was observed. *M. catarrhalis* growth was completely inhibited by two cigarettes/100 ml growth medium. No difference in growth was observed between *Prevotella* spp +/- CSE. A marked increase in *P. aeruginosa* resistance to tetracycline and doxycycline was observed after repeated CSE exposure: resistance to tetracycline and doxycycline increased from 24 to >256 µg/ml, and 48–>256 µg/ml, respectively.

Conclusions The growth of principal bacteria isolated from COPD patients were not affected by concentrations of CSE utilised in this study, but changes in the susceptibility of *P. aeruginosa* to tetracyclines was observed. This increase in resistance may be mediated by efflux pump up-regulation, and may lead to cross-resistance with other antibiotics. Work currently underway aims to determine whether CSE induces other key phenotypic changes (virulence factor expression and/or biofilm production) which might enhance the pathogenicity of these bacteria in the presence of CSE and result in poorer outcomes for patients with COPD.

Sleep disordered breathing – assessment and treatment

**RESULTS OF A NATIONAL SURVEY OF PRE-OPERATIVE SCREENING FOR OBSTRUCTIVE SLEEP APNOEA**

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10.1136/thoraxjnl-2014-206260.29

Introduction and objectives There is currently no UK guidance (from BTS, BSS or RCA) regarding screening for obstructive sleep apnoea in the pre-operative setting. Evidence suggests that undiagnosed OSA is associated with increased post-operative complications but no trials have examined whether screening the UK’s general surgical population is justifiable. We sought to examine current UK practice and opinion in this regard.

Methods A postal survey was sent to all 180 UK sleep service providers asking whether they had a hospital policy for pre-operative screening for OSA and what this consisted of. If there was no policy they were asked how pre-operative patients with suspected OSA were identified. Further details regarding diagnostic confirmation and opinion regarding practice were sought.

Results We received 84 replies. There is a spectrum of current practice amongst respondents. There were 31 centres (37%) with a policy for screening for OSA. Of these, 42% screened all patients with a questionnaire e.g. STOP BANG, 23% screened only patients undergoing certain operations, 13% screened patients with high BMI only. Of those with a policy who

**Abstract S21 Table 1**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>COPD</th>
<th>HV</th>
<th>HS</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1/FVC Ratio</td>
<td>1.90 ± 0.63</td>
<td>2.66 ± 0.51</td>
<td>2.51 ± 0.34</td>
</tr>
<tr>
<td>FEV1</td>
<td>1.46 ± 0.45</td>
<td>3.12 ± 0.55</td>
<td>3.20 ± 0.71</td>
</tr>
<tr>
<td>SW</td>
<td>71 ± 16</td>
<td>69 ± 13</td>
<td>69 ± 16</td>
</tr>
<tr>
<td>SW % Predicted</td>
<td>58 ± 17</td>
<td>98 ± 6</td>
<td>95 ± 13</td>
</tr>
<tr>
<td>SW/FVC Ratio</td>
<td>0.51 ± 0.08</td>
<td>0.82 ± 0.06</td>
<td>0.79 ± 0.06</td>
</tr>
</tbody>
</table>

in the lower airways of patients with COPD, healthy non-smokers and smokers.

Methods Bronchial wash samples were collected from patients with COPD (GOLD 1–3; *n = 18*), healthy non-smokers (HV; *n = 11*) and healthy smokers (HS; *n = 8*). Samples were processed using the Illumina MiSeq platform. The Shannon-Wiener Index (SW) of diversity, lung obstruction (FEV1/FVC ratio) and ordination by Non-Metric Multidimensional Scaling (NMDS) on Bray-Curtis dissimilarity indices were analysed to evaluate how samples were related. Principal component analysis (PCA) was performed to assess the effect specific taxa had within each cohort. Characteristics of each cohort are shown in Table 1.

Results There was no difference in taxa richness between cohorts (range: 69–71; *p = 0.954*). Diversity (SW Index) was significantly lower in COPD samples compared to samples from HV and HS (*p = 0.009* and *p = 0.033*, respectively). There was no significant difference between HV and HS (*p = 0.186*). The FEV1/FVC ratio was significantly lower for COPD compared to HV (*p = 9.10^-5*) and HS (*p = 2.10^-6*), respectively. NMDS analysis showed that communities belonging to either of the healthy groups were more similar to each other than they were to samples belonging to the COPD group. PCA analysis showed that members of *Streptococcus* sp. and *Haemophilus* sp. had the largest effect on the variance explained in COPD. In HS, *Hae-mophilus* sp., *Fusobacterium* sp., *Actinomyces* sp., *Prevotella* sp. and *Veillonella* sp. had the largest effect on the variance explained, while in HV *Neisseria* sp., *Porphyromonas* sp., *Actino-myces* sp., *Atopobium* sp., *Prevotella* and *Veillonella* sp. had the largest effect on the variance explained.

Conclusions The study demonstrates that microbial communities in the lower airways of patients with COPD are significantly different from that seen in healthy comparison groups. Patients with COPD had lower microbial diversity than either of the healthy comparison groups, higher relative abundance of members of *Streptococcus* sp. and lower relative abundance of a number of key anaerobes.

**THE EFFECT OF CIGARETTE SMOKE ON IMPORTANT PATHOGENS IN COPD LUNG INFECTION**

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10.1136/thoraxjnl-2014-206260.28

Introduction The leading cause of COPD in developed nations is exposure to tobacco smoke. COPD is characterised by acute periods of exacerbation, which are often bacterial in aetiology. The direct effect of cigarette smoke on bacteria present in the COPD lung, and how this may drive disease progression, has not been determined. This preliminary study aimed to determine the effect of cigarette smoke extract (CSE) on the growth and antibiotic susceptibility of COPD bacterial lung pathogens.
estimated the number of referred patients, 60% saw more than >5 per month. Of centres with no policy only 26% estimated that they received >5 referrals per month. Without a policy 72% of referrals came from clinical suspicion alone.

Overall 96% of respondents felt that all patients at high risk of OSA should be screened for OSA. 56 respondents thought it would be ethical to randomise identified cases of OSA to a potential trial of peri-operative CPAP or no CPAP, compared with 40 who did not.

**Conclusions** There is no established UK standard practice for screening for OSA pre-operatively, despite a majority opinion amongst questionnaire responders that high risk patients should be. There would be cost implications if National pre-operative OSA screening was implemented and therefore needs to be clear evidence based benefit before proceeding.

**S24** REPEATABILITY AND EFFECT OF INCENTIVES ON AN OFFICE BASED ADVANCED DRIVING SIMULATOR (MINIUOLDS) TO ASSESS DRIVING PERFORMANCE IN OBSTRUCTIVE SLEEP APNOEA SYNDROME (OSAS)

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10.1136/thoraxjnl-2014-206260.30

**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 continuously measured variables in an advanced PC-based driving simulator the at risk patients can be identified with a high degree of accuracy.

We have investigated whether this finding is repeatable. Individuals may “raise their game” if they know that their licence is at stake. We have therefore also investigated the effect of an incentive on the test.

**Methods** 150 untreated OSAS patients (males-131) were randomised to either the repeatability (n = 50) or incentive arm (n = 100). All performed a simulator run, after initial acclimatisation. In the repeatability arm, patients performed the simulator run on two separate occasions with no knowledge of the results. In the incentive arm, patients performed the simulator run on two separate occasions but just prior to the second run were told about their performance and offered a prize if they could improve their performance by 10%.

SDLP in epoch 3 and “veer” reaction time (Veer-RT) were the co-primary outcome variables. Classification of patients into “pass”, “fail” and “indeterminate” were the secondary outcome variables. Results were analysed using paired and unpaired T tests with the level of significance set at p < 0.05.

**Results** 137 patients (repeatability arm-48, incentive arm-89) completed the trial. The median duration between the two simulator runs was 13 days (range, 5–55). SDLP in epoch 3 and Veer-RT were repeatable (P = 0.54, Δ SDLP, 0.01 and P = 0.37, Δ Veer-RT: 0.13) respectively. There was no effect of an incentive on SDLP in epoch 3 (P=0.18) and Veer-RT (P=0.57). There was no difference in the simulator outcome between the two runs [pass (P = 0.70), indeterminate (0.06), fail (P = 0.16)].

**Conclusions** SDLP and Veer-RT are consistent between runs on the MiniUoLDS and this is not affected by a simple incentive. Advanced office PC based simulators may be helpful when advising patients with OSAS about driving.

**S25** SLEEPY SNORERS WITH “FLOW LIMITATION SYNDROME”: A MISSED OPPORTUNITY FOR CPAP?

R Yadavilli, B Chakrabarti, S McDougall, H Home, S Emegbo, N Duffy, R Parker, O’Kelly. Aintree Chest Centre, University Hospital Aintree, Liverpool, UK; University of Liverpool, Liverpool, UK

10.1136/thoraxjnl-2014-206260.31

**Background** The apnoea-hypopnoea index (AHI) is used to define Obstructive Sleep Apnoea Syndrome (OSAS). Some subjects however, present primarily with excessive daytime sleepiness (EDS) and loud snoring, but investigation may reveal an elevated Respiratory Disturbance Index (RDI) with most events comprising Flow limitations. Little UK based data exists regarding treatment outcomes in this group.

**Methodology** 118 subjects (mean age 52 years; Epworth sleepiness score scale score (ESS) 13.58 (5.30); 80% male) presented between November 2011–October 2013 to the Sleep Service with EDS as a primary symptom, loud snoring, RDI > 15 with AHI ≤11 (Mean RDI 21.77 (9.43)); AHI 8.03(2.74); ODI 6.72 (4.49) and were treated with CPAP. At 30 day compliance review, 60% (71/118) had benefited from CPAP with mean ESS pre-CPAP 14.13 (5.12) falling to 7.70 (4.82) following CPAP. The mean BMI was found to be significantly higher in those 71 subjects benefiting from CPAP (33.20 (SD 8.13) v 30.26 (SD 7.40); p = 0.04) but no significant differences were noted in baseline Epworth score, age, gender, AHI, RDI, ODI and Pulse Transit Time (PTT).

This “Flow Limitation” cohort was compared with 261 subjects (mean age 56 years; ESS 12.47(5.61); 82%Male) diagnosed with OSAS during the same time period (Mean AHI 37.11 (19.94); mean ODI 31.15 (19.74) and treated with CPAP. 76% (199/261) of the OSAS group reported benefit from CPAP; ESS fell from 13.24 (5.35) to 6.60 (4.74) following CPAP therapy.

Comparing the “Flow Limitation” group with the “OSA” group, the mean BMI (32.03(7.94) v 34.70(8.65); p = 0.04) and age (51.75(12.34) v 56.20(12.18); p = 0.001) were significantly lower in the “Flow Limitation” subjects but no significant difference was noted in baseline ESS. Those deriving benefit from CPAP in the OSAS group demonstrated significantly higher CPAP usage (4.45(2.24) v 3.83(2.13) hours/night; p = 0.04).

**Conclusion** Basing treatment decisions on AHI rather than RDI may miss a proportion of patients exhibiting similar levels of EDS as those with OSAS who would otherwise have gained benefit from CPAP. Despite the observed benefit, CPAP usage appeared lower in this “Flow Limitation” cohort who appeared overall to be a younger group with a lower BMI compared to those with OSAS.

**S26** WHAT ARE THE PREDICTORS OF DEVELOPING HYPOVENTILATION IN OBESITY?

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10.1136/thoraxjnl-2014-206260.32

**Introduction** Obesity Hypoventilation Syndrome (OHS) is conventionally defined by the combination of obesity (BMI >30 kg/m²) and daytime hypercapnia (PaCO₂ ≥6 kPa, with no alternative explanation); sleep-disordered breathing may or may not be included in the definition. The development of ventilatory failure in obese individuals is highly variable, and the additional factors responsible have not been comprehensively studied. In obese
Obese out-patients referred for possible OSA had vHCO₃⁻ measured. Patients with a vHCO₃⁻ ≥27 mmol/l underwent arterial blood gas (ABG) analysis. Those with pCO₂ >6.2 kPa underwent further assessments to identify the cause of ventilatory impairment. None had been referred specifically for investigation of OHS. Patients had domiciliary or in-patient sleep studies as per standard practice.

Results There were 288 patients included: 65% males, mean (SD) age 50 years (range 21–79 years), BMI 39.2 kg/m² (7.8), Epworth Sleepiness Scale 13 (6), daytime SpO₂ on air 97% (2.1). Sleep study results showed the Apnoea-Hypopnoea Index (AHI) to be ≥5 in 88%, and ≥30 in 49%. Mean vHCO₃⁻ was 26.2 mmol/l (2.7), vHCO₃⁻ correlated significantly (r = 0.3–0.4, p < 0.005) with daytime SpO₂, mean overnight SpO₂, time spent <80% and <90%, but not AHI or ODI.

vHCO₃⁻ was ≥27 mmol/l in 123 (43%), of whom 80 had an ABG measurement; mean pCO₂ 5.4 kPa (0.8), ten patients >6.2 kPa. Ventilatory impairment was due to OHS in four (5% of ABG cohort); there was additional lung or chest wall disease in the other six. Overall, 25 patients had a base excess ≥3. The vHCO₃⁻ range was 28–36 mmol/l in patients with OHS, with a BMI range of 38–53 kg/m².

Three additional outpatients with BMI ≥30 kg/m² were diagnosed with OHS on ABG without vHCO₃⁻ measurement. In all seven OHS patients, CPAP was initiated. One was non-compliant, four improved and two required home non-invasive ventilation due to non-improvement in ABG.

Conclusions In this large cohort of patients assessed for OSA, 43% had a vHCO₃⁻ ≥27 mmol/l indicating possible OHS, but only 5% were actually diagnosed with OHS. In isolation this strategy to identify OHS seems inefficient. An increased vHCO₃⁻ in combination with sleep study data may be superior.

Literature suggests 10–25% of patients assessed for Obstructive Sleep Apnoea (OSA) have OHS, with significantly increased morbidity and mortality. Early identification may be beneficial. Studies suggest venous bicarbonate (vHCO₃⁻) ≥27 mmol/l can be used to screen for OHS. We assessed the impact of incorporating this measurement into patient assessments.

Methods Obese out-patients referred for possible OSA had vHCO₃⁻ measured. Patients with a vHCO₃⁻ ≥27 mmol/l underwent arterial blood gas (ABG) analysis. Those with pCO₂ >6.2 kPa underwent further assessments to identify the cause of ventilatory impairment. None had been referred specifically for investigation of OHS. Patients had domiciliary or in-patient sleep studies as per standard practice.
3.0 mg produced significantly greater weight loss compared with placebo (Table) and enabled more individuals to reach ≥5% and >10% weight loss targets after 32 weeks (p < 0.0001, both). Oxygen saturation, polysomnographic measures, HbA1c and systolic blood pressure (SBP) at 32 weeks are summarised (Table). Nausea and diarrhoea were the most common adverse events with liraglutide 3.0 mg (27% and 17% of individuals, respectively).

Discussion Liraglutide 3.0 mg produced significantly greater reductions than placebo in AHI, body weight, SBP and HbA1c in obese individuals with moderate/severe OSA and was generally well tolerated.

'Blood and spit' – what to measure in AECOPD

<table>
<thead>
<tr>
<th>Abstract S28 Table 1</th>
<th>Change from baseline at 32 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Liraglutide 3.0 mg</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td><strong>n</strong></td>
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<tr>
<td>Observed means (LOCF)</td>
<td>Observed means (LOCF)</td>
</tr>
<tr>
<td><strong>AHI3 (events/h)</strong></td>
<td>–12.2</td>
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<tr>
<td><strong>Oxygen desaturation</strong></td>
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<tr>
<td>≥4% index (events/h)</td>
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<tr>
<td><strong>Total sleep time (min)</strong></td>
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<tr>
<td><strong>Sleep onset (%)</strong></td>
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<td><strong>Body weight (%)</strong></td>
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<td>≥5% body weight loss (%)</td>
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<td>&gt;10% body weight loss (%)</td>
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<tr>
<td>HbA1c (%)</td>
<td>0.4</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
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1ANCOVA model
2Logistic regression model
3Definitions of apnoea and hypopnoea from the 2007 AASM Manual for the Scoring of Sleep and Associated Events were used

Methods Admission platelet counts were categorised as low (<150), normal (150–400), or high (>400) x10^10 cells/mm^3 and odds ratios assessed for inpatient and, among those surviving to discharge, 1-year mortality (normal platelet count=reference). For inpatient mortality, platelet category and DECAF indices were included in multivariate logistic regression. The areas under the ROC curves for DECAF and DECAF+Platelets were compared by the method of DeLong. Associations with thrombocytosis were analysed using Mann-Whitney or Fisher’s exact test. Causes of death at 1-year due to respiratory, cardiac or malignant disease were recorded.

Results Thrombocytosis was associated with inpatient (OR 1.83, 95% CI 1.12–3.00, p = 0.016) and 1-year mortality (OR 1.62 95% CI 1.09–2.30, p = 0.017). Thrombocytopenia was associated with inpatient (OR 3.5, 95% CI 1.51–8.12, p = 0.004), but not 1-year mortality (OR 1.81, 95% CI 0.76–4.312.08, p = 0.181). On multivariate analysis, thrombocytosis (OR 1.85, 95% CI 1.03–3.33 p = 0.039) and thrombocytopenia (OR 3.00 95% CI 1.09–8.24 p = 0.033) independently predicted inpatient mortality, but did not improve predictive power of DECAF (AUROC: DECAF=0.86, DECAF+Platelets=0.86; p = 0.93).

Thrombocytosis was associated with a higher white cell count (p<0.001) and eMRCD score (i.e. more breathless when stable; p = 0.001), lower: albumin (p = 0.004), BMI (p = 0.002), FEV1 (p = 0.010), haemoglobin (p<0.001), and a lower proportion of women (p = 0.004), and patients with cosinopenia (<0.05 x 10^9/l) (p = 0.008), cardiac death (p = 0.044), current smoking (p = 0.046), AF (p = 0.029) and diabetes (p = 0.006). Thrombocytosis was not related to cardiovascular disease, prior exacerbation and readmission rates or LTOT use, admission PaO2, pH or NIV, or length of stay.

Discussion Thrombocytosis was an independent predictor of both inpatient mortality and, amongst survivors to discharge, 1-year mortality. Thrombocytosis was not associated with cardiovascular disease and the higher 1-year mortality was not due excess cardiovascular or cancer deaths, suggesting that other mechanisms are responsible. Whilst thrombocytosis was not associated with LTOT use or PaO2, it was associated with other indices of disease severity, including breathlessness and lower FEV1, BMI and albumin level.

REFERENCES
1 Harrison Thorax 2014
2 Steer Thorax 2012

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REFERENCES
1 Harrison Thorax 2014
2 Steer Thorax 2012

Abstract S29 Table 1 | Platelet category and cause of death
---|---
Platelet count (x10^10 cells/mm^3) | Total patients | Inpatient deaths, n (% of total) | Deaths at 1 year, n (% of total) | Respiratory deaths, n (% of all deaths at 1 year) | Cardiovascular deaths, n (% of all deaths at 1 year) | Cancer deaths, n (% of all deaths at 1 year) |
---|---|---|---|---|---|---|
<150 | 32 | 25.0 | 50.0 | 81.3 | 12.5 | 6.3 |
150–400 | 713 | 8.7 | 28.5 | 75.4 | 11.8 | 7.4 |
400 | 175 | 14.9 | 41.1 | 84.7 | 4.2 | 6.9 |
has been associated with an adverse prognosis in cardiac and respiratory disease, including COPD. We have assessed its value in AECOPD and whether adding RDW improves the predictive power of the DECAF score.

**Methods**

We studied 2 groups of patients with AECOPD, the “derivation cohort” (n = 920) in whom DECAF was derived and the “internal validation cohort” (n = 880) in whom its prognostic value was confirmed.

In the validation cohort RDW was collected prospectively and relationships to mortality assessed by univariate and multivariate logistic regression. RDW values were dichotomised by visual inspection of the receiver operator characteristic (ROC) curve which showed the optimal prognostic threshold for hospital mortality to be 15.5%, consistent with other studies. “RDW score (15.5% or less=0, greater than 15.5%=1) was added to the DECAF score and the areas under the ROC (AUROC) curves for the DECAF and DECAF-RDW scores were compared by the method of DeLong.

In the derivation cohort RDW was collected from laboratory records and the prognostic utility assessed separately by logistic regression.

**Results**

In the validation cohort RDW >15.5% was a strong predictor of inpatient mortality in both univariate (OR 2.70, 95% CI 1.68–4.32, p < 0.001) and multivariate analysis (OR 2.16, 95% CI 1.28–3.64, p = 0.004). However, there was no difference between the AUROC curves for the DECAF and DECAF-RDW scores (Figure 1; p = 0.63).

In the derivation cohort RDW >15.5% showed a non-significant trend towards higher inpatient mortality on univariate analysis (OR 1.55, 95% CI 0.96–2.50, p = 0.07), but there was no association on multivariate analysis (OR 1.05, 95% CI 0.60–1.84, p = 0.86).** Discussion**

The significant association of RDW with inpatient mortality in AECOPD in one cohort but not the other suggests limited value in this population. When forced into the DECAF model, RDW did not improve its predictive power and is a weaker prognostic index than the component parts of DECAF.

**REFERENCES**

1 Seyhan COPD 2013
2 Steer Thorax 2012
3 Echevarria Thorax 2013(68:A138)

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**Introduction and objectives**

A number of clinical prediction rules have been described to predict adverse outcomes in patients admitted to hospital with an acute exacerbation of COPD (AECOPD). None are used routinely, perhaps because of limitations including setting (confined to intensive care), use of subjectively defined or difficult to access clinical measurements and lack of external validation. None have undergone impact assessment.

The National Early Warning Score (NEWS) in unselected medical admissions accurately predicts risk of in-patient mortality. The NEWS is less discriminating in patients with COPD. We hypothesised that patients admitted with an AECOPD could be more accurately risk stratified based on a combination of the NEWS and other parameters.

**Methods**

This was a twin site observational cohort study, over a two-year period (March 2012 – February 2014). 2361 admissions with COPD were identified.

**Results**

123 died during admission (5.2%) and a further 36 (1.5%) were escalated to Intensive Care (ICU) and survived to discharge. We analysed these 159 patients against a control group (n = 159) matched only for month of admission (to address seasonal fluctuations in disease severity).

Major results of the study are summarised in Table 1. Those who died or had care escalated were older, had a higher NEWS and respiratory rate. Neutrophils, lymphocyte count, neutrophil-lymphocyte ratio, urea, albumin and CRP were significantly different between the two groups studied. On multivariable analysis lymphocyte count, urea, NEWS and age were independent predictors of adverse outcome.

**Abstract S31 Table 1**

Admission parameters for patients with AECOPD - comparison between those who died or had care escalated versus those who remained on the ward and survived to discharge. Results given as Mean (Standard deviation). NLR = neutrophil-lymphocyte ratio, NEWS = National Early Warning Score

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Died / escalated (n=159)</th>
<th>Control group (n=159)</th>
<th>T-test or Mann-Whitney U test*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutrophils (x10⁶/l)</td>
<td>12 (4.5)</td>
<td>9.9 (5.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Lymphocytes (x10⁹/l)</td>
<td>1.0 (0.4)</td>
<td>1.5 (0.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>NLR</td>
<td>17.2 (18.8)</td>
<td>9.7 (9.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sodium (mmol/l)</td>
<td>136.6 (7.3)</td>
<td>136.7 (4.7)</td>
<td>0.913</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>35.0 (5.7)</td>
<td>36.7 (4.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Urea (mmol/l)</td>
<td>10.3 (6.8)</td>
<td>6.9 (4.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP (mg/l)</td>
<td>84.0 (90.4)</td>
<td>53.4 (58.8)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Age</td>
<td>76.1 (10.8)</td>
<td>71.8 (10.4)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>NEWS</td>
<td>6.2 (3.2)</td>
<td>4.1 (2.6)</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Respiratory Rate (per minute)</td>
<td>22.1 (5.3)</td>
<td>20.6 (4)</td>
<td>0.011</td>
</tr>
</tbody>
</table>

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**Abstract S30 Figure 1**
Conclusions Age, admission NEWS and blood parameters differed significantly between those who were managed on the ward with AECOPD and those who either died or whose care was escalated to ICU. This could form the basis for a prediction score, automatically calculable on admission to hospital using available technology to highlight those patients judged at greatest risk of deterioration.

REFERENCE
1 Steer J, Gibson GJ, Bourke SC. Predicting outcomes following hospitalization for acute exacerbations of COPD. QJM 2010;103(11):817-29

S32 THE RELATIONSHIP BETWEEN EXERCISE CAPACITY AND INFLAMMATORY MARKERS AT COPD EXACERBATION

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Introduction Chronic obstructive pulmonary disease (COPD) is characterised by breathlessness, fatigue and reduced daily activity which worsens acutely at exacerbation. A three year observational study has shown a reduction in 6MWT over time that correlates with increase over the same period in plasma Interleukin-6 and C-reactive protein (CRP) levels (Ferrari, Tanni et al. 2013). We therefore investigated whether acute changes in 6MWT at exacerbation were associated with changes in systemic inflammatory markers and the perception of fatigue.

Methods Forty four patients from the London COPD cohort who had a mean age of (±SD) 71(±7) years; FEV1 52(±17)% predicted; male gender 72% and still smoking 30% were asked to performed a 6MWT and completed a FACIT-F questionnaire when stable (baseline) and 3 days after first presenting with the exacerbation. Blood was drawn for assay of CRP and fibrinogen.

6MWT was performed according to ATS protocols. Exacerbations were defined by our usual symptom criteria (Seemungal, Donaldson et al. 1998). High scores in the FACIT-F questionnaire indicate low fatigue. Stable COPD was defined as having no exacerbations in the preceding six weeks or subsequent two weeks. Data was analysed by paired t-test, Wilcoxon sign rank test and Spearman correlation.

Results The 6MWT was significantly lower at 3 day post exacerbation compared to baseline measurements [414(SD±111) vs 359(SD±1222) metres; p ≤ 0.001] and fatigue was worse [37 (9.3) vs 35(9.1); p = 0.037]. Inflammatory markers were significantly higher at the exacerbation recovery visit compared to stable state, CRP [median (IQR)] [3.0 (1–8) vs 8.0(3–37) mg/L; p < 0.001] and fibrinogen [3.5 (3–4) vs 4.3 (3–5) g/l; p = 0.003].

The fall in exercise capacity from baseline to exacerbation recovery visit was positively correlated with greater increases in CRP [rho= -0.41; p = 0.021] (Figure 1A) and in fibrinogen [rho= -0.42, p = 0.025] (Figure 1B). Also, the falls in exercise capacity between baseline and exacerbation were associated with increased in fatigue levels [r = 0.44; p = 0.013] (Figure 1C).

Conclusions These findings suggest that changes in inflammatory markers and other metabolites in the body at exacerbation altering the perception of fatigue and reducing the patient exercise capacity.

S33 SPUTUM COLOUR IN THE LIGHT OF THE HEALTH RELATED QUALITY OF LIFE, AIRWAYS AND SYSTEMIC BIOMARKERS IN EXACERBATIONS OF COPD

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Abstract S32 Figure 1 The correlation between six minute walk test (6MWT) and inflammatory markers (1A) CRP, (1B) fibrinogen and (1C) fatigue

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10.1136/thoraxjnl-2014-206260.39
Introduction Acute exacerbations of COPD have a major impact on patients’ health related quality of life (HRQoL), and the utilisation of health care resources. Current guidelines recommend oral corticosteroids and/or antibiotics for the treatment of acute exacerbations of COPD based on patients’ symptoms. With increasing bacterial resistance to antibiotics and the rising costs of COPD treatment, further research into diagnostic tools to aid the management of COPD in its stable and exacerbating states is required. Sputum colour (SC) is an accessible marker of underlying bronchial inflammation. We investigated the contribution of objective measures of SC as a component of the clinical assessment of exacerbations and relationships with symptom severity.

Methods Data from 36 patients with moderate to very severe COPD was assessed in this prospective observational cohort study (AERIS). There were 122 exacerbations in total over a year. Sputum and blood sampling were performed at enrolment, routine follow up and exacerbation visits. A five-point sputum colour chart was developed to objectively report the SC. Sputum samples from all visits were graded against this chart by the trained laboratory staff. Data from mild, moderate and severe exacerbations were included in the analysis.

Results We found a correlation between SC at exacerbations and disease severity (FEV1%) at exacerbations. SC was also related to sputum neutrophilia at exacerbations. SC was significantly associated with systemic markers such as blood neutrophilia, CRP and fibrinogen. Interestingly, we observed no statistically significant correlation between SC and Procalcitonin levels. We also found no statistically significant relationship between SC and symptom scores (CAT and EXACT-PRO) at exacerbations. However, we found a significant association between CAT and EXACT-PRO scores (rho 0.46; p < 0.01).

Conclusion We observed that visual colour score of sputum at exacerbations is related to underlying airway and systemic inflammation but not to symptom scores. The use of a SC combined with other clinical and laboratory biomarkers, as part of a multicomponent diagnostic tool, may further improve its clinical utility to better guide effective exacerbation treatment. Further analysis of the full AERIS cohort will explore this.

Abstract 533 Table 1 Spearman’s correlation for sputum colour at all exacerbations

<table>
<thead>
<tr>
<th>Sputum Colour</th>
<th>rho</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1%</td>
<td>0.26</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Sputum Neutrophils (count)</td>
<td>0.66</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Neutrophils (%)</td>
<td>0.62</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Macrophages (count)</td>
<td>-0.38</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Lymphocytes (count)</td>
<td>-0.22</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td>-0.23</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Blood Neutrophils (10^9/L)</td>
<td>0.20</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>0.47</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Fibrinogen (g/L)</td>
<td>0.32</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Procalcitonin (ng/ml)</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>EXACT-PRO</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>CAT</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

FEV1: Forced Expiratory Volume in 1 second; CRP: C Reactive Protein; EXACT-PRO: The Exacerbations of Chronic Pulmonary Disease Tool Patient Reported Outcome; CAT: The COPD Assessment Tool; NS: No significance

Pulmonary arterial hypertension: scientific advances

BMTR-II DEFICIENCY LEADS TO AN INCREASE IN LUNG EGG DEPOSITION, PULMONARY VASCULAR REMODELLING AND AN ABNORMAL LIVER VASCULATURE IN MICE CHRONICALLY INFECTED WITH S. MANSONI

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10.1136/thoraxjnl-2014-206260.40

Rationale and objectives Schistosomiasis is the world-wide leading cause of pulmonary arterial hypertension (PAH) and is particularly prevalent in developing countries. More than 80% of patients with familial PAH in the western-world have a mutation in bone morphogenetic protein type-II receptor (BMPR-II), which is a member of the transforming growth receptor-beta (TGF-b) superfamily and is important in cell proliferation and differentiation. The aim of the study was to determine if mice with a heterozygous null mutation in BMPR-II are more susceptible to pulmonary vascular remodelling induced by S. mansoni infection, compared with wild-type littermates.

Methods Wild-type (BMPR-II +/-) and BMPR-II heterozygous (BMPR-II +/-) C57/BL6 mice were infected percutaneously with S. mansoni. Seventeen weeks post-infection right ventricular systolic pressure (RVSP), right ventricular hypertrophy (RVH), liver and lung egg counts were measured. Pulmonary vascular remodelling and liver histology were assessed by morphometry, following immunohistochemistry. Lung, liver and serum cytokines were also measured. A macrophage phagocytosis assay and in vivo bead assay were also performed.

Measurements and main results At 17 weeks post-infection there was a significant increase in pulmonary vascular remodelling associated with a significant increase in egg deposition and cytokines in the lung, in BMPR-II +/- mice. Furthermore, there was a positive correlation between lung egg deposition and pulmonary vascular wall thickness. Additionally, there was a significant dilatation of the central hepatic vein in the BMPR-II +/- infected mice compared with the BMPR-II +/- infected mice. However, no differences in RVSP, RVH or liver egg deposition were found.

Conclusions This study has shown that mice deficient in BMPR-II are more susceptible to pulmonary vascular remodelling induced by S. mansoni which is directly correlated to an increase in egg burden in these mice. Additionally, we have shown that BMPR-II +/- mice have an abnormal liver vasculature, which may be responsible for increased egg shunting into the lungs.

BMPS9 AND BMP10 MEDIATE CONNEXIN EXPRESSION IN ENDOTHELIAL CELLS: IMPLICATIONS FOR PAH AND HHT


10.1136/thoraxjnl-2014-206260.41

Background Germ-line mutations in the bone morphogenetic protein type-II receptor, BMPR-II, underlie 80% of heritable...
pulmonary arterial hypertension (PAH) cases and approximately 25% of idiopathic PAH cases. PAH may arise due to endothelial dysfunction as mice with BMPR-II deficiency exhibit increased pulmonary vascular permeability.

BMP9 is an endothelial quiescence factor and is thought to maintain the integrity of the endothelium. We previously reported that BMPR-II and ALK1 are the key receptors through which BMP9 inhibits the proliferation of human pulmonary artery endothelial cells (hPAECs). We hypothesised that BMPR-II deficiency impacts on endothelial cell connectivity and may contribute to endothelial dysfunction in PAH.

**Methods** Human pulmonary artery endothelial cells were obtained from Lonza and blood outgrowth endothelial cells (BOECs) were isolated from peripheral blood of unaffected controls or PAH patients with identified BMPR-II mutations. Cells were transfected with siRNAs targeting BMPR-II followed by stimulation with BMP9. RNA was extracted and the expression of candidate genes determined by quantitative PCR. Further siRNA studies were performed for ALK1 and endoglin siRNAs. The promotion of gap junction assembly by BMP9 and BMP10 were assessed by immunofluorescence, Western blotting and functionally using parachute assays.

**Results** Screening of candidate BMP9-induced junctional and structural proteins highlighted a subset of endothelial connexins that are BMP9 and BMP10-responsive and dependent on BMPR-II and ALK1. BMP9 and BMP10 increased the expression of the connexins, assessed by Western blotting and immunostaining. In addition, BMP9 and BMP10 significantly increased the transfer of calcine from labelled donor cells to unlabelled acceptor cells, indicating a promotion of endothelial cell connectivity.

**Conclusion** In addition to their roles promoting endothelial quiescence, BMP9 and BMP10 directly promote endothelial cell connectivity by increasing connexin expression and assembly. The central contributions of BMPR-II and ALK1 to this process may implicate impaired endothelial connectivity as a pathological component of PAH and HHT.

**S36** FERROPORTIN IS EXPRESSED IN HUMAN PULMONARY ARTERY SMOOTH MUSCLE CELLS: IMPLICATIONS FOR PULMONARY ARTERIAL HYPERTENSION

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Background Pulmonary Arterial Hypertension (PAH) is a rare but fatal condition manifested by pulmonary vascular remodeling, increased pulmonary vascular resistance and right-heart failure. Disruption in iron handling and anaemia, caused by elevated iron-regulatory hormone hepcidin, is observed in PAH. Ferroportin is the only known cellular iron-export protein that is downregulated by hepcidin. As such, iron supplementation as a therapy is currently under clinical trial. However, it is also known that iron is both pro-oxidant and pro-proliferative. Recent evidence also points to sub-clinical haemolysis and the presence of free haemoglobin in PAH patients. We hypothesised that ferroportin would be expressed; be responsive to hepcidin challenge and have implications for the proliferation of human pulmonary artery smooth cells (hPASMCs).

**Methods** The mRNA levels of ferroportin was measured by RT-PCR, the protein expression was detected by western-blot analysis and quantified by ELISA. The sub-cellular distribution of ferroportin was visualised by immunocytochemistry (ICC). hPASMCs were pre-incubated with or without free haemoglobin and further challenged with increasing doses of hepcidin and the proliferative responses assessed by cyquant and/or BrdU incorporation assays. Some cells were also pre-incubated with LY2928057 (monoclonal antibody against ferroportin that stabilises cellular expression, Eli-Lilly) in proliferation assays.

**Results** Basal ferroportin mRNA was detected in hPASMCs, but the mRNA levels were largely unaltered with hepcidin exposure (n = 3). A ~50KDa protein band representing ferroportin was detected under resting conditions while hepcidin challenge caused decrease in ferroportin protein levels (Figure 1). Basal ferroportin was uniformly distributed in the cells; however hepcidin challenge led to intense punctate/vesicular staining (n = 3). Finally, exposure to free haemoglobin alone or along with hepcidin increased proliferation of hPASMCs by 13.6% and 12.4% (p < 0.05, n = 3) respectively. Interestingly, pre-incubation of the cells with LY2928057 partly reversed this effect.

**Conclusion** This is the first report of ferroportin expression and regulation in hPASMCs. We suggest that targeting and manipulating the hepcidin-ferroportin axis using LY2928057 might prove a novel therapeutic approach for PAH.

**S37** VASCULAR ENDOTHELIAL CELL GROWTH FACTOR-A (VEGF-A) SIGNALLING AND NEOVASCULARISATION OF PULMONARY ENDARTERECTOMY MATERIAL IN CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION (CTEPH)

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Background Despite recent advances in the medical treatment of patients with CTEPH, relatively little is understood surrounding the underlying pathological mechanisms. Many patients have a historical documented venous thromboembolic event (VTE) and consequently, failed resolution of an acute VTE has been proposed as a key initiating factor in the subsequent development of CTEPH. Here we investigated VEGF-A levels, a key regulator of angiogenesis, in CTEPH patients prior to and following...
The role of soluble guanylate cyclase stimulator Bay 41–2272 on remodelling processes relevant to the pathogenesis of pulmonary arterial hypertension

D Shao, SI Wort. Imperial College London, London, UK

10.1136/thoraxjnl-2014-206260.45

Introduction and objectives Pulmonary arterial hypertension (PAH) is characterised by remodelling of small, muscular pre-capillary blood vessels. The subsequent rise in pulmonary vascular resistance leads to right ventricular failure and death. The aetiology of the remodelling process is largely unknown although defects in the bone morphogenetic protein receptor II (BMPR II) pathway are likely to be involved. Most of the therapies used thus far are aimed at pulmonary vasodilation. However it is unclear how much of the benefit seen with these medications is related to reverse remodelling. Riociguat is a “first in class” drug that stimulates soluble guanylate cyclase, with a consequent increase in cyclic GMP (and vasodilation). Riociguat has recently been shown to improve haemodynamics and exercise capacity in patients with idiopathic PAH and chronic thromboembolic PH (PATENT and CHEST). Here we sought to

Abstract S39 Figure 1 Bay41–2272 induces HPASMCs DNA fragmentation (apoptosis), data were presented as mean±SEM n = 3.

*p < 0.005; **p < 0.001
determine the effects of Bay 41–2272, the tool compound for riociguat, on remodelling processes in pulmonary vascular cells. Methods We used primary human endothelial (HPAECs) and smooth muscle cells (HPASMCs) as our target cells. Proliferation was measured using the CyQUANT proliferation kit after cells were treated with various concentration of Bay 41–2272 (kind gifted by Bayer Pharmaceuticals Ltd) for 72 h in the presence of 15% serum. Apoptosis was measured using cell death ELISA kit and DAPI staining after cells were treated with various concentration of Bay 41–2272 for 24 and 48 h in the absence of serum.

Results Bay 41–2272 treatment increased HPASMC apoptosis after 24 and 48 h (Figure 1) by Cell death ELISA; this was further confirmed by DNA condensation assay (DAPI staining). Bay 41–2272 treatment also increased HPAEC apoptosis at 24 h. It was not clear at 48 h treatment whether HPAEC cell death was significant in the absence of serum. Bay 41–2272 treatment reduced HPASMC proliferation (Figure 2), but had no effect on HPAECs.

Conclusions Our preliminary indicate that Bay 41–2272 increases apoptosis and inhibits proliferation, at least in HPASMCs, in vitro. Further studies are needed to fully characterise these effects on remodelling processes and to compare sGC stimulators, such as Bay 41–2272 to Type V phosphodiesterases.

Images in pleural disease

Improving the patient journey: thoracic ultrasonography as an adjunct to decision making and diagnostic pathways in pleural disease

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Background and method Pleural disease represents a growing source of referrals to respiratory services. Physicians increasingly provide many of the diagnostic and therapeutic interventions these patients require independent of colleagues in radiology or thoracic surgery. This changing practice can streamline diagnostic pathways within individual centres, and is reflected in BTS guidelines and the need for respiratory physicians to train in thoracic ultrasonography (TUS). Patients referred to our tertiary-level service undergo in-depth TUS to help determine their diagnostic pathway; assessing factors including the nature of any pleural fluid, positioning of intercostal vessels, and movement of the underlying lung. We reviewed our procedural database (January 2010 to June 2014) and clinical records to identify cases where TUS influenced clinical decision making or subsequent investigations. Results Procedural triage: 359 patients underwent assessment for diagnostic procedures to obtain pleural tissue during the study period. 64 patients were directed to have TUS-guided cutting needle pleural biopsies due to co-morbidity or after TUS identified heavily septated fluid and/or absent lung sliding (representative of adherent lung) that would prevent local anaesthetic thoracoscopy (LAT). One patient was referred for surgical biopsies after TUS identified septated fluid and an at-risk intercostal vessel that would prevent safe intervention by the physician team.

Advanced LAT: 294 LATs were scheduled during the study period. Four LATs were converted “on the table” to TUS-guided cutting needle biopsies after TUS identified increasing septation within the pleural space; a secure diagnosis was obtained in all cases. 95 LATs (32.3%) required Boutin needle pneumothorax induction under TUS guidance. This was successful in 77 cases (81.1%); in those LATs (n = 18) where pneumothorax formation failed an attempt to obtain pleural tissue was made in 10 cases using TUS-guided cutting needle biopsies, making a secure diagnosis in 6 patients.

Conclusion TUS can greatly improve the patient’s journey from presentation with pleural disease to diagnosis and should be utilised in all cases. TUS allows selection of the most appropriate means of obtaining diagnostic pleural tissue and facilitates more complex procedures. As interventional respiratory physicians become familiar with the capabilities of TUS this type of advanced practice may become increasingly widespread.

Looking beyond the pleura – a systematic review of thoracic ultrasonography to diagnose lung consolidation in respiratory failure

IP Corcoran, PD Wallbridge, NM Rahman, SS Mallet, M Hew. Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Trust, Oxford, UK; Department of Respiratory Medicine, Royal Melbourne Hospital, Melbourne, Australia; Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK; Allergy, Immunology and Respiratory Medicine (AIRMED), The Alfred Hospital, Melbourne, Australia

Background and method The use of thoracic ultrasound (TUS) by physicians is increasingly commonplace in light of recent BTS guidelines and changes to training curricula. At its simplest, TUS enhances patient safety during interventions through the identification of pleural fluid and underlying structures. However, TUS training documents in the UK (Royal College of Radiologists) and US (American College of Chest Physicians) acknowledge a need for the ultrasonographer to recognise features of underlying lung, including consolidation.
Pneumonia leading to respiratory failure is a common cause of admission to medical and intensive care units worldwide and associated with significant morbidity and mortality, particularly when diagnosis is delayed. Diagnosis can be challenging and existing tools (clinical examination, CXR or CT) have their recognised flaws. TUS may be an alternative solution, offering patients a bedside investigation that provides clinicians with instant feedback to inform treatment decisions.

We searched MEDLINE, EMBASE and the Science Citation Index Expanded (inception to October 2013) for studies relating to the diagnostic use of TUS in adults with acute respiratory failure due to radiographic consolidation, focusing on studies using CT as their reference standard. Two reviewers independently extracted data from eligible studies and assessed study quality using QUADAS-2.

Results Three cohort studies, all based in an ICU setting, with a total of 134 participants met inclusion criteria. Two studies were at high risk of potential bias, whilst the third had limitations of applicability. The reported sensitivity (0.91 to 1.00) and specificity (0.78–1.00) of TUS in expert hands for CT-detected consolidation was superior to that for CXR (sensitivity 0.38 and 0.68; specificity 0.89 and 0.95). Outside the inclusion criteria, a number of studies of patients with consolidation but no respiratory failure also suggested TUS might have greater diagnostic sensitivity than CXR.

Conclusion TUS remains, at present, a technology with limited applicability. The reported sensitivity (0.91 to 1.00) and specificity (0.78–1.00) of TUS in expert hands for CT-detected consolidation was superior to that for CXR (sensitivity 0.38 and 0.68; specificity 0.89 and 0.95). Outside the inclusion criteria, a number of studies of patients with consolidation but no respiratory failure also suggested TUS might have greater diagnostic sensitivity than CXR.

Given the increasing importance of establishing a microbiological aetiology in pneumonia, we undertook a study assessing the safety and acceptability of bedside ultrasound-guided TLNA (REC No. 09/H0605/12). TLNA has previously reported to have been predominantly undertaken without radiological control.

Methods Participants with community- or hospital-acquired pneumonia completed a baseline assessment of chest pain and pain associated with phlebotomy using a 10 cm visual analogue scale (VAS). Post procedure, participants assessed pain associated with TLNA, and undertook a Likert-based evaluation of the procedure.

Up to 3 mg/kg lidocaine was used to anaesthetise the skin and pleura. An ultrafine 25G needle, attached to a 20 ml luer lock syringe containing 3.5 ml 0.9% sodium chloride solution was inserted into consolidated lung under direct ultrasound guidance by a Respiratory Physician. 0.5 ml of the sodium chloride was injected followed by aspiration with gentle agitation (3 mL of sodium chloride remaining in the syringe as a carrier solution). The needle was then withdrawn. Any pleural fluid present was also aspirated separately.

Samples underwent culture and 16S rRNA gene analysis.

At day 30, one patient had mild ongoing pain at the site of both TLNA and subsequent chest tube insertion, although the relative contribution of each procedure to this pain was unclear.

TLNA increased culture or sequencing-based aetiological diagnosis from 3/28 to 14/28 (18/28 when including pleural fluid analysis). TLNA appears safe and well-tolerated.

Patients presenting with pleural disease on a background of asbestos exposure pose a diagnostic dilemma. Malignant mesothelioma and benign pleural disease have similar radiological appearances but markedly different prognoses. Definitive histological diagnosis is gold standard, however, there are small case series where PET-CT has been compared to pleural biopsy. These have suggested cut-off standardised uptake values (SUV) of 2.0–3.0, with reported sensitivity of 94.1–100% and specificity of 94–100% for excluding pleural malignancy. It has been suggested that where the CT appearances are more in keeping with a benign aetiology, pleural avidity on PET-CT may be able to adequately distinguish between benign and malignant disease, identifying a low-risk population that can be observed in preference to proceeding to thoracoscopy.

We are a cardiothoracic centre which utilises PET-CT in this way. We aimed to review our single-centre experience to see if our outcomes were consistent with the reported data.

Abstract S42 Figure 1
All PET-CT reports carried out since 2007 with the mention of pleura/pleural within the request or report were reviewed. Radiological reports and patient records were examined, scans requested primarily for assessment of the pleura were included. Indication, radiological diagnosis, final diagnosis, presence of histological confirmation and duration of follow-up were determined. All patients with at least 6 months follow-up were analysed.

185 PET CT scan reports were reviewed, of which 28 were carried out primarily for assessment of pleural disease. 9 were found to have high SUVs suggestive of malignancy. 7 of which were demonstrated to be mesothelioma, 1 pleural tumour, 1 recurrence of non-small cell lung cancer. The remaining 19 were reported to have low SUVs, consistent with benign pleural disease.

For those with PET findings consistent with benign pleural disease, follow up data was available for a median of 12 months (Min 6–Max 66). One patient underwent pleural biopsy, which was consistent with benign disease. None of those designated as benign pleural disease based on PET-CT appearances were subsequently found to have pleural malignancy.

Our findings are consistent with previously published data and support the utility of PET-CT scanning in differentiating benign from malignant pleural disease in a clinical setting.

Introduction and objectives The biology of Malignant Pleural Mesothelioma (MPM) is poorly understood, reflected in inexplicable heterogeneity in survival and therapeutic responses. Tumour angiogenesis has been identified as a therapeutic target and high tumour vascularity-to-stroma ratio is a poor prognosis marker. We report preliminary results of a pilot study conducted to establish and validate dynamic contrast-enhanced (CE) magnetic resonance imaging (MRI) methodology for the non-invasive assessment of MPM tumour vascularity.

Methods 15 patients with suspected MPM were recruited prospectively. All had Pleural MRI (3T Siemens) 3–5 days prior to Medical Thoracoscopy (MT). Imaging protocols were developed utilising patients 1–6. In the remaining 9, T1-weighted VIBE images were acquired (single isotropic volume in the coronal plane) at baseline and 4.5, 9 and 13.5 min post-injection of Gadolinium contrast (0.1 mmol/kg). Signal Intensity (SI) was measured within 15 regions of interest containing representative tissues.
pleural tissue at each time point and summarised as Mean (+/-SD).

Pleural biopsies were obtained at MT in 8/9 patients who underwent complete CE-MRI. Paraffin-embedded tissue was available for 6/8 and stained with Factor VIII and CD34 immunostains. Blood vessel numbers and total vessel area were measured using quantitative image-analysis software (Leica Biosystems, U. K.) and correlated against contrast kinetic parameters (early SI increment (0–4.5 min) and peak SI), using Spearman’s test. Patients were followed-up in a specialist pleural clinic and survival recorded.

Results Mean age was 75 years (+/- 7). 93% (n = 14) were male. Final diagnoses were: MPM (n = 6), lung adenocarcinoma (n = 1), breast adenocarcinoma (n = 1), renal cell carcinoma (n = 1), Benign Asbestos Pleural Effusion (n = 4), rheumatoid arthritis-related effusion (n = 1) and haemothorax (n = 1).

Figure 1 demonstrates relationships identified between contrast kinetic parameters and tissue vascularity. Mean follow-up was 267 (+/- 149) days, over which time mortality for MPM patients exhibiting early peak CE was 100% (n = 2/2) vs. 0% (n = 0/1) for late peak CE (log rank p = 0.2).

Conclusions We have established a functional MRI protocol for use in MPM. Within the limitations of this pilot study, early CE kinetics appear to reflect pleural tissue vascularity. Further work is ongoing to fully assess the diagnostic, prognostic and predictive value of this imaging biomarker.
Abstract S46 Figure 1 Phagocytosis of unopsonised SA by blood neutrophils over 60 min

20), or Escherichia coli bioparticles (EC, n = 10) and fluorescently labelled disease-relevant bacteria, Haemophilus influenzae (HI, n = 10) and Streptococcus pneumoniae (SP, n = 10) was assessed, at regular intervals over 60 min, using flow-cytometry. Results were confirmed using time-lapse video microscopy.

Results Peak phagocytosis was achieved at 60 min for unopsonised bacteria and 30 min for opsonised bacteria. There were no differences in time to peak phagocytosis between bacterial species. Blood neutrophils from patients with COPD and HC displayed similar phagocytic ability, in both percentage of neutrophils with phagocytic activity and the amount of SA, EC, HI or SP ingested (as indicated by MFI) (COPD vs. HC, p > 0.05 for all). This was ubiquitous to both opsonin independent and opsonin-dependant phagocytosis, and was consistent across all time points measured. A typical comparison is shown in figure one, with unopsonised SA data.

Conclusions Phagocytic activity of blood neutrophils from patients with COPD to ingest Staphylococcus aureus, Escherichia coli, Streptococcus pneumoniae and Haemophilus influenzae is not altered compared to age-matched healthy controls. This should be replicated in lung neutrophils to assess whether transmigration to the tissues affects function.

S47

ENHANCED IL-6/CCL3 SIGNALLING IN THE PLASMA OF PATIENTS WITH COPD

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10.1136/thoraxjnl-2014-206260.53

Rationale IL-6 is a pro-inflammatory cytokine that signals through soluble (sIL-6R/gp80) and membrane bound (gp80) receptors to promote recruitment of mononuclear cells. IL-6 induces expression of CCL3, a monocyte chemokine. Monocytes are precursors of macrophages and dendritic cells. They can be classified into three subtypes according to surface expression of CD14 (LPS receptor) and CD16 (FgammaRIII): CD14++CD16-, CD14+CD16+, CD14-CD16++. We measured plasma levels of IL-6, sIL-6R and CCL3 and determined the chemokine receptor expression profile of circulating monocytes in COPD.

Methods 70 COPD patients and 30 healthy controls comprising 15 smokers (S) and 15 healthy non-smokers (HNS) underwent plasma sampling. Levels of IL-6, sIL-6R and CCL3 were determined by multiplex analysis (MSD) of plasma. Multi-colour flow cytometry was performed on whole blood obtained from 32 COPD patients, 8 S and 8 HNS to measure surface expression levels of chemokine receptors CCR1, CCR2, CCR7, CXCR1 and CX3CR1 on CD14++CD16-, CD14+CD16+ and CD14-CD16++ monocytes.

Results COPD patients had the greatest levels of IL-6 and sIL-6R. CCL3 was not detected in any controls, but was present in a subset of COPD patients. Surface expression of the CCL3 receptor CCR1 measured on CD14++CD16-, CD14+CD16+ and CD14-CD16++ monocytes of COPD patients was greater than those of HNS (p = 0.04). There were no significant differences in expression levels of other chemokine receptors.

Conclusions We report evidence of enhanced IL-6 signalling in the plasma of COPD patients and increased plasma CCL3 in a subset of individuals from this disease group. Furthermore, there was increased CCR1 expression on COPD monocytes. Enhanced IL-6 may co-ordinate the mononuclear component of the inflammatory response in COPD.

Abstract S47 Table 1

<table>
<thead>
<tr>
<th></th>
<th>COPD</th>
<th>S</th>
<th>HNS</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6 (pg/ml)</td>
<td>33.7(190.3)</td>
<td>3.8(1.9)</td>
<td>0*</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>sIL-6R (pg/ml)</td>
<td>5338(950.3)</td>
<td>4453(613.2)</td>
<td>4853(856.8)</td>
<td>p = 0.0005</td>
</tr>
<tr>
<td>CCL3 (pg/ml)</td>
<td>74.8(111.9)**</td>
<td>0*</td>
<td>0*</td>
<td>-</td>
</tr>
</tbody>
</table>

Data expressed as mean (SD) * lower limit of quantification of the assay **CCL3 levels registered above the assay’s lower limit of quantification in 7/70 COPD patients.

S48

AIR POLLUTION PARTICULATE MATTER PROMOTES DC MATURATION AND ENHANCES THEIR STIMULATION OF CD8 LYMPHOCYTE RESPONSES

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10.1136/thoraxjnl-2014-206260.54

Background High levels of ambient urban particulate matter (UPM), a component of air pollution, are associated with respiratory tract infections and exacerbations of airways diseases. Dendritic cells (DCs) exposed to inhaled UPM orchestrate the resulting immune response. We have previously shown that UPM-stimulation of DCs results in enhanced proliferation of naïve CD4 lymphocytes but decreased priming of IFNγ-producing CD4 lymphocytes. These CD4 lymphocytes are important in anti-viral immune responses; however, Tc1 CD8 lymphocytes have more direct anti-viral action. In this research we have studied the effect of UPM on DC priming of CD8 lymphocytes.

Methods CD11c peripheral blood DCs were isolated, cultured in the presence/absence of UPM stimulation, with GM-CSF or in medium alone. DC expression of CD83, CCR7, CD40 and MHC Class I were measured by flow-cytometry at 24 h. Pretreated DCs were also cultured with naïve CD8 lymphocytes in

Abstract S48 Table 1

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>UPM</th>
<th>GM-CSF</th>
<th>UPM + GM-CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFα (pg/ml)</td>
<td>77.6(60.2-256)</td>
<td>149(72.3-853)</td>
<td>904(148-1425)</td>
<td>241.1(434-4869)</td>
</tr>
<tr>
<td>IFNγ (pg/ml)</td>
<td>843(44.9-195)</td>
<td>225 (73.6-1537)</td>
<td>1009 (66.25-1477)</td>
<td>2343 (189-8726)</td>
</tr>
<tr>
<td>IL-13 (pg/ml)</td>
<td>25.9 (5.88-106)</td>
<td>59.0 (25.3-335)</td>
<td>939 (45.8-384)</td>
<td>638 (74.6-1266)</td>
</tr>
</tbody>
</table>
an allogeneic mixed-lymphocyte reaction (MLR). Lymphocyte proliferation (flow-cytometric measurement of CFSE) and cytotoxic killing (multiplex bead array) were assessed at day 5. The proportion of lymphocytes primed to produce IFNγ was measured at day 7 (intracellular staining).

**Results** UPM-stimulation increased DC expression of CCR7 (p = 0.008), and the production of IFNγ, TNFα and IL-13 by CD8 lymphocytes in MLR at day 5 (all p < 0.05; Table 1). The proportion of CD8 lymphocytes primed to produce IFNγ was also increased by UPM-stimulation of DCs (p = 0.034).

**Conclusion** No evidence of an impaired Tc1 response was seen with UPM-stimulated DCs, in contrast to our previous findings with CD4 T lymphocytes. This may be because CD8 lymphocytes are more primed to respond and produce cytokines at baseline. However, UPM-treatment of DCs did significantly increase DC expression of CCR7, which directs DCs to lymph nodes, and increased the priming of Tc1 and Tc2 responses in the absence of any other stimulation. Inhalation of UPM may give rise to pathological CD8 responses to otherwise innocuous novel antigens.

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**S49 TELOMERE ATTRITION IN CIRCULATING WHITE BLOOD CELLS IN COPD RELATES TO LUNG FUNCTION AND OUTCOMES**

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10.1136/thoraxjnl-2014-206260.55

**Introduction** Increasing evidence suggests accelerated ageing as a pathogenic mechanism in COPD. **Methods and results** Telomere length in circulating WBC, a marker of biological ageing, was assessed in 200 ex-smoker COPD patients (108 male, age 61.5 ± 6.4 years, FEV1 45.6 ± 17.1% predicted), 30 ex-smokers with normal lung function (27 male, age 59.9 ± 7.3 years, FEV1 109.1 ± 13.4% predicted) and 50 non-smoker healthy subjects (27 male, age 59.3 ± 8.3 years, FEV1 113.2 ± 13.1% predicted). TL was assessed by qPCR and expressed as relative T/S ratio.

TL was shorter in COPD (0.77 ± 0.2 relative T/S ratio) than in both ex-smokers (0.83 ± 0.2 relative T/S ratio) and non-smokers (0.84 ± 0.2 relative T/S ratio) (p < 0.05). Furthermore TL correlated negatively with age (r = -0.17, p = 0.007), emphysema score (r = -0.217, p = 0.001), number of exacerbations in the previous year to inclusion in the study (r = -0.129, p = 0.04), number of hospitalisations over 3 years follow-up (r = -0.167, p = 0.004) and positively with FEV1 (r = 0.135, p = 0.03) and arterial oxygen saturation (r = 0.161, p = 0.01). **Conclusion** COPD patients have evidence of premature ageing (shortened TL) compared to normal subjects irrespective of their smoking history. TL relates to FEV1, SaO2, exacerbation rate and hospitalisations.

The ECLIPSE study (GSK Study No. SCO104960, NCT00292352) was sponsored by GlaxoSmithKline.

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**S50 AIRWAY SMOOTH MUSCLE INFLAMMATION IS CONTROLLED BY MICRORNA-145 TARGETING OF SMAD3 IN COPD**

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10.1136/thoraxjnl-2014-206260.56

**Introduction and objectives** Airway smooth muscle cells (ASMCs) may contribute to the pathological airway inflammation and remodelling in COPD through the secretion of inflammatory cytokines and increased proliferation. Our previous work demonstrated that ASMCs from patients with COPD release greater amounts of IL-6 and CXCL8 compared to those from healthy subjects and are in a state of hyperproliferation. MicroRNAs (miRNAs) have recently emerged as important homeostatic regulatory molecules in COPD, and we have previously demonstrated the role of these in controlling ASMC proliferation in asthma. We hypothesise that microRNA-145 (miR-145) controls the aberrant phenotype observed in ASMCs from patients with COPD by targeting SMAD3, an important downstream signalling molecule of the TGF-β pathway.

**Methods** Human primary ASMCs were grown from individuals classified as being healthy non-smokers, healthy smokers, or those with COPD (n = 9 per group). Cells were stimulated with TGF-β and foetal calf serum, and miRNA and mRNA expression levels were measured by RT-PCR. IL-6 and CXCL8 release was measured by ELISA. Transfection of miR-145 mimics and inhibitors were used to model the effects of miR-145 over-expression and knock-down, respectively.

**Results** Low concentrations of TGF-β significantly upregulated SMAD3 expression in ASMCs from patients with COPD. Higher concentrations of TGF-β led to a suppression of SMAD3 expression, with a concomitant increase in miR-145 expression in these cells, to a greater degree than in healthy subjects.

Inhibiting miR-145 in ASMCs from COPD patients reduced the increased IL-6 and CXCL8 release and proliferation back to levels comparable to that of healthy individuals.

**Conclusions** This is the first time that miR-145 has been demonstrated to be important in controlling the increased inflammatory state of ASMC cells from COPD patients. This miRNA may not only act as a novel biomarker for COPD, but may also be a novel target for treatment.

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**S51 CIRCULATING DESMOSINE RELATES TO CARDIOVASCULAR COMORBIDITY, CORONARY ARTERY CALCIIFICATION SCORE (CACS), SYSTEMIC INFLAMMATION AND MORTALITY IN PATIENTS WITH COPD**

1Roberto A Rabinovich, 1Bruce E Miller, 1Karolina Wrobel, 1Gourab Choudhury, 1Kareema Ranjit, 3Ellen M Drost, 1Lisa E Edwards, 3David A Lomas, 3Stephen I Remond, 1Aivar Agusti, 2Ruth Tal-Singer, 1Jorgen Vestbo, 1Emiel Wouters, 1Edwin Van Beeck, 1John T Murchison, 1William MacNee, 1Jeffrey TJ Huang. 1Edinburgh Lung and the Environment Group Initiative (ELEGI), Centre for Inflammation and Research, Queens Medical Research Institute, Edinburgh, Edinburgh, UK; 1GlassoSmithKline, King of Prussia, Pennsylvania, USA; 1Medical Research Institute, School of Medicine, University of Dundee, Dundee, UK; 1Faculty of Medical Sciences, University College London, London, UK; 1Division of Pulmonary, Critical Care, Sleep and Allergy, University of Nebraska, Omaha, Nebraska, USA; 1ospital Clinic, IDIBAPS, Universitat de Barcelona and CIBER Enfermedades Respiratorias, FSB, Mallorca, Spain; 1Department of Respiratory Medicine, Odense University and University of Southern Denmark, Odense, Denmark; 1Department of Respiratory Medicine, Maastricht University Medical Centre, Maastricht, The Netherlands; 1Clinical Research Imaging Centre, Queens Medical Research Institute, Edinburgh, UK; 1Royal Infirmary of Edinburgh, Scotland, Edinburgh, UK

10.1136/thoraxjnl-2014-206260.57
Spoken sessions
Abstract S52 Table 1

Abstract S51 Figure 1 Differences in pDES between patients with
very high CACS and lower CACS levels (* p < 0.01)
Introduction COPD is a risk factor for cardiovascular comorbidities. Elastin degradation represents a shared mechanism for the
pulmonary and vascular features.
Methods and Results Plasma desmosine (pDES), a marker of
elastin degradation, was measured in 955 COPD patients (609
male, age 63.1 ± 7.2 years, FEV1 50.6 ± 15.1%predicted) by
an isotope dilution LC-MS/MS method. Coronary artery calcification (CACS), a surrogate of atherosclerosis, was assessed in
440 standard CT scan images (low 1000 AU).
Results pDES was elevated in patients with cardiovascular
comorbidities (p < 0.01) and correlated with FEV1 (r = 0.39, p
< 0.0001), MMRC (r = 0.16, p < 0.0001), 6MWD (r=-0.16, p
< 0.0001), BODE index (r = 0.10, p < 0.005), fibrinogen, IL6,
IL8, CCL18, and SPD but not with emphysema. These variables
showed significant higher values in the patients in the highest
pDES quartile. pDES was elevated in patients with very high
CACS in comparison with patients with lower CACS (Figure 1)
and in patients that died during a 3 year follow-up (p < 0.0001).
Conclusion pDES relates to lung function, systemic inflammation, cardiovascular comorbidities, and CACS in patients with
COPD. pDES is a predictor of all cause overall mortality.
The ECLIPSE study (GSK Study No. SCO104960,
NCT00292552) was sponsored by GlaxoSmithKline.

How does clinical respiratory physiology
help the clinician?
S52

IS A RAISED BICARBONATE, WITHOUT HYPERCAPNIA,
PART OF THE PHYSIOLOGICAL SPECTRUM OF OBESITYRELATED HYPOVENTILATION?

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and sleep-disordered breathing may or may not be included. OHS
patients have a higher morbidity, mortality, and health care utilisation compared with non-hypercapnic obese subjects. We hypothesised that in obese patients, even in the absence of a raised daytime
PaCO2, the presence of a raised plasma standard bicarbonate, or
base excess (BE, as a biomarker of whole body acid-base balance)
would be associated with some well-recognised features of OHS
(reduced ventilatory drives to hypoxia and hypercapnia, and nocturnal hypoventilation), thus suggesting they represent ‘early’ OHS.
Methods Obese subjects (BMI >30 kgs/m2) were identified from a
variety of sources, and divided into those with: 1) normal arterial
blood gases and normal acid-base balance, 2) an isolated raised
arterial BE (≥2 mmol/L), and 3) awake arterial hypercapnia (>6
kPa, i.e. established OHS). Two-point ventilatory responses to
hypoxia (15 min poikilocapnic response to 15% O2) and hypercapnia (15 min response to 5%CO2 in O2) were performed.
Derivatives included the fall in SaO2 and rise in end-tidal CO2
when stable, and conventional ventilatory drive calculations. Polygraphic sleep studies were done with the derivatives of intermittent
(oxygen desaturation index) and prolonged hypoxia (time below
90% SaO2) reported here.
Results 71 subjects (BMI 47.2, SD 9.8; age 52.1, SD 8.8) were
recruited into the above three groups (33, 22, and 16 respectively). The table shows the BMI, PaCO2 and BE for the three
groups, along with the selected derivatives of the ventilatory
drive measurements and sleep studies. For nearly all the ventilatory response and sleep study derivatives, group 2 (with only an
isolated raised BE) represented a middling group, and for some
of the measures this middle group was more similar to group 3,
with established OHS, rather than group 1.
Conclusion This study shows that obese individuals with raised
BE, but without awake hypercapnia, probably represent an intermediary stage towards overt obesity-hypoventilation syndrome.
Further studies will be required to establish if early intervention
for this group is beneficial.

S53

1

NEURAL RESPIRATORY DRIVE AND SYMPTOMS
LIMITING EXERCISE CAPACITY IN CHRONIC
OBSTRUCTIVE PULMONARY DISEASE

1

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King’s College London, London, UK; 2Guangzhou Medical College, Guangzhou, China;
3
Guy’s and St Thomas’ NHS Foundation Trust, London, UK; 4Addenbrookes Hospital,
Cambridge, UK; 5Royal Brompton and Harefield NHS Foundation Trust, London, UK
1

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Introduction Obesity Hypoventilation Syndrome (OHS) is conventionally defined by the combination of obesity (BMI >30 kg/m2) and
daytime hypercapnia (PaCO2 >6 kPa, with no other explanation)
Thorax 2014;69(Suppl 2):A1–A236

10.1136/thoraxjnl-2014-206260.59

A29


Introduction Exercise capacity in chronic obstructive pulmonary disease (COPD) is limited both by abnormal pulmonary mechanics, reported as breathlessness, and by leg muscle fatigue. To improve functional capacity it is important to understand the primary physiological constraint. Neural respiratory drive (NRD), measured using the diaphragm electromyogram expressed as a proportion of maximum (EMGdi%max), quantifies the load on the respiratory muscles imposed by abnormal pulmonary mechanics, and relates closely to breathlessness. We hypothesised that end-exercise EMGdi%max would be higher in patients stopping because of breathlessness than in those stopping because of leg fatigue. Methods EMGdi, ventilation (V̇e), oxygen consumption (VO₂) and ventilatory reserve (V̇e/MVV%) were measured in 23 COPD breathlessness (n = 12, EMGdi%max 75.7 (69.5 to 77.1)%) optimised by improving pulmonary mechanics rather than inter-costal spaces bilaterally. Mean peak root mean square EMG-diaphragm (EMGdi) was measured during five minutes of tidal breathing. Results EMGdi%max was higher in patients stopping because of breathlessness (n = 12, EMGdi%max 75.7 (69.5 to 77.1)%) than in those stopping because of leg fatigue (n = 8, EMGdi%max 44.1 (39.4 to 63.3)%, p < 0.05). There were no significant differences in end-exercise V̇e or VO₂, V̇e/MVV% tended to higher levels in the breathless group. Discussion These results suggest that patients limited by breathlessness due to ventilatory constraints can be identified as those reaching near-maximal levels of NRD during exercise. Measurement of EMGdi%max during exercise could prove useful in identifying patients whose functional performance would be best optimised by improving pulmonary mechanics rather than interventions to train peripheral muscle groups.

**S54 NEURAL RESPIRATORY DRIVE MEASURED USING PARASTERNAL INTERCOSTAL MUSCLE ELECTROMYOGRAPHY IN PATIENTS WITH INTERSTITIAL LUNG DISEASE**


Introduction Forced vital capacity (FVC) and gas transfer (TLCO) are often used to assess disease severity and monitor progression in patients with interstitial lung disease (ILD). Difficulty in performing the required manoeuvres, particularly in severe disease, and inherent measurement variability makes detection of clinically important changes difficult using these parameters. There is, therefore, a need for new biomarkers in this patient group. Neural respiratory drive (NRD) reflects the load on the respiratory system and the capacity of the respiratory muscles. Parasternal intercostal muscle electromyography (EMGpara) provides a non-invasive measure of NRD which relates to disease severity and breathlessness in obstructive lung diseases. Measurements of EMGpara in ILD could potentially quantify overall disease severity. Aim The aim of the study was to investigate the relationships between EMGpara, lung function, breathlessness, functional status and quality of life (QoL) in ILD. Method EMGpara was measured in 45 patients with a range of fibrotic lung diseases using surface electrodes placed in the second intercostal spaces bilaterally. Mean peak root mean square EMGpara per breath was calculated and expressed as a percentage of maximum EMGpara (EMGpara%max). The neural respiratory drive index (NRDI) was derived by multiplying EMGpara%max by the respiratory rate. Spirometry and lung gas transfer were performed and the composite physiologic index (CPI) calculated. Six minute walk test (6MWT) and 4 metre gait speed (4MGS) were used to determine functional status. Health-related quality of life was assessed with the King’s Brief Interstitial Lung Disease (K-BILD) and the St George’s Respiratory Questionnaires (SGRQ). The Base-line Dyspnea Index (BDI) was used to grade breathlessness. Results NRDI correlated significantly with VC%predicted (r = -0.36, p = 0.018) and the CPI (r = 0.40, p = 0.01) No significant correlations were found between EMGpara or NRDI and breathlessness, QoL or functional status. Conclusion EMGpara is a feasible measure in ILD. EMGpara correlates with prognostic markers suggesting potential value as a biomarker integrating important pathophysiological changes in lung mechanics in fibrotic ILDs. The lack of association with QoL measures and BDI requires further investigation.

**S55 NEURAL RESPIRATORY DRIVE USING PARASTERNAL ELECTROMYOGRAPHY IN CLINICALLY STABLE CYSTIC FIBROSIS PATIENTS: A PHYSIOLOGICAL MARKER OF LUNG DISEASE SEVERITY AND EXERCISE CAPACITY**


Introduction Measurement of neural respiratory drive, using parasternal intercostal muscle electromyography (EMGpara), has previously been shown to relate to pulmonary function impairment and exercise-induced breathlessness in advanced cystic fibrosis (CF). This measure reflects the load on the respiratory system and the capacity of the respiratory muscles and therefore may provide a composite measure of overall lung disease severity. In order to utilise EMGpara clinically in CF, its relationship to standard physiological outcome measures requires further investigation across a broad range of disease severities. Aim: To investigate the relationships between EMGpara and standard measures of pulmonary function and exercise performance in patients with CF. Methods Thirty patients with clinically stable CF were recruited. EMGpara was recorded during five minutes of tidal breathing using electrodes positioned in the second intercostal space directly lateral to the sternum. Peak EMGpara per breath was averaged over the final minute of the recording and expressed as a percentage of EMGpara recorded during a maximal inspiratory manoeuvre (EMGpara%max). Spirometry, lung volumes by body...
S56 DIFFERENCES IN FORCED OSCILLATION TECHNIQUE BETWEEN HEALTHY INDIVIDUALS, OBSTRUCTIVE SLEEP APNOEA AND OBESITY HYPOVENTILATION SYNDROME

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10.1136/thoraxjnl-2014-206260.63

Introduction Forced oscillation technique has been used to demonstrate expiratory flow limitation (EFL) by measurement of $\Delta X_n$. With the method of improving aerobic exercise performance in this group, there is poor understanding on the trajectory of changes in chronic obstructive pulmonary disease, however, this technique has not been widely used in the obese population. Obese individuals breathe at lower lung volumes and are therefore likely to develop EFL. We have previously demonstrated EFL occurs in individuals with obesity hypoventilation syndrome (OHS) but wished to determine if this also occurred in those with obstructive sleep apnoea (OSA) and compare differences between these groups.

Method Subjects with established OSA, OHS and healthy volunteers were recruited from the Lane Fox Respiratory Unit and Sleep Disorders Centre, St Thomas’ Hospital. Subjects underwent measurements of height, weight, spirometry and EFL (ResmonPro, ResTech, Milan, Italy).

Results Eleven healthy (HC), 8 OSA and 9 OHS subjects were recruited, age 23.6 ± 4.2, 31.4 ± 8.0 and 58.9 ± 10.4 years respectively. Body mass index (BMI): healthy subjects 17.9 ± 2.9; OSA group 41.4 ± 8.0; OHS group; 46.8 ± 9.3 kg/m², there were significant differences in BMI between the HC and OSA and OHS groups (p < 0.001) but no difference between OSA and OHS. Spirometry (FEV1, FVC): HC 3.54 ± 1.15, 4.35 ± 1.47, OSA 2.55 ± 0.85, 3.27 ± 1.03 OHS 2.04 ± 0.74, 2.58 ± 0.85. In both the OSA and OHS groups DXn increased with recumbency, as did the percentage of flow limited breaths (Table 1). Each group significantly increased their inspiratory resistance with the supine position compared to the upright seated position. There was a significant difference in DXn between HC and OHS only in upright, 45° and supine positions (p < 0.05). There was also a difference in the percentage of EFL breaths between HC and OHS in the 45° and supine positions and between OSA and OHS in the 45° position (p < 0.05).

Conclusion Patients with obesity and sleep disordered breathing experience EFL, which was more evident in the OHS group compared to the OSA group. This may be a consequence of their higher BMI impacting their lung volumes to a greater extent. Furthermore, the impact of position was greater in the OHS group suggesting that EFL may be a contributing factor in the development of hypercapnic respiratory failure in these individuals.

Abstract S56 Table 1 Differences in expiratory flow limitation, as demonstrated by $\Delta X_n$, between healthy controls, OSA and OHS

<table>
<thead>
<tr>
<th>Healthy controls</th>
<th>Obstructive Sleep Apnoea</th>
<th>Obesity Hypoventilation Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Upright Seated</strong></td>
<td><strong>45°</strong></td>
<td><strong>Supine</strong></td>
</tr>
<tr>
<td>$\Delta X_n$ (mH2O.L⁻¹)</td>
<td>-0.15 ± 0.13</td>
<td>0.04 ± 0.21*</td>
</tr>
<tr>
<td>% of EFL breaths</td>
<td>0 ± 0</td>
<td>0 ± 0</td>
</tr>
<tr>
<td>Inspiratory Reactance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$X_{res}$ (cmH2O.L⁻¹)</td>
<td>-0.55 ± 0.21</td>
<td>-0.67 ± 0.43</td>
</tr>
<tr>
<td>$X_{res}$ (cmH2O.L⁻¹)</td>
<td>2.71 ± 0.55</td>
<td>3.45 ± 0.66</td>
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<tr>
<td>$R_5$ (l/min)</td>
<td>-0.23 ± 0.18</td>
<td>0.04 ± 0.21</td>
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<tr>
<td>$R_T$ (l/min)</td>
<td>0.44 ± 0.04</td>
<td>0.45 ± 0.05</td>
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<tr>
<td>$R_T$ (l/min)</td>
<td>14.26 ± 7.06</td>
<td>13.5 ± 5.19</td>
</tr>
<tr>
<td>RR (bpm)</td>
<td>15.75 ± 1.99</td>
<td>17.9 ± 2.93</td>
</tr>
</tbody>
</table>

*Significantly different from seated position within group (ANOVA, p < 0.05).

Abbreviations: EFL=Expiratory Flow Limitation, VE=minute ventilation, RR=Respiratory Rate
made in exercise performance between COPD and Healthy controls (HC), during aerobic training and more importantly limited data exists on the rates of detraining between the groups.

**Methods** This study measures sub-maximal and maximal performance in response to an aerobic training programme and to a period of detraining.

COPD and HC undertook 8 weeks of supervised cycling exercise training three times a week. There consequently followed a 4 week period of detraining, and resumption of pre cycling habitual activity (not engaging in regular exercise). A symptom limited incremental cycle (ramp protocol) and constant work rate (sub-maximal/endurance) cardiopulmonary exercise tests (CPET) were performed at baseline, after 4 and 8 weeks of training and after detraining. Cycling training intensity and CPET endurance work were equivalent to 65% of the Work (in Watts (W)) at VO2 Peak during the baseline CPET ramp test. Training intensity was re-set if there was any improvement during the 4-week CPET ramp test.

**Results** 10 COPD patients (MRC 3, 2 males, age 74 years, FEV1 63.3% predicted) and 7 HC (MRC 1, 4 males, age 71 years, FEV1 111% predicted) completed the study. COPD group had lower starting training workloads (59.5 vs 121 Watts, p<0.05) compared to HC. HC showed a significant increase in Peak VO2 uptake in the ramp but COPD patients only showed an increasing trend. There were however increases in the time achieved during sub-maximal testing in both groups during the 8 week training period. However during detraining, there was relative preservation in the HC but a significant reduction in endurance time in the COPD group.

**Conclusion/discussion** Exercising training at moderate intensities showed no changes in maximal performance in COPD groups, compared to HC. However gains in sub-maximal performance were seen in both groups. Training induced gains in sub-maximal performance may be better preserved in HC during detraining, when compared to the COPD groups.

Abstract 557 Figure 1  Sub-Maximal Test

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**Spoken sessions**

**Latent TB and biomarkers**

**558** PROSPECTIVE HEALTH ECONOMIC EVALUATION OF DIFFERENT RECOMMENDED STRATEGIES FOR TB TESTING IN A CONTEMPORARY HIV POSITIVE COHORT

"J Capocos, 1L Sewell, 2C Smith, 1C Cropley, 1S Bhagani, 1S Morris, 1M Johnson, 1MCI Lipman. 1Royal Free London NHS Foundation Trust, London, UK; 2University College London, London, UK"

10.1136/thoraxjnl-2014-206260.64

**Introduction** The risk of active tuberculosis (TB) disease is estimated to be increased 40-fold in people with HIV (PHIV). Effective antiretroviral treatment (ART) may reduce this significantly. UK national guidance recommends using blood interferon gamma release assay (IGRA) +/- tuberculin skin testing (TST) for latent TB (LTBI) diagnosis but there are little supporting health economic data. We sought to evaluate the cost-effectiveness of different testing strategies using data from a prospective contemporary cohort.

**Methods** Subjects receiving ambulatory HIV care were recruited by stratified selection within our HIV centre. TST, IGRA (TSpot, TB), frontal chest radiograph (CXR) and single induced sputum for mycobacterial culture were performed. The yield was used to model a screening programme that utilised current UK HIV demographics (Public Health England). Costs were based on the BNF, local costs or published literature (TST £16, IGRA £60, CXR £50, induced sputum £42, treatment for latent and active TB £786 and £7619 respectively). Uptake and LTBI treatment efficacy were both estimated at 65%. We assumed a lifetime reactivation rate with TST+/IGRA+ of 10% and TST+/IGRA- of 2%; and that all those with evidence of LTBI would be given treatment.

**Results** Over 13 months, 211 people were recruited. 26% were female and 26% black African. LTBI rates amongst subjects from sub-Saharan Africa, medium and low TB incidence countries were 8/55 (15%), 2/31 (6%) and 4/125 (3%) respectively. One patient had a persistently indeterminate IGRA. Subclinical TB disease was diagnosed in two (1%) subjects.

Using these data to model TB testing nationally, the British HIV Association (BHIVA) testing algorithm was the most cost-effective with an incremental cost effectiveness ratio (ICER) of £21,475. The NICE algorithm both cost more and prevented fewer cases of active TB (Table 1). More comprehensive strategies were associated with increasing cost.

**Conclusion** Testing only those at highest risk of progression to active TB disease in an HIV population with high ART use was cost-effective, whilst most strategies testing all comers and for active TB cost considerably more than the £20–30,000/QALY gained threshold used in the UK.

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**EVALUATING THE CLINICAL UTILITY OF XPERT® MTB/RIF FOR THE DIAGNOSIS AND MANAGEMENT OF TUBERCULOSIS IN A HIGH BURDEN REGION OF THE UK**

"J Kim, B O’Connor, H Patel, N Perera, M Wiseoka, G Woltmann, P Haldar. University of Leicester, Leicester, UK"

10.1136/thoraxjnl-2014-206260.65

**Introduction** The importance of Xpert® MTB/RIF (GeneXpert) for the rapid confirmation of tuberculosis (TB) and indicator for drug resistance is now well established for high burden, resource poor countries, with a high prevalence of smear positive pulmonary disease. The phenotype of disease differs significantly in high income countries like the UK with fewer smear positive cases and more extra-pulmonary disease. The role of GX in this setting is unclear.

**Objectives** To evaluate how GeneXpert was being used in local practice and determine factors that influenced test performance.

**Methods** We performed a retrospective analysis of all GeneXpert tested patient samples between October 2011 and April 2014. Our area sample requests and unprocessed specimens were excluded. Positive GeneXpert results were categorised as very low, low, medium and high. Sensitivity and specificity analyses excluded clinically diagnosed TB without supporting evidence and stratified samples by type and smear status. Statistical analyses were computed on SPSS (v.16)."
Results 217 assays from 193 patients were included for analysis. 101 patients (52%) were treated for TB (74 pulmonary). A clinical diagnosis of TB was made in 14 patients. 145 samples (68%) were from the respiratory tract. The remainder were categorised as: fluid (44); tissue (15) and pus (9). Overall 68 (32%) samples were AFB smear positive and 111 (52%) samples were mycobacteria culture positive (80 *M. tuberculosis*). There were 78 (36%) GeneXpert positive results. The assay had superior performance for diagnosis of TB and predicting *M. tuberculosis* culture positive outcomes in AFB smear positive compared with smear negative samples (table). For smear negative, culture positive samples, false negative GeneXpert results were associated with a significantly longer time to culture (mean difference 10.4 days, p = 0.006). For smear negative GeneXpert positive samples, the mean time to positive diagnosis was reduced by 13.3 days but this did not alter the time to starting treatment.

Conclusion In our practice, GeneXpert has high specificity to reliably inform a positive TB diagnosis but lacks sensitivity in smear negative disease to reliably exclude the diagnosis. The decision to start treatment continues to be governed by clinical suspicion in this group.
**Background**

There are high rates of active tuberculosis (TB) in London’s hard to reach groups (homeless people, substance misusers and prisoners). However no systematic data are available regarding the prevalence of latent TB infection (LTBI) and blood borne viruses (BBVs) within homeless hostels, drug services and a prison in London. We also investigated management outcomes in those referred on to healthcare services.

**Design/method**

Recruitment took place from May 2011–June 2013. Service users screened for TB on a mobile chest x-ray unit and in prison using the static digital x-ray machine were approached and, with consent, blood was drawn for IGRA (Quantiferon In-Tube) and HIV, HCV and HBV. Results were provided to participants with onward referral to healthcare services in line with current guidance. Treatment outcomes were collected via telephone follow up one year post referral for the positive cases.

**Results**

Prison (n = 511) (Table 1)

LTBI: 65(13%) participants were IGRA positive [3(5%) co-infected with HCV]. Of these, 37(57%) were referred for preventive treatment, 16(43%) did not attend (DNA) appointments and were discharged or were lost to follow up (LFU). Of the 15 who commenced treatment, 9(60%) completed treatment.

HCV: 22 participants were positive and referred, of which 11 (50%) DNA/LFU, 11(50%) were under review and none commenced treatment.

HBV: 10 participants were positive, of which 6(60%) DNA/LFU, 4(40%) were under review and none commenced treatment.

There were no HIV positives.

**Conclusion**

The prevalence of LTBI, BBVs and co-infection within the hard to reach group is high compared to the general population with fewer patients starting TB prophylaxis/HCV treatment. The high overall rates of DNA/LFU (47%) seen indicate that current approaches to onward referral and retention in care for this group appear to be poor and effective measures to improve engagement with clinical services are essential.

This study was supported by NIHR Programme Grant for Applied Research (RP-PG-0407–10340).

**RISK FACTORS FOR IGRA POSITIVITY IN CONTACTS OF ACTIVE TUBERCULOSIS IN A UK HIGH-PREVALENCE SETTING**

AC Repossi, RD Turner, GH Bothamley. Homerton University Hospital NHS Foundation Trust, London, UK

10.1136/thoraxjnl-2014-206260.68

**Background**

Interferon-gamma release assays (IGRAs) are being used to confirm significant exposure to tuberculosis (TB) after a positive tuberculin skin test (TST). We explored the variability...
of a positive test in a large UK TB clinic amongst contacts of active disease.

Methods The records of all individuals notified with active TB and of their screened contacts from 2012–3 were reviewed retrospectively. Uni- and multivariate analysis identified variables associated with active TB and/or QuantiFERON® test positivity in contacts.

Results Of 203 notified tuberculosis index cases, 470 contacts were screened. 116 had immunological evidence of TB exposure including 11 with active disease. The estimated background rate of positive TB immune response was 18% and was the same in contacts of index cases who were later denotified (7/39) as in contacts of extrapulmonary disease (24/132).

On univariate analysis, index case variables associated with a positive TST and IGRA were a pulmonary vs. extrapulmonary site of disease (OR 2.1; 95% confidence interval 1.3–3.5) and, for contacts of pulmonary TB (PTB), presence of cough (2.5; 1.1–4.0), duration of cough (p = 0.04), sputum smear positivity (1.7; 1–2.8), sputum smear grade (p = 0.02), radiographic extent of disease (p = 0.008), and perhaps pulmonary cavities (1.6; 1–2.6). No effect was detected of gender, smoking status, or TB strain of the index case (Beijing or Cameroon vs. other lineage), or nature of contact (household vs. other), even when considering only child contacts.

Contact variables associated with positive tests were birth in a high TB prevalence country (2.3; 1.3–4.0), age ≥12 years (2.0; 1.2–3.3), smoking (2.2; 1.0–5.1) and perhaps alcohol excess (3.2; 0.9–10.7), but not diabetes or BCG vaccination. There were insufficient data to investigate an effect of HIV and homelessness. Contact country of birth (1.9; 1.1–3.1) and index site of disease (2.0; 1.2–3.4), sputum smear positivity (2.6; 1.3–5.6) and radiographic extent of disease (p = 0.008) remained significant on multi-variate analysis.

Conclusion The likelihood of significant TB exposure is a consequence of bacillary load, radiographic extent of disease and coughing behaviour.

Introduction In screening for tuberculosis (TB), we need to distinguish between active and latent TB. In those with a positive interferon-gamma release assay (IGRA) additional tests are required to identify active TB. Proteomic fingerprinting suggested that four proteins (C-reactive protein (CRP), transthyretin, neopterin, and serum amyloid A (SAA)) might be able to distinguish active from latent disease.1

Methods Patients were grouped to reflect different stages of infection and those with latent TB were followed for over eight years. These groups were: 1) Smear-positive TB (n = 20), 2) Smear-negative/culture-positive TB (n = 12), 3) Recent TB contacts with positive interferon-gamma release assay (IGRA) (n = 15), and 4) No TB detected with firm alternative diagnosis (n = 12). All patients in groups 1 to 3 and 25% of group 4 were IGRA positive. Serum samples were collected and enzyme-linked immunosorbent assays (ELISAs) were performed to measure C-reactive protein, transthyretin, neopterin, and serum amyloid A found in the serum samples from each group. Standard cut-off values were used for each protein and results labelled as either positive or negative. Chi-square calculations were used to determine the significance of the results in differentiating between active TB, latent TB, and absence of TB infection.

Abstract S63 Table 1

<table>
<thead>
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<th>Investigation</th>
<th>Smear-positive TB</th>
<th>Smear-negative/culture-positive TB</th>
<th>Recent contact/IGRA positive</th>
<th>TB considered but firm alternative diagnosis reached</th>
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<tbody>
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<td>IGRA positive</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>25</td>
</tr>
<tr>
<td>C-reactive protein (&gt;5 mg/L)</td>
<td>100</td>
<td>90</td>
<td>33</td>
<td>50</td>
</tr>
<tr>
<td>Transferrin (&lt;200 mg/L)</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>92</td>
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<tr>
<td>Serum amyloid A (&lt;80 mg/L)</td>
<td>100</td>
<td>100</td>
<td>66</td>
<td>66</td>
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<tr>
<td>Neopterin (&lt;10 nmol/L)</td>
<td>100</td>
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</table>
Clinical trials and outcome measures in paediatric lung disease

Eosinophil cationic protein and cytokine analysis in exhaled breath condensate in paediatric asthma

Background Sputum eosinophil counts are unstable in childhood asthma. This makes sputum induction to quantify sputum eosinophils an unsuitable test to guide anti-inflammatory therapy.

While eosinophils may be cleared following apoptosis, free eosinophil granules, containing effector proteins, may persist in the airway lumen. We speculated that inflammatory mediators in exhaled breath condensate, released by eosinophils (such as eosinophil cationic protein (ECP)) could aid risk-profiling in children with asthma. We therefore sought to assess whether ECP is present in EBC from asthmatic children, alongside an assessment of pro-inflammatory cytokines.

Methods Children with asthma aged 7–15 and age matched healthy controls underwent spirometry, sputum induction, collection exhaled breath condensate (EBC), and completed the childhood asthma control test. Exhaled breath was tested for eosinophil cationic protein (ECP) using an immunoassay. A cytokine analysis of the exhaled breath condensate was also carried out in addition to a sputum leucocyte differential.

Exhaled breath condensate (EBC) was collected in an R-tube following manufacturer protocol,over 10 min.

Results Sputum leucocyte counts were performed in 33 children with asthma. Suitable samples (visible airway plugs) were obtained from 14 children at baseline who concurrently provided EBC samples. Of these, 7/14 (50%) were eosinophilic and 7/14 (50%) were non-eosinophilic. The cytokine analysis showed that IL-4 did not differ between groups. IL-13 was raised in children who had sputum eosinophilia (2.54 ± 1.18 vs. 0.87 ± 1.49 pg/ml, mean±sd, p = 0.0387, unpaired t-test).

Exhaled breath condensate was collected in 26 asthmatic children and 10 controls. ECP was detected in EBC from 5/26 asthmatic children and 0/10 healthy children. In 2 asthmatic children, detectable ECP was associated with sputum eosinophilia (>2.5%). In one child ECP was detectable with no induced sputum eosinophils. (Table 1).

Discussion ECP may be identified in EBC from children with asthma, and is not exclusively associated with concurrent sputum eosinophilia. Eosinophilia may be identified non-invasively by measuring Th2 cytokines in EBC. These techniques may provide additional insights into underlying airway inflammation and identify children who may benefit from specific anti-Th2 cytokine monoclonal antibody therapies.

REFERENCES

Abstract S64 Table 1 Eosinophil cationic protein (ECP) assay using exhaled breath. The threshold for detection in the assay was 50.7 pg/ml

<table>
<thead>
<tr>
<th>Patient</th>
<th>Mean ECP (pg/ml)</th>
<th>Sputum Eosinophils (%)</th>
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<tr>
<td>Child 1</td>
<td>65 (unknown)</td>
<td></td>
</tr>
<tr>
<td>Child 2</td>
<td>505</td>
<td>18.96</td>
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<tr>
<td>Child 3</td>
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<td>Child 4</td>
<td>1113</td>
<td>0.21</td>
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THE GLI SPIROMETRY REFERENCE EQUATIONS INFLUENCE THE APPARENT RATE OF DECLINE IN FEV1 AMONG CHILDREN AND ADOLESCENTS WITH CYSTIC FIBROSIS

1GD a v i e s ,1PA u r o r a ,2AM c D o n a l d ,3A Prasad, 4D Bilton, 1J Stocks, 2S Stanojevic.

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10.1136/thoraxjnl-2014-206260.72

Abstract S66 Figure 1 (A) Urine 15dPGJ2 at baseline is significantly lower in children who have an asthma exacerbation within 3 months. (B) ROC curve for 15dPGJ2. ROC AUC=0.858, p=0.005. PG:prostaglandin. Bar represents median, comparison by Mann-Whitney test. *p=0.01.

Background In patients with cystic fibrosis (CF), interpretation of cross-sectional FEV1 data is greatly influenced by choice of spirometry reference equation, particularly during childhood (Stanojevic; J Cyst Fibros 2014). We hypothesised that availability of the Global Lung Function Initiative (GLI) spirometry reference equations (Quanjer; ERJ 2012) will also affect the apparent rate of decline in lung function over time, thereby potentially altering our understanding of disease progression in CF.

Methods Data were extracted from two patient registries: the UK CF Registry (n = 6043 subjects; 20,013 test occasions over a period of 5 years) and the Toronto CF database (n = 1023 subjects; 27,868 test occasions over a period of 23 years). Spirometric outcomes were interpreted using%predicted FEV1 calculated from GLI, Knudson (as currently used by the UK CF Registry), and Wang-Hankinson (as used by the US CF Foundation) reference equations. Patients >30 yrs or with FEV1 > 130% predicted were excluded. We used a non-linear mixed effects model to describe the average change in FEV1 with age. To illustrate the importance of reference equation in evaluating risk factors, FEV1 decline according to patient gender was also explored.

Results The pattern of lung function decline at the population level differed according to selected equation (Figure). Average rate of decline was steeper with Knudson or Wang-Hankinson than GLI. Importantly, GLI equations showed a steady decline in FEV1 starting at 6 yrs, whereas the other equations suggest greater decline during adolescence. Similar patterns were observed in both UK and Toronto populations. When analysed according to gender, the rate of lung function decline was steeper in females during early adolescence compared with males where the decline was steady.

Conclusions In both datasets, Knudson and Wang-Hankinson reference equations suggest relative preservation of spirometry in childhood followed by rapid decline in adolescence. However using the more robust GLI equations, steady decline throughout childhood with a less dramatic acceleration during adolescence is seen, with differences in pattern of change over time according to patient gender. Accurate identification of critical periods of lung function decline offers novel opportunities to target care.

Funded by the UK CF Trust.

LUNG CLEARANCE INDEX (LCI) IS A SENSITIVE PREDICTOR OF HIGH RESOLUTION COMPUTED TOMOGRAPHY (HRCT) SCORES IN CHILDREN WITH NON-CF BRONCHIECTASIS

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10.1136/thoraxjnl-2014-206260.73

Introduction and objectives LCI is a sensitive predictor of early cystic fibrosis (CF) lung disease, and correlates with HRCT better than spirometry (Thorax. 2008;63:129–134). The same is true in adults with non-CF bronchiectasis (Am J Respir Crit Care Med. 2014;189:586–592.), but by contrast, in PCD there were no relationships between LCI, HRCT or spirometry (Am J Respir Crit Care Med. 2013;188:545–549). It is unclear whether these differences reflect primary versus secondary cilary dyskinesia, or CFTR versus non-CFTR disease. We hypothesised that in children with non-CF bronchiectasis, relationships between spirometry, LCI and HRCT will be similar to those in CF children and non-CF bronchiectasis adults, rather than PCD patients.

Methods 12 children with non-CF bronchiectasis performed LCI and spirometry and underwent thoracic HRCT. HRCT scans were scored quantitatively (Thorax. 2013;68:532–539). Results were compared with those from large CF (n = 125) and PCD (n = 38) cohorts.

Results In non-CF bronchiectasis there was a correlation between first second forced expired volume (FEV1) and LCI (p = 0.009, r=-0.6), similar to that seen in CF (p < 0.0001,
Abstract S67 Figure 1 Correlation between LCI and FEV1 in children with non-CF, non-PCD bronchiectasis (A), CF (B) and PCD (C)

r = -0.6) but not in PCD (Figure). In non-CF bronchiectasis LCI was more significantly correlated with HRCT (extent and severity of bronchiectasis (p = 0.002, r = 0.8 and p = 0.01, r = 0.7 respectively), airway wall thickening (p = 0.01, r = 0.7) and air trapping (p = 0.0006, r = 0.8)) than was spirometry (only correlation with air trapping (p = 0.03, r = -0.6)). As shown previously, there were good correlations between HRCT and LCI in CF, but in PCD only air trapping correlated with LCI, and there were no correlations with FEV1.

Conclusions LCI is a good marker of structural lung disease in children with non-CF bronchiectasis and is more sensitive to HRCT abnormalities than spirometry, similar to adults, and CF at all ages. This suggests the different relationships seen in PCD result from the effects of primary versus secondary ciliary dyskinesia rather than CFTR versus non-CFTR lung disease. LCI may be useful in monitoring children with non-CF bronchiectasis, but this needs to be confirmed longitudinally. The results illustrate the importance of not extrapolating between different airway diseases.

THE HI-FLO STUDY: A PROSPECTIVE OPEN RANDOMISED CONTROLLED TRIAL OF HIGH FLOW NASAL CANNULA OXYGEN THERAPY AGAINST STANDARD CARE IN BRONCHIOLITIS

C Hathorn, G Ernst, S Hasan, D Wong, M Seear. British Columbia Children’s Hospital, Vancouver, Canada

Introduction High flow nasal cannula (HFNC) oxygen therapy is increasingly used as a form of respiratory support with limited evidence to support its use. Data from retrospective studies suggest that HFNC reduces rates of intubation and respiratory parameters in infants with bronchiolitis. It is well-tolerated, easy to use, and has very few adverse effects.

Objective To determine if HFNC therapy reduces work of breathing, oxygen requirement and time to resolution of respiratory distress more quickly than standard care in bronchiolitis.

Methods We conducted a prospective open randomised controlled trial to compare HFNC oxygen therapy with standard care for children with bronchiolitis in ward environments in a tertiary referral children’s hospital over a two-year study period. Patients under 18 months of age with a clinical diagnosis of bronchiolitis were eligible. Subjects were randomised to standard supportive care with low flow oxygen (up to 2 litres/minute) or HFNC oxygen at 8 litres/minute. Fractional inspired concentration of oxygen was titrated to maintain saturations >92%. A validated composite clinical score (modified Tal) was measured every 3 h.

Results 72 patients were recruited, 36 in each treatment arm. The mean age of subjects was 4 months, range 0.5–12.9 months. 42% were male, and all but two were born at term. 79% were RSV positive. 3 patients in the control group, and 4 in the intervention group required admission to intensive care. There was no improvement in time to resolution of respiratory distress or oxygen requirement in patients receiving HFNC oxygen therapy. There was a trend towards lower clinical scores in the first 3 h following initiation of treatment in the intervention group. There were no adverse effects from HFNC therapy, and it was found to be safe in a ward environment.

Conclusion HFNC oxygen therapy may improve clinical parameters during the first hours of treatment, but it did not significantly reduce time to resolution of respiratory distress or oxygen requirement.

REFERENCE


Lung cancer: how are we doing and what’s next?

THE NATIONAL LUNG CANCER AUDIT

S68 RISING STANDARDS OF CARE CONTINUE IN YEAR 9 OF THE NATIONAL LUNG CANCER AUDIT

P Beckett, A Yelland, J Wootton, MD Peake. Royal College of Physicians, London, UK; Information Centre for Health and Social Care, Leeds, UK

Introduction The National Lung Cancer Audit, now in its 9th year, is run jointly by the Royal College of Physicians and The Information Centre for Health and Social Care (HSCIC), and commissioned by the Healthcare Quality Improvement Partnership (HQIP). Over this period, the rich data of increasing quality has charted improving standards of care for patients, as well as persistent variation across organisations which in most cases is independent of case-mix.

Methods Although several other countries also submit data to the audit, this abstract presents provisional results for England only for patients first seen in 2013.

Results 30,508 patient records were submitted with more than 93% having performance status and the same number having disease stage recorded (see Table 1). Spirometry is available for 65% of Stage I-II/PS 0–1 NSCLC patients, allowing more detailed risk-adjustment to be carried out in future. The histological confirmation rate remains steady at 75%, and the proportion with non-subtyped NSCLC continues to fall. There has been a small but incremental rise in the resection rate in histologically-confirmed NSCLC which now stands at 23%, and in the proportions of patients with SCLC receiving chemotherapy (70%). Patient access to specialist nurses appears to have improved but demonstrates a continuing unmet need. The proportion having CT scan before bronchoscopy continues to rise (91%) as does the proportion having chemotherapy for locally advanced NSCLC with good PS (60%). Variation in practice still exists – for example, the resection rate in Stage I-II NSCLC varies from 46% to 66% across the cancer networks, although the range is narrower than the previous year (35% to 62%).

Our final presentation will contain further analyses of survival across the audit lifespan.

Conclusions In contrast to the early years of the audit where standards of care appeared to improve rapidly and were partly related to improvements in data quality, recent years have shown only small incremental improvements. A reconfiguration of the
audit as part of a new commissioning process, and the linkage with other developing datasets will allow the project to continue to realise the goal of improved and less variable outcomes and for patients with lung cancer.

S70 RESULTS FROM THE FIRST NATIONAL LUNG CANCER ORGANISATIONAL AUDIT


10.1136/thoraxjnl-2014-206260.76

Background National Lung Cancer Audit reports consistently demonstrate variation in diagnostic pathways, treatment rates and outcomes which are not wholly explained by case-mix. One possible explanation for this variation is different access to diagnostics and treatment specialists, however little is known about the provision of these services across England and Wales lung cancer services.

Methods An electronic survey was sent to all lung cancer lead clinicians in England and Wales in January 2014. The survey included seven questions for all MDTs on service provision, diagnostic services, staging services, and lung cancer treatment. There were a further 3 questions for treatment centres. Two reminders were sent and the survey closed in May 2014.

Results 128 records were submitted from 176 trusts. After removal of duplicate and empty records 101 were available for analysis. Mean (range) average number of patients discussed per MDT meeting is 26 (5–88) and 29% Trusts have a separate diagnostic service. Mean (range) average number of patients discussed per MDT meeting is 26 (5–88) and 29% Trusts have a separate diagnostic service.

Process and Outcomes

<table>
<thead>
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<th>Data Completeness</th>
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<td>20,639</td>
<td>25,757</td>
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<td>89%</td>
<td>91%</td>
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<td>77%</td>
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<td>Treatment</td>
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<td>72%</td>
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<td>89%</td>
<td>89%</td>
<td>91%</td>
<td>91%</td>
<td>92%</td>
</tr>
</tbody>
</table>

Conclusion The data provide a moderately representative snapshot of diagnostic and treatment services available for lung cancer patients in England and Wales. There is significant variation in the number of specialists available and some patients do not have access to key treatment modalities e.g. VAT lobectomy. Further work is required to determine how this relates to patient experience and outcomes. All Trusts are encouraged to submit validated data for the next round of organisational audit.

S71 ARE QUALITY STANDARDS AND ACCREDITED CENTRES FOR MEDIASTINAL STAGING WITH EBUS NEEDED? A REPORT FROM THE MANCHESTER CANCER EBUS GROUP

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10.1136/thoraxjnl-2014-206260.77

Introduction Mediastinal staging in lung cancer is a core function of EBUS-TBNA. There has been an explosion of EBUS-TBNA services across the UK over recent years. However, quality standards and adherence to such standards are not widely known. The aim of this study was to describe the current practice of four independent EBUS centres serving a large UK cancer network.

Materials and Methods In 2012, the number of centres providing EBUS-TBNA in this Network increased from one to four. This prompted the development of an EBUS sub-group and service specification that mandates the collection of pre-defined data for all EBUS procedures. Analysis of this prospective maintained database was undertaken for this report.

Results 741 lung cancer patients underwent EBUS-TBNA in the study period. 56.4% (418/741) were for nodal staging, with the remaining performed for pathological confirmation of lung cancer. The proportion of staging procedures performed at each centre varied significantly (range 4.8% - 80.3%, p < 0.0001). In those patients undergoing EBUS for mediastinal staging, the average number of lymph stations sampled per procedure varied from 1.3 to 1.9 across the four centres and the proportion of...
S72  CLINICAL PREDICTION MODELS FOR MALIGNANCY IN SOLITARY PULMONARY NODULES – A VALIDATION STUDY IN A UK POPULATION

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Background  Management of solitary pulmonary nodules (SPNs) depends critically on the pre-test probability of malignancy. Several quantitative prediction models have been developed using clinical and radiological criteria. Three models include CT criteria (Mayo, Veterans Association, Brock University) with a fourth model (Herder) incorporating FDG avidity on CT-PET scan in addition. These models have not been validated in a UK population, and the current study aimed to compare their performance in a population of patients recruited from a UK teaching hospital.

Methods  Patients with SPNs (4–30 mm) were retrospectively identified from the lung cancer MDT and a nodule follow-up clinic (n = 246). All patients had a final diagnosis confirmed by histology or radiological stability on a 2-year follow up. For each patient, the probability of the pulmonary nodule being malignant was calculated using the four models described. The models were used both in a restricted cohort of patients based on their respective exclusion criteria, and in the total cohort of patients. The accuracy of each model was assessed by calculating the area under the receiver operating characteristic (ROC) curve.

Discussion  There is variability in practice in all parameters of EBUS practice examined in our Network, in the absence of agreed standards and protocols for mediastinal staging. Such protocols and standards have now been agreed and implemented across our Network and the EBUS sub-group is committed to ongoing data collection and publication to drive quality outcomes in this pivotal lung cancer service.

Abstract S72 Figure 1  Malignancy prediction models comparison

S73  INFRARED SPECTROSCOPY FOR THE DETECTION OF EXTENDED FIELD CARCINOGENESIS: A NEW PARADIGM FOR LUNG CANCER SCREENING?


Background  Computerised Tomography (CT) has been shown to be the only lung cancer screening modality to be effective in reducing lung cancer specific mortality. 1 A minimally invasive technique to stratify those at greatest risk within the population of adult smokers may help to target CT screening more effectively.

Rationale  Tobacco smoke exposure causes a field of injury to the Airways (including nose and mouth) that if detected may inform an individual’s risk of lung cancer. 2 Infrared spectroscopy (IR) is a technique that can detect subtle biochemical alterations in macroscopically normal cells.

Methods  Buccal cells were exfoliated from 76 patients including 38 smokers without and 38 with lung cancer (matched for age, gender and pack years). The cells were fixed onto IR windows and spectra recorded using synchrotron radiation (Diamond facility, Oxford). Data was acquired using x36 objective and 15 × 15 μm aperture in transmission mode; 256 interferograms at 4 cm⁻¹ resolution were recorded for 50 cells per sample. All samples analysed were confirmed to be cytologically normal. Outlying data was removed using principal component analysis and a prediction model built using partial least squares discriminant analysis.

Results  Smokers with lung cancer could be differentiated from matched smokers without lung cancer with a diagnostic accuracy of 80%. The spectral region showing greatest difference between groups was in the 1200–900 cm⁻¹ region; comparison to reference spectra shows that this is likely to represent a metabolic change caused by an increased abundance of glycogen or its derivatives.

Conclusions  We have shown for the first time that IR spectroscopy of macroscopically normal upper respiratory tract cells may have a role to play in the early detection of lung cancer. Future work will validate these findings and aim to develop this.
CIRCULATING TUMOUR CELLS IN PERIPHERAL AND PULMONARY VENOUS BLOOD PREDICT POOR LONG-TERM SURVIVAL IN SURGICALLY RESECTED NON-SMALL CELL LUNG CANCER PATIENTS

1ZD Liu, 1SF Xu, 1RD Zhang, 1YS Li, 1Y Han, 1CY Su, 1Z Chen, 1H Wang, 1SK Liu, 1QY Zhao, 1S Zhou, 1DZ Zhen, 1DF Yu, 1N Xiao, 1XY Song, 1M Qin. 1Beijing Chest Hospital, Capital Medical University, Beijing, China; 2Beijing Children’s Hospital, Capital Medical University, Beijing, China; 3Clinical Genomics Unit, Head and Neck Surgery Branch, National Institute on Deafness and Communication Disorders, National Institutes of Health, Bethesda, Maryland, USA; 4Ludespei Hematology Oncology Center, Hebei, China

10.1136/thoraxjnl-2014-206260.80

Background We tested the hypothesis that the circulating tumour cells (CTCs) in preoperative peripheral blood (PPB) and intraoperative pulmonary venous blood (IPVB) could predict poor long-term survival in surgically resected NSCLC patients.

Method CTCs were separated from the blood using magnetic beads coated by antibody against epithelial-cell adhesion molecule (EpCAM) through magnetic activated cell sorting (MACS). The CTCs were quantified with fluorescence labelled antibodies against pan-cytokeratin through flow cytometry. CTCs were prospectively quantified in PPB and IPVB in 23 consecutive stage I-IIIA patients with surgically resected NSCLC. Association between CTCs and prognosis of these patients was evaluated after 5-year follow-up.

Results In the NSCLC patients, outcomes were assessed according to levels of CTCs at surgery, and compared with CTCs detected in benign pulmonary diseases, and healthy volunteers, where the mean and 95% CI of CTCs counts were all 5 CTCs/15 mL in PPB and >50 CTCs/15 mL in IPVB. Univariate Cox proportional-hazards regression analysis showed that CTCs count in PPB or IPVB was an independent risk factor for tumour-free and overall survivals. The high risk group of patients had a shorter median tumour-free survival (22 months vs. >60.0 months, P < 0.0012) and shorter overall survival (27 months vs. >60 months, P < 0.0015).

Conclusions CTCs countin PPBand IPVB was an independent risk factor for tumour-free and overall survivalin surgically resected NSCLC patients.
Clinical TB

**S75** RISK FACTORS AND THERAPEUTIC IMPLICATIONS OF VITAMIN D DEFICIENCY IN MALAWIAN ADULTS WITH PULMONARY TUBERCULOSIS

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Introduction and objectives Pre-treatment Vitamin D deficiency (VDD) is well described amongst adult TB patients in Malawi and has been associated with impaired mycobacterial immunity. Anti-TB drugs and antiretroviral therapy (ART) for HIV may induce hepatic Vitamin D metabolism, further reducing the serum concentration of active metabolites including 25-OH D3. This study identified risk factors for baseline VDD, assessed the effect of therapy on 25-OH D3 concentrations, and evaluated whether VDD deficiency has prognostic implications for treatment response.

Methods Adults with pulmonary TB were treated with standard 6 month therapy. Serum 25-OH D3 concentrations were measured at baseline, 8 weeks and end of treatment. Serial sputum samples were used to model the rate of bacterial elimination for each patient. Patients were followed until 1 year post-treatment. Patients were stratified by HIV status and ART use and analysed using multivariable regression analysis.

Results 133 patients were studied. 75 (56%) were HIV-infected and 24 (18%) were on ART. 118 (89%) had favourable and 15 (11%) had unfavourable outcomes. The median baseline 25-OH D3 concentration was 57.3 nmol/l. 47 (28%) patients had concentrations <50 nmol/l, representing VDD. On multivariate analysis, neither HIV status nor ART influenced baseline 25-OH D3 levels, but lower concentrations were reported in patients who were recruited during the cold months of July/August (p = 0.001), suffered food insecurity (p = 0.035) or had a lower baseline Body Mass Index (p = 0.047). Without specific supplementation, 25-OH D3 levels improved during TB therapy (see figure). There were no associations between 25-OH D3 levels at any time-point and the sputum bacillary elimination rate or final clinical outcome.

Conclusions 1. The presence and extent of VDD in Malawian TB patients was determined by environmental factors (sunlight exposure and dietary intake) rather than HIV status or ART.
2. 25 OH D3 levels improved during therapy, suggesting that induction of Vitamin D metabolites by anti-TB drugs or ART is adequately compensated by improved Vitamin D uptake during disease recovery.
3. VDD did not have prognostic implications for treatment response.

Abstract S75 Figure 1 Time on therapy

**S76** TB INFECTION IN THE NEPALI POPULATION IN SOUTHEAST LONDON DISPLAYS DIFFERENT CHARACTERISTICS COMPARED TO THE TB POPULATION IN NEPAL

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Introduction The World Health Organisation classifies Nepal as having high Tuberculosis (TB) burden (Estimated incidence 163/100,000). TB within the Nepali population in the UK has not been formally characterised but a recent study indicates unique characteristics compared to overall UK data. These include higher rates of multi-drug resistant (MDR) TB (4.7% vs 1.6%), and lower rates of TB/HIV co-infection (1.1% vs 8%). We sought to investigate if these differences were also found in the TB population in Nepal or were unique to the immigrant population in SE London.

Methods Retrospective cohort analysis was performed of all Nepali TB patients in Greenwich between 2007–2012. Data collected included site, drug resistance, HIV co-infection and completion rates. Results were compared to Nepal National Tuberculosis Programme (NTP) data from 2012. Data analysis was conducted as part of an Internship with the Britain Nepal Medical Trust.

Results 86 UK patient records were analysed and compared to NTP 2012 data (n = 34,245). TB patients in Greenwich were younger than patients in Nepal; 91.8% age <55 yrs compared with 72.5% of patients in Nepal.

Of the patients diagnosed with pulmonary TB in Greenwich, only 19.7% had sputum smear positive disease, compared to 68% in Nepal. UK patients had higher rates of extrapulmonary disease compared to Nepal (41% vs. 23.8%).

The rate of MDR TB in new diagnoses shows a marked difference; Greenwich having rates of 4.7% compared to 2.2% in Nepal. Despite the higher rates, risk factors for MDR TB were low in UK immigrants (HIV 1.1%, previous TB treatment 0% and MDR TB contact 0%).

Treatment completion in Greenwich was 98% compared with 91% in Nepal, who run a national DOTS programme.

Conclusion Nepali expatriate TB patients display different characteristics to both UK and Nepal TB populations, and have high rates of MDR TB which cannot be accounted for by increased risk factors. Further studies are required to identify if this reflect differences in TB diagnostics or relate to the migration status of the Nepali patients.

REFERENCES
Abstract S76 Table 1

<table>
<thead>
<tr>
<th>Age</th>
<th>Greenwich (%)</th>
<th>Nepal (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>-14</td>
<td>1.2</td>
<td>2.5</td>
</tr>
<tr>
<td>15–24</td>
<td>34.9</td>
<td>20.5</td>
</tr>
<tr>
<td>25–34</td>
<td>34.9</td>
<td>18.0</td>
</tr>
<tr>
<td>35–44</td>
<td>10.5</td>
<td>12.0</td>
</tr>
<tr>
<td>45–54</td>
<td>10.5</td>
<td>15.5</td>
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<tr>
<td>55–64</td>
<td>3.5</td>
<td>15.5</td>
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<tr>
<td>65+</td>
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<td>12.0</td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary Smear +ve</td>
<td>11.6</td>
<td>51.8</td>
</tr>
<tr>
<td>Pulmonary Smear -ve</td>
<td>47.4</td>
<td>24.4</td>
</tr>
<tr>
<td>Extrapulmonary</td>
<td>41.0</td>
<td>23.8</td>
</tr>
<tr>
<td>Other</td>
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<td></td>
</tr>
<tr>
<td>Treatment completion</td>
<td>98</td>
<td>91</td>
</tr>
<tr>
<td>TB/HIV co-infection</td>
<td>1.1</td>
<td>2.4</td>
</tr>
<tr>
<td>MDR</td>
<td>4.7</td>
<td>2.6</td>
</tr>
</tbody>
</table>

**Background**

Chest radiographs are commonly used for the diagnosis of tuberculosis and to assess the extent of disease. A relationship between the extent of disease as determined by smear grade and cavitation has been shown to predict 2-month smear results but little has been done to determine whether radiological severity reflects the bacterial burden at diagnosis.

**Design/methods**

Pre-treatment chest X-rays from 1837 subjects with smear positive pulmonary tuberculosis enrolled into the REMoxTB trial were reviewed retrospectively. Two clinicians blinded to clinical details using the Ralph et al. scoring system (1) (comprised of the percentage of affected lung field and presence of cavitation) performed separate readings. An independent reader (a radiologist) reviewed discrepant results for quality assurance.

**Results**

Matching sets of data were available for 1422 subjects. The median severity score was 53.75/140 (IQR 32.03–66.25) and median time to culture positivity 117 h (4.88 days). CXR p was higher in those without cavitation (difference 23.7 h, p < 0.0001). Time to positivity was higher in those without cavitation (difference 23.7 h, p < 0.0001) and those with a low area affected (difference 12.1 h, p < 0.0001).

**Conclusions**

The radiological severity of pulmonary tuberculosis at diagnosis is weakly correlated with bacterial load as measured by TTP. This suggests that, in addition to bacterial burden, other factors such as immune response influence radiological appearances.

**REFERENCES**


S78

**DO TUBERCULOSIS CASES MANAGED BY CLINICIANS WITH AVERAGE ANNUAL CASELOADS BELOW 10 HAVE POORER TREATMENT OUTCOMES?**

1. HR Stagg, HJ Thomas, D Pedrazzoli, LF Anderson, A Albakar, CS Mele. University College London, London, UK; Public Health England, London, UK; London School of Hygiene and Tropical Medicine, London, UK

10.1136/thoraxjnl-2014-206260.84

**Introduction and objectives**

The 2007 Department of Health Tuberculosis Toolkit advises that clinicians should not be solely managing tuberculosis (TB) cases if their average caseload is less than 10 per year. A systematic evaluation of whether these guidelines are being followed, and how effective such a threshold is, has not been undertaken in the UK.

**Methods**

All UK TB cases notified 2003–2011 were extracted from Public Health England’s Enhanced Tuberculosis Surveillance system. Mean caseload for each clinician was calculated over the preceding year and three years by using case notification date. 12 month TB treatment outcomes were categorised as unfavourable or good/neutral. Cases without clinician information and resistant to rifampicin were excluded, the latter due to UK recommendations on the length of treatment. The proportion of cases managed by clinicians with a caseload under 10 was analysed, then random effects logistic regression utilised to determine the relationship between caseload and treatment outcomes, adjusting for clustering by clinician and confounding.

**Results**

74,550 TB cases were notified 2003–11. The proportion of TB cases seen by a clinician who had a low caseload (less than 10) in the preceding year declined gradually 2004–11 (42 to 28%), with no apparent acceleration post-Toolkit. Univariate modelling demonstrated very strong evidence of increased odds of an unfavourable treatment outcome among cases seen by a clinician who had a low caseload over the preceding three years (cluster-specific odds ratio 1.23 (95% confidence interval 1.14–1.33), p-value <0.001); this relationship was upheld in a model adjusted for demographic, temporal and clinical confounders (1.14 (1.05–1.23), <0.001; 44,184 cases), and additionally when a sensitivity analysis was performed looking at second assigned clinician, if present.

**Conclusions**

Our analysis indicates that TB cases managed by clinicians with a mean caseload of under 10 were analysed, then random effects logistic regression utilised to determine the relationship between caseload and treatment outcomes, adjusting for clustering by clinician and confounding.

**REFERENCES**

1. Ditah, Thorax 2008;63:440–446

S79

**COUGH PREVALENCE AND FREQUENCY IN PULMONARY TUBERCULOSIS**

1. RD Turner, AC Repossi, S Mats, S Bining, GH Bothamyk. Homerton University Hospital NHS Foundation Trust, London, UK; IEETA, University of Aveiro, Aveiro, Portugal; King’s College London, London, UK

10.1136/thoraxjnl-2014-206260.85
Abstract 579 Figure 1 24-hour cough frequency in sputum smear-positive and smear-negative pulmonary TB and latent TB infection. Error bars: median and IQR

Introduction Patterns of cough in tuberculosis influence transmission of disease yet have been little studied. We report the prevalence, duration, severity and frequency of coughing in tuberculosis.

Method The first part was a retrospective review of the medical records of all individuals diagnosed with pulmonary tuberculosis (PTB) at our hospital during 2012–3. The reported presence and duration of coughing was noted. In the second part of the study, successive patients with an ultimate diagnosis of PTB were asked to wear the Leicester Cough Monitor for 24 h prior to commencing treatment. Controls had latent TB infection (LTBI). Participants rated their cough severity from 0–100 with a visual analogue scale (VAS). Cough characteristics were compared with other clinical variables.

Results 108 cases of PTB from 2012–3 were included. 82 reported cough of median (IQR) duration 4 (1–8) weeks. There was a significant association of the presence of cough with TB sputum culture positivity (odds ratio, 11.0; 95% confidence interval, 2.5–50.0) but not gender, smoking, smear positivity, cavitary disease or extent of radiographic change. No predictor of the duration of cough was identified and there were too few patients to estimate the effect of TB strain.

Cough frequency was measured in subjects with sputum smear positive PTB (S+; n = 20), smear negative PTB (S−; n = 10) and LTBI (n = 11). Variability was high: median (IQR) cough rates were 238 (121–701), 126 (15–395) and 11 (7–56) coughs/24 h, respectively, and not significantly different for S+ vs. S− (figure). For active TB, cough rates were reduced overnight (2.8 [0.2–12.4] vs. 12.7 [3.3–23.4] coughs/h for night vs. day, respectively; p = 0.01). No effect of smoking was detected, nor was there a correlation between cough frequency and radiographic extent of disease, cavities or time to sputum culture positivity. Cough severity was higher for S+ than S− but also variable and the difference not statistically significant (VAS: 60 [13–94] vs. 22 [1.5–70] respectively; p = 0.41). Severity correlated with cough frequency in active tuberculosis (Spearman’s r = 0.60, p = 0.001).

Conclusion Cough in TB reduces overnight and is related to culture positivity. Bacterial burden and extent of disease may not be important. Other determinants of cough await characterisation.
Predicting and preventing re-admissions in COPD – what is the real cost?

S81 GAIT SPEED IS A PREDICTOR OF MORTALITY FOLLOWING HOSPITALISATION FOR ACUTE EXACERBATIONS OF COPD

1SSC Kon, 2SE Jones, 2SJ Schofield, 1JI Canavan, 1CM Nolan, 1MJ Dickson, 2BM Haselden, 1Mi Polkey, 1PP Cullinan, 1WD-C Man. 1NIHR Respiratory Biomedical Research Unit, Royal Brompton and Harefield NHS Foundation Trust and Imperial College, Harefield, Middlesex, UK; 2Department of Occupational and Environmental Medicine, Imperial College, London, UK; 3The Hillingdon Hospital NHS Foundation Trust, Uxbridge, UK. 10.1136/thoraxjnl-2014-206260.87

Background Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are associated with significant morbidity, mortality, and high resource utilisation. More accurate prediction of prognosis following hospital discharge may help optimise clinical management and individualise post-discharge care. Physical performance is potentially amenable to change and may help stratify patients at risk of early mortality. In community-dwelling older adults, the 4-metre gait speed (4MGS) is a well-established physical performance measure and a consistent predictor of mortality. We hypothesised that 4MGS at discharge predicts 1 year mortality in patients hospitalised with AECOPD.

Methods 213 patients admitted to one hospital with a primary diagnosis of AECOPD were recruited prospectively. 4MGS was measured on the day of hospital discharge. Data on all-cause mortality at one year were obtained from the patient care summary record, hospital and GP records, and corroborated by patients and their families. Logistic regression models were used to assess the association between 4MGS and death.

Results Baseline characteristics: 111 males/102 females; mean (SD) age 72 (11) years, 4MGS 0.61 ms$^{-1}$ (0.26) and median (IQR) FEV$_{1}$% predicted 35 (26, 49). 35 patients (16%) were not alive at 1 year. 4MGS at hospital discharge was significantly lower in these patients compared to survivors (mean (SD) 0.47 (0.24) vs 0.63 (0.26) ms$^{-1}$; p < 0.001). All-cause mortality at 1 year increased with decreasing quartiles of 4MGS (Q4 4%; Q3 9%; Q2 21%; Q1 32%; p < 0.001). Multivariate logistic regression demonstrated a significant trend in the age adjusted odds of death with decreasing quartiles of gait speed (p < 0.001) (see Table 1). Increased odds of death at 1 year were seen with each 0.1 ms$^{-1}$ decline in gait speed (OR 1.26 (1.06 to 1.49), p = 0.008).

Conclusion The 4MGS measured at discharge predicts 1 year mortality in patients hospitalised with acute exacerbation of COPD. Given the simplicity of the 4MGS, it is a potentially useful tool to risk stratify patients with COPD in the acute setting and tailor post discharge care.

Abstract S81 Table 1 Multivariable logistic regression model predicting all cause mortality at 1 year by gait speed

<table>
<thead>
<tr>
<th>Gait speed (quartiles)</th>
<th>Crude odds ratio (95% CI)</th>
<th>Adjusted odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (median 0.32)</td>
<td>11.49 (2.50–52.81)</td>
<td>8.67 (1.81–41.62)</td>
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</tr>
<tr>
<td>2 (median 0.50)</td>
<td>6.55 (1.37–31.21)</td>
<td>4.87 (0.97–24.34)</td>
<td>0.007</td>
</tr>
<tr>
<td>3 (median 0.69)</td>
<td>2.55 (0.47–13.78)</td>
<td>2.34 (0.43–12.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4 (median 0.91)</td>
<td>1</td>
<td>1</td>
<td>trend</td>
</tr>
<tr>
<td>Gait speed continuous per 0.1 m/s decline</td>
<td>1.32 (1.12–1.55)</td>
<td>1.26 (1.06–1.49)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

This abstract summarises independent research funded by the National Institute for Health Research (NIHR) under its HTA Programme (Ref 11/27/01). The views expressed are those of the author (s) and not necessarily those of the NHS, the NIHR or the Department of Health.

S82 AN ECONOMIC EVALUATION OF SELF-MANAGEMENT PROGRAMS DELIVERED AT DISCHARGE AFTER ACUTE EXACERBATION, IN COPD PATIENTS IN THE UK


This model found that self-management delivered at discharge was more costly, but resulted in better outcomes, with a £683 cost difference and a gain of 0.0831 QALYs. To be cost-effective it would need to cost £2200 or less if the hazard ratio remained at 0.82. Sensitivity analysis found that self-management had a 68% probability of being cost-effective at a threshold of £20,000 per QALY, with most of this uncertainty being around the effect, duration of effect and cost.

Conclusion If self-management interventions are effective in reducing readmissions for up to two years, they are likely to be cost-effective. This speculative economic model describes the uncertainty around this conclusion.
This abstract summarises independent research funded by the National Institute for Health Research (NIHR) under its HTA Programme (Ref 11/27/01). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

**Background** NIV is an established treatment for the management of acute exacerbation of COPD but less is known about the effectiveness of NIV in the home setting. Many clinicians consider domiciliary NIV to be cost-effective in patients that have experienced three or more exacerbations however no economic evaluations, using decision modelling have been conducted.

**Methods** The findings of a systematic clinical review of the clinical effectiveness of domiciliary NIV in COPD were applied in a Markov model, to estimate cost-effectiveness, from a UK perspective, when compared to usual care. Outcomes were measured in Quality Adjust Life Years (QALYs). Two end-stage COPD populations were considered; patients that were stable for at least twelve weeks (stable population) and those recently discharged for exacerbation (post-admission population). Given the uncertainty around the effect of domiciliary NIV on admissions and mortality in both populations, extensive sensitivity analysis was conducted to quantify and likelihood of NIV being cost-effective at a thresholds of £30,000 per QALY and the model’s sensitivity to key parameters.

**Results** This model indicated that domiciliary NIV is unlikely to be cost-effective in stable populations but is more likely to be cost-effective post-admission. However, there was considerable uncertainty around the results for both populations. The model was most sensitive to changes in the risk ratio for admission and the duration of the effect but was also sensitive to changes in baseline risk of admissions.

**Conclusion** This model indicates that domiciliary NIV is unlikely to be cost-effective in stable patients but maybe cost-effective in patients with a history of admissions. This speculative economic model describes the uncertainty around these conclusions.
2013, Thorax). We secured funding to pilot PEPR in our local DGH population. Here, we present the initial five months data.

Aims and objectives This study aimed to investigate the impact of PEPR on exercise tolerance, QoL and health care utilisation in a local DGH population.

Methods Data were collected prospectively from successive patients referred for PEPR between December 2012 and May 2014. Outcome measures consisted of ISWT and QoL (CAT). Healthcare utilisation was measured through 30 and 90 day readmission and A&E attendance rates. Descriptive statistics and significance values were calculated in SPSS (version 22) using paired t-test and Chi².

Results 64 patients were referred to PEPR. 53% (n = 34) decline to attend, 15% (n = 10) failed to complete the programme. Subsequently 31% (n = 20) patients completed PEPR which is comparable to standard PR. Exercise tolerance was significantly improved (difference between the means 46 m 95% CI +/-3.1 m p = 0.009). QoL was significantly improved (difference between the means 46 m 95% CI +/-3.1 m p = 0.002). Table 1 demonstrates the impact of PEPR on healthcare utilisation. Both 30 and 90 day readmissions were significantly reduced. 90 day A&E attendances were significantly reduced. Average LoS following readmission in the group who declined PEPR was 11 days compared to an average LoS following readmission in PEPR group of 1 day. Considering the savings associated with bed days alone and staffing expenses the cost benefit of PEPR was £21309 pa.

Conclusions Results suggest PEPR in a DGH population has a significant impact on QoL. and exercise tolerance with reductions in healthcare utilisation and associated cost benefits.

Pulmonary infection: discovery science

S86 THE INFLAMMATORY RESPONSE TO STREPTOCOCCUS PNEUMONIAE IS EXAGGERATED BY THE POLYSACCHARIDE CAPSULE


Streptococcus pneumoniae infections characteristically cause a high degree of inflammation. The S. pneumoniae polysaccharide capsule prevents opsonophagocytosis and is essential for virulence. The capsule might also be expected to reduce the host’s inflammatory response by inhibiting bacterial interactions with pro-inflammatory signalling proteins eg toll-like receptors (TLR), which this has not previously been investigated. Using isogenic unencapsulated strains and in vitro and in vivo models of infection we have characterised capsule effects on the inflammatory response to S. pneumoniae.

Surprisingly, although the unencapsulated (Δcps) S. pneumoniae strain was much more sensitive to phagocytosis by macrophages and induced a stronger NFkB response by human monocyte derived macrophages (MDMs) it caused similar levels of stimulation of a TLR2 reporter cell line as the encapsulated strain TIGR4. In addition, microarrays demonstrated increased transcription of pro-inflammatory cytokines by MDMs in response to TIGR4 compared to the Δcps strain, and quantitative PCR and ELISAs confirmed stronger TNF, IL1β, and IL6 responses by MDMs to TIGR4. Furthermore, compared to the Δcps strain the TIGR4 strain caused greater neutrophil recruitment and higher cytokine levels in the lungs in a mouse model of pneumonia, as well as higher serum cytokine levels with worse hypotension in a rat model of sepsis. Additional in vitro experiments excluded antibody, complement, pneumolysin, the inflammasome, and lectin-mediated signalling as mechanisms driving differences in inflammatory responses between TIGR4 and Δcps. Expression of the TIGR4 capsule in Streptococcus mitis did not increase MDM or murine inflammatory responses. Notably, preventing phagocytosis with cytochalasin D did not alter differences in the inflammatory response between TIGR4 and the Δcps strains, and in silico analysis suggested the Δcps strain activated a wider range of transcription factors.

Overall, the data indicate that unencapsulated S. pneumoniae stimulate a wider range of host cell signalling pathways than encapsulated bacteria, some of which are likely to be anti-inflammatory. Hence the capsule, rather than reducing inflammation, causes increased pro-inflammatory responses and subsequent disturbances to host physiology during S. pneumoniae infection. Targeting the mechanisms responsible for capsule-dependent inflammation could offer novel treatment options for reducing the morbidity and mortality associated with S. pneumoniae infections.

S87 A FUNCTIONAL COMPARISON OF NEONATAL AND ADULT NEUTROPHIL RESPONSES TO RESPIRATORY SYNCYTIAL VIRUS

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10.1136/thoraxjnl-2014-206260.93
Introduction and objectives

Respiratory Syncytial Virus (RSV) is a major cause of lower respiratory tract infection during infancy. Neutrophils are the predominant cell type within the RSV-infected airway, 80% of inflammatory cells from BAL of intubated infants being neutrophils. Despite extensive research unpicking innate viral responses to RSV little is known about the specific role the neutrophil plays. The aim of this work was to investigate the response of neutrophils to RSV using an in vitro model utilising neutrophils from adult volunteers. To investigate whether relative immaturity of infant neutrophils leads to impaired responses we are now comparing adult neutrophils with neonatal neutrophils, isolated from cord blood.

Methods

Highly purified neutrophils from whole blood of healthy adult donors were incubated with RSV. Samples were taken at 2, 4, and 20 h for QT-PCR of RSV N gene, western blot analysis and cytospin slides for confocal imaging of RSV F protein. Experiments were then replicated using neutrophils purified from cord blood, collected from the placenta following elective caesarean section, of healthy term neonates. Supernatants were stored for measurement of the cytokine response of the neutrophil to RSV.

Results

Uptake of RSV by adult neutrophils was shown by both western blot and quantitative RT-PCR. Maximal uptake was at 4 h with a reduction by 20 h. Confocal microscopy was undertaken, using a primary monoclonal antibody to RSV fusion protein. This showed that RSV was internalised inside the cytoplasm in a distribution suggestive of endosomal uptake (see figure). Preliminary data suggests that neonatal neutrophils are also capable of this viral uptake but work is ongoing to determine differences between the two models.

Conclusions

We have shown that neutrophils may be involved in viral clearance as part of the immune response to viral invasion. They appear to take up virus with kinetics suggestive of endocytosis. Work is ongoing to establish the mechanism of entry using a panel of inhibitors. Initial results would suggest that neonatal neutrophils may respond similarly but work continues to establish whether this is the case and if there is any functional impairment that may explain infants’ propensity to severe disease.

Abstract S88 Figure 1

Indirect fluorescent confocal microscopy was carried out on cytospins of neutrophils purified from adult blood and incubated with RSV for a 2 h in the presence of GM-CSF. Z stacks were taken using a Leica confocal and Z-projection images produced using Imaris software. RSV (white arrow) is identified in all depths of the cytoplasm in this orthogonal view throughout the cell in discrete pockets suggestive of endosomes.
all patients with a DNAH11 defect (n = 5) compared to healthy controls (n = 3) and patients with PCD due to a defect of the central pair or nexin link (n = 3) (Figure 1). A reduction in outer dynein arm volume of 30% was identified compared to central pair or nexin link (n = 3) (Figure 1). A reduction in healthy and PCD controls (n = 3) and patients with PCD due to a defect of the DNAH11 gene was detectable in breath taken directly from patients. This pilot study demonstrated an ionic spectrum from volatile organic compounds that may be detectable in breath taken directly from patients. This pilot study demonstrated the potential of SIFT-MS to identify 5 PPMs, incubated separately for 24 hr.

**Methods** Training set: Haemophilus influenzae (HI), Moraxella catarrhalis (MC), Streptococcus pneumoniae (SP), Staphylococcus aureus (SA) and Pseudomonas aeruginosa (PA) cultures with a negative control incubated at 37°C on chocolate agar plates in sealed bags for 24 hr, 48 hr and 72 hr. Plates were opened after 10 min at room temperature before ionic spectra of the gas above the culture dishes in the range 15 to 200 mass units were recorded using SIFT-MS and standardised to operating conditions. Test set: the same five PPMs and a negative control were incubated in triplicate for 24 hr only and analysed as above.

**Results** Using the spectra generated with HSO+ ionisation, 6 ion sets were identified. The sum of ions within each set, expressed as a percentage of the total ion sum of masses 15 to 200 (excluding reagent ions) fell into ranges that, in combination, differentiated between the PPMs. This set of conditions was incorporated into an algorithm that was then applied to the test set of triplicate plates. The algorithm correctly differentiated all 24 hr plates with MC, SA and PA from each other and from the negative control and HI plates with 100% accuracy. Negative control and HI could not be differentiated.

**Conclusion** This pilot study illustrates the potential for SIFT-MS to identify monocultures of 4 common PPMs within a short incubation time and encourages further study with a wider range of pathogens alone and in combination. Early identification of PPMs in culture, and translation to potentially detect carriage or infection with specific pathogens in breath may improve management of respiratory infections.

**Introduction** Asthma is an inflammatory disease of the conducting airways which is exacerbated by environmental exposures, such as viral infections. Bronchial epithelial cells (BECs) together with underlying fibroblasts form an epithelial mesenchymal trophic unit (EMTU) that maintains normal tissue homeostasis. In asthma the EMTU is dysregulated. Recent evidence suggests that viral infections activate the epithelial barrier resulting in mediator release which could potentially activate fibroblasts. Therefore, we hypothesised that exposure to viruses activates inflammatory and anti-viral responses in the EMTU.

**Methods** The EMTU was modelled using a co-culture system of polarised BECs (16HBE14o-) and fibroblasts (MRC5s) maintained on the apical and basolateral surface of a nanoporous membrane respectively. After 6 days the model was challenged apically with poly (I:C) (a viral mimetic) and barrier responses were determined by measuring transepithelial resistance (TER) while cytokine release was determined by ELISA.

**Results** Following poly (I:C) stimulation a significant reduction in TER was observed in both the EMTU model and BEC monocultures. However, the EMTU model maintained a higher TER at 6–24 h after challenge. With regards to cytokine secretion, poly (I:C) stimulation significantly induced pro-inflammatory (IL-6, IL-8, GM-CSF and IL-1α) and anti-viral (IP-10) mediator release from BEC but not fibroblast monocultures. In the EMTU model, basolateral IL-6, IL-8, GM-CSF and IP-10 responses to poly (I:C) were significantly enhanced compared to BEC monocultures. In addition, basolateral pro-inflammatory (IL-6, IL-8 and GM-CSF) but not anti-viral (IP-10) responses were mediated by epithelial-derived IL-1α.

**Conclusions** Poly (I:C) activates inflammatory and anti-viral responses in BEC monocultures and fibroblast co-culture models of the EMTU. These responses were enhanced in the co-culture model suggesting that the EMTU is activated. Inflammatory but not anti-viral responses were mediated by epithelial-derived IL-1α acting on the underlying fibroblasts. This may have important consequences in promotion of inflammation and airway remodelling in viral-induced exacerbations of asthma.

**New asthma treatments**

**Role of IL-1α in Viral-Induced Inflammatory Responses in a Co-Culture Model of the Airway Mucosa**

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**Once-Daily Tiotropium Respimat® Add-On to ICS + LABA Improves Symptom Control and Reduces Exacerbations in Patients with Symptomatic Asthma**

D. Price, M. Engel, M. Moroni-Zentgraf, H. Schmidt, R. Dahl, P. Paggiaro, M. Vandevalker, HAMK Kerstjens, A. Kaplan. Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK; Boehringer Ingelheim Pharma GmbH and Co. KG, Biberach an der Riss, Germany; Odense University Hospital, Odense, Denmark; University of Pisa, Pisa, Italy; Clinical Research of the Orkneys, Colombia, USA; University Medical Center Groningen, Groningen, The Netherlands; Family Physician Airways Group of Canada, Ontario, Canada

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Background We evaluated the effect of once-daily tiotropium Respimat® 5 µg on lung function, asthma exacerbation and asthma symptom control among patients with symptomatic asthma receiving inhaled corticosteroids (ICS; ≥800 µg/day budesonide or equivalent) + long-acting β2-agonist (LABA). 

Methods Data were pooled from two replicate, double-blind, placebo-controlled, 48-week, parallel-group studies of once-daily tiotropium 5 µg versus placebo, both delivered via the Respimat® SoftMist™ inhaler (PrimoTinA-asthma®; NCT00772538, NCT00776984). Eligible patients had: ≥5-year history of asthma diagnosed before the age of 40 years; seven-question Asthma Control Questionnaire (ACQ-7) score of ≥1.5; experienced ≥1 exacerbation during the previous year. Patients were either lifelong non-smokers, or ex-smokers (>10 pack-years) who quit smoking ≥1 year before study enrolment. Exclusion criteria included diagnosis of chronic obstructive pulmonary disease. Co-primary end points in individual trials: peak forced expiratory volume in 1 second (FEV₁) within 3 h post-dose (0–3 h) and trough FEV₁. A co-primary end point in pooled data was time to first severe exacerbation; secondary end points included time to first episode of asthma worsening and ACQ-7 response. Post hoc efficacy analyses were performed. 

Results 912 patients were randomised to receive tiotropium Respimat® (n = 456) or placebo Respimat® (n = 456). At Week 48, tiotropium Respimat® was associated with statistically significant improvements versus placebo Respimat® in peak FEV₁(0–3h) (adjusted mean difference 100 mL; 95% confidence interval: 52, 148; p < 0.0001) and trough FEV₁ (adjusted mean difference 62 mL; 95% confidence interval: 18, 106; p = 0.006). Time to first severe asthma exacerbation was significantly longer with tiotropium Respimat® versus placebo Respimat® (282 vs 226 days, respectively; hazard ratio 0.79; p = 0.034), as was time to first episode of asthma worsening (315 vs 181 days, respectively; hazard ratio 0.69; p < 0.0001). At Week 24, ACQ-7 responder rate was significantly higher with tiotropium Respimat® (53.9%) versus placebo Respimat® (46.9%; odds ratio 1.32; p = 0.0427). 

Conclusion Once-daily tiotropium Respimat® add-on to ICS + LABA improves lung function, reduces risk of severe asthma exacerbation and asthma worsening, and significantly improves asthma symptom control compared with placebo Respimat® in patients with symptomatic asthma.

#S92 Efficacy of Once-Daily Tiotropium Respimat® 5 µg from Five Phase III Trials in Adults with Symptomatic Asthma

<table>
<thead>
<tr>
<th>Table</th>
<th>Adjusted mean of difference in response from placebo (mL)</th>
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<tr>
<td></td>
<td>Tiotropium Respimat®5 µg (n = 456)</td>
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<tr>
<td>Peak FEV₁(0–3h)</td>
<td>110 (p = 0.0001)</td>
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<tr>
<td>Trough FEV₁</td>
<td>93 (p = 0.0058)</td>
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<tr>
<td>FEV₁, AUC(0–24)</td>
<td>107 (p = 0.0001)</td>
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<tr>
<td>Peak FVC(0–24)</td>
<td>87 (p = 0.0050)</td>
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</table>

Abstract S92 Table 1

Pooled data: AUC, area under the curve; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

$\text{SoftMist™ inhaler}$ in adults with symptomatic asthma on inhaled corticosteroid (ICS) $\pm$ long-acting β2-agonist (LABA) maintenance therapy.

Methods Two 48-week trials of tiotropium Respimat® 5 µg (PrimoTinA-asthma®; NCT00776984, NCT00772538) in patients on high-dose ICS (≥800 µg budesonide or equivalent) + LABA; two 24-week trials of tiotropium Respimat® 5 µg and 2.5 µg (MezzoTinA-asthma®; NCT01172808, NCT01172821) in patients on moderate-dose ICS (400–800 µg budesonide or equivalent); one 12-week trial of tiotropium Respimat® 5 µg and 2.5 µg (GraziaTinA-asthma®; NCT01316380) in patients on low-dose ICS (200–400 µg budesonide or equivalent).

Results 3476 patients were treated, of whom 1128 received tiotropium Respimat® 5 µg. Once-daily tiotropium Respimat® 5 µg significantly improved lung function (Table) in patients with not fully controlled asthma receiving low- to high-dose ICS. In addition, tiotropium Respimat® 5 µg reduced the risk of severe exacerbations versus placebo (co-primary end point) in patients on high-dose ICS + LABA (hazard ratio 0.79; p = 0.0343), and there was an increase in ACQ-7 responder rate (co-primary end point) with the5 µg dose (odds ratio 1.32; p = 0.0308) compared with placebo in patients on moderate-dose ICS.

Conclusion Once-daily tiotropium Respimat® significantly improves lung function in adult patients with symptomatic asthma receiving a range of doses of ICS, including even high-dose ICS + LABA, suggesting a potential role for this treatment as add-on to ICS in adults with symptomatic asthma.

## Abstract S93

**A Prospective Study Investigating Exacerbations, Healthcare Utilisation and Health Economic Indicators in Omalizumab Treated Severe Allergic Asthma Patients – Results from an Interim Analysis of the Apex II Study**

**Methods**

Treated Severe Allergic Asthma Patients – Results from an Interim Analysis of the Apex II Study

**Background**

A previous retrospective study of UK clinical practice demonstrated that omalizumab was associated with reduced exacerbations and healthcare utilisation in severe allergic asthma.
Aim This multicentre observational study was conducted to confirm the observed retrospective findings prospectively in UK clinical practice.

Methods Retrospective data were collected in the 12 months prior to and prospective data for up to 12 months following omalizumab initiation. The primary endpoint was the change in mean daily OCS dosage (reported previously). Secondary endpoints included changes in mean exacerbation frequency (defined as requiring hospital admission or Accident and Emergency (A&E) attendance and/or a course of OCS (dosage increase of at least 10 mg/day for at least 3 days)), healthcare utilisation and missed days in education or at work.

Results 235 patients were enrolled in the study at end December 2013 in 22 UK centres. Data for interim analysis were examined from patients with 12 months of assessment at database lock (n = 85, females, 54%, mean (±SD) age 44 yr (±13.2), mean (±SD) duration of asthma 26 yr (±14.0)). At the 16 weeks assessment 74/85 (87%) patients were classified as responders to omalizumab treatment. Comparing the 12 month periods prior to and following initiation of omalizumab, mean total exacerbations decreased by 51% from (mean, ±SD) 4.25 ± 2.73 to 2.07 ± 2.01 (mean difference 2.18, p < 0.001), while mean exacerbations involving hospital visits decreased by 61% from 1.52 ± 2.00 to 0.59 ± 1.25 (difference 0.93, p < 0.001). A&E attendances were reduced from 54 to 19 (p < 0.01) and inpatient hospitalisations from 85 to 36 (p < 0.001). The percentage of average days absent from work or education due to sickness was more than halved in the 12 months pre and post omalizumab initiation reducing from 19.6% to 7.72% (n = 27, p < 0.05).

Conclusions The data prospectively confirms that omalizumab is associated with significant reduction in exacerbations, healthcare utilisation and societal burden in severe allergic asthma patients as was reported in the retrospective study.
**Results** Participants were allocated to vitamin D3 vs. placebo in equal numbers; 82% were vitamin D insufficient at baseline. Vitamin D3 supplementation did not influence time to first severe exacerbation (aHR 1.02, 95% CI 0.69–1.53, P = 0.91) or time to first URI (aHR 0.87, 95% CI 0.64–1.16, P = 0.34). The influence of vitamin D3 on co-primary outcomes was not modified by baseline vitamin D status or genotype. Of 16 pre-specified secondary outcomes, only one showed a difference between arms: vitamin D3 supplementation induced a modest improvement in respiratory quality of life as evidenced by a reduction in mean total score for the St George’s Respiratory Questionnaire at 2 months (-3.9 points, p = 0.005), 6 months (-3.7 points, p = 0.038) and 12 months (-3.3 points, p = 0.060).

**Conclusions** Vitamin D3 supplementation did not influence time to exacerbation or URI in a population of adults with ICS-treated asthma with a high prevalence of baseline vitamin D insufficiency.

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**S96** BRONCHIAL THERMOPLASTY REDUCES PERIPHERAL BLOOD EOSINOPHILS IN SEVERE ASTHMA DEMONSTRATING SYSTEMIC EFFECTS OF A LOCALISED THERAPY

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10.1136/thoraxjnl-2014-206260.102

**Introduction** Severe Asthma, characterised by persistent symptoms despite maximal medical therapy, represents 5% of asthma cases. Bronchial Thermoplasty (BT) is a novel therapy, NICE approved for Severe Asthma patients uncontrolled despite step 4/5 of British Guideline on Asthma Management. BT delivers radiofrequency thermal energy to airways distal to the mainstem bronchi, permanently reducing airway smooth muscle mass. It is unknown whether treatment of smooth muscle hypertrophy impacts persistently upon systemic signs of allergic inflammation. Peripheral blood eosinophils (PBEs) are a marker of allergic inflammation in asthma. We asked: does BT modify signs of allergic inflammation as measured by PBEs and if so, does this effect persist over time?

**Method** A retrospective review of 15 consecutive Severe Asthma cases treated with BT was performed. Serial PBEs measured before and up to 1 year after BT were compared. Blood eosinophil levels taken peri-procedure were excluded from analysis due to standard protocol concomitant steroid therapy. For time to first detectable high PBE all available post-BT PBE levels were assessed.

**Results** 13 patients had PBE data before and after BT, with an average of 9 and 12 serial PBE levels pre and post-BT respectively. Mean PBE 1 year pre-BT was 0.33 x 10^9/L falling to a mean of 0.16 x 10^9/L 1 year post-BT (p < 0.05) (see Figure). 9 of 13 patients had a fall in mean PBE, in 2 of 13 levels rose and 1 of 13 mean PBEs were unchanged post-BT. In 6 patients who converted from normal to high PBE post-BT, average time to first high PBE (≥0.4 x 10^9/L) was 7 months (range 1–13 months). In 5 patients (38%) PBE remained within normal range persistently post BT.

**Conclusions** Severe Asthma patients undergoing BT had a significant reduction in average peripheral blood eosinophil levels from baseline. In over 1/3 of cases this effect was persistent 1 year post procedure. These findings support the concept that BT not only reduces asthma-associated smooth muscle hypertrophy but impacts upon systemic markers of allergic inflammation.

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**Mechanistic insights in acute lung injury**

**S97** LONG TERM SURVIVAL IN PATIENTS WHO UNDERGO OESOPHAGECTOMY IS LOWER IN PATIENTS WHO DEVELOP POST-OPERATIVE ACUTE RESPIRATORY DISTRESS SYNDROME

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10.1136/thoraxjnl-2014-206260.103

Oesophagectomy is a complicated procedure with high risk of complications in the immediate post-operative period. We have previously shown that patients undergoing oesophagectomy have ~ 25% risk of Acute Respiratory Distress Syndrome (ARDS) post op. Post-operative complications have been shown to decrease long term post-operative survival following major surgery. We hypothesised that long term survival would be reduced in patients who develop ARDS post oesophagectomy.

We analysed data from 55 patients recruited to the translational sub-study of the BALTI prevention trial. 26 of the 55 patients (47%) died within 2 years of their operation. Patients who died within two years of their oesophagectomy were more likely to have required ventilation for ARDS during their hospital admission. In addition, patients who survived less than two years were more likely to have developed a surgical complication (e.g. anastomotic leak, wound infection, chyle leak) post-op. There was no difference in age, lung function, BMI or cancer staging. Patients who did not survive more than 2 years post-op were more likely to be smoking at the time of the operation, but there was no difference in pack year smoking history between the two groups.

Perioperative markers of alveolar epithelial damage (PICCO EVLWI and PVPI), and the severity of both local (BAL CRP) and systemic inflammation (IL-17, ICAM-1, and TNF\(\alpha\)-1/2) were associated with outcome.

In conclusion, complications during recovery from oesophagectomy have an adverse effect on the chances of long term survival. Development of strategies to reduce post-operative morbidity may improve long term outcomes.
A NOVEL HUMAN MODEL TO STUDY ALVEOLAR INJURY AND REPAIR

1 Alçada, JP Ng-Blichfeldt, AG Proudfoot, MJD Griffiths, CH Dean, M Hind. Leucocyte Biology, National Heart and Lung Institute, Imperial College London, London, UK

Introduction The development of regenerative therapies holds promise for the future treatment of parenchymal lung diseases. However, encouraging preclinical data from animal models have translated poorly in clinical trials. The cellular and molecular response to lung injury is difficult to study in man. To address this fundamental question, we have developed a novel in vitro human model. Precision cut lung slice (PCLS) culture is a well-established tool in airway biology and pharmacology. Here, we demonstrate lung parenchyma can be maintained and manipulated in vitro generating a tractable model, which allows study of lung injury and repair in man.

Methods PCLS (500 μm) were generated from agarose-inflated lung lobes from human lungs maintained ex-vivo by perfusion and ventilation (EVLP). The slices were cultured in serum-free medium in a rotating incubator (37°C, 5% CO2) and analysed at days 1, 3 and 7. Cell specific immunofluorescence markers were used to identify smooth muscle, type I and type II alveolar epithelial cells (AT1, AT2), vascular endothelial cells and proliferating cells (using αSMA, Aquaporin5, ProSPC, PECAM1 and Phospho-histone H3 respectively). Slice viability was confirmed using MitoTracker, LDH and Live/Dead assays.

Results All of the expected cell types were identified in PCLS by immunofluorescence demonstrating that human PCLS maintained cellular differentiation in culture. Pro-SPC was predominant in the alveolar wall cells, particularly in the alveolar septal junctions, corresponding to known location of AT2 cells; AQ5 was distributed in thin bands lining the alveolar walls suggestive of the apical membrane of AT1 cells; αSMA was positive around airways, the known location of smooth muscle cells (SMCs); PECAM-1 was positive within alveolar walls corresponding to microvascular capillaries within alveolar septae. There was no significant cell proliferation during culture under basal conditions. Finally, cell viability studies demonstrated that PCLS can be maintained for up to 1 week in serum-free culture.

Conclusion PCLS of human lung parenchyma remain differentiated and viable for up to 7 days in serum-free culture. In future, human PCLS derived from normal and injured regions of lung from the EVLP model may provide a novel means of studying alveolar repair in human lung in vitro.

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A NOVEL HUMAN MODEL TO STUDY ALVEOLAR INJURY AND REPAIR

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REFERENCES

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EFFECTS OF DIFFERENTIAL TNF RECEPTOR SIGNALLING IN MODULATING NEUTROPHIL-ENDOTHELIAL INTERACTIONS IN THE PULMONARY MICROVASCULATURE

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Neutrophil recruitment into the bronchoalveolar space is central to the pathogenesis of acute respiratory distress syndrome injury (ARDS), and occurs via interaction with the lung microvascular endothelium. Tumour Necrosis Factor (TNF) is a key mediator in these processes, activating endothelial cells and inducing changes in microvascular permeability, as well as priming neutrophils (a pre-requisite for neutrophil-mediated tissue damage) and modulating neutrophil lifespan. TNF signals through two cell surface receptors, TNFR1 and TNFR2 initiating distinct signalling pathways and cellular responses. In a human in vivo model of ARDS, selective TNFR1 antagonism attenuated pulmonary inflammation (O’Kane et al, Thorax 2013; 63:A50). Using TNF receptor specific muteins and a novel highly selective TNFR1 antagonist, we investigated the role of differential TNFR signalling on neutrophil-pulmonary microvascular endothelial cell interactions.

TNF-induced alterations in the expression of the neutrophil cell surface molecules CD11b, CD62L, TNFR1 and TNFR2 were all modulated via TNFR1. TNFR1 was also the dominant receptor mediating reactive oxygen species generation by TNF-primed, FMLP-stimulated neutrophils. We further examined the role of TNF receptors in modulating neutrophil apoptosis; whilst engagement of both TNFR1 and 2 was required to induce early neutrophil apoptosis, TNFR1 antagonism reversed TNF-induced late survival to constitutive levels of apoptosis. TNFR1 antagonism of human pulmonary microvascular endothelial monolayers significantly reduced TNF-induced production of IL-1beta, IL-6 and IL-8 (p < 0.05), endothelial permeability and the release of the endothelial injury markers sICAM-1, sVCAM-1 and sE-selectin (p

Collectively, these results suggest that TNFR1 regulates multiple components of neutrophil-endothelial interactions. Selective TNFR1 antagonism may offer a novel therapeutic approach in ARDS; phase II clinical trials of this therapy are scheduled.
Methods and Results  The role of neutrophilic inflammation and PAR-1 was investigated in two models of murine pneumococcal pneumonia (serotype 2 (D39) and serotype 19F (EF3030)) by using the most clinically advanced PAR-1 antagonist, SCH530348. Neutrophil depletion and chemokine neutralisation studies were also performed. Samples were analysed by immunohistochemistry, cytology, flow cytometry, ELISA and microbiological techniques. Our models were characterised by evidence of intra-alveolar coagulation, increased neutrophil recruitment to areas of bacterial infection and increased PAR-1 expression (demonstrated by quantitative image-analysis). Neutrophil deple- tion protected mice against barrier disruption but resulted in compromised host defence. In contrast, PAR-1 antagonist treatment significantly reduced neutrophil recruitment to the bronchoalveolar space without being detrimental to host defence. Markers of alveolar leak, coagulation activation and pro-inflammatory cytokines and chemokines (IL-1β, CCCL1, CCL2 and CCL7) were also attenuated. Neutralisation studies demonstrated that IL-1β and CCL7, but not CXCL1 and CCL2, played a key role in neutrophil recruitment to the airspace in this model. Translational studies were performed to examine by flow cytometry the CXC and CC chemokine receptor expression on neutrophils from blood and BALF of mechanically ventilated CAP-induced ARDS patients and controls. CXCXR1 and CXCXR2 expression on BALF neutrophils was higher in CAP-ARDS patients compared to controls. Additionally, chemokine expression patterns on neutrophils from CAP-ARDS patients changed within different compartments, evidenced by decreased expression of CXCR1 and increased expression of CXCXR2, CCR1, CCR2 and CCR3 on neutrophils from BALF compared with blood.

Conclusion These data provide preclinical proof-of-concept that recently developed PAR-1 antagonists may offer a novel therapeutic approach for controlling or preventing alveolar barrier dysfunction and excessive neutrophilic inflammation in pneumo-
coccal pneumonia without compromising host defence. Furthermore, they highlight a role for chemokine receptor switching in CAP-ARDS with important implications for future targeting of these chemokine receptors.

SRC/BCR-ABL INHIBITION WITH DASATINIB IN STERILE AND NON-STERILE ACUTE LUNG INFLAMMATION

Introduction and objectives  Adult respiratory distress syndrome (ARDS) is a commonly fatal complication of lung infection and inflammation, with no effective treatment. It is characterised by excessive neutrophil influx and degranulation into the lungs, with alveolar leak and severe hypoxia. Src family tyrosine kinases are critical in integrin-dependent neutrophil degranulation. Dasatinib is a Src/Bcr-abl inhibitor used in chronic myeloid leukaemia. We investigated our hypothesis that extracellular neutrophil degranulation could be inhibited by dasatinib in vitro and would modulate the inflammatory response in vivo in models of infective and sterile lung injury.

Methods  Whole blood and isolated blood neutrophils from healthy volunteers were pre-treated with dasatinib and treated with neutrophil stimuli or live bacteria. Degranulation was measured by granule receptor expression and presence of extracellular granule products. Other neutrophil functions were assessed, including adhesion, L-selectin shedding, chemotaxis, phagocytosis, oxidative burst, bacterial killing and apoptosis. Neutrophil lung inflammation was induced in mice using intra-tracheal E. coli or hydrochloric acid.

Results  In vitro, dasatinib inhibited neutrophil degranulation in response to lipopolysaccharide derived from E. Coli 026:B6, fMLF and Staphylococcus aureus at concentrations above 100 nM, with no effect on neutrophil viability or apoptosis. Integrin-dependent functions including adhesion, chemotaxis and phago-
cytosis in adherent conditions were impaired, but phagocytosis was unaffected in whole blood. Intracellular oxidative burst was maintained, with normal bacterial killing, but extracellular superoxide anion release was impaired.

In vivo, dasatinib had modest effects on the pro-inflammatory response to E. coli, reducing interstitial neutrophils, alveolar myeloperoxidase and TNFα at 1 mg/kg and alveolar lactoferrin at 10 mg/kg. Bacterial killing was impaired in a dose dependent fashion, with associated alveolar leak and systemic toxicity at 10 mg/kg. In sterile acid injury, 5 mg/kg dasatinib reduced neutrophil infiltration, degranulation (interstitial CD11b/alveolar lactoferrin) and monocyto-chemotactic protein-1 (MCP-1) in the alveolar space, but induced detrimental effects at 10 mg/kg.

Conclusions The pan-Src kinase inhibitor dasatinib modifies multiple pro-inflammatory neutrophil functions in vitro and in vivo with an impairment in bacterial killing observed in infective lung injury. In the context of sterile inflammation, manipulation of neutrophil degranulation also alters the inflammatory environment and this approach warrants further study as a therapeutic strategy in ARDS.

LIPOXIN A4 IMPROVES EFFEROCYTOSIS VIA INHIBITION OF THE HMGB1 IN HUMAN ALVEOLAR MACROPHAGES

Introduction  Effective clearance of apoptotic cells by macrophages, termed efferocytosis, is a pre-requisite for successful res-
olution of inflammation. High mobility group box protein 1 (HMGB1), is an alarmin that may promote inflammation as well as suppress phagocytosis. Lipoxin A4, represents one of a unique class of lipid mediators that possess a wide spectrum of anti-
inflammatory and pro-resolution actions. We hypothesised that lipoxin A4 may promote both apoptosis in neutrophils, and stim-
ulate macrophage efferocytosis, acting as an antagonist to HMGB-1.

Methods  Neutrophils were obtained from healthy volunteers and cultured for 24 h with or without lipoxin A4. Apoptosis of neutrophils was determined with Annexin V/SyTox staining by flow cytometry. HMGB-1 levels in Acute Respiratory Distress Syndrome (ARDS) bronchoalveolar lavage fluid (BALF) was measured by ELISA. The effects of HMGB-1 and lipoxin A4 upon alveolar macrophage efferocytosis was assessed by measur-
ing the ingestion of CMFDA labelled apoptotic neutrophils by flow cytometry. The P3K (PI3K) protein expression was meas-
ured by western blotting.
Results Treatment of lipoxin A4 (100 nM) increased the apoptosis of neutrophils (p = 0.0244), and reduced the dead (p = 0.0238) and necrotic neutrophils (p = 0.0358) compared to control (n = 8). BALF from patients with ARDS suppressed efferocytosis of apoptotic neutrophils. The effects of BALF correlated with HMGB-1 levels in the BALF fluid. HMGB-1 decreased efferocytosis (p < 0.05) in a dose dependent manner, and reached a significant effect at 150 ng/ml (p = 0.008). Lipoxin A4 increased the efferocytosis (p < 0.05) of alveolar macrophages in a dose dependent manner, and reached the maximal effect at 100 nM (p = 0.008). Moreover, lipoxin A4 (100 nM) blocked the decreased efferocytosis response to HMGB-1 (150 ng/ml) (p = 0.005, n = 8). The lipoxin A4 beneficial effects were abrogated by ALX antagonist, BOC-2 (p < 0.05) and PI3K inhibitor (p < 0.05).

Conclusions Lipoxin A4 in vitro promotes the apoptosis but not necrosis of neutrophils. In tandem it stimulates efferocytosis of alveolar macrophages. Elevated HMGB-1 in ARDS BALF suppress efferocytosis. Lipoxin A4 can block these effects of HMGB-1. The effect of lipoxin A4 increasing efferocytosis was through ALX–PI3K signalling pathways. Lipoxin A4 may therefore have potential as a therapeutic agent to promote the resolution of neutrophil inflammation in ARDS.

COPD outcomes

NO LOSS IN EFFICACY FOLLOWING SWITCH FROM SALMETEROL/FLUTICASONE COMBINATION TO INDACATEROL MONOTHERAPY IN PATIENTS WITH MODERATE COPD: THE INSTEAD STUDY

Introduction Many patients with low risk of COPD exacerbations receive twice-daily (bid) LABA/ICS, salmeterol/fluticasone (SFC), for maintenance treatment. This study evaluated the effect of switching these patients to a once-daily (od) LABA, indacaterol, monotherapy.

Methods INSTEAD was a 26-week double-blind, double-dummy study in patients aged ≥40 years, with moderate COPD (post-bronchodilator FEV₁, 50–80% predicted) and no exacerbations in the past 12 months, who were receiving SFC 50/500 µg bid for ≥3 months prior to study entry. Patients were randomised (1:1) to continue with SFC 50/500 µg or to be switched (with no washout) to indacaterol 150 µg. The primary objective was to demonstrate non-inferiority of indacaterol to SFC, measured by trough FEV₁ after 12 weeks (non-inferiority margin: 60 mL). Trough FEV₁ was also evaluated at 4, 8 and 26 weeks. TDI and SGRQ-C total scores were evaluated at Weeks 12 and 26; the annualised rate of exacerbations and safety were evaluated over 26 weeks.

Results A total of 581 patients were randomised (indacaterol: 293; SFC: 288); 85.4% completed the study. The primary endpoint was met, with a LSM difference in trough FEV₁ between indacaterol and SFC of −9 mL (95% CI: −45 to 26 mL; p = 0.002 for NI). There were no significant differences between treatments in trough FEV₁ at any of the other visits (Baseline and Weeks 4, 8 and 26). The TDI and SGRQ-C total scores and their responder rates were similar between two treatments, at both Weeks 12 and 26 (Table 1). During the 26 week treatment period, 79.5% and 74.7% of patients in the indacaterol and SFC groups, respectively, experienced no exacerbations. There was no statistically significant difference between treatments in the rate of all COPD exacerbations per year, with rates of 0.57 vs 0.67, respectively (RR 0.86 [95% CI 0.62, 1.20]; p = 0.367). Adverse events (AEs) and serious AEs were comparable between the treatment arms.

Conclusion Indacaterol was non-inferior to SFC in terms of bronchodilatation and showed similar efficacy in terms of breathlessness, health status, and exacerbation rate indicating that this group of patients can be switched from SFC to indacaterol 150 µg with no loss in efficacy.

DOUBLE-BLIND MULTI-CENTRE RANDOMISED CONTROLLED TRIAL OF VITAMIN D3 SUPPLEMENTATION IN COPD (VIDICO)

Introduction and objectives Inadequate vitamin D status is common in patients with COPD, and it associates with susceptibility to upper respiratory infection (URI) – a major precipitant of exacerbation. Multi-centre trials of vitamin D supplementation for prevention of exacerbation and URI in COPD are lacking. We therefore conducted a multi-centre double-blind randomised placebo-controlled trial of vitamin D supplementation for the prevention of moderate/severe exacerbation and URI in adults with COPD.

Methods Two hundred and forty patients were allocated to receive a 2-monthly oral dose of 3 mg vitamin D₃ or placebo for one year. Co-primary outcomes were time to first moderate/
severe exacerbation and time to first URI. Secondary outcomes included peak severity and area under the curve for exacerbation symptoms. A pre-specified sub-group analysis was conducted to determine whether effects of the intervention on co-primary outcomes were modified by baseline vitamin D status. This trial is registered with ClinicalTrials.gov (NCT00977873).

Results 122 participants were allocated to the intervention arm of the trial, and 118 to the control arm. Vitamin D supplementation did not influence time to first exacerbation (HR 0.86, 95% CI 0.60–1.24, p = 0.42) or time to first URI (HR 0.95, 95% CI 0.69–1.31, p = 0.75) in the study population as a whole, but it did reduce peak severity (p = 0.042) and area under the curve (p = 0.032) for exacerbation symptoms. Pre-specified sub-group analysis revealed that vitamin D supplementation was protective against moderate/severe exacerbation among the 148 participants with baseline serum 25-hydroxyvitamin D (25(OH)D) concentration < 50 nmol/L (aHR 0.57, 95% CI 0.35 to 0.92, p = 0.021), but not among the 92 participants with baseline serum 25(OH)D ≥ 50 nmol/L (aHR 1.45, 95% CI 0.81 to 2.62, p = 0.21; P for interaction = 0.021). Baseline vitamin D status did not modify the effect of vitamin D supplementation on risk of URI (P for interaction = 0.41).

Conclusions Vitamin D supplementation protected against moderate/severe exacerbation, but not upper respiratory infection, in COPD patients with baseline 25(OH)D < 50 nmol/L. It also modestly reduced peak severity and area under the curve for exacerbation symptom scores, irrespective of baseline vitamin D status.

Abstract S105 Table 1 Mean changes in, FVC, at IOS 5Hz and IOS 20hz, FeNO and PWV after exposures began in Oxford Street (OS) and Hyde Park (HP)

<table>
<thead>
<tr>
<th></th>
<th>Healthy</th>
<th>COPD</th>
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<tr>
<td></td>
<td>OS HP Δd</td>
<td>p</td>
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</table>
| Spirometry (Δ%)
| FEV1 1 h      | 0.78 ± 0.21 | 0.09 | -2.30 ± 0.68 | -4.00 ± 0.01 * |
| FEV1 2 h      | 0.49 ± 0.28 | 0.17 | -1.43 ± 0.38 | -1.05 ± 0.39 |
| FEV1 6 h      | 1.84 ± 0.35 | 0.01 * | 1.68 ± 0.20 | 2.08 ± 0.41 |
| FEV1 24 h     | 0.05 ± 0.11 | 0.01 * | 0.85 ± 0.93 | 0.93 ± 0.65 |
| PWV (difference m/s)
| IOS 5Hz 4 h   | -0.01 ± 0.00 | 0.00 | -0.03 ± 0.02 | 0.05 ± 0.01 * |
| IOS 20Hz 4 h  | -0.01 ± 0.00 | 0.00 | -0.01 ± 0.02 | 0.04 ± 0.03 |
| IOS 20Hz (difference kPa/l/s) 4 h | -0.01 ± 0.00 | 0.00 | -0.01 ± 0.01 | 0.03 ± 0.02 | 0.04 * |
| IOS 5hz (difference kPa/l/s) 4 h | -0.01 ± 0.00 | 0.00 | -0.03 ± 0.02 | 0.03 ± 0.02 |
| PWV (difference m/s)
| 3 h           | -0.1 ± 0.02 | 0.47 | 0.1 ± 0.6 | 0.08 ± 0.03 * |
| 6h            | 0.3 ± 0.03  | 0.32 | 0.2 ± 0.3 | 0.03 ± 0.03 * |
| 24 h          | 0.6 ± 0.04  | 1.0 ± 0.04 * | 0.3 ± 0.7 | 0.32  |

*p < 0.05
Δ d Mean difference of difference between each exposure site

Introduction and objectives We studied the changes in lung function and cardiovascular responses in healthy volunteers and patients with COPD exposed to the high pollution levels in a busy London street.

Methods Using a cross-over design, 37 healthy volunteers and 37 COPD patients (walked along Oxford Street (diesel only traffic) and, on a separate occasion, in Hyde Park (low or little traffic), London for two hours. Cardio-respiratory measurements were performed at baseline, and during and after each exposure, alongside personal particulate and gaseous exposure measurements.

Findings Compared to Hyde Park, mean exposures on Oxford Street had higher levels of black carbon (10.4 µg/m³ vs. 1.2 µg/m³, p < 0.001) and ultrafine particle counts (25472/cm³ vs 5709/cm³, p < 0.001).

In comparison with Hyde Park the healthy subjects had a mean fall in FEV1 from baseline of 6.05% (p = 0.01) 6 h and a fall of 4.17% (p = 0.01) 24 h after arrival in Oxford St. There was no associated drop in FVC. Arterial stiffness measured by pulse wave velocity (PWV) increased 24 h after arriving on Oxford Street.

In volunteers with COPD, there was a mean fall in FEV1 of 4% (p = 0.01) with an associated drop in FVC of 3.4% (p = 0.02) one hour after the start of exposure on Oxford Street, compared to Hyde Park. Measurement of impulse oscillometry in volunteers with COPD demonstrated increased arterial resistance at 5 Hz of 0.05 kPa/L/s (p = 0.01) four hours and at 20 Hz of 0.02 (p = 0.04) 24 h after exposure began on Oxford Street. PWV increased by 0.8 m/s and 0.5 m/s three hours and six hours after exposure started on Oxford street respectively.

There were no changes in FeNO in either group between the two sites.

Preliminary multivariate analysis has so far found no associations with individual particulate measurements.

Conclusions These findings show that airways obstruction occurred in both the healthy volunteers and COPD patients exposed to ambient levels of diesel pollution on a busy London Street. The associated vascular dysfunction was more prominent in COPD patients. Further analyses of markers of inflammation in the collected samples are now needed to ascertain the mechanistic cause of the pathophysiological findings.
Introduction and objectives

The major cost to health services of COPD care is hospital admission for exacerbation. Reducing length of stay (LOS) will reduce cost, yet there is wide variability across patients and hospitals. We test the hypothesis that these variations may be attributed to either patient characteristics, hospital characteristics and/or the so-called hospital-clustering effect, which indicates that patients with similar characteristics may experience different processes of care and outcomes depending on the hospital to which they are admitted.

Methods

The European COPD Audit which was carried out in 432 hospitals from 13 countries, included data from 16,018 patients admitted over an 8 week period. The recorded variables included information on the patient and disease characteristics, resources available and clinical practice. Variables in each category associated with LOS were evaluated by a multivariate multi-level analysis and expressed as odds ratios (OR).

Results

Mean LOS was 8.7 days (median: 7, standard deviation: 8.3, interquartile range: 4–11). Factors associated with an LOS higher than the median (see figure) were clinical with the highest impact in patients with use of mechanical ventilation (OR: 4.74) and higher oxygen flows (OR 2.63). In-hospital treatments, comorbidities and patient-related variables including GOLD class IV (OR 1.77) were also significant. These relationships were maintained with respect to longer LOS (> 21 days). Neither the day of admission, nor any of the resource variables were associated with significant differences in LOS. The crude variability of LOS between the different countries was reduced after accounting for these clinical factors and the clustering effect.

Conclusions

This study demonstrates a noteworthy reduction in the observed crude inter-hospital variation in LOS after accounting for the hospital-cluster effect and patient related variables. This emphasises the predictor importance of the patients’ clinical conditions and interventions, and underestates the impacts of hospital resources and organisational factors. This “real-life” reflection may highlight some valid learning points that may help us to determine which achievable strategies are most relevant to improve outcomes.

Abstract S107 Table 1

<table>
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<tr>
<th></th>
<th>Minimally adjusted OR (95% CI)</th>
<th>Adjusted for in-hospital factors OR (95% CI)</th>
<th>Adjusted for use of secondary prevention OR (95% CI)</th>
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<td>1.16 (1.07–1.26)</td>
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<td>180 day mortality</td>
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<td>1.39 (1.31–1.47)</td>
<td>1.35 (1.24–1.46)</td>
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Introduction

COPD patients are at increased risk of myocardial infarction (MI) and have increased mortality after an MI. Although some of this increased risk may be due to COPD itself, differences in management after an MI may play a role. We therefore investigated whether the increased in-hospital and 180 day mortality for COPD patients could be explained by differences in in-hospital and discharge treatment.

Methods

Patients with a first MI between 2003–2013 were identified from the UK MINAP database. COPD patients had a record of obstructive airway disease, smoking history and were aged >35 years. Logistic regression was used to compare mortality in-hospital and at 180 days post-discharge between COPD and non-COPD patients. All models were adjusted for age, sex, smoking, previous cardiovascular disease, renal failure, diabetes and cardiovascular drugs used on admission. Variables relating to in-hospital management (delay in diagnosis, use of reperfusion and time to reperfusion/use of angiography in-hospital) and use of secondary prevention of MI were investigated.

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MIF as the key regulator for mesenchymal stem cells expressing full length TRAIL – a promising therapy for cancer

ZQ Yuan, KK Kolluri, SM Janes. University College London, London, UK

Bone marrow derived mesenchymal stem cells (MSCs) are promising tools for lung cancer therapy considering their tendencies for tumour homing and low immunogenicity. Tumour necrosis factor related apoptosis inducing ligand (TRAIL) is a pro-apoptotic protein that induces selective apoptosis of tumour cells, while sparing normal cells. Therefore, it is expected that MSCs engineered to produce TRAIL will home to and kill cancer cells.

In this study, two lentiviral vectors were constructed to express the full-length (fIT) or a truncated soluble form of TRAIL (sIT) driven by a CMV promoter/enhancer. A secretion targeting sequence and an isoleucine zipper (ILZ) peptide were sequentially added to the N-terminal of the soluble TRAIL to produce secreted and trimerised TRAIL. TRAIL lentiviruses were prepared and human BM-MSCs were transduced with a multiplicity of infection (MOI) of 2. FACS analysis by anti-TRAIL antibody staining demonstrated that over 99% of fIT or sIT viruses transduced cells are positive for TRAIL expression. TRAIL expression was further confirmed by Western blotting and ELISA assays. The fIT or sIT expressing MSCs both showed similar level of cellular TRAIL expression (~350 ng TRAIL per 1 mg of total cellular protein).

Co-culture of cancer cells with transduced MSCs determined the cancer killing efficacy of MSCs expressing fIT or sIT. Twenty cancer cell lines were tested and classified into four TRAIL response groups; high, medium, low, and no sensitivity to recombinant TRAIL (rTRAIL) at the concentration of 50 ng/ml. At the co-culture ratio of 4:1 cancer to MSC cells, MSC-sIT treatment showed no or only marginal cancer cell killing effect, in contrast, MSC-fIT showed promising effects on all tested cell lines, with an apoptosis induction rate ranging between 35–75%. In groups designated as high, moderate and low, MSC-fIT are as effective as rTRAIL and induced marked cell death (p < 0.001) in cell lines which showed no sensitivity to rTRAIL (Figure).

In conclusion, these results demonstrate MSC-fIT is a promising cell therapy and have great potential for clinical treatment of lung cancers and pleural metastases.
DYSREGULATED IRON METABOLISM MEDIATED BY IRP2 MAY INFLUENCE LUNG CANCER PROGRESSION, PARTICULARLY IN THE CONTEXT OF CIGARETTE SMOKE EXPOSURE

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10.1136/thoraxjnl-2014-206260.116

Background Iron is required for cell growth, and various cancers have been shown to proliferate more readily when iron replete. We have shown this previously in lung cancer and further demonstrated that this was reduced by either iron chelation or knockdown of IREB2, an iron regulatory gene. Differences in iron content of bronchoalveolar lavage (BAL) fluid have been reported in smokers compared to non-smokers, so we hypothesised that iron dysregulation might be an active mechanism of cancer progression in smokers.

Methods Two lung cancer cell lines were cultured with either ferrous (Fe2+) or ferric (Fe3+) forms of iron, or with cigarette smoke extract (CSE). Proliferation, apoptosis, necrosis and migration were assessed by BRDU assay, FACS and scratch wound assay respectively. Iron regulation was assessed by means of gene expression and Western blot for IREB2 (protein product IRP2), ferritin and transferrin receptor.

Results Cancer cells proliferated more in the presence of ferrous iron or 5% CSE (p = 0.045) and survival poorer (p = 0.079).

Conclusions Proliferation of cancer cells driven by iron dysregulation may be a clinically relevant mechanism in lung cancer, particularly in smokers.

REFERENCES

METHODS TO ISOLATE BASAL CELLS FROM THE RESPIRATORY EPITHELIUM

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10.1136/thoraxjnl-2014-206260.117

Introduction and objectives Maintenance of a healthy respiratory epithelium is essential in the prevention of airway disease. Perturbations in airway homeostasis have been linked to the pathogenesis of airway disease including asthma, fibrosis and lung cancer. The ‘stem cell hypothesis’ describes how a change within cells responsible for airway maintenance and repair can lead to development of cancer. Basal stem/progenitor cells in the upper airways are suggested to represent the cell of origin in squamous cell carcinoma and therefore are of research interest.

Isolation of this cell type has been hampered because established airway enzymatic digestion methods destroy epitopes of interest on the surface of basal cells. We sought an optimised method of digestion for the isolation of viable basal cells from murine, and then human, airway epithelium.

Methods Conventional enzymatic digestion of the murine upper respiratory epithelium involves an overnight pronase incubation. Using flow cytometry, we compared this strategy to other reported methods: a dispase/trypsin digest, collagenase incubation and a combination of these.

A method allowing selection of a pure basal cell population in the murine trachea was subsequently translated to human airways to assess its efficacy.

Results Following pronase digestion, only 2% of epithelial cells were basal cells, probably as a result of enzymatic epitope removal. Optimal extraction of murine basal cells involved removal of the epithelium through a dispase/trypsin incubation followed by incubation of tracheal remnants in collagenase to release the remaining basal cells from submucosal glands. We identified a well-defined basal cell population representing 30% of the airway epithelium, consistent with known airway basal cell frequency, which can be isolated by fluorescence-activated cell sorting.

Application of this strategy to digest human airways revealed a comparable population of basal cells and allowed sorting of a viable cell population.

Conclusions We optimised a method to facilitate the extraction of basal epithelial cells from both mouse and human airways. This strategy allows sorting of a pure, viable basal cell population for use in further assays.

REFERENCE
1. Hegab AE et al. Isolation of basal cells and submucosal gland duct cells from mouse trachea. JOVE, 2012;67

MMP12 AND LMO7 ARE KEY GENES INVOLVED IN THE EARLY PATHOGENESIS OF SQUAMOUS CELL CARCINOMA OF THE LUNG

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10.1136/thoraxjnl-2014-206260.118

Lung cancer is the most lethal cancer type worldwide. In order to improve patient survival it is important to enhance our understanding of the early changes associated with lung cancer progression. UCLH has a unique cohort of patients with pre-invasive lung squamous cell carcinoma (SCC) lesions. Within this cohort there is a discrepancy between the prevalence of pre-invasive lesions and the incidence of invasive lung cancer, which suggests that not all pre-invasive lesions progress to invasive carcinomas. The aim of this study was to identify and characterise key genes involved in the early pathogenesis of lung SCC.

We performed genome-wide gene expression Illumina Whole-Genome DASL® arrays in 19 regressive and 20 progressive pre-invasive lung SCC lesions. The expression of matrix metalloepitidase 12 (MMP12) and LIM domain 7 (LMO7) was also determined in the 39 pre-invasive lung cancer lesions by immunostaining analysis. The functional role of MMP12 and LMO7 in cell migration and invasion was demonstrated by MMP12 and LMO7 knockdown in different squamous cell carcinoma cell lines and human bronchial epithelial cells (HBECs), respectively.

We found 939 genes significantly differently expressed between the progressive and the regressive pre-invasive lung SCC lesions. We identified a remarkably elevated expression of a spectrum of genes in the progressive lung SCC lesions involved in different
related cancer pathways including chromosome instability, p53 signalling and Wnt/b-catenin signalling. MMP12 and LMO7 were found within the highest significantly differently expressed genes and were therefore chosen to pursue studies focused on understanding the potential mechanisms leading to the development of lung SCC. In agreement with the gene expression data the expression of MMP12 and LMO7 proteins were up-regulated and down-regulated, respectively, in progressive when compared with regressive lesions. Inhibiting MMP12 by MMP12 knockdown significantly reduced the migration and invasion of different squamous cell carcinoma cell lines (A431, H357 and H376). We also established HBECs knockdown targeting LMO7. We observed a significant increase in the migration and invasion of HBECs cells in the LMO7 shRNA knockdown compared to control.

Our results suggest that MMP12 and LMO7 may be potential therapeutic markers for lung cancer at early stage.

Infection of the pleural space in disease and on purpose

**S113 PREDICTORS OF BACTERIAL ‘LOAD’ IN PLEURAL INFECTION**


10.1136/thoraxjnl-2014-206260.119

Pleural infection is usually defined using pleural fluid biochemical characteristics, given that only ~30% of cases are culture positive, but the relationship between these characteristics and pleural space bacterial concentration is unclear.

We developed an assay to estimate bacterial ‘load’ using quantitative polymerase chain reaction (qPCR) to determine 16S rRNA gene copy number in pleural fluid samples (this gene is present in all bacteria). This enabled us to explore the relationship between patient characteristics and pleural fluid bacterial ‘load’.

**Methods** Pleural infection samples were obtained from the Second Multicentre Intrapleural Sepsis randomised controlled Trial (MIST2), REC no. 04/MRE5/53. DNA was extracted using the FastDNA SPIN Kit. Quantitative PCR (qPCR) of the 16S rRNA gene was undertaken using the ultra-pure Power SYBR Green PCR reagent and primers that amplified the 467 nt V3–4 region of the 16S rRNA gene. A 3-step thermal cycling profile was empirically determined to give optimal results. Ten-fold dilutions of *Acidothermus cellulolyticus* DNA were used to estimate sample 16S rRNA gene concentration. All PCRs were performed in duplicate. Melt-curve analyses and agarose gel electrophoresis of qPCR amplicons were used to ensure absence of non-specific PCR products.

**Results** 172 pleural fluid samples were analysed. Pleural fluid pH, culture status, appearance, LDH and glucose were all predictive of bacterial load (see Table). Patient C-reactive protein (CRP) and white cell count (WCC) were not significantly associated with bacterial load.

**Conclusions** Bacterial ‘load’ was associated with acknowledged predictors for pleural infection. Such findings add further support to the utility of pH, glucose and LDH values as proxies for pleural infection, in the correct clinical context. Patient WCC and CRP were not significantly associated with bacterial ‘load’.

This assay is limited in that it assesses total bacterial DNA (from viable and dead bacteria), rather than quantifying viable

| Abstract S113 Table 1 Relationships between copies of 16S rRNA gene (base 10 logarithmic values) and characteristics of patients and pleural fluid (PF) samples |
|---------------------------------|------------------------------|-----------------|-----------------|-----------------|-----------------|
|                                | Number | Copies of 16S rRNA gene, measured by qPCR | Geometric mean | 95% CI | p value |
|                                |        | % change per unit | 95% CI         | Geometric mean | 95% CI | p value |
| PF pH                          | 97     | -89.6 | -97.6, -55.5 | 0.003 |
| PF culture status              |        |        |                |                |                |            |
| Negative                       | 110    | 2.8 × 10^3 | 1.9 × 10^3, 4.0 × 10^3 | 0.0001 |
| Positive                       | 44     | 2.2 × 10^3 | 1.2 × 10^3, 4.0 × 10^3 | 0.0001 |
| PF appearance                  |        |        |                |                |                |            |
| Non-purulent                   | 74     | 1.9 × 10^3 | 1.2 × 10^3, 2.9 × 10^3 | 0.0001 |
| Purulent                       | 76     | 1.4 × 10^3 | 8.8 × 10^2, 2.2 × 10^3 | 0.0001 |
| PF LDH                         |        |        |                |                |                |            |
| ≤1000                          | 26     | 1.4 × 10^3 | 6.9 × 10^2, 2.8 × 10^3 | 0.0001 |
| 1000–5000                      | 41     | 4.1 × 10^3 | 2.3 × 10^3, 7.1 × 10^3 | 0.0007 |
| >5000                          | 36     | 6.2 × 10^3 | 3.4 × 10^3, 1.1 × 10^4 | 0.0007 |
| PF glucose                     |        |        |                |                |                |            |
| ≤1.0                           | 43     | 5.9 × 10^3 | 3.4 × 10^3, 1.0 × 10^4 | 0.0007 |
| 1.0–2.2                        | 14     | 2.9 × 10^3 | 1.1 × 10^3, 7.3 × 10^3 | 0.0007 |
| >2.2                           | 35     | 1.5 × 10^3 | 8.5 × 10^2, 2.8 × 10^3 | 0.0007 |
| Patient CRP                    |        |        |                |                |                |            |
| ≤100                           | 28     | 3.5 × 10^3 | 1.6 × 10^3, 7.5 × 10^3 | 0.372 |
| 100–160                        | 27     | 3.5 × 10^3 | 1.6 × 10^3, 7.7 × 10^3 | 0.372 |
| ≥160                           | 87     | 5.8 × 10^3 | 3.7 × 10^3, 8.9 × 10^3 | 0.372 |
| Patient WCC                    |        |        |                |                |                |            |
| ≤11.0                          | 41     | 3.7 × 10^3 | 1.9 × 10^3, 7.0 × 10^3 | 0.215 |
| 11.0–16.5                      | 58     | 4.6 × 10^3 | 2.7 × 10^3, 7.9 × 10^3 | 0.215 |
| >16.5                          | 53     | 7.7 × 10^3 | 4.4 × 10^3, 1.4 × 10^4 | 0.215 |

1% change in 16S rRNA gene copies number per unit increase in the specified variable. CI = confidence interval. p values for tests of linear trend (continuous variables) and for tests of heterogeneity (categorical variables). LDH units – IU/L; glucose units – mmol/L; CRP units – mg/L; WCC units – x 10^9/L.
bacteria. Further, bacteria vary in their copy number of the 16S rRNA gene, dependent on species. Despite these limitations, our associations have reached a strong level of significance.

PREVIOUSLY UNRECOGNISED ORAL ANAEROBES IN PLEURAL INFECTION
10.1136/thoraxjnl-2014-206260.120

Laboratory culture of pleural infection samples is positive in only 30% of cases, probably related to antibiotic usage and fastidious or unculturable organisms such as some anaerobes. Previous studies using capillary sequencing of the 16S rRNA gene improves rates of organism identification, but is unable to resolve the polymicrobiality thought to be present in anaerobic infection.

We used ultra-deep pyrosequencing to definitively characterise anaerobic pleural infection.

Methods Pleural infection samples were obtained from the Second Multicentre Intrapleural Sepsis randomised controlled Trial (MIST2), REC no. 04/MRE5/53. DNA was extracted using the FastDNA SPIN Kit. Modified ‘fusion’ primers amplified the V4–6 regions of the 16S rRNA gene. Subsequent pyrosequencing was performed on the Roche 454 GS FLX instrument. Data analyses were performed using the open source ‘Quantitative Insights Into Microbial Ecology’ platform. Strategies were used to control for contamination.

Results 172 pleural fluid samples were available, 98 of which were successfully sequenced. 32/98 samples contained anaerobes (defined when ≥10% of sequences in a sample represented anaerobes).

Fusobacteirales, particularly *Fusobacterium nucleatum*, and Bacteroidales, particularly *Prevotella* spp. were commonly found although other anaerobes were seen (see Figure). Anaerobic pleural infection was usually polymicrobial, with an estimated 4–5 operational taxonomic units (“species”) per sample. Particular patterns of co-infection were *Fusobacterium nucleatum* and *Streptococcus milleri* group although *Prevotella* spp. ± *Fusobacterium* spp. ± *Porphyromonas* spp. ± *Treponema* spp. also co-infected several samples.

Many species were found that have not been previously documented, including *Atopobium rimae*, *Cryptobacterium curatum*, *Lactobacillus* spp., *Stomatobaculum* spp., *Oribacterium* spp., *Prevotella baronae*, *Prevotella dentalis/Hallella seregens*, *Prevotella scopos*, *Fretibacterium* spp., *Tanerella forsythia*, *Treponema denticola*, *lecitinolyticum*, *maltophilum*, *medium* and *socra*nskii. Intriguingly, the original isolation and description of almost all these anaerobes were from the oropharynx and some have never been detected at other body sites.

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**Abstract S114 Figure 1** Individual bacteriology of all samples that had anaerobes account for at least 10% of sequence reads.
Conclusions Anaerobic infection occurs in ∼33% of cases of pleural infection and is typically polymicrobial. Sequencing revealed many anaerobic bacteria never previously isolated in the pleural space. These bacteria have a strong association with the oropharynx, particularly the gingival crevices. Such findings add to our understanding of the mechanism of development of pleural infection.

Discussion This is the first study examining the diagnostic utility of pleural fluid ADA in a low TB incidence area. The chance of an effusion with an ADA under 35 IU/L being of tuberculous aetiology was negligible and empirical anti-TB therapy could be avoided in such cases. A pleural ADA of over 35 IU/L in lymphocyte-predominant pleural fluid gives a strong suspicion of tuberculous aetiology. In patients who are unsuitable for more invasive procedures this could be used as an indication to start therapy.

Abstract S115

PLEURAL FLUID ADENOSINE DEAMINASE (ADA) IN THE DIAGNOSIS OF TUBERCULOUS PLEURAL EFFUSIONS IN A LOW INCIDENCE POPULATION

Introduction Numerous studies have assessed the diagnostic ability of pleural adenosine deaminase (ADA) in detecting tuberculous pleural effusions, with good specificity and sensitivity reported. However, in the UK (UK) ADA is not routinely used in the investigation of a patient with a pleural effusion, mainly due to a lack of evidence as to its utility in areas where tuberculous (TB) incidence is low.

Methods Patients presenting with an undiagnosed pleural effusion to a tertiary pleural centre in South-West England over a 3 year period, were prospectively recruited to a pleural biomarker study, in which baseline pleural fluid samples were collected and stored. Samples from consecutive patients with robust 12-month follow up data and confirmed diagnoses were sent for ADA analysis.

Results Of 338 patients enrolled, 7 had confirmed tuberculous pleural effusion (2%). All 7 TB effusions were lymphocyte predominant with a median ADA of 72.0 IU/L (range- 26.7 to 91.5) compared to a population median of 12.0 IU/L (range- 0.3 to 568.4). Using the established cut off of 35 IU/L, ADA was shown to have a negative predictive value (NPV) of 99.7% (95% CI; 98.2–99.9%) for the exclusion of TB, and sensitivity of 85.7% (95% CI; 42.2–97.6%) with an area under the curve of 0.88 (95% CI; 0.732–1.000). In the context of a lymphocytic effusion an ADA over 35 IU/L had a sensitivity and positive predictive value of 85.7% (95% CI; 42.2–97.6%), see figure. Bacterial pleural infection was the main alternative cause of raised ADA in our cohort.

Discussion This is the first study examining the diagnostic utility of pleural fluid ADA in a low TB incidence area. The chance of an effusion with an ADA under 35 IU/L being of tuberculous aetiology was negligible and empirical anti-TB therapy could be avoided in such cases. A pleural ADA of over 35 IU/L in lymphocyte-predominant pleural fluid gives a strong suspicion of tuberculous aetiology. In patients who are unsuitable for more invasive procedures this could be used as an indication to start therapy.

Abstract S116

SYSTEMIC CHEMOTHERAPY AND THE RISK OF PLEURAL INFECTION WITH INDWELLING PLEURAL CATHETERS (IPCS)

Methods A detailed retrospective review was performed of the first 100 patients treated with an IPC from February 2011 to December 2013 at Queen Alexandra Hospital, Portsmouth.

Results 11 of the 100 IPC insertions developed pleural infection (11%), four of whom had received chemotherapy (see table). Overall 15 patients received chemotherapy after IPC insertion with an interval varying from 0 days (same day) to 43 days, with a median of 9 days. The 2 × 2 table compared the proportion of patients developing pleural infection with and without chemotherapy.

Further analyses assessed the interval from chemotherapy to IPC insertion and whether it influenced the numbers of pleural infections, using cut-off points at 7, 14, 21 and 28 days. There was no significant difference at any of these time-points (p=NS).

Conclusions The pleural infection rate with an IPC was slightly higher than previous published series. There was however no significant increase in pleural infection in those receiving chemotherapy, although these analyses did not account for variability in tumour type, tumour stage, performance, co-morbidity and leucopenia at time of insertion. While the analyses were not significant, this needs to be retested in larger or combined registries of patients treated with IPCs for pleural malignancy.
SURVIVAL IN PATIENTS WITH MALIGNANT PLEURAL EFFUSIONS WHO DEVELOPED PLEURAL INFECTION: A RETROSPECTIVE CASE REVIEW FROM 6 UK CENTRES

Abstract S117 Figure 1 Survival in patients with malignant pleural effusions who developed pleural infection: a retrospective case review from six UK Centres

Background The incidence of malignant pleural effusions (MPE) is increasing and overall prognosis remains poor. In-dwelling pleural catheters (IPCs) relieve symptoms, but increase the risk of pleural infection. We reviewed survival times of cases of pleural infection in patients with IPCs for MPE from 6 UK centres.

Methods Baseline data were collected for all IPC insertions from 1/1/05 to 31/1/14. Survival times were analysed by underlying tumour. Results were compared with national data, and with data from a cohort of 789 patients with MPE (the LENT cohort). LENT scores were used to calculate individual predicted life expectancy, which was compared with actual survival.

Results Of 672 IPCs inserted across 6 centres during the study period, 25 patients (3.6%) experienced pleural infection. 19/25 were male, median age 69 (range 35-79). 12/25 had mesothelioma, 8/25 lung cancer, 3/25 breast cancer, 1/25 lymphoma and 1/25 thyroid cancer. 18/25 had a performance status of 0-1, and 19/25 received oncological treatment.

Survival with MPE and pleural infection compared favourably with the LENT cohort (see figure 1). Median survival with mesothelioma and pleural infection was 753 days (95% confidence interval 446-1089) compared with 339 days in the LENT cohort (95% CI 267-442) and less than 365 days in nationally reported data. Patients with lung cancer and pleural infection also outlived their LENT counterparts; median survival of 138 days (95% CI 62-479) versus 74 days (95% CI 60-90). Patients with breast cancer had similar survival times (167 vs 192 days).

LENT scores were calculated where possible. 9/13 (69%) outlived their predicted life expectancy. 16/25 (64%) developed infection within 90 days of IPC insertion. There was no difference in survival times between patients with early and late infection (p = 0.6).

Discussion In this series of patients with IPCs, pleural infection was associated with longer survival with mesothelioma and lung cancer, but not breast cancer. Most patients experienced early infection, suggesting this result isn’t simply a result of higher infection rates in patients who survive longer with an IPC in situ. We propose that pleural infection stimulates a local immune response, which acts against tumour. Further studies are planned to investigate this hypothesis further.

Clinical investigations and outcomes in pulmonary vascular disease

Abstract S118 INCREASED INCIDENCE AND SEVERITY OF CHRONIC THROMBOEMBOLIC PULMONARY HYPERTENSION FOLLOWING THE INTRODUCTION OF A ONE-STOP CLINIC FOR ACUTE PULMONARY EMBOLISM

Introduction The management and follow-up of pulmonary embolism (PE) is delivered by various specialities resulting in both under and over investigation for suspected chronic thromboembolic pulmonary hypertension (CTEPH). To standardise our approach to long-term PE management a “one-stop” clinic was established in Sheffield in March 2010 to review all patients approximately 3 months after their presentation with acute PE. The aim of this study was to evaluate the incidence and severity of CTEPH identified from a one-stop clinic using an investigative strategy based on careful clinical assessment.

Methods Consecutive patients attending the one-stop PE clinic following hospital admission with acute PE were identified. During the one-stop consultation a haematologist and respiratory physician reviewed the patient jointly. The need for further investigation was based on clinical assessment. CTEPH was defined as mean pulmonary artery pressure (mPAP) at right heart catheterisation ≥25 mmHg and required multimodality imaging (isotope perfusion scanning, CT pulmonary angiography and MR imaging including MRA and MR perfusion mapping) demonstrating classical features of CTEPH.

Results Over a 3-year period between March 2010 and March 2013, 616 patients (mean age 67.7 years, 50% male) attended the one-stop PE clinic approximately 3 months following their acute presentation. 16 patients were diagnosed with CTEPH. An overall diagnostic rate of CTEPH of 2.6% for patients seen at the clinic and an annual incidence of 8.9/million/year was observed based on a referral population of 600,000. This compares to an annual incidence of CTEPH of 4.8/million/year in patients referred to the SPVDU over the same time period, based on a referral population of 15 million. The 16 patients with CTEPH had mPAP 37 ± 11 mmHg, pulmonary vascular resistance (PVR) 362 ± 240 dynes, significantly lower than patients with CTEPH diagnosed at the SPVDU until 2010 (n = 242) mPAP 48 ± 11 mmHg and PVR 735 ± 389 dynes (Hurdman et al Eur Respir J 2012;39(4):945-955).

Conclusion Introduction of a one-stop PE clinic for routine follow-up of patients with acute pulmonary embolism identifies
patients with higher rates of CTEPH with less severe pulmonary haemodynamic changes.

**S119** LEFT VENTRICULAR DYSFUNCTION INFLUENCES SURVIVAL IN CONNECTIVE TISSUE DISEASE ASSOCIATED PULMONARY ARTERIAL HYPERTENSION BUT NOT IDIOPATHIC PULMONARY ARTERIAL HYPERTENSION

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**Background** Connective tissue disease – associated pulmonary artery hypertension (CTD-PAH) has a worse prognosis compared with idiopathic pulmonary arterial hypertension (IPAH). We investigated the prognostic significance of left and right cardiac dysfunction in IPAH and CTD-PAH.

**Methods and results** Between 2003 and 2011, patients with a new suspected diagnosis of pulmonary hypertension underwent diagnostic assessment including cardiac magnetic resonance (CMR) imaging and right heart catheterization (RHC). 138 patients fulfilled the criteria for pulmonary arterial hypertension, of which 74 were diagnosed with IPAH and 38 were diagnosed with CTD-PAH. At baseline, there was no significant difference in age, functional class, lung function or six-minute walk distance between the two groups. At CMR, both groups had right ventricular (RV) dilatation and impaired RV systolic function, but well preserved left ventricular (LV) ejection fraction. Patients with IPAH had greater right ventricular hypertrophy than those with CTD-PAH (VMI 1.16 v 0.99, p = 0.03). Left atrial volume, a marker of LV diastolic dysfunction, was lower in IPAH than CTD-PAH (23 v 33 ml/m², p < 0.0001). At RHC, mean pulmonary artery pressure was higher in IPAH than CTD-PAH (50 v 43 mmHg, p = 0.01).

There was no difference in the distribution of initial disease-targeted therapies between the groups. Survival was better in IPAH than in CTD-PAH (p = 0.03), with rates of 83% at 1 yr and 74% at 3 yrs in IPAH, but 75% at 1 yr and 53% at 3 yrs in CTD-PAH. Poor baseline right ventricular function was associated with reduced survival in both conditions. However, poor left ventricular function, as measured by left ventricular stroke volume index (LVSVI), only influenced survival in CTD-PAH (p = 0.002) and not in IPAH (p = 0.21).

**Conclusions** Poor LVSVI at diagnosis is associated with impaired survival in CTD-PAH but not IPAH. Intrinsic LV problems, particularly diastolic dysfunction, may contribute to the excess mortality in CTD-PAH.

**S120** RIGHT VENTRICULAR DYSFUNCTION IN PULMONARY HYPERTENSION WITH COMBINED PULMONARY FIBROSIS AND EMPHYSEMA SYNDROME

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**Introduction** Recent studies have suggested that the coexistence of emphysema and fibrosis alters clinical outcome. The aim of this study was to investigate the comparative clinical characteristics, pulmonary function, haemodynamics and right ventricular (RV) function and outcome in patients with pulmonary hypertension associated with combined pulmonary fibrosis and emphysema (PH–CPFE), chronic obstructive pulmonary disease (PH–COPD) and interstitial lung disease (PH–ILD).

**Methods** In 79, incident patients with pulmonary hypertension associated with respiratory disease, cardiovascular magnetic resonance imaging was performed at 1.5T. Emphysema and fibrosis were scored on high resolution computed tomography scans. Demographic data, lung function tests and right heart catheterisation were also performed.

**Results** Patients with pulmonary hypertension associated with combined pulmonary fibrosis and emphysema syndrome had lower right ventricular ejection fraction when compared to both patients with PH–COPD and PH –ILD (p < 0.05). At Kaplan–Meier analysis, patients with PH–CPFE patients had significantly
worse outcome than those with PH-COPD (p = 0.015), and borderline worse outcome than patients with PH-ILD (p = 0.050). Figure. 48 of 94 patients were diagnosed with severe PH-RESP defined at mPAP≥40 mmHg. WHO functional class (p = 0.036), DLCO (p = 0.019), RVEF (p = 0.033) were significant independent predictors of outcome in patients with severe PH-RESP.

Conclusion Patients with severe PH-RESP have a dire clinical outcome. RVEF is an independent predictor of adverse outcome in these patients and may be a powerful biomarker for use in clinical trials of targeted therapy in patients with pulmonary hypertension associated with lung disease, particularly given the unreliable performance of echocardiography in patients with advanced lung disease.

THE UTILITY OF THE INCREMENTAL SHUTTLE WALKING TEST IN PULMONARY HYPERTENSION: RESULTS FROM THE ASPIRE REGISTRY

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Introduction The Incremental Shuttle Walk Test (ISWT) has been evaluated in a number of diseases and found to be a safe, reproducible test which correlates better with VO₂ max than the Six-Minute Walk Test (6MWT). We aimed to evaluate the utility of the ISWT as a prognostic indicator in pulmonary hypertension (PH).

Methods Data was retrieved for consecutive cases of PH diagnosed in our unit from 2001–2010, a cohort previously described. ISWT was performed routinely as part of baseline assessment according to the modified protocol of Singh et al. Data was analysed in 5 Groups according to the distance achieved based on ISWT level. A p-value of was deemed statistically significant.

Results 1002 of 1,344 patients diagnosed with PH underwent baseline ISWT within 3 months of cardiac catheterization and prior to pulmonary vascular therapy. Complete baseline data was available for 998 patients.

Kaplan-Meier analysis showed that increasing level of ISWT was associated with increased survival (Figure 1), including the PAH sub-group, with no ceiling effect.

ISWT distance correlated with WHO Functional Class, right atrial pressure, pulmonary vascular resistance, cardiac index, mixed venous oxygen saturation and percent predicted carbon monoxide diffusion (DLco) (p all ≤0.01). Multivariate Cox regression survival analysis including sex, body mass index, age, haemodynamic parameters and percent predicted DLco, demonstrated that ISWT distance was an independent predictor of survival.

One year follow-up data was available for 397 patients. Kaplan-Meier analysis showed that ISWT level on treatment at 1 year was predictive of survival (p < 0.001). Survival was also superior in patients whose ISWT distance improved from baseline ≥30 m compared to those whose distance remained stable (-20 to +20 m) or declined by ≥30 m (p = 0.20).

Conclusion Baseline ISWT distance correlates with WHO functional class and pulmonary haemodynamics with no ceiling effect. It is an independent predictor of survival and change in ISWT predicts outcome. These features make it a viable alternative to the 6MWT in the assessment of patients with pulmonary hypertension, with a number of potential advantages.

REFERENCES

OUTCOME AFTER PULMONARY ENDARTERECTOMY (PEA): LONG TERM FOLLOW-UP OF THE UK NATIONAL COHORT


Introduction Chronic thromboembolic pulmonary hypertension (CTEPH) is a life threatening condition that historically has a poor outcome with supportive medical treatment. Pulmonary endarterectomy (PEA) is the treatment of choice and offers the only chance of cure. Data on the predictors of long term survival after PEA are limited. We analysed the long-term data from the UK PEA cohort.

Method All patients who underwent a PEA for CTEPH at Papworth hospital between January 1997 and December 2012 were included. Pre- and post-operative data on haemodynamics, exercise capacity, functional class and targeted PAH therapies taken were obtained from databases of the UK PH centres. The NHS spine summary care record tracking system was used for survival data and causes of death from the England and Scotland General Register Offices. The causes of death were further classified into 4 groups: 1. Post operative, 2. Right ventricular failure away from operative period, 3. Related to anticoagulation, 4. Unrelated to CTEPH e.g. malignancy.

Results 880 patients underwent PEA over the 15 year period. The mean age was 57 (range 15–84) and 53% were male. 89% were in WHO functional class 3 or 4 before surgery with a mean mPAP of 47 mmHg and PVR of 830 dynes. Post surgery 84% of patients...
DOES EXERCISING WITH DOMICILIARY NON-INVASIVE VENTILATION (NIV) IMPROVE QUALITY OF LIFE (QOL) IN PATIENTS WITH SEVERE CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)?

Introduction and objectives Patients with severe COPD experience breathlessness leading to exercise limitation impacting on QoL. Pulmonary rehabilitation (PR) can improve QoL, but those with the severest disease are frequently hospitalised and cannot readily access PR. Previous studies have trialled positive pressure as a means of relieving ventilatory load, allowing more severe COPD patients to exercise. Studies have assessed mixed pathology or stable COPD patients. In this study, we have assessed patients with severe COPD admitted to hospital with Type 2 respiratory failure and acidosis treated with acute NIV.

Methods Sixty five COPD patients were randomly assigned to endurance training (ET) or to endurance + strength training (EST). All Patients underwent 3 sessions per week. For ET, as upper intensity training limits were considered 40–50% heart rate reserve and 50% 1RM. Before training programs, at FU1 and at FU2, all patients underwent clinical assessment, respiratory functionality tests, maximal cardiopulmonary test. Repeated measures ANOVA during hospital admission and continued this at home for 3 months post-discharge. Exercising included weights, pedal cycling and walking. QoL was assessed using the St Georges Respiratory Questionnaire (SGRQ) and the London Chest Activities of Daily Living Questionnaire (LCADL). Mean changes in total scores for SGRQ and LCADL were compared between baseline and at 3 months (M3). Data are mean±SD or mean (range).

Results The group (n = 18) age was 66.5 years [46–97], FEV1: 25% predicted [9–51%] and MRC score 3 [1–4]. 3/18 patients died during the study. The results are presented in Table 1.

Conclusion Patients exercising with NIV, in hospital and at home twice weekly (Group 3) showed the greatest improvement in QoL, compared to the other two groups. The use of NIV during exercise at home may assist patients unable to access pulmonary rehabilitation.

REFERENCES

EFFECTS OF TWO ADAPTED PHYSICAL ACTIVITY TRAINING PROGRAMS ON PULMONARY FUNCTIONALITY AND EXERCISE CAPACITY IN PATIENTS AFFECTED BY CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Introduction It has been reported the efficacy of adapted physical activity (APA) in exercise capacity improvement. Nevertheless, there is still no consensus on training modalities and intensities to be prescribed in patients affected by chronic obstructive pulmonary disease (COPD). The aim of the study was to assess the effects of two 16 weeks APA training programs (endurance vs endurance +strength) on respiratory parameters (FVC%, FEV1%, FEV1/FVC %) and exercise capacity (VO2 peak) immediately after APA training program (first follow up: FU1) and after six months (second follow up: FU2).

Methods Sixty five COPD patients were randomly assigned to endurance training (ET) or to endurance + strength training (EST). All Patients underwent 3 sessions per week. For ET, as upper intensity training limits were considered 40–50% heart rate reserve; for EST training limits were considered 40–50% heart rate reserve and 50% 1RM. Before training programs, at FU1 and at FU2, all patients underwent: clinical assessment, respiratory functionality tests, maximal cardiopulmonary test. Repeated measures ANOVA during hospital admission and continued this at home for 3 months post-discharge. Exercising included weights, pedal cycling and walking. QoL was assessed using the St Georges Respiratory Questionnaire (SGRQ) and the London Chest Activities of Daily Living Questionnaire (LCADL). Mean changes in total scores for SGRQ and LCADL were compared between baseline and at 3 months (M3). Data are mean±SD or mean (range).

Results The group (n = 18) age was 66.5 years [46–97], FEV1: 25% predicted [9–51%] and MRC score 3 [1–4]. 3/18 patients died during the study. The results are presented in Table 1.

Conclusion Patients exercising with NIV, in hospital and at home twice weekly (Group 3) showed the greatest improvement in QoL, compared to the other two groups. The use of NIV during exercise at home may assist patients unable to access pulmonary rehabilitation.
was adopted to assess parameters’ variations. Statistical significance was set for \( p < 0.05 \).

**Results** Thirty-five patients (14M/21F; age 71 ± 9 y; FEV₁ 61 ± 14% of predicted) completed the ET program; 30 patients (18M/12F; age 74 ± 6 y; FEV₁ 59 ± 18% of predicted) completed the EST program. In both ET and EST, respiratory parameters did not change. ET FVC\%, FEV₁\%, FEV₁/FVC\% values at FU1 were 76 ± 14, 61 ± 16, 64 ± 12 respectively; at FU2 76 ± 16, 59 ± 16, 61 ± 12. For EST FVC\%, FEV₁\%, FEV₁/FVC\% values at FU1 were 79 ± 14, 59 ± 16, 58 ± 13 respectively; at FU2 83 ± 12, 64 ± 16, 60 ± 13. In ET \( V\text{O}_2\text{peak} \) showed significant variations: 17.7 ± 3.1, 18.8 ± 3.4, 16.3 ± 3.3, before training, at FU1 and at FU2 respectively (\( p < 0.0001 \)). In EST: 19.1 ± 4.9, 20.3 ± 5.9, 18.2 ± 5.5, before training, at FU1 and at FU2 respectively (\( p < 0.008 \)).

**Conclusion** Both ET and EST produced a significant improvement in exercise capacity (\( V\text{O}_2\text{peak} \)) at FU1. Unfortunately, both ET and EST worsened at FU2 vs FU1. However FU2 data were better than at baseline.

**REFERENCES**


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**A COMPARISON BETWEEN WEIGHT SUPPORTED AND UNSUPPORTED EXERCISE ON ENERGY EXPENDITURE AND CARDIORESPIRATORY RESPONSE DURING EXERCISE IN OBESE ADULTS WITH TREATED OBSTRUCTIVE SLEEP APNEA**

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**Background** Weight loss and improving cardiorespiratory fitness are key treatment outcomes for obese individuals with Obstructive Sleep Apnoea (OSA). We investigated the total energy expenditure and cardiorespiratory response to weight supported (cycling) and unsupported (walking) at two different intensities.

**Methods** Individuals with treated OSA and a BMI >30 kg/m\(^2\) performed an incremental cardiopulmonary exercise test on a cycle ergometer (ICE) and a treadmill (ITM) with expired gas analysis to determine the peak oxygen uptake (\( V\text{O}_2\text{peak} \)). Participants completed two endurance tests on each modality matched at 80% and 60% of the highest \( V\text{O}_2\text{peak} \) determined by the incremental tests. The cardiorespiratory responses were measured and total energy expenditure was estimated from the \( V\text{O}_2 \).

**Results** 16 participants (8 male) completed all six tests: mean [SD] age 57[13]y and median [IQ range] BMI 33.3[30.8 to 35.3]kg·m\(^{-2}\). The \( V\text{O}_2\text{pk} \) on the ITM vs ICE was 2268[574] vs 1775[430] ml·min\(^{-1}\), respectively. Participants endured treadmill walking at 80% and 60% \( V\text{O}_2\text{pk} \) for four and nearly three times as long, respectively, compared to cycling with similar cardiovascular responses. The pattern of energy expenditure during rest, exercise and recovery at matched intensities (Figure 1) was similar between modalities at matched intensities.

Total energy expenditure during treadmill walking was greater than cycling at both high (158[101] versus 29[15]kcal) and moderate (178[100] versus 85[59]kcal) intensities. For a thrice weekly exercise regimen of at least moderate intensity, treadmill exercise would typically result in a total of 388 and 277 kcal/week greater energy expenditure than cycle exercise at 80% and 60% \( V\text{O}_2\text{pk} \), respectively.

**Conclusion** Contrary to current guidelines, walking might be the preferred training modality for achieving the combination of weight loss and increased cardiorespiratory fitness in obese adults with OSA.

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**DEVELOPING HEALTHY LIFESTYLE INTERVENTIONS FOR OVERWEIGHT PATIENTS WITH OBSTRUCTIVE SLEEP APNEA (OSA): A SURVEY OF PATIENT ATTITUDES AND CURRENT PRACTICE**

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**Background** Current BTS/SIGN guidelines suggest the inclusion of behavioural interventions as part of the management for overweight patients with Obstructive Sleep Apnoea Syndrome (OSAS). Healthy lifestyle interventions are widely available in a variety of settings for other chronic diseases.

Our aims were to assess:

1. patients’ views and their experience with weight loss and lifestyle changes.
2. Internet and Information Technology (IT) access to investigate if a web-based lifestyle intervention would be feasible.
3. current clinical practice regarding healthy lifestyle advice.
Methods A questionnaire was developed to assess patients’ experience of lifestyle changes, their preferences and willingness to take part in a healthy lifestyle intervention, and their internet and IT usage. This was administered to patients with treated OSAS attending a sleep clinic. The MRC dyspnoea scale grade and Veterans Specific Activity Questionnaire (VSAQ) (1) were measured. Current practice regarding lifestyle advice and interventions, and serial weights were assessed by a case-note review of sequential overweight patients with treated OSAS attending a sleep clinic.

Results 112 patients with treated OSAS completed the survey (results shown in Table 1): 80.5% male, 76% aged 50 to 79 years, mean estimated BMI 35 kg m$^{-2}$, median [IQR] MRC dyspnoea scale 3[2–3] and VSAQ score 5[3–7] indicating being unable to walk briskly. 75% of individuals had access to broadband Internet (Table 1) and over 40% would be interested in a web-based healthy lifestyle intervention. 33 case-notes were reviewed with a mean follow up of 5 years. 27/33 individuals had been given healthy lifestyle advice of which 24/27 was to lose weight. Only two individuals had been recommended to join a leisure programme. Weight remained unchanged over five years after diagnosis, ANOVA p = 0.90.

Conclusions Breathlessness causing reduced physical activity was commonly reported in overweight patients with OSAS. Weight loss is not currently achieved after simple advice from a healthcare professional, and advice or support regarding increasing physical activity is rarely provided. Further support with healthy lifestyle interventions should be explored, and attitudes and Internet access would favour development of a web-based intervention.

REFERENCE

DOES THE TIME OF DAY OF ALLERGEN CHALLENGE INFLUENCE RESPIRATORY INFLAMMATION?

**Introduction**

Circadian variations in immune parameters such as lymphocyte proliferation, antigen presentation and cytokine gene expression have been described. Recently, an association between the molecular circadian clock, immunity and inflammation has been recognised. To date research in this area has focussed on the innate immune response. However, the time at which the lung is exposed to an allergen might significantly affect the ability of the lung to mount an adequate immune response. Furthermore, this line of investigation might provide valuable insight into asthma, a common disease with a strong circadian rhythm.

**Method**

We used a well-defined mouse model of allergic lung inflammation, the ovalbumin challenge model. After initial intraperitoneal sensitisation, 4 groups of C57BL/6 mice received ovalbumin challenge at one of four time points, repeated at the same time for 3 consecutive days. The timepoints used were: 1 am, 6 am, 1 pm or 6 pm. Measurements of airway hyper-responsiveness were recorded, bronchoalveolar lavage was performed and lungs were harvested for immunohistochemistry and for gene analysis by PCR. Experiments were repeated in clock gene knockout mice, *rev-erbα*−/−.

**Results**

- C57BL/6 mice challenged at 1 am develop increased AHR
- This suggests that allergic airway inflammation is under clock control
- *Rev-erbα*−/− mice show identical responses, suggesting that REV-ERBα is not critical to the development of airway inflammation in this model
- C57BL/6 mice challenged at 6 pm develop the most profound inflammatory response within the lung (Figure 1)
- This suggests that allergic inflammation within the lung is caused by a different mechanism to that within the airway, yet is also under clock control

**Discussion**

Understanding the mechanism underlying clock control of allergic lung inflammation and its possible translation to asthma, provides a new therapeutic opportunity. Furthermore, targeting earlier stages in the circadian pathway might narrow the therapeutic window for timing of existing drug delivery, reducing drug dose and minimising side effects by giving shorter acting agents and the most efficacious time of day.
Peripheral Blood Mononuclear Cells from Children with Severe Asthma Exhibit an Impaired Corticosteroid Sensitivity, Which Also Correlates with Increasing Body Mass Index

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Introduction Corticosteroid (CS) insensitivity contributes to the difficulty in managing children with severe asthma. A better understanding of the molecular mechanisms driving this defective response could provide novel therapeutic options for these patients. Peripheral blood mononuclear cells (PBMCs) from adults with severe asthma have been used to demonstrate an impaired sensitivity to CS, enabling the delineation of potential underlying mechanisms. Whether CS insensitivity exists in PBMCs from severely asthmatic children, however, requires further validation.

Objective To determine whether PBMCs from children with severe asthma have an impaired in vitro responsiveness to corticosteroids.

Methods We conducted an observational feasibility study comparing the corticosteroid sensitivity of PBMCs from asthmatic children on British Thoracic Society treatment step 4–5 (n = 7) with healthy controls (n = 5). PBMCs from 5 ml of venous blood were plated in the presence of 100 ng/ml of lipopolysaccharide (LPS), and in the absence or presence of either 10–8 M or 10–6 M of dexamethasone (DEX). ELISA assays were used to determine the levels of TNF-α and IL-8, and the % suppression of these by DEX. Pearson product-moment correlation tests...
were conducted to determine the correlation between in vitro CS sensitivity and different clinical parameters. **Results** There was no difference in baseline or LPS-induced cytokine release from PBMCs between the two groups. The inhibition of TNF-α release by DEX was significantly diminished in children with asthma compared to healthy controls at 10⁻⁶ M concentration (p = 0.018) but no differences were noticed at 10⁻⁸ M concentration, or on LPS-induced IL-8 production. A significant inverse correlation between % inhibition of TNF-α and body mass index (BMI) at 10⁻⁶ M (rs = -0.84, p = 0.02) and 10⁻⁸ M (rs = -0.82, p = 0.02) was found. **Conclusions** Our results show the existence of an impaired CS sensitivity in PBMCs from children with severe asthma, suggesting that these cells can be used for mechanistic investigations. Interestingly, we observed a negative correlation between CS sensitivity and BMI, a novel in vitro finding which supports the association between overweight/obese asthmatic children and a decreased clinical response to CS therapy. Together, these results merit further studies with a larger sample size.

**REFERENCES**
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**S132**

**SPUTUM AND BRONCHIAL BIOPSY EXPRESSION OF 8-OXO-7, 8-DIHYDRO-2'-DEOXYGUANOSINE (8-OXODG) IN ASTHMA IS RELATED TO NEUTROPHILIC INFLAMMATION AND POOR ASTHMA CONTROL**

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**Introduction and objectives** Oxidative stress has been implicated in the pathogenesis of asthma. Validated sputum biomarkers are required to assess this and its relationship to other clinical variables.

We sought to compare sputum and bronchial 8-oxodG expression in asthma and health; assess the sputum repeatability; and explore its relationship with induced sputum inflammatory cells counts and exacerbations.

**Methods** Asthmatics and healthy controls were recruited from a single centre and underwent clinical characterisation including sputum induction (asthma n = 58, health n = 27) and bronchial biopsy (asthma n = 16, health n = 10).

Sputum and epithelial 8-oxodG expression was measured by ELISA and Immunohistochemistry respectively. Sputum asthmatics were assessed at a repeat stable visit at 6 months.

**Results** Between health and asthma, there were no significant differences in the median (IQR) sputum 8-oxodG levels [12 (16)] ng/ml⁻¹ vs. [11 (15)] ng/ml⁻¹, p = 0.36) or the mean (SEM) percentage area of epithelium reaching threshold intensity for 8-oxodG (2.0 (0.7)% vs. 4.4 (1.0)% p = 0.12).

Asthma sputum 8-oxodG correlated with the sputum total cell count (rs = 0.53, p < 0.01), sputum neutrophils (rs = 0.27, p = 0.04), sputum macrophages (rs = -0.31, p = 0.02) and serum IgE (rs = -0.27, p = 0.04). Epithelial 8-oxodG correlated to the number of exacerbations in the previous year (rs = 0.70, p < 0.01) and the ACQ 6 (rs = -0.52, p = 0.04).

The upper 95th confidence interval of sputum 8-oxodG and epithelium 8-oxodG reaching threshold in healthy controls was used to split asthma patients into 8-oxodG high and low groups. The sputum 8-oxodG high group (n = 13) had significantly higher sputum total cells 8.08 [8.41] x 10⁶ g⁻¹ vs. 2.25 [2.91] x 10⁶ g⁻¹, p < 0.01, higher sputum neutrophils (82.25 [32.75]% vs. 55.50 [29.75]%, p < 0.01) and lower serum IgE (30 [76.50] KUL⁻¹ vs. 157 [212.90] KUL⁻¹, p < 0.01). The epithelial 8-oxodG high group (n = 8) had significantly more exacerbations 3.9 (0.3) p < 0.01 and a lower ACQ 6 score 1.4 (0.3) vs. 2.4 (0.3) p = 0.04.

In the asthmatic group, the intra-class correlation coefficient of sputum 8-oxodG between the 2 visits was 0.51 (p < 0.01).

**Conclusions** 8-oxodG expression in sputum and bronchial biopsies was not different between asthma and health, although we did identify an 8-oxodG high group in asthma. Interestingly, expression in asthma was associated with neutrophilic inflammation and poor asthma control.

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**S133**

**β2-ADRENERGIC RECEPTOR GLY16ARG POLYMORPHISM IS NOT ASSOCIATED WITH IMPAIRED ASTHMA CONTROL IN CORTICOSTEROID TREATED ADULT ASTHMATICS**

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**Introduction** The Arg-16 β2-adrenergic receptor allele is associated with increased exacerbations in asthmatic children exposed to combination therapy with long-acting beta-agonists (LABA) and inhaled corticosteroids (ICS). We evaluated whether the Gly16Arg polymorphism is associated with impaired asthma control in ICS treated adult asthmatics and whether this was influenced by concomitant LABA use.
Kinase Selectivity Profiles of Nintedanib and Imatinib

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Introduction

Tyrosine kinase inhibition has shown inconsistent success in the treatment of idiopathic pulmonary fibrosis (IPF). While a study of imatinib showed no impact on survival or lung function in a placebo-controlled study, two recently announced placebo-controlled phase 3 trials of nintedanib demonstrated statistically significant impact on forced vital capacity. Comparing the kinase target profiles could inform future target selection for drugs in IPF.

Methods

In vitro kinase selectivity data of nintedanib and imatinib were collected using the kinomescan platform (DiscoveRx Inc). Binding data (% binding) for 451 human kinases (~80% of the human kinome) were initially collected at a single concentration (10 uM). For kinases that displayed significant binding, potencies (KD) were measured in dose-response format.

Results

At a common concentration of 100 nM, imatinib and nintedanib bound to 12 and 50 kinases, respectively. Maximal drug concentrations (Cmax) observed in patients were used to project therapeutically relevant kinase inhibition for both drugs. Using these criteria, nintedanib binds 44 kinases at drug levels seen in patients (KD < Cmax of 64 nM). Imatinib binds 34 kinases at drug levels seen in patients (KD < Cmax of 7500 nM). 14 kinases were bound by both compounds, including PDGFRα, PDGFRβ and VEGFR2.

Conclusions

Our results suggest that nintedanib and imatinib have partially overlapping inhibition profiles; the kinases that are targeted by both agents are unlikely to be responsible for efficacy differences. Further work is required to identify which of the remaining kinase target(s) are responsible for efficacy in IPF and could therefore represent targets for follow-up compounds.

Basic mechanisms of IPF

Idiopathic pulmonary fibrosis (IPF) has a complex pathophysiology with epithelial-mesenchymal transition (EMT) thought to be important to the pathogenesis of fibrotic lesions. CD248 is a membrane-bound receptor that has collagen and lectins as ligands and is a stromal cell marker, whose expression is up-regulated post-natally during tissue inflammation and/or-remodelling. A role of CD248 is emerging in kidney fibrosis, but its function in the lung is unknown. We hypothesised that CD248 is a mesenchymal marker of IPF severity and that CD248 contributes to IPF pathogenesis.

Methods

CD248 expression was investigated in 23 IPF patient lung samples using immunohistochemistry (IHC) and qualitatively scored. Expression was assessed in cultured normal human lung fibroblasts (NHLFs), A549 cells, IPF derived fibroblasts and normal human primary ATII s, treated with or without TGF-β1 and PDGF-BB, using flow cytometry and qRT-PCR. siRNA CD248 knock down (KD) on NHLF mesenchymal marker expression and proliferation was evaluated using qRT-PCR and BrdU assays.

Results

IHC revealed strong CD248 expression by fibroblasts in both fibrotic areas and physiological structures of IPF lung tissue (pericytes and pleural tissue). Expression was greatest in samples from lung transplant explants. In vitro, CD248 protein levels were significantly greater in IPF derived lung fibroblasts vs NHLFs (p < 0.01). CD248 KD significantly reduced proliferation of control, PDGF-BB and/or TGF-β1 treated NHLFs (p < 0.001), but collagen and αSMA mRNA levels were unaffected (p > 0.05). The alveolar epithelium did not express CD248 on the protein level and minimal CD248 mRNA levels were detected in cultured A549 cells and ATII s, which remained unchanged during TGF-β1 induced EMT.

Summary

CD248 expression is elevated in the lungs of IPF patients especially in severe disease. CD248 expression appears specific for fibroblasts compared to epithelial cells and does not change during EMT. CD248 KD reduced fibroblast proliferation, but not myofibroblast differentiation.

We conclude that CD248 over-expression is involved in the pathogenesis of IPF – and that it has potential as a marker of mesenchymal/fibroblast lineage. Given that CD248 ligands are collagen type I, IV and fibronectin, we hypothesise that CD248 signalling represents a novel matrix-fibroblast interaction that may be a potential therapeutic target in IPF.
MTOR SIGNALLING IS AN ESSENTIAL PATHWAY FOR TGF-β1 INDUCED αSMA AND COLLAGEN GENE EXPRESSION

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Emerging evidence suggests a role for PI3K/mTOR signalling in the pathology of organ fibrosis. The aim of this study was to delineate PI3K/mTOR signalling in response to TGF-β1 stimulation of primary human lung fibroblasts (HLFs), and to investigate the role of this pathway in TGF-β1 mediated myofibroblast differentiation and collagen synthesis.

A time-course of SMAD 2/3 and Akt (Ser473) phosphorylation, the major downstream effector of the PI3K/mTOR pathway, was constructed to assess TGF-β1 induced signalling kinetics in HLFs. TGF-β1 (1 ng/ml) induced rapid phosphorylation of SMAD2/3, peaking at 1 h, followed by Akt phosphorylation which peaked 12 h after initial stimulation. Maximal expression of ACTA2 and COL1A1 was observed 36 h after TGF-β1 stimulation, correlating with the delayed time-course of Akt phosphorylation.

To investigate the role of the PI3K/mTOR pathway in TGF-β1 induced myofibroblast differentiation and collagen gene expression, HLFs were treated with pharmacological titrations of potent pathway inhibitors. Maximal Akt signalling and expression of ACTA2 and COL1A1 were significantly inhibited by a dual PI3K/mTOR inhibitor, while SMAD phosphorylation was unaffected. Treatment with an ATP competitive mTOR inhibitor also resulted in significantly reduced Akt phosphorylation and expression of ACTA2 and COL1A1, in response to TGF-β1. In contrast, treatment of HLFs with either an allosteric or ATP competitive Akt inhibitor showed no inhibitory effect on TGF-β1 induced gene expression.

These data suggest PI3 kinase/mTOR signalling is an important component in TGF-β1 induced αSMA and collagen gene expression and that an mTOR dependent, Akt independent pathway mediates this functional response in primary HLFs.

VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) EXPRESSION IN THE IPF LUNG – A ROLE FOR ANTI-ANGIOGENIC ISOFORMS?

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10.1136/thoraxjnl-2014-206260.143

Introduction VEGF has been implicated in the development of IPF. Differential splicing of the VEGF gene produces an alternative family of isoforms (VEGFαsb) that have anti-angiogenic properties, in contrast to conventional isoforms (VEGFαss). Currently available literature on the role of VEGF in IPF has not differentiated between these families of isoforms and thus a degree of literature re-appraisal is required.

Hypotheses
- The balance of VEGFαss:VEGFαsb isoforms may be important in IPF pathogenesis
- VEGFαsb isoforms may abrogate the development of IPF
Congenital diaphragmatic hernia (CDH) is a developmental diaphragmatic anomaly resulting in pulmonary hypoplasia and consequent pulmonary hypertension and respiratory failure sequelae. Despite advances in treatment, CDH remains associated with high morbidity and mortality rates. Reduced levels of vascular endothelial growth factor (VEGF) have been implicated in CDH pathogenesis. Animal studies have shown that intraterrorine VEGF replacement enhances pulmonary vascularisation and lung epithelial cell proliferation. This study aimed to deliver VEGF through the engineering of a biocompatible and slow releasing nanodiamond (ND) platform, in a rat model of CDH.

NDs were either fluorescently labelled (ND-FL) or conjugated to recombinant VEGF164 (ND-VEGF; 2 µg/mL, VEGF164). Nitrofen was administered to pregnant Wistar rats at E9 (term=E22) to induce fetal CDH. At E19, maternal hysterotomy was performed, and NDs (75 µg/mL in 50 µL vehicle/saline) were administered intratracheally followed by fetal tracheal occlusion (TO). Blinded assessment of lung-to-body weight ratio (LBWR) was performed at E21.5 in CDH offspring.

Prenatal ND administration did not have overt adverse effects. ND-FL biodistribution indicated that NDs localised in type II pneumocytes. ND-VEGF+TO was associated with improved lung growth (LBWR: 5.9 ± 0.2%), which was greater than that observed in VEGF+TO (3.5 ± 0.4%; p < 0.01), vehicle+TO (3.9 ± 0.1%; p < 0.01), and sham surgery (2.0 ± 0.2%; p < 0.001) groups. Moreover, ND-VEGF+TO resulted in thinner alveolar septa (mean transection length/airspace: 18.9 ± 0.5) and increased alveolar size (mean airspace chord length: 31.4 ± 0.6) compared to other treatment groups (p).

This is the first study to show that nanoparticle-mediated prenatal delivery of VEGF induces significant lung growth in CDH and suggests that sustained cargo release is pivotal in mimicking the temporal expression of VEGF in normal lung development.

**New insights in skeletal muscle wasting and weakness**

A PARADOXICAL RISE IN RECTUS FEMORIS MYOSTATIN (GDF-8) AND GDF-15 IN RESPONSE TO NEUROMUSCULAR ELECTRICAL STIMULATION IN CRITICAL CARE

**Introduction** Neuromuscular electrical stimulation (NMES) is widely used in rehabilitation and muscle disease. Recently there is increasing interest in its use as a prevention and treatment for intensive care unit acquired weakness (ICUAW). ICUAW is a common and often devastating disease resulting as a consequence of critical illness. The molecular mechanisms are not understood, however early mobilisation and rehabilitation are to date the most effective treatments. NMES has been shown to help prevent muscle wasting in some clinical studies in the ICU setting, however the evidence is inconclusive. We hypothesised that the NMES of a single leg in critical care patients would be associated with reduced muscle wasting and down regulation of molecular pathways involved in muscle breakdown. Specifically myostatin (GDF-8), a potent negative regulator of muscle mass, and GDF-15, a potential novel driver of muscle atrophy.

**Methods** We conducted a single-blinded, single leg, contralateral controlled trial of NMES in patients admitted to a specialist cardiothoracic ICU. Patients were recruited prior to elective high-risk cardiac surgery or during ICU admission. Baseline bilateral rectus femoris cross sectional area (RF_{csa}) was measured by ultrasound and rectus femoris biopsies were taken. 2 × 1 hour sessions of NMES were then conducted for 1 week and ultrasound and biopsies were repeated. Biopsy specimens were examined for mRNA expression of genes of interest and results analysed in paired analysis relative to baseline. (NCT01321320).

**Results** 12 patients completed the study protocol. Myostatin and GDF-15 mRNA expression were both significantly elevated in NMES legs compared to baseline (p = 0.03 and p = 0.04 respectively), but remained unchanged in control legs. There was no significant change in RF_{csa}.

**Discussion** It is believed that NMES will have beneficial effects in the ICU setting in terms of preservation of muscle function. However it is recognised to also have potential to cause muscle damage. In the setting of sedated patients who cannot report pain or those in whom the nutritional and metabolic status of the muscle may be expected to be poor, researchers should be aware that NMES may promote muscle breakdown.
**Introduction**

Intensive care unit acquired weakness (ICUAW) is common and associated with significant morbidity. We previously identified GDF-15, a TGF-β super-family member, as a potential driver of acute muscle wasting in a novel human model of ICUAW (Crit Care Med 2013; 41:982). In the current study we investigated the potential mechanisms by which GDF-15 may contribute to the development of ICUAW.

Dysregulation of muscle microRNAs has been described in muscle disorders. MicroRNAs are essential for muscle homeostasis and their expression can be influenced by inflammatory cytokines. Furthermore muscle microRNAs may down-regulate TGF-β signalling. However, the function of microRNAs in ICUAW has not previously been described. We hypothesised that down-regulation of muscle microRNAs, driven by GDF-15, would lead to increased sensitivity to TGF-β signalling in muscle of patients with ICUAW.

**Methods**

We conducted an observational study of 20 patients with ICUAW and 7 elective surgical controls. Subjects underwent rectus femoris muscle biopsy and blood sampling. Muscle specimens were examined for mRNA and microRNA expression of target genes by qPCR. Plasma samples were tested for GDF-15 concentration (ELISA). Histology samples were stained for pSMAD2/3 nuclear positivity. To examine the effects of GDF-15 on target genes, differentiated C2C12 myotubes were treated with GDF-15 for 4 days. The effect of over-expression of miR-181a in C2C12 myoblasts on TGF-β signalling was also examined.

**Results**

Compared with controls, patients with ICUAW had greater GDF-15 mRNA expression in muscle (median 2-fold higher; *p = 0.006) and concentration in plasma (median 7239 vs. 2454 pg/ml; *p = 0.001). MicroRNAs involved in muscle homeostasis were significantly lower in muscle from patients with ICUAW. Both log[GDF-15 mRNA] and log[plasma GDF-15] were significantly negatively correlated with log[microRNA expression]. GDF-15 treatment of myotubes significantly elevated expression of muscle atrophy-related genes and down-regulated expression of muscle microRNAs. miR-181a suppressed TGF-β responses in myotubes, suggesting increased sensitivity to TGF-β in ICUAW muscle. Consistent with this, nuclear phospho-SMAD2/3 and CYR61 mRNA expression were increased in ICUAW muscle.

**Discussion**

By suppressing expression of muscle microRNAs GDF-15 may increase sensitivity to TGF-β signalling, thus promoting muscle wasting in ICUAW. This study identifies both GDF-15 and associated microRNA as potential therapeutic targets in ICUAW.
**Introduction**

Muscle wasting, that is present in a subgroup of patients with COPD, is an independent predictor of health related quality of life and survival. The two-dimensional fluorescence difference in gel electrophoresis (2D-DIGE) technology is now recognised as an accurate method to determine and quantify proteins.

**Methods and results**

With the aim of identifying proteins potentially involved in the process of muscle wasting, we performed 2D-DIGE protein expression profiling in the vastus lateralis of 10 patients with COPD and low fat free mass index (FFMI) (COPD<sub>≤</sub>) (FEV<sub>1</sub> 33 ± 4.3%pred, FFMI 15 ± 0.2 Kg.m<sup>-2</sup>) in comparison with both 8 patients with preserved FFMI (COPD<sub>≥</sub>) (FEV<sub>1</sub> 47 ± 7.3%pred, FFMI 19 ± 0.6 Kg.m<sup>-2</sup>) and 9 age and gender-matched healthy sedentary subjects (C) (FEV<sub>1</sub> 96 ± 4.0%pred, FFMI 20 ± 0.9 Kg.m<sup>-2</sup>). Data analysis was performed using DeCyder software and for protein identification MALDI-TOF mass spectrometry (MS).

Ten proteins, whose expression was significantly changed in COPD<sub>≤</sub>, were identified; serum albumin (ALBU), heat shock protein beta-1 (HSPB1), pereoxiredoxin-6 (PRDX6), Alpha-crystallin B chain (CRYAB) and Alpha-1-antitrypsin (A1AT) were increased while Histone-lysine N-methyltransferase (DOT1L), Troponin T (TNNT1), Myozenin-1 (MYOZ1), Myosin light chain 1 (MYL1) and mitochondrial ATP synthase subunit alpha (ATPα) were decreased.

**Conclusion**

Our results showed a down-regulation of structural muscle proteins, proteins involved in myofibrillogenesis, cell cycle arrest and energy production and up-regulation of proteins reacting to cell stress and proteins involved in oxidative stress protection.

Supported by Chief Scientist Office (CSO) Scolt06/S1103/5 and FIS P108/0320.

**Abstract S143 Figure 1**

Telomere Length analysis in HSKMC

**Conclusion**

We have developed a novel in vitro model of ageing skeletal muscle cells, which will help us to assess the role of accelerated ageing in muscle dysfunction and wasting in COPD patients.

Dr Lakhdar was funded by an LTERS fellowship grant.
**RESULTS**

In the 12 patients with data so far available in this study, QOL measured by the total SGRQ score correlated significantly with QMVC/BMI ($r = -0.75$, $p = 0.005$), FFMI ($r = -0.71$, $p = 0.009$) and USRF ($r = -0.88$, $p = 0.0002$) (Figure 1A). There was no significant correlation between total SGRQ score and Sensedwear measured steps per day ($r = -0.62$, $p = 0.08$) (Figure 1B) TEE ($r = -0.62$, $p = 0.08$) or AEE (rho = -0.41, $p > 0.05$) in the 9 patients with data available. Furthermore, there was no significant correlation between BNP or resting echocardiographic parameters and total SGRQ QOL.

**Discussion**

We have shown that muscle size and function are directly related to QOL in patients with IPAH. This work suggests that muscle function may be an important determinant of QOL in these patients, making it a potential target for therapeutic intervention. Further data is needed to define the association between physical activity and QOL in patients with IPAH.

**Cough – mechanisms and therapies**

**P1**

**A NOVEL CAPSAICIN COUGH CHALLENGE IN HEALTHY ADULTS: BEYOND THE CS**

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**Introduction**

We have developed a novel cough challenge methodology and previously showed that evoked maximal cough responses, defined as $E_{\text{max}}$, better discriminate health from disease than traditional endpoints. It is unclear how other factors influence $E_{\text{max}}$ or how it relates to the low cough rates observed in health. Therefore, we aimed to investigate the variability, repeatability and influences on $E_{\text{max}}$ in a larger group of healthy volunteers.

**Objective**

To assess maximum cough responses to capsaicin in a group of healthy adults representing a wide range of ages.

**Method**

Doubling doses of capsaicin 0.49 to 10000 [micro]M were inhaled sequentially up to the maximum tolerated dose. Four inhalations of each dose were administered 30 seconds apart and the number of coughs evoked within 15 seconds was recorded. The maximum number of coughs evoked by each dose of capsaicin ($E_{\text{max}}$) and the dose that elicited half of the $E_{\text{max}}$ defined as ED50 were calculated. General linear models were used to assess the influence of subject demographics on these endpoints.

**Results**

Forty seven healthy volunteers performed the capsaicin challenge; median age 38 years (range 20–74), 17 males, median FEV1, 103% predicted (97–115), median BMI 25.0 (22.2–28.6), and median total cough rate 0.2 c/h (0.0–0.1). The median $E_{\text{max}}$ was 11 coughs (IQR, 8–19) with an ED50 of 15.6 [micro]M (7.8–109.4). The intraclase correlation coefficients for $E_{\text{max}}$ and ED50 were 0.89 and 0.96 respectively which were highly significant ($p < 0.001$). Age, gender, FEV1 and BMI had no significant influence on $E_{\text{max}}$.

In contrast, gender ($p < 0.001$) and BMI ($p = 0.029$) both significantly influenced ED50 explaining 41.7% of the variation. Those subjects with a higher BMI and females were in health. We therefore aimed to investigate the variability, repeatability and influences on $E_{\text{max}}$ in a larger group of healthy volunteers.

**Conclusion**

Data collected to date has demonstrated that in healthy volunteers, $E_{\text{max}}$ and ED50 are stable measures over time however $E_{\text{max}}$ has the advantage of being independent of patient factors. Intere sting, objective cough frequency in healthy volunteers seems to be unrelated to capsaicin evoked coughing.

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**Introduction and objectives**

Activation of afferent fibres from the lungs are involved in the cough reflex. In vivo studies in guinea-pig have demonstrated that there are various sub-types of $A\delta$-fibres (RARs, nociceptive and cough) and $C$-fibres (either nodose or jugular ganglia derived), however, little is known about their equivalent characteristics in vivo. This study aims to characterise the responsiveness of airway sensory nerves, in vivo, ultimately providing a better insight into understanding the role/contribution of the various types/subtypes of $A\delta$- and $C$-fibres in airway reflexes such as cough.

**Methods**

Male guinea-pigs were anaesthetized with urethane (1.5 g kg$^{-1}$), paralysed and artificially ventilated via a tracheal cannula. A vagus nerve was isolated: single fibres were identified as originating from $A\delta$- and $C$-fibres using several criteria. Action potentials were recorded and agents were administered to the airways by aerosol.

**Results**

Fibre types were classified according to their conduction velocities (Table 1). All $C$-fibres examined were activated by capsaicin, whereas in the $A\delta$-fibres studies there were both capsaicin responsive and non-responsive fibres, irrespective of their CV range. All fibres exposed to CA responded strongly. There were marked differences in the responsiveness to the TRPV4 agonist, GSK1016790A: $A\delta$-fibres from all subgroups responded vigorously, but the $C$-fibres examined were not activated. Interestingly, administration of hypotonic solutions activated all of the $A\delta$-fibres, but had no effect on $C$-fibres. In contrast, all $C$-fibres responded to the TRPA1 agonist, acrolein, with no effect on $A\delta$-fibres.

**Conclusion**

Several vagal afferent nerve subtypes have been identified in guinea-pig airways in vivo, although the classification does not appear as obvious to that observed in vitro. It is clear that there is a marked variation in their sensitivity to TRP channel agonists, TRPV1, TRPA1 and TRPV4, which have been shown to evoke cough in a preclinical model in conscious guinea-pigs. It seems probable, therefore, that the different afferent pathways all regulate cough to a greater or lesser degree depending on the nature of the stimulus and underlying cause of the cough.

**REFERENCES**


**Abstract P2 Table 1**

Characteristics of vagal afferent neuronal subtypes innervating the airways and lungs of guinea pigs in vivo

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<th>$CV &lt; 1 \text{m s}^{-1}$</th>
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<tbody>
<tr>
<td>RARs</td>
<td>Classical RARs</td>
<td>Classical RARs</td>
<td>Classical RARs</td>
</tr>
<tr>
<td>Capsaicin-responsive</td>
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<td>Capsaicin non-responsive</td>
<td>Capsaicin non-responsive</td>
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<tr>
<td>(nociceptor)</td>
<td>(mechanoreceptor?)</td>
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</table>
P3  Efficacy of a physiotherapy, speech and language therapy intervention (PSALTI) on health related quality of life (HRQoL) for patients with refractory chronic cough: a randomised control trial

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Introduction Refractory chronic cough has a significant negative impact on HRQoL. There are currently limited effective antitussive therapies. Few studies have explored the effectiveness of nonpharmacological interventions for refractory chronic cough. This study investigated the efficacy of PSALTI on HRQoL for people with refractory chronic cough in a multi-centred RCT.

Methods Participants were recruited across five NHS hospitals trusts. 76 participants were randomised to PSALTI or placebo (equal attention) intervention. PSALTI consisted of education, laryngeal hygiene and hydration advice, cough control techniques and psycho-educational counselling. Placebo consisted of general education on exercise, diet, stress and relaxation. Both groups attended 4 weekly sessions of 1:1 therapy. HRQoL was measured at baseline, four weeks (end of treatment) and 3 months follow up by Leicester cough questionnaire (LCQ). Cough reflex sensitivity was assessed at baseline and four weeks by capsaicin cough challenge (C2, C5, concentration that caused first urge to cough (Cu)) and was analysed by geometric means (GM). Outcomes between groups were analysed using ANCOVA.

Results The PSALTI (n = 35) and Placebo groups (n = 41) were well matched (p > 0.05) for age [mean (SD)] 58 (15) vs. 56 (11) years; gender 71% vs. 63% females; cough duration [median (IQR)] 60 (30 to 126) vs. 48 (24 to 126) months and baseline LCQ [mean (SD)] 10.4 (3.6) vs. 11.9 (3.5). At four weeks HRQoL improved in both groups, mean LCQ increase in PSALTI was 3.4 (95% CI 2.26 to 4.53) vs placebo 1.7 (95% CI 0.78 to 2.54); difference in LCQ change between groups was 1.5 (95% CI 0.27 to 2.71). The cough sensitivity to capsaicin was greater in PSALTI group compared to placebo (GM (SD) 2.5 (5.07) vs. 0.612 μM (3.26), p = 0.02). There was no significant difference in cough reflex sensitivity between the groups (C2, p = 0.46; C5, p = 0.74).

Conclusions PSALTI significantly improved HRQoL compared with equal attention placebo intervention and this improvement was sustained at three months. PSALTI also significantly increased Cu compared to placebo.

10.1136/thoraxjnl-2014-206260.153

P4  Establishing a role for TRPV1 on sensory nerves in COPD associated chronic cough

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Background An increase in cough reflex sensitivity to capsaicin in COPD has been described in some studies, suggesting a role for TRPV1 in the disease phenotype. We utilised a guinea-pig cigarette-smoke (CS) exposure COPD model to investigate an enhanced cough phenotype, and evaluate the role of TRPV1 using a novel clinical-ready inhibitor, XEN-D0501. Furthermore, we confirmed enhanced cough responses in COPD patients using a dose-response capsaicin challenge to determine E_{max}.

Methods Guinea-pigs were exposed to air/cigarette smoke (CS) for 1 hour, twice daily, for 8 days. Coughs evoked by aerosolised capsaicin (30 μM), depolarisation of isolated vagus nerve tissue induced by capsaicin (1 μM), or increases in intracellular calcium [Ca^{2+}]_{i}, to capsaicin (1 μM) in airway-terminating (i.e. Dil stained) jugular and nodose neurons were evaluated. Vagus nerve was obtained from human non-smoker/smoker subjects for similar assessment. Coughs evoked by capsaicin (4 inhalations, 0.49–1000 μM) were recorded in COPD and compared with healthy controls.

10.1136/thoraxjnl-2014-206260.154

Abstract P4 Figure 1 (A) Human coughs to capsaicin — healthy controls; n = 15, median age 56 (IQR 39–60) females, mean FEV_{1} 109.5% (±17.0). COPD patient n = 15, median age 69 (64–72), 5 females, mean FEV_{1} 58% (±11.2), p < 0.001 (General Estimating Equations). (B)Guinea-pig coughs to capsaicin (30 μM);*p < 0.05 compared to Veh control (Kruskal-Wallis with Dunn’s post-test) n = 8.
Results Capsaicin-evoked cough was increased in COPD patients (Fig.1A) and in CS-exposed guinea-pigs (Fig.1B) compared to controls. Capsaicin induced greater depolarisation in nerve tissue from CS-exposed guinea-pigs, and in human vagus nerves from smokers, compared to controls. Capsaicin also induced greater (Ca^{2+}), increases in airway-terminating jugular and nodose (which are normally capsaicin-unresponsive) neurons from CS-exposed guinea-pigs. XEN-D0501 (i.p. 1 h before cough recording) almost completely inhibited the cough response to capsaicin in both air- and CS-exposed guinea-pigs (Fig.1B).

Conclusions CS-exposure evoked increased cough to capsaicin in guinea-pigs, mimicking the enhanced cough phenotype observed in COPD patients. This was parallelised by enhanced capsaicin responses in isolated vagus nerves and airway neurons from CS-exposed guinea-pigs and in human vagus from smokers suggesting the enhanced cough phenotype is due to increased TRPV1-mediated sensory nerve responsiveness. Inhibition of the CS-enhanced cough response by XEN-D0501 further implicated a role for TRPV1. This data, together with the finding that TRPV1 KO mice display less inflammation in a similar pre-clinical model of CS-exposure, indicates the potential utility of TRPV1 antagonists in the treatment of COPD, which is currently being evaluated in an ongoing COPD clinical trial.

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P5 LIPID-LADEN MACROPHAGES IN BRONCHOALVEOLAR LAVAGE FLUID ARE NOT DIAGNOSTIC OF AIRWAY REFLUX

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Aims Demonstration of lipid-laden macrophages in respiratory secretions has been suggested to be a marker of reflux and aspiration. However studies looking at the diagnostic value of quantifying macrophage ingested lipids have been inconclusive. We wanted to look evaluate the utility of this technique in diagnosing airway reflux.

Methods In this prospective study bronchoalveolar lavage samples were collected from patient’s undergoing flexible bronchoscopy for various indications (lung cancer, chronic cough, ILD etc). Cells collected were stained with Oil-Red-O. Lipid-laden macrophage index (LLMI) was used to quantify lipid accumulation. This is calculated by grading the amount of intracellular Oil-Red-O positive particles per 100 alveolar macrophages. A score of 0 (no opacification) to 4 (total opacification) is assigned to each macrophage. The sum of the scores yields the LLMI. Patients were asked to complete the Hull Airways Reflux Questionnaire (HARQ), a validated tool to diagnose airways reflux. One of the investigators, blind to the analysis, independently reviewed the clinical notes to establish a diagnosis of associated airway reflux. The investigator performing cell analysis was blind to the clinical details. The groups with and without a clinical diagnosis of airway reflux were compared. Correlations between the HARQ score and LLMI were sought.

Results Twenty nine patients (19 females, mean age 64 years) were included in the study. Of these in 11 a clinical diagnosis of associated airway reflux was made. The mean [SD] LLMI in the group with airway reflux (95[105]) was not significantly different from those without airway reflux (90[75]). There was a weak correlation observed between the HARQ score and the LLMI (0.09) which was not statistically significant (p = 0.69).

Conclusions We fail to demonstrate significant association between LLMI and either a clinical diagnosis of airway reflux or the HARQ score. This could be due to the fact that macrophages scavenge both exogenous and endogenous material. However our study is limited by small numbers and disparate underlying clinical diagnoses. The small correlation of LLMI with HARQ scores merits further evaluation. Whether the proportion of macrophages phagocytising lipids or the degree of lipid ingestion by the macrophages is more important needs further study.

P6 MENTHOL HAS BENEFICIAL EFFECTS IN THE AIRWAYS THROUGH A TRPM8-INDEPENDENT MECHANISM

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Introduction Asthma is a debilitating disease of the airways characterised by symptoms such as bronchoconstriction, hyperresponsiveness and cough. Current therapies are associated with significant side effects and are ineffective in severe disease highlighting the need for novel treatments. Menthol, a cooling compound found in medicinal products, is commonly thought to activate the thermo-sensing cation-permeable Transient Receptor Potential Melastatin 8 (TRPM8) channel. Furthermore, menthol is known for its beneficial effects in the airways such as bronchodilation and suppression of nerve activation and cough, however the mechanism of action is unknown.

Aim To pharmacologically characterise the role of TRPM8 and menthol in the airways.

Methods TRPM8 gene expression was measured using Taqman real-time PCR. Mouse and guinea pig isolated vagal nerves were mounted in a grease-gap chamber and depolarisation (mV) recorded as an indicator of sensory nerve activity. Segments of murine and guinea pig trachea were attached to a force transducer in an organ bath and relaxation of carbachol-induced tone recorded (mg).

Results TRPM8 is expressed in mouse and guinea pig vagal ganglia. The selective TRPM8 agonist, WS3, caused activation of guinea pig and mouse isolated vagal nerves, which was inhibited by the TRPM8 antagonist, JNJ41876666. Furthermore, WS3-induced depolarisation was abolished in isolated vagal nerves from T rpm8−/− mice. (−)-menthol (active form) caused a small depolarisation of mouse and guinea pig isolated vagal nerves, which was blocked by JNJ41876666. Interestingly, pre-incubation of (−)-menthol inhibited vagal nerve activation induced by the tussive stimulus, capsaicin, an effect that was not inhibited by JNJ41876666. WS3 and (−)-menthol caused a concentration-dependent relaxation of murine and guinea pig trachea, which was not abolished by JNJ41876666 nor in the T rpm8−/− mouse airway. No expression of TRPM8 was detected in guinea pig or mouse airway smooth muscle.

Conclusions (−)-menthol caused a small TRPM8-dependent activation but a robust TRPM8-independent inhibition of vagal sensory nerve activity and relaxation of airway smooth muscle. Elucidating the mechanism behind the beneficial effects of (−)-menthol could lead to the development of promising new therapeutic targets for airway diseases such as asthma.
**P7** NEURONAL DYSFUNCTION IN ASTHMA; INSIGHTS FROM THE STUDY OF THE COUGH REFLEX

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Introduction Cough in asthma is common, troublesome, predicts severity and poor prognosis, yet remarkably little is understood about the underlying neuronal mechanism. Currently available asthma medications are not designed to directly treat cough, the archetypal airway neuronal reflex. Previous studies have commonly used the dose of capsaicin that evokes two coughs (C2) or five coughs (C5) as the standard measure to assess the sensitivity of the cough reflex. These measures poorly discriminate between health and disease, and correlate only weakly with objective cough rates. A novel challenge methodology that uses the maximum number of evoked coughs (Emax) as an end point better discriminates between health and disease and correlates strongly with subjective cough measures.

Objective To assess the differences in the maximum cough responses evoked by capsaicin (Emax) between asthmatics and healthy volunteers.

Method A capsaicin inhalational challenge (doubling doses 0.49 to 1000μM) was performed. Four inhalations 30 seconds apart were performed at each concentration and the total coughs evoked at each dose were recorded and verified using a cough monitor. The highest total number of coughs evoked at any dose of capsaicin is denoted Emax.

Results Forty nine asthmatics were compared with 47 healthy volunteers. There was a significant difference in the median age between groups (asthmatics 22.9 (IQR 20–27), healthy volunteers 38.0 (29–47) p < 0.001). Equal ratios of females were recruited in both groups (31 in asthmatics and 30 in healthy volunteers). There were no significant differences in gender, body mass index, smoking history or lung function. Asthmatics were of the mild to moderate category (BTS steps 1/2/3, 45/39/16%). There was a significant difference in the Emax between asthmatics (mean coughs 20.5 (SD±10.1) and healthy volunteers 13.1 (±7.2) (p < 0.001). See Figure 1.

Conclusion Using this novel full dose response methodology, this data suggests that even during stability, asthmatics have an exaggerated cough response to capsaicin. This suggests that subgroups of asthmatics have neuronal dysfunction which can be identified by this capsaicin challenge.

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**P8** OBJECTIVE COUGH FREQUENCY MONITORING IN BRONCHIECTASIS

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Introduction and objectives Cough is a major symptom in bronchiectasis. Cough monitors are emerging as an important tool that assesses cough objectively. The aim of this cross-sectional study was to assess cough frequency in non-cystic fibrosis bronchiectasis, investigate its association with patient-reported symptoms and health-related quality of life (HRQOL), and investigate potential factors of cough frequency variability.

Methods Patients with non-cystic fibrosis bronchiectasis were recruited from 2 outpatient bronchiectasis clinics. All patients underwent 24-hour ambulatory cough monitoring with the Leicester Cough Monitor, and reported sleeping time in a diary. The patients also completed the Leicester Cough Questionnaire (HRQOL), and visual analogue score (VAS) for sputum and cough severity. Sputum bacteria colonisation status was assessed, and defined as at least 2 positive cultures, minimum 3 months apart and within one year.

Results 49 patients were recruited; median (IQR) age 65 (52, 70) years, 64% female. The aetiology of bronchiectasis were: idiopathic (45%), post infective (29%) and other (25%). The prevalence of sputum colonisation were: pseudomonas aeruginosa (mean coughs 20.5 (SD±10.1) and healthy volunteers 13.1 (±7.2) (p < 0.001). See Figure 1.

Conclusion Using this novel full dose response methodology, this data suggests that even during stability, asthmatics have an exaggerated cough response to capsaicin. This suggests that subgroups of asthmatics have neuronal dysfunction which can be identified by this capsaicin challenge.

**REFERENCES**

Interestingly both NSIP and IPF cohort reported cough; however, proportionally NSIP patients have less cough (14/51, 27.4%) compared with IPF (37/261, 14%).

Conclusions Cough occurs in a huge majority of patients with both IPF and NSIP. Cough appears to be a greater problem in older patients.

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Introduction Chronic cough is a troublesome condition that reduces patient quality of life. Recent evidence suggests that healthy females cough more than healthy males but the mechanism underlying this is unclear. We hypothesise that opioid-sensitive inhibitory control mechanisms determine capsaicin-evoked cough responses in healthy subjects.

Aim To show that in healthy males the number of capsaicin-evoked coughs is increased following administration of naltrexone, an opiate receptor antagonist, compared with placebo.

Method 15 male subjects (median age 30 yrs (21–59)) were recruited in to a randomised double blind cross-over trial of single doses of naltrexone vs. placebo given 1 week apart. A capsaicin inhalational challenge (doubling doses 0.48 to 125[micro]M) was performed 60 min after ingestion of naltrexone/placebo using a dosimeter. Four inhalations 30 seconds apart were performed at each concentration and the total coughs evoked at each dose were recorded and verified using a cough monitor.

Results There was a tendency for subjects to cough more when treated with naltrexone (16.7 ± 2.7 (SEM) compared with placebo (13.7 ± 1.6), (p = 0.11, general estimating equations). See Figure 1

Abstract P10

Figure 1

Poster sessions
Conclusion This small pilot study suggest that opiate sensitive inhibitory mechanisms may have a role in controlling the cough reflex even in healthy subjects.

REFERENCES


P11 THE ROLE OF GABAB RECEPTOR MECHANISMS IN THE HUMAN COUGH REPLEX

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Background Chronic cough represents an important unmet clinical need. Gamma-aminobutyric acid is a major inhibitory neurotransmitter in the central nervous system (CNS). GABAB receptors have been identified peripherally, as well as centrally. Studies in guinea-pigs, have suggested that the activation of GABAB receptors in the CNS and PNS can inhibit cough. The only clinically available GABAB agonist is Baclofen, and although it has been shown to suppress cough in animals and humans, it causes drowsiness as it is centrally acting. Lesogaberan, is a novel, predominantly peripherally acting GABAB agonist.

Objective To determine whether both peripherally acting (Lesogaberan) and centrally acting (Baclofen) GABAB agonists modulate cough responses to inhaled capsaicin compared with placebo in healthy volunteers.

Methods Single centre, double-blind, double-dummy, three-way crossover trial in healthy controls of Lesogaberan (120 mg MR), Baclofen (40 mg) and placebo. Subjects were treated with single doses of each study medication with a washout period of ≥7 days between doses. Cough responses to inhaled capsaicin were assessed using a novel challenge protocol (1) measured at screening and 2 hrs post dosing (tmax) on each study day. The primary end point was the maximum number of coughs evoked at any concentration of capsaicin (Emax). The secondary end point was the concentration of capsaicin evoking 50% of the maximal response (ED50).

Results There were 15 patients enrolled onto the study with a median age of 29 years old (IQR25–44); 7 female; mean BMI was 24.6 (±3.0).

Lesogaberan treatment was associated with a small, statistically significant increase in Emax (mean 13.4 coughs, 95% CI 10.1–17.9) compared with placebo (11.8, 95% CI 8.8–15.9) (p = 0.04), but had no effect on ED50 (geometric mean 47.4 μM 95% CI 24.4–91.7 vs Placebo 37.6 95% CI 19.2–73.5 p = 0.37), see Figure 1.

In contrast, Baclofen had no significant effect on Emax (11.1, CI8.1–15.4) (p = 0.23), but, ED50 was significantly increased compared with placebo (geometric mean 75.2 μM 95% CI 37.2–151.8 p = 0.002).

Conclusion This data suggests the anti-tussive actions of GABAB agonists, against capsaicin-induced cough in healthy volunteers, occurs in the central rather than the peripheral nervous system.

REFERENCES


P12 THE USEFULNESS OF HEARTBURN AS A MARKER OF THE SUCCESS OF ACID SUPPRESSION THERAPY IN CHRONIC COUGH

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Background A recent retrospective analysis of randomised controlled trials has suggested that patients with chronic cough reporting heartburn are more likely to benefit from acid suppressive treatment than those without heartburn. Therefore we set out to investigate the response rate to acid suppression treatment (PPI and or H2 antagonists) in patients attending our specialist cough clinic.

Objective To determine the relationship between reported responses to acid suppression treatment and the presence or absence of heartburn.

Methods We performed a retrospective review of 59 consecutive new referrals to the clinic. The presence or absence of heartburn is collected routinely in our standard clinic proforma. Patients who were treated with acid suppression either at our clinic or previously at another centre were included, together with their reported response to treatment. A Fisher’s exact test was used to assess whether those with heartburn were more likely to report a response of their cough to acid suppression treatment than those without heartburn.

Results Of 59 new referrals (median age 58 (range 26–76), 44 female), 21 (35.6%) reported heartburn, whereas 38 (64.4%) did not. Forty-four subjects had completed a trial of acid suppression therapy; 7 (15.9%) reported either a partial or complete resolution of their cough, but 37 (84.0%) reported no response. Of those reporting heartburn, 5/21 (23.8%) also reported a response to acid suppression. Of those not reporting heartburn, 2/23 (8.7%) reported a response to acid suppression. Although a greater proportion of those with heartburn reported improvement of cough with acid suppression, this did not reach statistical significance (p = 0.23).

Conclusion This data suggests that in the setting of a specialist cough clinic few patients report a response of their cough to
Introduction There is considerable interest surrounding the role of chronic mucus hypersecretion (CMH) in the development of COPD but varying definitions of CMH have created uncertainty regarding its prevalence. Some studies characterise CMH as chronic phlegm production whilst others as chronic cough (CC) productive of phlegm. By understanding how these symptom groups relate to each other, we may be better equipped to interpret existing data and search for therapeutic targets. We report the prevalence and overlap of CMH and CC over 43 years of adult life from age 20 years within the nationally representative MRC NSHD birth cohort.

Methods The MRC NSHD is a birth cohort study of men and women born during one week in March 1946 within England, Scotland and Wales. CMH and CC presence was determined by completion of the MRC questionnaire on respiratory symptoms in the following years (study member age in years): 1966(20), 1971(25), 1982(36), 1989(43), 1999(53) and 2009(63). The MRC questionnaire defines CMH as the production of phlegm from the chest on most days for three months of each year and defines CC as cough on most days for three months of each year.

Results 1394 subjects (47% male) completed questionnaires on all six occasions between 1966 and 2009. 398 study members (26.8%) reported either symptom at least once with a majority of CMH reporters concurrently reporting CC (See Table 1). The percentage of CMH reporters concurrently reporting CC increased with age (0.5%/year increase, CI 0.18–0.82, p = 0.001).

Conclusion Most chronic phlegm producers report concurrent CC, and this percentage increases with age. Restricting CMH definition to those with CC, however, misses the substantial proportion of the population who report chronic phlegm production without CC. The requirement for a chronic cough to define CMH may underestimate the total prevalence of chronic sputum producers and hence those potentially at risk of COPD development or progression.

Basic mechanisms of acute lung injury, interstitial lung disease and PAH

Introduction and objectives Concern about the DNA quality for next-generation sequencing encourages use of dedicated preparative kits. The purpose of this study was to attempt to sequence ten stored DNA samples that had been prepared from human blood using phenol chloroform methods 12–17 years earlier, frozen at -70 C and not subjected to special treatments.

Methods The ten DNA samples that had been defrosted on multiple occasions, were defrosted again for library preparations using the Agilent SureSelect Target Enrichment System for Illumina paired-end multiplexed sequencing. Sequencing was performed on an Illumina HiSeq 2000 instrument for 2 x 100 base reads. Sequencing data were processed with RTA version 1.7.45 with default filter and quality settings, aligned to the human genome for each sample, approximately 8 million primary sequence reads uniquely mapped to the captured region of interest.

Conclusions Extremely high quality DNA sequences can be obtained using stored DNA samples prepared many years earlier, and not subjected to any special treatments in the intervening years. The findings will be of particular importance to research communities where acquisition of new samples is not always possible.
Methods Triplicate confluent primary human microvascular endothelial cells (Promocell GmbH) were cultured in the presence and absence of TGF-beta stimuli relevant to pulmonary arteriovenous malformations and hereditary haemorrhagic telangiectasia (HHT). Following rRNA-depletion of total RNA, seven libraries were prepared using Illumina reagents, and 8 pM of each library used for cluster generation and sequencing on Genome Analyser II. Algorithms for aligning reads to NCBI36/hg18 and GRCh37/hg19 included Bowtie, TopHat and Seqmap. Validations were performed using quantitative rt-PCR.

Results More than 2 Gigabases of sequence was generated. Transcriptome-wide profiles were similar between libraries, with sixteen types of RNA species detected including 146 micro (mi) RNA families (47 broadly conserved), and 10,749 protein-encoding mRNAs representing ~5.5% of mapped reads. Alignments to endothelial mRNAs/miRNAs were substantially higher than to gene loci for non-endothelial mRNAs/miRNAs. mRNA exon alignments demonstrated sharp exon boundary delineation, but required alignments to non-annotated intronic regions involved in multi-exon deletions in HHT patients. There was an inverse relationship between alignments depths and qPCT cycle thresholds (Ct), where single alignments were detectable, and Ct values of 20 generated by 0.02 nM spiked RNA. Across all experiments in replicate donor/treatment RNAs, for a panel of single open reading frame miRNA genes, RNASeq alignments (gene strand read counts normalised to the total number of valid reads and exon/locus size) explained 72% of the variance of qPCT cycle threshold (p < 0.0001). Dynamic whole transcriptome profiling is in progress.

Conclusions These novel directional next generation RNA sequencing methods provide new insights for mutational mechanisms, and a systems approach to dissection of regulatory and target RNA networks relevant to human disease.

Abstract P16 Table 1 Cytokine levels pre and post pulmonary endarterectomy

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<td>16</td>
<td>±1.00</td>
<td>±1.10</td>
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Data presented as mean ± SD, p = Wilcoxon rank-sum test. IL = interleukin; TNFα = tumour necrosis factor α; GM-CSF = granulocyte-macrophage colony-stimulating factor; IFNγ = interferon

P17 MOLECULAR COMPLEXITIES IDENTIFIED THROUGH TARGETED GENOMIC SEQUENCING OF THE HHT3 LOCUS ON CHROMOSOME 5

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Introduction The pathogenesis of chronic thromboembolic pulmonary hypertension (CTEPH) is poorly understood. Idiopathic pulmonary arterial hypertension (IPAH) is associated with systemic and localised inflammation. Distal vasculopathy is seen in IPAH and CTEPH (2 compartment model). Inflammation has been implicated in CTEPH pathogenesis. We undertook a whole transcriptome approach to systematically identify inflammation-related gene loci and networks in PAH and CTEPH.

Methods To identify gene loci relevant to CTEPH, we sequenced exomes and targeted transcriptomes as part of the HHT310 project. Mutational analyses were performed on five surgically resected CTEPH lung autopsies. Whole transcriptome sequencing was performed on PEA specimens and explanted lungs (5 CTEPH, 11 IPAH). Formalin fixed samples were immunostained with antibodies to CD45 (inflammatory cell), CD79a (B cell), CD68 (macrophage) or CD3 (T cell) to evaluate inflammation in the lung parenchyma. Perivascular and parenchymal cell counts showed non-significant reductions of CD3+ cells in CTEPH (p = 0.19 and 0.08 respectively). More CD68+ cells were seen in the parenchyma in CTEPH (p = 0.03). Few CD20+ cells were seen in parenchyma with no difference.

Results Neovascularisation correlated to CD45+ cells in PEA specimens when normalised to specimen area (r = 0.4, p = 0.01). Conclusions In CTEPH, most serum cytokines were not elevated sufficiently to suggest systemic inflammation is important in pathogenesis. The change in IL10 and TNFα are possibly due to improvement in cardiac function post PEA as described previously. The relative lack of CD3+ T cells in the media of small arteries in CTEPH suggests that localised inflammation is also less important. The significance of CD68+ cells in CTEPH lung parenchyma needs further assessment.

Conclusions These novel directional next generation RNA sequencing methods provide new insights for mutational mechanisms, and a systems approach to dissection of regulatory and target RNA networks relevant to human disease.
Introduction and objectives New methods of high throughput sequencing provide unparalleled access to the human genome and transcriptome. We hypothesised that next generation DNA sequencing technologies would allow us to identify an elusive novel disease gene for a pulmonary vascular disease inherited as an autosomal dominant trait: The HHT3 interval on chromosome 5 is predicted by linkage studies to contain a mutation causing pulmonary arteriovenous malformations and hereditary haemorrhagic telangiectasia.\(^1,2\)

Methods Published expressed sequence tag (EST) databases and tiling array data were used to supplement sequencing analysis of the HHT3 interval. Sheared, Agilent SureSelect adaptor-ligated genomic DNAs from six related patients and four controls were hybridised to single stranded biotinylated RNA baits. Samples were pooled for multiplexed sequencing on an Illumina HiSeq2000. Sequence data were processed with RTA version 1.7.45, CASAVA Eland pair algorithm, and CASAVA 1.7 demultiplexing algorithms. Validations of sequence variants were performed using conventional PCR and Sanger sequencing.

Results Conventional exon-based sequencing strategies did not identify the HHT3 causative gene mutation. For individual candidate genes, up to 108 alternatively spliced transcripts per gene were predicted from EST databases. For intergenic regions, tiling array data indicated that up to 44 different transcribed fragments were present in the nucleus and/or cytoplasm of different cell types. For each NextGen sequencing DNA sample, ~8 million reads per sample uniquely mapped to the HHT3 interval which represents ~1/5,000 of the genome. Using a 2:1 threshold, an average of ~4,000 differences to NCBI36/hg18 were identified in each sample. 113 differences to NCBI36/hg18 were present in all six HHT3-affected individuals and absent in all four controls. 60% of novel shared variants were validated by wet lab PCR. Following exclusion in 100 normal chromosomes, and computational predictions of potential function, multiple candidate sequence variants remain.

Conclusions Genomic sequencing capturing intrinsic sequences yields challenging numbers of sequence variants for wet lab validations, even when multiple replicate chromosomal strategies are employed.

REFERENCES
2 Govani et al. J Angiogen Res 2010;11(2):15

P18 ROBO1/ROBO4-SLIT2 EXPRESSION IN PULMONARY VASCULAR CELLS: IMPLICATIONS FOR PAH?
10.1136/thoraxjnl-2014-206260.167

Introduction and objectives Pulmonary artery hypertension (PAH) is associated with inappropriate vascular remodelling and inflammation. Recent studies have shown that vascular cells express the transmembrane roundabout (Robo) proteins, Robo1 and Robo4, and that interaction with a secreted glycoprotein ligand, Slit2, controls cell migratory and inflammatory response. We hypothesise that Robo1, Robo4 and Slit2 are expressed on pulmonary artery (PA) endothelial cells (EC) and smooth muscle cells (SMC). We also hypothesise that Slit2 will modulate PAEC and PASMC migration and inflammatory mediator release.

Methods Real-time-PCR determination of Robo1, Robo4 and Slit2 expression and the house-keeping gene, GAPDH, in PAEC, PASMC and for comparison, human umbilical vein endothelial cells (HUVEC); following incubation with TNFα (10ng/ml) or Slit2N (10nM) for 2h. Enzyme-linked immunosorbent assay measurements of granulocyte-macrophage-colony stimulating factor (GM-CSF) in supernatants of HUVEC, PAEC or PASMC pre-treated (1h) with Slit2N, followed by TNFα (17h). Migration assays (PAEC or PASMC) towards serum-containing medium (0.05 and 0.02%, respectively), for 4h with/ without Slit2N.

Results Basal mRNA expression of Robo1, Robo4 and Slit2 was detected in PAEC, PASMC and HUVEC (n = 3–4). Slit2N (2h) significantly (p < 0.05, n = 3) decreased Robo4 and Slit2 mRNA expression, but not Robo1, by 35% in PAEC; and had no effect on HUVEC or PASMC. TNFα had no significant effects on Robo1, Robo4 or Slit2, regardless of cell type. Despite a small (23%), but significant (p < 0.05) reduction of GM-CSF release from TNFα-activated HUVEC (n = 7), no similar effects were seen in PAEC or PASMC (n = 3). Moreover, whilst PAEC or PASMC migration to serum-containing medium increased (2.7- and 5.3-fold, respectively), co-incubation with Slit2 had no significant effect.

Conclusion The novel discovery of Robo1, Robo4 and Slit2 mRNA in PAEC and PASMC; and that Slit2 down-regulated Robo4 and Slit2 in PAEC, but not PASMC/HUVEC, might suggest negative feedback on the Robo4-Slit2 axis unique to PAEC. That neither PAEC nor PASMC responded to Slit2 in functional assays could reflect limitations in experimental assays. However, down-regulation of Robo4-Slit2 in PAEC might also explain lack of effect on GM-CSF release, when compared with HUVEC. Further studies to better delineate the role of the Robo-Slit2 pathway in PAH are required.

P19 THE ROLE OF DIFFERENTIAL TNFR SIGNALLING IN MAINTENANCE OF ALVEOLAR EPITHELIAL HOMEOSTASIS

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10.1136/thoraxjnl-2014-206260.168

Alveolar epithelial activation and disruption of the alveolar epithelial barrier promote recruitment of neutrophils into the alveolar space and cause alveolar oedema respectively thereby playing key roles in the pathogenesis of Acute Respiratory Distress Syndrome (ARDS). Tumour necrosis factor alpha (TNF) is an early mediator of inflammation in ARDS. TNF signals through two cell surface receptors, TNFR1 and TNFR2 initiating distinct signalling pathways and cellular responses.

Using a novel, highly selective TNFR1 domain antibody (dAb\(^\s{34}\)), a dummy dAb and the dual TNFR antagonist Adalimumab\(^\s{63}\), we investigated the role of differential TNFR signalling on human pulmonary alveolar epithelial cell (human alveolar type 2 cells and A549 cell line) activation, permeability and repair.

Human alveolar epithelial type 2 cells (haT2) expressed both TNFR, whilst A549 cells only expressed TNFR1. TNFR1 signalling mediated release of the neutrophil chemokines IL-8 and GMCSF as well as IL-6 in haT2 (pin vitro scratch model of epithelial (haT2) wound repair.

TNFR1 signalling induced pro-inflammatory cytokine expression from alveolar epithelial cells and mediated increased epithelial permeability. TNFR1 induced permeability did not appear to
be due to disruption of epithelial junctional proteins; we speculate that this may alternatively be due to TNFR1 induced cell death.

**Abstract P19 Figure 1** A549 cells plated on an iCelligence 8-well gold electrode coated plate were incubated with TNFR1 dAb™, a dummy dAb or Adalimumab™ for 1 h then exposed to exogenous TNF or vehicle control. Electrical impedance was measured continuously over 50 h. Trough normalised impedance was measured over 50 h post treatment (n = 3–5). Data are presented as mean ±SEM analysed by Kruskal-Wallis (Dunns). *p < 0.05, **p < 0.01

**Background** Acute respiratory distress syndrome (ARDS) remains an often fatal condition without effective pharmacological therapies. Characteristically, a neutrophil-dominant disorder, it is associated with a dysregulated inflammatory response and tissue injury. Neutrophil migration into inflammatory sites is controlled by a variety of factors; in sterile tissue injury mitochondrial formylated peptides are released following necrotic cell death and bind to formyl peptide receptor 1 (FPR1) on neutrophils to induce migration and activation.

**Hypothesis** That mitochondrial formylated peptides are elevated in ARDS and drive FPR1-mediated neutrophil recruitment. Inhibition of FPR1 in sterile lung injury would therefore attenuate the inflammatory response through multiple FPR1-mediated effects.

**Methods** Mitochondrial DNA and formylated peptides were quantified in plasma of ARDS patients and healthy controls by qPCR, western blot and LC-MS/MS. Healthy volunteer neutrophils were stimulated with mitochondrial formylated peptides and chemotaxis assays and flow cytometry used to assess neutrophil function. Intracellular signalling was assessed by western blotting. Mouse models of infective (E. coli) and sterile (hydrochloric acid) acute lung injury were used.

**Results** Free mitochondrial DNA and formylated peptides were elevated in ARDS patients. Mitochondrial formylated peptides induced FPR1-dependent neutrophil chemotaxis through PI3K- and MAPK-mediated control of the β3-integrin heterodimer Mac1. In sterile acid-induced injury FPR1 inhibition resulted in reduced neutrophil migration, pulmonary haemorrhage, protein leak and pro-inflammatory cytokine expression. Furthermore, acid-induced reduction in alveolar macrophage number was inhibited while interstitial macrophages displayed an alternatively activated phenotype. FPR1 was also found to be expressed on mouse type 1 alveolar epithelial cells suggesting further possible mechanisms through which FPR1-mediated alveolar leak occurs. Importantly, delivery of FPR1 antagonists 12 h after injury also reduced acute lung inflammation demonstrating potential therapeutic relevance. In non-sterile E. coli-mediated lung injury partial antagonism of FPR1 resulted in reduced alveolar neutrophil numbers and attenuated vascular leak without altering bacterial clearance.

**Conclusions** Mitochondrial formylated peptides and FPR1 play an important role in the pathogenesis of sterile acute lung injury. This appears to be predominantly through neutrophil-dependent means but their role in macrophage and epithelial cell function could also be important. FPR1 antagonism may therefore represent a multi-cellular therapeutic target in the treatment of ARDS.

**P20**

**DELINEATING THE CONTRIBUTION OF FORMYLATED PEPTIDES AND FORMYL PEPTIDE RECEPTOR 1 TO THE PATHOGENESIS OF ACUTE LUNG INJURY**

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**Abstract**

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**P21**

**HYPOXIA-INDUCED NEUTROPHIL SURVIVAL IS DEPENDENT ON PHOSPHOINOSITIDE 3-KINASE (PI3-K)-MEDIATED SIGNALLING**

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**Introduction and objectives** Neutrophils (PMNs) are a key component of the innate immune response to invading pathogens. They accumulate at sites of inflammation and infection, which are typically characterised by low oxygen tensions (e.g. in the acute respiratory distress syndrome (ARDS)). Human PMNs undergo constitutive apoptosis, their survival contingent upon pro-survival and pro-apoptotic signals derived from their microenvironment. Hypoxia profoundly delays PMN apoptosis, resulting in persistence of PMNs at inflammatory foci and this may perpetuate hypoxia-mediated lung injury. Given the importance of phosphoinositide 3-kinase (PI3-K) signalling in cytokine-mediated neutrophil survival, we hypothesised that hypoxia-induced PMN survival may also involve PI3-K-mediated signalling.

**Methods** Highly pure PMNs isolated from healthy volunteers were incubated for 20 h under normoxic (20 kPa) and physiologically relevant hypoxic (3 kPa) conditions with a pan-PI3-K inhibitor (LY294002 at 10 µM), a novel pan-Class I PI3-K inhibitor (ZSTK474 at 1 µM, 3 µM and 10 µM) or novel PI3-K Class I isoform-selective inhibitors (PI3-Kβ at 1 µM; PI3-Kγ at 3 µM and 10 µM, or PI3-Kδ at 3 µM). PMNs were also incubated in normoxia and hypoxia in the presence of GM-CSF (1 ng/ml) with the same panel of inhibitors, allowing comparison with GM-CSF mediated survival, which is largely PI3-K dependent. PMN apoptosis was assessed using two complementary techniques – morphology and flow cytometry following annexin V-FITC and propidium iodide staining.
**Results** Compared with normoxia, hypoxia promoted PMN survival (mean% ± SEM apoptotic cells at 20 h: 30.9 ± 1.9 vs. 59.0 ± 1.8 respectively, p < 0.0001). Both pan-PI3-K inhibitors reversed the pro-survival effect of hypoxia in a concentration-dependent manner, LY294002 (10 µM; 60.3 ± 4.0, p < 0.0001) and ZSTK474 (10 µM; 58.3 ± 2.6, p < 0.0001) without affecting the basal rate of apoptosis. This effect was not seen with the dual PI3-K inhibitor (3 µM; 43.8 ± 7.6) or individual PI3-Kδ (1 µM; 43.0 ± 5.8) and γ inhibitors (3 µM; 34.9 ± 4.5 and 10 µM; 32.6 ± 3.6).

**Conclusions** Our results indicate that hypoxia-induced PMN survival is PI3-K dependent. Targeting this pathway may accelerate PMN apoptosis, resulting in resolution of inflammation.

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Idiopathic pulmonary fibrosis (IPF) and non-specific interstitial pneumonia (NSIP) are forms of idiopathic interstitial pneumonias that have distinct histopathological features and outcomes. It is unknown if these idiopathic interstitial pneumonias have common mechanisms of fibrosis. Endoplasmic reticulum (ER) stress has been implicated in the pathogenesis of sporadic and familial idiopathic pulmonary fibrosis. In response to endoplasmic reticulum (ER) stress, cells trigger the unfolded protein response (UPR) with upregulation of chaperones, such as BiP, and the phosphatase growth arrest and DNA damage 34 (GADD34) in determining the severity of the fibrotic response. We hypothesised that ER stress may also be involved in the pathogenesis of NSIP.

Paraffin embedded lung biopsy sections from 4 patients with sporadic idiopathic pulmonary fibrosis (IPF) (UPI histopathology) and 4 non-specific interstitial pneumonia (NSIP) histopathology were evaluated for the ER stress markers BiP and GADD34 by immunohistochemistry. For each biopsy sample, six high power fields (x 200 magnification) were scored for fibrosis and inflammation as well as BiP and GADD34 using semi-quantitative analysis by 2 blinded, independent investigators.

BiP and GADD34 were expressed in areas of fibrosis, localised to reactive type II pneumocytes and endothelial cells. No staining was detected in fibroblasts or fibroblastic foci. In sporadic IPF (UPI), levels of BiP within the epithelium correlated with fibrosis ($r^2 0.56$, p = 0.0001, Figure 1a) more than inflammation ($r^2 0.38$, p = 0.0013). In contrast, epithelial GADD34 was more strongly associated with NSIP fibrosis ($r^2 0.56$, p < 0.0001, Figure 1b). There was no association between the ER stress markers and inflammation in NSIP.

These data suggest that ER stress and the unfolded protein response are features of NSIP as well as IPF and may play a role in determining the severity of the fibrotic response.
VITAMIN D LEVELS ARE LOW IN SARCOIDOSIS AND CONTRIBUTE TO ABNORMAL MONOCYTE ACTIVITY

Introduction Sarcoidosis is a multisystem inflammatory disorder. We showed recently that monocytes from patients with sarcoidosis exhibited reduced IL-10 production, and were less able to suppress T cell proliferation. Vitamin D is reduced in a number of inflammatory and autoimmune disorders and has been shown to influence the activity of immune cells, including monocytes. We had observed reduced Vitamin D levels in our sarcoidosis patients and hypothesised that this may contribute to immune-pathology by altering monocyte function.

Methods Forty-six steroid-naïve, non-smoking individuals with histology-confirmed sarcoidosis were recruited from our Sarcoidosis-ILD service at first presentation. Serum calcidiol levels were compared with age and gender matched healthy controls. Patients and hypothesised that this may contribute to immune-mediated disease makes functional characterisation of monocyte activity score 2 were recruited: gene expression profiles compared with age and gender matched healthy controls. All donors were Caucasian, corticosteroid (and other immunomodulatory treatment) naïve-non-smokers. Monocytes were isolated by CD14-negative magnetic selection within 3 h of venesection, RNA extracted using a proprietary kit and stored at -80°C prior to single batch hybridisation with illumina humanHT-12 v4 chips.

Results A total of 3437 genes were differentially expressed in sarcoidosis monocytes compared with controls (adjusted p value of <0.05). Filtering by Log2 fold change of at least 1.5 identified 151 differentially expressed genes among these. Principal component analysis demonstrated clear segregation between sarcoidosis and controls, and between those with high and low activity, with low activity clustering closer to healthy controls. IL-6 was the most significantly upregulated gene (Log2 FC 4.723 adjusted p < 0.001). Other significantly upregulated genes included the pro-inflammatory cytokines IL1A (2.987, 0.001) and IL1B (2.952, 0.001); and the monocyte chemotactic factors CCL20 (4.212, 0.002), CXCL2 (4.057, <0.001) and CCL3 (3.470, 0.003). Gene set enrichment analysis identified gene ontology (GO) gene sets relating to inflammatory and immune system responses to be amongst the most positively enriched genes in the monocytes from patients with active disease (p < 0.001, normalised enrichment score [NES] 2.22 and 2.20 respectively).

Conclusions Sarcoidosis monocytes sarcoidosis have a distinct gene expression profile exhibiting a pro-inflammatory, chemotactic phenotype. IL-6 may be implicated in the initiation and maintenance of alveolitis and hypergammaglobulinemia in sarcoidosis and the recent interest in the use of humanised anti-IL-6R antibodies in the treatment of rheumatoid arthritis and other immune mediated disease makes functional characterisation of the role of IL-6 in the pathogenesis of sarcoidosis an exciting prospect.

REFERENCES

DISTINCT PRO-INFLAMMATORY GENE EXPRESSION PROFILE IN MONOCYTES FROM SARCOIDOSIS PATIENTS WITH ACTIVE DISEASE

Introduction Monocytes are potential key cellular players in the early pathogenesis of sarcoidosis. Having previously identified altered monocyte activity in sarcoidosis, we now examine monocyte whole genome expression profile in order to determine potential processes and pathways involved in the perturbed immune activity of these cells.

Methods Patients with tissue-confirmed sarcoidosis (three high-activity, three low-activity, identified by a predefined clinical activity score)2 were recruited: gene expression profiles compared with age and gender matched healthy controls. All donors were Caucasian, corticosteroid (and other immunomodulatory treatment) naïve-non-smokers. Monocytes were isolated by CD14-negative magnetic selection within 3 h of venesection, RNA extracted using a proprietary kit and stored at -80°C prior to single batch hybridisation with illumina humanHT-12 v4 chips.

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REFERENCES

P26

P26 MAPK INHIBITION ENHANCES CORTICOSTEROID EFFECTS IN HUMAN EPITHELIAL CELLS VIA INCREASED GR NUCLEAR LOCALISATION

Background Phospho-p38 MAPK expression is increased in airway epithelial cells in patients with severe asthma and in COPD patients compared to controls. Increased p38 MAPK activation may lead to reduced corticosteroid responsiveness. We have used a human cell bronchial epithelial cell line to investigate the effects of a p38 MAPK inhibitor in combination with a corticosteroid on inflammatory cytokine stimulation.

Methods The human epithelial cell line 16HBE14o was used to determine the effects of dexamethasone (0.1–1000 nM) alone, the p38 MAPK inhibitor BIRB-796 (1–1000 nM) alone and both drugs combined at all concentrations on LPS (1 μg/ml), Poly I:C
(100 µg/ml) or TNFα (10 ng/ml) induced IL-6, IL-8 and RANTES. 16HBE14o- cells were treated with BIRB-796 (1–1000 nM) alone and in combination with dexamethasone (0.1 nM) for 30 min and glucocorticoid receptor (GR) nuclear translocation determined by immunofluorescence. The effects of TNFα stimulation on the phosphorylation of p38 and GR (serine 226) in 16HBE14o- cells were determined by Western blot analysis.

**Results** Maximum inhibition of dexamethasone and BIRB-796 in combination was significantly greater than either drug alone for LPS and TNFα induced IL-6 and IL-8 and for Poly I:C induced RANTES (p < 0.05 all comparisons). BIRB-796 (1000 nM) alone had no effect on GR translocation. BIRB-796 (1000 nM) used in combination with dexamethasone (0.1 nM) significantly increased nuclear GR (76.6% nuclear staining) compared to dexamethasone (0.1 nM) alone (4% nuclear staining). TNFα stimulation increased both p38 and GR serine 226 phosphorylation by 15 min. Pre-incubation with BIRB-796 abolished p38 phosphorylation and reduced GR serine 226 phosphorylation.

**Conclusion** P38 MAPK inhibition enhances the effect of corticosteroids on inflammatory cytokines in human epithelial cells. This enhancement is due to inhibition of p38 dependent phosphorylation of GR serine 226 which leads to increased nuclear localisation of GR.

Keeping your distance: telemonitoring and telehealth

**P27 THE USE OF TELEMONITORING TO ASSIST IN THE EARLY SUPPORTED DISCHARGE FOR PATIENTS ADMITTED WITH AN EXACERBATION OF COPD**

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10.1136/thoraxjnl-2014-206260.176

**Introduction** In 2011 the Whole Systems Demonstrator programme findings showed that, if used correctly, Telehealth can deliver 14% reduction in bed days and an 8% reduction in tariff costs in patients with chronic conditions. However little data is available on using Telehealth to assist in the acute setting of early supported discharge of COPD patients as most previous studies focused on its use to assist the long term case management of these patients.

**Methods** After training of staff within the COPD early support discharge (ESD) team in Salford (CAST), 17 HomePods were made available for this 12 months pilot starting in 2013. Patients were selected based on their ability to use the technology and on availability of HomePods. Pods were left with patients for 30 days and provided remote real-time monitoring of patients before they were re-deployed again to another patients. During the deployment period, patients were supported by a combination of telephone calls and home visits.

**Objectives**

- Measure the impact of Telehealth on 30 day readmission rates in this cohort
- Test the impact of new technology on caseload/ work load of CAST
- Test the acceptability of Telehealth on this cohort and on CAST
- Assess impact on ability to selfcare
- Measure patients’ satisfaction

**Outcomes** 73/285 (25%) patients received this intervention with the CAST team
- 30 day re-admission rates within the intervention group was 3% compared to 8% in the other ESD patients, and 18% within the Respiratory directorate.
- Those in the telehealth group accounted for 5% of all home visits and 25% of all phone calls made by CAST
- The capacity of CAST was increased from 15 Cases to 18 cases at any one time (20%)
- Patients’ survey showed excellent impact on patients
  - Patients’ satisfaction
  - Confidence in self care
  - Patients acceptability and likeability to Telehealth
  - Good suggestions were made by patients for improvement

**Conclusions** The use of Telehealth in the context of ESD for COPD patients admitted with an exacerbation appears to have favourable effect on relevant outcomes without impact on workload and therefore might me a useful tool to consider.

**P28 THE USE OF SMARTPHONE APPLICATION (COPD ASSIST) TO SUPPORT THE IMPLEMENTATION OF LOCAL PRIMARY CARE GUIDELINES ON THE MANAGEMENT OF PATIENTS WITH COPD**

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10.1136/thoraxjnl-2014-206260.177

**Introduction** Smartphone applications (apps) have become increasingly popular and offer us up-to-date access to information “on the go”. Many national and international societies, medical journals and healthcare organisations develop their own apps; However using apps on a local level to promote implementation of local COPD guidelines and education has not been previously evaluated.

**Methods** Funding was provided by Salford’s CCG innovation fund. A Smartphone app developing firm was commissioned and a development plan was agreed as follows:

1. Close liaison with the lead respiratory physician throughout the project.
2. A primary care focus group helped develop a Beta version for testing prior to launch.
3. App launched as “COPD Assist”.
4. Promotion to primary care clinicians via newsletter articles, press releases, seminars, and the intranet.
5. Regular data collection on app downloads to measure usability
6. Users’ feedback and suggestions via app reviews
7. App downloads initially restricted to Salford clinicians

**Objectives**

1. Provide primary care clinicians with access to local guidelines and relevant contact details for COPD services anytime, anywhere.
2. Provide the most up-to-date guidelines
3. Offer clinicians access to educational material including videos (inhaler technique, spirometry, and pulmonary rehabilitation) and the opportunity to share this information with patients.
4. Provide up to date pricing of various inhaled therapies
Outcomes COPD Assist was launched in March 2014, then published to all Salford’s primary care clinicians supported by 5 training seminars with over 70 clinicians attending.

Within 4 months following its launch, COPD assist was downloaded 622 times by different users, with an average use time of 7 min and average of 9 screens viewed per session. 52% of users have used the app more than once.

Feedback was excellent, particularly ease of use and simplicity.

Conclusions This bespoke smartphone app to support the implementation of local primary care COPD guidelines appears to be widely acceptable to users and could potentially promote these guidelines. However, more research around clinically meaningful outcomes, such as adherence to guidelines and impact on prescribing, is required to assess the true impact of such technology on the management of COPD in primary care.

Results 45/48 (94%) of CCG practices took part. Data from 372 patients on COPD registers reviewed over 25 virtual clinics is presented. 321 (86%) patients had confirmed COPD (including 33 with COPD and asthma), 34 had asthma, 15 needed more spirometry and 2 had another diagnosis. 279/321 (87%) patients had a recommendation made: 64 (23%) referred for PR, 53 (19%) for spirometry, and 45 (16%) for smoking cessation. Changes to drug therapies were also recommended: 42 (15%) patients had a LAMA recommended, 16 (5%) a LABA, and while 117/321 COPD patients (37%) required no change to ICS therapy, a graduated step down/stop was suggested for 198 (63%). The outcomes associated with this are in Table 1.

Overall, from Q4 13/14 prescribing data, there was a 4% decrease in high dose ICS (as proportion of total ICS use) resulting in a saving of £50,000.

Conclusion Integrated working through respiratory virtual clinics offers huge scope to improve high value care for COPD patients. Overuse of ICS in COPD is common and GP-led withdrawal of high dose ICS where appropriate is feasible, acceptable and well tolerated by patients.

Abstract P29 Table 1 Outcomes associated with the ICS gradual withdrawal recommendation

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of patients (n = 198)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICS successfully stopped</td>
<td>61</td>
</tr>
<tr>
<td>ICS stopped</td>
<td>58</td>
</tr>
<tr>
<td>Patient due for step down at time of data submission</td>
<td>33</td>
</tr>
<tr>
<td>Patient was not stepped down, but reason not given</td>
<td>19</td>
</tr>
<tr>
<td>Patient asked not to have ICS stopped</td>
<td>9</td>
</tr>
<tr>
<td>Patient did not tolerate lower dose</td>
<td>9</td>
</tr>
<tr>
<td>Patient included as no-longer fulfilled inclusion criteria</td>
<td>7</td>
</tr>
<tr>
<td>Patient could not be contacted</td>
<td>2</td>
</tr>
</tbody>
</table>

Abstract P30 Table 1

<table>
<thead>
<tr>
<th>County</th>
<th>County 1</th>
<th>County 2</th>
<th>County 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>County 1</td>
<td>2010/11</td>
<td>2011/12</td>
<td>2012/13</td>
<td>2013/14</td>
</tr>
<tr>
<td>2010/11</td>
<td>24,788</td>
<td>22,272</td>
<td>23,884</td>
<td>20,820</td>
</tr>
<tr>
<td>2011/12</td>
<td>17,976</td>
<td>16,764</td>
<td>16,996</td>
<td>14,300</td>
</tr>
<tr>
<td>2012/13</td>
<td>11,596</td>
<td>11,888</td>
<td>11,912</td>
<td>10,380</td>
</tr>
<tr>
<td>2013/14</td>
<td>54,360</td>
<td>50,924</td>
<td>52,792</td>
<td>45,500</td>
</tr>
</tbody>
</table>

Large scale change is difficult to bring about. The regional Respiratory Programme began in 2011 with the aim of improving outcomes in COPD and asthma. We designed a COPD dashboard with key metrics aiming to track progress and encourage involvement in service improvement. The Quality Observatory maintain the dashboard and release quarterly updates which we email out to our network members and other key people (n = 396) accompanied by commentary indicating issues for consideration and highlighting trends. The target audience includes clinicians in primary, secondary and community care plus managers and commissioners. This work is supplemented by running oxygen and pulmonary rehabilitation clinical networks which provide support and training to clinicians plus a quarterly educational and information sharing epublication ‘Breathing Matters’. We track trends in metrics. COPD bed days are a key outcome measure and the table below shows the yearly value since the program commenced.

Looking at the admission figures on a population basis i.e. admissions per 1,000 COPD population (population weighted for prevalence of COPD using ERPHO modelled estimates and projections) there is a similar trend:

County 1 2010/11 17.9 per 1000 vs 13.2 per 1000 in 2013/14

County 2 2010/11: 12.5 per 1000 vs 10.3 per 1000 in 2013/14

County 3 2010/11: 15.8 per 1000 vs 13.8 per 1000 2013/14
INTELLIGENCE BASED INFORMATION SYSTEM (IBIS) REDUCES RESPIRATORY PATIENTS’ USE OF SECONDARY HEALTH CARE RESOURCES

Background IBIS is a database developed by South East Coast Ambulance Service (SECAmb) to facilitate communication of individual patient care plans between SECAmb, the Respiratory Care Team (RCT) and secondary care. It aims to reduce the number of patients conveyed to hospital.

Aims and objectives The investigation aimed to establish the impact of IBIS on respiratory patients’ use of secondary care in our locality.

Methods Respiratory patients uploaded into IBIS between May and November 2013 were included. Data were collected from the Patient Administration System including, number of A&E attendances and admissions in the three months preceding and three months after patient care plans were included in IBIS. Data were analysed with descriptive statistics and Wilcoxon Paired Test utilising SPSS version 22.

Results 65 patients were included in the study. Table 1 demonstrates the impact of IBIS on A&E attendances and admissions. There was a significant reduction in admissions (p = 0.011). A reduction in A&E attendances was observed (p = 0.064). A sub-analysis of patients already utilising secondary care resources was undertaken. In this patient group a significant reduction in both A&E attendances (p = 0.000) and admissions (p = 0.000) was observed.

Conclusions IBIS assists in reducing respiratory patients A&E attendances and admissions. The impact of IBIS is more profound in patients who have already utilised secondary health care resources.

A NOVEL AUTOMATED REFERRAL SYSTEM USING THE ELECTRONIC PRESCRIPTION OF PREDNISOLONE ≥30 MG AND NEBULISED BRONCHODILATORS TO THE RESPIRATORY SPECIALIST TEAM IS ROBUST AND EFFECTIVE

RC Colclough, T Avent, K Breese, C Caddick, D Curry, K Swindells, S Gomperz. Queen Elizabeth Hospital Birmingham, Birmingham, UK

Introduction Patients admitted to hospital with an exacerbation of COPD should be cared for by respiratory teams (COPD Quality Standard 10, NICE 2011). The earlier the patient is reviewed by a specialist the greater the impact on length of stay (COPD NICE guideline 101, 2010). A rigorous and rapid referral system is required.

A new electronic referral system triggered by the prescription of prednisolone ≥30 mg AND nebulised bronchodilators (salbutamol and/or ipratropium) via our Prescribing Information Communication System (PICS) was implemented. This replaced the laborious paper sift of the admissions book for admissions with airway exacerbations. The general medical team was also permitted to refer directly to the respiratory team via email.

Referral numbers were compared over a 2-month period to ensure that the new automated system is robust.

Method
1. The new automated referral was created.
2. Data was collected from the three referral routes a) paper sift, b) automated referral system, c) email from general medical team.
3. Comparison between: a) monthly automated and email referrals was made, b) paper sift and automated referrals route was made.

Results Each month there were:
1. 262 (mean) admissions screened via paper sift of which 96 (mean) were inappropriate (36%).
2. No patients identified by paper sift or email were missed by the automated system.
3. 138 (mean) automated referrals- time from admission to automated referral 13 h (mean) 10–16 h (range).
4. 75 (mean) email referrals - time from admission to email referral 104 h (mean) 96–112 (range).

Conclusion Paper sift is time costly and laborious with a third of referrals inappropriate. Automated referrals are sent 91 (mean) hours quicker than email referrals. Automated referrals reduce the delay between admission and specialist review. They can be received from any location in the hospital throughout the day using Smart Phones.

The automated referral eliminates the need for once daily paper sifting of the admission book, and replaces it with a more timely and robust method of directing the specialist respiratory team to the patient’s bedside.
**Poster sessions**

**P33** 'LIGHT TOUCH' TELEMONITORING FOR PEOPLE WITH COPD IN LOTHIAN: A PILOT EVALUATION WITH NESTED QUALITATIVE STUDY

1HJ Pinnock, 1M MacNab, 1S Lee, 2J McCloaghan, 2J Hanley, 1A Lindsay, 1B McGinstry. 1The University of Edinburgh, Edinburgh, UK; 2Edinburgh Napier University, Edinburgh, UK; 3NHS Lothian, Edinburgh, UK

Background and aim Professionally monitored telehealthcare has significant workload implications, but qualitative work suggested that pulse oximetry could potentially contribute to self-monitoring. We aimed to evaluate the acceptability and perceived utility of a COPD ‘Light Touch’ service.

‘Light Touch’ intervention People with COPD used a pulse oximeter and symptom diary to self-monitor and self-refer according to a self-management plan. The service was overseen (though not actively monitored) by community-based respiratory/long-term conditions teams who were contactable by a telephone helpline.

Method We undertook a before-and-after study with quantitative data collection at baseline and six-months. Outcomes were St George’s Respiratory Questionnaire (SGRQ), Hospital Anxiety and Depression Scale (HADS) and service use. Nested semi-structured interviews with patients (at baseline and six-months) and managers, and a focus group of healthcare professionals explored perceptions of the service.

Results We recruited 51 patients. Quality-of-Life (SGRQ): 21 (46%) participants improved by ≥4 (the minimum important difference); 12 (26%) deteriorated by ≥4. HADS improved: more participants had normal scores for anxiety (65%) and depression (80%) at 6 months than at baseline (51% and 64%). There were fewer surgery consultations and more telephone consultations, antibiotic, oral steroid and nebulised therapy prescriptions recorded during the study period compared to the previous year. Only 18 (39%) contacted the Light-Touch Helpline.

We conducted interviews with 20 participants (36 interviews), 6 managers, and a focus group of 8 clinicians. Patients were generally positive and embraced ‘Light-Touch’ telemonitoring as part of their daily self-surveillance. The readings were reassuring and gave them confidence to make self-management decisions. Most patients did daily checks though several had stopped routine monitoring preferring to ‘check their readings as and when the need arises’. Healthcare professionals were concerned that patients had disengaged with their service. Few patients contacted the clinical teams for help or advice during the study and 6-monthly telephone reviews were introduced to maintain contact.

Conclusion In contrast to professionally-monitored telehealthcare, ‘Light-Touch’ seemed to reduce the contacts between patients and professionals. Whilst this may represent effective self-management, there were concerns that loss of engagement with healthcare services may be detrimental to achieving prompt management of exacerbations.

**P44** ASSESSMENT OF SPIROMETRY AND IMPULSE OSCILLOMETRY IN RELATION TO ASTHMA CONTROL

A Manoharan, WJ Anderson, J Lipworth, BJ Lipworth. University of Dundee, Dundee, UK

Background Guidelines advocate the use of spirometry to assess pulmonary function in asthmatic patients. Commonly used measures include forced expiratory volume in 1 second (FEV1), forced expiratory ratio (FEV1/FVC) and forced mid-expiratory flow between 25% and 75% of forced vital capacity (FEF25–75). Impulse oscillometry (IOS) is an effort independent test performed during tidal breathing. IOS may be used to assess the total and central airway resistance at 5 Hz (R5) and 20 Hz (R20) respectively and hence derive the peripheral airway resistance from the difference (R5–R20).

Objective To compare spirometry and IOS as tests of global airway function (i.e., FEV1, FEV1/FVC, R5) and putative measures of small airways function (i.e., FEF25–75, R5–R20) and their relationship to long-term asthma control.

**P34** WHAT IS INTEGRATED CARE AND WHAT IS THE VALUE OF AN INTEGRATED RESPIRATORY SPECIALIST?

1NJ Roberts, 1M Ward, 5S Patel, 5J Yorke, 1J Williams, 1R Walters, 5M McKewitt, 5Edwards, 1Glasgow Caledonian University, Glasgow, UK; 5Sherwood Forest Hospitals, Sutton in Ashfield, UK; 1Kings College Hospital London, London, UK; 1University of Manchester, Manchester, UK; 1Halton General Hospital, Runcorn, UK; 4Mansfield Community Hospital, Mansfield, UK; 2British Lung Foundation, London, UK; 3British Thoracic Society, London, UK

Aim The way we deliver healthcare in the UK is changing, joining up care between the different health sectors has created a new field of “integrated care”. Recent publications from the Kings Fund, Nuffield Trust and National Voices has shown that it is difficult to define “integrated care”. This project surveyed health professionals on their views about integrated care and the value of integrated respiratory specialists.

Method A questionnaire was sent to all BTS members in Oct 2013 on the role of integrated care specialists, 216 responses were received.

Results Most respondents (82.5%, 178/216) included integration of primary and secondary care in their definition of integrated care, only 36.3% (65/178) included community, and a smaller number included social care as part of the definition. In the free-text there was also emphasis on the bridging role of the post, and providing “seamless care” across sectors.

62% (86/139) agreed that integrated respiratory specialists had added value (compared to respiratory specialist roles); providing continuity of care for a defined population (87%, 121/139), and 77% (106/138) agreed that they improve outcomes for patients with a long term condition. Eighty-nine percent (124/140) also agreed that integrated specialists improve relationships between primary and secondary care. When asked the most important role that an integrated respiratory specialist should undertake (98 comments), the provision of specialist leadership, clinical decision-making and supervision (20 comments) were highly rated. Teaching (10 comments) and providing liaison support for the whole pathway were also important (9 comments).

Conclusion 82% of respondents (178/216) included integration of primary and secondary care in their definition of integrated care. However 14.4% were unsure of what integrated care was. Considerable more work is needed to promote this new way of working and potential career pathway. However of those who did know about these roles, a large majority agreed that these roles had added value compared to traditional specialist roles.

Funded by the BTS.

Abstracts M35 to M43 can be found on pages A208–A211.
Methods
Spirometry and IOS measurements from asthmatics were linked to a health informatics database for oral steroid and short-acting beta agonist use (SABA) use 1 year prior to the measurements.

Results
442 patients had both spirometry and IOS, mean FEV₁ = 86% predicted, 94% on ICS, median dose 800 μg/day. IOS and spirometry measures were equally predictive of impaired asthma control for both oral steroid and SABA use. For oral steroid use, the adjusted odds ratio (95% CI) for oral steroid (A) and short-acting beta-agonist use (B) in the year preceding measurements were linked to a health informatics database for oral steroid and SABA use 1 year prior to the measurements.

Abstract P44 Figure 1 Adjusted odds ratios (95% CI) for oral steroid (A) and short-acting beta-agonist use (B) in the year preceding measurements of FEV₁ (<80% predicted, n = 140 vs >80% predicted, n = 302), FEV₁/FVC (<0.70, n = 131 vs >0.70, n = 311), FEV₁/FVC <60% predicted, n = 238 vs >60% predicted, n = 204), R5 (>150% predicted, n = 183 vs <150% predicted, n = 259) and R5-R20 (<0.10 kPa·L⁻¹·s, n = 185 vs <0.10 kPa·L⁻¹·s, n = 257). The 95% CIs which exclude unity are defined as being of statistical significance.

Conclusion
Spirometry or IOS measurements are equally useful for patients able to produce a sputum sample, some patients cannot produce a sample. As a result we looked at developing an alternative method of monitoring using nasal lavage samples to study the intra-individual changes in inflammation in severe asthma.

Methods
Patients requiring sputum monitoring as part of their clinical management were invited to take part in this pilot and to provide an additional nasal lavage sample obtained using an olive method. Participants were clear of infection at time of sampling. Sputum was either spontaneous or induced using the traditional 3%-4%-5% nebulised sodium chloride procedure. ECP (Eosinophil Cationic Protein) was measured in sputum and nasal supernatants using a commercial ELISA kit (Mesacup, MBL). Differential cell count (DCC) was attempted for both sputum and nasal sample types.

Results
This abstract shows the results obtained for the first 32 consecutive patients. Our patient population is described in Table 1, 69% female, 69% atopic (as defined by positive RAST). No patient was immunosuppressed or on IM Tramcinolone.

ECP levels were as follows:

- Sputum: median 2650 (min:20.76–28603 ng/ml), 100% of samples had detectable levels.
- Nasal lavage: 0(0–7.6), 20%.

DCC were as follows:

- Sputum: 38% patients were eosinophil positive (as defined by >3%),
- Nasal lavage: no eosinophil was detected, 38.5% of samples had a DCC but interpretation was hindered by low cell yield.

Sputum DCC/ECP did not correlate significantly with nasal ECP (Pearson R=0.168, p = 0.374 and R=-0.048, p = 0.807 respectively). Nasal DCC data could not be computed as no patient was eosinophil positive.

Conclusions
At this stage of our pilot, intermediate data analysis shows that nasal sampling does not appear to be a successful alternative to sputum monitoring in severe asthma.
THE INFLUENCE OF AGE AND GENDER ON ALLERGY TEST RESULTS: IMPLICATIONS FOR THE USE AS BIOMARKERS IN CHILDHOOD ASTHMA

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Introduction Skin prick tests (SPTs) and measurement of allergen-specific serum (s)IgE are the main diagnostic tools for confirming atopy. Results of both tests are usually reported as dichotomous (sensitised/not sensitised), using arbitrary cut-offs which are the same across different ages and genders (SPT >3 mm, sIgE >0.35 kU/L). We investigated the influence of age and gender on allergy test results as biomarkers of asthma during childhood.

Methods Children in a population-based birth cohort (n = 1051) were followed from birth to age 11 years. Information on asthma/wheeze (questionnaires), SPTs and sIgE to inhalant allergens (mite, cat, dog) were collected at ages 3, 5, 8 and 11 years. We investigated the association between quantitative atopy (sum of SPT mean wheal diameters [MWD]/titres of sIgE) and wheeze/asthma across ages and genders.

Results There was a significant association between the SPT MWD/sIgE titre and wheeze/asthma at all ages and for both genders. However, the strength of this association was age and gender-dependent. For SPTs, the strength of the association between SPT MWD and asthma increased with increasing age (OR 1.14 – 1.20, p = 0.002); we observed the opposite pattern for sIgE titre (OR 0.97–0.99, p = 0.04). For any given SPT/sIgE level, boys were significantly more likely to express clinical symptoms, particularly in early life; this difference between males and females appeared to diminish with age, and was no longer significant by age 11 years.

Conclusions Age and gender have to be taken into account when interpreting the results of allergy tests (skin tests and IgE measurement) in the context of asthma during childhood.

CONTINUOUS LARYNGOSCOPY DURING EXERCISE (CLE): A PRACTICAL AND VALUABLE TEST IN A RESPIRATORY SERVICE?

B Panchasara, GS Haji, S Ward, A Menzies-Gow, JH Hull. Royal Brompton Hospital, London, UK

Introduction and rationale Exertional wheeze and dyspnoea are most frequently attributed to exercise induced bronchoconstriction (EIB), yet may arise secondarily to a temporary closure of the larynx. This condition, termed Exercise induced laryngeal obstruction (EILO), is best characterised by the gold standard technique of direct and continuous laryngoscopy during exercise (CLE). To date most descriptions of the utility of CLE are in subjects with unexplained and/or disproportionate exertional dyspnoea in a general respiratory population (i.e. not confined to athletes).

Objectives Assessment of the safety, utility and application of CLE in subjects with unexplained and/or disproportionate exertional dyspnoea in a general respiratory population (i.e. not confined to athletes).

Methods and measurements Patients referred for CLE with unexplained breathlessness and other respiratory diagnosis including treatment refractory asthma and COPD were identified. Thereafter clinical and physiological assessments were reviewed.

Results In total 83 referrals (October 2012–February 2014) for CLE studies were analysed. The overall median (range) age was 43 (17–71) years. The majority of subjects were female (n = 56). Only a total of 4 (5%) subjects were athletes. We made a diagnosis of EILO in 30 (36%) of subjects studied. Prior to CLE 32 (39%) had been given a diagnosis of EIB, and of these we identified 17 (53%) actually had a diagnosis of EILO. Only one minor complication (pre-syncopal episode) was encountered during the procedure.

Conclusion CLE is a safe effective method for the assessment of disproportionate exercise induced dyspnoea. It is a sensitive diagnostic tool and should not be reserved for use in a highly athletic population. It appears to be particularly useful in patients diagnosed with EIB who are not responding to treatment. Therapeutic intervention in the form of physiotherapy once the diagnosis is made offers the potential for symptomatic improvement and the withdrawal of unneeded pharmacological agents.
rs10500804 (OR 1.85, p = 0.02); AG genotype for CYP2R1 SNP rs10766197 (OR 1.82, p = 0.03); AA genotype for VDR SNP rs7975322 (OR 2.15, p = 0.02).

Conclusions Over half of participating asthma patients were vitamin D deficient. Obesity, winter sampling, fair skin, and SNP in DBP, CYP2R1 and VDR genes were risk factors for deficiency. Caucasian ethnicity, sun seeking behaviour, modest daily supplement doses and recent tanning bed use were protective.

P49 CAN THE ASTHMA CONTROL QUESTIONNAIRE (ACQ) AND/OR THE BLOOD EOSINOPHIL COUNT ACCURATELY DETECT SPUMT EOSINOPHILIA?

JR Anderson, DB Hodgson, EE Wilson, TW Harrison, DE Shaw. Nottingham Respiratory Research Unit, Nottingham, UK

10.1136/thoraxjnl-2014-206260.189

Induced sputum differential cell counts provide important information about airway inflammation and future risk in asthma, but are not universally available. We set out to ascertain the sensitivity and specificity of the Juniper Asthma Control Questionnaire (ACQ) and/or the peripheral blood eosinophil count to detect a sputum eosinophil count >3%.

Methods We performed a retrospective, cross-sectional study of 165 subjects with asthma, aged 18–80, prescribed as-required bronchodilators, long-acting β-agonists, 0–4000 mcg inhaled beclometasone dipropionate equivalent or maintenance oral steroids (0–20 mg prednisolone) from our database. Current smokers were excluded. Spirometry, FeNO at 50 ml flow, sputum induction, Asthma Control Questionnaire (ACQ) and blood eosinophils (BEos) were recorded.

Induced sputum eosinophils (SEos) defined eosinophilic (EA, SEos ≥3%) and non-eosinophilic (NEA, SEos <3%) groups. BEos, SEos and FeNO were log10 transformed and groups were compared with t-tests or Mann-Whitney-U using STATA and GraphPad. Receiver operating characteristic (ROC) curves determined cut-points of ACQ and BEos that identified SEos ≥3%, and these were tested retrospectively in a second population of adults with asthma (n = 48, 40% EA, mean FEV1 82.6% predicted).

Results The 31% with EA had a lower FEV1% predicted and FEV1/FVC ratio, a higher FeNO, BEos and ACQ compared to NEA (Table 1). There was a significant correlation between ACQ and sputum eosinophils (Pearson r 0.32, p < 0.0001).

The optimal cut-points of ACQ and BEos identifying a SEos of 3% were an ACQ ≥1.57 (sensitivity 55%, specificity 78%) and BEos ≥0.22 × 109/L (sensitivity 84% and specificity 68%) respectively. Individuals with both ACQ of ≥1.57 AND BEos of ≥0.22 the sensitivity was 45% and specificity of 100% for a SEos of 3%.

Testing in the second population the ACQ≥1.57 had a sensitivity 47% and specificity 86% for SEos ≥3% while BEos ≥0.22 had sensitivity 68% and specificity 45%. The combination of ACQ ≥1.57 AND BEos ≥0.22 had a lower sensitivity of 37%.

Abstract P49 Table 1

<table>
<thead>
<tr>
<th>Number of observations</th>
<th>All</th>
<th>Sputum eosinophils &gt;3%</th>
<th>Sputum eosinophils &gt;3%</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>56.2 ± 13.4</td>
<td>57.4 ± 13.75</td>
<td>53.5 ± 12.2</td>
<td>0.081</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male n (%)</td>
<td>81 (49.1%)</td>
<td>53 (66.5%)</td>
<td>28 (54.9%)</td>
<td></td>
</tr>
<tr>
<td>Female n (%)</td>
<td>84 (50.9%)</td>
<td>61 (53.5%)</td>
<td>22 (45.1%)</td>
<td></td>
</tr>
<tr>
<td>FEV1 (Litre)</td>
<td>2.39 ± 0.85</td>
<td>2.46 ± 0.87</td>
<td>2.23 ± 0.79</td>
<td>0.12</td>
</tr>
<tr>
<td>FEV1% predicted</td>
<td>80.5 ± 20.7</td>
<td>83.54 ± 19.4</td>
<td>73.7 ± 23.2</td>
<td>0.005*</td>
</tr>
<tr>
<td>FVC (Litre)</td>
<td>3.46 ± 1.03</td>
<td>3.49 ± 1.06</td>
<td>3.36 ± 0.95</td>
<td>0.46</td>
</tr>
<tr>
<td>FVC% predicted</td>
<td>95.1 ± 18.8</td>
<td>96.9 ± 17.5</td>
<td>91.0 ± 21.09</td>
<td>0.062</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>68.7 ± 9.9</td>
<td>70 ± 9.8</td>
<td>65.7 ± 9.4</td>
<td>0.008*</td>
</tr>
<tr>
<td>Body-mass index (Kgm⁻²)</td>
<td>28.6 ± 5.1</td>
<td>28.8 ± 4.0</td>
<td>26.9 ± 3.0</td>
<td>0.54</td>
</tr>
<tr>
<td>History of smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Pack-years)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>(0,20)</td>
<td>(0,20)</td>
<td>(0,15)</td>
<td>0.87*</td>
</tr>
<tr>
<td>Daily inhaled corticosteroid dose (Becolmetasone dipropionate equivalent (mcg/day))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>(0,3200)</td>
<td>(0,3200)</td>
<td>(0,3200)</td>
<td>0.05*</td>
</tr>
<tr>
<td>Oral Prednisolone</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>(0,28)</td>
<td>(0,15)</td>
<td>(0,20)</td>
<td></td>
</tr>
<tr>
<td>Juniper ACQ® score</td>
<td>1.4 ± 1.0</td>
<td>1.1 ± 0.9</td>
<td>1.9 ± 1.2</td>
<td>-0.001*</td>
</tr>
<tr>
<td>Exhaled nitric oxide FeNO at 50ml flow (ppb) Geometric mean (95% CI)</td>
<td>25.7 (22.9, 28.8)</td>
<td>20.0 (17.8, 22.9)</td>
<td>44.7 (35.5, 56.23)</td>
<td>-0.001*</td>
</tr>
<tr>
<td>Sputum differential eosinophil count %</td>
<td>1.24 (0.95, 1.62)</td>
<td>0.47 (0.39, 0.55)</td>
<td>11.0 (8.3, 14.13)</td>
<td>-0.001*</td>
</tr>
<tr>
<td>Blood eosinophils (x10⁹/L)</td>
<td>0.24 (0.22, 0.28)</td>
<td>0.19 (0.18, 0.21)</td>
<td>0.43 (0.36, 0.5)</td>
<td>-0.001*</td>
</tr>
</tbody>
</table>

Arithmetic mean values reported as mean unless specified
* Standard deviation
Geometric means are reported with a 95% Confidence Interval (CI)
The difference between means compared with t-test unless specified with a
# Juniper Asthma Control Questionnaire- A validated questionnaire providing a numerical assessment of asthma control over the preceding 7 days. The mean score ranges from 0 (fully controlled) to 6 (poorly controlled)
† Mann-Whitney U
p < 0.05
FEV1 Forced expiratory volume in one second
FVC Forced vital capacity
ppb Parts per billion
but a high specificity of 93% and could be useful to exclude rather than identify the presence of sputum eosinophilia.

Conclusion Combined testing using ACQ and BEos only identifies eosinophilia in 37% and can’t replace induced sputum, but may be useful to exclude sputum eosinophilia and prospective study is warranted.

Background “Difficult asthma” is defined as persistent symptoms and/or frequent exacerbations in patients with a diagnosis of asthma, despite treatment at step 4 or 5 of the BTS/SIGN guidelines. “Difficult asthma” clinics have been set up in many UK hospitals, but there is no published evidence to suggest their effectiveness at reducing exacerbations or hospital admissions.

Aims To determine whether a regional difficult asthma clinic led to a reduction in prescription of oral steroid for exacerbations and a reduction in hospital admissions for asthma.

Methods A retrospective analysis of patients who attended this regional difficult asthma clinic between August 2009 and May 2013 was performed. Medical notes and GP letters were scrutinised to ascertain the number of hospital admissions two years before and two years after the first clinic appointment. For oral steroids, one year before and after was used. To compare these data Wilcoxon tests were used due to the skewed data.

Results For hospital admissions, data was available for 44 patients, mean (SD) age 44.2 (14.1) and 66% female. The median (inter-quartile range (IQR)) number of hospital admissions in the two years prior to clinic was 2 (0.3) compared to 0 (0,1) in the two years following clinic visit (p = 0.014). Oral steroid prescription data was available for 54 patients, mean (SD) age 43.5 (14.4), 70% female. The median (IQR) number of oral steroid courses required in the year prior to first clinic appointment was 6 (3,7.5,10), which reduced to 2 (0,4) in the year after first appointment (p < 0.001).

Conclusion Our regional difficult asthma clinic significantly reduced both hospital admissions for asthma two years after first clinic appointment and number of oral steroid prescriptions one year after first clinic appointment. This study, although small, highlights the benefit of such clinics to patients and the potential for the reduction in use of NHS resources. They should be encouraged in all major centres.

REFERENCE

1 Prys-Picard CO, Campbell SM, Ayres JG, Miles JF, Niven RM. Consensus Difficult Asthma Consortium UK: Defining and investigating difficult asthma: developing quality indicators. Respiratory Medicine 2006;100(7):1254-61

PS1

BARRIERS AND FACILITATORS TO EFFECTIVE SELF-MANAGEMENT OF ASTHMA – A SYSTEMATIC REVIEW AND THEMATIC SYNTHESIS

SE Kirby1, C Miles1, E Arden-Close1, L Yardley1, A Bruton1, M Hankins6, DM Thomas. 1Department of Psychology, University of Southampton, UK; 2NHf Southampton Respiratory Biomedical Research Unit, UK; 3Department of Psychology, University of Southampton, UK; 4Faculty of Health Sciences, University of Southampton, UK; 5NHf Southampton Respiratory Biomedical Research Unit, UK; 6Real-World Evidence Solutions, IMS Health, UK; 7Department of Primary Medical Care, University of Southampton, UK, NHf Southampton Respiratory Biomedical Research Unit, UK

Introduction and objectives Self-management is an established approach to controlling asthma, recommended in guidelines. Despite the reported effectiveness of self-management, its promotion, uptake and use among patients, carers, and health-care professionals remain low. We conducted a systematic review and thematic synthesis of qualitative research into self-management in adults, children and adolescents with asthma. Our objective was to identify the perceived barriers and facilitators associated with reduced or improved effectiveness of asthma self-management.

Method Electronic databases (Medline, EMBASE, AMED, CINAHL, and PsycINFO; 1996 – August 2013) and British Thoracic Society guidelines were searched for qualitative literature that explored factors relevant to facilitators and barriers to uptake, adherence, or outcomes of self-management in adults, children and adolescents with asthma. We assessed the methodological strengths of the studies using the Critical Appraisal Skills Programme (CASP) tool for qualitative studies, and conducted a thematic synthesis of included studies.

Results Of the 1532 studies initially identified, 34 papers were included in the review. Thematic synthesis identified 10 overarching themes (Figure 1) which suggest that barriers and facilitators of self-management included the perceived quality of the relationship between health-care professionals and patients, the perceived adequacy of education around self-management and medications, and positive and negative beliefs about asthma with regards to self-management and existing interventions. Self-management could also be helped or hindered by the amount and type of social support and perceived ease of access to healthcare. In addition, having a co-morbidity, mood/anxiety problems, and encountering professional barriers within the health care system (such as consultation time and access to lung function testing), are perceived to hinder successful self-management of asthma.

Conclusion Perceived barriers and facilitators occur at the level of individuals with asthma (and carers), health-care professionals, and organisations. These findings contribute to our understanding of why existing self-management interventions may not always be effective, and can be used to inform future study into areas where further intervention may improve the adoption of self-management of asthma. For example, future work could include addressing patient and carer beliefs in educational interventions and decisions involving treatment, or greater use of pharmacist educators, patient advocates, and technological interventions.

<table>
<thead>
<tr>
<th>Professional factors</th>
<th>Partnership between the patient/carer and their health care professional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Access to healthcare</td>
<td>Education regarding asthma and its management</td>
</tr>
<tr>
<td>Social support</td>
<td>Health beliefs about asthma and self-management</td>
</tr>
<tr>
<td>Mood disorders and anxiety</td>
<td>Self-management interventions</td>
</tr>
</tbody>
</table>

Abstract PS1 Figure 1 Overarching themes identified during thematic synthesis
Asthma self-management is effective in clinical trials, widely recommended by guidelines but poorly implemented. We aimed to synthesise the evidence from implementation studies of asthma self-management support interventions to inform delivery in routine clinical practice.

Methods Using systematic review methodology (Cochrane Handbook) we searched eight electronic databases, performed snowball and manual searches, and searched research databases for unpublished and on-going work. We included studies with a range of methodologies, and which evaluated the introduction of an asthma self-management support intervention in routine clinical practice. We assessed included papers for quality (Downs and Black), extracted and synthesised data on process (e.g. number of action plans issued) and clinical outcomes (e.g. measures of asthma control, unscheduled healthcare). Narrative synthesis used the whole systems approach as a framework. [PROSPERO registration: CRD42012002898].

Result: We included 18 studies (7 randomised trials, 8 longitudinal database studies, 3 uncontrolled studies) from primary, secondary, community and managed care settings in six countries. Interventions which explicitly addressed patient, professional and organisational factors (n = 7 studies) showed the most consistent improvement in both process and clinical outcomes. Targeting professionals (n = 2 studies) improved process but not clinical outcomes. Targeting patients (n = 6 studies) had inconsistent impact on process/clinical outcomes. Targeting the organisation (n = 3 studies) improved process, and had a small effect on clinical outcomes. Authors highlighted the importance of a healthcare system committed to supporting self-management, skills training for professionals, patient education programmes supported by regular reviews, and on-going evaluation of the implementation process.

Conclusion: Effective interventions were complex: actively engaging patients, and training and motivating professionals within the context of an organisation which prioritised supported self-management. Commissioners and providers of services for people with asthma should consider how they can promote a culture of supporting self-management as a normal, expected, monitored and remunerated aspect of the provision of care.

Funding: NIHR HS&DR programme (project number 11/1014/04). The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the Hs and DR programme, NIHR, NHS or the Department of Health.
Asthma is a heterogeneous condition, with a variety of clusters of clinical presentations and courses, objective measures and treatment responses. A common feature of asthma is the under-reporting of poor symptom control by patients and under-recognition by clinicians. Poor asthma control in the preceding 12 months prior to admission has been linked to asthma related deaths. The significance of measuring asthma control independently from asthma severity has been demonstrated. However, considerable differences in perceived and actual control are apparent. There is a need to identify patient groups at risk of under-reporting symptoms and not recognising poor control.

**Aim** To establish which patient features are associated with over-estimation of disease control.

**Setting** Secondary care consultant led asthma clinic.

**Population** 108 patients recruited over 10 weeks.

**Measures** Objective measures of disease severity were mapped against perceived symptom control using the Asthma Control Test; age, gender, co-morbidities, medications, induced sputum, lung function, IgE, blood eosinophil, histamine challenge test, exhaled nitric oxide, ECG CXR, smoking status and BMI.

**Analysis** Significant associations between patient groups and perceptions of symptom control are described.

**Results** 61 (56.6%) of patients had difficult asthma according to BTS guidance. 95 (88.0%) had poorly controlled asthma, with 70 (64.8%) of these perceiving adequate control of symptoms.

All patients with good perceived and actual control of symptoms; 13 (12.0%), had never smoked. 85.5% of patients who perceived symptoms prevalence were overweight, obese or morbidly obese.

All patients with raised IgE or blood eosinophilia had poorly controlled asthma; though 58.6% of this group perceived good control.

**Conclusion** This single centre cross-sectional study suggests smokers, overweight patients and those with inflammation predominant asthma are most likely to under-report severity. These findings are in keeping with the cluster analyses of Haldar and Moore. Further work is required to follow-up these patients to establish if poor perception of symptoms changes over time, or is associated with future asthma attack frequency.

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**P55** IS PRESCRIPTION UPTAKE AND MEDICATION ADHERENCE RATING SCALE (MARS) A USEFUL TOOL IN ASSESSING ASTHMA CONTROL IN CHILDREN WITH PROBLEMATIC SEVERE ASTHMA (PSA)?

P55 NagaKumar, H Hall, M Bracken, S Kagani, A Bush, E Fleming. Royal Brompton Hospital, London, UK; National Heart and Lung Institute, Imperial College, London, UK

10.1136/thoraxjnl-2014-206260.195

**Introduction** Sub-optimal adherence to medications results in poor asthma control, however objective measurement of adherence is challenging.

**Aim** To assess adherence to inhaled corticosteroids (ICS) in children with problematic severe asthma (PSA) using prescription uptake and the Medicines Adherence Rating Scale (MARS) (self-reported adherence) and relate them to measures of asthma control.

**Methods** 160 patients assessed as part of the established RBH difficult asthma protocol (2008–2013) were included [Arch Dis Child 2009;94:780–4]. Adherence was assessed using prescription uptake data (GP and local hospital) and MARS. Sub-optimal adherence was defined as a prescription uptake of <80%. Spirometry (FEV1, pre bronchodilator), bronchodilator reversibility (BDR), and exhaled nitric oxide (FENO) were measured. The Asthma Control Test (ACT), Paediatric Asthma Quality of Life Questionnaire (PAQLQ) was used to evaluate control. Number of courses of oral steroids and hospital admissions in the previous 12 months were recorded.

**Results** Median age was 11.6 yr (5–16). 66% were male. 52% had prescription uptake of <80%.

MARS score showed only a weak correlation with prescription uptake (n = 48, r² = 0.03, p = 0.29), even in patients with prescription uptake of <50% (n = 23, r² = 0.09, p = 0.32). No relationship was found between prescription uptake and ACT, MARS, FEV1, rescue courses of OCS, FENO or BDR (Table 1).

**Conclusion** Poor prescription uptake was not related to any measure of asthma control, meaning that we could not differentiate the genuine therapy resistant from the non-adherent. But it is not possible to assess how much ICS was actually inhaled. Patterns of ICS use may be a more important determinant of control. Self-reported adherence, as measured by MARS was high even in those with very poor (<50%) prescription uptake highlighting the limitations of this questionnaire. More objective means of assessing adherence should be incorporated into protocols for assessing severe asthma.

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**P56** IMPACT OF PHARMACIST-LED ASThma AND COPD REVIEWS IN GENERAL PRACTICE

H Khach, Barts Health NHS Trust, London, UK

10.1136/thoraxjnl-2014-206260.196

**Introduction** Asthma and chronic obstructive pulmonary disease (COPD) account for a significant burden of disease in the UK. In a local initiative, a respiratory pharmacist carried out structured asthma and COPD reviews aimed at improving clinical outcomes in a primary care setting.

**Aims and objectives** This study aims to assess the impact of asthma and COPD reviews in accordance with national guidelines and standards of care.

**Methods** The study was carried out prospectively, during one day a week basis, over a twelve month period across six GP surgeries. Patients were included based on use of high dose inhaled corticosteroid and bronchodilator preparations (ICS/LABA) and/or presence of previous exacerbations, accident and emergency (A&E) or hospital admissions.

**Results** 231 patients with asthma (n = 146, 63.2%) and COPD (n = 85, 36.8%) were reviewed, with 370 consultations carried
Table 1, below, shows a significant proportion of patients had uncontrolled disease. This was likely to be due to poor adherence to maintenance inhalers and poor inhaler technique in a large proportion of patients. Interventions were made in all patients, including reducing the beclomethasone dipropionate (BDP) equivalence in the asthma group by 625.8 mcg (37.5%). Annual drug cost savings attributed to appropriate step down and cessation of therapy showed amounted to £51.8 K (asthma: £36.4 K; COPD: £15.4 K). Follow up exacerbation data is ongoing, with 48 patients (20.8%) at the 6 or 12 month stage, showing significant reductions from 1.7% to 0.04% and 3.0% to 0.14% in asthma and COPD respectively.

Conclusions Structured asthma and COPD reviews have shown that a significant proportion of patients have uncontrolled disease despite use of extensive and high dose pharmacological therapy. Structured reviews by the pharmacist resulted in significant interventions that improved ACT and CAT scores and reduced unwarranted healthcare utilisation. Furthermore, it showed that appropriate prescribing and disease management in line with national standards of care also resulted in significant drug cost savings.

Background Asthma exacerbations pose a significant burden to the NHS, however the factors that underpin inpatient length of stay remain poorly understood. We undertook a service improvement project using hospital episode statistics to evaluate the demographics of the asthma hospital exacerbation population in Leicester hospitals and risk factors that influence length of stay.

Methods Hospital episode statistics were generated using an ACCESS database query set capturing a range of clinical metadata including length of stay, ICD-10 coding for two types of asthma admission (asthma and status asthmaticus), sex, age, ethnicitity, financial year quarter of admission. In addition comorbidity was calculated by cross referencing spell diagnoses to the Charlson comorbidity index score. This database was subsequently linked to pathology data reporting blood eosinophils, neutrophils, CRP at admission and the highest ever historical blood eosinophil count. A backwards logistic regression model was used to identify factors associated with length of stay.

Results Analysis showed significant differences for baseline characteristics of patients admitted with asthma and COPD. Baseline ACT and CAT scores were significantly lower in the asthma group compared to the COPD group, indicating worse asthma control and less airway obstruction. Baseline FEV1 was also significantly lower in the COPD group. A number of factors were independent predictors of length of stay in the model, including female sex, age over 50 years, asthma diagnosis, and COPD diagnosis. However, the majority of patients admitted with asthma or COPD had at least one comorbidity.

Conclusions The findings of this study raise important questions about the reasons for hospitalisation in both asthma and COPD exacerbations. The study demonstrates the complexity of exacerbations and needs for future research to further understand the factors influencing hospital stay.

**Abstract P56**

**Table 1**

<table>
<thead>
<tr>
<th>Exacerbations in previous 12 months</th>
<th>Asthma (n = 146)</th>
<th>COPD (n = 85)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of A&amp;E attendances, n (mean/patient)</td>
<td>33 (0.23)</td>
<td>33 (0.39)</td>
</tr>
<tr>
<td>Number of hospital admissions, n (mean/patient)</td>
<td>14 (0.10)</td>
<td>26 (0.31)</td>
</tr>
<tr>
<td>Good technique, n (%)</td>
<td>27.6% (48)</td>
<td>23.8% (20)</td>
</tr>
<tr>
<td>Moderate technique, n (%)</td>
<td>16.5% (24)</td>
<td>25.0% (21)</td>
</tr>
<tr>
<td>Poor technique, n (%)</td>
<td>55.9% (81)</td>
<td>51.2% (43)</td>
</tr>
<tr>
<td>Pre review (range: 200–4000)</td>
<td>1669.9 mcg</td>
<td>NA</td>
</tr>
<tr>
<td>Post review (range: 400–2000)</td>
<td>1044.1 mcg</td>
<td>NA</td>
</tr>
<tr>
<td>Current, n (%)</td>
<td>24.7% (36)</td>
<td>36.5% (31)</td>
</tr>
<tr>
<td>Quit rates (for ≥3 months) post follow up, n (%)</td>
<td>50.0% (18)</td>
<td>58.1% (18)</td>
</tr>
<tr>
<td>Ex smoker, n (%)</td>
<td>17.8% (26)</td>
<td>56.5% (48)</td>
</tr>
<tr>
<td>Mean pack year history, n (%)</td>
<td>30.1</td>
<td>57.1</td>
</tr>
<tr>
<td>Maintenance ICS/LABA or ICS, n (%)</td>
<td>7.9 (7.0)</td>
<td>8.4 (0.8)</td>
</tr>
<tr>
<td>Long acting antimuscarinic, n (%)</td>
<td>NA</td>
<td>9.8 (10.0)</td>
</tr>
<tr>
<td>Mean adherence to medicines in previous 12 months (median)</td>
<td>7.9 (7.0)</td>
<td>8.4 (10.0)</td>
</tr>
<tr>
<td>Reliever inhaler, n (%)</td>
<td>9.3 (7.0)</td>
<td>14.3 (12.5)</td>
</tr>
<tr>
<td>Reliever Inhaler Use (times per day)</td>
<td>2.2</td>
<td>3.0</td>
</tr>
</tbody>
</table>

**Factors Influencing Length of Hospital Stay in Asthma Exacerbations: Results of a Service Improvement Project**

AJ Hanson, Y Vali, JRA Fisher-Black, G Woltema, M Richardson, AJ Wardlaw, S Siddiqui. University Hospitals of Leicester NHS Trust and NIHR Respiratory Biomedical Research Unit, Leicester, UK

10.1136/thoraxjnl-2014-206260.197
COPD phenotyping

**A COMPARISON BETWEEN THE CLINICAL FEATURES OF PI SZ AND PI ZZ PATIENTS WITH ALPHA-1 ANTITRYPSIN DEFICIENCY**

J Vayalapa, KG Edgar, D Griffiths, RA Stockley, AM Turner. University of Birmingham, Birmingham, UK; University Hospitals Birmingham NHS Foundation Trust, Birmingham, UK

Introduction Alpha-1 antitrypsin deficiency (AATD) is a hereditary disorder affecting about 1 in 3000 people in the UK commonly associated with early-onset emphysema. There are two common deficiency alleles - PiS and PiZ. PiZZ patients have severe AATD, with levels of 10–15% normal. PiSZ patients have less severe deficiency (40% normal) and are generally thought to have a minimal risk. We hypothesised that if PiSZ patients were at lower risk of COPD than PiZZ, and their lung disease would be more characteristic of usual COPD than that of PiZZ patients.

Method 104 PiSZ patients and 638 PiZZ patients from the UK AATD registry (ADAPT) were compared for their demographics, lung function, risk factors for COPD (e.g. smoking, occupation), co-morbidities associated with COPD, index status (i.e. if diagnosed due to lung disease or family screening) and CT densitometry (where available). Outcome in terms of lung function decline and mortality was also assessed. Univariate statistics were used to guide subsequent regression analyses.

Results Emphysema was more likely in PiZZ than PiSZ patients (OR 11.0 (5.7–21.3); p < 0.001) in the regression analysis after accounting for age, pack years and lung index status. PiZZ patients also had significantly worse FEV1 and DLCO than PiSZ patients in similar regression models (both p < 0.01). Emphysema was more severe in both upper and lower zone (both p < 0.01), and proportionately greater in the lower zone (UZ/LZ VI = 1.5 v 1.2) in PiZZ patients. Mortality and DLCO decline were also greater in PiZZ patients.

Conclusion PiSZ patients have a milder form of AATD associated with better lung function. The data suggests the pattern of emphysema is closer to usual COPD than classical AATD. Further analyses comparing PiSZ to PiMM are now ongoing.

**UTILITY OF FIB4 SCORE AND LIVER DISEASE IN ALPHA-1 ANTITRYPSIN DEFICIENCY (A1ATD)**


Introduction A1ATD is an autosomal co-dominant condition where homozygosity for the Z-allele results, classically, in emphysematous lung involvement, and liver fibrosis dependant on polymerisation rate of aberrant protein.1 The FIB4 score non-invasively estimates risk of liver fibrosis,2 but has not previously been investigated in A1ATD. We completed preliminary assessment of the utility of FIB4 in our A1ATD cohort. Whilst the standard of care in A1ATD should be joint respiratory-hepatology services, not all patients are able to access this. A simple tool to guide referral to hepatology services could therefore be clinically useful to the respiratory community.

Methods We report data from 30 PiZZ patients with ultrasound (US) characterisation of liver disease. An abnormal USS was considered as any abnormality other than cysts, thus including features of cirrhosis and fatty infiltration. FIB4 was calculated as [Age (years) × AST (U/l)]/[Platelets (109) × ALT (U/l)]. The most recent lung physiology was recorded as FEV1 (%predicted), diffusion coefficient (KCO,%predicted) and residual volume (RV,% predicted). Body mass index (BMI) was calculated.

Results The 30 patients had a mean age of 54 ± 12.4 years, 14 were male. Lung function showed mean FEV1 1.85 ± 1.12 L

Abstract P59 Figure 1 ROC of the FIB4 index for detection of abnormal USS

**ROC of the FIB4 index for detection of abnormal USS**
Cannabis lung causing debilitating emphysema: Are we on the verge of an epidemic?

Narendra Babu Chinnappa, Kasia Zalewska, Damian Mckeon. Ysbyty Gwynedd, Bangor, UK
10.1136/thoraxjnl-2014-206260.200

Introduction and objectives Cannabis (or marijuana) is the world's most widely-used illicit drug, according to UN drug report 2012 prevalence of cannabis use between 15–64 years of age is around 1.7% in Europe and 2.6% in USA. It is particularly prevalent amongst adolescents and young adults. As societies reconsider the legal status of cannabis, policy makers and clinicians require sound knowledge of the acute and chronic effects of cannabis. There has been surprisingly little research into its effects on respiratory health. In a rural region of North Wales we have noticed an increasing number of young patients presenting with precocious bullous emphysema associated with very high tobacco and cannabis usage.

Methods A series of 8 patients presenting through the Emergency Department with an exacerbation of COPD were noted to have precocious COPD associated with high cannabis use. The age was between 35–48, all had both physiological and radiological signs of advanced emphysema. All had at least 10–20 years of cannabis usage smoking more than 5 'joints' per day. Of these, 4 patients were significantly impaired to require long term oxygen therapy, and one is actively listed for a single lung transplant. All had normal levels of alpha 1 antitrypsin and chymotrypsin.

Results We found young patients with debilitating COPD secondary to cannabis use i.e. as less as 10 years of use. We postulate that cannabis smoking leads to severe COPD in young patients independent of genetic susceptibility, which is on the verge of increase.

Conclusions The addition of cannabis to the tobacco, and high usage at a young age is leading to increase in the incidence of COPD in general and bullous emphysema as a phenotype in particular. We are concerned that the dangers of cannabis inhalation and these risks are not being appreciated by the wider health community. More research is needed to know the mechanisms of the inflammatory response secondary to cannabis smoking.
ASSESSMENT OF REGIONAL VARIABILITY IN MATRIX METALLOPROTEINASE CONCENTRATIONS BY CT INFORMED BRONCHOALVEOLAR LAVAGE IN PATIENTS WITH COPD

Abstract

Purpose

Saliva is increasingly promoted as a suitable alternative diagnostic bio-sample to blood, yet its role in respiratory disease is still to be elucidated.

Background

Matrix metalloproteinases (MMPs) are a family of proteolytic enzymes involved in the normal physiological turnover of the pulmonary extracellular matrix. They have been implicated in animal models of emphysema. However, there have been conflicting results in human studies, largely due to the anatomical regional variability and heterogeneity of COPD not being taken into account. This study aims to understand the role of MMPs in COPD by using CT analysis to guide regional bronchoalveolar lavage (BAL) and employing multiplex profiling of this fluid.

Methods

Twelve mild-to-moderate COPD patients (FEV1/FVC ratio <0.7, FEV1 >50%) underwent high resolution spiral chest CT. This was reported by a thoracic radiologist and lobes with most and least evidence of disease (emphysema or bronchial wall thickening) were identified. During bronchoscopy 100 ml of saline was instilled into each of these lobes and the BAL was collected. This fluid was filtered and then concentrated 2-fold by lyophilisation. MMP-1, -2, -3, -7, -8 and -9 were measured using a multiplex ELISA. Sample protein concentration was determined using a Bradford assay. MMP concentration was corrected for BAL protein concentration.

Results

MMPs and protein were successfully detected in BAL. Median values for MMP-1, -2, -3, -7, -8 and -9 were all increased in the diseased lobe compared to the relatively preserved lobe. This was significant for MMP-2 and -3 and trended towards significance for MMP-1 and -7 (Table 1).

Conclusion

These results suggest that certain MMPs are present in greater quantities in areas of the lungs most affected by COPD, adding to the evidence that they may be involved in the pathogenesis of the disease. This study also demonstrates the regional anatomical variability of COPD in respect to imaging abnormalities and the underlying disease processes. Regional sampling needs to be considered in future studies to enable full understanding of the heterogeneous pathological mechanisms involved in COPD.
Salivary levels of C-Reactive Protein (CRP), Procalcitonin (PCT) and Neutrophil Elastase (NE) were assessed in patients with COPD to determine if saliva could provide an alternative diagnostic bio-sample to blood. As the clinical usefulness of biomarkers relies on correlation to patient events, we also explored the relationship between target saliva analyte levels and wellbeing scores on breathing and activities of daily living (ADL), recorded in a purposeful diary.

The study included 139 subjects: 17 healthy non-smokers; 24 healthy smokers; 98 patients with COPD [Global Initiative for Chronic Obstructive Lung Disease (GOLD) Stage I, 16; Stage II, 32; Stage III, 39; Stage IV, 11]. Participants were assessed over 3 visits, one week apart and involving patient completion of a self-assessment diary, spirometry and, saliva sampling. 22 randomly selected COPD subjects provided simultaneous blood samples. Each salivary biomarker could distinguish across the 3 health status groups; however when adjusted for confounding factors this significance only remained for salivary NE, which was increased in healthy smokers compared to healthy non-smokers (p < 0.001) and stable COPD subjects (p < 0.001). Patients with an acute exacerbation of COPD (n = 36) had a median increase in all 3 salivary biomarkers (p < 0.001). CRP: median 5.74 ng/ml, interquartile range 2.86–12.25, (95% Confidence Interval (CI): 3.72–11.47; PCT 0.38 ng/ml, [0.22–0.94], (95% CI: 0.31–0.54) and NE 539 ng/ml [112.25–1264], (95% CI: 169–982). Salivary CRP and PCT concentrations strongly correlated with their serum counterparts; salivary NE did not. Salivary CRP and PCT levels correlated with breathing scores (r = 0.14, p < 0.02; r = 0.13, p < 0.03 respectively) but not with activities of daily living. Salivary NE showed no relationship to wellbeing scores.

Salivary CRP, PCT and NE provide clinically relevant information on disease status in COPD, and additionally NE on smoking status in healthy individuals. These results provide the conceptual basis for saliva to be used as a bio-sample in COPD monitoring.

**Abstract P64 Table 1** COPD matched subjects stable/exacerbation

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Stable (n = 36)</th>
<th>Exacerbation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1, % predicted</td>
<td>53 ± 23</td>
<td>48 ± 19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRC score</td>
<td>5.00 ± 1.25</td>
<td>5.00 ± 1.25</td>
<td>&lt;0.16</td>
</tr>
<tr>
<td>Breathing score</td>
<td>3.00 ± 0.00</td>
<td>4.00 ± 1.00</td>
<td>&lt;0.006</td>
</tr>
<tr>
<td>ADL score</td>
<td>3.00 ± 1.00</td>
<td>4.00 ± 2.00</td>
<td>&lt;0.014</td>
</tr>
<tr>
<td>Sputum</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amount</td>
<td>2.00 ± 2.00</td>
<td>3.00 ± 2.25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Texture</td>
<td>1.94 ± 0.33</td>
<td>2.06 ± 0.41</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Colour</td>
<td>3.00 ± 1.00</td>
<td>4.00 ± 1.50</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Salivary Biomarkers a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP, ng/ml</td>
<td>1.61 ± 1.10</td>
<td>7.35 ± 10.04</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCT, ng/ml</td>
<td>0.09 ± 0.06</td>
<td>0.50 ± 0.71</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NE, ng/ml</td>
<td>128 ± 1.90</td>
<td>769 ± 1680</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Abstract P65 Table 1** Clinical characteristics of patients with impaired and preserved static balance expressed as mean (SD) or median (25th, 75th centiles)

<table>
<thead>
<tr>
<th></th>
<th>Impaired balance (n = 42)</th>
<th>Completed Tandem stand (n = 132)</th>
<th>Mean difference (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>74 (9)</td>
<td>69 (9)</td>
<td>5.1 (2 to 8)</td>
<td>0.002</td>
</tr>
<tr>
<td>FEV1, % predicted</td>
<td>55 (39, 77)</td>
<td>48 (30, 61)</td>
<td>9 (4)</td>
<td>0.02</td>
</tr>
<tr>
<td>ISW (metres)</td>
<td>166 (109)</td>
<td>252 (127)</td>
<td>-90 (-130 to -40)</td>
<td>0.0001</td>
</tr>
<tr>
<td>CAT</td>
<td>20.3 (7.7)</td>
<td>20.4 (7.4)</td>
<td>-0.1 (-2.7 to 2.5)</td>
<td>0.95</td>
</tr>
<tr>
<td>Peak QMVC (kg)</td>
<td>21.8 (8.9)</td>
<td>25.3 (9.0)</td>
<td>-4.7 (-8.5 to -0.9)</td>
<td>0.02</td>
</tr>
<tr>
<td>4MGS (m/s)</td>
<td>0.81 (0.2)</td>
<td>0.98 (0.2)</td>
<td>0.17 (0.1 to 0.04)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Activity in 3METS</td>
<td>110 (40, 344)</td>
<td>285 (104, 567)</td>
<td>14 (-272 to 301)</td>
<td>0.92</td>
</tr>
<tr>
<td>Number reporting falls in 12 months</td>
<td>8</td>
<td>12</td>
<td>-</td>
<td>0.10</td>
</tr>
</tbody>
</table>

a, Mean ± standard deviation  
b, Median, interquartile range  
COPD = Chronic Obstructive Pulmonary Disease; FEV1 = Forced Expiratory Volume in 1 second; MRC = Medical Research Council; ADL = Activity of Daily Living; CRP = C-Reactive Protein; PCT = Procalcitonin; NE = Neutrophil Elastase. P values represent the difference between stable and exacerbation phase.
Sarcopenia is age-related loss of skeletal muscle mass leading to increased risk of physical disability, poor health status and death. Although sarcopenia is primarily an age-related condition, it is recognised that there are multiple contributing factors, notably from immobility and the effects of chronic disease. International consensus working groups have defined sarcopenia as a loss of muscle mass and reduced muscle strength or function. Although skeletal muscle dysfunction is well recognised in chronic obstructive pulmonary disease (COPD), the prevalence of sarcopenia (defined using international consensus guidelines) and the impact of sarcopenia upon functional capacity and health related quality of life (HRQoL) have not been previously described in patients with COPD. Furthermore, it is not known whether sarcopenia affects the response to pulmonary rehabilitation (PR).

Methods Sarcopenia was determined using the European Working Group on Sarcopenia in Older People (EWGSOP) algorithm in 622 outpatients with stable COPD. Other measurements included incremental shuttle walk (ISW), five-repetition sit-to-stand (5STS), quadriceps maximum voluntary contraction (QMVC) and HRQoL (St George’s Respiratory Disease (SGRQ) and COPD Assessment Test (CAT)). Response to PR was determined in 43 patients with sarcopenia and compared with a control group identified using propensity score matching. Baseline characteristics and change pre- to post-PR were compared between groups.

Results Prevalence of sarcopenia was 14.5% (16.1% men and 12.3% women; p = 0.20), which increased with advancing quartiles of age and GOLD spirometric stage. Patients with sarcopenia were older, had worse air flow obstruction, reduced QMVC, exercise capacity and HRQoL (Table 1). Both sarcopenic patients and controls showed significant improvements in exercise capacity, functional performance, QMVC and HRQoL with PR, with no between group differences. Following PR, 12/43 (28%) patients no longer met EWGSOP criteria for sarcopenia.

Conclusion There is a high prevalence of sarcopenia in patients with COPD which is associated with reduced exercise capacity and HRQoL. Sarcopenia does not impact upon response to pulmonary rehabilitation in COPD.
Improving lung cancer outcomes

P69 A STUDY OF THE EFFECT OF THE 2013 ‘BE CLEAR ON LUNG CANCER’ CAMPAIGN ON 2 WEEK WAIT REFERRALS TO AN INNER NORTH WEST LONDON CANCER CENTRE

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10.1136/thoraxjnl-2014-206260.209

Introduction The first national ‘Be Clear on Cancer’ lung cancer campaign ran for 6 weeks from May 2012 with the message ‘Been coughing for 3 weeks? Tell your doctor’. During this time there was a 32% increase in 2 week wait (2 WW) referrals, with approximately 700 additional cancers diagnosed compared to 2011.

Method We studied the effect of the 6 week campaign in 2013 on 2 WW referrals to Imperial College NHS trust, comparing with referrals in the 6 week period prior to the campaign. We assessed quality of the referral based on completeness of the 2 WW proforma (scored out of 10), and the outcome of the referral. Direct radiology referrals were not included.

Results The campaign period was 2nd July to mid-August 2013. We studied from 15th May until 15th August 2013. Our referrals increased by 52% during the campaign (25 vs 38). The referral quality was unchanged (average score 6.24 pre-campaign and 6.65 during the campaign, p = 0.41). The proforma was used in 20/25 referrals pre-campaign and 30/38 during the campaign.

Table 1 shows the results of the patient information section. Patients received less information during the campaign (p=ns).

Diagnoses There were more referrals diagnosed with lung cancer pre-campaign than during it (37.5% vs 13.9% p = 0.055). One patient in the campaign group was diagnosed with lymphoma. The pre-campaign group had normal investigations in 16.7% patients, with other diagnoses made in 45.8% compared to the campaign group which had 22.2% (p = 0.6) and 61.1% (p = 0.25) respectively.

There was no significant increase in referrals with a cough as the only symptom (7/25 vs 11/38 p = 0.95).

In the campaign group, in patients diagnosed with lung cancer, we found a significant improvement in referral score compared to those without cancer (8 vs 4.87, p = 0.01). There was no change in the pre-campaign group.

Conclusion Our 2 WW referrals increased during the campaign but fewer patients were diagnosed with lung cancer and more received a non-cancer diagnosis. During the campaign, referral forms for those without cancer were poorly completed which may represent pressure on GPs to refer coughs through the 2 WW pathway despite low suspicion.

Abstract P69 Table 1 Patient Information

<table>
<thead>
<tr>
<th></th>
<th>6 weeks pre-campaign</th>
<th>6 weeks of campaign</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. patients told that cancer was being investigated</td>
<td>602 (30%)</td>
<td>1330 (20%)</td>
<td>0.34</td>
</tr>
<tr>
<td>No. patients given 2WW information</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>leaflet (if on form)</td>
<td>417 (23.5%)</td>
<td>624 (16.7%)</td>
<td>0.61</td>
</tr>
<tr>
<td>No. patients told they’d be seen in 2 weeks</td>
<td>12/20 (60%)</td>
<td>19/30 (40%)</td>
<td>0.82</td>
</tr>
</tbody>
</table>
IMPROVED LUNG CANCER REFERRAL RATES AND EARLY DIAGNOSIS IN A DISTRICT GENERAL HOSPITAL
MS Sidhu, AG Gulati, PH Hawkins, SC Cooper. Colchester General Hospital, Colchester, Essex, CO45JL, UK
10.1136/thoraxjnl-2014-206260.210

Background Survival rates from lung cancer are poor in England with 5 year survival of 8% of men and 9% of women. We hypothesised that greater awareness of lung cancer symptoms resulting from local (2011) and national (2012) campaigns had increased our 2 week wait (2 WW) referrals and may have led to earlier diagnosis and better survival rates.

Methods We carried out a retrospective analysis of data between 2008 and 2013 of all patients referred with a new diagnosis of lung cancer. For all new referrals; the number of 2 week GP referrals, patient demographics, treatment modality, survival, and time to first outpatient appointment were examined.

Results 2 WW referrals increased by 26% from 108 in 2008 to 421 in 2013, (peak 447 in 2012) and the number of confirmed lung cancer cases was 236 and 272 respectively, with 253 in 2012. 29.8% of patients presented as an emergency in 2013 compared to 39.4% in 2008. During 2008 and 2010 4.2(mean) [0.75](SD)% patients presented with stage IA disease compared to 6.3[0.7]% during 2011 and 2013 (p = 0.05). The rate of presentation with stage IV disease did not change significantly (50% vs56.6%, 2008 and 2013 respectively). 15.1% cases underwent curative treatment (surgical) in 2013 compared with 10.1% in 2008. Survival at 6 and 12 months was unchanged. The time to first outpatient appointment was not significantly different (mean of 8 days).

Conclusion The peak of 2 WW referrals coincided with local and national awareness campaigns. Although there was an increase in 2 WW referrals this was not reflected in the number of confirmed lung cancer cases. However, there has been an increase in the percentage of Stage IA diagnoses and resection rates which may have been a result of the campaigns increasing awareness amongst physicians and leading to earlier referrals.

REFERENCE

POPULATION BASED EPIDEMIOLOGY, TREATMENT AND PROGNOSIS OF MALIGNANT MESOTHELIOMA IN LEEDS, UK - A MATCHED HISTORICAL COMPARISON
RS Raju, MEJ Callister. St James’s University Hospital, Leeds, UK
10.1136/thoraxjnl-2014-206260.211

Introduction and objectives Since 2006 the National Lung Cancer Audit has provided increasingly comprehensive data on diagnosis, management and survival in patients with malignant mesothelioma on the UK. However, comparisons over a longer time period are hindered by a lack of comparable data. A previous population-based study of mesothelioma in Leeds, UK provided information on patients diagnosed between 2002 and 2005 (Thorax 2008;63:435). This current study describes the results of a matched analysis covering the years 2008–2013, allowing comparison with a historical cohort.

Methods 140 patients diagnosed with malignant pleural mesothelioma within the geographical boundaries of Leeds (CCG) were identified from 2008 to 2013 using Cancer Registry and National Lung Cancer Audit data. Clinical records from Leeds Teaching Hospitals (n = 136) or surrounding district hospitals (n = 4) were reviewed for information relating to disease characteristics at presentation, management and survival.

Results Clinical information for the current cohort is shown in Table 1 alongside data from the matched historical cohort from 2002–2005. The incidence per 100,000 population fell from 4.9
in 2002–2005 to 2.9 in 2008–2013. This partly reflects an increase in the population of the area covered over the time period (from 750,000 as described in the previous study to 806,683 in the current period).

Comparing earlier and later cohorts, there was a significant increase in the proportion of patients with a specific histological subtype (36% vs 86% respectively, p < 0.001) with a large rise in the proportion of epithelioid cases (32% vs 71% respectively). Similarly, comparing management of pleural effusion, the use of talc insufflation remained similar (38% vs 44% respectively) with increased use of indwelling pleural catheters (12% vs 22% respectively) and a reduction in talc slurry pleurodesis (15% vs 1% respectively). Overall treatment rates with palliative chemotherapy rose from 18% to 38% (p = 0.0002). Median survival rose from 267 days (95% CI 178–356) to 380 days (95% CI 252–397) between the two cohorts.

**Conclusions** The current study shows an unexpected reduction in measured incidence in Leeds, raising the possibility of incomplete case ascertainment in this study period. Specific histological subtyping, rates of palliative chemotherapy, and median survival increased between the cohorts.

## P72

**INCIDENTAL DETECTION OF EARLY STAGE NON-SMALL CELL LUNG CANCER – TIME TO IMPLEMENT SCREENING?**

1RM Thakrar, 1JM Brown, 2SV Brazil, 3D Lawrence, 4PJ George, 5SM Jans, 6N Nwah, 1Lungs for Living Research Centre, University College London, UK; 2Department of Life Sciences, University College London, UK; 3MRC Clinical Trials Unit, London, UK; 4The Heart Hospital, London, UK; 5University College London Hospital, London, UK

10.1136/thoraxjnl-2014-206260.212

**Introduction** Early detection is the key to survival in non-small cell lung cancer (NSCLC) where surgical resection can be undertaken. However, stage I and II disease combined account for only 25–30% of patients presenting with lung cancer. Although, clinical pathways from primary care exist to facilitate expeditious management of patients, the role of other referral pathways to diagnosis of surgically treatable lung cancers is not known.

**Methods** Patients suitable for surgical resection for curative intent for primary lung cancer were identified between 2007 and 2011 at this institution. Patients diagnosed ‘incidentally’ on radiology were compared to those detected through the standard ‘two week’ wait target referral system. Specific data on demographics, diagnostics utilised, pathological stage, and lung cancer mortality were recorded.

**Results** Eighty-four patients were treated with surgical resection for non-small cell cancer. The ‘two-week’ wait referrals accounted for one quarter (n = 21; 95% CI 17–35%) of the all the referrals, whilst 61% (n = 51; 95% CI 50–70%) of patients were found to have lung cancer detected incidentally through investigations performed by other specialties in the hospital. The presentation of patients to hospital with cancer related symptoms whether they had operable disease or not, had significantly higher lung cancer specific mortality (p = 0.02; see figure).

**Conclusion** We demonstrate that patients who have cancer-related symptoms have a worse outlook. Whilst asymptomatic patients diagnosed by chance have better prospects for cure by surgical resection, thus highlighting the promise of CT screening for lung cancer in patients with high risk factors.

## P73

**THE RATE OF INCIDENTAL SYNCHRONOUS PATHOLOGY ON PET-CT SCANS PERFORMED FOR THORACIC MALIGNANCY AND SUBSEQUENT IMPACT ON LUNG CANCER PATHWAYS**

TRE Jones, HI Curtis, Queen Elizabeth Hospital, Gateshead, UK

10.1136/thoraxjnl-2014-206260.213

**Introduction** NICE (CG121) recommends that all patients potentially suitable for curative intent treatments are offered PET-CT, and that they are treated within 62 days of their urgent referral and within 31 days of the decision to treat. There are case reports and three large studies regarding incidental findings on PET-CT performed for thoracic malignancy. These studies were based in Sheffield, Australia and Switzerland, with a rate of significant incidental findings of 21%, 12% and 9% respectively. There are no studies regarding the impact on referral pathways.

We aimed to identify the rate of incidental synchronous pathology on PET-CT for thoracic malignancy in our local population of 190,000 and the impact of these on referral pathways. We serve a local authority district ranked 43/326 in the English Index Multiple Deprivation in 2010 (rank of 1 being most deprived).

**Methods** Identifying patients from our thoracic MDT database, we retrospectively analysed electronic patient records for those with synchronous pathology on PET-CT between November 2012 and October 2013. Data collected included primary
diagnosis, synchronous pathology, referral timelines and reasons for delays.

**Results**

- 108 patients had a PET-CT for investigation of thoracic malignancy.
- 29 incidental findings were found in 28 patients (28/108;26%); see chart-1.
- 20 patients (20/108;19%) required further investigation/referral for their synchronous pathology.
- 22 of these 28 patients were ultimately diagnosed and treated for thoracic malignancy.
- Referral to treatment was delayed in 8 patients (8/108;7%), but only in 1 (1/108;1%) as a direct result of management for their synchronous pathology.

**Conclusions** A high number of patients undergoing PET-CT have synchronous pathology. Compared with previous UK data we found a higher rate of synchronous pathology. This may reflect a higher burden of disease in the North East of England.

Synchronous findings have a limited impact on referral to treatment pathways. However they can result in more investigations and trips to hospital, which may have a psychological impact on patients already going through a stressful life event. Perhaps this should be highlighted at time of decision to perform PET-CT.

**P74**

**FOLLOW-UP OF LUNG CANCER PATIENTS POST SURGERY**

R Aslam, AR Biswas, P Biall. Mid Yorkshire NHS Trust, Wakefield, UK

10.1136/thoraxjnl-2014-206260.214

**Rationale** Over 50% of patients undergoing surgery for lung cancer die from recurrence or a second episode of lung cancer within 5 yrs.1 There is little evidence based guidelines regarding the follow up of post surgical resection. Most follow up with physical examination and plain radiographs. Few recommend follow up with CTs. Within Mid Yorkshire NHS trust, patients are followed up post-operatively for 5 years. In the initial 2 years CTs are performed at 3, 12 and 24 months and chest radiographs at 3 to 6 monthly intervals for 5 years. The aim of this study was to assess the benefits of cross sectional imaging.

**Methods** A retrospective analysis was conducted of 109 patients undergoing surgery for lung cancer within Mid Yorkshire NHS hospital trust between 2009 and 2012.

**Results** 109 patients were included in total (42% female). Types of surgery were lobectomy (80%), wedge resection (10%) and pneumonectomy (10%) Recurrence occurred in 37% of patients (85% pulmonary).

60% of recurrences were adenocarcinomas and 33% squamous cell carcinomas. The majority of patients were asymptomatic (78%). Dyspnoea was the most frequent symptom (19%). The most commonly staged tumour was 1B (pT2A 53%, pN0 50%).

53% of recurrences were identified at the 3 month post-operative CT, 8% at 6 months, 28% at 12 months and 3% at 24 months. Chest radiographs identified recurrence at 6 (3%), 9 (3%) 18 (3%) and 21 months (3%). Total mortality within the recurrence group was 25%.

54% of patients had treatment with curative intent (surgery; 23% radiotherapy; 18% chemotherapy; 10% chemoradiotherapy 5%). 23% received palliative treatment, chemotherapy/ radiotherapy.

Conclusions There are substantial benefits of imaging in identifying recurrences in cancer patients. The post-operative CT imaging at 3 and 12 months is advantageous as they identified 53% and 28% of the recurrences respectively. However, the benefit of regular chest radiographs and surveillance CT at 24 months is questionable as they were less effective.

**REFERENCE**


**P75**

**PROGNOSTIC IMPLICATIONS OF THE MODIFIED GLASGOW PROGNOSTIC SCORE IN EARLY STAGE NON-SMALL CELL LUNG CANCER**

AM MacKenzie, E Johnson, S Tsim, KG Blyth. Department of Respiratory Medicine, Southern General Hospital, Glasgow, UK

10.1136/thoraxjnl-2014-206260.215

**Introduction and objectives** Up to 50% of patients treated radically for non-small cell lung cancer (NSCLC) subsequently present with metastatic disease. This is despite rigorous case-

selection and the use of adjuvant therapies based on clinical and/or surgical staging. A simple, objective biomarker that identified patients at higher risk of recurrence might facilitate more effective multi-modality radical treatment.

Since inflammation-based biomarkers offer robust prognostication in metastatic NSCLC, we hypothesised that the modified Glasgow Prognostic Score (mGPS), Neutrophil:Lymphocyte Ratio (NLR) and/or Platelet:Lymphocyte Ratio (PLR), measured prior to radical treatment would have utility in this regard.

**Methods** Utilising a radiology database, we retrospectively identified all patients with Stage I-IIa NSCLC who underwent...
radical treatment between August 2011 and August 2012. Electronic records were reviewed and baseline parameters, including blood results were recorded. mGPS (based on CRP and Albumin), NLR and PLR were calculated. All cases were subject to multidisciplinary assessment, detailed staging and 2-year follow-up. Kaplan-Meier plots were generated for mGPS, NLR, PLR and compared using log-rank for trend and log rank. Differences in mortality were quantified using Hazard Ratios (HR). Differences in stage proportion were compared using the Chi-Square z test.

Results 97 patients were identified. 44/97 (45%) were male, mean age 70 (± 8) years. 54/97 (56%) underwent surgery, 43/97 (44%) underwent radical RT. NLR and PLR provided no useful prognostic information. In surgical patients only, increasing mGPS was associated with decreasing 2-year survival (see Figure 1(a)), with curve separation occurring 1 year post-resection. Pre-operative mGPS 1 and 2 were associated with HR for death of 3.9 (95% CI 0.8–39.5, p = 0.095) and 5.8 (95% CI 1.38–106, p = 0.02) relative to mGPS 0. There were less Stage I and more Stage II patients in the mGPS 1 group (see Figure 1(b)), mGPS 0 and 2 appeared well matched for stage.

Conclusion These data suggest that pre-operative mGPS may be useful in risk-stratifying patients with early stage NSCLC. The late survival curve separation observed suggests recurrent malignancy rather than post-operative complications are likely to explain this. If confirmed prospectively, integration of mGPS into staging algorithms might allow more effective targeting of adjuvant therapies.

Introduction We have previously shown that the majority of recurrent disease occurs within the 2 years of lung cancer resection. Follow-up protocols vary between centres but often involve serial CXR examinations. At Salford we also perform a CT scan at one year after surgery. Given that the prognosis for early stage lung cancer is good, the question arises as to when it’s safe to discharge such patients from follow-up? Traditionally this has been set at 3 years.

The Salford Lung Cancer database provides comprehensive data on all patients in Salford undergoing surgical resection including outcomes during follow-up. To date, 255 patients have undergone resection of non-small cell lung cancer and the rate of resection is increasing year on year. This audit sets out to review the data following introduction of routine PET scans to clinical practice.

Methods All patients undergoing surgical resection were first identified from March 2006 to July 2010. Those with a post-operative stage 1A or 1B disease were then extracted; allowing a 4 year follow up for each patient. Those patients dying within 4 years of surgery from non-cancer and non-lung cancer causes were excluded to produce a selected cohort of patients. 1, 2, 3 and 4 years survival figures were then produced for each category of disease (1A, 1B and 1A+1B) to observe for any serial changes.

Results A total of 89 patients underwent surgical resection during the study period of which 55 (62%) were 1A or 1B disease. After exclusions, 43 patients (23 × 1A and 20 × 1B) were available for analysis. As expected, relapse rates were low and occurred in the first 2 years. Survival rates were high but remained stable after 2 years of follow up (see Table). The use of 1 year CT scans detected just 2 relapses.

Conclusions Allowing for the small numbers, the above audit supports a move away from traditional follow-up protocols to discharge alive and well patients with resected early stage disease from the clinic at 2 years. The role of imaging surveillance during the first 2 years requires further exploration.

REFERENCES
1 Tunney R et al. P195 Temporal Trends and Distribution of Recurrent Disease Following Lung Cancer Surgery and Relationship to Pre-Operative PET-CT. Thorax 2010;65:A159–A160

P76 WHEN IS IT SAFE TO DISCHARGE RESECTED STAGE 1A/1B NSCLC FROM THE CLINIC?
1G Kamalatharan, 1CS Moorcroft, 2R Shah, 3SCO Taggart. 1University of Manchester, Manchester, UK; 2University Hospital of South Manchester, Manchester, UK; 3Salford Royal NHS Foundation Trust, Salford, UK

Introduction When it might be safe to discontinue regular follow-up of early stage lung cancer is good, the question arises as to when it’s safe to discharge such patients from follow-up? Traditionally this has not been defined.

Methods All patients undergoing surgical resection were first identified from March 2006 to July 2010. Those with a post-operative stage 1A or 1B disease were then extracted; allowing a 4 year follow up for each patient. Those patients dying within 4 years of surgery from non-cancer and non-lung cancer causes were excluded to produce a selected cohort of patients. 1, 2, 3 and 4 years survival figures were then produced for each category of disease (1A, 1B and 1A+1B) to observe for any serial changes.

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REFERENCES
1 Tunney R et al. P195 Temporal Trends and Distribution of Recurrent Disease Following Lung Cancer Surgery and Relationship to Pre-Operative PET-CT. Thorax 2010;65:A159–A160

P77 CARCINOMA IN-SITU AT THE BRONCHIAL RESECTION MARGIN – A CASE FOR ROUTINE SURVEILLANCE WITH AUTOFLUORESCENCE BRONCHOSCOPY
1RM Thakrar, 1JM Brown, 2H Apperley, 3M Falzon, 4PJ George, 5N Navari, 6SM Janes. 1Lungs for Living Research Centre, University College London, UK; 2Bristol Medical School, University of Bristol, UK; 3Thoracic Medicine, University College London Hospital, UK; 4The Heart Hospital, University College London Hospital, UK

Introduction Lung cancer is the leading cause of cancer mortality worldwide, with squamous cell carcinomas commonly arising in the central airways and accounting for nearly 30% of cases. Progression from normal bronchial epithelium to carcinoma in situ (CIS) has been well described, and is found at the resection margin after lobectomy in up to 2.5% of cases; however, its fate has not been defined.

Method Cases referred to the autofluorescence bronchoscopy (AFB) surveillance programme at this institution were analysed retrospectively from 1999–2012, for all those shown to have CIS at the resection margin following surgery for TxN0M0 squamous cell carcinoma. Patients underwent longitudinal assessment of the tracheobronchial tree to (a) confirm CIS at the resection margin and track its fate over time (b) characterise development of other preinvasive lesions.

Results Twenty-two cases were identified with a median interval of 6 months (range 3–9) from surgical resection to first AFB. Thirteen patients (59%) were confirmed to have CIS on biopsy at the bronchial resection margin during the first AFB. Eleven (85%) of these progressed to invasion over a median interval of 37 months (range 4–83). A subgroup of these (5 patients) developed 8 invasive cancers at sites distant to the anastomotic site and 9 patients had >1 CIS lesion at a distant site. Two patients (9%) found to have CIS after initial post-resection AFB, persisted after follow-up of 36–45 months. Although no progression...
has been seen, both have developed CIS at distant sites to the resection margin. Nine patients (41%) were found to have no evidence of CIS at the resection margin and during a median surveillance period of 37 months (range 19–126), all were found to have normal bronchial epithelium. One patient in this group developed a second primary lung cancer that was surgically resected.

**Conclusion** CIS at the bronchial resection margin is a strong indicator of its fate to progression to invasive carcinoma. Its persistence sets precedent for the development of multiple, consecutive CIS lesions and invasive squamous cell carcinomas, and highlights the importance of routine AFB surveillance following surgery in these cases.

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**P78** CAN PET STANDARD UPTAKE VARIABLE (SUV) PREDICT DISEASE PROGRESSION IN EARLY-STAGE NON-SMALL CELL LUNG CANCER (NSCLC)?

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10.1136/thoraxjnl-2014-206260.218

**Introduction** The correlation between SUV on PET-CT and prognosis in NSCLC has been the subject of much debate. We were interested in whether SUVmax values could be used to determine which cases of early stage (1–2) NSCLC were likely to progress.

**Methods** We reviewed all 93 histologically proven early stage NSCLCs seen at our tertiary centre over a one year period. We defined those with SUVmax in the upper quartile as the high SUV group and compared these with the remainder. Historical data were considered to allow subsequent outcomes to be established.

**Results** Median follow up was 772 days during which time there was a 17% mortality rate [all-cause median time to death 338 days]. The median SUVmax for the cohort was 10.1, and those in the upper quartile all had results over 15.0.

The high SUV group (n = 27) and low SUV group (n = 68) had similar baseline characteristics, received similar treatment regimens and there were no significant differences in tumour size between the groups. Disease progression and mortality were both significantly higher in those with SUVmax in the upper quartile, despite this group tending to have earlier disease (see Table 1).

Retrospective analysis using Youdin’s index suggested that the optimal threshold for predicting disease progression was not significantly different when cases with nodal involvement were excluded [SUVmax 15.0 vs 15.5].

**Conclusions** Our results suggest that SUVmax may indeed help identify those patients with early stage NSCLC at higher risk of progression. In our large cohort those with an SUVmax of >15 were over 3 times more likely to develop progressive disease than those with lower results and this was independent of tumour size or nodal involvement. Whether individuals in the higher-risk group would benefit from increased surveillance or adjuvant therapy remains to be established.

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**Clinical management of pulmonary infection**

**P79** BRONCHIECTASIS SEVERITY IN PRIMARY IMMUNODEFICIENCY - A TWO CENTRE STUDY

1AD Saleh, 1JR Hurst, 2J Davison, 3C Stroud, 4D Lowe, 5A De Soyza. 1University College London, London, UK; 2Freeman Hospital Adult Bronchiectasis Service, Newcastle, UK; 3Immunology Department Royal Victoria Infirmary, Newcastle, UK; 4Institute for Immunity and Transplantation, Royal Free Hospital, London, UK; 5Institute of Cellular Medicine, Newcastle University and Freeman Hospital Adult Bronchiectasis Service, Newcastle, UK

10.1136/thoraxjnl-2014-206260.219

**Introduction** Up to 70% of patients with Primary Immunodeficiency syndromes such as Common Variable Immunodeficiency (CVID) have bronchiectasis. Within this population it is a major driver of morbidity.1

The Bronchiectasis Severity Index (BSI) is capable of accurately categorising non-cystic fibrosis bronchiectasis patients into three severity groups that predict risk of hospitalisation and mortality at one and four years.2 It consists of nine clinical parameters, and was derived and validated in a diverse international bronchiectasis population. Mild disease is defined as a BSI score of <4, moderate 5–8 and severe >9.

This study aims to assess the relative severity of bronchiectasis associated with primary immunodeficiency.

**Methods** 24 Patients from the Royal Free Hospital, London and 22 patients from the Freeman Hospital Newcastle were recruited. Age, body mass index, predicted FEV1, number of hospitalisations in the last 2 years, number of exacerbations in the last year, medical research council dyspnoea (MRC) score, Pseudomonas and other pathogen colonisation status and number or lobes involved on CT chest were obtained to calculate the BSI. Statistical analysis was carried out using SPSS V11.

**Results** The 46 patients were 67.4% female with a mean age of 55.9. There were no significant differences in age, gender or disease severity between the two centres. The median BSI was 4 (i.e. mild disease).

56% of patients had mild disease, 21.7% were moderate and 21.7% severe bronchiectasis. These patients had markedly less severe disease than the mixed aetiology population of 603 patients used to derive the scoring tool.

**Conclusion** Patients with Primary Immunodeficiency associated bronchiectasis were younger with less severe disease compared to the BSI cohort population previously reported. This suggests good multidisciplinary care in Primary Immunodeficiency with earlier referral to respiratory specialists. It also correlates with our prior longitudinal data that FEV1 decline in immunodeficiency-related bronchiectasis is less rapid than other aetiologies.1

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**Abstract P78 Table 1 Early stage NSCLC**

<table>
<thead>
<tr>
<th>Age</th>
<th>% female</th>
<th>Predicted FEV1%</th>
<th>Median PS</th>
<th>%treated with curative intent</th>
<th>Median Stage</th>
<th>Disease Progression*</th>
<th>All cause Mortality*</th>
</tr>
</thead>
<tbody>
<tr>
<td>High SUV* (n = 27)</td>
<td>70.5</td>
<td>50%</td>
<td>80.8%</td>
<td>1</td>
<td>89.5%</td>
<td>1b</td>
<td>40.7%</td>
</tr>
<tr>
<td>Low SUV* (n = 68)</td>
<td>70.8</td>
<td>53%</td>
<td>77.6%</td>
<td>1</td>
<td>92.3%</td>
<td>2a</td>
<td>13.2%</td>
</tr>
</tbody>
</table>

1Cut off SUVmax =15; *Denotes significant statistical difference p < 0.05.
Introduction and objectives | NHS England have been looking at using the EQ-5D-5L as a measure of health outcome across the NHS. It is a simple measure which patients complete at the start and end of treatment to evaluate quality and effectiveness of interventions. To date there is no evidence on its use in Bronchiectasis (Bx). Moreover, evaluation of exercise performance is also vital as this can be associated with increased dyspnoea, reduced lung function or increased malaise. Sit to stand (5STS) and six minute walk test (6MWT) can be used to evaluate exercise performance but there is limited guidance on responsiveness and feasibility in Bx. This abstract provides novel data for these outcome measures (OM) in Bx patients during a routine inpatient stay.

Methods | 20 Bx inpatients (Male: Female 20:20, Median age: 63 (29–74) Median FEV1: 1.26 (0.51–2.9) were assessed. 6MWT, 5STS and EQ-5D-5L were completed on all patients during their initial and final assessment.

Results | Median length of stay was 10 days. Data is presented as median difference and comparisons were made using Wilcoxon Signed Rank tests.

Conclusion | The EQ-5D-5L improved but did not show a significant difference, moreover there is currently no reported MCID for this OM. Significant differences were seen in both the 6MWT and 5STS. The 5STS is quick and feasible to complete and therefore maybe more preferable to use than the 6MWT. More understanding is needed on the utility of the EQ-5D-5L in this population.
length of stay was calculated by dividing the total number of bed days by the total number of admissions for each calendar period. Linear regression was used to test for changes over time in mean age at admission and average length of stay.

**Results** In 2004 the total number of admissions was 8611 (11,147 after standardisation) and this increased progressively up to 2011 when the number was 15,885 (see Figure 1). The overall annual increase was 9% (Rate Ratio [RR] 1.09, 95% Confidence Interval [CI] 1.08 to 1.10; p < 0.0001). During the study period, the mean age at admission increased from 62 years to 65 years and the average length of stay decreased from 6.5 days to 4.7 days (p = 0.001). 60% of admissions were in women and admissions were more common in individuals over 60 years.

**Conclusions** Data on hospital admissions from bronchiectasis suggest that the disease burden is increasing. The cost of inpatient care, combined with outpatient disease monitoring and prescription of antibiotics pose a large burden on healthcare services.

**REFERENCE**

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**P83**

**EFFECT OF A STANDARDISED CHEST CLEARANCE PATHWAY ON QUALITY OF LIFE AND HOSPITAL ADMISSIONS IN PATIENTS WITH NON CYSTIC FIBROSIS BRONCHIECTASIS**

1. LT Yeo, 2K Bentley, 2L Borill. 1University of Manchester, Manchester, UK; 2Pennine Acute Hospitals NHS Trust, Manchester, UK

10.1136/thoraxjnl-2014-206260.222

British Thoracic Society guidelines for non-cystic fibrosis bronchiectasis (NCFB) recommend airway clearance taught by a physiotherapist for patients with chronic sputum production or mucus plugging on CT. Various techniques and adjuncts are available and the evidence for the effectiveness of these is inconsistent. We designed a stepwise chest clearance pathway for use in a specialist NCFB clinic in a large district general hospital trust. Patients were taught and commenced on active cycle breathing technique with postural drainage, positive expiratory pressure device, mucolytic and nebulised hypertonic saline, progression to each step until chest clearance was felt to be optimised. Quality of life was assessed using Leicester cough questionnaire (LCQ) at baseline and after each intervention including the point of optimisation. Hospital admission and general practice antibiotic prescription data were retrospectively collected for 12 months pre and post initiation of the pathway. Data were compared using Wilcoxon signed rank test.

105 patients (mean age 67, 53 female, mean FEV1 1.62l) were included although data were incomplete. Total LCQ score significantly improved at the point where chest clearance was felt to be optimised, compared to baseline, with a median difference of 1.3. Subgroup analysis revealed that patients with lower baseline LCQ showed greater improvement. Further analysis revealed that all steps in the pathway resulted in significant improvements in LCQ with the exception of mucolytics. Hospital admissions for NCFB were significantly reduced in the 12 months following initiation of the pathway. There was no significant difference in antibiotic usage according to GP prescriptions.

This retrospective study suggests that the use of a standardised chest clearance pathway may result in improved quality of life and reduction in hospital admissions in patients with NCFB.
IS THE CURB-65 SCORE A RELIABLE TOOL FOR GUIDING INITIAL ANTIBIOTIC THERAPY IN ACUTELY UNWELL PATIENTS WITH COMMUNITY ACQUIRED PNEUMONIA?

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10.1136/thoraxjnl-2014-206260.224

Introduction Prompt appropriate antibiotics for community acquired pneumonia (CAP) reduces mortality, length of stay and adverse events. Antibiotic choice is directed by the CURB-65 score and clinical judgement. Admission is recommended for most CURB-65 ≥2. Recent national data showed an unexplained non-compliance of 40% (>2000 patients) with CAP antibiotic guidelines using CURB-65 scores alone. Antimicrobial misuse and resistance are a global concern. We investigated compliance with our Trust CAP guidelines and used an early warning score (EWS) to quantify clinical judgement.

Methods Data were collected retrospectively for adults attending the emergency department with CAP over 4 months. The CURB-65 and the Trust’s EWS (Physiological Observations Track and Trigger system – POTTS) were calculated at presentation. A POTTS score of 2 triggers escalation of care. Prescriptions were compliant when the initial antibiotic concurred with the Trust guidelines. Patients receiving broader spectrum agents than recommended were ‘over-treated’. Admission was noted.

Results (Table 1) Of 77 patients with CAP, 11 (14%) received ‘compliant’ antibiotics (Table 1). 38 (49%) patients were over-treated, 25 (66%) of whom had POTTS ≥2, though 15 (60%) of these patients had low severity CURB-65 of 0–1. Of 49 patients with POTTS ≥2, 27 (55%) had a CURB-65 of 0–1, 26% a CURB-65 of 2. 44% and 68% of those with a CURB-65 of 0 or 1 were admitted, with higher average POTTS than those discharged.

Conclusion The majority of patients incorrectly prescribed broad spectrum antibiotics had a CURB-65 score that failed to categorise them as sick enough to warrant them despite an EWS ≥2. Hospital admission demonstrated similar findings. Over half of those with an elevated EWS had a low severity CURB-65. We did not collect outcome data but the ‘over-treatment’ and admission appear appropriate. Prompt, effective and empiric antimicrobials for septic patients give better clinical outcomes. Seemingly non-compliant antimicrobial prescriptions may have punitive implications for Trusts. We suggest that CURB-65 under-recognises sepsis syndrome and thus the EWS should be included and further validated in CAP guidelines and audits.

REFERENCE
1 BTS CAP guidelines

P85 HIV-RELATED ACUTE RESPIRATORY ADMISSIONS – GOOD OUTCOMES AND AN OPPORTUNITY FOR TESTING

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10.1136/thoraxjnl-2014-206260.225

Introduction The burden, changing pattern and outcome of HIV-associated lung disease following the introduction of antiretroviral therapy (ART) remains to be defined. We sought to investigate these factors in an unselected cohort of individuals admitted acutely to our London teaching hospital.

Methods Consecutive admissions were prospectively collected between June 2013 and May 2014. In those where the cause for admission was an acute respiratory illness, patient notes and electronic records were interrogated. Patients were allowed ≥1 diagnoses and in-hospital outcomes only were reported.

Results Fifty-three of 149 (35%) acute HIV admissions were with respiratory causes, (3 patients had 2 admissions >30 days apart). Median age was 45 years and 28% (15) were female. Median CD4 count was 109 (range 3–867) cells/μL; 14 (26%) had fully suppressed HIV loads (VL <20 copies/ml).

4 of 53 (8%) were admitted with non-infectious diagnoses: 2 with lung cancer, 1 non-infective COPD exacerbation and 1 non-specific interstitial pneumonia. The remainder had infections: 12 (23%) had culture-confirmed bacterial pneumonia, 11 (21%) were treated for PCP, 8 (15%) had culture-confirmed Mycobacterium tuberculosis (1 MDR), 4 had confirmed viral pneumonia (8%). 20 (38%) patients completed treatment for pneumonia with no specific laboratory confirmation. The most common bacterial isolates were streptococcus pneumoniae (4 cases), haemophilus influenzae (3), pseudomonas aureginosa (2) and klebsiella pneumoniae (2). In 11 of 53 (22%) a new diagnosis of HIV was made at the time of admission, 10 of whom presented as acute community acquired pneumonia (CAP). In 9 of 11 (82%) CD4 count was <200 cells/μL and 6 of 11 (55%) required ICU care. In total 20 of 53 (38%) were admitted to ICU, and 8 (15%) required mechanical ventilation. Median length of stay in hospital was 9 (2–397) days. 1 patient died.

Conclusions Acute respiratory illness remains a significant cause of HIV admissions, with opportunistic and non-opportunistic pathogens commonly identified. Outcomes were reassuringly good despite the frequent need for ICU support. We believe our data underlines the important opportunity that a presentation with acute respiratory illness provides to test for and diagnose HIV infection.
Airway assessment by a SALT team was performed in 4 patients within 48 h of admission. None of the patients underwent video fluoroscopy. An initial dietetic review within 72 h of admission was observed in 6 patients (18%). Median hospital stay was 8 days and in hospital mortality was 41%.

**Conclusion**
The study demonstrates a significant inconsistency in the initial management of patients hospitalised with AP. The lack of early intervention by SALT and dietetic services and routine video fluoroscopy use in the majority of patients is of concern. A specific guideline with an evidence-based diagnostic pathway and management needed for patients at high risk for AP.

---

**Abstract P87 Table 1**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Geometric mean KPN CFU cm⁻²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Contact time (hours)</td>
</tr>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td><strong>Control</strong></td>
<td>1.8 × 10⁵</td>
</tr>
<tr>
<td><strong>ACP</strong></td>
<td>1.8 × 10⁵</td>
</tr>
<tr>
<td><strong>A2A</strong></td>
<td>1.8 × 10⁵</td>
</tr>
</tbody>
</table>

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**Smoothing the process: clinical management of COPD and bronchiectasis**

**Introduction**
Asthma and COPD account for a significant proportion of inpatient admissions in the UK. A national review of asthma deaths found that a significant proportion of patients die without seeking medical assistance or before emergency medical care could be provided.¹

**Objectives** Establish the pathway that patients undertake to access care in the lead up to an A and E attendance and/or inpatient admission.

**Method**
Patients attending A and E and/or following an inpatient admission due to an exacerbation of asthma or COPD were reviewed by a respiratory pharmacist during weekday working hours. Patients were identified post take ward rounds and using hospital electronic systems. All analyses were conducted using SPSS 22. Ethics approval was not required.

**Results**
Over the six-month period, 539 (138 asthma and 403 COPD) presentations for exacerbations of asthma and COPD were reviewed. As Table 1 shows, only 48% (n = 66) and 46% (n = 185) of asthma and COPD patients respectively, received medical attention and/or had an active intervention (e.g. administration of rescue pack of oral corticosteroids and/or antibiotics) prior to presenting to hospital. The remaining 52% (n = 72) and 54% (n = 218) respectively either did not seek medical attention or were unable to be reviewed (e.g. unable to obtain an appointment with their general practitioner, GP) prior to their attendance. The results also show that the majority of patients were registered with a GP.

**Conclusion**
Despite the majority of patients having access to a GP, a significant proportion of asthma and COPD patients either did not seek medical attention prior to presenting to hospital, or were unable to be reviewed by their GP. These findings correlate with those found in the national review of asthma deaths.¹ At a time of increasing demands on healthcare resources, these results pose the question of how we can better triage patients to the body polymer material. The clinical implications of these findings are relevant to VHC hygiene and patient health, and require further investigation.
appropiate care settings to minimise unscheduled care and improve patient access and care.

REFERENCE

P89 ATTENDANCE OF SECONDARY CARE RESPIRATORY OUTPATIENT APPOINTMENTS IN ILLICIT DRUG USERS WITH RECURRENT HOSPITAL ADMISSIONS WITH ‘COPD’ AT A CITY CENTRE TEACHING HOSPITAL

R Huang, AM Collins, N Williams, N Gamer, T Perry, H Burhan. Royal Respiratory Research (RHR), The Royal Liverpool and Broadgreen University Hospital Trust, Liverpool, UK
10.1136/thoraxjnl-2014-206260.229

Introduction
Non-attendance at outpatient appointments (OPA) costs the NHS an estimated £600 m a year, with over 94,000 missed (first) OPAs in England from 2013 to 2014.1 We reviewed the arrangement and attendance of OPAs for illicit drug smokers, after hospital re-admission with an ‘exacerbation of chronic obstructive pulmonary disease (COPD)’. Methods All illicit drug smokers re-admitted between January 2009 and September 2011 with a presumptive diagnosis of ‘exacerbation of COPD’ were included. Planned respiratory OPAs were reviewed retrospectively from our COPD admission database to determine the number attended or unattended. Unattended OPAs were classified as (a) hospital cancellation (b) patient cancellation (c) patient did not attend (DNA) or (d) ‘unknown’.

Results
Of 89 patients, no OPA was arranged in 28 (31.5%). 334 respiratory appointments were made for 61 patients (mean = 5.5 per patient); of these, only 86 (25.7%) were attended (see Table).

Conclusion
High recurrent admission rates suggest that these patients should all have specialist respiratory OPAs arranged at discharge, with the aim of preventing re-admission and improving their respiratory health. In our cohort we noted poor OPA attendance with a DNA rate of 52.0% compared with around 8.6% for first OPAs overall in England in 2012.2 This suggests alternative approaches are needed in order to engage with these patients such as community based secondary care outreach services. We will now study the effects of an intensive community-based secondary care outreach services; involving smoking cessation, targeted pulmonary rehabilitation, specialist respiratory (consultant and nurse) involvement, vaccination, inhaler technique reviews, medication concordance checks/ prescription and health trainers.

REFERENCES

Abstract P89 Table 1

<table>
<thead>
<tr>
<th>Reason</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital cancelled</td>
<td>92 (37.1%)</td>
</tr>
<tr>
<td>Patient cancelled</td>
<td>8 (3.2%)</td>
</tr>
<tr>
<td>DNA</td>
<td>129 (52.0%)</td>
</tr>
<tr>
<td>Unknown</td>
<td>19 (7.7%)</td>
</tr>
</tbody>
</table>

P90 CATCH – COMMUNITY ACCESS TO CT CHEST

1CS Moorcroft, 2G Kamalatharen, 3S Elliot, 4A Walsham, 5A Shama, 7SCO Taggart.
2Manchester Medical School, Manchester, UK; 3Salford Clinical Commissioning Group, Salford, UK; 7Salford Royal NHS Foundation Trust, Salford, UK
10.1136/thoraxjnl-2014-206260.230

Introduction
Rates of lung cancer diagnosis for two week wait (2WW) referrals are low although referrals are increasing. Many 2WW’s are potentially exposed to unnecessary anxiety as the referral requires the G. P. to inform the patient of the possibility of cancer. CATCH (Community Access To CT Chest) is a new protocol of care that has been developed by the Salford lung cancer team in collaboration with the Salford C. C. G. whereby abnormal “low risk” CXR reports are communicated to G. Ps with instructions for them to request a CT scan, which is then fast tracked allowing rapid performance and reporting of the scan with appropriate advice to the GP.

Methods
A d-base was set up to capture the performance of CATCH from its introduction on 05.02.2014 to 05.07.2014. Demographic details were collected for dates of CXR, CXR report, CT request, CT report, relevant outcomes and 2WW activity for same time (2011–2014). Participating patients were interviewed by telephone using a structured questionnaire (supported by a postal questionnaire for non-responders).

Results
53 patients underwent an abnormal CXR with advice to enter into the CATCH protocol and of these 7 bypassed CATCH having been referred directly into the 2WW system by their G. Ps. For the 46 patients completing CATCH, seven (15%) urgent 2WW referrals were recommended. In the remaining 39 patients, 28 required no follow up, 9 non-urgent referral to the chest clinic and 2 repeat community CXRs. Timelines for performance of CT scans were acceptable (see Table) and detected cancer in 5/46 (10.9%) and were normal in 8/46 (17.4%). 23–26 patients interviewed to date rated the service overall as either very good or excellent. During same points in 2011, 2012, 2013 and 2014 2WW numbers were 69, 84, 89 and 81 respectively.

Conclusions
Our provisional data support the role of CATCH as a new system of care for managing ‘low risk’ CXR reports that might otherwise be referred into growing 2WW clinics. Thus far, the protocol moves at a rapid pace and has been well received by the patient (although we await the results of the postal survey in due course).

Abstract P90 Table 1

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean time (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR performed to CXR report</td>
<td>3.1</td>
</tr>
<tr>
<td>CXR report to CT request</td>
<td>5.1</td>
</tr>
<tr>
<td>CT request to CT appointment</td>
<td>5.8</td>
</tr>
<tr>
<td>CXR report to CT appointment</td>
<td>13.0</td>
</tr>
</tbody>
</table>

P91 DEVELOPMENT AND IMPLEMENTATION OF A STRUCTURED, ANNUAL ‘COMPREHENSIVE RESPIRATORY ASSESSMENT’ FOR INDIVIDUALS WITH ADVANCED COPD

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10.1136/thoraxjnl-2014-206260.231

Introduction
Disease burden, polypharmacy, co-morbidities and complex social needs are significant in patients with advanced COPD and predict morbidity, mortality and health care
utilisation. Our first aim was to develop a structured annual assessment for patients with advanced COPD: the ‘Comprehensive Respiratory Assessment (CRA)’ to systematically assess disease burden, co-morbidities and social care needs akin to the ‘Comprehensive Geriatric Assessment’. The second aim was to use the CRA in an out-patient setting to inform an individualised care plan. We report our first year experience of implementing an Advanced COPD Clinic with an annual CRA.

**Methods** A multi-disciplinary team developed the Comprehensive Respiratory Assessment (CRA) for patients with advanced COPD which was defined as an FEV1 of <50% predicted with one of the following: MRC ≥ 4, Respiratory Failure, ≥ 2 hospital admissions with an acute exacerbation of COPD, current smoking history, and a low BMI or significant weight loss. A bespoke electronic patient record (the airways disease database [ADD]) was developed to support the CRA. The CRA was performed annually by an advanced COPD nurse and subsequently reviewed in an out-patient clinic by a respiratory physician supported by a multi-disciplinary team whereby an individualised care plan was agreed with the patient. Ethical approval was sought and written consent provided.

**Results** The Advanced COPD service and CRA was established in June 2013 in Leicester, UK. The CRA is categorised into four principal domains which are: (1) exercise and activity, (2) exacerbations, (3) co-morbidities and extra-pulmonary manifestations, and (4) prognostic indicators and end of life care needs. At one year 155 referrals have been made with 71 annual CRAs completed to date. The baseline data of the patient cohort are described in Table 1.

**Conclusion** The innovation of an advanced COPD service, with a multi-disciplinary team, supported by an annual Comprehensive Respiratory Assessment and bespoke electronic patient record is feasible and allows systematic assessment, development of individualised treatment plans, and further characterisation of this cohort.

**Abstract P91 Table 1** Characteristics of an advanced COPD cohort

<table>
<thead>
<tr>
<th>Baseline Characteristics</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66 (9)</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>51%</td>
</tr>
<tr>
<td>MRC Grade (median and IQR)</td>
<td>4 (4-4)</td>
</tr>
<tr>
<td>FEV1 (% predicted)</td>
<td>32 (12)</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>25.5 (7.7)</td>
</tr>
<tr>
<td>Current smokers (%)</td>
<td>25%</td>
</tr>
<tr>
<td>Pack years (years)</td>
<td>39 (17)</td>
</tr>
<tr>
<td>Living arrangements (% living alone)</td>
<td>31%</td>
</tr>
<tr>
<td>Oxygen use (% LTOT)</td>
<td>39%</td>
</tr>
<tr>
<td>Number of exacerbations in previous year (median and IQR)</td>
<td>4.5 (2.0-8.0)</td>
</tr>
<tr>
<td>Number of hospitalisations in previous year (median and IQR)</td>
<td>0.5 (0.0-1.0)</td>
</tr>
<tr>
<td>Incremental shuttle walk test (m)</td>
<td>128 (91)</td>
</tr>
<tr>
<td>Quadriceps strength (Kg)</td>
<td>19 (8)</td>
</tr>
<tr>
<td>CAT score</td>
<td>25 (7)</td>
</tr>
<tr>
<td>Chronic Respiratory Questionnaire (CRQ)</td>
<td>2.1 (0.7)</td>
</tr>
<tr>
<td>CRQ dyspnoea</td>
<td>2.9 (1.2)</td>
</tr>
<tr>
<td>CRQ fatigue</td>
<td>3.7 (1.4)</td>
</tr>
<tr>
<td>CRQ emotion</td>
<td>3.7 (1.5)</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>9.5 (4.4)</td>
</tr>
<tr>
<td>HADS depression</td>
<td>8.1 (3.5)</td>
</tr>
</tbody>
</table>

MRC: Medical Research Council, FEV1: Forced Expiratory Volume in 1 sec, CAT: COPD Assessment Tool, CRQ: Chronic Respiratory Questionnaire, HADS: Hospital Anxiety and Depression Scale

**Abstract P92 Figure 1** Accuracy of diagnoses and management of NIECOPD, IECOPD and CAP on AMU before and after a right care approach

**Introduction** COPD is the second most common cause of emergency admission and 5th cause of readmission to hospital. Appropriate identification and treatment is crucial to make every bed day count and reduce the burden of COPD. Characterising COPD exacerbations (ECOPD) and excluding differential diagnoses in acutely unwell co-morbid patients can be challenging. This study aimed to evaluate the accuracy of diagnoses/management of patients on the acute medical unit (AMU) in an inner London teaching hospital with 300 ECOPD admissions/yr, and to develop an improvement plan.

**Methods** Admission records for COPD patients admitted acutely with increased shortness of breath, cough and/or wheeze over 6 weeks (Jan/Feb 2014) were reviewed. Diagnostic criteria and treatment were compared to national standards. 21 AMU junior staff completed a COPD knowledge questionnaire. An ECOPD pathway was developed, highlighting diagnostic and treatment differences between infective (IECOPD), non-infective COPD exacerbations (NIECOPD) and community acquired pneumonia (CAP), supported by electronic prescribing order sets. An online learning module was developed to support junior doctors.

**Results** 44 COPD patients (26M, 18F) were admitted to AMU. 20% had an incorrect diagnosis. Of NIECOPD patients (20%): 66% received antibiotics; 11% did not receive prednisolone. Of IECOPD patients (47%): 65% received iv or incorrect oral antibiotics; 14% did not receive prednisolone. Of CAP patients (32%): in CURB <3 89% received iv antibiotics. 5 CAP patients were documented as IECOPD; 2 were undertreated. 2 IECOPD patients were diagnosed with CAP and over treated. Only 13/21 (62%) of AMU junior doctors understood the difference between NIECOPD, IECOPD and CAP. After the improvement plan, incorrect diagnosis fell from 20% to 7%. Of NIECOPD patients (28%): only 18% received antibiotic therapy; 100% received prednisolone. Of IECOPD patients (48%): 74% received correct antibiotics; 100% received prednisolone. Of
SUPPORTING PATIENT INVOLVEMENT IN SERVICE DEVELOPMENT: ELICITING PATIENT-CENTRED INFORMATION TO INFORM COMMISSIONING OF COPD SERVICES

F Early, T Watts, K Homan, A Green, M Brookes, J Fuld. Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK; British Lung Foundation, London, UK; Cambridgeshire and Peterborough CCG, Cambridge, UK

Introduction Patient involvement in population level health care decisions often involves consultation rather than interactive decision-making. Lack of insight into appropriate methods is a barrier to patient involvement.

Working Together for Change (WTfC) is a person-centred process to inform service development. Information from person-centred reviews (PCRs) is themed in a two-day co-production workshop. It is effective in social care and mental health but has not been applied in physical health. We tested its feasibility to improve the quality of person-centred information for COPD commissioners and of patient involvement.

Methods Forty COPD patients recruited from GP lists, secondary care and support groups participated in one-to-one PCRs. PCRs identified their priorities for what's working in their life regarding COPD, what's not working, what's important to the future.

These patients, health service professionals and third sector organisations involved in COPD support were then invited to attend the two one-day workshops. Patients’ priorities were themed collaboratively. Root cause analysis of what was not working was followed by statements of what success would look like if root causes were addressed. Action plans were created.

Qualitative data from workshop observations and participant interviews were analysed using thematic analysis.

Results Service priorities included information, holistic care, access, dietary support, access to patient information for HCPs.

The improved quality of the person-centred information was evident in the ways in which professionals’ understanding of patient needs was enhanced through close, informal interaction with patients and carers, e.g. witnessing difficulties such as simultaneously eating and breathing and other physical limitations that prevent patients following healthcare advice (Table 1). Participation was positive for patients and professionals (Table 1) experiencing it as engaging and collaborative. Patients felt

**Abstract P93 Table 1 Table of Themes**

<table>
<thead>
<tr>
<th>Sub-themes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>New insights</td>
<td>There was surprise among professionals at some of the issues highlighted that they were not previously aware of or of which they had not appreciated the importance. This included a greater understanding of why, due to practical or physical limitations, patients cannot always follow the medically advised course of action and mental health aspects of COPD.</td>
</tr>
<tr>
<td>Firsthand knowledge ‘from the horse’s mouth’</td>
<td>Through close interaction professionals could hear the issues that patients had and the changes they wanted made and could see the reality of their lives and the issues they dealt with (e.g. using oxygen, eating and breathing and moving around). The impact was emotional and humbling.</td>
</tr>
<tr>
<td>Appreciation of the range of patient experience</td>
<td>This was achieved through interaction with patients with a range of disease severity from mild to more severe and hearing of their differing challenges and experiences.</td>
</tr>
<tr>
<td>Hearing hard to reach voices</td>
<td>The process included the voices (either personally present or through PCRs) of patients who would not typically attend a focus group or consultation event.</td>
</tr>
<tr>
<td>Varied perspectives</td>
<td>Having a greater number of patients present elevated the patient input from token representation to a meaningful voice.</td>
</tr>
<tr>
<td>Positive experience of participation for patients and professionals</td>
<td></td>
</tr>
<tr>
<td>Collaboration, inclusivity and egalitarianism</td>
<td>Participants enjoyed working with each other in a pleasant, friendly atmosphere, with openness and sharing.</td>
</tr>
<tr>
<td>Mutual understanding</td>
<td>This came through mutual learning amongst both patients and professionals, seeing people’s reality and hearing a range of perspectives from a variety of participants. Patients learned about commissioning and professionals learned about the reality of patients’ and carers’ lives.</td>
</tr>
<tr>
<td>Engaging and stimulating</td>
<td>Active engagement helped by strong facilitation (not just sitting listening).</td>
</tr>
<tr>
<td>Freedom for ideas to emerge</td>
<td>There was no pre-determined end point and anonymous voting gave a sense of freedom.</td>
</tr>
<tr>
<td>Power to make a contribution</td>
<td>Patients felt they were contributing to a process that could result in something influential.</td>
</tr>
<tr>
<td>Being heard</td>
<td>Patients felt that all information was precious and their issues were not “lost” or “dropped” even if they did not end up in the final outcomes.</td>
</tr>
<tr>
<td>Problems with participation</td>
<td></td>
</tr>
<tr>
<td>Confusion</td>
<td>In the early stages of the workshop it took a while for some participants to fully comprehend the process.</td>
</tr>
<tr>
<td>Dot voting</td>
<td>Some participants felt this encouraged herd mentality</td>
</tr>
<tr>
<td>Physical difficulties</td>
<td>Some patients experienced mobility difficulties in a building with long corridors</td>
</tr>
<tr>
<td>Immediate benefits to patients from taking part</td>
<td></td>
</tr>
<tr>
<td>Learning about support and resources and treatments</td>
<td>This came from material presented and discussed at the workshop, and from interactions with professionals. This could have a bigger impact than leaflets or literature.</td>
</tr>
<tr>
<td>Peer support</td>
<td>Reassurance from knowing that other people have similar issues and the opportunity to share these.</td>
</tr>
</tbody>
</table>
both heard and empowered and felt all the information they offered was precious.

**Discussion** Patients found it a powerful experience and felt they made a contribution for the future. Professionals gained emotional and practical insights which inspired motivation for change in service delivery. The process tapped into strong motivations for mutual understanding. It is an effective element in developing person-centred COPD services and is transferable to other LTCs.

Supported by grant from the Health Foundation

**P94**

**PATIENT AGENDA SETTING AND CLINIC EFFICIENCY IN OUTPATIENTS: AN INDIVIDUAL RANDOMISED CONTROLLED TRIAL**

A Everden, F Early, K Homan, J Fuld. Cambridge University Hospitals NHS Foundation Trust, Cambridge, UK

10.1136/thoraxjnl-2014-206260.234

**Introduction** Most patients have issues to raise in a consultation but may not actually raise them, adversely affecting the consultation outcome. Evidence suggests that methods to help patients consider their information needs before a consultation can increase satisfaction without increasing consultation length but there is a need to assess a wider range of outcome measures and to measure consultation length accurately.

We studied the impact of a paper agenda form to prompt question asking in a respiratory outpatient clinic. The primary objective was to identify whether this increased agreement that “My doctor discussed the issues that were important to me”. Secondary endpoints included consultation length and post-consultation confidence to self-manage (0–10 scale).

**Method** Patients were randomised to receive the agenda form or usual care by blocked randomization (block size 6), stratified by consultant. Patients receiving the form had a written brief inviting them to complete it in the waiting room. PROMs were collected post-consultation. Consultations were timed by an observer outside the room. As planned in the protocol, categorical data were analysed using Fisher’s exact test and continuous data were analysed using a t-test. Exploratory analyses to assess the effects of a number of factors used mixed model ANOVA.

**Results** Groups were well matched at baseline for age, gender and respiratory diagnosis. There was no significant effect of agenda form use on the primary or secondary endpoints (Table 1). Exploratory analyses identified that in new patients (but not in follow-up patients) the form was associated with shorter consultation length (LS mean=15.2 mins) than usual care (LS mean=21.3 mins) (p = 0.017) and with lower confidence to self-manage (LS mean=6.6) than usual care (LS mean=9.2) (p = 0.001).

**Conclusion** There was no overall benefit from the form and a risk of detrimental impact on patient experience for some patients. This resonates with reports from other more complex self-management interventions that have found unexpected detrimental effects in some patients. There is a need for greater understanding of what works for whom with regard to self-management support. It cannot be assumed that the impact will be universally beneficial at best or neutral at worst.

**REFERENCE**

1 Trial reference: REC reference: 13/WA/0171

**P95**

**NON CF BRONCHIECTASIS**

CJ Baggott, E Harris, J Suntharalingam, AS Malin. Royal United Hospitals Bath, Bath, UK

10.1136/thoraxjnl-2014-206260.235

**Background** Bronchiectasis is said to affect 100/100 000, however the true prevalence is probably significantly higher. Our previous BTS bronchiectasis audit identified that a significant service improvement was required. This led to the introduction of a home intravenous antibiotic pilot, a bronchiectasis working group, and enhanced teaching and information sharing with primary care. Despite this, these patients remain poorly served both in the community and hospital.

From 2009–13 there were 330 bronchiectasis admissions to our hospital. A significant proportion of these could have been managed in the community, substantially reducing the cost to the NHS.

**Aims** We are developing an integrated bronchiectasis service between hospital and community. The vision has been to create a primary and secondary care interface, utilising the usual multidisciplinary team plus psychology and dietetic support, a ‘hospital without walls’ model and an online, multi-faceted communication tool.

**Abstract P94 Table 1** Analysis of primary and secondary outcomes measures

<table>
<thead>
<tr>
<th></th>
<th>Agenda form</th>
<th>B – 3</th>
<th>Usual care</th>
<th>N - 80</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>My doctor discussed the issues that were important to me</td>
<td>SD</td>
<td>3 (72.4%)</td>
<td>21 (28.1%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>37 (20.9%)</td>
<td>21 (70.0%)</td>
<td>0.4567</td>
<td></td>
</tr>
<tr>
<td>I raised with my doctor the issues that were important to me</td>
<td>SD</td>
<td>3 (17.6%)</td>
<td>18 (12.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>23 (25.2%)</td>
<td>18 (22.5%)</td>
<td>0.6464</td>
<td></td>
</tr>
<tr>
<td>I got the outcome I wanted from my consultation</td>
<td>D</td>
<td>2 (2.9%)</td>
<td>21 (2.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A</td>
<td>18 (23.7%)</td>
<td>24 (30.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>SA</td>
<td>54 (69.6%)</td>
<td>56 (67.3%)</td>
<td>0.4993</td>
<td></td>
</tr>
<tr>
<td>How confident do you feel that you can take steps to manage your condition as a result of today’s visit?</td>
<td>n</td>
<td>79</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>6 (11.92)</td>
<td>8 (11.34)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>10</td>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min, Max</td>
<td>3, 10</td>
<td>5, 10</td>
<td>0.795</td>
<td></td>
</tr>
<tr>
<td>Consultation duration (mins)</td>
<td>n</td>
<td>83</td>
<td>78</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>55.2 (17.69)</td>
<td>15.3 (7.58)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>13</td>
<td>14.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Min, Max</td>
<td>3, 40</td>
<td>7, 44</td>
<td>0.908</td>
<td></td>
</tr>
</tbody>
</table>

*SD* (Strongly Disagree)

**D** (Disagree)

**A** (Agree)

**SA** (Strongly Agree)

Abstract P95 Figure 1

Integrated bronchiectasis care pathway
Outputs We provided *Pseudomonas* eradication therapy (previously published – White et al. 2012) and have piloted a home intravenous antibiotic service providing treatment for exacerbations which saved 497 hospital bed days in 2013. Twenty one patients received 37 home intravenous courses; of these, 17 courses were self-administered. Overall we reduced annual bronchiectasis admissions by 30% when comparing with 2011–12, equivalent to 23 fewer admissions over the year.

We have developed an online database and clinical record tool which can be shared and updated by hospital and community alike. As well as allowing rapid communication, the database shows trend analysis, logging of microbiology/antibiotic use and is a valuable audit and research resource.

We held a recent workshop comprising CCG, community partners and hospital stakeholders. We developed a new dynamic care pathway showing a combined “community/hospital hub” which will work with partners in primary and secondary care (Figure 1). We propose that such shared care working represents a useful model for broad application elsewhere.

**Getting to grips with paediatric lung disease**

**P96** A NEW INTERACTIVE GAME DEVICE MAY IMPROVE COMPLIANCE WITH SPACER DEVICES IN VERY YOUNG CHILDREN

1CS Murray, 2S Shakir, 3TA Islam. 1University of Manchester and Central Manchester University Hospitals NHS Foundation Trust, Manchester, UK; 2Penine Acute Hospitals NHS Trust, Manchester, UK

10.1136/thoraxjnl-2014-206260.236

**Background** The use of spacers in young children is not always easy and can result in distressed children and parents. We aimed to develop and assess an interactive electronic game to improve ease of use and potentially compliance with inhalers in young children.

**Methods** The Respiratory Aid For Inhalers (RAFIhaler) consists of an electronic sensor adjacent to the outflow valve of a spacer mask, providing input every 0.1 seconds to a custom designed android application on a smartphone that is mounted, in full view of the child, on top of the spacer. The application displays on-screen characters designed to respond to correct breathing as part of a game storyline, for example by blowing away characters unfriendly to the hero (RAFI) or blowing his boat across a river. The RAFIhaler was developed through iterative testing and redesigns of hardware and software until a satisfactory final module was completed.

This module was tested on 14 children admitted to hospital with acute wheeze by an independent researcher, along with a survey to assess the child’s reaction and the parent and child’s perceived benefit from RAFIhaler. Open-ended questions allowed further feedback.

**Results** Fourteen children (2–7 yrs, 7M:7F) participated; 13 children and 14 parents completed the survey. All children stated they enjoyed the activity. Eleven children responded further; 10 (91%) felt the RAFIhaler helped them taking medication. All but one parent felt that RAFIhaler helped their child use the spacer. Of the thirteen parents who felt the RAFIhaler helped, three felt their child previously really struggled with the inhaler. Some benefits of RAFIhaler voiced by parents were: enjoyable (3); good distraction (3); made child calmer (2); helped in breathing/inspiration (3); helped child relax (3); made medication easier (3); good distraction (3); made child calmer (2); helped in breathing/inspiration (3), and was really useful at home (1). One parent felt RAFIhaler was not of benefit as they felt their child already took their inhaler well.

**Conclusions** Children universally found using the RAFIhaler with their spacer enjoyable. The majority of parents felt the RAFIhaler helped their child take their medicine. The RAFIhaler may be of use both in encouraging young children to use their inhaler/spacer, and in combatting anxiety and stress associated with their use.

**P97** DIVERGING TRENDS IN PREVALENCES OF ASTHMA, ECZEMA AND HAYFEVER IN CHILDREN AGED 9–12 YEARS

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10.1136/thoraxjnl-2014-206260.237

**Introduction** The prevalences of childhood asthma, eczema and hayfever have been recorded in our local population since 1964. The prevalence of a lifetime history of asthma rose from 4% in 1964 to a peak of 28% in 2004 before falling back to 22% in 2009. Wheeze in the past 12 months fell from 19% in 2004 to 16% in 2009. Lifetime prevalences of eczema and hay fever were approximately 5% in 1964 and had risen to 30% and 25% in 2004 and 2009. Here we present the results of our 2014 survey where we tested the hypothesis that eczema and hayfever prevalence will have followed the earlier trend for asthma and fallen since 2009.

**Methods** Children aged 9 to 12 years attending local primary schools were eligible. The questionnaire used in previous surveys was distributed to children by teaching staff, completed by parents at home and returned directly to the researchers.

**Results** Forty-seven schools were invited to participate of whom 41 took part. There were 4175 questionnaires distributed and 1378 returned (33%). The mean (SD) age was 10.9 (1.1) and 50% were boys. A lifetime history of asthma was reported in 17%. Lifetime prevalences of eczema and hay fever were 31% and 30% respectively. Wheeze in the past 12 months was reported in 13%.

**Conclusions** The proportion of children with a history of ever having had asthma and of recent wheeze continues to fall in our population at a time when the prevalences of eczema and...
hayfever remained static (see Figure). There was a low response rate in this survey and the results should be interpreted with some caution but the findings suggest different underlying mechanisms for asthma and other “allergic” conditions.

P98 A QUESTIONNAIRE SURVEY OF PARENT EXPERIENCES AND PERSPECTIVES IN CHILDREN DIAGNOSED WITH INTERSTITIAL LUNG DISEASE (ILD)

C Gilbert, A Bush, S Cunningham. chILD Lung Foundation, Wirral, UK; Royal Brompton and Harefield Trust NHS, London, UK; Royal Hospital for Sick Children, Edinburgh, UK

Background and objectives Paediatric ILD is rare, so even clinicians in large centres will see very few cases. We aimed to report the experience of parents of children diagnosed with ILD in order to inform current clinical practice, and future planning of health care.

Methods Between February 2014 and March 2014, UK based families with children given a diagnosis of ILD completed an anonymous comprehensive web-based survey developed by the chILD Lung Foundation. The survey consisted of mainly closed questions, with some open qualitative questions.

Results Of the 37 families who completed the questionnaire, 70% of participants reported that they were very happy/happy with the overall management of their child. Diagnoses: unknown 38% (n = 14), neuroendocrine hyperplasia of infancy 16% (n = 6), ABCA3 mutations 8% (n = 3), obliterative bronchiolitis (OB) 24% (n = 9), follicular bronchiolitis 3% (n = 1), pulmonary interstitial glycogenosis 3% (n = 1), surfactant protein C mutations (SP-C) 5% (n = 2) and chronic bronchiolitis 3% (n = 1). Median age at diagnosis was 35 weeks (range 1 week to 8 years), with 25 weeks the median time from first symptoms to diagnosis (range 1 week to 8 years), with 25 weeks the median time from first symptoms to diagnosis (range 1 week to 8 years). Areas of concern were (a) communication; care plans/treatment strategies were provided by a respiratory consultant in only 19 of 37 cases, (b) written information: >50% families could not recall receiving any written information on ILD or their child’s specific disease after diagnosis or information on their child’s prognosis, (c) psychological support; 91% of respondents reported significant/moderate anxiety, however psychological services were reported as offered to only 7 of 37 families, (d) feeding issues; reported by 77% of families (which is not a feature of ILD described in the literature) and these persisted in 35%, mostly long-term gastrostomy dependency and oral aversion. Qualitative responses included requests for better written communication between hospitals and training for smaller hospitals, and improved specialist nurse support of children with ILD.

Conclusion These data provide a broader understanding of parent experiences and perspectives, which should be important now for professionals looking after children with ILD as well as for those planning of future services.

P99 COMPARISON OF MULTIPLE BREATH WASHOUT USING A COMMERCIAL DEVICE AND A MASS SPECTROMETER IN SCHOOL AGE CHILDREN WITH CYSTIC FIBROSIS

J Duncan, E Raywood, A Bush, Stocks, Aurora. UCL Institute of Child Health and Great Ormond Street Hospital for Children, London, UK; Imperial College and Royal Brompton and Harefield Hospital NHS Foundation Trust, London, UK; UCL Institute of Child Health, London, UK

Background Lung clearance index (LCI) measured by multiple breath washout (MBW) is a sensitive indicator of early lung disease in Cystic Fibrosis (CF). MBW using sulphur hexafluoride (SF6) and mass spectrometry (MS) is currently the gold standard, but equipment is limited to a few centres. Although commercial devices based on SF6 have been developed, use of SF6 is expensive and restricted in some countries. Commercial devices using nitrogen (N2), which is cheaper and widely available, have been developed recently to increase accessibility of this test in research and clinical practice but have yet to be validated in children. The aim of this study was to compare values of LCI and Functional Residual Capacity (FRC) in children using the N2-MBW EasyOne Pro® LAB system (ndd Medical Technologies) and the MS (AMIS 2000, Innovision ApS).

Methods School-age children with CF and healthy controls completed MBW in triplicate on both the EasyOne Pro® and MS in random order on the same occasion. Within-subject agreement between devices for LCI and FRC was assessed by Bland-Altman analysis.

Results Of the 50 children recruited, all completed testing using MS, while 5 failed quality control on the EasyOne Pro®. Paired results from both devices were obtained in 26 children with CF (mean age [range]) 13.3y[7.8y-17.4y]) and 19 controls.

Abstract P99 Figure 1 Bland-Altman comparison of LCI and FRC between MBW devices. Limits of agreement not shown as variability of the differences are proportional to mean values.
(14.8y [12.5y–16.7y]). LCI was significantly higher in those with CF when using both devices (mean difference [95% CI], CF-controls): 2.47 [1.4;3.5] for the MS-SF₆ and 2.20 [1.2–3.2] for N₂-MBW.

There were no significant group differences between devices for either LCI (mean difference [95% CI] -0.14 [-0.45;0.16] or FRC -0.15L [-0.2;0.08]. Within-subject variability was proportional to mean values (see Figure) and ranged from 0.4–15.7% for LCI and 0.0–19.6% for FRC.

Conclusion Despite some previous reports that N₂-washout results in higher LCI values than MS-SF₆ washout, on average, we found similar values in both healthy school-age children and those with CF. Further work is required to examine causes of within-subject variability and assess validity and sensitivity over a wider age range, including preschool children, before commercial N₂-MBW devices can be confidently used in multi-centre trials.

REFERENCE
1 Aurora et al. Am J Respir Crit Care Med. 2011;183:752–8

Background Multiple breath inert-gas washout (MBW) using sulphur hexafluoride (SF₆) measured by mass spectrometry (MS), is sensitive to early lung disease in children with Cystic Fibrosis (CF) but is not widely available. To increase the accessibility of MBW, commercial devices have been adapted using nitrogen-washout (N₂-MBW). Our aim was to assess the feasibility of two commercial N₂-MBW devices as supplied by the manufacturers compared to a custom-built MS system in school-aged children.

Methods Patients with CF and controls performed MBW on three devices; the Exhalyzer®D (ECO MEDICS AG); the EasyOne Pro®LAB (ndd Medizintechnik AG) and the MS system (AMIS 2000, Innovaop ApS) on the same test occasion (order randomised). Attempts were made to obtain 3 technically acceptable runs/device (maximum 8 attempts on each).

During testing children watched a DVD and were encouraged to breathe normally. Data were analysed using the ‘clinical application’ setting for both commercial devices, and customised software for the MS. Quality control was in accordance with the ATS/ERS consensus statement and manufacturers’ guidelines.

Results 14 control (mean [range] age: 15.0 [12.5–16.7] yrs) and 18 children with CF (13.5 [7.8–17.4] yrs) were assessed. The median (range) number of runs attempted were: MS 3(3–8), Exhalyzer®D 4(3–6), EasyOne Pro®LAB 4(3–8). Average calibration time was shorter for EasyOne Pro®LAB (5 min) than either MS (11 mins) or Exhalyzer®D (12 min). Total test duration was similar between devices and dependent on disease severity.

3 acceptable MBW runs were achieved in all children using the MS, 75% with the EasyOne Pro®LAB, and 47% on the Exhalyzer®D system (see Table). Reasons for failure with Exhalyzer®D were usually due to technical/equipment problems, whereas for the EasyOne Pro®LAB these were generally associated with marked changes of breathing pattern at commencement of washout, leading to exclusion of one or more runs.

Discussion Despite use in an experienced MBW centre, our initial attempts to implement commercial MBW devices according

<table>
<thead>
<tr>
<th>Abstract P100 Table 1</th>
<th>Number (n) of technically satisfactory runs according to MBW device</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MS</td>
</tr>
<tr>
<td>n = 3</td>
<td>32</td>
</tr>
<tr>
<td>n = 2</td>
<td>0</td>
</tr>
<tr>
<td>n = 1</td>
<td>0</td>
</tr>
<tr>
<td>None acceptable</td>
<td>0</td>
</tr>
</tbody>
</table>

to manufacturers’ guidelines resulted in a relatively low success rate in schoolchildren when compared to MS. Subsequent feedback to manufacturers has led to further adaptations which should improve feasibility in future, although this has yet to be assessed in very young children.

REFERENCE
1 Robinson et al. Eur Resp J 2013

Poster sessions

P100 THE FEASIBILITY OF USING COMMERCIAL MULTIPLE BREATH NITROGEN WASHOUT DEVICES IN SCHOOL-AGED CHILDREN

1E Raywood, 1I Duncan, 5S Legg, 2P Aurora, 1J Stocks. 1Institute of Child Health, University College London, London, UK; 2Great Ormond Street Hospital and NHS Foundation Trust, London, UK

Assessment of ventilation inhomogeneity using the multiple breath washout (MBW) technique has been shown to be more sensitive than spirometry in detecting early cystic fibrosis lung disease throughout childhood. The current “gold standard” interface for school age children and adults is a mouthpiece. Although masks are better tolerated by infants and younger children, their use increases equipment deadspace which could influence measured values and hence interpretation of results. The aim of this study was to examine the effect of using a mask vs. mouthpiece on values of functional residual capacity (FRC) and the lung clearance index (LCI) derived from MBW.

Method Comparisons were performed in healthy adults. The study design incorporated repeated measures as well as interface comparison. The mask was selected to mimic measurement conditions in infants, the deadspace of 8.5 ml being approximately 1–2 ml/kg in adults. Mouthpiece (MP) deadspace was ~5 ml. Subjects were randomly allocated to group A (Mask-Mouthpiece-Mouthpiece) or group B (Mouthpiece-Mouthpiece-Mask) protocols. Each subject performed a total of 9 MBW runs, in 3 sets, each consisting of 3 runs, with a 5-minute break between each set. MBW was performed using a mass spectrometer as described previously (Aurora 2005 AJRCCM). Paired t-tests with 95% limits of agreement were used to establish repeatability (MP1 vs. MP2) and any differences between Mask vs. Mouthpiece. This study was approved by the local research ethics committee and written consent obtained from subjects.

Results Technically satisfactory comparative data were obtained on 15 occasions in 14 adults (36% males; age: 22–56 years). Respiratory rate and tidal volume were similar using either approach. Repeatability: Both FRC and LCI were repeatable using the mouthpiece ([Mean (95% CI) diff: FRC: 0.012L (-0.05;0.07); LCI: -0.1[-0.3; 0.1]); Figure 1A and B. Mask vs. Mouthpiece: FRC and LCI were both significantly higher when assessments were made using a mask compared with a mouthpiece: FRC: 0.101L (0; 0.202); LCI: 0.4 (0.2;0.7); Figure 1C and D.

Conclusion The increase in LCI when using a facemask exceeded normal within test variability in adults and could
influence interpretation of results especially if different patient interfaces are used when collecting data in younger children.

**P102**

**RECOVERY OF BASELINE LUNG FUNCTION AFTER A PULMONARY EXACERBATION IN CHILDREN WITH PRIMARY CILIARY DYSKINESIA (PCD)**

M Sunther, S Carr, C Hogg, A Bush. Royal Brompton Hospital, London, UK

10.1136/thoraxjnl-2014-206260.242

**Rationale**

Spirometry in children with cystic fibrosis (CF) frequently fails to return to baseline after treatment for a pulmonary exacerbation [Am J Respir Crit Care Med 2010; 182: 627–32]. It is unclear however how often lung function returns to previous baseline levels after treatment of a pulmonary exacerbation with intravenous antibiotics in children with PCD.

**Objectives**

To determine in children with PCD: (1) the proportion treated for a pulmonary exacerbation who recover to baseline FEV1 within 3 months and at 12 months and (2) to try to identify factors which are associated with failure to recover spirometry.

**Methods**

Cohort study using the PCD database for children at the Royal Brompton Hospital from 2003 to 2013. We selected the first clinically diagnosed pulmonary exacerbation treated with intravenous antibiotics. The best FEV1 in the 3 months after treatment and at 12 months was compared to the best FEV1 in the 12 months before treatment (baseline). Recovery to baseline was defined as any FEV1 after treatment that was greater than or equal to 90% of the baseline FEV1.

**Results**

Of the 30 children treated for pulmonary exacerbations, 77% recovered to baseline lung function within 3 months and 73% at 12 months. There were no significant differences between the responders and non-responders in terms of age, sex, ethnicity, BMI, baseline FEV1, persistent sputum infection or use of antibiotic prophylaxis or mucolytic agent (Table).

**Conclusions**

Similar to findings in CF, around 25% PCD patients fail to recover to baseline lung function after treatment of a pulmonary exacerbation with intravenous antibiotics. Better treatment strategies are needed, and the results also suggest that prevention of exacerbations would be a useful end-point in clinical trials.

**P103**

**DO CHILDREN WITH PRIMARY CILIARY DYSKINESIA HARBOUR THE SAME PATHOGENS IN THE UPPER AND LOWER AIRWAY?**

GS Marsh, NL Collins, A Bush, C Hogg, SB Carr. Royal Brompton Hospital, London, UK

10.1136/thoraxjnl-2014-206260.244

**Background**

Primary ciliary dyskinesia (PCD) is characterised by chronic nasal discharge and lower respiratory tract infections. We aimed to assess the prevalence and concordance of pathogens present in samples from the upper (UA) and lower airway (LA) of children with PCD.

**Method**

Microbiology samples from UA (naso-sinal lavage or nasal swab) and LA (sputum or cough swabs) were taken at the same time from children attending a specialist PCD centre, diagnosed on standard criteria (Eur Respir J 2009:34:1264–1276).

**Results**

70 children (30 male), median age 10.7 yrs (range 1–18), were studied. 36/70 were prescribed long term prophylactic oral antibiotics. 42 (60%) of UA samples were culture positive compared to 21 (30%) positive LA samples. The UA positive group were not statistically different in age or FEV1% pred (11.1 vs 10 yrs and 78% vs 75%). 14 patients were culture positive in both UA and LA, 10 of which had matched pathogens and 4 were unmatched. 20 were matched culture negative. The range of pathogens and where they were isolated are shown in the Table, some samples had more than one isolate.

**Conclusion**

In PCD, pathogens are isolated far more commonly from the UA than the LA. The clinical impact of these pathogens in the long term is unknown. 11 (16%) had PA in UA with only 2 of these having PA in their LA. We speculate that the UA may be, at least in some children, the source of LA infection. Clinical trials of eradication therapy after positive nasal cultures are indicated.

**Abstract P102 Table 1**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Responder (n=23)</th>
<th>Non responder (n=7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, yr</td>
<td>11.4</td>
<td>12.2</td>
</tr>
<tr>
<td>Median BMI, kg/m²</td>
<td>17.7</td>
<td>16.8</td>
</tr>
<tr>
<td>Female sex</td>
<td>4 (60)</td>
<td>4 (57)</td>
</tr>
<tr>
<td>Caucasian</td>
<td>12 (62)</td>
<td>4 (57)</td>
</tr>
<tr>
<td>FEV1 &lt; 40%</td>
<td>2 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Persistent infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>5 (22)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>1 (4)</td>
<td>1 (14)</td>
</tr>
<tr>
<td>Staphylococcus pneumoniae</td>
<td>2 (9)</td>
<td>0</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>0</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Prophylactic antibiotic</td>
<td>17 (78)</td>
<td>6 (86)</td>
</tr>
<tr>
<td>Mucolytic agent</td>
<td>7 (30)</td>
<td>1 (14)</td>
</tr>
</tbody>
</table>

**Abstract P103 Table 1**

<table>
<thead>
<tr>
<th>Micro-organism</th>
<th>UA+, LA+</th>
<th>UA+, LA-</th>
<th>UA-, LA+</th>
<th>UA-, LA-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strep pneumoniae</td>
<td>4</td>
<td>14</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>H Influenza</td>
<td>4</td>
<td>11</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Staph. Aureus</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Ps. Aeruginosa</td>
<td>2</td>
<td>9</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Moraxella</td>
<td>2</td>
<td>4</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>3</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
COMPARISON OF THE UPPER AND LOWER AIRWAY MICROBIOTA IN CHILDREN

Introduction The lower airway microbiota is important in chronic lung disease but young children do not expectorate, making longitudinal studies difficult. Upper airway samples, of uncertain reliability, are used as a surrogate. Whilst throat swabs (TS) have shown differences in the microbiota between healthy and wheezing children [PLoS One 2012;7(10):e46803], the role of cough swabs (CS) is at present unclear. This study assessed the correlation between upper and lower airway samples as a prelude to a longitudinal study. We hypothesised that upper airway samples reflect the lower airway microbiota.

Methods TS and lower airway samples (bronchoalveolar lavage fluid, bronchial brushings or both) were collected from 55 children undergoing a clinically indicated fibre-optic bronchoscopy (FOB), including CS from 35 children. Bacterial DNA was extracted for quantitative PCR (qPCR) and 454 FLX pyrosequencing of the V3-V5 region of the 16S rRNA bacterial gene. Data analysis was performed with Quantitative Insights Into Microbial Ecology (QIIME) and Phyloseq in R.

Results FOB indications included: recurrent lower respiratory tract infections (47%); cystic fibrosis (CF) (35%), and Primary Ciliary Dyskinesia (PCD) (11%). Only seven CS amplified successfully, 375,268 high quality 16S rRNA sequences were obtained from 132 upper and lower airway samples. No significant difference was seen in richness ($H = 1.352, 2\ d.f., p = 0.509$), evenness ($H = 3.942, 2\ d.f., p = 0.139$), Shannon’s diversity index ($H = 1.38, 2\ d.f., p = 0.501$), and Inverse Simpson’s diversity index ($F_{2,91} = 0.547, p = 0.581$) between TS and lower airway samples. Beta-diversity (diversity between samples) was significantly different; $\leq 7.2\%$ of variation in diversity attributed to the sampling method ($p = 0.002$). Greater variation was observed between underlying pathologies and between patients ($\leq 41.2\%$ and $68.3\%$ respectively, $p = 0.001$).

Conclusions CS are not useful for pyrosequencing. TS are predictive of the lower airway microbiota and can differentiate diseases. TS are therefore potentially useful in studying longitudinal changes in the microbiota in children with chronic lung diseases.

Safety, Feasibility and Quality of Sputum Induction in Preschool Children with Obstructive Airways Disease

Introduction Airway infection and inflammation in infancy and preschool years contribute to the pathogenesis of cystic fibrosis (CF), severe wheezing and recurrent cough. However, the use of sputum induction (SI) to guide management in preschool children with obstructive airways disease remains under-explored. We hypothesised that SI can be performed safely in preschool children with obstructive airways disease, and that samples of sufficient quality to assess infection and inflammation can be obtained.

Methods SI was performed using nebulised hypertonic saline, 3.5% if there was a history of wheeze or 7% if the child had no wheeze or a diagnosis of CF. The procedure was undertaken for 15 min and safety was assessed using pulse-oximetry and auscultation. Physiotherapy, followed by a cough/oropharyngeal swab (CS), and oropharyngeal suction (OS) were undertaken to obtain samples. All samples were analysed for bacterial culture and viral PCR, a sub-set were processed for cytology.

Results 35 children (16 males), median age 32 months (range 7–70 months) were included. 32/35 (91%) completed the procedure. The remaining three did not complete nebulisation as they became too upset, but underwent sample collection. None of the patients had any drop in oxygen saturation or increased respiratory symptoms. 16/35 (46%) patients had positive pathogen identification (22 separate bacterial or viral isolates) from SI samples obtained by OS. Only 3/35 (9%) positive isolates were identified from CS. 29/35 samples were able to be processed for cytology (see Table 1). Performance of SI was safe, feasible and well tolerated by preschool children with a range of obstructive airways diseases. Pathogen identification was significantly higher in samples obtained by OS compared to CS. Samples were of sufficient quality for cytological analysis in approximately half the patients. Future work will determine the clinical utility of SI as a non-invasive sample to guide therapy in preschool obstructive airways disease.
reported as a useful and safe technique in young children with CF, but it is not yet widely used.

Hypothesis

As part of a quality improvement initiative, we hypothesised that SI would reduce the need for BAL in school-aged CF children with deteriorating lung function and no significant bacterial growth on CS.

Methods

After CS and bronchodilator, 7% hypertonic saline was nebulised via an ultrasonic Ultraneb (DeVilbiss Healthcare) for 15 min. Spirometry was performed pre, post and at 5 min intervals throughout. Sputum was collected at 5 min intervals, and at the end of the procedure physiotherapy was performed to collect more sputum. If a child was unable to expectorate then a CS or oropharyngeal (OP) suction was performed.

Results

39 children (41% male), median age 11 years (range 5–16 years), median FEV1 85% (range 39–125%) performed SI from June 2102 to July 2014. Significant bronchoconstriction occurred in 11%. 2 adverse events occurred (vomiting and dizziness). The procedure took a mean of 90 min including equipment set up and cleaning.

34/39 (87%) expectorated a sputum sample of which 15 (38.5%) had a positive bacterial culture; only 3 of these patients (20%) grew the same organism on the preceding CS. Five patients avoided planned BAL due to a positive SI result and 2 avoided an admission for intravenous antibiotics.

Conclusion

SI is well tolerated in the majority of school-aged children with CF. It has a higher rate of positive bacterial culture than same-day CS and, in this cohort, avoided the need for bronchoscopy in a significant proportion. It is a time-consuming procedure, but based on these data, we consider that establishing SI as a clinical procedure will be a priority for our service.

Integrated knowledge in practice

P107 KNOWLEDGE OF NON INVASIVE VENTILATION IN A DISTRICT GENERAL HOSPITAL – A CAUSE FOR CONCERN?

RC Jones, A Stanton, M Juniper. Great Western Hospitals NHS Foundation Trust, Swindon, UK

Introduction

Non Invasive Ventilation (NIV) is being used more widely in acute areas by medical staff with varied training and experience in initiation and ongoing management of ventilatory failure.

Aims

To investigate doctors’ knowledge of NIV in an emergency department (ED) and general medical wards, specifically indications for use, appropriate set up and ongoing care.

Methods

An anonymous online and written questionnaire was distributed to all doctors working in general medicine and in the ED at a UK district general hospital in Spring 2014. Participants were asked to identify appropriate indications for NIV and then led through a scenario of managing a patient with COPD and decompensated ventilatory failure.

Results

40/116 (34%) of doctors responded across all grades. On a 6-point scale, self-identified confidence in managing NIV improves with seniority (5.2 (ST3+) vs 3.3 (FY1-ST2)) and past job experience in ICU (4.1 vs 3.6). Doctors were unclear about indications for NIV outside ICU/HDU. Whilst the majority (95%) correctly identified COPD exacerbations as an indicator, doctors at all grades would also use NIV for: asthma (10%), significant hypoxia (10%) and pneumothorax (3%). A fifth (18%) would start NIV without initial medical therapy. Only 55% (22/40) could identify appropriate initial ventilatory pressures (initial IPAP range 4–16, initial EPAP range 4–16). Suggesting a value for back up rate was more problematic with 43% (17/40) unable to provide any value and 9/23 (39%) suggesting an inappropriate value (range 8–18). Only 53% (22/40) could correctly alter settings when 23% (9/40) of doctors altered both IPAP and EPAP by equal amounts. 50% (4/8) ED/medical registrars could not alter settings correctly.

Conclusion

Knowledge of appropriate use of NIV is sub optimal across all grades working in the ED and general medicine in our institution, and probably reflects the increasing use of a specialist intervention in the hands of non-specialists. There are a number of doctors whose use of NIV could compromise patient safety. Urgent education across all grades is needed alongside review of how NIV is delivered in the DGH setting.

P108 ACUTE NIV PRACTICES AT A DISTRICT GENERAL HOSPITAL AND THE IMPACT OF REGULAR ELECTRONIC FEEDBACK ON PATIENT OUTCOME

TJC Ward, VW Sandoo, SF Hussain. Kettering General Hospital NHS Foundation Trust, Kettering, UK

10.1136/thoraxjnl-2014-206260.249

Background

Non-invasive ventilation (NIV) has become the standard of care for management of acute type 2 respiratory failure. There is evidence that junior doctors receive inadequate training and confidence in the use of NIV is low. National audits have shown consistent shortcomings in NIV management.

Aims

To assess initiation of acute NIV in a District General Hospital setting, to provide prompt structured feedback to doctors initiating NIV and to assess whether feedback leads to improvement.

Methods

A total of 72 acute NIV initiations were prospectively assessed between January and June 2014. Data from patient records was collected using a structured pro-forma to assess nine parameters (described below). A feedback email with total score out of nine along with brief written feedback was sent to all doctors initiating NIV.

Results

Performance was reported for each of the nine criteria; documented indication for NIV (94%); documented NIV start time (90%); BTS recommended NIV pressures achieved (61%); ABG immediately prior to therapy (93%); ABG performed at 1–2 h (75%) and at 4–6 h (79%); documented ceiling of treatment (70%) and discussion with patient/relatives (67%); improvement in pH at 6 h (58%). Use of correct pressures led to an improvement in pH in 68% compared to 43% when inadequate pressures were used (p < 0.05), pH at 6 h improved in 81% when all initial 8 parameters were met compared to 0% with a score of 4 or less (p < 0.01). There was a trend towards increased survival with higher scores.

Scores steadily improved over the first 3 months however fell at the beginning of April, coinciding with the rotation of junior doctors, rising again towards the end of the study period.

Conclusion

Better adherence with BTS guidelines led to improvements in patient outcomes. Structured feedback led to improvement in NIV initiation scores.
CAN A THEORY-INFORMED INTERACTIVE ANIMATION EXPOSURE TO COMMUNITY COPD DURING SPECIALTY TRAINING?

Introduction There has been an exponential growth in Community COPD care delivered by respiratory consultants in the last 5 years. Despite this rapid expansion, little is known about trainees’ exposure to these services even though a proportion of them will go on to work in or set up such posts after completing their training.

Methods We conducted a national survey of respiratory trainees to assess their views and experience of Community COPD, including the commissioning process which forms an integral part of establishing such services.

Results We obtained 59 responses from trainees in 12 different regions (including all four home nations): 17% less than full time (LTFT), 81% ST5+, and 53% female. Despite the majority (64%) being aware of an expansion in services locally over 86% had no experience of Community COPD and most (75%) had no direct involvement in the commissioning process. Unsurprisingly, over three quarters felt their exposure to Community COPD services during specialty training was inadequate.

Of 8 who had attended Community COPD clinics, 7 had to organise ad hoc sessions themselves. Some trainees perceived a reluctance to facilitate formal training opportunities due to hospital service delivery requirements or a concern that community services were commissioned to be consultant-delivered.

While over 22% of respondents stated that they would not apply for a consultant post that included any Community COPD sessions, this did not include any LTFT trainees and this group were also more likely to consider a job wholly based in the community [50% vs. 27%].

Discussion This survey suggests that most respiratory trainees, especially those in LTFT, would be willing to work in Community COPD roles as consultants, but are struggling to obtain adequate experience during training. It is envisaged that there will be further expansion of community respiratory services to improve patient access and to facilitate integration between primary and secondary care in the future. We suggest that training programme directors consider making experience of Community COPD a formal requirement and that the curriculum is updated to better reflect the needs of trainees.

Acknowledgements We would like to thank the Respiratory Trainees’ National Support Team, and the 8 who volunteered to have Community COPD sessions for the first time.

Thorax 2014;69(Suppl 2):A1–A236 A125

P110 EXPOSURE TO COMMUNITY COPD DURING SPECIALTY TRAINING

1G Hoskins, 2B Williams, 3J Murray, 5S Skar, 4M McGhee, 6G Gauld, 7G Brown, 8S Treweek, 9F Sniehotta, 10LCameron, 11A Sheik, 12S Hagen. 1University of Stirling, Stirling, Scotland, UK; 2University of Dundee, Dundee, Scotland, UK; 3Asthma UK Scotland, Edinburgh, Scotland, UK; 4University of Aberdeen, Aberdeen, Scotland, UK; 5University of New South Wales, Sydney, Australia; 6University of Dundee, Dundee, Scotland, UK; 7Asthma UK Scotland, Edinburgh, Scotland, UK; 8University of Aberdeen, Aberdeen, Scotland, UK; 9University of Newcastle, Newcastle, England, UK; 10University of California Merced, California, USA; 11University of Edinburgh, Edinburgh, Scotland, UK; 12Glasgow Caledonian University, Glasgow, Scotland, UK

10.1136/thoraxjnl-2014-206260.251

Background Participation in regular physical activity improves aerobic fitness and well-being. For people with asthma the benefits also include reduced hospital admissions, absenteeism, medication use, and improved ability to cope with the disease. However, although people with asthma can exercise safely, children and young people with asthma are less likely to be physically active than their peers. Integrating the principles of user-centred design and the MRC Framework for Complex interventions a theoretically-informed interactive animation was developed to encourage young people aged 12–18 years with asthma to engage in physical activity.

Methods A mixed-methods two stage approach was used. In stage 1 a user group (young people with asthma, parents, health professionals) used online consultation and discussion methods to inform the development of the intervention in a highly iterative manner (modelling). The theoretical basis for the intervention was then refined and converted into a 3D animation with accompanying action plan and volitional help sheet. In stage 2 a web-based Interactive Modelling Experiment evaluated effectiveness in three key areas: knowledge about asthma, inhaler use, and intention to increase physical activity. One-to-one interviews and focus groups were used to evaluate the acceptability of the animation and whether the theoretical basis was effective.

Results Twenty three people were recruited to the user group. Facilitated by multiple online consultation methods the group was highly engaged throughout. Fifty-three individuals were randomised online to receive the intervention or control; 26 completed follow-up questionnaires (49%). The pilot online experiment supported the evidence base for the intervention but demonstrated that recruitment methods and loss to follow-up need addressed before a future trial. Though not powered to detect an effect on intentions and behaviour, the study revealed an impact on intentions to be active (increase) and on safe inhaler use (decrease). Qualitative feedback was positive across all groups, the intervention being well received and regarded as understandable, meaningful, engaging and potentially very useful within an asthma review.

Conclusion We have developed a high quality, two part intervention regarded as meaningful, acceptable and potentially useful. Future work is needed to establish whether acceptability levels and perceived effectiveness translate into behaviour change.
Background and method Intercostal chest drain (ICD) insertion has long been considered a core skill for the general physician to master. The NPSA alert in 2008 highlighted potential hazards associated with this procedure, whilst recent guidelines¹ advocate the use of thoracic ultrasound to reduce complications. These developments have occurred at a time when trainees report a growing lack of confidence in their clinical experience and procedural capabilities, alongside a decline in training opportunities² that might address the latter concern. Nonetheless, competence in ICD insertion remains a compulsory or highly desirable procedural skill to acquire on a number of UK specialty training curricula including that for (general) internal medicine.

We carried out a survey of consultants and trainees who contribute to general medical services in hospitals across the Thames Valley region. This survey assessed factors including physicians’ attitudes towards ICD insertion; prior and recent procedural experience; training opportunities; and clinical knowledge.

Results 90 clinicians (26 consultants; 41 registrars (ST3+); 23 core medical trainees (CT1/2)) responded to the survey. Most clinicians (94% of responses) felt that placing >5 ICDs was necessary to attain initial competence at the procedure; before continuing to place >5 ICDs on an annual basis in order to maintain that competence (78% of responses). However, only 17% of medical registrars surveyed reached this basic combined standard. Other key findings are summarised in Table 1.

Conclusion Our findings demonstrate a disparity between clinical reality and the expectations junior doctors and consultants have of the physician in training with regards to ICD competence. Most trainees cannot achieve the number of procedures they feel are required to attain independence, nor maintain that independence on an annual basis; whilst access to training in thoracic ultrasound is limited outside certain specialties. This inexperience is manifest in variable clinical understanding and procedural confidence.

Consideration needs to be given as to how medical training programmes might address these issues, and whether ICD insertion is even a skill that all general physicians can maintain competence in performing in the modern clinical environment.

REFERENCES
1. Thorax 2010;65 Suppl 2:i61–76

Poster sessions

P111 PROCEDURAL EXPERIENCE, TRAINING OPPORTUNITIES AND ATTITUDES TOWARDS INTERCOASTAL CHEST DRAIN INSERTION: VARIATIONS BETWEEN CONSULTANTS, TRAINEES AND MEDICAL SUB-SPECIALTIES

1J P Corcoran, 2R J Hallifax, 3A Takkar, 1P Posladis, 4A Sykes, 1NM Rahman. 1Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Trust, Oxford, UK; 2Department of Respiratory Medicine, Buckinghamshire Healthcare NHS Trust, Aylesbury, UK; 3Department of Respiratory Medicine, Royal Berkshire NHS Foundation Trust, Reading, UK

10.1136/thoraxjnl-2014-206260.252

Abstract P111 Table 1 Sample of key findings from a survey of 90 clinicians relating to intercostal chest drain (ICD) insertion. Answers to clinical questions were derived using BTS Pleural Disease Guidelines (2010) and consensus between three respiratory physicians specialising in pleural disease

<table>
<thead>
<tr>
<th>ATTITUDES (answers on a Likert-type scale; 1 = strongly agree to 5 = strongly disagree)</th>
<th>Consultants (ST3+)</th>
<th>SHOs (CT1/2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;ICD insertion is a core skill that all general medical registrars should be able to perform&quot;</td>
<td>1.9 ± 1.3(SD)</td>
<td>2.3 ± 1.2</td>
</tr>
<tr>
<td>&quot;ICD insertion is a specialist skill only a select group of physicians should perform in future&quot;</td>
<td>3.5 ± 1.2(SD)</td>
<td>3.1 ± 1.2</td>
</tr>
<tr>
<td>TRAINING and EXPERIENCE (trainees only)</td>
<td>SpRs</td>
<td>SHOs</td>
</tr>
<tr>
<td>None</td>
<td>20 (49%)</td>
<td>5 (22%)</td>
</tr>
<tr>
<td>&lt;5</td>
<td>14 (34%)</td>
<td>12 (52%)</td>
</tr>
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<td>5 to 10</td>
<td>5 (12%)</td>
<td>5 (22%)</td>
</tr>
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<td>10 to 20</td>
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</tr>
<tr>
<td>Yes</td>
<td>22 (54%)</td>
<td>12 (52%)</td>
</tr>
<tr>
<td>No</td>
<td>19 (46%)</td>
<td>11 (48%)</td>
</tr>
<tr>
<td>Yes + qualification</td>
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<td>0 (0%)</td>
</tr>
<tr>
<td>Yes, not qualified</td>
<td>13 (32%)</td>
<td>5 (22%)</td>
</tr>
<tr>
<td>No</td>
<td>23 (56%)</td>
<td>18 (78%)</td>
</tr>
<tr>
<td>CLINICAL KNOWLEDGE (best of 5 questions, trainees only)</td>
<td>SpRs</td>
<td>SHOs</td>
</tr>
<tr>
<td>Scenario 1: Small (≤2cm) asymptomatic 1° pneumothorax in 22yo male correct answer: observation only</td>
<td>Correct</td>
<td>11 (27%)</td>
</tr>
<tr>
<td>Incorrect</td>
<td>30 (73%)</td>
<td>21 (91%)</td>
</tr>
<tr>
<td>Scenario 2: Patient with suspected pleural infection and &quot;x&quot; marked in radiology as site for aspiration by medical team on ward. correct answer: repeat USS to identify safe site and immediate aspiration +/− ICD</td>
<td>Correct</td>
<td>25 (61%)</td>
</tr>
<tr>
<td>Incorrect</td>
<td>16 (39%)</td>
<td>4 (17%)</td>
</tr>
</tbody>
</table>

P112 SPEECH AND LANGUAGE THERAPY BY SKYPE™ FOR VOCAL CORD DYSFUNCTION AND CHRONIC COUGH

SF Lillie, I Haines, A Vyas, SJ Fowler. Lancashire Teaching Hospitals Trust, Preston, UK

10.1136/thoraxjnl-2014-206260.252

Introduction The Airways Service at Royal Preston Hospital receives tertiary referrals from across the UK. When a diagnosis of vocal cord dysfunction (VCD) or chronic cough is made and speech and language therapy (SLT) required, patients undergo weekly therapy (minimum four sessions), which some may struggle to attend due to pre-existing commitments and/or travel time. As SLT typically does not require ‘hands-on’ therapy we felt that Skype™ videoconferencing may be a useful mode of treatment delivery. We present our initial experience of this service.

Methods A six-month pilot was completed whereby patients were offered SLT over Skype. Prior to therapy all patients were seen by the respiratory consultant and speech and language therapist for assessment and flexible laryngoscopy. Patients required confidential webcam access and proficiency. Symptom questionnaires were completed pre and post therapy (for VCD
the 12 item VCDQ; for chronic cough the 19-item LCQ), and patient satisfaction questionnaires and flexible laryngoscopy performed post therapy.

Results Eleven people have completed SLT over Skype to date, and all demonstrated improvement in symptoms following therapy. Patients with VCD showed a decrease in score on the VCDQ from median (range) 48 (12–53) pre therapy to 40 (7–42) post therapy [minimal clinical important difference (MCID) 5]. Patients with chronic cough showed an increase on the LCQ from median (range) 6.4 (4.6–8.2) pre therapy to 12.2 (10–14.6) post therapy (MCID 1.3). Improvements in laryngeal tension and sensitivity were noted in all cases. All patients gave positive feedback in their patient satisfaction questionnaire scoring “very satisfied” or greater. On three occasions Skype connection problems delayed sessions by a few days.

Conclusions Virtual consultations provide the opportunity to treat patients in a more time efficient and practical way, and improvements in patient-reported symptoms and laryngeal appearances were similar to those of patients attending therapy sessions in chest clinic. This data gives support to pursue formalised tariffs for a specialised telehealth service. We feel that Skype should continue as a regular therapy option for patients and other members of the multi-disciplinary team (MDT) should consider this method of therapy delivery.

**THE USE OF LOCAL ANAESTHESIA IN IMPROVING THE PATIENT EXPERIENCE OF ARTERIAL BLOOD GASES: STUDENTS AND TRAINERS ARE STILL NOT GETTING THE MESSAGE**

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Background BTS guidelines (2008) states that “local anaesthesia (LA) should be used for all arterial blood gas (ABG) specimens except in emergencies” as it improves the patient experience. A survey conducted in 2012 revealed only 5% of junior doctors regularly use LA with ABGs. We were interested to determine if this has improved and establish whether medical students are being orientated to this practice.

**Methodology** This is a multicentre prospective study. A questionnaire survey was distributed to 4th year medical students and junior doctors affiliated with UCL Medical School. Questions related to their actual experiences of using LA with ABGs and barriers to using LA.

**Results** 94 medical students completed the questionnaire. Students used LA 17% of the time out of 54 supervised procedures. 29% were actively discouraged from using LA by their supervising doctor. 10% felt the general culture amongst supervising doctors was resistant to using LA.

Amongst the 86 surveyed doctors, 91% never or rarely (<10% of the time) used LA, 5% sometimes (~25% of the time) and 3% used it regularly (>75% of the time). 65% of doctors were not aware that LA was advised in national guidance. 40% of respondents felt it would not reduce the pain of the procedure and 38% did not know the technique involved of using LA.

**Conclusion** The use of LA is extremely poor as has been found previously. The reasons reflect a lack of awareness and a culture that is experienced from the moment the enter the clinical environment as medical students. In order to improve the patient experience we have introduced an intervention at the level of the medical school and junior doctor teaching which includes mandatory training and encouraging affiliated trusts to help create a culture where giving LA is the norm.

We will fully report on the results and success of our interventions.

**REFERENCES**


**WHAT SKILLS, EXPERIENCE AND TRAINING ARE NEED TO WORK IN INTEGRATED RESPIRATORY SPECIALIST ROLES AND HOW CAN WE ROLL THESE POSTS OUT IN THE UK?**

NJ Roberts, M Ward, S Patel, J Yorke, J Williams, R Walters, M McKevitt, S Edwards, Glasgow Caledonian University, Glasgow, UK; Sherwood Forest Hospitals, Sutton in Ashfield, UK; Kings College Hospital London, London, UK; University of Manchester, Manchester, UK; Halton General Hospital, Runcorn, UK; Mansfield Community Hospital, Mansfield, UK; British Lung Foundation, London, UK; British Thoracic Society, London, UK

Aims There is an increased drive towards healthcare integration in the UK (UK) to adapt to new health care needs. In response to this, new ways of delivering care have been developed such as the provision of integrated respiratory specialists. This project set out to describe these roles, the key skills needed and how junior staff can aspire to these roles.

**Methods** Semi-structured telephone interviews with 12 integrated care specialists or those currently working with integrated respiratory care teams were undertaken to explore and discuss the role of integrated respiratory specialists.

**Results** Nine integrated specialists were interviewed (6 physicians, 2 nurses, 1 physiotherapist). One Specialist Trainee (SrR), a general practitioner (GP) and a pharmacist were also interviewed. The integrated role was variable for participants; most were involved in MDTs, education for staff and developing guidance, with some involved in community or virtual clinics. Physicians were more likely to be involved in Acute Medical Unit reviews. Five interviewees had two joint leads with either two physicians, or a physician and a nurse.

Key skills identified by the interviewees included respiratory specialist knowledge, prior primary care experience as well as knowledge of the NHS, commissioning and social services processes. Specific training included conflict management, advanced communication and research and evaluation skills (health economics and service evaluation). Three areas were highlighted to support the establishment of new posts: clear details about the posts and standards of care; embedding integrated care into training; increasing visibility of this new area and gaining support from appropriate organisations.

**Conclusions** Interviewees highlighted that existing posts should be used as exemplars to provide junior staff with more information about these roles. Greater collaboration with professional societies such as the BTS, ERS and PCRS for education as well as to promote and advance these new potential career pathways should be undertaken.

Funded by the British Thoracic Society.
Clinical delivery of pulmonary rehabilitation

**P115 EVIDENCE OF POST-CODE LOTTERY IN THE AVAILABILITY OF PULMONARY REHABILITATION (PR) IN THE EAST OF ENGLAND (EOE)**

1J Jongejan, 2R Barlow, 1EoE Respiratory Strategic Clinical Network, Cambridge, UK; 2PROVIDE, Chelmsford, UK

10.1136/thoraxjnl-2014-206260.255

Introduction and objectives Pulmonary Rehabilitation (PR) should be made available to all suitable people with COPD and various other chronic respiratory conditions.1 Recommendations have been made on the quality of the provision and commissioning of PR. Indicative benchmark rates have been developed2 to support commissioners determine local need. We compared the local availability of PR across the EoE.

Methods A regional PR group was formed to promote best practice, offer peer support and enable improvements through the collection of meaningful regional data. Data was collected from 17/18 (94%) providers on the number of PR places commissioned per CCG(s). In 13 providers PR was commissioned. In 4 providers PR was provided under Payment by Result and in the collection of meaningful regional data. Data was collected from 17/18 (94%) providers on the number of PR places commissioned per CCG(s). In 13 providers PR was commissioned. In 4 providers PR was provided under Payment by Result and these maximum capacity was calculated using a 1:8 staff:patient ratio. Comparison was made between availability and indicative benchmark rates in each locality. Where providers covered more than one CCG, data was aggregated for analysis purposes.

Results In the EoE the average number of people expected to benefit from PR/year is 11,748 (192 per 100,000 population/year).3 However, our data showed a maximum of 6,165 PR places were available (101 per 100,000/year). Local provision varied 2.8-fold across the CCGs, ranging between 60 per 100,000/year and 171 per 100,000/year. This was not explained by local variation based on actual provision/local target varied 3.1-fold [27.2%-85.4%].

Conclusions There was evidence of post-code lottery in the provision of PR with a 2.8-fold variation between localities. There was also an overall insufficient availability throughout the region (average 52.5% of the proposed target). Provision compared to local targets varied more than 3-fold. Provision was less than 50% of local target in 50% of localities. This data will be shared with local commissioners and providers, so that this deficiency can be addressed.

REFERENCES


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**P116 DIFFERENCES IN PATIENT OUTCOMES BETWEEN A 6, 7 AND 8 WEEK PULMONARY REHABILITATION PROGRAMME**

1R Barlow, 1E Easton, 2L Andrews. 1Provide, Chelmsford, UK; 2University of Essex, Colchester, Essex

10.1136/thoraxjnl-2014-206260.256

**Background** NICE (2010) recommend that pulmonary rehabilitation programmes run between 6–12 weeks in duration. To date, there is no consensus in the research to the optimal duration of a programme.

**Objectives** To investigate changes in patient outcomes over time for 6, 7 and 8 week pulmonary rehabilitation programmes.

To investigate differences in patient outcomes between 6, 7 and 8 week pulmonary rehabilitation programmes in order to identify optimal duration.

**Setting:** Community based pulmonary rehabilitation programmes in the East of England.

Participants: In total 363 participants completed one of the three pulmonary rehabilitation programmes. Patients with a chronic respiratory condition showing a commitment to the pulmonary rehabilitation programme and had no contraindications to exercise were included.

**Intervention:** Pulmonary rehabilitation twice a week for 6, 7 or 8 weeks.

Main outcome measures: St Georges Respiratory Questionnaire (SGRQ), Clinical COPD Questionnaire (CCQ), Hospital Anxiety and Depression Score (HADS) and Incremental Shuttle Walk Test (ISWT).

**Results** The t-tests indicated a statistically significant improvement in patients’ exercise capacity (measured by the ISWT) for all 3 programmes (p < 0.001). Patients attending the 8 week programme improved the most (increasing by 74.43 metres), followed by the 6 then 7 week programme (increasing by 57.24 and 48.96 metres respectively). The minimal clinically significant change for the ISWT is 47.5 metres so all the programmes improved by a clinically significant amount. When controlling for baseline ISWT scores the 8 week programme showed statistically significant improvements on post-rehabilitation ISWT scores above the 6 or 7 week programmes (F(2,341) = 6.72, p = 0.001).

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### Abstract P116 Table 1 Meas (SDs) and T-tests for all measures pre and post intervention for each programme

<table>
<thead>
<tr>
<th></th>
<th>6 week pulmonary rehabilitation</th>
<th>7 week pulmonary rehabilitation</th>
<th>8 week pulmonary rehabilitation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
<td>Pre</td>
</tr>
<tr>
<td><strong>Measure</strong></td>
<td>Mean (SD)</td>
<td>t (df)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>SGRQ</td>
<td>55.44 (17.48)</td>
<td>54.27 (16.93)</td>
<td>1.17 (129)</td>
</tr>
<tr>
<td>ISWT</td>
<td>110.13 (79.47)</td>
<td>168.37 (86.39)</td>
<td>-14.20 (131)**</td>
</tr>
<tr>
<td>CCQ</td>
<td>2.87 (1.36)</td>
<td>2.75 (1.20)</td>
<td>1.27 (135)</td>
</tr>
<tr>
<td>HADS Anxiety</td>
<td>6.17 (4.23)</td>
<td>6.13 (4.11)</td>
<td>0.14 (135)</td>
</tr>
<tr>
<td>HADS Depression</td>
<td>7.04 (3.75)</td>
<td>6.62 (3.67)</td>
<td>1.75 (135)</td>
</tr>
</tbody>
</table>

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**Poster sessions**
Conclusions Findings show that greatest improvements in terms of exercise capacity may be seen from 8 week pulmonary rehabilitation programmes, but that improvement for the ISWT can be obtained from 6, 7 or 8 week programmes.

REFERENCES

Abstract P117 Figure 1

Introduction and objectives Pulmonary Rehabilitation (PR) should be made available to all suitable people with COPD and various other chronic respiratory conditions. An abundance of guidelines has been produced making recommendation on the quality of both the provision and commissioning of PR. Limited data is available on PR programme adherence rates and most study rates post COPD exacerbation. Recent IMPRESS Guidance suggested a target completion rate of 75% of offered sessions and stated the national average being less than 50%. Our aim was to get an accurate regional perspective of completion rates of all PR service providers to use as a lever for improvement.

Methods Prior to 2013/14 a regional PR group was formed to promote best practice, offer peer support and enable improvements through the collection of meaningful regional data. A data set was agreed and defined and during 2013/14 quarterly data was collected. Referring GPs were also asked to provide recent spirometry results, a dyspnoea score, exacerbation frequency and current medication were collected. An assessment was made based on the information provided as to whether the patient could be listed immediately for pulmonary rehabilitation, whether further assessment was required, or whether the referral was inappropriate.

Results A sample of 250 GP referral forms out of a total of 545 patients referred did not have COPD based on the spirometry results supplied. Compared with the baseline referral rate to PR from secondary care consultants, the rate of referral from GPs improved from 37% to 91%. 24% had a completion rate of 75% or above.

Conclusions Completion rate varied widely with a 2.5-fold variation between the best and worst performers. 34.8% of referrals needed further assessment and 24.4% were inappropriate. 22.4% of all referrals were evaluated of which 51% of patients were male and the mean age was 69 years (range 31–90). 40.8% of GP referrals could be listed immediately for PR, 34.8% of referrals needed further assessment and 24.4% were inappropriate. 22.4% of all patients referred did not have COPD based on the spirometry results supplied. Compared with the baseline referral rate to PR from secondary care consultants, the rate of referral from GPs

Abstract P118 Figure 1

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Introduction Referring suitable patients for Pulmonary Rehabilitation (PR) has formed part of the Quality and Outcomes Framework (QOF) reward for General Practitioners (GPs) in Wales since April 2013. Patients with Chronic Obstructive Pulmonary Disease (COPD) that have a Medical Research Council (MRC) dyspnoea score of 3 or above, or those with an MRC score of 2 and recently discharged from hospital for COPD are eligible. We sought to determine the impact of this change on the referral pattern to our PR programme, which traditionally had only accepted referrals from secondary care respiratory consultants.

Methods A standardised form was prospectively designed and distributed to enable primary care providers to refer suitable patients to the PR programme. Data on patient demographics, respiratory diagnosis, co-morbid conditions, MRC dyspnoea score, exacerbation frequency and current medication were collected. Referring GPs were also asked to provide recent spirometry values for patients that were referred. An assessment was made based on the information provided as to whether the patient could be listed immediately for pulmonary rehabilitation, whether further assessment was required, or whether the referral was inappropriate.

Results A sample of 250 GP referral forms out of a total of 545 were evaluated of which 51% of patients were male and the mean age was 69 years (range 31–90). 40.8% of GP referrals could be listed immediately for PR, 34.8% of referrals needed further assessment and 24.4% were inappropriate. 22.4% of all patients referred did not have COPD based on the spirometry results supplied. Compared with the baseline referral rate to PR from secondary care consultants, the rate of referral from GPs

Abstract P118 Figure 1

REFERENCES
1 NICE. COPD: management of COPD in adults in primary and secondary care. 2010 [http://www.nice.org.uk/guidance/CG101]
showed a sharp increase, particularly toward the end of the financial year (difference in slope -0.77 (95% CI -2.16 to 0.61) versus 9.53 (6.03 to 13.03), p < 0.0001) [Figure]. 36.8% of patients were found to be on off-label inhaled therapy for COPD.

Conclusion The number of referrals to PR increased significantly following inclusion in QOF. The majority of the referrals from GPs either require further evaluation or are inappropriate. The spirometry data suggests there is a high misdiagnosis rate of COPD in primary care.

P119 IS A PRACTICE INCREMENTAL SHUTTLE WALK TEST NEEDED FOR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ADMITTED TO HOSPITAL FOR AN ACUTE EXACERBATION?

1V Johnson-Warrington, 2K Mitchell, 2S Singh. 1University Hospitals Coventry and Warwickshire, Coventry, UK; 2Centre for Exercise and Rehabilitation Science, University Hospitals of Leicester NHS Trust, Leicester, UK

Introduction The Incremental Shuttle Walk Test (ISWT) assesses exercise capacity in patients with Chronic Obstructive Pulmonary Disease (COPD). Guidelines suggest 2 ISWTs should be performed. However, in patients who have been admitted with an acute exacerbation, it is unknown if 2 ISWTs are required.

Objective To investigate if a practice ISWT is needed for inpatients with an acute exacerbation of COPD.

Methods Patients admitted to hospital with an acute exacerbation completed 2 ISWTs, prior to discharge. Patients gave written informed consent (ISRCTN84599369) and were included if they used the same oxygen and mobility aid (if any) between tests.

Results 37 inpatients with COPD (19 male) were included: mean (SD) 67.89(8.02) years with BMI 24.66(6.60), FEV1 was 1.07(0.44)(41.94(13.72)% predicted), FEV1/FVC 47.11 (11.70)% median (inter-quartile range) MRC dyspnoea grade 4 (3–5), resting Borg breathlessness 2(0.5–3) and 11 had never exercised.

Participants achieved ISWT1 92.16(97.67)m, post-HR 108.64 (14.33), post-SaO2 90.33(3.89), post-Borg breathlessness 4(3–5) and post-Rated Perceived Exertion (RPE) 13(13–15). There was a statistically significant increase of 14.59(29.12)m for ISWT2 (p < 0.05) but no significant differences in HR, SaO2, Borg or RPE. Bland Altman plot (Figure 1a) shows acceptable agreement between the ISWTs.

When calculating Endurance Shuttle Walk Test (ESWT) level at 85% VO2 peak as estimated from ISWT1 and ISWT2, there was a significant increase of one level (p < 0.05).

Multiple regression explained 92.1% of the variance (F(9–18)0 < 0.001, R2 0.921) of the difference between ISWTs using FEV1%predicted, FEV1/FVC%, BMI, exercise history, resting SaO2, ISWT1 distance, ISWT1 post-SaO2, post-Borg and post-RPE (p < 0.05). Using the multiple regression equation to calculate predicted ISWT2, there was good agreement (Figure 1b) and no significance difference between this and actual ISWT2 (0.04 m, p > 0.05).

Conclusions There was a small but statistically significant increase between ISWTs, which was below the minimal clinically important difference. However, this difference changed the ESWT level for some patients which would have had consequences for exercise prescription.

This exploratory work has shown that we can predict the difference between ISWTs using a multiple regression equation which could substitute the need for a second ISWT; this needs to be confirmed prospectively. A practice ISWT is therefore not necessarily needed in this patient group.

P120 SHARED DECISION MAKING IN A PULMONARY REHABILITATION SETTING FOR COPD PATIENTS

CL Madsen, J Tomkinson. Bristol Community Health, Bristol, UK

Title: Evidence of Shared Decision Making in a COPD education and supported self-management group setting.

Authors: Jen Tomkinson, Advanced Respiratory Physiotherapist, Specialist Services (Long Term Conditions) Bristol Community Health CIC; Claire Madsen, Consultant Physiotherapist; Bristol Community Health CIC

Introduction and objectives Shared Decision Making (SDM) is a patient centred, research based approach which empowers patients to work in partnership with health professionals to manage their long term conditions. There is no published data of
Poster sessions

Abstract P120 Table 1

<table>
<thead>
<tr>
<th>Shared Decision Making Descriptor</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of patients felt that the clinician addressed what was important to them at their appointment</td>
<td>90%</td>
</tr>
<tr>
<td>% of patients felt that their expectations were met during their appointment</td>
<td>90%</td>
</tr>
<tr>
<td>% of patients felt able to make a decision that was right for them with their clinician</td>
<td>90%</td>
</tr>
<tr>
<td>% of patients felt that the clinician shared their expertise with them enough to help the patient feel that they were making the right choice for them</td>
<td>90%</td>
</tr>
<tr>
<td>% of patients felt that they fully understood the pros and cons of each treatment option</td>
<td>88%</td>
</tr>
<tr>
<td>% of patients were happy that there was enough time to help them feel confident in making their treatment choice</td>
<td>90%</td>
</tr>
<tr>
<td>% of patients reported that the information they received led to them changing their decision regarding treatment choices</td>
<td>45%</td>
</tr>
<tr>
<td>% of patients felt more confident to manage their condition after attending an education and self-management group</td>
<td>90%</td>
</tr>
<tr>
<td>% of patients reporting that they now do things differently as a result of their consultations showing changes in lifestyle and health behaviours</td>
<td>95%</td>
</tr>
<tr>
<td>% of patients reporting high confidence scores in self-managing their condition at the start of the group</td>
<td>5%</td>
</tr>
<tr>
<td>% of patients reporting high confidence scores in self-managing their condition at the end of the group</td>
<td>90%</td>
</tr>
</tbody>
</table>

shared decision making within group education for COPD patients to date.

Methods 20 semi-structured interviews were performed to obtain quantitative and qualitative data from COPD patients who had recently attended an education and supported self-management group held over six weeks. Data collection was performed by allied health professionals who do not work in the COPD clinic. Questionnaires were reviewed and amended by a Questionnaire Users, Interviews and Surveys group prior to use.

Results (see Table) Qualitative feedback provided by patients supported the quantitative results and ranged from neutral to highly positive in nature, with several patients reporting significant impact on their quality of life, confidence in supported self-management, increased exercise participation, physical function, and social participation.

Conclusion COPD patients attending a six weeks education and supported self-management group reported significant understanding of information, increased understanding of treatment options, and increased education and ability to self-manage.

REFERENCES
Collins A (2011)The Kings Fund Report: ‘Making shared decision-making a reality: No decision about me, without me’

P121 SPEECH AND LANGUAGE THERAPY IN PULMONARY REHABILITATION: THE IMPLICATION OF EDUCATION SESSIONS ON DYSPHAGIA MANAGEMENT
SF Lillie, J Haines, A Vyas, SJ Fowler. Lancashire Teaching Hospitals Trust, Preston, UK
10.1136/thoraxjnl-2014-206260.261

Introduction Pulmonary rehabilitation (PR) programs use multi-disciplinary teams to optimise physical and social functioning of patients with chronic respiratory impairment. Such patients demonstrate an increased prevalence of oropharyngeal dysphagia as a consequence of impaired co-ordination between respiration and swallowing function. Often patients will not be aware of the warning signs of dysphagia and unfortunately will not be seen by a speech and language therapist until they are admitted to hospital. We report the outcomes of a pilot scheme whereby such patients underwent education, assessment and treatment for dysphagia as part of their PR programme.

Methods The pilot scheme ran between June 2013 and May 2014. Intervention consisted of: (1) a one hour group education session on the signs, symptoms and risks of dysphagia; (2) screening for oropharyngeal dysphagia; and (3) individual out-patient management in Airways Clinic. The majority of patients attending the education sessions had a diagnosis of Chronic Obstructive Pulmonary Disease (COPD).

Results The education programme was delivered to 72 patients, and resulted in a significant improvement in dysphagia knowledge. The average score pre education was 3/11 and post education was 8/11. Fourteen patients (19%) exhibited or reported symptoms of dysphagia. Of these two patients were overtly aspirating and required food/fluid modification and seven patient's required instrumental assessment in the form of fibre endoscopic evaluation of swallowing (FEES). During FEES, three patients showed penetration of food/ fluids and were at risk of silent aspiration. These patients attended for further SLT where diet/ fluids were modified, posture was assessed and dysphagia therapy was introduced.

Conclusions Dysphagia education and management of patients in PR can contribute the early identification, patient awareness and self-management of dysphagia. We have confirmed that undiagnosed but clinically important dysphagia is present in patients undergoing PR. We are investigating whether improved dysphagia knowledge and early identification of dysphagia symptoms leads to reduced exacerbations and improved quality of life.

P122 A SURVEY OF PULMONARY REHABILITATION (PR) SERVICES IN KENT, SURREY, SUSSEX (KSS)
J-P Crofton-Biwer, E Lazar, J Bott. Kent Surrey Sussex Academic Health Science Network, Crawley, UK
10.1136/thoraxjnl-2014-206260.262

Introduction and objectives There is no agreed model for Pulmonary Rehabilitation (PR) and wide variation in services exists. A regional PR network was established 4 years ago, with the aim to drive up standards and reduce variation. An audit was undertaken of all PR services in the region to determine costs of services and factors influencing variance.

Method In June 2013 e-questionnaires were sent to all 16 known PR providers; fifty questions requested average annual/ weekly data including: staff pay bands, time spent on exercise, education, administration, travel and other identifiable costs, numbers failing to complete (drop-out) and clinical outcomes. All costs were calculated in terms of cost-per-patient. Providers
were assured actual costs and their identity would not be revealed.

Results

1. PR regionally serviced 3712 patients annually
2. Many providers total per patient costs were above the national tariff
3. Administration formed the highest share of providers total cost (24%) 
4. Administration time per patient per course varied widely (1 – 14 h)
5. There was a wide range of drop-out, 10 – 42%, mean 23% 
6. The mean (£76) and range (£23–£255) of drop-out cost per patient was high, rising at an ever increasing rate for every dropout (Figure) 
7. Both larger patient numbers and rolling programmes were associated with higher per patient cost, the latter accountable to higher admin costs surpassing savings in exercise session costs. 
8. Inconsistent reporting of clinical outcome data by providers.

Conclusion Our analysis demonstrates significant variation in the makeup of providers’ individual costs, with the majority of the variation between providers’ total cost per patient attributed to dropouts. Administration and drop-out were the greatest contributory factors to higher service costs. Higher cost was associated with larger patient numbers and rolling programmes.

Discussion Insufficient clinical outcome data were received to make any meaningful comparison of cost with outcome. Further work in this area is therefore required. Providers expected that providing services for larger numbers of patients and using rolling programmes would have lower costs, but the reverse was true. Administration costs for PR are very significant and may frequently be the key driver behind cost differences.
DO WE NEED A PRACTICE INCREMENTAL SHUTTLE WALK TEST FOR PATIENTS WITH INTERSTITIAL LUNG DISEASE?

**Objective** To investigate if a practice ISWT is needed for patients with ILD referred to PR.

**Methods** Patients with ILD recorded on our PR database, who attended a PR assessment and performed 2 ISWTs, were selected. Patients were included if they had 2 recorded ISWTs using the same oxygen prescription and mobility aid (if any) between tests and provided written consent. Hospital notes were retrieved, diagnosis confirmed and relevant data extracted and validated.

**Discussion** Examination of data available demonstrates that patients with ILD achieve the minimum important difference of the ISWT (>47.5 m) and were close to achieving the minimum important difference of the SGRQ (>4). ILD patients have a greater benefit in terms of reduction in symptoms as measured by SGRQ, than the cohort as a whole. Limitations to generalisation of conclusions due to small sample size are acknowledged.

**Conclusion** ILD patients who completed a 6-week community based, PR programme within a mixed respiratory disease cohort demonstrate a clinically significant improvement in exercise capacity and make gains in health related quality of life.

**REFERENCES**


**Abstract P123 Table 1** Summary of mean values Pre-PR, Post-PR and change after PR for ISWT and SGRQ

<table>
<thead>
<tr>
<th></th>
<th>ILD patients (n = 21)</th>
<th>Whole cohort (n = 344)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ISWT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-PR</td>
<td>197.62</td>
<td>202.48</td>
</tr>
<tr>
<td>Post-PR</td>
<td>254.29</td>
<td>266.25</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td>56.67</td>
<td>63.77</td>
</tr>
<tr>
<td><strong>SGRQ symptoms</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-PR</td>
<td>50.48</td>
<td>60.77</td>
</tr>
<tr>
<td>Post-PR</td>
<td>39.15</td>
<td>55.23</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td>11.90</td>
<td>5.54</td>
</tr>
<tr>
<td><strong>SGRQ activity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-PR</td>
<td>69.14</td>
<td>70.34</td>
</tr>
<tr>
<td>Post-PR</td>
<td>66.70</td>
<td>66.61</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td>2.90</td>
<td>3.71</td>
</tr>
<tr>
<td><strong>SGRQ Impact</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-PR</td>
<td>34.95</td>
<td>39.66</td>
</tr>
<tr>
<td>Post-PR</td>
<td>34.55</td>
<td>34.44</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td>1.40</td>
<td>5.22</td>
</tr>
<tr>
<td><strong>SGRQ Total</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-PR</td>
<td>48.00</td>
<td>52.42</td>
</tr>
<tr>
<td>Post-PR</td>
<td>44.90</td>
<td>47.71</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td>3.85</td>
<td>4.71</td>
</tr>
</tbody>
</table>

**Abstract P124 Figure 1** Bland-Altman plot showing agreement between the two ISWTs

**Results** 43 patients (24 male) were included, 18 with Idiopathic Pulmonary Fibrosis. Participants were mean (SD) 72.17(10.54) years, Forced Vital Capacity was 2.28(0.87)l [77.24(25.46)% predicted], Transfer factor for the Lung for Carbon Monoxide 3.60(1.07)ml/mmHg [44.79(12.80)% predicted], median (interquartile range) Medical Research Council dyspnoea grade 3.5 (3–4) and 29 used oxygen therapy.

Participants achieved 165.12(123.89)m on ISWT1 with post-SaO2 87.86(5.86)% and heart rate 97.03(14.71), Borg breathlessness 4(3–5) and Rated Perceived Exertion (RPE) 13(11.25—15). There was a change of 28.84(31.71)m between the two ISWTs (p < 0.001); 72.1% of patients walked further on their second ISWT. Backward linear regression only explained 42% of this variance (R², 426).

For those who did not improve, ISWT1 was ≤210 m. Bland-Altman plot showed good agreement between the ISWTs, however the limits of agreement were wide. There was a significant difference in Endurance Shuttle Walk Test levels when calculated at 85% of VO₂ peak as estimated from ISWT1 and ISWT2 (p < 0.001).

**Conclusions** For patients with ILD, we have shown that there are significant differences between the first and second ISWT and therefore a practice ISWT is needed in order to accurately assess exercise capacity, prescribe an exercise programme and ensure services and interventions are correctly evaluated. We were unable to predict those who did not need to complete 2 ISWTs.

**REFERENCE**


**Abstract P125** THE IRISH LUNG FIBROSIS ASSOCIATION’S 2000 STEPS A DAY CHALLENGE: A PILOT STUDY TO EVALUATE A NOVEL HOME EXERCISE PROGRAMME FOR LUNG FIBROSIS PATIENTS

**REFERENCE**

1 Cassidy, 2 Byrne, 3 Danaher, 2 Egan. Irish Lung Fibrosis Association, Dublin, Ireland; 4 Mater Misericordiae University Hospital, Dublin, Ireland

10.1136/thoraxjnl-2014-206260.264

10.1136/thoraxjnl-2014-206260.265
Idiopathic Pulmonary Fibrosis (IPF) is a progressive, debilitating interstitial lung disease of unknown aetiology that results in irreversible scarring of the lungs. Patients develop impaired oxygen exchange and subsequent functional limitations including dyspnoea, hypoxia and fatigue. Patients’ fear of breathlessness leads to avoidance of physical activity yet, exercise is crucial to maintain health, strength, and mobility. Pulmonary rehabilitation is advocated for IPF patients but access to such programmes is difficult and restricted.

Methods The Irish Lung Fibrosis Association (ILFA) in collaboration with the physiotherapy department at the Mater Misericordiae University Hospital developed the 2000 Steps a Day Challenge as a new and innovative home-based exercise programme for IPF patients. The 2000 Steps a Day pack includes a pedometer, guidance and a diary to progress the step programme, and a Contract for Success to encourage commitment. Positive language and inspirational messages were used to motivate patients to make it part of their daily routine and reassure and support those experiencing setbacks. The programme was piloted by 15 ambulatory patients (11 male: 4 female) for 4-weeks. 10/15 patients required supplementary oxygen, 6/15 patients were on the lung transplant list and 3/15 patients were post-lung transplant. Patients were asked to record their baseline daily step count for 1-week, to gradually incorporate an additional 2000 steps (equivalent to 1 mile of walking) into their daily routine, and to complete a questionnaire on the suitability of the new exercise programme.

Results 12/15 patients completed the pilot phase and successfully added at least 2000 steps extra to their daily routine. 10/12 patients completed the questionnaire. 90% said the written materials were clear and understandable, 70% said the programme was easy to incorporate into their lives, 80% were motivated to exercise every day, 90% considered the pedometer a good motivational tool, 70% found the diary practical, 80% reported improved confidence, 100% felt a sense of achievement after reaching their target, 100% would recommend the programme to another patient. To date, over 200 walking packs have been requested. The ILFA 2000 Steps a Day Challenge is a novel, safe, effective and achievable home-based exercise solution for IPF patients.

The lungs at work: occupational lung disease

P126 BREATHLESSNESS AND LUNG FUNCTION PREDICTS FUTURE WORK DISABILITY IN OLDER WORKERS: DETECTION, INTERVENTION, RETENTION?

1 JS Ramirez, 2 SJ Schofield, 3 APM Woods, 4 P Cullinan. Royal Brompton and Harefield NHS Foundation Trust, London, UK; 2 National Heart and Lung Institute, Imperial College, London, UK

10.1136/thoraxjnl-2014-206260.266

Economic pressures and the ageing population have increased the importance of maintaining fitness to work in older adults. Dyspnoea and airflow limitation are associated with disability particularly in individuals with diagnosed disease. A cross-sectional general population survey of 51–60 year olds demonstrated significant associations between breathlessness, airflow obstruction and work performance; a follow-up survey was completed 18 months later to examine changes in work.

Participants from the first study were sent a postal questionnaire asking about job and employment changes. Questionnaire and spirometry results from the initial study were used to define breathlessness (modified MRC scale) and airflow obstruction (GOLD stage) respectively. Information from the follow up questionnaire was also used to identify cases, defined as those who had experienced a change in employment, and frequency matched controls of the same gender, who reported no change in work circumstances (with a ratio of two controls per case).

Results from respondents to the follow up questionnaire (1663/1773 (94%)), all of whom had been in full time work at the time of the first study) showed that the majority (78.5%) continued in full time employment; however 10.6% were working part time and 10.9% were no longer in paid employment at follow up. Of the participants still in employment who reported changing their hours or activity at work, 9.3% stated that this change had been to their health. Prevalence of economic inactivity rose with increasing breathlessness and with increasing airflow obstruction in workers of both sexes; these relationships were statistically significant in all cases except for airflow obstruction in women (Figure). The odds of GOLD stage 1 or greater airflow obstruction was significantly higher in cases than in controls (unadjusted OR 1.71, 95% CI 1.10–2.77, p = 0.02).

These findings suggest that breathlessness and airflow obstruction are associated with subsequent job instability and premature loss from the workforce in older workers. A focused surveillance programme could identify those at higher risk of employment problems with the intention of ameliorating them – providing that there are suitable interventions available to support continuing workforce activity in adults in their sixth decade of life and beyond.
inhaled exposures at an individual level, and the attitudes of workers with and without COPD to these issues.

Aim The aim of this work was to explore attitudes to workplaces, and to other aspects of the management of long-term respiratory problems, from individuals within a large population study with and without COPD.

Methods The primary aim of this population-based study was to assess the contribution made by inhaled occupational exposures to the development of COPD. The study was based in Sheffield, historically an industrialised part of the UK. A sub sample of cases of self reported COPD (n = 66) and non cases of COPD (n = 224) were asked to rate their views to a set of 36 pre defined statements, each rated between “don’t agree” and “completely agree” on a five point scale. Statements included enquiry about attitudes to chronic respiratory ill health, smoking, general health issues and the influences of the workplace on health.

Results 290 individuals, all 55 years old or greater, participated, 172 (59%) of whom were male. The majority of participants generally agreed or completely agreed with most statements, although various differences emerged between those with and without COPD. For example, those with self reported COPD were more likely, as anticipated, to identify this condition as a longer term health problem, but less likely to agree that workers with possible breathing problems should talk to their employer about these or undergo regular spirometry to identify these.

Conclusions This study has identified a set of attitudes and beliefs from those with and without COPD relating to chronic respiratory problems at work. Knowledge of these semi-quantitative data will assist the development of better workplace interventions to reduce the burden of this condition.

Introduction and objectives Spirometry is frequently carried out as part of workplace-based respiratory surveillance programmes for the detection of both obstructive and restrictive lung diseases. However, the performance of spirometry to detect restrictive lung diseases is generally poor and especially so if the prevalence of the disease in the tested population is low such as in many working populations.

Our aim was to increase the specificity and the positive predictive value (PPV) of current spirometry-based algorithms to diagnose restrictive lung diseases in the occupational health setting to reduce false positives and so the number of unnecessary and expensive referrals for lung volume measurements in hospital.

Methods We re-analysed two prospective studies of 259 and 265 tertiary care hospital consecutive patients, respectively used to derive and validate the current standard spirometry-based algorithm (FVC <85% predicted and FEV1/FVC >55%) to diagnose restrictive lung diseases (Glady CA, et al. Chest 2003). We used true lung restrictive cases (TLC <LLN predicted) as a gold standard in 2 × 2 contingency tables to estimate sensitivity, specificity, positive and negative predictive values for each potential diagnostic cut-off. Predicted values for spirometry parameters were calculated by using both Crapo and Hankinson equations. Because our target population is active workers we tested the performance of each diagnostic algorithm among subjects under 65 years old and with a simulated prevalence of restrictive disease of 10% and 1%. In addition, we compared the performance of our best diagnostic algorithm to the ones previously reported by using receiver operating characteristic (ROC) curves.

Results Our best diagnostic algorithm (FVC <70% predicted and FEV1/FVC<0.7) had a higher specificity (96% using Hankinson prediction equation) and PPV (80% and 27%) for a disease prevalence of 10% and 1%, respectively) compared to previous algorithms. For example, compared to Glady’s algorithm, among 184 people tested, ours produced only 6 (3%) false positives vs. 64 (34%), and correctly classified 91% subjects vs. 65%, corresponding to an area under the ROC curve of 0.83 vs. 0.77. The results were confirmed in the validation dataset.

Conclusions Our proposed spirometry-based algorithm accurately excludes pulmonary restriction and reduces unnecessary lung volume testing in occupational health clinical setting.
FEASIBILITY STUDY OF A PRIMARY CARE SCREENING TOOL FOR OCCUPATIONAL ASTHMA

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Introduction Occupational asthma (OA) accounts for 1 in 6 cases of adult-onset asthma and is associated with an estimated societal cost in the UK of £100 million/annum.1 However many workers with OA go undiagnosed or experience a lengthy delay in diagnosis,2 and primary healthcare professionals fail to enquire about patients’ occupations and the effect of work on asthma symptoms.3 We evaluated the feasibility of introducing an electronic screening tool for OA in primary care.

Methods A prospective feasibility study was undertaken over a 3-month period in 4 primary care practices in Birmingham, UK. Practices modified their existing electronic health records (one of: EMIS, SystmOne, Vision) with a customised asthma review template embedding the questions “What is your occupation?” and “Are your symptoms better away from work on days away/on holiday?” Baseline practice-level data were gathered and at the end of the study period all exposed healthcare professionals (GPs, practice nurses) were invited to complete an online questionnaire intended to evaluate utility and willingness to use the tool.

Results Prevalence of Read-coded asthma was 5.6–8.2% and Read-coded OA was 0–0.7%. All 4 practices incorporated the screening tool without any technical difficulty. 24/52 (46%) exposed GPs/nurses returned questionnaires, of whom 10 (42%) had used the tool; uptake was higher (85%) in those professionals who were given brief training. Healthcare professionals who did use the screening tool found it to be user-friendly (clear, concise, logical) with no perceived procedural or IT difficulties or significant added burden. Responders were less confident (44% agreed/strongly agreed) about how to act when patients had work-related asthma symptoms and 78% agreed/strongly agreed that further training in managing health aspects of suspected occupational asthma would improve the screening tool.

Conclusion An electronic screening tool for OA can be easily and quickly incorporated into existing asthma disease management systems. Its utility could be greatly improved by user instruction and training in further clinical management of the patient with work-related asthma symptoms.

REFERENCES
1 Ayres et al. Thorax 2011;66(2):128–33
2 Fishwick et al. Prim Care Respir J 2007;16:304–10
A number of epidemiological investigations have identified asthma prevalence in cleaners around 1.5–2.0 times those of reference populations. There are around 700,000 cleaners in the UK, asthma prevalence is around 8%, and that suggests a high burden of work-related disease. However, a clinical diagnosis of occupational asthma in cleaners is established relatively rarely. We have investigated the hypothesis that this discrepancy occurs because cleaner’s asthma is a form of low dose irritant asthma that is visible to epidemiologists but does not have the typical clinical features of occupational asthma. A questionnaire was sent to 1400 cleaners working in local hospitals and universities. 14% had a previous diagnosis of asthma, and in 32% of these the asthma started after they began work as a cleaner. Investigations for possible occupational asthma comprised paired measurements of airway responsiveness at and away from work (n = 13), serial PEF analysed using OASYS-2 (n = 13) and a structured clinical history (n = 10). 5 subjects had a greater than 3 fold improvement in PD20 away from work, and 2 subjects had OASYS score >2.5 indicating a probable occupational effect. 1 subject had both. The clinical histories were sent to 9 physicians with an interest in occupational asthma who were asked to score them for the likelihood of occupational asthma on a scale 0 to100% with and without the OASYS scores and the airway responsiveness measurements. Before seeing the investigation results, 7 of the 90 individual scores (9 physicians x 10 subjects) were above 50% indicating that the diagnosis of occupational asthma was thought likely. After seeing the investigation results, 29 of the 90 scores were above 50%. The mean probability score based on the history alone did not exceed 50% for any cleaner but was above 50% for 2 cleaners when the investigations were taken into account. These findings support the view that cleaner’s asthma has features that make it difficult to identify from the clinical history.

**P133** LONGITUDINAL DECLINE IN FEV1 IN OCCUPATIONAL ASThma DUE TO IRRITANTS IS NOT ALTERED BY REMOval FROM EXPOSure

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Introduction Airborne irritants and allergens in the workplace can induce and trigger occupational asthma (OA). OA due to sensitisation is associated with an accelerated rate of decline in FEV1 (100 ml/yr) compared with healthy controls (25 ml/yr), which improves on removal from exposure. We sought to describe the rate of FEV1 decline in patients with irritant-induced OA before and after their removal from exposure.

Methods Cases of irritant-induced OA reported between 1991 and 2011 were identified from the SHIELD database (a voluntary reporting scheme for OA) and their demographic characteristics and serial FEV1 measurements were gathered. Generalised estimating equations with an exchangeable correlation structure were used to calculate an average rate of FEV1 decline for all patients before and after removal from exposure.

Results A total of 526 FEV1 readings (179 prior to removal, 347 post removal) were gathered from 52 patients. 30 patients had FEV1 data both before and after removal; 5 patients had FEV1 data only before removal, and 17 patients had FEV1 data only after removal; demographics were not significantly different between the groups. FEV1 decline prior to removal of the irritant was 44 ml/year (95% CI: 32–58) and FEV1 decline after removal was 49 ml/year (95% CI: 36–62). There was no significant difference between the intercepts of the two lines, implying no improvement in FEV1 after removal from exposure.

Conclusion In this cohort, irritant-induced OA was associated with an accelerated decline in FEV1, which persisted after removal from the irritant. These results might be attributed to differences in the underlying pathology of sensitisation and irritant-induced OA, differences in patient behaviour, or differences in treatments offered to the two groups.

**REFERENCE**

1. Anees W et al. FEV1 decline in occupational asthma. Thorax 2006;61:751–5

**P134** SENSITISATION TO CROSS-REACTIVE CARBOHYDRATE DETERMINANTS IN BRITAIN’S Bakers: THE IMPLICATIONS FOR HEALTH SURVEILLANCE

1H Harrison, 1J Welch, 2S Schofield, 2J Cannon, 2B Fitzgerald, 1M Jones. 1Imperial College, London, UK; 2Royal Brompton and Harefield NHS Trust, London, UK

Introduction and objectives The diagnosis of baker’s asthma as part of health surveillance schemes in some UK supermarkets relies on determining sensitisation to wheat flour and/or alpha amylase. Recently, data have emerged suggesting that serum IgE analysis in bakers may be complicated by the presence of clinically irrelevant specific IgE to cross-reactive carbohydrate determinants (CCDs), which are complex-type Asn (N)-linked glycan structures commonly formed in plants. Potentially this might lead to false positive flour specific IgE assays, which would have an impact on bakers undergoing surveillance. The aim of this study was to identify the prevalence of CCD sensitisation in UK bakers and investigate the impact of CCD specific IgE within a health surveillance setting.

Methods Serum samples from UK bakers attending our occupational asthma clinic (n = 209) were analysed for specific IgE to CCD (MUXF) using ImmunoCAP assay (Phadia). Any positive samples were further tested for specific IgE to grass pollen, and competitive inhibition assays were used to determine cross-reactivity between CCD, flour and grass pollen.

Results Sensitisation rates to CCD in our population of UK bakers were low (7%) despite high sensitisation rates to grass pollen (48%) and flour (60%). Sensitisation to CCD was more prevalent in those sensitised to either flour or grass than in those not sensitised to flour (11.5% vs 0%, p < 0.001) or grass (10.9% vs 2.8%, p = 0.025). We observed cross reactivity between flour and grass pollen and competitive inhibition assays between CCD and flour or grass pollen revealed cross-reactivity in some but not all sensitised bakers.

Conclusions Our study demonstrated that a minority of bakers were sensitised to CCD and, Interestingly, this was associated with being co-sensitised with both flour and grass. It is unlikely that CCDs have major implications for the health surveillance for UK bakers. In the minority of bakers with CCD specific IgE, there was some suggestion that CCDs may play a role in the cross-reactivity between flour and grass pollen, although in others it was less likely. Within the clinical setting, it may be prudent to measure CCD specific IgE in bakers who are co-sensitised to both flour and grass pollen.
**P135** PREVALENCE OF SENSITISATION TO SOYA FLOUR IN THE BAKING INDUSTRY WITHIN THE UK

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Introduction Soya flour is routinely used as a baking additive to increase shelf life, improve colour and add a nutty flavour to bread. Although a large number of bakers are exposed to soya flour, there is little information as to the prevalence of sensitisation to soya flour in the baking industry. One study reports sensitisation to soya flour in four bakers who were sensitised to flour and alpha amylase and a bronchial challenge to soya flour elicited an immediate or dual asthmatic response. Studies in soy processing plant (slightly different to bakeries) report soy-specific IgE in 21% of soy processing workers compared with only 4% in health care workers, suggesting soya is an important occupational allergen in the soy processing industry.

Methods To determine prevalence of sensitisation to soya flour in bakery workers, we carried out skin prick testing to soya flour (Allergopharma 598) in bakery workers exposed to soya flour (n = 196) and in non-bakery controls (n = 50), who attended an occupational lung disease clinic. Skin tests were categorised as positive if they induced a wheal with a mean diameter of ≥2 mm greater than the response to a negative (saline) control and histamine was used as a positive control.

Results In a total of one hundred and ninety five bakery workers exposed to soya, forty two bakers were sensitised to soya flour (21%), and forty of those bakers were also sensitised to either flour and or alpha amylase (95%) In comparison, none of the control group (n = 50) were sensitised to soya flour.

Conclusion In our preliminary study of bakery workers exposed to soya flour, we found that around a fifth of the population were sensitised to soya flour. The clinical significance of soya flour need further investigation, although it seems prudent to include soya flour in the diagnostic tests for bakers asthma.

**P136** ASTHMA IN ROYAL AIR FORCE (RAF) PERSONNEL: MEASURING SEVERITY, CONTROL AND PREVIOUS IMPACT ON SERVICE CAREER

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10.1136/thoraxjnl-2014-206260.276

Background The overwhelming majority of UK military recruitment occurs in the age group (18–24) in which the recent increases in childhood asthma have been greatest. Concerns about operational risks associated with asthmatic individuals are reflected in selection policies excluding applicants taking asthma treatment, reporting symptoms in the last five years or since the age of 16. This study was designed to characterise the severity and impact of asthma on current RAF serving personnel.

Methods Questionnaires were sent to all current service personnel with a diagnosis of asthma on their medical record; an equivalent number of non-asthmatic personnel (matched on age and sex) were also surveyed to provide a referent population. Information on asthma symptoms and treatment, reported change in deployment, medical fitness category and career intention was collected.

Results Of 463 asthmatics who responded to the survey, 167 (36.1%) were not currently on asthma treatment, 63 (13.6%) were on reliever therapy only and 233 (50.3%) were on regular asthma treatment. Two-thirds reported adult onset asthma. Those on regular treatment were more likely to have needed urgent/unscheduled treatment, been unable to work due to their asthma and have a current ACQ score indicating uncontrolled disease; whilst this group were more likely to be currently downgraded, they were no more likely to have returned early from deployment than those in other groups (Figure). Comparing individuals with asthma and matched referents, those with disease were significantly more likely to be downgraded (OR 2.36 (95% CI 1.48–3.77), p < 0.001), prevented from deploying for medical reasons (OR 2.47 (95% CI 1.41–4.34), p = 0.006) and be assigned unfit (OR 1.79 (95% CI 1.20–2.73, p = 0.006)). Very few individuals had to return early from deployment, suggesting that restrictions were effective in mitigating risks posed by uncontrolled asthma.

Conclusions The findings from this cohort suggest that asthmatics in the RAF, particularly those taking regular treatment, are being restricted from some jobs and environments; this affects few individuals and does not appear to have a negative impact on service career. Decisions at recruitment are likely to have greater impact and would benefit from being studied prospectively.

**P149** CHARACTERISTIC AND PROGNOSIS OF PATIENTS WITH COPD AND TYPE 2 RESPIRATORY FAILURE

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10.1136/thoraxjnl-2014-206260.277

Introduction Factors associated with type 2 respiratory failure (T2RF) in COPD have been poorly described. Co-existent obstructive sleep apnoea is thought to play a part, and episodes of worsening hypercapnia, associated with acidosis (AHRF), at the time of exacerbations is a well recognised feature. We hypothesised that the development of hypercapnia or type 2 respiratory failure would associate with a higher risk of subsequent AHRF and higher mortality.

Methods 292 patients who had been prescribed oxygen for their COPD during 2006–2010 were studied. Medical records were
HOSPITAL RE-ADMISSIONS WITH EXACERBATION OF OBSTRUCTIVE PULMONARY DISEASE IN ILLICIT DRUG SMOKERS

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Poster sessions

10.1136/thoraxjnl-2014-206260.278

Introduction Patients with obstructive pulmonary disease (asthma or chronic obstructive pulmonary disease – COPD) who smoke illicit drugs are at an increased risk of hospital admissions.

We compared hospital re-admission rates due to exacerbations of obstructive pulmonary disease amongst current/ex- illicit drug smokers versus current/ex-tobacco smokers.

Hypothesis ‘Are those who smoke illicit drugs admitted to hospital with a clinical diagnosis of exacerbation of COPD more likely to be readmitted with a further exacerbation than current/ex-tobacco smokers?’

Methods Re-admission was defined as any admission, after the first, with an exacerbation of obstructive pulmonary disease during the study period. All admissions with a presumptive diagnosis of ‘exacerbation of COPD’ between January 2009 and September 2011 were reviewed. This was performed retrospectively using our COPD admission database.

Results There were 950 sequential hospital admissions in 709 patients over a 33 month period. We found 250 ex-tobacco smokers, 370 current tobacco smokers and 89 current or ex-illicit drug smokers. Re-admission rates with exacerbation of obstructive pulmonary disease were higher in illicit drug smokers compared to current/ex-tobacco smokers (1.00 v. 0.22/0.26, p < 0.001). Illicit drug smokers were younger (50 v. 72.9/69.9 [mean 71.2] years, p < 0.001) and had shorter length of hospital stay (7.44 v. 9.28/10.69 [mean 9.87] days, p = 0.038). Illicit drug smokers with FEV1 < 1 litre (L) had higher readmissions (2.56) than ex/current tobacco smokers (0.6) with FEV1 < 1L (p < 0.001) [Table 1]. Illicit drug smokers with FEV1 > 1L did not show this trend (p = 0.236). Tobacco pack years were higher in tobacco smokers (40.22) compared to illicit drug smokers (22.47), p.

Admissions requiring non-invasive ventilation (NIV) for type 2 respiratory failure were more common in illicit drug smokers (8.4 v. 3%, p < 0.002).

Conclusion We have shown that readmission rates in illicit drug smokers are higher than in tobacco smokers. These patients tend to be younger, have a male predominance, have shorter length of hospital stay and are more likely to require NIV; readmissions were more predominant in illicit drug smokers with an FEV1 < 1L.

Abstract P1540 Figure 1

reviewed for lung function, blood gases in the stable state, episodes of AHRF and mortality up to the end of March 2014. Cross-sectional analyses seeking associations of hypercapnia and T2RF were carried out, together with comparisons of FEV1 decline, AHRF and mortality between those with and without T2RF.

Results Mean follow up duration was 6.7 years. 164 patients died and 90 had one or more episodes of AHRF; AHRF was more common in T2RF (p = 0.046). Cox regression analysis, adjusting for age, demonstrated that death was more likely in those with T2RF compared to T1RF (Figure 1; p = 0.018). A rise in CO2 after administration of oxygen during the test of LTOT eligibility showed a similar association, but it was less strong (p = 0.041). Lung function was strongly associated with T2RF and subsequent use of NIV for AHRF; 53% of those with T2RF and high risk dependant on their admission score.

References

**Abstract P151 Table 1** The use of DECAF score to risk stratify patients admitted with COPD exacerbation

<table>
<thead>
<tr>
<th>Patient Risk</th>
<th>Total No of patients n (%)</th>
<th>No of inpatient deaths n (%)</th>
<th>Required NIV n (%)</th>
<th>Re-admitted within 3 months n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>99 (62.3%)</td>
<td>4 (4.0%)</td>
<td>9 (8.1%)</td>
<td>41 (43.1%)</td>
</tr>
<tr>
<td>Intermediate Risk</td>
<td>35 (22.0%)</td>
<td>1 (2.6%)</td>
<td>5 (14.2%)</td>
<td>12 (35.3%)</td>
</tr>
<tr>
<td>High Risk</td>
<td>25 (15.7%)</td>
<td>1 (40%)</td>
<td>4 (16%)</td>
<td>7 (46.7%)</td>
</tr>
</tbody>
</table>

**Introduction and objectives** Although socioeconomic factors are known to influence clinical outcome in COPD patients, few studies have addressed the impact of educational attainment. This is particularly relevant in light of the fact that telehealth, using often complex technologies, are increasingly used in the management of chronic diseases. We therefore aimed to ascertain the proportion of patients hospitalised with AECOPD who have formal educational qualifications and access to information technologies.

**Method** Clinical and physiological data were prospectively gathered from consecutive patients admitted to a metropolitan teaching hospital with AECOPD between April and December 2013. Patient data were analysed according to the possession of educational qualifications, and access to a personal computer and the internet.

**Results** 100 patients were admitted with AECOPD (40% female, age 70.5 ± 9.3 years). 51% of patients lived alone, 38% were current smokers with a FEV1 0.70 ± 0.39 L at admission, and 13% were receiving long term oxygen therapy. Median symptomatic days prior to admission was 4.0 (IQR 1 to 14), with an annual admission frequency of 2.0 (IQR 1 to 6). 14% of patients had access to both a computer and the internet. Patients with no access to these technologies were older (71.2 ± 9.2 vs. 64.8 ± 7.7 years, p < 0.02). Patients with no educational qualifications had a lower %predicted FEV1 (31.2 ± 23.6 vs. 38.7 ± 20.9, p < 0.05), and were less likely to have access to information technologies (7% vs. 93%, p < 0.05). They were more likely to be readmitted within 28 days (11% vs 3%, p=ns), but presented with a lower symptom burden on admission as measured by the numerical rating scale (3.6/10 vs. 5.0/10, p=ns).

**Conclusion** These data suggest there may be difficulties in implementing the use of telehealth within this metropolitan COPD population. Only 14% had access to a computer and the internet. Patients with no educational qualifications had worse spirometry at admission, but surprisingly a lower symptom burden. This may be due to the fact that those with educational qualifications...
Background Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are characterised by an acute worsening of symptoms beyond the normal day-to-day variability. Pneumonic episodes, confirmed by new chest X-ray (CXR) infiltrates, are common in patients with COPD but are difficult to distinguish in primary care from non-pneumonic exacerbations. It is uncertain whether AECOPD and pneumonic episodes in COPD patients are distinct clinical events in terms of aetiology and/or response to oral therapy. We performed a longitudinal study to characterise these events and to determine clinically meaningful differences associated with CXR changes in the outpatient setting.

Methods The Acute Exacerbation and Respiratory Infections in COPD (AERIS) study is a longitudinal epidemiological study to assess how changes in the COPD airway microbiome contribute to the incidence and severity of AECOPD. Patients with moderate to very severe COPD aged 40–85 years were followed monthly for 2 years, and reviewed within 72 h of onset of symptoms of AECOPD. We compared markers of systemic and airway inflammation between pneumonia AECOPD characterised by new CXR infiltrates, and non-pneumonic AECOPD, in a sub-cohort of 36 patients.

Results In the first year of study participation 122 exacerbations were recognised of which 120 had a CXR performed. Of these, 20 (16.7%, n = 12 patients) were identified as having new CXR infiltrates, and non-pneumonic AECOPD, in a sub-cohort of 36 patients. Statistically significant differences occurred in mean white blood cell count, blood neutrophil count, C-reactive protein, fibrinogen and sputum percentage neutrophil count between those AECOPD with new CXR infiltrates and those without (Table 1). Furthermore, there was a trend towards more severe symptom scores with pneumonic episodes using the EXACT-PRO score (p = 0.057).

Conclusion Pneumonic episodes are common in the context of clinical events presenting as outpatient AECOPD. The profile of airway and systemic inflammation is greater during these events than those without CXR changes. Understanding whether the biology and clinical course of these events is distinct from other exacerbations is key, particularly as patients are encouraged to self-manage based on symptom changes alone. Further study of the AERIS cohort will investigate links between aetiology, outcomes and prognostic markers at exacerbation including radiological and clinical indices.
Discussion Two-thirds of patients completed a discharge bundle during the Trust’s busiest quarter for COPD admission. Patients completing the discharge bundle had a significantly lower rate of 30-day readmission.

Poster sessions

Abstract P154 Table 1 Characteristics and readmission details of patients who were reviewed by the COPD specialist nurse and completed the discharge bundle

<table>
<thead>
<tr>
<th></th>
<th>Discharge Bundle (N=103)</th>
<th>No Discharge Bundle (N=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Area (Surrey/Hants/berk%)</td>
<td>59/31/10</td>
<td>53/90/17</td>
</tr>
<tr>
<td>Age in years (mean, SD)</td>
<td>75 (10)</td>
<td>76 (10)</td>
</tr>
<tr>
<td>Sex (male/female%)</td>
<td>45/55</td>
<td>46/51</td>
</tr>
<tr>
<td>&gt;1 admission in previous year (%)</td>
<td>27</td>
<td>28</td>
</tr>
<tr>
<td>Length of stay in days (median, range)</td>
<td>5 (1–71)</td>
<td>4 (1–26)</td>
</tr>
<tr>
<td>Short (0/1 day) length of stay (%)</td>
<td>18</td>
<td>17</td>
</tr>
<tr>
<td>30-day readmission (%)</td>
<td>17.5</td>
<td>34.0*</td>
</tr>
<tr>
<td>3-month readmission (%)</td>
<td>36.9</td>
<td>52.8**</td>
</tr>
<tr>
<td>Days to readmission (mean, SD)</td>
<td>33 (25)</td>
<td>28 (10)</td>
</tr>
<tr>
<td>Readmissions/patient (mean, SD)</td>
<td>0.55 (0.95)</td>
<td>0.68 (0.83)</td>
</tr>
<tr>
<td>Hospital days/patient (mean, SD)</td>
<td>9 (10)</td>
<td>9 (8)</td>
</tr>
</tbody>
</table>

* P = 0.027; ** P = 0.062

Introduction Theophylline therapy has a role in COPD patients who fail to respond adequately to inhaled bronchodilators and show symptomatic benefit from a trial of the drug. Treatment is complicated by drug interactions and its narrow therapeutic range (10–20 mg/L). High serum levels increase the risk of toxicity, demonstrating numerous symptoms such as nausea, vomiting, headaches, dyspepsia, insomnia and behavioural disturbances. Serious adverse effects such as cardiac arrhythmias and epileptic seizures tend to occur at serum levels above this reference range. NICE guidelines for COPD state that a theophylline level should be measured on admission in patients admitted for acute exacerbation of COPD (AE-COPD). The aim of this study was to audit compliance with these guidelines.

Methods Patients with a diagnosis of AE-COPD were retrospectively analysed over a 6-month period (June–December 2013) at a university hospital. Those who were prescribed theophylline within 24 h of admission were included in the study. Further information was gathered including theophylline level, date of request, and subsequent dose adjustment. Paper and computerised medical and prescribing records were reviewed using a set pro-forma.

Results Of a total of 54 patients in the study, 23 patients (43%) had theophylline levels checked during their hospital admission. Only 5 (9%) patients had theophylline levels within 24 h of admission, with the mean number of days from admission to assessment being 4.69 (SD+ 5.29). Of those patients, 13 patients (56.5%) had a level within subtherapeutic range (<10 mg/L), and 8 patients (61%) receiving subsequent dose adjustment. There were no patients found to have a theophylline level above therapeutic range (>20 mg/L).

Conclusion Improvement is needed in compliance with guidelines for the theophylline monitoring in patients with AE-COPD, as more than half of patients did not have levels checked during their hospital admission. Furthermore, dose adjustments were made in only 2 of 3 patients. Changes can be implemented through education to junior doctors, implementation of electronic prescribing alerts, and adding this to our MDT COPD bundle checklist. Further prospective audit cycle will be performed to assess improvements.

REFERENCE
1 NICE Guidelines [CG101]2010

P155 COMPLIANCE WITH GUIDELINES FOR THE MANAGEMENT OF THEOPHYLLINE IN PATIENTS WITH ACUTE EXACERBATIONS OF COPD

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10.1136/thoraxjnl-2014-206260.283

Introduction Theophylline therapy has a role in COPD patients who fail to respond adequately to bronchodilators and show symptomatic benefit from a trial of the drug. Treatment is complicated by drug interactions and its narrow therapeutic range (10–20 mg/L). High serum levels increase the risk of toxicity, demonstrating numerous symptoms such as nausea, vomiting, headaches, dyspepsia, insomnia and behavioural disturbances. Serious adverse effects such as cardiac arrhythmias and epileptic seizures tend to occur at serum levels above this reference range. NICE guidelines for COPD state that a theophylline level should be measured on admission in patients admitted for acute exacerbation of COPD (AE-COPD).1 The aim of this study was to audit compliance with these guidelines.

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1 NICE Guidelines [CG101]2010

P156 CAN SPECIALIST NURSES PREDICT WHICH PATIENTS WILL READMIT FOLLOWING DELIVERY OF A COPD CARE BUNDLE?

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Introduction Adequate follow up is a key element of COPD care bundles (CB). COPD nurse specialists responsible for completing follow up consultations may be able to utilise clinical judgment and measures of health status to predict which patients are at greater risk of readmission. Objective We explored whether COPD nurse specialists working in the Respiratory Discharge Service (REDS), who delivered the CB, could predict whether patients would readmit within 15 days post discharge. We also explored levels of health and psychological status for those patients who the REDS team thought were and were not at risk of readmission.

Methods This was a retrospective audit of patients who received a COPD discharge CB from April 2013 to March 2014. Readmission likelihood was recorded by the REDS team after completion of a 2 day post-discharge phone consultation. Patients also completed the COPD Assessment Test (CAT), MRC breathlessness scale and the Hospital Anxiety and Depression Scale (HADS).

Results Readmission risk was recorded for 1003 patients who received the CB prior to discharge. A total of 100 patients of these 1003 readmitted (readmission rate of 9.7%). The REDS team correctly predicted that 39 of these 100 patients would be readmitted. There were statistically significant between-group differences for the ‘will admit’ and ‘will not admit’ groups were analysed using independent t-tests.

Abstract P156 Table 1 Characteristics and readmission details of patients who were reviewed by the COPD specialist nurse and completed the discharge bundle

<table>
<thead>
<tr>
<th></th>
<th>REDs &quot;Will readmit&quot;</th>
<th>REDs &quot;Will not readmit&quot;</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRC score</td>
<td>4.28 (0.68)</td>
<td>3.75 (0.90)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CAT score</td>
<td>25.25 (8.97)</td>
<td>22.91 (7.55)</td>
<td>0.012</td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>7.97 (4.95)</td>
<td>5.86 (4.23)</td>
<td>0.001</td>
</tr>
<tr>
<td>HADS depression</td>
<td>7.94 (4.14)</td>
<td>5.27 (3.40)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Discussion Two-thirds of patients completed a discharge bundle during the Trust’s busiest quarter for COPD admission. Patients completing the discharge bundle had a significantly lower rate of 30-day readmission.
This suggests other factors must be important in predicting COPD readmissions.

**P157**  
**CANCER PATIENTS WITH SEVERE COMMUNITY ACQUIRED PNEUMONIA HAVE POORER OUTCOMES DUE TO INCREASED ILLNESS SEVERITY AND SEPTIC SHOCK AT ADMISSION TO INTENSIVE CARE**

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**Introduction**  
Patients with community acquired pneumonia (CAP) and an underlying diagnosis of cancer have worse outcomes. However, the characteristics of cancer patients with severe CAP admitted to intensive care units are not well defined. **Methods** An observational study of patients admitted to a University hospital ICU with a primary diagnosis of CAP between January 2006 and October 2011. **Results** 96 patients met our inclusion criteria for a diagnosis of severe CAP (19.8%).60% had cancer at the time of admission to ICU (57.9% with haematological malignancy and 42.1% with solid organ cancer). There were no statistically significant differences in age, gender or co-morbidities between those with and those without cancer. Patients with cancer had significantly higher median [IQR] APACHE II (25 [20–19] vs 20 [16–24]; p = 0.009), SAPS (51 [42–62] vs 42 [34–53]; p = 0.039) and SOFA (12 [10–13] vs 9 [4–12]; p = 0.018) scores and a longer median [IQR] time interval between hospital and ICU admission (2 [1–5] vs 1 [0–3] days; p = 0.049). There were no statistically significant differences in the proportion of patients receiving mechanical ventilation or renal support and no differences in the duration of mechanical ventilation or duration of ICU or hospital stay. Patients with cancer included a significantly greater proportion of patients receiving vasopressors (89.5% vs 63.6%, p = 0.030) and a markedly increased ICU (68.4% vs 31.2%, p = 0.004) and hospital mortality (78.9% vs 33.8%, p = 0.001). There were no significant differences in leucocyte counts, CRP, clotting (PT, APTT and INR), renal function (urea and creatinine) or liver function (AST and ALT). There were no significant differences in heart rate, temperature, systolic blood pressure or oxygenation index. However, patients with cancer had significantly lower median diastolic blood pressure (40 mmHg vs 50 mmHg, p = 0.026).

**Conclusion**  
Cancer patients with severe CAP continue to have an increased risk of death that appears to be related to increased illness severity at the time of ICU admission associated with septic shock. A delay in recognising the need for intensive care support in cancer patients with severe CAP may possibly explain the increased illness severity at the time of ICU admission.

**P158**  
**EVALUATION OF VITAL CAPACITY CHANGES IN SPINAL INJURED PATIENTS DURING EPISODE OF SEPSIS**

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10.1136/thoraxjnl-2014-206260.286

**Introduction**  
Respiratory complications have been suggested as cause of death in approximately 60% of spinal cord injured patients requiring ventilation after spinal cord injury.1 The vast majority of these respiratory complications are due to infections i.e. pneumonias. It has been postulated that infections trigger a general inflammatory response which directly affects respiratory muscle strength and worsens respiratory function, which can cause respiratory failure.2 All patients with a high spinal injury (> T1) or respiratory impairment have their vital capacity (VC) measured routinely at least once daily. We designed a project to assess if significant forced vital capacity (FVC) changes occur in spinal injury patients during an episode of sepsis.

**Methods** In this retrospective review we collected data from all our spinal injury patients with an episode of sepsis (pneumonia or urinary) between March 2010 and February 2013. **Results** A total of 16 episodes were recorded in 14 patients (2 female, 12 male) with an average age of 61.8. Level of spinal cord injury varied from C4-T9 and the majority had ASIA (American Spinal Injury Association) grade A. Of all 16 episodes of sepsis, 6 (37.5%) were diagnosed as pneumonia. 10 (62.5%) were of urinary tract origin with positive urine culture. Blood cultures were positive in 4 cases, negative in 11 and not available in 1. FVC ranged from 4000 ml to 1200 ml. VC changes were more profound with respiratory infection as we observed an average FVC change of 1450 ml (50–77%) for the diagnosis of pneumonia and 862 ml (2.3–58%) for urinary tract infection.

**Conclusions** Systemic infection causes significant changes in vital capacity suggesting direct effect of the inflammatory process on diaphragmatic and respiratory muscle function. These VC changes are more profound with respiratory infection as we observed an average FVC change of 1450 ml (50–77%) for the diagnosis of pneumonia and 862 ml (2.3–58%) for urinary tract infection.

**REFERENCES**

1 Wat J et al., Spinal Cord 2011;49:404–10

**Abstract P158 Table 1**

<table>
<thead>
<tr>
<th>Level</th>
<th>ASIA</th>
<th>Baseline VC</th>
<th>VC when unwell</th>
<th>Change in VC (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C4</td>
<td>A</td>
<td>1200</td>
<td>600</td>
<td>600 (50%)</td>
</tr>
<tr>
<td>C4</td>
<td>A</td>
<td>2200</td>
<td>500</td>
<td>1700 (77%)</td>
</tr>
<tr>
<td>C4</td>
<td>C</td>
<td>2500</td>
<td>650</td>
<td>1850 (74%)</td>
</tr>
<tr>
<td>C4</td>
<td>A</td>
<td>2900</td>
<td>1500</td>
<td>1400 (48%)</td>
</tr>
<tr>
<td>C4</td>
<td>C</td>
<td>1630</td>
<td>980</td>
<td>650 (40%)</td>
</tr>
<tr>
<td>C4</td>
<td>A</td>
<td>3000</td>
<td>2930</td>
<td>70 (2.3%)</td>
</tr>
<tr>
<td>C4</td>
<td>A</td>
<td>1200</td>
<td>1000</td>
<td>200 (16%)</td>
</tr>
<tr>
<td>C4</td>
<td>A</td>
<td>3000</td>
<td>1590</td>
<td>1410 (47%)</td>
</tr>
<tr>
<td>C4</td>
<td>A</td>
<td>2550</td>
<td>1750</td>
<td>800 (31%)</td>
</tr>
<tr>
<td>C6</td>
<td>B</td>
<td>1800</td>
<td>650</td>
<td>1150 (63%)</td>
</tr>
<tr>
<td>C6</td>
<td>B</td>
<td>3400</td>
<td>800</td>
<td>2600 (76%)</td>
</tr>
<tr>
<td>C6</td>
<td>B</td>
<td>3570</td>
<td>2650</td>
<td>890 (25%)</td>
</tr>
<tr>
<td>T4</td>
<td>A</td>
<td>4000</td>
<td>3480</td>
<td>520 (13%)</td>
</tr>
<tr>
<td>T8</td>
<td>A</td>
<td>4000</td>
<td>1680</td>
<td>2320 (58%)</td>
</tr>
<tr>
<td>T8</td>
<td>C</td>
<td>3250</td>
<td>1920</td>
<td>1330 (41%)</td>
</tr>
<tr>
<td>T9</td>
<td>D</td>
<td>1400</td>
<td>800</td>
<td>600 (43%)</td>
</tr>
</tbody>
</table>

**P159**  
**WEANING AND LONG TERM VENTILATION OUTCOMES IN SPINAL INJURY PATIENTS AFTER REFERRAL TO A REGIONAL SPINAL INJURY CENTRE**

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Difficult and slow weaning of ventilated patient will have been observed by staff in many critical care units. A National Association for Medical Direction of Respiratory Care (NAMDRC) Consensus Conference suggested that 20% of such patients had neurological disease.

The incidence of respiratory failure following acute cervical spinal cord injury (ASCI) ranges between 22.6% and 57% and the average time to wean from ventilator support was found to be 36 days. Weaning for such patients should therefore take place in an intermediate care facility and be slow paced. Previous data from our unit did suggest a successful wean in about 70% of patients admitted to this regional spinal injury unit. We therefore wanted to review our recent results (Nov 2009 – Nov 2012) with previous standards.

Methods We performed a retrospective review of all patients admitted from November 2009 to November 2012 for respiratory weans following spinal cord insult.

Results 43 patients (33 male and 8 female) were admitted to the spinal critical care unit for weaning (14.33 patients per year). Average age was 54.7 years for male and 55.4 years for females. The level of injury is illustrated in the table below:

<table>
<thead>
<tr>
<th>Level of Injury</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1–3</td>
<td>10</td>
<td>23%</td>
</tr>
<tr>
<td>C4–5</td>
<td>23</td>
<td>54%</td>
</tr>
<tr>
<td>&gt;C5</td>
<td>10</td>
<td>23%</td>
</tr>
</tbody>
</table>

Of the 43 patients, 35 were successfully weaned; the rest were either partially weaned or not weaned.

7 of the 10 Level C1–3 injury patients were not weaned or were only partially weaned. The remaining 3 patients of Level C1–3 injury (incomplete) were weaned. 1 patient with Level C6 injury was only partially weaned but was 77 years of age.

Conclusions Review of the period from 2009–2012 is very encouraging, suggesting weaning success in line with national and international centres. Further reviews will focus on duration of wean and the effect of co-morbidities and age on the weaning outcome. Further attention needs to focus on quality of life in the weaned and not weaned patient group.

REFERENCES

Pulmonary arterial hypertension: diagnosis, management and outcomes

The role of specialist palliative care services in the management of patients with pulmonary arterial hypertension: a review of current practice

SC Woolcock, J De Soysa, R Crackett, M Day, AJ Fisher, J Lordan, G MacGowan, PA Corris. National Pulmonary Hypertension Service (Newcastle), Institute of Cellular Medicine, Newcastle University and the NUTH NHS Foundation Trust, Newcastle Upon Tyne, UK

Introduction and objectives Pulmonary Arterial Hypertension (PAH) is a severe, progressive condition characterised by increased pulmonary vascular resistance, right ventricular failure and death. Survival is strongly linked to functional class with patients persisting in WHO class IV surviving less than one year. Such patients commonly require repeated hospital admissions with intractable symptoms due to right heart failure. Although specialist palliative care involvement is recommended in current guidelines for the management of PAH, no formal recommendations exist presently to guide clinicians on timing of referral.

The aim of this study was to outline current practice in this area and define the potential workload and role of specialist palliative care services.

Methods Data was collected retrospectively for all patients within our national PAH service who died over a one year period (June 2013–June 2014). We specifically looked at timing of referral and involvement of palliative care specialists, WHO functional class, clinical course prior to death and prognostic indicators of deterioration.

Suitable patients were identified from the PAH and palliative care databases. Patient notes were reviewed to identify WHO class, clinical course prior to death and documented evidence of specialist palliative care involvement.

Results
- 31 patients were identified; (14 male, 17 female; 19 (61%) WHO IV, 9 (29%) WHO III, 3 (10%) WHO II).
- Only 11 (35%) had documented evidence of specialist palliative care involvement.
- 7 (22%) received input whilst in hospital, 4 (13%) in the community.

Conclusions The majority of our patients did not receive specialist palliative care support during the final stages of their disease. Whilst the majority (61%) of patients were functional class IV prior to death, 39% were functional class II or III. Progressive deterioration and increased burden of symptoms over time preceding death were commonly noted. Whilst the specialist PAH nurses and clinicians offer palliative care and support, our data suggests that a review of the timing, organisation and documentation of referral to specialist palliative care services requires consideration.

Assessment of age-adjusted D-dimer cut-off values in investigating venous thromboembolism in older patients: a retrospective analysis

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Introduction and objectives The specificity of D-dimer testing in detecting venous thromboembolism (VTE) appears to fall in older patients as D-dimer concentrations increase with age. There has been interest in the use of age-adjusted D-dimer cut-off values to increase the specificity in older patients. The objective of this study was to review the diagnostic accuracy of D-dimer testing in older patients with suspected VTE in our population, comparing conventional and age-adjusted D-dimer cut-off values.

Methods A retrospective study from a large teaching hospital in the UK was undertaken. 389 data episodes were compiled from suspected VTE presentations during two months in 2013. Patients were assessed using a combination of clinical probability scores and D-dimer measurement (D-dimer HS assay, Instrumentation Laboratories). Conventional (230 ng/ml and age-adjusted...
(age x 10 ng/ml) cut-off values were applied to patients ≥50 years, and specificity and sensitivity were calculated.

Results (Table 1) Of the 389 presentations, 229 (58.9%) were from patients aged ≥50 years. 13 (11.5%) patients with positive D-dimers using the conventional cut-off, had VTE as confirmed by imaging tests. The sensitivity of the conventional D-dimer cut-off value was 100% in this older cohort, with a specificity of 53.7%. The age x10-adjusted cut-off improved specificity to 84.7%; however sensitivity was markedly reduced to 76.9%, with 3 patients (23.1%) with non-high clinical probability of VTE missed. Further analysis suggested that an age-adjusted cut-off factor of x3 would maintain sensitivity at 100%; however specificity was only 47.7%.

Conclusions We have identified that an age-adjusted cut-off factor of x10 significantly increased D-dimer specificity in older patients; however the sensitivity of this test was unacceptably compromised. A cut-off factor of x3 maintained sensitivity, but specificity was unsatisfactory compared to conventional values, although still higher than in most published studies. We conclude that we cannot use an age-adjusted cut-off of x10 in our ≥50 year old population using this assay. Further work is required to identify an appropriate cut-off, concentrating on the >75 year old patients only. This would help to reduce the number of unnecessary tests and anxiety in this vulnerable group of patients.


ddimer= (mg/l); CRP=0–5 mg/l; WCC=4–11 g/l; D-dimer= (mg/l); CRP=0–5 mg/l

P163 ACCURACY OF INFLAMMATORY MARKERS TO DISTINGUISH BETWEEN PNEUMONIA AND PULMONARY EMBOLISM IN ACUTE SETTINGS

Introduction Pulmonary Embolisms (PE) are clinically difficult to diagnose and associated with significant morbidity and mortality. Computed Tomography Pulmonary Angiogram (CTPA) is routinely used to investigate suspected PE. Clinical concern and the increased availability of CTPA may mean that more patients may be receiving unnecessary radiation: a CTPA is approximately 15 mSv, equivalent to 750 chest radiographs. In addition, detection of other pathology by CTPA/VQ. However, it is increasingly recognised

P162 A TWO MONTH PROSPECTIVE STUDY: ARE CTPAS REQUESTED APPROPRIATELY AND IF NOT DO THEY DIAGNOSE ALTERNATIVE PATHOLOGIES?

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10.1136/thoraxjnl-2014-206260.290

Abstract P162 Table 1 Characteristics of conventional and age-adjusted D-dimer cut-off values in patients ≥50 years old

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>Age x 10-adjusted</th>
<th>Age x 3-adjusted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity (%)</td>
<td>100</td>
<td>76.9</td>
<td>100</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>53.7</td>
<td>84.7</td>
<td>47.7</td>
</tr>
<tr>
<td>Positive Predictive Value (%)</td>
<td>11.5</td>
<td>23.3</td>
<td>10.3</td>
</tr>
<tr>
<td>Negative Predictive Value (%)</td>
<td>100</td>
<td>98.4</td>
<td>100</td>
</tr>
</tbody>
</table>

P163 ACCURACY OF INFLAMMATORY MARKERS TO DISTINGUISH BETWEEN PNEUMONIA AND PULMONARY EMBOLISM IN ACUTE SETTINGS

Abstract P163 Table 1 Comparison of inflammatory markers and d-dimer levels between PE, CAP and ARTI

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PE (n = 167)</th>
<th>CAP (n = 58)</th>
<th>ARTI (n = 63)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, male (%)</td>
<td>84 (50.3)</td>
<td>31 (53.4)</td>
<td>40 (63.5)</td>
<td>0.358</td>
</tr>
<tr>
<td>Age (yrs), mean (sd)</td>
<td>66.9 (16.6)</td>
<td>73.4 (17)</td>
<td>63 (23)</td>
<td>0.016</td>
</tr>
<tr>
<td>Hospital stay (days), median (range)</td>
<td>5.31 (0–34)</td>
<td>7.08 (0–34)</td>
<td>1.51 (0–29)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>30 day mortality, n (%)</td>
<td>7 (4.2)</td>
<td>16 (27.6)</td>
<td>9 (14.3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CRP (mg/l), median (range)</td>
<td>67.3 (4–412)</td>
<td>88.9 (12–417)</td>
<td>68.8 (9–284)</td>
<td>0.322</td>
</tr>
<tr>
<td>WCC (g/l), mean (sd)</td>
<td>10.9 (4.8)</td>
<td>11.8 (5.2)</td>
<td>12.17 (4.9)</td>
<td>0.2</td>
</tr>
<tr>
<td>D-dimer (mg/l), median (range)</td>
<td>1000 (255–1000)</td>
<td>518 (150–1000)</td>
<td>170 (100–1000)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Positive d-dimer (%)</td>
<td>123 (96.6)</td>
<td>8 (53.3)</td>
<td>3 (18.8)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

WCC=white cell count, CRP=C-reactive protein, Acute LRTI=symptoms of acute chest infection with normal CXR. Normal range: WCC=4–11 g/l; D-dimer= (mg/l); CRP=0–5 mg/l
that PE is associated with abnormal concentrations of many proteins involved in inflammation and vascular injury, yet there is inadequate data describing the difference in these proteins from infective processes.

Aims We aimed to determine whether there is a difference in inflammatory markers between acute PE and community acquired pneumonia (CAP) or acute lower respiratory infection (LRTI).

Methods A random sample of emergency departments (ED) and patients evaluated for acute PE at our institution (January 2013–December 2013) were retrospectively evaluated for D-dimer, C-reactive protein (CRP) and serum white cell (WCC) levels. PE was diagnosed by a positive CTPA in all cases. Inflammatory markers in confirmed PE cases were compared and matched with those of community acquired pneumonia (CAP) and acute lower respiratory infection (LRTI). We excluded all cases with incidental, chronic or previous PE.

Results A total of 295 patients were included (mean age 67.7 ± 18.45 yrs; 159 males), of which 167 (56.6%) had PE, 58 (19.7%) had CAP, 63 (21.4%) LRTI and seven (2.4%) had incidental, chronic or previous PE.

Conclusions In patients suspected of acute PE, unlike D-dimer, NTproBNP were significantly higher in PE than CAP or ARTI (p = 0.000). There were no significant differences among disease groups for median CRP levels (mg/l); PE (67.3 (4–412); CAP (88.9 (12–417) and acute LRTI (median 68.9 (9–284), (p = 0.322). In contrast, levels of D-dimer were significantly higher in PE than CAP or ARTI (p = 0.000).

P164 ΔNTproBNP PREDICTS SURVIVAL AND MORE ACCURATELY REFLECTS CHANGING RIGHT VENTRICULAR STRUCTURE AND FUNCTION THAN Δ6MWD IN PULMONARY HYPERTENSION

MJ Brewis, MK Johnson, AJ Peacock. Scottish Pulmonary Vascular Unit, Glasgow, UK

10.1136/thoraxjnl-2014-206260.292

Right ventricular (RV) function is known to predict survival in pulmonary hypertension (PH). Furthermore, increasing right ventricular volumes (RVEDVI, RV end diastolic volume and RVESVI, RV end systolic volume index) and falling ejection fraction (RVEF) whilst on treatment have been shown to determine poorer outcome. Measurement of RV function by cardiac MRI (CMR) is not widely available and often poorly tolerated in very breathless patients. Monitoring of PH patients traditionally focuses on serial 6 min walk testing (6MWD) and N terminal pro brain natriuretic peptide (NTproBNP), a biomarker that has been shown to reflect RV function and structure. We hypothesised that ΔNTproBNP is a superior non invasive marker of ΔRV function than Δ6MWD, and predicts survival.

Methods 59 patients with pre-capillary PH whom underwent serial CMR between 2004 and 2014 with 6MWD and/or NTproBNP sampling within 1 month of scan were retrospectively included. 146 ΔRV function values were calculated. For survival analysis, patients were censored at last day of study (24/6/14) or if lost to follow up. Survival was taken from the date of the second CMR scan. Due to the interaction between cardiac MRI values, only univariate survival analysis was performed.

Results ΔNTproBNP correlates more closely with ΔRVEF, ΔRVEDVI, ΔRVESVI than 6MWD (table1). Both ΔNTproBNP and Δ6MWD predicted survival [HR 1.001 95% CI 1.001–1.002 p 0.0001].

Conclusion ΔNTproBNP is superior to Δ6MWD as a surrogate marker of changing RV function which can be easily evaluated in the clinic setting. Both ΔNTproBNP and Δ 6MWD predict survival in PH.

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P165 AMBULATORY MANAGEMENT OF SUSPECTED PULMONARY EMBOLISM AT A DISTRICT GENERAL HOSPITAL: A 2 YEAR REVIEW

A Griffiths. Royal Glamorgan Hospital, Llantrisant, UK

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Background Studies have suggested that outpatient (OP) management of suspected pulmonary embolism (PE) is feasible. At our DGH (popn 289400) in 2012 we found that over a 2 month period most suspected PE patients (suitable for ambulatory care) were being identified resulting in significant (17 nights) bed savings.

The aims of repeating our study were:

1) to ascertain the proportion of patients who had a CTPA that were managed as OP and subsequent nights saved 2) to identify any further patients that could have been managed as OP and potential nights saved 3) a comparison with 2012

Methods RADIS was used to collect all CTPA’s performed between 1st Jan 2014 and 28th February 2014. Inclusion criteria: Ambulatory, normal heart rate, respiratory rate, blood pressure and oxygen saturations, any patient who was managed as an OP. Simplified PESI Score <1. Exclusion criteria: Pre-existing in-patients that had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE; patients who had their CTPA on the same day of discharge, OP CTPA where in-patients that had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE, patients who had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE, patients who had their CTPA on the same day of discharge, OP CTPA where in-patients that had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE, patients who had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE, patients who had their CTPA on the same day of discharge, OP CTPA where in-patients that had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE, patients who had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE, patients who had their CTPA on the same day of discharge, OP CTPA where in-patients that had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE, patients who had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE, patients who had their CTPA on the same day of discharge, OP CTPA where in-patients that had a CTPA ordered where the primary admission (and in-patient stay) was not for suspected PE.

Results For the above period 102 CTPA’s were performed (105 in 2012). Average time from request to CTPA was 4.7 h (0.5–24 h, 4.1 hrs in 2012) Figure 1 shows the excluded patients. 9 patients were included;7 were female, average age 47 years (23–66 years). All had a sPESI score
Conclusion  The number of ambulatory patients investigated for PE has reduced from 2012 to 2014 which probably reflects an increased acute physician presence at our DGH but some bed savings (7 nights over our 2 month period) were still made. Over 2 years approximately 180 ambulatory patients have been investigated and managed for PE at our DGH with no adverse incidents to date.

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2 Benjamin JA et al. Thorax 2012;67:A123

P165 PATIENTS WITH CONFIRMED AND SUSPECTED PULMONARY EMBOLI HAVE THE SAME TWO-YEAR MORTALITY

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10.1136/thoraxjnl-2014-206260.294

Introduction  There is limited information regarding long-term survival following Pulmonary Embolism (PE), and no data on survival of patients that have undergone CT Pulmonary Angiography (CTPA) but found to be thrombus negative. The positive rate of PE detection in patients undergoing CTPA is variable, ranging from 4.7–25.8% and there is a high reported incidence of incidental pathology discovered during this investigation. We sought to determine the comparative survival of patient undergoing CTPA that were thrombus positive compared with those without a PE. We also sought to determine the rate of PE detection and characterise the nature of incidental findings found in patients undergoing CTPA.

Methods  We retrospectively reviewed data on all CTPA investigations conducted between April 2010 and April 2012. All abnormalities reported on CTPA were reviewed and compared with previous imaging from the last 6 months to determine if they were new findings. Follow-up investigations and out-patient attendances were obtained for all new findings reported on the index CTPA, and 2 year mortality rates were established from regional registry data.

Results  Of the 1043 patients suitable for analysis, 241 (22.4%) were thrombus positive. The thrombus positive cohort consisted of 47.7% males compared with 40.7% in the thrombus negative group (difference 7.1% [-0.0 to 14.2, p = 0.52]). Survival at 2 years following CTPA was 67.6% in thrombus positive patients and 65.9% in thrombus negative patients with a hazard ratio of 0.96 (95% CI, 0.74 to 1.23, p = 0.721) (Figure). Incidental findings were detected in 51.1% of CTPA examinations including: consolidation/collapse (19.5%), effusion (16.7%), neoplasia (13.5%), lymphadenopathy (9.8%), heart failure (7.6%) and pulmonary nodules (6.6%). 47.7% of incidental findings were deemed significant as determined by the need for further follow-up of clinical intervention.

Conclusion  There is no difference in the 2 year mortality between thrombus positive and thrombus negative patients undergoing CTPA. Many incidental findings found on CTPA are clinically significant.

P166 OUTCOMES AND PREDICTORS OF MORTALITY IN CANCER PATIENTS WITH INCIDENTAL PULMONARY EMBOLISM

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10.1136/thoraxjnl-2014-206260.295

Objectives  Incidental pulmonary emboli (iPE) are detected in a significant minority of contrast CT scans performed during the management of patients with cancer. These patients are reported to have an increased mortality compared to matched controls. This study investigates outcomes and predictors of mortality following iPE.

Methods  Reports of all contrast-enhanced CT scans including the chest, excluding dedicated CT pulmonary angiography, performed between 1st May 2012 and 30th September 2013, were searched for prospectively identified iPE. Clinical data was collected from multiple sources, including clinic letters, discharge summaries, and the hospital patient database. Patients presenting with acute symptoms consistent with PE or those already receiving therapeutic anticoagulation were excluded. Potential clinical and radiological predictors of mortality were defined pre-hoc and tested using Student’s t-test and Cox proportional-hazard regression.

Results  There were 160 cancer patients with iPE. Anticoagulation treatment was given in 97% of cases. Overall 30-day and 6-month mortality following iPE was 20.6% (95% confidence interval 15.0–27.6%) and 52.5% (44.8–60.1%), respectively. Increased 30-day and 6-month mortality was observed in scans performed on inpatients compared to outpatients (38.2% vs 11.4%, p = 0.0004 and 78.2% vs 40.0%, p < 0.0001). 6-month mortality was also increased if this was a new diagnosis of
malignancy at the time of the CT scan compared to patients with known malignancy (69.4% vs 46.0%, \( p = 0.0046 \)), or if metastases were present at the time of CT scan (58.3% vs 26.7%, \( p = 0.0012 \)).

There were 86 (53.8%) central (main or lobar pulmonary arteries), 60 (37.5%) segmental, and 14 (8.8%) subsegmental pulmonary emboli. No significant mortality difference was observed between these radiological features.

**Conclusion** This study has assessed potential poor prognostic features in patients with cancer and iPE. Despite the vast majority receiving therapeutic anticoagulation, there is a high 30-day and 6-month mortality. The benefits of conventional treatment in this clinical situation are as yet unclear.

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**Poster sessions**

**P168** REDUCED GAS TRANSFER (TLCO) PREDICTS POOR OUTCOME IN PATIENTS WITH PULMONARY HYPERTENSION AND HEART FAILURE WITH PRESERVED EF FRACTION

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10.1136/thoraxjnl-2014-206260.296

**Rationale** There is limited data on predictors of survival in patients with Pulmonary Hypertension (PH) in the context of Heart Failure and Preserved Ejection Fraction (HF-pEF). Simple non-invasive tests to aid the physician in prognostication would be valuable. The aim of this study was to examine demographic and non-invasive predictors of outcome in PH-HF-pEF in a large well phenotyped PH registry.

**Method** In the ASPIRE Registry (Hurdman J et al Eur Resp J, 2012), 1737 consecutive, incident, treatment-naive patients with suspected PH underwent diagnostic evaluation between February 2001 and 2010. Patients were diagnosed as PH-HF-pEF if no other causes of PH could be identified and they fulfilled the following criteria: signs and symptoms of heart failure; mean pulmonary artery pressure \( \geq 25 \) mmHg at rest and pulmonary arterial wedge pressure >15 mmHg by RHC; preserved left ventricular systolic function (ejection fraction \( \geq 50\% \)) by echocardiography or CMR. Predictors of survival were assessed using forward stepwise Cox regression analysis. Variables with a p-value

**Results** 98 patients who fulfilled the diagnostic criteria for PH-HF-pEF were identified. Maximum duration of follow-up was 10 years with a mean follow up 4.9 \( \pm 2.3 \) years, during which 33 (34%) patients died. After multivariate analysis, only ISWT distance HR 0.99 CI (0.99–1.00) and TLCO HR 0.96 CI(0.94–0.98) at baseline, were predictors of outcome (\( p < 0.01 \)). Median predicted TLCO in the PH-HF-pEF population was 65%. The 5-year survival in those with a TLCO <65% predicted was 60%, compared with 85% in those whose TLCO was \( \geq 65\% \) (\( p < 0.01 \)).

**Conclusions** Simple non-invasive testing such as TLCO and exercise capacity measured by the ISWT predict outcome in patients with PH-HF-pEF.

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**P169** RATES OF RECOVERY OF OXYGEN CONSUMPTION AND HEART RATE AFTER CARDIOPULMONARY EXERCISE TESTING PREDICT SURVIVAL IN PATIENTS WITH PRECAPILLARY PULMONARY HYPERTENSION

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10.1136/thoraxjnl-2014-206260.297

**Abstract P169 Table 1**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Significance level</th>
<th>Variable</th>
<th>Significance level</th>
</tr>
</thead>
<tbody>
<tr>
<td>VO2 R 30</td>
<td>0.729</td>
<td>OUES</td>
<td>0.026</td>
</tr>
<tr>
<td>HRR 30*</td>
<td>0.300</td>
<td>Peak VO2</td>
<td>0.024</td>
</tr>
<tr>
<td>VO2 R 60</td>
<td>0.084</td>
<td>VE/VO2 at AT</td>
<td>0.032</td>
</tr>
<tr>
<td>HRR 60</td>
<td>0.058</td>
<td>Peak heart rate</td>
<td>0.067</td>
</tr>
<tr>
<td>VO2 120</td>
<td>0.021</td>
<td>Diagnosis</td>
<td>0.055</td>
</tr>
<tr>
<td>HRR 120</td>
<td>0.003</td>
<td>Age</td>
<td>&lt;0.001</td>
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<tr>
<td>DLCO (% pred)</td>
<td>0.002</td>
<td>logNTproBNP</td>
<td>0.064</td>
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<tr>
<td>SvO2</td>
<td>0.115</td>
<td>Cardiac index</td>
<td>0.278</td>
</tr>
<tr>
<td>RAP</td>
<td>0.401</td>
<td>mPAP</td>
<td>0.532</td>
</tr>
<tr>
<td>6MWD</td>
<td>0.205</td>
<td>WHO FC</td>
<td>0.428</td>
</tr>
</tbody>
</table>

**P170** HEART RATE RECOVERY AT ONE MINUTE FOLLOWING INCREMENTAL SHUTTLE WALK TEST PREDICTS OUTCOME IN PULMONARY HYPERTENSION

CG Billings, J Hurdman, M Austin, J Armstrong, CA Ellicot, RA Condliffe, DG Kiely. Sheffield Pulmonary Vascular Disease Unit, Sheffield, UK

10.1136/thoraxjnl-2014-206260.298

**Background** Heart-rate recovery during the first minute of rest (HRR1) after a six minute walk test (6MWT) has been shown to

**Introduction** Several cardiopulmonary exercise testing (CPET) variables have been shown to predict prognosis in pulmonary hypertension (PH). Recently published data suggests that novel variables such as oxygen uptake efficiency slope (OUES), i.e. the relationship between VO2 and log-transformed ventilation and heart rate recovery (HRR), the rate of decline of heart rate at one minute after an incremental CPET, have been shown to predict survival in a cohort of PH patients.

We aimed to study the prognostic significance of the rate of recovery of VO2 after incremental CPET alongside HRR and OUES in a large cohort of patients with precapillary PH. We hypothesised that a slower VO2 recovery would be associated with poorer survival and that we could confirm that lower HRR and OUES are significantly associated with a worse outcome.

**Method** Retrospective analysis was undertaken of data from 108 incident patients who underwent CPET at the time of diagnosis of Group I or IV PH. Univariate Cox proportional hazard analyses were undertaken to assess the prognostic significance of the variables considered and the results are shown in Table 1.

**Results** [Table 1]

**Conclusions** The degree of VO2 recovery at 120 seconds after incremental CPET is predictive of survival in this relatively large group of patients with precapillary PH. We have also confirmed the findings seen in another centre of a significant influence of heart rate recovery and OUES on survival. Further work should focus on whether these variables provide additional prognostic information over their more traditionally studied counterparts.

**REFERENCES**

be a strong predictor of clinical worsening in patients with pulmonary arterial hypertension.\(^1\) No data as yet has been published regarding the utility of HRR1 as a predictor of mortality.

**Aim**

To assess the prognostic value of HRR1 after an Incremental Shuttle Walk Test (ISWT) in patients with pulmonary hypertension (PH).

**Methods**

Data was retrieved for consecutive cases of PH diagnosed in our unit from 2001–2010. ISWT was performed routinely as part of baseline assessment according to a modified protocol of Singh et al.\(^2\) Only treatment-naive patients with ISWT and HRR data from -90 to +30 days from date of diagnosis were included. HRR1 was defined as the difference between ISWT and HRR data from -90 to +30 days from date of diagnosis. Using a cut-off point of 18 bpm, the Kaplan Meier graph for HRR1 >18 bpm (n = 179) was significantly better than HRR1 ≤18 bpm (n = 312), p = 0.007 (Figure 1) for all patients and for diagnostic Groups 1 and 2 separately (p = 0.045, p = 0.006).

Using univariate Cox proportional hazard analysis for all patients HRR1 (continuous data) had a Hazard Ratio for mortality (HR) of 0.990 with a confidence interval (CI) of 0.962–0.997, p = 0.008. Compared to patients with HRR1 >18, those with HRR1≤18 had a HR of 1.559 (CI 1.127–2.156) p = 0.007.

Grouping patients by median distance walked and HRR1–18 demonstrated that the HRR1 proved a useful predictor only in patients who walked less than 180 m.

**Conclusion**

HRR1 following ISWT predicts outcome in patients with pulmonary hypertension with more severe disease.

**REFERENCES**

1. Minai OA et al. Am J Respir Crit Care Med. 2012;185:400-408

**Abstract P171 Table 1**

<table>
<thead>
<tr>
<th></th>
<th>NPH group</th>
<th>PAH group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>153</td>
<td>718</td>
<td></td>
</tr>
<tr>
<td>Age-yrs</td>
<td>52.6 ± 13.0</td>
<td>60.4 ± 14.6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>sPAP-mmHg</td>
<td>24.3 ± 3.5</td>
<td>68.2 ± 21.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>dPAP-mmHg</td>
<td>9.7 ± 2.4</td>
<td>25.3 ± 8.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>mPAP-mmHg</td>
<td>15.9 ± 2.4</td>
<td>41.1 ± 12.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>PCWP-mmHg</td>
<td>7.3 ± 2.4</td>
<td>10.5 ± 2.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CO-L.min(^{-1})</td>
<td>4.6 ± 1.0</td>
<td>4.3 ± 1.3</td>
<td>0.008</td>
</tr>
<tr>
<td>HR-bpm</td>
<td>74.9 ± 13.1</td>
<td>78.5 ± 13.3</td>
<td>0.005</td>
</tr>
<tr>
<td>PVR-Wood units</td>
<td>1.9 ± 0.5</td>
<td>8.0 ± 4.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ca-ml.mmHg(^{-1})</td>
<td>4.6 ± 1.7</td>
<td>1.6 ± 0.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RC time-s</td>
<td>0.4 ± 0.1</td>
<td>0.5 ± 0.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV power total-W</td>
<td>0.2 ± 0.07</td>
<td>0.6 ± 0.24</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV power mean-W</td>
<td>0.16 ± 0.05</td>
<td>0.39 ± 0.14</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV power oscillary-W</td>
<td>0.08 ± 0.03</td>
<td>0.25 ± 0.11</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV oscillatory power fraction</td>
<td>0.34 ± 0.08</td>
<td>0.39 ± 0.06</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

NPH group - normal pulmonary haemodynamics group; PAH group - pulmonary arterial hypertension group; sPAP - systolic pulmonary artery pressure; dPAP - diastolic pulmonary artery pressure; mPAP - mean pulmonary artery pressure; PCWP - pulmonary capillary wedge pressure; CO - cardiac output; HR - heart rate; PVR - pulmonary vascular resistance; Ca - pulmonary artery compliance; W - watts.
Conclusions RC-time is not constant between health and pulmonary vascular disease. A reduction in RC-time, in the context of PAH, is associated with a decrease in cardiac efficiency. RVOPF is lower in the NPH group compared to the PAH group. This implies better cardiac efficiency in the NPH group possibly due to less pulsatile loading of the RV. Haemodynamic assessments which include measures of compliance may be of utility in understanding the progression of right heart failure in PAH.

The combination of systolic pulmonary artery pressure (sPAP), the PA-area at HRCT and the ratio of the diameter of segmental artery to the adjacent bronchus in the apicoposterior segment of the left upper lobe was strongly correlated to mPAP ($R^2=0.785163$; $p = 0.0001$). The contribution of other echocardiographic-parameters (longitudinal STRAIN and Time-to-Peak STRAIN values, TTP) in multivariate regression analysis was not statistically significant, probably because of the small number of patients.

Using the ROC Analysis we found that 931.6 is the upper limit of normal (ULN) for the PA-area, with a 86% sensitivity and 61% specificity (0.839 AUC); while 20.34 is the ULN for the ratio of the PA-area to the ascending aorta diameter, with a 100% sensitivity and 50% specificity (0.804 AUC).

Conclusion (S) HRCT remains an useful tool to identify patients with PH, however the combination of HRCT and echocardiography improves accuracy in PH diagnosis.

In the pleural zone

**P173** AMBULATORY MANAGEMENT OF SPONTANEOUS PNEUMOTHORAX

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10.1136/thoraxjnl-2014-206260.301

Introduction There is no clear consensus on the management of Spontaneous pneumothorax. BTS recommends insertion of chest drain following failure of initial aspiration in large primary spontaneous pneumothorax (PSP) and in all patients with symptomatic/ large secondary spontaneous pneumothorax (SSP). These patients are usually admitted to hospital following chest drain insertion.

Objective To study the feasibility and safety of early discharge of spontaneous pneumothorax patients requiring chest drain on the ambulatory pathway with a Heimlich valve (pneumostat device).

Methods Patients were initially managed as per BTS guidelines. Patients who had a chest drain inserted were admitted until review by the respiratory team. All PSP patients and some SSP patients with good performance status (WHO scale 0–1) were eligible for the ambulatory pathway. Those with continuing air leak are fitted with a Heimlich valve and discharged home. They were reassessed every two days with a CXR on arrival in the ambulatory care unit. The chest drain was removed once the air leak stopped for at least 24 h.

Results 21 episodes of spontaneous pneumothorax in 18 patients (10 PSP and 8 SSP) were treated on the ambulatory pathway between May’13 and June’14. The healthcare usage of patients on ambulatory pathway is listed in the table. The pneumothorax resolved successfully in 82% (17 episodes). There were three recurrences requiring repeat management on the ambulatory pathway. A total of 10 patients were referred to the surgeon including four with continuing air leak and six due to

<table>
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<th>Abstract P173 Table 1</th>
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<tr>
<td><strong>Duration in hospital (days)</strong></td>
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<tr>
<td><strong>Duration in community (days)</strong></td>
</tr>
<tr>
<td><strong>Number of reviews</strong></td>
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</table>
recurrence. Patients with continuing air leak remained in the community until admission for thoracic surgery. Complications included pain in two patients and allergic reaction to the dressing used in one patient. The patient with allergic reaction had accidental dislodgement of chest drain during dressing change necessitating reinsertion of chest drain.

**Conclusion** It is feasible for most patients with large PSP and many patients with SSP to be managed on an ambulatory care pathway with a Heimlich valve until their pneumothorax heals or is definitively treated.

**REFERENCE**

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### Abstract P174 Table 1

<table>
<thead>
<tr>
<th>NA as first intervention</th>
<th>ICD as first intervention</th>
<th>P value</th>
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</thead>
<tbody>
<tr>
<td>Median age, years (IQR)</td>
<td></td>
<td>0.66</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td></td>
<td>0.41</td>
</tr>
<tr>
<td>Right sided, n (%)</td>
<td></td>
<td>0.99</td>
</tr>
<tr>
<td>Previous pneumothorax, n (%)</td>
<td></td>
<td>0.72</td>
</tr>
</tbody>
</table>

**Methods** We conducted a retrospective observational study of 735 consecutive pneumothorax episodes between March 2008 and December 2013. Those with secondary spontaneous pneumothorax, history of trauma and iatrogenic pneumothorax were excluded. Pneumothorax with no visible aerated ipsilateral lung on plain chest radiograph was defined as ‘PSP with complete lung collapse’. Patient case records and plain chest radiographs were reviewed. Values of p < 0.05 were considered statistically significant.

**Results** Of the 735 episodes, 233 (32%) were PSP. 61 PSP patients were identified to have complete lung collapse on chest radiograph. 32 patients had NA and 29 ICD as the first intervention. There was no statistically significant difference between the two groups in terms of age, sex, smoking history and symptoms. Compared to the NA group, patients with ICD had significantly better immediate success rate (66% vs. 10%; p < 0.0001) and lower rate of recurrence (3% vs. 31%; p = 0.0064). Median length of stay was similar in both groups. Almost a third of the patients in both groups required a definitive surgical intervention.

**Conclusion** Our results suggest significantly better success with ICD as the first intervention in the management of PSP with complete lung collapse and there was no added benefit of NA. We propose a further sub group of PSP with complete lung collapse in which NA should not be attempted.

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### Abstract P175

**Measurement of air leak post-thoracic surgery: Implications for medical management of pneumothorax**

1. RJ Hallifax, 2J Mitchell, 3JP Corcoran, 1Psallidas, 1NM Rahman, 1E Belcher. 1Oxford Centre for Respiratory Medicine, Oxford, UK, 2Department of Thoracic Surgery, Oxford, UK

10.1136/thoraxjnl-2014-206260.303

**Introduction** Use of digital suction devices post-thoracic surgery is widespread, allowing patients to be more mobile and potentially reducing the time to chest drain removal post-op (in comparison with standard underwater seal).

Spontaneous pneumothorax (SP) is common (5,000/yr in the UK). However, there are no good predictors of outcome for patients with pneumothorax. Measurement of early air leak could potentially predict which patients who will not resolve spontaneously and will require surgery. Post-surgical data may provide an interesting analogy to ongoing air leak in spontaneous pneumothorax. The hypothesis is that reduction in air leak to <50 ml/min within 30 min of attachment can predict air leak over next 48 h and overall drain duration.

**Methods** Retrospective review of the use of digital suction device (Thopaz, Medela UK) post-op in the Thoracic Surgical department of a tertiary referral centre between May and December 2012. The detailed air leak measurements were assessed against duration of drainage.

**Results** Operations included 88 lung resections (wedge resections, lobectomies and metastasectomies via VATS and thoracotomy), 28 pleural procedures (VATS pleurodesis +/- bulbectomy) and 12 empyema drainage/decortication. Average air leak over the entire duration was significantly different between the groups: 80.6 ml/min, 54.3 ml/min and 304.5 ml/min respectively (p = 0.01).

Patients with early reduction of air leak (i.e. reduced to <50 ml/min within the initial 30 mins) were compared to patients
with >50 ml/min air leak (see Table). The mean air leak over the subsequent 48 h was significantly different between the groups for patients post-lung resection (34.4 vs 164.9 ml/min, p = 0.01), and post-pleural operation (9.1 vs 196.7 ml/min, p = 0.03); but not after empyema surgery (9.8 vs 1001.4 ml/min, p = 0.08). The duration of chest drain in situ post-op was lower in the group with early reduction in air leak (but did not reach statistical significance).

**Conclusion** This sample of post-surgical data suggests that early resolution of air leak is associated with ongoing low air leak (and early drain removal). Equivalent prospective studies are now required in the medical management of pneumothorax to determine whether early physiological measurements can predict outcome.

**P176** IATROGENIC PNEUMOTHORAX POST CT-GUIDED LUNG BIOPSY – HOW DO WE MANAGE IT?

AM Lewis, AA Ionescu. Royal Gwent Hospital, Aneurin Bevan University Health Board, Newport, UK

10.1136/thoraxjnl-2014-206260.304

**Introduction** Iatrogenic Pneumothoraces (IP) are a common complication of computerised tomography (CT)-guided lung biopsy. Management depends on size, underlying lung disease, and symptoms.

The British Thoracic Society (BTS) Guidelines comment that the majority of IPs do not require intervention. If needed aspiration is successful in 89%.(1). Size of pneumothorax is assessed differently by the BTS and The American College of Chest Physicians (ACCP),(1, 2). This study reports the management of IP over a 15-month period.

**Methods** All IP over 15-months were analysed. Data extraction forms for each IP episode utilised electronic clinical, MDT notes and radiological images.

**Results** 160 day-case CT-guided lung biopsies were performed. There were 32 IPs, 20% of all biopsies.

Five IPs were >2 cm at hilar level, classified as large by BTS guidance. Fifteen were >3 cm apically, described as large by ACCP classification.

There was poor agreement between BTS and ACCP sizing of pneumothoraces, (kappa 0.26).

All BTS-classified large pneumothoraces, and 9(60%), of ACCP-classified large pneumothoraces required intervention.

Fifteen (47%) patients with IP, all asymptomatic with pneumothoraces

Nine (28%) IPs underwent inpatient observation. Three subsequently required intervention, all of which were small at hilar level but large apically, or symptomatic.

Aspiration was performed in 4 patients, one being >2 cm at hilar level and all >3 cm apically. Two required subsequent tube drainage.

Five (16%) IPs were treated initially with intercostal chest drainage. Four had pneumothoraces >2 cm at hilar level, and the other had a large apical pneumothorax. Only one was symptomatic.

Five patients were initially observed or had simple aspiration but subsequently required tube drainage.

**Conclusions** Two-thirds of the IPs were managed conservatively. Thirteen percent of patients had aspiration of which three-quarters needed subsequent intervention. Symptoms or FEV1 did not predict need for intervention. The BTS and ACCP criteria for size assessment had poor agreement and clinical judgement was used to decide on treatment.
PATIENT-RELATED OUTCOME MEASUREMENTS IN PLEURAL EFFUSIONS


Introduction Pleural disease is a common health problem in the general population and the number of pleural interventions available to physicians is rapidly expanding. Most clinical studies to date have focused on the generation of successful treatments for pleural diseases without considering patient-centred assessments of symptomatic relief in a procedure undertaken for patient benefit. Patient-related outcome measures (PROMs) such as the assessment of pain and difference in dyspnoea have been used in other disease areas to estimate effectiveness and guide interventions. This prospective study measured PROMs after pleural interventions using a specific survey questionnaire.

Methods Data were collected from 95 patients treated in a tertiary referral centre from December 2013 to June 2014. Pleural interventions included diagnostic aspiration, therapeutic aspiration, thoracoscopy, intercostal chest drain insertion and indwelling pleural catheter insertion. We gathered information on pain, dyspnoea, expected improvement and willingness to repeat the procedure if needed using a 100 mm visual analogue scale (VAS). Clinical, radiological and histological data were recorded and categorised the patients with pleural effusions to either: malignant, infected, heart failure and undiagnosed. Patients with pneumothorax were classified to either primary or secondary. Data are presented as mean ± SD.

Results Data were collected from 31 therapeutic aspirations, 30 intercostal drain insertions, 17 diagnostic/simple aspirations, 14 thorascopies and 3 indwelling catheter insertion groups. The results showed the procedure associated with the most pain is medical thoracoscopy (VAS: 20 ± 20.3 mms) whereas diagnostic aspiration (VAS: 2.52 ± 4.78 mms) was the least uncomfortable. Pain measurements were similar in intercostal and indwelling pleural catheter insertion groups (p: 0.75). VAS score for dyspnoea demonstrated that intercostal drain insertion had the greatest effect on patients’ breathlessness compared to the other procedures (VAS difference pre and post-procedure: 50.8 ± 27 mms). 99.8% of the patients would repeat any of the pleural procedures if needed.

Conclusion Our study, the first to prospectively assess patient-related outcomes in pleural procedures, demonstrates that different pleural procedures significantly improve symptoms alongside a high degree of patient satisfaction. Pleural PROMs may represent a standardised way of measuring symptomatic benefit which can be used in both clinical practice and future research.

CLINICIAN AND PATIENT EXPERIENCE IN THE DELIVERY OF A DAY-CASE LOCAL ANAESTHETIC THORACOSCOPY SERVICE AT A SPECIALIST PLEURAL UNIT

I Psallidas, JP Corcoran, RJ Hallifax, A Takeas, A Sykes, NM Rahman. Oxford Centre for Respiratory Medicine, Oxford University Hospitals NHS Trust, Oxford, UK

Background and method Local anaesthetic thoracoscopy (LAT) is utilised by an increasing number of respiratory physicians for diagnostic and therapeutic purposes in the setting of pleural disease. Although guidelines [1] allow for day-case LAT (i.e. procedure and discharge home on the same day), the majority of UK centres electively admit patients for overnight observation post-procedure. This impacts on service provision by increasing bed occupancy and limiting procedural capacity; whilst affecting patients by incurring a hospital stay they might not need. Reasons for centres not offering day-case LAT are unclear but may include clinician experience and limitations in the available guidelines.

Day-case LAT has been offered by our tertiary centre-based pleural service for a number of years. Patients are routinely considered for this approach if their procedure is for purely diagnostic purposes, as opposed to being therapeutic in addition (i.e. whether talc poudrage pleurodesis is anticipated). Other factors considered in the decision-making process include performance status, co-morbidities and social background. A review of our procedural database from January 2010 to June 2014 was...
performed to identify the number of day-case LATs and define the characteristics of the patient population offered this approach.

Results Of 294 LATs booked during this period, 127 (43.2%) were planned as a day-case procedure. 113 day-case LATs went ahead with 7 patients (6.2%) requiring an “unplanned” hospital admission for reasons outlined in Figure 1. Patients planned for day-case LAT tended to be younger (68.1 vs. 72.4 years, p = 0.12, unpaired t-test) with fewer co-morbidities and better social support than the general population having this procedure. No patient declined a day-case procedure having been offered one, whilst the process on the day proved acceptable with most patients valuing the opportunity to avoid an overnight hospital stay.

Conclusion With careful case selection day-case LAT can be provided successfully, benefiting patients and clinicians whilst saving bed days and healthcare costs. Centres with the appropriate case mix and experience may wish to develop day-case LAT as part of their service. Future guidelines should acknowledge this need and offer advice on patient selection and logistical requirements.

REFERENCE
1 Thorax 2010; 65 Suppl 2:i54–60

Poster sessions

P179 DOES DAY-CASE THORACOSCOPY REDUCE THE NUMBER OF HOSPITAL BED DAYS FOR PATIENTS UNDER INVESTIGATION FOR UNILATERAL PLEURAL EFFUSION?
J Fallon, J Pepperell. Musgrove Park Hospital, Taunton, UK
10.1136/thoraxjnl-2014-206260.307

Introduction and objectives Medical thoracoscopy is the investigation of choice for diagnosis of exudative pleural effusions where pleural cytology is negative and malignancy is suspected. Over the past 18 months, our centre has offered day-case thoracoscopy to suitable patients, with the aim of reducing elective admissions and overall hospital bed days for patients undergoing this procedure. A review of practice has been performed to evaluate whether day-case thoracoscopy is effective in reducing bed days in this cohort of patients.

Methods Data was retrospectively collected from patients attending our centre for medical thoracoscopy over a 12 month period (Feb 2013 – Feb 2014). Information on the number of bed days required, readmission rates and repeat procedures was reviewed for those attending for day-case thoracoscopy and compared with those electively admitted for overnight stay +/- talc pleurodesis.

Results Of 53 patients undergoing medical thoracoscopy at our centre, 31 patients were electively admitted for thoracoscopy, with an average stay of 3.8 bed days. 23 (74%) of this group underwent talc pleurodesis during their initial admission. 13 (42%) patients required readmission within 6 months, extending their total length of stay in this period to 7.3 bed days. 11 (35%) of these patients required further pleural procedure (s) within 6 months of initial thoracoscopy. 22 patients underwent day-case thoracoscopy (initial stay of 0 bed days). 9 (41%) of these patients required re-admission within 6 months, with an average total length of stay of 3.8 bed days. 11 (50%) of these patients went on to require further pleural procedure (s). For the 22 patients attending for day-case thoracoscopy, the number of bed days saved (number of patients x average length of elective admission) was 83.6 bed days.

Abstract P179 Table 1 Comparison of elective admission for thoracoscopy with day-case thoracoscopy

<table>
<thead>
<tr>
<th></th>
<th>Elective admissions</th>
<th>Day-case admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thoracoscopy patients (n = 53)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Initial admission bed days (average)</td>
<td>3.8</td>
<td>0</td>
</tr>
<tr>
<td>Re-admission within 6 months</td>
<td>13 (42%)</td>
<td>9 (41%)</td>
</tr>
<tr>
<td>Re-admission bed days (average)</td>
<td>3.5</td>
<td>3.8</td>
</tr>
<tr>
<td>Total bed days (average)</td>
<td>7.3</td>
<td>3.8</td>
</tr>
<tr>
<td>Further pleural procedure (s) within 6 months</td>
<td>11 (55%)</td>
<td>11 (50%)</td>
</tr>
</tbody>
</table>

Conclusions Day-case thoracoscopy reduces the number of hospital bed days in patients under investigation for unilateral pleural effusion and does not lead to increased rates of re-admission for this cohort of patients. Those undergoing day-case thoracoscopy are more likely to require a further pleural procedure, as talc pleurodesis is not performed in this group.

P180 THE IMPORTANCE OF ACCURATE PRE-OPERATIVE BIOPSY IN THE RADICAL MANAGEMENT OF MESOTHELIOMA – DON’T BLAME THE PHYSICIAN JUST KEEP TAKING MORE BITES
Aj Sharkey, R Vaja, V Joshi, J Le Quesne, S Muller, C Richards, D Wailer. Glenfield Hospital, Leicester, UK
10.1136/thoraxjnl-2014-206260.308

Introduction Histological subtype is an independent prognostic factor in malignant pleural mesothelioma (MPM). Accurate typing is required to offer appropriate therapy, with surgery generally being reserved for epithelioid disease due to the poor survival in biphasic and sarcomatoid MPM. Preoperative tissue can be obtained by a variety of methods which may yield suboptimal specimens.

We aimed to investigate whether the mode of biopsy influenced the accuracy of diagnosis.

Methods We reviewed clinicopathological data from all patients who underwent radical surgery for MPM from 2000–2014, and compared subtyping from biopsies and resection specimens. In addition, a subspecialty expert consultant histopathologist reviewed biopsies from all biphasic cases.

Results In total, 335 patients had available pathological data available.
61 (18.2%) showed discordance in subtyping between the diagnostic biopsy and the resection specimen. In 53 patients a poorer prognosis cell type was identified at resection (see Table).

There was poorer survival in the discordant group; median survival 8.2 vs 15.2 month (p = 0.001 HR=1.659 95% CI 1.227–2.243).

Discordance was found to be an independent predictor of survival on multivariate analysis (HR 1.653 95% CI 1.207–2.264 p = 0.002).

There was no effect of method of pre-operative biopsy on concordance (p = 0.306). There was also no difference in the accuracy of the diagnosis if a surgical biopsy was performed versus medical thoracoscopy or a radiologically guided biopsy (p = 0.768).

In 26 (18.4%) cases there was discordance between pre-operative biopsy and post-operative histological subtype. In 22 patients a poorer prognosis cell type was identified.

Conclusion These data demonstrate potential inaccuracy of current biopsy practice with accompanying impaired patient
outcome. This correlates with our existing knowledge of the heterogeneity of MPM and the difficulty of subtyping from small biopsies. A wide distribution of biopsy sites within the hemithorax is likely to be more significant in obtaining an accurate histological diagnosis than the mode of biopsy itself.

**Abstract P180 Table 1**

<table>
<thead>
<tr>
<th>Pre-op histology</th>
<th>Epithelioid</th>
<th>Biphassic</th>
<th>Sarcomatoid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epithelioid</td>
<td>243</td>
<td>49</td>
<td>0</td>
</tr>
<tr>
<td>Biphassic</td>
<td>4</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>Sarcomatoid</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
</tbody>
</table>

There was a significant difference in survival between the low risk group and the high and medium risk groups combined (24.2 vs 14.5 months p = 0.031).

Survival was similar between those with known asbestos exposure and those who reported no asbestos exposure; 14.7 vs 15.2 months p = 0.573.

**Conclusion** This is the first study to demonstrate that those patients who worked in occupations at highest risk of developing mesothelioma also have the worst comparative survival from radical surgery. The causation remains a topic for further research. It is also of note that patients with no reported asbestos exposure had an unexpectedly poor survival. The importance of a careful occupational history of asbestos exposure is emphasised.

**REFERENCE**


**P181** **DOES THE DEGREE OF OCCUPATIONAL ASBESTOS EXPOSURE AFFECT THE OUTCOME OF RADICAL SURGERY FOR MALIGNANT PLEURAL MESOTHELIOMA?**

Al Sharkey, R Vaja, A Nakas, D Waller. Glenfield Hospital, Leicester, UK

10.1136/thoraxjnl-2014-206260.309

**Introduction** Malignant Pleural Mesothelioma (MPM) is associated with variable exposure to asbestos and a spectrum of prognosis which may be extended by radical surgery. Proportional mortality ratios have been used in the past to estimate the risk of developing mesothelioma, and more recently specific occupational risk groups have been described.

We aimed to determine whether those at highest risk of developing mesothelioma by virtue of working in high exposure occupations also fared worse after radical surgery for mesothelioma.

**Methods** Case notes were reviewed for all patients undergoing radical surgery for MPM between 1999 and 2014. Prior asbestos exposure had been determined by histories taken by the multidisciplinary team. Patients were separated into one of 8 groups, using modified versions of the categories proposed by Rake et al. in 2009. Comparative outcome was assessed for each group.

**Results** History of asbestos exposure was available for 262 patients. Thirteen patients were excluded from further analysis having died in hospital.

Of the remaining 249 patients, 84.3% were male, and median age was 62 years (range 14–81 years). The only significant intergroup difference was gender, with more females in the low risk and no exposure groups (p = 0.021). However, in our cohort of surgically treated patients, gender had no effect on survival (p = 0.476).

**Abstract P181 Table 1**

<table>
<thead>
<tr>
<th>Exposure Group (Rake et al)</th>
<th>Asbestos exposure</th>
<th>Median survival (months) p</th>
<th>Risk Group</th>
<th>Median survival (months) p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Any non-construction high-risk job</td>
<td>60</td>
<td>14.4</td>
<td>High Risk</td>
<td>14.4</td>
</tr>
<tr>
<td>2 Carpenter</td>
<td>34</td>
<td>15.8</td>
<td>Medium risk</td>
<td>14.8</td>
</tr>
<tr>
<td>3 Plumber, electrician, painter or decorator</td>
<td>17</td>
<td>14.0</td>
<td>Low risk</td>
<td>24.2</td>
</tr>
<tr>
<td>4 Other construction</td>
<td>35</td>
<td>13.2</td>
<td>None</td>
<td>15.2</td>
</tr>
<tr>
<td>5 Any medium-risk industrial job</td>
<td>21</td>
<td>14.8</td>
<td>None</td>
<td>15.2</td>
</tr>
<tr>
<td>6 Any low-risk industrial job</td>
<td>7</td>
<td>32.0</td>
<td>None</td>
<td>15.2</td>
</tr>
<tr>
<td>7 Domestic exposure</td>
<td>12</td>
<td>24.2</td>
<td>None</td>
<td>0.167</td>
</tr>
<tr>
<td>8 None of the above</td>
<td>63</td>
<td>15.2</td>
<td>None</td>
<td>0.447</td>
</tr>
</tbody>
</table>

**P182** **APPRAISAL OF AN INDIWELLING PLEURAL CATHETER (IPC) SERVICE AT A LARGE ACUTE TRUST**

RM Mercer, S Gunatilake, LJ Bishop, KS Babu, A Chauhan. Queen Alexandra Hospital, Portsmouth, UK

10.1136/thoraxjnl-2014-206260.310

**Introduction** Data on indications, outcomes and complications of IPCs from clinical trials has been published. This audit examined differences in practice and outcomes between clinical trials and day-to-day working which may influence the pleural service and provide information to other hospitals considering introducing this service.

**Method** We retrospectively reviewed patient-related data and outcomes for IPCs inserted at our hospital from February 2011 until December 2013. We compared the findings to secondary outcomes of the IPC arm of the TIME2 trial.

**Results** 102 IPCs were placed into 93 patients: 43 as inpatients; 59 as outpatients. 20 inpatients and 23 outpatients had previous talc pleurodesis.

10 patients had microbiological isolation of pleural fluid throughout a total of 27.3 IPC years; not all were associated with clinical signs of a pleural infection. Only 12 (50%) patients with a C-reactive protein of >200 mg/l had a sample of their pleural fluid sent for culture.

Drain removal occurred in 23% of the inpatient IPCs and 29% of the outpatient compared to 57% in the TIME2 trial.

The median inpatient stay after elective pleurodesis in an outpatient was 1.3 nights in 2011 (range 0–11), 1 night in 2012 (range 0–5) and 0 nights in 2013 (range 0–5).
Conclusion The TIME2 cost analysis was based on a median stay of 0 nights which has been replicated in our hospital this year. The optimisation of community support and increasing confidence with the procedure led to reductions in inpatient stays.

The rate of IPC removal was substantially less common in our cohort and the indication for removal was often not due to spontaneous pleurodesis alone unlike the TIME2 trial. Indications for removal included infection, pain and blockage as well as pleurodesis. The data from our centre did not exclude any patients, including those who died, and the follow up period often continued beyond 6 months.

Some large differences exist between the TIME2 trial data and our cohort. While this could reflect a different patient population and setting, it could also highlight differences in outcomes between controlled clinical trials and day-to-day practice.

REFERENCE
1. Davies HE et al. JAMA 2012;307(22):2383–9

TB: non pulmonary and hepatotoxicity

Abstract P182 Table 1

<table>
<thead>
<tr>
<th>Indication for IPC</th>
<th>Inpatient</th>
<th>Elective</th>
<th>Missing data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung cancer</td>
<td>5</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>7</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Other cancer</td>
<td>26</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Benign or unknown</td>
<td>1</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Number of IPCs</td>
<td>43</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>IPC number removed</td>
<td>10 (23%)</td>
<td>17 (29%)</td>
<td>1 displaced</td>
</tr>
<tr>
<td>Removed due to spontaneous pleurodesis</td>
<td>3 (7%)</td>
<td>5 (9%)</td>
<td></td>
</tr>
<tr>
<td>Median days in situ until removal (range)</td>
<td>97.5 (3–168)</td>
<td>92.5 (22–340)</td>
<td>1 unknown</td>
</tr>
<tr>
<td>IPC in situ at time of death</td>
<td>31 (72%)</td>
<td>35 (59%)</td>
<td>5 lost to follow up</td>
</tr>
<tr>
<td>Median days in situ until death (range)</td>
<td>22 (7–317)</td>
<td>79 (2–346)</td>
<td></td>
</tr>
</tbody>
</table>

Introduction Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is now the standard of care for investigating intra-thoracic lymphadenopathy. Although well validated in malignancy and sarcoidosis, the literature for intra-thoracic tuberculous lymphadenitis is limited. Previous work from neighbouring London boroughs reported a sensitivity (histology or microbiology consistent with tuberculosis (TB)) for TB of 94% with positive TB culture in 47% of 156 patients.

Methods We examined retrospectively all EBUS-TBNA procedures performed at a London district general hospital between April 2010 and January 2014. Patients were referred to our EBUS service from our own hospital and two local centres. All patients were assessed clinically prior to the procedure and underwent a CT scan. Bronchoscopy reporting software was used to identify all EBUS procedures. Patient notes, clinic letters, electronic patient records and the London TB Register (LTBR) were used to obtain clinical information then matched with pathological and microbiological results. All patients were followed up for a minimum of 6 months.

Results 363 patients were included. The overall sample yield (either lymph node or tumour identified) was 94%. 63 cases of tuberculosis were identified and EBUS-TBNA had been diagnostic in 57 (90%). Pathological findings were consistent with TB in 84% of cases and culture was positive in 62%. Culture identified 5 cases of drug resistance. Where caseating granulomas were identified, 18/25 cases were culture positive and 15/23 where non-caseating granulomas were identified (p = 0.76). In addition, where necrotic material was obtained 3/5 samples were culture positive and where reactive lymph nodes were identified 4/9 samples were culture positive.

Conclusion EBUS-TBNA is a useful tool in the investigation of intra-thoracic tuberculous lymphadenitis. We show the possibility of achieving higher culture positivity from that reported in the literature. It highlights the importance of the TB culture for definitive diagnosis and detecting drug resistance. It is important to examine these findings in the context of appropriate clinical information and investigations.

P184 FEMALE GENITAL TUBERCULOSIS: THE LONG ROAD TO DIAGNOSIS

10.1136/thoraxjnl-2014-206260.312

Introduction Female genital tuberculosis (TB) is rarely encountered in the UK but early diagnosis and treatment can prevent significant morbidity.

Methods We conducted a retrospective study of all patients treated at our institution for female genital TB between 2004 and 2014. Data including demographics, symptoms, microbiological and histological diagnoses and treatment outcomes were recorded.

Results 10 cases of female genital TB were identified. These account for approximately 0.71% of our TB cases, giving a local incidence of female genital TB of approximately 0.5/100,000 population. Mean age was 37.9 +/-14.3. Five patients were from Bangladesh, two from India and one from Pakistan, Cyprus and Somalia. Mean duration of symptoms prior to diagnosis was 24.3 months, range: 0–84. Presenting symptoms included infertility (50%), menorrhagia (10%), amenorrhoea (20%), irregular menstrual bleeding (40%), dyspareunia (20%), vaginal discharge (10%), post coital bleeding (10%) and lower abdominal pain (50%). Patients also experienced fevers (30%), night sweats (10%) and weight loss (10%). All patients had either a laparoscopy or hysteroscopy with biopsy of the endometrium in nine cases and the ovary in one case. Seven cases were found to have necrotising granuloma on biopsy of which two were positive for Ziehl-Neelsen (ZN) staining, two were negative and three were not performed. Non-necrotising granuloma was seen in one case and histology was unrecorded for two cases but PCR was positive in both these biopsies. Samples were sent for culture in three cases and all had fully sensitive TB. All cases were treated with standard TB treatment. In two cases treatment is ongoing. One patient died from a co-existing condition. Seven patients completed treatment, of which four had full symptom
resolation, two remain under the infertility team and one has ongoing abdominal pain. Median treatment duration was six months.

Conclusion This case series highlights the delay in diagnosis and the significant morbidity – particularly infertility – experienced by patients with genital TB. Samples were frequently not sent for culture. Raising awareness of TB within obstetrics and gynaecology and highlighting the importance of considering TB in patients from high incidence countries may help reduce diagnostic delay for these women.

**P185** IMPROVING THE ACCURACY OF MICROBIOLOGICAL DIAGNOSIS OF TB LYMPHADENITIS – IS A MULTIDISCIPLINARY APPROACH NECESSARY?

A Saigal, HS Kasi, R Sands, A Jayaratnam. Barking, Havering and Redbridge NHS Trust, Romford, UK

10.1136/thoraxjnl-2014-206260.313

Introduction The gold standard for diagnosing tuberculosis (TB) is from culture of the organism from fluid or tissue. Histological analysis of surgical specimens is well-established, but microbiological analysis is less frequent. Our trust serves a population with a high incidence of TB. Therefore, patients who present with lymphadenopathy should always be considered for a diagnosis of TB and all specimens sent for microbiological and histological diagnosis.

Methods A retrospective analysis was undertaken of all patients diagnosed with TB lymphadenitis between 2009–2013 using the London TB Register (LTBR), case notes and laboratory data to identify the proportion diagnosed with microbiology data compared with histology data.

Results 324 patients were diagnosed with TB lymphadenitis from LTBR, of which 73% (235/324) had lymph node (LN) specimens taken for microbiological or histological diagnosis. 233 patients had extrathoracic disease alone, of which 62% (144/233) had LN tissue sent for microbiology with 74% yielding a positive culture. In both groups, a greater percentage of LN tissue was sent for histo-cytological analysis than microbiology (see figure).

75% (12/16) of patients with combined extrathoracic and intrathoracic disease had specimens sent for microbiology. 83% (11/16) gained a positive microbiological diagnosis from lymph node sampling.

Conclusion Microbiological specimens were more likely to be sent in patients with extrathoracic disease compared to those with intrathoracic disease. This may partly be explained by the fact that all intrathoracic lymph node sampling during this study period was undertaken at other centres, mostly through referrals from the lung cancer MDT. Therefore TB may not have been considered as a possible diagnosis.

However, a significant proportion of surgical samples taken locally did not have microbiology specimens sent, which potentially may have impacted on treatment outcomes.

This review highlights that more education should be undertaken locally with surgical and radiology departments and the lung MDT, emphasising the need for all lymph node specimens to be sent for both microbiological and histological analysis.

**P186** INTRATHORACIC LYMPH NODE TUBERCULOSIS – A COMPREHENSIVE CLINICAL DESCRIPTION

K Kow, D Connell, A Singanayagam, D Ap Dayfyl, H Janus, M O’Donoghue, M Wickremasinghe, A Lanfear, OM Kan. Imperial College London, London, UK; St Mary’s Hospital, Imperial College Healthcare NHS Trust, London, UK

10.1136/thoraxjnl-2014-206260.314

Background Intrathoracic lymph node tuberculosis (ITLNTB) is an extra-pulmonary manifestation of tuberculosis (TB) and a predominant feature of primary TB in children. Historical literature supports the key role of lymph nodes in tuberculosis pathogenesis yet there is a paucity of literature describing ITLNTB in adults.

Methods This study comprehensively reviewed the clinical, radiological and pathological features of ITLNTB from 2009–2012 at a busy urban tuberculosis clinic.

Results 113 adult patients with ITLNTB were identified between 2009–2012. Patients were usually male, with a mean age of 41.5 ± 15.8 years and mostly from White, Black-African or Indian ethnic groups. 86% were non-UK born and most presented within 5–10 years of entering the country. 43% were asymptomatic. A subgroup of patients who were mycobacterial culture positive on endobronchial ultrasound sampling (EBUS) of intrathoracic lymph nodes were identified as patients with definite mycobacterial infection of the lymph nodes (n = 27).

Comparisons between symptomatic and asymptomatic groups in the whole cohort and EBUS culture positive subgroup demonstrated significant associations between symptoms and disease dissemination (p = 0.0002 and p = 0.01 respectively); and symptoms and pathological response in the lymph nodes (p = 0.02 and p = 0.01 respectively), suggesting the presence of a spectrum of disease reflected in congruent clinical and pathological responses (Table 1). Comparisons between disease sites affected also showed a significant association between host response in the lymph nodes and disease dissemination (p = 0.006).

The presence of radiological necrosis, number of affected nodal stations, and largest node size were significantly greater in symptomatic patients in the whole cohort; with a similar trend observed in the EBUS culture positive subgroup.

In the EBUS culture positive subgroup, asymptomatic patients were identified significantly earlier following entry to the UK (p = 0.01).

Discussion This study provides the first comprehensive clinical description of ITLNTB in adults. There is a spectrum of disease

**Abstract P185 Table 1** Table demonstrating numbers of patients with TB lymphadenitis having lymph node samples sent for microbiological or histological analysis and diagnostic yield

<table>
<thead>
<tr>
<th>2009–2013</th>
<th>Number &amp; Percentage of samples sent for</th>
<th>Number &amp; Percentage of samples with positive culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>LN biopsy</td>
<td>Microbiology</td>
<td>Histology</td>
</tr>
<tr>
<td>Combined</td>
<td>M (193)</td>
<td>152 (79%)</td>
</tr>
<tr>
<td>Intrathoracic</td>
<td>M (193)</td>
<td>152 (79%)</td>
</tr>
<tr>
<td>Extrathoracic</td>
<td>M (193)</td>
<td>152 (79%)</td>
</tr>
</tbody>
</table>

IM = Microbiology; HM = Histology; LN = Lymph Node
The use of moxifloxacin for the treatment of increased pulmonary M. avium-intracellulare

Thorax A158

= 17). 32 patients on moxifloxacin had ECGs of which 6 between regimens with moxifloxacin (n = 43) or without it (n = 27). There was no significant difference in either the success of treatment (p = 0.102) or the risk of hepatotoxicity (p = 0.264). We recommend a treatment regimen including moxifloxacin followed by 10 months of rifampicin, isoniazid and pyrazinamide. A response to treatment, with no evidence of disease recurrence on cessation of therapy, was seen in 78.3% of cases (72/92). 12.5% of patients reported possible side effects including gastrointestinal symptoms (n = 12), headache (n = 1), and rash (n = 1). No serious side effects were reported. Maximum QTc was never found to be above 500 milliseconds and there were no episodes of documented arrhythmias or syncope.

Conclusions We recommend a treatment regimen including moxifloxacin in place of ethambutol so that any reported visual change is unlikely to be related to treatment, and we propose continuing moxifloxacin beyond the intensive phase, if tolerated, when culture is unavailable. We treat ophthalmic TB for the same duration as central nervous system TB. Our data shows that this is a safe and effective regimen but more evidence is required before recommending definitive guidelines.

Poster sessions

Abstract P187 Table 1 Comparison between symptomatic and asymptomatic groups from EBUS culture positive subcohort

<table>
<thead>
<tr>
<th>Symptomatic (n = 13)</th>
<th>Asymptomatic (n = 26)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>55.4 ± 12.8</td>
<td>56.0 ± 9.3</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>White 10 (77%)</td>
<td>23%</td>
</tr>
<tr>
<td>Black-African</td>
<td>26.5%</td>
<td>37.5%</td>
</tr>
<tr>
<td>Indian</td>
<td>31.8%</td>
<td>29%</td>
</tr>
<tr>
<td>Born in UK</td>
<td>U 89.4%</td>
<td>97.5%</td>
</tr>
<tr>
<td>Duration in UK (median, IQS)</td>
<td>12 (4-18.5)</td>
<td>2 (1-4)</td>
</tr>
<tr>
<td>Exposures</td>
<td>Diabetes 0%</td>
<td>14.29%</td>
</tr>
<tr>
<td></td>
<td>HIV 5.26%</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Travel endemic</td>
<td>65.42%</td>
</tr>
<tr>
<td></td>
<td>Smoking</td>
<td>13.33%</td>
</tr>
<tr>
<td></td>
<td>Tuberculosis</td>
<td>37.5%</td>
</tr>
<tr>
<td>Disease sites</td>
<td>Pulmonary</td>
<td>67.37%</td>
</tr>
<tr>
<td></td>
<td>Pleural</td>
<td>5.26%</td>
</tr>
<tr>
<td></td>
<td>ETNL</td>
<td>26.32%</td>
</tr>
<tr>
<td></td>
<td>Skin</td>
<td>0%</td>
</tr>
<tr>
<td></td>
<td>Eye</td>
<td>5.26%</td>
</tr>
<tr>
<td>% Isolated</td>
<td>PTB (HIV and EPTB)</td>
<td>42.11%</td>
</tr>
<tr>
<td>% Extrapulmonary TB</td>
<td>5.26%</td>
<td>0%</td>
</tr>
<tr>
<td>Cytology</td>
<td>Granulomatous with caseation</td>
<td>62.3%</td>
</tr>
<tr>
<td></td>
<td>Granulomatous without caseation</td>
<td>26.32%</td>
</tr>
</tbody>
</table>

Based on clinical severity, disease phenotype and diagnostic and radiological findings. Host response in the lymph nodes is reflected by both symptom manifestation and disease dissemination, implicating the lymph nodes in a critical role in the natural history of TB infection. Finally, a subclinical phenotype was identified, suggesting an early stage of disease progression in TB.

P187 THE USE OF MOXIFLOXACIN FOR THE TREATMENT OF OPHTHALMIC TUBERCULOSIS

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10.1136/thoraxjnl-2014-206260.315

Background The number of patients we are treating for ophthalmic tuberculosis (TB) have increased year on year, from two in 2009 to twenty in 2013. A recent global review of the strategies used in the diagnosis and treatment of ophthalmic TB showed a wide disparity of diagnostic and treatment strategies. We present a review of our current practice and justification for our treatment regimens.

Methods We identified all the cases in our hospital treated for ophthalmic TB between 2009 and 2013. Age, gender, ophthalmic TB diagnosis findings, blood tests, treatment regimens, including durations and outcomes, and adverse drug reactions were collected and analysed.

Results A total of 60 cases were identified. Mean age was 45.0 +/- 14.4 years. 61.7% were male. The most commonly used regimen was 2 months rifampicin, isoniazid, pyrazinamide and moxifloxacin followed by 10 months of rifampicin, isoniazid and moxifloxacin. A response to treatment, with no evidence of disease recurrence on cessation of therapy, was seen in 78.3% of cases. 5% experienced hepatotoxicity requiring a change in treatment. There was no significant difference in either the success of treatment (p = 0.102) or the risk of hepatotoxicity (p = 0.264) between regimens with moxifloxacin (n = 43) or without it (n = 17). 32 patients on moxifloxacin had ECGs of which 6 (18.8%) newly developed a raised QTc. This resulted in moxifloxacin being stopped during the step-down phase of treatment in two patients. Maximum QTc was never found to be above 500 milliseconds and there were no episodes of documented arrhythmias or syncope.

Conclusions We recommend a treatment regimen including moxifloxacin in place of ethambutol so that any reported visual change is unlikely to be related to treatment, and we propose continuing moxifloxacin beyond the intensive phase, if tolerated, when culture is unavailable. We treat ophthalmic TB for the same duration as central nervous system TB. Our data shows that this is a safe and effective regimen but more evidence is required before recommending definitive guidelines.

Introduction The incidence of nontuberculous mycobacteria (NTM) isolation from humans is increasing worldwide. In England, Wales and Northern Ireland (EW and NI) the reported rate of NTM more than doubled between 1996 and 2006. It is unclear if this trend has continued. We present an updated analysis with national NTM data from 2007 to 2012.

Methods All individuals with culture positive NTM isolates between 2007–2012 reported to Public Health England by the five mycobacterial reference laboratories serving EW and NI, were included. The annual incidence of NTM was calculated based on the year of the first positive NTM isolate from each individual.

Results 21,024 individuals had NTM culture positive samples. Over the study period the incidence rose from 5.57 (n = 3126) to 7.63 (n = 4454) per 100,000 population. The majority were male (57%) and older (71% >50 years of age). 77% of individuals had a pulmonary isolate – and here the incidence increased from 3.97 to 6.05 per 100,000 population between 2007 and 2012. In those with extra-pulmonary samples it remained stable from 3.97 to 6.05 per 100,000 population between 2007 and 2012. In those with extra-pulmonary samples it remained stable at 1.61 per 100,000 population. In patients

Table 1 indicates the seven most frequently reported organisms; M. avium-intracellulare (MAI) accounted for 35% of isolates (75% in people >50 years). 78% of these were from pulmonary samples. 42% of M. abscessus isolates were in patients 60 years.

Abstract P188 Table 1 Most common NTM reported from total samples 2007–2012

<table>
<thead>
<tr>
<th>Organism</th>
<th>Total number of samples 2007–12</th>
<th>2007 incidence (per 100,000 population)</th>
<th>2012 incidence (per 100,000 population)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M. avium-intracellulare</td>
<td>7400</td>
<td>1.90</td>
<td>2.80</td>
</tr>
<tr>
<td>M. gordonia</td>
<td>3373</td>
<td>0.74</td>
<td>1.38</td>
</tr>
<tr>
<td>M. chelonae</td>
<td>2318</td>
<td>0.60</td>
<td>0.9</td>
</tr>
<tr>
<td>M. fortuitum</td>
<td>1681</td>
<td>0.47</td>
<td>0.58</td>
</tr>
<tr>
<td>M. kansasii</td>
<td>1299</td>
<td>0.42</td>
<td>0.29</td>
</tr>
<tr>
<td>M. xenopi</td>
<td>1065</td>
<td>0.34</td>
<td>0.34</td>
</tr>
<tr>
<td>M. abscessus</td>
<td>986</td>
<td>0.26</td>
<td>0.38</td>
</tr>
</tbody>
</table>
Conclusion The incidence of NTM has continued to rise since the last national survey. This represents an almost ten-fold increase since 1995. The majority of these are pulmonary isolates (in particular MAI). Possible explanations include greater awareness amongst clinicians leading to increased sampling, improvements in laboratory techniques for speciation or laboratory reporting practices. However, such a large increase most likely reflects a genuine rise in NTM infection in the population. Given this change in culture confirmation, it is imperative that a comprehensive clinical database is set up to provide national monitoring of clinically significant infections, and establish the true burden of disease present in EW and NI.

**P189** SHOULD SCREENING FOR CHRONIC VIRAL HEPATITIS IN PATIENTS WITH TUBERCULOSIS BE INTRODUCED TO NICE GUIDELINES?


10.1136/thoraxjnl-2014-206260.317

Background Screening for viral hepatitis is not routinely recommended in patients diagnosed with tuberculosis (TB). However there are significant similarities in the global distribution of TB and hepatitis B (HBV) and C (HCV). It remains unclear whether co-infection with HBV or HCV is a risk factor for hepatotoxicity in patients receiving anti-tuberculous therapy and significant morbidity and mortality is associated with a late diagnosis.

Objectives To determine the prevalence of HBV and HCV infection among new cases of active TB across treatment centres in East London and to assess the adverse drug reactions to anti-tuberculous treatment experienced by this population.

Methods We conducted a retrospective study including all patients diagnosed with active TB during 2013 in two TB clinics in London. Data on demographic characteristics, HBV surface antigen (HBsAg), HCV antibody, human immunodeficiency virus (HIV) and adverse drug reactions were retrospectively analysed.

Results In total, 472 cases of active TB were notified during 2013. The mean age was 37.7 (+/- 15.3) years (range: 5-92). Males accounted for 62.3% of our cohort. 84.7% of patients were born outside of the UK with the majority of patients being born in either Bangladesh (16.5%), India (27.8%) or Pakistan (15.9%). Overall, 304 patients were screened for HBV, 302 for HCV, and 447 for HIV. Of those screened, HBSAg was detected in 3.3%, HCV antibody in 2.0% and HIV in 3.4%. All patients infected with HBV or HCV were foreign born. Hepatotoxicity was defined as an ALT greater than 5 times the upper limit of normal or requiring a change in treatment. There was no significant difference in rates of hepatotoxicity in either HepBsAg status (p = 0.371), HCV status (p = 0.597) or HIV status (p = 0.413) but numbers of HBV and HCV infection were small.

Conclusions The prevalence of HBV and HCV was significantly higher in our cohort of TB patients than the background UK prevalence, which is 0.4% for HCV, 0.3% for HBV and 0.15% for HIV. Routine screening for HBV and HCV on an opt-out basis would be justified in our setting given the high proportion of foreign-born patients. Further research into the magnitude of HBV/HCV co-infection with active or latent TB, any increased risk in drug-induced hepatotoxicity and the cost-effectiveness of routine screening is needed.

**P190** DRUG INDUCED LIVER INJURY IN THE TREATMENT OF TUBERCULOSIS IN A BUSY UK CENTRE

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10.1136/thoraxjnl-2014-206260.318

Introduction We describe the incidence and management of drug induced liver injury (DILI) in active TB at the largest UK centre, using a nurse-led local protocol derived from 1998 BTS guidelines.

Methods All active TB cases were identified from April 2010 to May 2014. Patients were identified with DILI by following criteria: Type 1 DILI (ALT >3x upper limit normal (ULN=55iu/l), Type 2 DILI (ALP >2x ULN(150 iu/l) and Bilirubin >21 iu/l)) or Type 3 DILI (Bilirubin >40 iu/l). Patient demographics, TB treatment (ATT), timing, management and outcomes of DILI were described. Baseline characteristics and ATT doses were matched with controls.

Results 105 individuals with DILI were identified out of 1529 patients with active TB (6.9%). 81% were on standard first line therapy (Rifampicin (R), Isoniazid (H), Pyrazinamide (Z) and Ethambutol (E)). 7.8% were on Moxifloxacin (M) instead of E and 1.9% were on RHME. Type 1 DILI was most frequent (81%) with median peak ALT 296 iu/l (IQR 227–505). Median time from treatment start to onset of DILI was 12.5 days (7-30). Symptoms at presentation included nausea/vomiting (54%), abdominal pain (18%) and jaundice (12.4%). 45.7% patients had all medication stopped, 7.6% continued ethambutol with amikacin (A), 26.7% continued all medication, 6.7% stopped Z only, 3.8% substituted Z for a quinolone. Median time from stopping to reintroduction was 10 days (6–17). Of 66 reintroduction patients, regimens included H >R (>E(45%), H> R=E-M (31%) and R=E-M (15%)). Median time from reintroduction to full treatment restart was 14 days (12–18). 81% of patients were uneventfully reintroduced, 3% suffered a 2nd DILI. 32% patients required hospital admission and 4(3.8%) died.

DILI cases were matched to 200 controls. Cases more likely (p < 0.05) to; be HIV positive, have quinolones in initial regimen and lower body weight. Quinolone use gave an adjusted hazard ratio 5.41 (2.96, 9.91).

Conclusion DILI remains the most important toxicity of ATT and usually occurs during the first month. The BTS guideline provides a useful template for the diagnosis and management of DILI which may be largely nurse led and ambulatory. Most patients are successfully reintroduced without pyrazinamide. HIV status, body weight and quinolone use are risk factors.

**P191** WITH A LOW INCIDENCE OF DRUG-INDUCED HEPATITIS, SHOULD WE BE OFFERING LATENT TB TREATMENT TO MORE PATIENTS OVER THE AGE OF 35?

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10.1136/thoraxjnl-2014-206260.319

Introduction NICE guidelines recommend patients >35 yrs at risk of tuberculosis (TB) on screening, but without active disease, should not be offered latent TB infection (LTBI) treatment unless a healthcare worker, or HIV positive. This is based on perceived
risks of drug-induced hepatitis, and reduced diagnostic sensitivity of LTBI in >35 yrs. 3 months Rifampicin/Isoniazid (3RH) is commonly used however in a review of LTBI treatment, only one Hong-Kong based study found 1766/100,000 (n = 170) had symptomatic hepatitis or alanine aminotransferase (ALT) >250 IU (Grade 3 hepatitis).1

Promoted by improved sensitivity of LTBI case finding with interferon gamma testing, and local case of active TB in a contact >35 yrs, we studied whether those >35 yrs with LTBI, treated with 3RH experienced greater hepatotoxicity than

Method We retrospectively analysed electronic patient records detailing LTBI patient treatments from June 2008–2013 from two hospitals, collecting baseline clinical data and ALT level >250 IU/L or symptoms) to the only previous study using the 3RH regimen and shows no age specific differences in ALT results. In light of this, we raise the question; with increasing rates of TB in the UK, a large proportion of which is attributable to latent infection, should we be offering LTBI treatment to more patients >35 yrs? This study suggests the need, and provides important information for, planning a larger study to help answer this question.

Discussion This study, although small, provides a similar rate of hepatitis (defined >250 IU/L or symptoms) to the only previous study using the 3RH regimen and shows no age specific differences in ALT results. In light of this, we raise the question; with increasing rates of TB in the UK, a large proportion of which is attributable to latent infection, should we be offering LTBI treatment to more patients >35 yrs? This study suggests the need, and provides important information for, planning a larger study to help answer this question.

REFERENCE

Abstract P191 Table 1

<table>
<thead>
<tr>
<th>Characteristics of cases (DILI) and controls</th>
<th>Controls (n = 200)</th>
<th>Cases (n = 105)</th>
<th>P-value</th>
</tr>
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<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Ethnic origin</td>
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<tr>
<td>HIV +ve</td>
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<tr>
<td>Quinolone use</td>
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<tr>
<td>Baseline ALT (IU/L)</td>
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<tr>
<td>Baseline ALP (IU/L)</td>
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<tr>
<td>Baseline BILI (μM/L)</td>
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<tr>
<td>Weight (kg)</td>
<td></td>
<td></td>
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<tr>
<td>Rifampicin dose per kg (if given)</td>
<td></td>
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<tr>
<td>Isoniazid dose per kg (if given)</td>
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<td>Pyrazinamide dose per kg (if given)</td>
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<tr>
<td>Moxifloxacin dose per kg (if given)</td>
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<tr>
<td>Odds ratios for exposures among DILI cases compared with controls</td>
<td></td>
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</tr>
</tbody>
</table>

Abstract P191 Table 1 Absolute ALT rise and number of patients whose peak ALT rose x2 upper limit of normal (>70 IU/L)

<table>
<thead>
<tr>
<th>Rise in ALT IU/L (≥95% CI)</th>
<th>&lt;35 (n = 98)</th>
<th>≥35 (n = 53)</th>
<th>Total (n = 151)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients with ALT &gt;70 IU/L (%)</td>
<td>10 (10.2)</td>
<td>3 (5.7)</td>
<td>13 (8.6)</td>
</tr>
<tr>
<td>Number of patients with ALT &gt;250 IU/L (%)</td>
<td>2 (2.1)</td>
<td>3 (1.8%)</td>
<td>3 (2.0%)</td>
</tr>
</tbody>
</table>

P192 ASIDE FROM AGE, DO OTHER FACTORS INCREASE THE RISK OF HEPATOTOXICITY IN PATIENTS TREATED FOR LATENT TB INFECTION?


10.1136/thoraxjnl-2014-206260.320

Background Reactivation of latent tuberculosis infection (LTBI) occurs in a number of at-risk groups including: tuberculosis (TB)
contacts, migrants from high prevalence countries and those who are immunosuppressed. The risk of hepatotoxicity in treating LTBI is thought to be low but much of this evidence is in patients treated with 6 months of isoniazid (6H) rather than 3 months of rifampicin and isoniazid (3RH). Equally, other than age, there is limited data on other factors which may contribute to the risk of developing hepatotoxicity.

**Methods** A retrospective study was performed at our centre. We analysed all patients treated with chemoprophylaxis, regardless of indication, between 2009 and 2013. Demographic data, treatment regimens and adverse drug reactions, including hepatotoxicity, were recorded. Severe hepatotoxicity was defined as either a rise in ALT five times greater than the upper limit of normal, or as any change in liver function that required an interruption or alteration in treatment. Liver function tests (LFTs) were routinely measured at baseline and then again at two weeks.

**Results** 290 cases were identified. 84.5% of patients were treated with 3RH, 12.1% were treated with 6H. 2.1% experienced severe hepatotoxicity 2 weeks into treatment. None had symptoms which prompted blood tests prior to our standard 2 week LFTs. Gender, age, documented co-existing liver disease, regimen choice, concomitant use of hepatotoxic drugs and reason for giving chemoprophylaxis were not significantly associated with an increased risk of hepatotoxicity. LTBI treatment was case managed by TB nurses with 91.7% of patients successfully completing treatment. There was no significant difference in treatment completion or adherence rates in those who developed hepatotoxicity compared with those who did not.

**Conclusions** Our review demonstrates a low incidence of hepatotoxicity associated with treatment of LTBI and highlights the difficulty in predicting those in whom it will occur. If management of LTBI moves from primary to secondary care it will remain important to perform LFTs at two weeks.

**Cystic fibrosis**

### P193

**LONGITUDINAL ASSOCIATIONS BETWEEN FEV1 AND HBA1C IN A UK COHORT OF YOUNG PEOPLE WITH CYSTIC FIBROSIS**

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10.1136/thoraxjnl-2014-206260.321

**Objectives** To interrogate the UK national data set and explore longitudinal relationships between FEV1, HbA1c and OGTT parameters in young people with CF up to the age of 23 years.

**Methods** The UK CF data set (2007 to 2012) recording annual measurements of height, weight, BMI,% predicted FEV1 and FVC, HbA1c and 2 h glucose (2 hrGlu) (>10 years only) was interrogated. HbA1c values >6.5% and 5.7-6.5% were used to define ‘undiagnosed’ diabetes and a pre-diabetic state respectively in patients not labelled as having CFRD. Data from cases with known CFRD were censored. Longitudinal models analysed %FEV1 and %FVC as dependent variables and HbA1c or 2 hrGlu, BMI SDS and age as covariates in patients with HbA1c in the pre-diabetic range.

**Results** 2105 patients (1097 males), 87.9% with DF508 mutations, median (range) age 13.7 (5.6–22) years, mean (SD) BMI Z score -0.11+/−1.1, %FEV1 82.1+/−20.3 at first visit were included. Median range follow up was 3 (1–5) years. 2 hrGlu was available in a subgroup (n = 636). Median HbA1c (Table 1) but not 2 hrGlu (slope -0.1, p = 0.3), within the pre-diabetic range (5.7–6.5%) were inversely associated with %FEV1.

**Conclusion** In this large UK data set, longitudinal increases in HbA1c within the pre-diabetic range were associated with declining lung function. Our findings support the rationale for trials to intervene early to manage hyperglycaemia in young CF patients with pre-diabetes.

### P194

**PREVALENCE OF UNDIAGNOSED PRE-DIABETES AND DIABETES IN A UK COHORT OF YOUNG PEOPLE WITH CYSTIC FIBROSIS**

1 Selby,* 1T Rootsey, 2R Williams, 3K Ong, 4D McShane. 1Cambridge University Hospitals NHSFT, Cambridge, UK; 2University of Cambridge, School of Clinical Medicine, Cambridge, UK; 3University of Cambridge, Department of Paediatrics, Cambridge, UK; 4University of Cambridge MRC Epidemiology Unit, Cambridge, UK

10.1136/thoraxjnl-2014-206260.322

**Background** In children with cystic fibrosis (CF), cystic fibrosis related diabetes (CFRD) typically develops from adolescence onwards and coincides with deteriorating lung function. Currently, diagnosis of CFRD is based on WHO oral glucose tolerance test criteria rather than HbA1c (used as part of the diagnostic criteria for diabetes mellitus).

**Objective** To interrogate a national data set and determine prevalence of pre-diabetes and diabetes in patients not diagnosed with CFRD as based on HbA1c.

**Methods** A national CF data set (2007 to 2012) recording annual measurements of height, weight, BMI,%predicted FEV1 and FVC and HbA1c was interrogated. Young people up to the age of 23 years were included. HbA1c values between 5.7-6.5% and >6.5% were used to diagnose pre-diabetes and diabetes respectively in patients not labelled as having CFRD. Prevalence of pre-diabetes, diabetes and%FVC were determined by age group using the first visit values for each individual.

**Results** 3759 patients (1627 males, 87.5% with DF508 mutations), median (range) age 14.5 years (4.5–23 years), BMI Z score -0.17 (~5.7 +/- 3.6) were included. Prevalences of known CFRD, pre-diabetes and undiagnosed diabetes are shown in Table 1. In cross sectional analyses adjusted for gender, age,
genotype and BMI, FEV1 was inversely associated with HbA1c, B=-5.0 (95% CI -6.0–3.0, p < 0.0001).

Conclusion In this large UK data set, an additional 6.6% of CF patients aged 16–23 years would be diagnosed with diabetes based on HbA1c values. Furthermore, the prevalence of undiagnosed pre-diabetes was high across all age groups and associated with lower %FEV1.

**P195** PROSPECTIVE EXAMINATION OF THE EFFECTS OF IVACAFTOR ON GLYCAEMIC HEALTH

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10.1136/thoraxjnl-2014-206260.324

Background The clinical benefits of the novel cystic fibrosis transmembrane conductance regulator (CFTR) have now been well established for patients carrying the G551D mutation through both phase 3 and real world clinical studies. Modulation of CFTR alters intestinal pH, which may assist in the function of pancreatic enzymes and which theoretically might have an impact on the absorption of nutrients in cystic fibrosis (CF). This may have significant impact on the glycaemic health of patients and early reports from a phase 2 study suggested a significant risk of hyperglycaemia in a patient with pre-existing diabetes.

Aim We aimed to prospectively assess the impact of ivacaftor on glycaemic health

Methods We conducted a prospective observational cohort study of subjects who commenced ivacaftor following NHS approval. Baseline measures were recorded including spirometric measures, weight and sweat chloride. Glycaemic control was assessed using HbA1c and repeated measures were recorded at 1, 3 and 6 months.

Results 24 subjects were included in the study. 17 subjects had normal glucose handling as defined by oral glucose tolerance test, 4 subjects had a pre-existing diagnosis of CF-related diabetes and 3 subjects had impaired glucose tolerance prior to ivacaftor commencement. Ivacaftor significantly increased FEV1 and BMI at 1.3 and 6 months compared to baseline, and decreased sweat chloride at 2 months, all indicating effective CFTR modulation.

There was a significant reduction in HbA1c from baseline to 6 months in the total cohort, (median 42.5 mmol/L versus 39.5 mmol/L, p = 0.004), but not at other time points. In the diabetic or IGT subgroups, there were no clinically significant changes in HbA1c.

Conclusion Ivacaftor is an effective treatment for CF patients carrying the G551D mutation. In normoglycaemic patients, Ivacaftor significantly reduces HbA1c at 6 months. There was no adverse effect on glucose control noted in diabetic or impaired glucose tolerance subgroups. This may be attributable to improved insulin secretion by CFTR related mechanisms or improved insulin sensitivity. These results are important and reassuring when commencing patients with diabetes on CFTR modulators.

**P197** THE INCIDENCE OF NEW PSEUDOMONAS AERUGINOSA INFECTION IN CHILDREN WITH CYSTIC FIBROSIS

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10.1136/thoraxjnl-2014-206260.326

Introduction Pseudomonas aeruginosa (PA) is one of the most important pathogens in cystic fibrosis (CF). Although there is a wealth of data about the prevalence of chronic PA infection, there is a paucity of evidence about the incidence of new PA infection.

Methods The SPACE (Sensitivity and specificity of PA detection using the hydrogen Cyanide concentration of Exhaled breath) study investigated if exhaled breath hydrogen cyanide is an early marker of PA infection in children with CF. Breath samples, clinical data and microbiology samples were collected at each outpatient appointment from a large cohort of children with CF who had not isolated PA for >12 months. This abstract reports the PA acquisition data.
Results 233 children were followed for a median of 2.0 (1.7–2.3) years. The median (IQR) age was 8.0 (5.0–12.2) years. 71 children isolated PA during the study period. The incidence rate (95% CI) of new PA infections was 0.15 (0.10–0.22) cases per patient year for those that had never previously isolated PA and 0.19 (0.13–0.27) cases per patient year for those that had been free from PA for >12 months. This rate varied between 0.08 (0.04–0.18) and 0.28 (0.14–0.49) cases per patient year at the 8 recruiting centres. 42% of children were asymptomatic at the time of PA acquisition. The median (IQR) number of antibiotic courses per patient year varied between the centres: 0.6 (0.2–1.3) to 3.6 (3.1–4.2) for oral and 0.0 (0–0) to 0.4 (0–1.2) for intravenous.

Conclusions This is the first prospective study to report the incidence of new PA infection in a large cohort of children with CF, considered to be free of PA airway infection. Incidence rate was higher in children who had isolated PA previously. The variation between centres is not easily explained and needs further investigation.

Acknowledgments We would like to thank the Principal Investigators, research nurses and co-ordinators at each of the recruiting centres as well as the children and their families.

P199 NEW APPROACHES TO THE CULTURE OF MYCOBACTERIUM ABSCESSUS COMPLEX FROM PATIENTS WITH CYSTIC FIBROSIS

1JE Foweraker, 1S Jalil, 1V Athithan, 1D Grugno, 1MC Curran, 1PA Rito. 1Papworth Hospital NHS Foundation Trust, Cambridge, UK; 2Cambridge Clinical Microbiology and Public Health Laboratory, Cambridge, UK

Introduction M. abscessus complex (Mab) are Rapid Growing Mycobacteria (RGM) that can cause severe infection. Prevalence is increasing and a recent study using whole genome sequencing showed cross infection between Cystic Fibrosis patients. Frequent surveillance for Mab infection may allow earlier diagnosis and prevent spread.

Automated broth (e.g. MGIT), is a sensitive rapid method for mycobacterial culture. Decontamination is needed to kill other bacteria and yeasts before culturing CF sputum in MGIT, but decontamination may reduce Mab numbers.

Other possibilities include chlorhexidine decontamination which yields more Mab but is incompatible with MGIT. Some mycobacteria grow directly from sputum on Burkholderia cepacia selective agar (Bcc) after extended incubation, without prior decontamination.

The aim of this study was to improve Mab culture from CF sputum.

Methods We compared MGIT culture of CF sputa with extended incubation of Bcc used in the routine laboratory. We compared growth of 30 known Mab on 3 formulations of Bcc and 2 Middlebrooke selective agars. We took 12 sputa from 9 CF patients with Mab infection and compared MGIT with culture on selective agars or chlorhexidine decontamination followed by culture onto non selective agar. Mycobacteria were identified by the National Mycobacterium Reference Laboratory and an in house PCR.

Results Eighteen of 515 CF sputa grew RGM (9 on Bcc agar and MGIT, 3 MGIT alone, 4 Bcc alone and 2 on Bcc with no MGIT culture). Contamination with other bacteria and fungi made it extremely difficult to see RGM on the routine Bcc.

Thirty sequenced M. abscessus abscessus, M. bolletii and M. massiliense all grew on the 3 commercial Bcc and 2 Middlebrooke agars.

One Bcc and one Middlebrooke agar successfully cultured RGM from all 12 sputa with fewest contaminants. Chlorhexidine decontamination and blood agar was effective but labour-intensive. Only 8 of 12 MGIT cultures grew RGM.

There was no difference in time to positive culture between agar and MGIT.

Conclusion Culture onto selective agar may be more sensitive than MGIT. It is quantitative and provides pure culture for identification, typing and susceptibility testing.

This may be a sensitive cost-effective way to screen sputa from patients at risk.

P199 MOLECULAR ANALYSIS DEMONSTRATES SHARED STRAINS OF MYCOBACTERIUM ABSCESSUS ISOLATES IN CYSTIC FIBROSIS PATIENTS ATTENDING A SINGLE CENTRE

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10.1136/thoraxjnl-2014-206260.328

Introduction and objectives The Mycobacterium abscessus complex is an emerging group of pathogens in cystic fibrosis (CF), which may cause cross infection. The aim of this study was to determine whether CF patients infected with M. abscessus attending a single UK adult CF centre harbour unique or shared strains of M. abscessus.

Methods Isolates were from 12 patients attending a single adult CF centre, who yielded one or more positive sputum cultures for M. abscessus complex during the period January 2010 to August 2013. Isolates were identified to subspecies level using hsp65-rpoB concatenated sequence cluster analysis. Variable Number Tandem Repeat (VNTR) analysis was used to compare these isolates and determine whether two or more patients were infected with the same strain.

Results 11 isolates were identified as M. abscessus subsp. abscessus. VNTR analysis demonstrated 2 clusters of 6 and 2 patients carrying the same strains of M. abscessus subsp. abscessus, both

Abstract P199 Table 1 Mycobacterium abscessus cluster sequence analysis and Variable Number Tandem Repeat profiling results

<table>
<thead>
<tr>
<th>Patient</th>
<th>M. abscessus subspecies</th>
<th>VNTR Profile</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>abscessus</td>
<td>2+, 5+, 3, 6, 2, 5, 1+, 2+, -</td>
</tr>
<tr>
<td>2</td>
<td>abscessus</td>
<td>2+, 5+, 3, 6, 2, 5, 1+, 2+, -</td>
</tr>
<tr>
<td>3</td>
<td>abscessus</td>
<td>2+, 5+, 3, 6, 2, 5, 1+, 2+, -</td>
</tr>
<tr>
<td>4</td>
<td>abscessus</td>
<td>2+, 5+, 3, 6, 2, 5, 1+, 2+, -</td>
</tr>
<tr>
<td>5</td>
<td>abscessus</td>
<td>2+, 5+, 3, 6, 2, 5, 1+, 2+, -</td>
</tr>
<tr>
<td>6</td>
<td>abscessus</td>
<td>2+, 5+, 3, 6, 2, 5, 1+, 2+, -</td>
</tr>
<tr>
<td>7</td>
<td>abscessus</td>
<td>3+, 4+, 3, - , 4+, 3+  2+, 2+, 2</td>
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<tr>
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</tr>
<tr>
<td>9</td>
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</tr>
<tr>
<td>10</td>
<td>abscessus</td>
<td>2+, 3, 4+, 2, 5, 1+, 2+, -</td>
</tr>
<tr>
<td>11</td>
<td>abscessus</td>
<td>1+, 4+, 2, 2, 4, 3+, 2+, 2+, 2</td>
</tr>
<tr>
<td>12</td>
<td>boletti</td>
<td>2+, 3, 5, 4, 3+, 1+, 2, 2+</td>
</tr>
</tbody>
</table>

Poster sessions

of which have also been isolated from CF patients from other UK hospitals. Isolates from the remaining 3 patients were unique. One additional isolate was identified as M. abscessus subsp. bolletii. No clear epidemiological connections between patients within each cluster at our centre have been identified to date.

**Conclusion** These results provide further evidence that some strains of *M. abscessus* complex may be isolated from multiple CF patients. However, there were no clear epidemiological connections between patients within clusters at our centre. The same strains have been isolated from patients at different UK CF centres. Further studies are required to determine the mode of acquisition of infection with these strains and whether there is a common environmental source of infection or cross infection between patients.

**P200 PRELIMINARY EVALUATION OF THE FUNGAL AIRWAY MICROBIOME IN ADULT CYSTIC FIBROSIS BY NEXT-GENERATION SEQUENCING, CULTURE AND STAINING TECHNIQUES**


**Introduction** The prevalence and diversity of fungal airway isolates is increasing in cystic fibrosis (CF). Amidst an extending spectrum of fungal complications, lack of standardised mycology methods and poor sensitivity of culture-dependent techniques renders interpretation of isolates challenging.

**Aims** To evaluate the diagnostic utility of fungal cytology and microbiology stains in addition to prolonged sputum culture from adult CF patients in comparison to standard mycology techniques.

Secondly, to develop a novel, next-generation sequencing assay targeting the ITS2 region of the fungal ribosomal-RNA gene to comprehensively profile the sputum fungal microbiota.

**Methods** Sputum samples were investigated by a panel of three mycology techniques: prolonged fungal culture (each examined at: Day7, D14, D21, D28); Calcofluor White (CFW) stain; Grocott’s Methenamine Silver (GMS) stain. A cohort of samples was also subject to broad-spectrum fungal next-generation sequencing.

**Results** 25 adult patients provided 45 sputum samples. Four fungal species were cultivatable: *Candida* species (26.6%); *Aspergillus fumigatus* (4.4%); *Scedosporium apiospermum* (15.5%) and *Exophiala dermatitidis* (11.1%).

Prolonged culture significantly increased overall fungal prevalence by 22% compared to standard duration (D7 p = 0.008). A significant increase of 11.1% in *S. apiospermum* prevalence was observed p = 0.02), whilst all *E. dermatitidis* isolates required prolonged culture. The sensitivity of GMS and CFW stains (85% and 93%) compared favourably to standard duration required prolonged culture. The sensitivity of GMS and CFW stains (85% and 93%) compared favourably to standard duration.

DNA extracted from a pilot group of these sputum samples (n = 14/45) was subject to PCR using barcode-indexed ITS2 primers designed for Illumina-MiSeq amplicon sequencing. Fungal taxa were detected in all samples, of which seven samples (50%) were negative after prolonged culture. Preliminary sequencing analysis of an extended sample cohort (n = 30) has detected 89 fungal taxa, from which only four species were cultured.

**Conclusions** Prolonged fungal culture is associated with a significant increase in fungal prevalence. The increased sensitivity is restricted to less common filamentous fungi associated with increasing pathogenicity: *S. apiospermum* and *E. dermatitidis*. The predictive value of stains in identifying samples positive at prolonged culture, but negative at standard duration illustrates their clinical utility.

Illumina-MiSeq ITS2-amplicon sequencing directly from sputum has identified a more diverse CF airways fungal microbiota. Preliminary analysis suggests that this is a highly sensitive tool for detecting fungi from sputum, including species which are refractory to standard and enhanced culture.

**P201 PNEUMOCYSTIS JIROVECII PREVALENCE IN A LARGE UK ADULT CYSTIC FIBROSIS CENTRE**

HD Green, PB Bright-Thomas, PJ Barry, HA Horley, K Mutton, IAM Jones. Manchester Adult Cystic Fibrosis Centre, University Hospital of South Manchester, Manchester, UK; Clinical Virology Department, Central Manchester University Hospitals NHS Trust, Manchester, UK.

**Introduction and objectives** *Pneumocystis jirovecii* (*P*) is an atypical fungus that causes pneumonia in immunocompromised patients. Its role in patients with cystic fibrosis (CF) is unclear. Its reported prevalence in CF ranges from 1–22% but has never been determined in the UK. Here we present preliminary cross-sectional data from an ongoing study at a UK adult CF centre.

**Abstract P201 Table 1 Comparison of characteristics for patients with positive and negative samples**

Pneumocystis jirovecii result

<table>
<thead>
<tr>
<th>Number</th>
<th>Negative</th>
<th>Positive</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender, n (%)</td>
<td>52 (55.9)</td>
<td>4 (57.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean age (yr), SD</td>
<td>33.8 ± 11.1</td>
<td>32.5 ± 10.1</td>
<td>NS</td>
</tr>
<tr>
<td>Spirometry and laboratory results</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean FEV1 (%, predicted), SD</td>
<td>56 ± 20.1</td>
<td>67 ± 29.5</td>
<td>NS</td>
</tr>
<tr>
<td>Mean BMI (kg/m2)</td>
<td>22.1 ± 3.2</td>
<td>22.2 ± 2.1</td>
<td>NS</td>
</tr>
<tr>
<td>WCC (x109/L) at recruitment</td>
<td>9.3 ± 3.1</td>
<td>9.3 ± 2.8</td>
<td>NS</td>
</tr>
<tr>
<td>CRP (mg/L) at recruitment</td>
<td>13.0 ± 16.8</td>
<td>7.9 ± 7.5</td>
<td>NS</td>
</tr>
<tr>
<td>Chronic colonisation, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>59 (63.4)</td>
<td>5 (71.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>24 (25.8)</td>
<td>1 (14.3)</td>
<td>NS</td>
</tr>
<tr>
<td>B. cepacia complex</td>
<td>14 (10.3)</td>
<td>2 (28.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Aspergillus fumigatus</td>
<td>6 (6.4)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Inhaled antibiotics</td>
<td>72 (77.4)</td>
<td>6 (85.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Oral steroids (continuous)</td>
<td>12 (12.9)</td>
<td>1 (14.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Prophylactic macrolide</td>
<td>4 (43.3)</td>
<td>1 (14.3)</td>
<td>NS</td>
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<tr>
<td>MRSA</td>
<td>1 (1.1)</td>
<td>1 (14.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Treatment, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azole therapy</td>
<td>8 (8.6)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Co-trimoxazole past 3 months</td>
<td>32 (34.4)</td>
<td>0</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Key: SD = standard deviation, WCC = serum white cell count, B cepacia complex = *Burkholderia cepacia* complex, NTM = Non-tuberculous mycobacteria, MRSA = Methicillin resistant *Staphylococcus aureus*, NS = not significant, p values < 0.1 are shown.
serving >400 patients, to establish prevalence and potential risk factors for infection.

**Methods** Sputum samples were obtained from 100 randomly selected CF outpatients and sent for routine microbiology and PJ DNA PCR assay at enrolment, subsequent visits, and pulmonary exacerbations requiring intravenous antibiotics within 4 months. Data were recorded for demographics, co-morbidities symptom score, spirometry, inflammatory markers, and prophylactic or recent therapeutic antibiotic therapy. Univariate comparisons were made between sputum PJ positive and negative patients. Chi square tests were used for categorical comparisons and independent sample t-tests for continuous independent variables.

**Results** Of the 100 patients, 4 of 100 had a positive sputum PJ PCR at baseline. 50 patients had a routine follow up sample between 1 and 4 months: 2 were positive for PJ. 22 patients had a sputum sample analysed at the onset of a pulmonary exacerbation of which 1 was positive for PJ. Hence, a total of 7 of 100 patients had a single positive sample by PCR for PJ. No patient has had >1 positive sample. None of the baseline parameters were significantly different between PJ positive and PJ negative patients at the level p.

**Conclusion** These results suggest that PJ is not an important infecting pathogen in this UK cohort of CF patients. This may be due to frequent use co-trimoxazole for pulmonary exacerbations and high prevalence of prophylactic macrolide antibiotic therapy at our centre compared to other published studies. These preliminary data were underpowered to accurately compare baseline characteristics between PJ positive and PJ negative patients.

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**P202**

**STUDYING THE RELATIONSHIP BETWEEN MATRIX METALLOPROTEINASES AND LUNG TISSUE DAMAGE DURING A CLINICAL EXACERBATION OF CYSTIC FIBROSIS**

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Abstract P202 Figure 1 The sputum concentration of MMP-9 (pg/ml) at sample time. Values at 3000 represent values above the level of detection. Significant values are represented with a line and an asterix (*). A significant decrease in MMP-9 concentration was found between Day 0 and Day 14 (p = 0.006). An increase in MMP-9 concentration was seen between day 14 and week 6 (p = 0.0412). There was a statistically significant decrease in MMP-9 concentration between day 0 and week 6 (p = 0.0453)

0 and day 14 (p = 0.0124); and between day 0 to week 6 (p = 0.0426).

**Conclusions** MMPs and other inflammatory markers are raised during exacerbations, and fall with treatment. High proteolytic activity might lead to a worsening lung function and contribute significantly to structural changes within the CF lung. Furthering our understanding of this diverse group of proteases could lead to potential novel therapeutic targets which could help prevent irreversible lung damage.

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**P203**

**DEVELOPMENT OF AN OPTIMAL F/HN PSEUDOTYPED SIV VECTOR FOR CF GENE THERAPY**

1SC Hyde, 1Ewfw Alton, 1AC Boyd, 1MM Connolly, 1M Chan, 1C Davies, 1LA Davies, 1S Geo-Sorl, 1U Griesenbach, 1M Hasegawa, 1JA Innes, 1M Inoue, 1G McLachlan, 1C Meng, 1J Pringle, 1SG Sumner-Jones, 1SG Tsugumine, 1DR Gill. 1UK Cystic Fibrosis Gene Therapy Consortium, Oxford, London and Edinburgh, UK; 2DNAVEC Corporation, Tsukuba, Japan

We are developing lung gene transfer vectors to treat acquired and inherited lung disorders such as cystic fibrosis, and have identified two platforms for efficient respiratory gene delivery: one non-viral system based on Cpg-free plasmid DNA combined with cationic lipids (pDNA/GL67A), which has recently completed evaluation in a Phase Ilb clinical study; and one novel viral system based on a recombinant simian immunodeficiency virus pseudotyped with the F/HN proteins of Sendai virus (rSIV. F/HN) to promote airway cell uptake. Here we report on the development of a “third generation” rSIV. F/HN vector suitable for use in the clinic. The vector is manufactured by transient transfection of cultured human cells using five producer plasmids, all of which have been engineered to be pharmacoepoeia compliant. A variety of vector configurations, including a range of enhancers/promoters and transgenes, were evaluated in a panel of airway models. rSIV. F/HN vectors directed high-level, robust gene expression in fully differentiated human airway cells,
human nasal brushings and human and sheep lung slices. In the mouse nose and lung, the preferred configuration directed up to x500-fold higher transgene expression than the non-viral platform, for the lifetime of the animal. Transgene expression was observed in 14.1% of lung epithelial cells (p < 0.0001 compared to controls). Repeated monthly administration (3X) was possible without loss of expression or significant histological inflammatory reactivity. Reassuringly, insertion site profiling from transduced cell lines and mouse nose/lung samples reveals a pattern of integration comparable to those reported for other lentiviral vectors in clinical development, with no evidence for enrichment of insertion at undesirable loci. The stability of rSIV. F/HN vectors was evaluated in two bronchoscope catheters and two aerosol generation devices. Encouragingly for clinical translation, no significant loss of transduction activity was noted with any of these clinically relevant delivery devices (p = 0.64). Delivery of rSIV. F/HN expressing CFTR to sheep lung resulted in CFTR mRNA at ~30% the levels of endogenous ovine CFTR (p < 0.0001 compared to non-treated lobes), exceeding presumed therapeutic levels. With the majority of translational hurdles addressed, we are now entering toxicology studies and the final stages of pharmaceutical development prior to entering clinical trials.

Although most CF patients express CFTR protein (albeit mutant) and should therefore not recognise the wild-type CFTR protein as foreign, there is an inherent risk of activation of T-cells against the recombinant wild-type protein after gene therapy. In addition, we have previously shown that approximately 10% of CF and non-CF subjects carry self-reactive T-cells, approximately 4 weeks after Dose 4 or 5, and 2 to 4 weeks after Dose 12 and the ELISPOT was performed. In addition anti-DNA antibodies were quantified. The Phase Ib trial will be unblinded in Summer 2014 to allow data analysis and all data will be presented at the conference.

Funded by the NIHR/EME Programme and the Cystic Fibrosis Trust.

Lung function testing: new approaches

Background Multiple-breath washout (MBW) is used to calculate a measure of ventilation heterogeneity, the lung clearance index (LCI), and requires tidal breathing until a previously inspired tracer gas concentration falls below 1/40th of the initial value, an arbitrary threshold. LCI is usually performed in triplicate, each taking 4–8 min to complete which may be taxing, particularly in young children and those with marked airflow obstruction. Shortened LCI is of interest since a reduction in the test time may increase feasibility and improve the clinical applicability of the measurement.

We hypothesised that LCI measurements could be reliably shortened. We also investigated whether shortened MBW was responsive to an intervention.

Patients and methods We calculated LCI from a fixed time point, and from a fixed number of breaths, as well as LCI and 25% (LCI0.25), 50% (LCI0.5) and 75% (LCI0.75) of 1/40th of the initial concentration of tracer gas (LCIstd) and the time saved, in children aged 6–16 years with asthma (n = 21), cystic fibrosis (CF, n = 20) and primary ciliary dyskinesia (PCD, n = 19), and healthy controls (n = 17), aged 3–18 years. Shortened LCI was also calculated in 29 asthmatic children pre and one month post one intra-muscular triamcinolone injection, part of our clinical severe asthma protocol.

Results Calculating shortened LCI from a fixed washout time or breath number was not reliable. However, all shortened LCI measurements from initial gas concentration correlated significantly with LCIstd in each disease group. LCI0.5 presented a balance between correlation with LCIstd (see figure) and time-saving. Mean proportion of time saved per washout, using LCI0.5, was 27% (asthma), 28% (CF) and 31% (PCD). Furthermore, LCI0.5 was significantly reduced after triamcinolone in children with severe asthma (mean LCI0.5 pre, 5.5 and 5.1 post triamcinolone, p = 0.02), and the change was similar to that demonstrated using LCIstd (mean LCIstd pre, 7.8 and post 7.0, p = 0.001).

Conclusion We show for the first time that LCI measurements can be shortened without loss of information in school-children with asthma, CF and PCD. LCI0.5 was the optimal surrogate measure for LCIstd when proportion of time saved, correlation number – NCT01621867). CF patients received 12 monthly doses of pGM169/GL67A (115 completed nine or more doses), or placebo by aerosol. PBMC were collected on two occasions prior to dose 1 to establish baseline levels for CFTR-specific T-cells, approximately 4 weeks after Dose 4 or 5, and 2 to 4 weeks after Dose 12 and the ELISPOT was performed. In addition anti-DNA antibodies were quantified. The Phase Ib trial will be unblinded in Summer 2014 to allow data analysis and all data will be presented at the conference.

Funded by the NIHR/EME Programme and the Cystic Fibrosis Trust.
with LCIstd and change following an intervention were considered.

**P206** CHANGES IN INDICES DERIVED FROM MULTIBREATH WASHOUT (MBW) FOLLOWING TREATMENT WITH IVACAFTOR IN PATIENTS WITH CYSTIC FIBROSIS

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10.1136/thoraxjnl-2014-206260.334

**Background** Lung clearance index (LCI) is a measure of gas mixing inhomogeneity derived from multi-breath washout (MBW) techniques, which has been shown to be more sensitive than conventional spirometry/FEV1. The potentiator, Ivacaftor, led to improvement in LCI in patients with mild cystic fibrosis (CF) lung disease however its utility as an outcome measure in more severe disease requires further investigation. Whilst LCI reflects overall ventilation heterogeneity, analysis of the phase III slopes of successive breaths in the MBW; known as Sacin and Scond; are thought to reflect the ventilation heterogeneity generated at branch points in the acinar and conductive lung zones respectively. This study aimed to explore changes in the indices derived from analysis of MBW following a year of treatment with Ivacaftor.

**Method** A prospective study was performed between March 2013 and April 2014 on patients with the G551D mutation and eligible for clinically prescribed Ivacaftor. MBW (Innocor SF6 technique) and spirometry were performed immediately prior to commencing Ivacaftor, and at a clinic visit following 9–12 months therapy. FEV1 is calculated using Stanojevic references and all data are expressed as mean (SD). Paired data were analysed with a Wilcoxon rank sum test and correlations with Spearman’s rank correlation. The null hypothesis was rejected at $p < 0.05$.

**Results** 8 patients were enrolled with ages ranging from 6–27 years. FEV1 increased from 68.7 (17.2)% before treatment to 80.1 (16.3)% after 9–12 months therapy ($p$1 and LCI did not correlate with each other.

**Discussion** Patients prescribed Ivacaftor demonstrated improvements in both conventional FEV1 and the newer measure of LCI; improvement was not limited to patients with milder disease and was seen throughout the group. In this study, the phase III slope measures did not appear to add further value to the LCI. It is possible that this reflects under powering in this small group; further data will be obtained.

**P207** RELIABILITY OF MEASUREMENTS USING INNOCOR BREATH BY BREATH ANALYSER DURING A MAXIMAL EXERCISE TEST IN CYSTIC FIBROSIS PATIENTS

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10.1136/thoraxjnl-2014-206260.335

**Introduction** Cardiopulmonary exercising testing (CPET) is considered the gold standard to study exercise capacity as an endpoint in clinical trials. Originally the UKCFGTC used the shuttle walk test for exercise capacity measurement but this proved inappropriate for mild, fit cystic fibrosis (CF) patients in our trial cohort (FEV1 50–90% predicted). The Innocor device uses photoacoustic gas detection technology and offers metabolic measurement but has not previously been validated for CPET in CF.

**Aim** To compare the Innocor with known reliable CPET machines to see if it is suitable to take forward into a multi dose clinical trial of gene therapy.

**Methods** 12 CF patients (7 Male, 14–47 years) participated in the study recruited from London and Edinburgh sites. They performed two incremental cycle ergometer exercise tests to exhaustion (adapted Godfrey protocol) with breath by breath analysis assessed using a reference system (Jaeger Masterscreen PFT, London; Pulmolink Medisoft, Edinburgh) or the Innocor device. All tests were randomly ordered, completed at least 24 h apart, with no more than two weeks’ separation.

**Results** VO2max and VE max were comparable between the Innocor and reference systems ($p = 0.1790$ and $p = 0.7642$ respectively; paired t tests). For VO2max, Bland Altman analysis showed the mean difference [Reference equipment-Innocor] was -0.026 l/min and the 95% confidence interval was -0.27 to 0.22 l/min (see Figure). In our experience the Innocor heart rate (HR)
recording (derived from saturation monitor) was unreliable; reading low during exercise compared to ECG-derived HR. **Conclusions** This small study confirms the Innocor device can produce measures of VO₂max comparable (95% confidence interval) with standard calibrated exercise systems in CF patients with mild to moderate lung disease. We found the method for Innocor to derive HR (pulse oximetry) was not reliable compared to reference ECG especially during heavy exercise. We were subsequently able to overcome this problem by interfacing the Innocor device with a separate electrocardiographic heart rate monitor.

**Methods** 38 PCD (14 male, group mean (range) age 21.8 (7.2–59.1) years, FEV1 Z score -3.18 (-6.0 – 17.0) and CF (14 male, group mean (range) age 10.9 (6.8 – 19.1) years, FEV1 Z score -2.72 (-5.4 – 0.9)) patients matched for P. aeruginosa status and 24 healthy controls recorded spirometry and MBW. LCI, Curv, Scond* and Sacin* were calculated.

**Results** There was no difference in LCI, FEV1 and Curv between the patient groups. LCI was correlated with Scond* (CF p = 0.0006, r = 0.5, PCD, p = 0.03 r = 0.3), Sacin* (CF p < 0.0001, r = 0.7, PCD p < 0.0001, r = 0.6) and Scond (CF p < 0.0001, r = 0.7, PCD p = 0.0003, r = 0.5), whereas Scond was not. There was no difference in Sacin* between the groups, but Scond* was significantly lower in PCD, approaching that of healthy controls.

**Conclusions** Curv is similarly impaired in PCD and CF. Scond* is nearly normal in PCD but not CF, supporting the hypothesis that there are differences in distal airway disease between these conditions. Finally, the results suggest that the new indices may be better discriminations between diseases in severe obstructive lung disease.

**Abstract P208 Figure 1** Gas concentration (y axis, log scale) over the course of an MBW, plotted against turnovers (x axis). Solid line shows gradient of line from start to LCl/2, dotted line shows gradient of line from LCl/2 to full LCl. Curv is expressed as the ratio of the slopes of these two lines. In health, slopes are similar and Curv is approaching zero, in disease, dotted slope is increasingly flat, giving an increased Curv value approaching 1.
AIRWAYS RESISTANCE IN BRONCHIAL CHALLENGE TESTING

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10.1136/thoraxjnl-2014-206260.338

Introduction Measurement of airways resistance is an alternative to spirometry to assess airflow obstruction. This can be measured by the interrupter technique (RInt) using a hand held device. We wished to know how RInt compared to forced expiratory volume in 1 second (FEV1) during a histamine challenge test.

Methods Twenty-nine (13 male) patients, aged 48.9 (SD 15.3) years, referred for a histamine challenge test were enrolled. Patients had measurement of RInt then FEV1 after administration of saline and following doubling concentrations of histamine from 0.06 mg/ml to 8 mg/ml. Extrapolation of the log dose-response curve was undertaken to calculate the concentration (Provocation Concentration – PC) causing an increase in airways resistance of 20, 40, 60, 80, 100, 120, 140 and 160% (RInt PC1.2 to RInt PC2.6) and a reduction in FEV1 by 20% (FEV1 PC20). The number of patients with a negative challenge (i.e. PC > 8 mg/ml histamine) was calculated for FEV1 and each change in airway resistance. Patients assessed their procedure provoked symptoms of breathlessness, dizziness and tiredness on a 100 mm visual analogue scale.

Results A total of 854 LCIs were performed during the trial, and technically acceptable measurements were achieved in 95.9% and 94.2% of tests at the two sites (mean 94.8%). 118 (13.8%) of LCIs were analysed independently by two operators, with a full range LCI values represented (range 7.24–19.21). The 95% limits of agreement (LoA) for LCI values were -0.04 to 0.04 (mean difference 0.00) and for FRC values were -0.01 to 0.01 (mean difference 0.00).

Conclusions Our results demonstrate that LCI is an achievable outcome measure in a multicentre trial in 94.8% of attempts. Separate offline analysis completed by two operators, with appropriate training and knowledge of the test, produces mean LCI and FRC inter-site differences of 0.00. LCI is feasible and appropriate for use as a surrogate endpoint in multicentre clinical trials using stringent methodology.

Abstract P210 Table 1

<table>
<thead>
<tr>
<th>Measure</th>
<th>Fall in FEV1 of 20% (FEV1 0.8)</th>
<th>RINT increase 20% (1.2)</th>
<th>RINT increase 40% (1.4)</th>
<th>RINT increase 60% (1.6)</th>
<th>RINT increase 80% (1.8)</th>
<th>RINT increase 100% (2.0)</th>
<th>RINT increase 120% (2.2)</th>
<th>RINT increase 140% (2.4)</th>
<th>RINT increase 160% (2.6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geom mg/ml</td>
<td>1.88</td>
<td>0.90</td>
<td>1.05</td>
<td>1.47</td>
<td>2.10</td>
<td>3.18</td>
<td>4.29</td>
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<td>1.46</td>
</tr>
<tr>
<td>(SEM)</td>
<td>0.51</td>
<td>0.37</td>
<td>0.39</td>
<td>0.48</td>
<td>0.63</td>
<td>0.80</td>
<td>0.87</td>
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<td>0.72</td>
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<tr>
<td>11</td>
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<td></td>
</tr>
<tr>
<td>PC20 &gt;8mg/ml (number of patients)*</td>
<td>13</td>
<td>12</td>
<td>13</td>
<td>14</td>
<td>16</td>
<td>19</td>
<td>21</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>0.39</td>
<td>0.24</td>
<td>0.24</td>
<td>0.24</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Kappa (p)</td>
<td>0.15 (0.41)</td>
<td>0.21 (0.26)</td>
<td>0.29 (0.11)</td>
<td>0.37 (0.039)</td>
<td>0.024</td>
<td>0.148</td>
<td>0.148</td>
<td>0.148</td>
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</tr>
</tbody>
</table>

FEV1: Forced expiratory volume in 1 second, RInt: airways resistance using the interrupter technique, Geom: geometric mean, mg: milligram, ml: millilitre, PC: provocation concentration (the concentration of histamine required to produce the desired effect). * The number of patients with a PC more than 8 mg/ml i.e. deemed not to have asthma.
In conclusion, FEV1/FVC index has a good correlation with ALSFRS-R (n = 20, r = -0.71, p < 0.001, FEV1/FVC = 1.630 - [0.018 * ALSFRS-R] ± 0.165).

**Abstract P212**
PARASTERNAL INTERCOSTAL ELECTROMYOGRAPHY TO ASSESS NEURAL RESPIRATORY DRIVE IN HEALTHY ADULT SUBJECTS

1V MacBean, 1C Hughes, 1G Nicol, 2CC Reilly, 1Gf Rafferty. 1King’s College London, London, UK; 2King’s College Hospital NHS Foundation Trust, London, UK

10.1136/thoraxjnl-2014-206260.340

Neural respiratory drive (NRD), measured using the parasternal intercostal muscle electromyogram (EMGpara), relates to lung disease severity as quantified by conventional methods in a range of diseases. Reference data from healthy populations are required for the technique to be used as an independent measure of lung disease severity. EMGpara has previously been expressed as a percentage of that obtained during a maximal inspiratory effort (EMGpara%max), restricting the use of the technique to subjects able to reliably perform such manoeuvres. The aim of this study was to investigate variability of both raw EMGpara (rEMGpara) and EMGpara%max in healthy adults.

EMGpara was measured during tidal breathing in 43 healthy adult non-smokers (25 females, median (range) age 32 (19–79) years, mean (SD) BMI 23.4 (3.5) kg/m²), using surface electrodes positioned bilaterally over the second interchondral space. Measurements were made with and without a mouthpiece/pneumotachograph in situ in 20 participants. Repeated measures were obtained within the same testing session in 27 subjects, and at least seven days later in 13 individuals. Spirometry, height, weight, BMI, fat free mass (FFM) via bioelectrical impedance and measures of regional fat distribution (waist/hip ratio and neck circumference) were also recorded.

Mean (SD) EMGpara%max and rEMGpara were 5.88 (3.63)% and 5.06 (2.26)µV respectively. Significant relationships were observed between anthropometric measures and EMGpara and EMGpara%max (Table 1). rEMGpara and EMGpara%max were unrelated to spirometry variables. Median (range) rEMGpara and EMGpara%max increased significantly with the pneumotachograph in place (4.86 (2.11–8.19)µV versus 5.62 (2.47–10.98) µV and 4.77 (1.68–17.00)% versus 6.78 (2.35–20.94)%, both p < 0.0001).

Analysis of variance by subject was used to assess within-subject variability. Measurement error was higher for EMGpara%max than rEMGpara (upper 95% confidence limit of difference between repeat measures of EMGpara%max 3.14%, versus 2.35 µV for rEMGpara; within-subject coefficient of variation EMGpara%max 30.8% versus rEMGpara 24.5%).

rEMGpara appears to be a reproducible marker of NRD. Both rEMGpara and EMGpara%max are influenced by subjects’ anthropometry. Further investigation is required to determine whether these influences are technical or physiological and must be considered when the technique is applied clinically or for research, or when developing reference values.

### Abstract P212 Table 1
Relationship of rEMGpara and EMGpara %max to anthropometric characteristics in 43 healthy adult subjects

<table>
<thead>
<tr>
<th>Correlation with raw EMGpara (r)</th>
<th>Correlation with EMGpara%max (r)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height</td>
<td>-0.38 (0.01)</td>
</tr>
<tr>
<td>Weight</td>
<td>-0.47 (0.001)</td>
</tr>
<tr>
<td>BMI</td>
<td>-0.46 (0.002)</td>
</tr>
<tr>
<td>FFM</td>
<td>-0.12 (ns)</td>
</tr>
<tr>
<td>Neck circumference</td>
<td>-0.43 (ns)</td>
</tr>
<tr>
<td>Waist/hip ratio</td>
<td>-0.23 (&lt;0.0001)</td>
</tr>
</tbody>
</table>

**Abstract P213**
THE IMPACT OF SLEEP DISORDERED BREATHING ON PERIPHERAL MUSCLE

1S Mandal, 2†Dhiri, 1A Vaughan-France, 1ES Suh, 1N Hart. 1Lancaster University, Lancaster, UK; 2King’s College London, London, UK

10.1136/thoraxjnl-2014-206260.341

Introduction Chronic obstructive pulmonary disease is characterised by peripheral muscle wasting with consequent reduction in muscle strength and function. In this cohort of patients a reduction in muscle strength correlates with morbidity and mortality. Less well known are the characteristics of muscle in patients with sleep disordered breathing (SDB), a disease state that can also be dominated by inflammation, breathlessness and hypoxia. We sought to examine the impact of sleep disordered breathing on peripheral muscle size and strength.

Method 51 subjects were recruited: 15 healthy controls (HC) with a normal body mass index (BMI, <25 kg/m²), 16 overweight and obese individuals with no SDB controls (SO), and 20 obese subjects with obstructive sleep apnoea (OSA). Subjects underwent measurements of Rectus Femoris Cross Sectional Area (RF CSA) and quadriceps maximal voluntary contraction (QMVC) (see Table 1).

### Abstract P213 Table 1 Differences between groups in demographics, muscle size and strength

<table>
<thead>
<tr>
<th></th>
<th>HC</th>
<th>SO</th>
<th>OSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>(20–33)</td>
<td>(23–40)</td>
<td>(48–67)</td>
</tr>
<tr>
<td>M:F</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>(19.6–23.6)</td>
<td>(25.5–32.7)</td>
<td>(35.8–42.6)</td>
</tr>
<tr>
<td>FEV₁(L)</td>
<td>(0.44–3.74)</td>
<td>(2.84–4.72)</td>
<td>(2.31–3.31)</td>
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<tr>
<td>FVC(L)</td>
<td>4.04</td>
<td>4.20</td>
<td>3.68</td>
</tr>
<tr>
<td>RF CSA (AU)</td>
<td>(2.17–4.27)</td>
<td>(2.66–5.56)</td>
<td>(2.79–4.12)</td>
</tr>
<tr>
<td>Hand grip strength/AU</td>
<td>7.6</td>
<td>8.59#</td>
<td>5.9#</td>
</tr>
<tr>
<td>SMWD (metres)</td>
<td>(529–648)</td>
<td>(513–607)</td>
<td>(278–515)</td>
</tr>
</tbody>
</table>

*significantly different from HC (p < 0.05); #significantly different from OSA (p < 0.05)

Abbreviations: HC=Healthy Controls, SO=Simple Obesity/Overweight, OSA=Obstructive Sleep Apnoea, BMI-Body Mass Index, RF CSA=Rectus Femoris Cross Sectional Area, QMVC=Quadriceps Maximal Voluntary Contraction, SMWD=Six Minute Walking Distance
Results As expected there were differences in BMI between the groups. There were also significant differences in muscle strength and RF_{CSA} when corrected for body weight between HC and OSA groups and between SO and OSA groups, but no differences between HC and SO groups (Table 1). The SO group demonstrated higher measurements of strength and RF_{CSA} than the HC group, however, the OSA group had lower measurements than both the HC and SO group. This translated to a functional difference as measured by the SMWD, again demonstrating the longest distance in the SO group and shortest in the OSA group.

Discussion This study has demonstrated that in those with BMI ≥ 25 kg/m^2 there appears to be a beneficial effect of excess weight on peripheral muscle size, strength and function; this may be due to the extra load carried by these individuals exerting a training effect on the muscles. However, in those who are obese with SDB, the SDB seems to exert a negative effect on muscle size, strength and function which may be a result of the inflammation and hypoxia SDB can cause.

**P214**

**UTILISATION OF CARDIO-PULMONARY EXERCISE TESTING (CPET) AT AN ENGLISH ACUTE HOSPITAL**

E Parkes, VC Moore, D Comer, F Raud, N Santana-Vaz, R Mukherjee. Birmingham Heartlands Hospital, Birmingham, UK

10.1136/thoraxjnl-2014-206260.342

**Background** CPET has been extensively used in the pre-operative (general anaesthesia) risk stratification. More recently, the utility of CPET has become more defined in the evaluation of unexplained dyspnoea and in prognosticating pulmonary hypertension in a rational manner which is also less invasive for patients. We set out to evaluate the utilisation pattern of CPET within a 709-bedded central England acute hospital Trust spread across 3 sites in the second year of the establishment of the service.

**Methods** The source of referral (and reason) for CPET were retrospectively recorded and analysed between 01 July 2013 and 31 May 2014 (ten months).

**Results** The total number of CPET referrals received was 178 out of which 150 (84%) were from surgical disciplines and 28 (16%) from medical disciplines. Vascular surgery submitted the majority of referrals (108, 61%) followed by colorectal surgery [see Figure]. Respiratory Medicine was the source of 11% of all referrals and Cardiology the source of 4%.

**Conclusions** The dominant utilisation of CPET by vascular surgery is expected, given the NHS evidence adoption centre and National Institute for Health and Care Excellence (NICE) 2009 recommendations on risk-stratification for Abdominal Aortic Aneurysm surgery mortality. However, CPET offers a unique assessment tool for the investigation of patients with unexplained dyspnoea and has a potential to pre-empt invasive, unnecessary and expensive assessment without definitive diagnosis [Thing JER, Mukherjee B, Murphy K et al. Thorax 2011; 66 (4): A144]. It appears that a lot of work needs to be done among the UK general respiratory and cardiology/heart failure communities to promote the awareness, understanding and utilisation of CPET.
trust for the same time period. From this data we could estimate the proportion of lung cancer patients from each trust that were referred for mediastinal staging with EBUS.

**Results** In 2012, 2,302 patients were diagnosed with lung cancer in this Network. In the same period, 193 patients were referred for EBUS mediastinal staging (8.4%). The proportion of lung cancer patients referred for mediastinal staging with EBUS varied significantly across the ten trusts ranging from 3.4% to 30.2% (p < 0.0001). The spearman co-efficient was 0.60 (p = 0.07) suggesting a possible relationship between the proportion of patients referred for EBUS and surgical resection (Figure 1). However, this may be due to a very high rate of staging EBUS at one trust, which if excluded yields a spearman co-efficient of 0.45 (p = 0.22).

**Discussion** It is highly concerning that only 8% of lung cancer patients underwent EBUS nodal staging in our network given 52% of UK patients with histologically confirmed NSCLC are stage I-III at the time of diagnosis. It is of note that the Trust with the highest proportion of patients undergoing EBUS nodal staging have the highest surgical resection rate and three of the four Trusts with the lowest resection rates refer <5% of patients for EBUS nodal staging. Standardisation of referral practice across the Network is a key future goal for the EBUS Sub-group.

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**Poster sessions**

**P216 LOCAL ENDOBRONCHIAL ULTRASOUND (EBUS) SERVICE REDUCES WAITING TIME FOR TEST RESULTS**

JL Dickson, M Lawson. Broomfield Hospital, MEHT, Chelmsford, UK

10.1136/thoraxjnl-2014-206260.344

**Introduction** Endobronchial ultrasound (EBUS) is increasingly used in investigating mediastinal lymphadenopathy. A recent Thorax paper suggested EBUS should only be performed in large centres to ensure quality. A recently established EBUS service at Broomfield Hospital appeared to reduce the time taken to obtain results compared to the regional service previously used. The service was audited to ensure quality and evaluate changes to pathway times.

**Objectives** Compare time from decision for EBUS to test result between local and regional service and ensure safety and accuracy.

**Methods** Data were collected prospectively for all EBUS cases after the local service was established in August 2013. Accuracy and safety of the service were audited based on the first 8.5 months of operation. Data were extracted from the MDT database for patients referred to the regional service between November 2013 and January 2014. Time from MDT decision for EBUS referral and subsequent MDT discussion of results were compared between both services. Data were compared using the Mann-Whitney U test using the statistics package in R.

**Results** Average time from decision to EBUS result was 19 days in the local service based on the first 21 cases performed. There was a 40 day average turnaround for the regional service based on the 10 cases referred between November 2013 and January 2014. This represented a statistically significant reduction in waiting time of 21 days (p = 0.0001). The local service was safe and accurate with no reported complications in 42 cases over the first 8.5 months and an overall accuracy of 88% increasing to 94% (31/33) in suspected cancer cases.

**Conclusions** Our recently established local EBUS service is safe and accurate but also significantly reduces the time between decision to EBUS and test results discussed in MDT compared to the regional referral service previously used. This is important for patients on the 62-day cancer pathway. A local service enables people to undergo investigations nearer to home. The establishment of national reference standards for EBUS is important to ensure optimal quality but this can be achieved in local services which may offer additional benefits to patients.
histological and surgical details were extracted from clinical records. Analysis was conducted on MedCalc software v13.3.1 and reviewed by an independent statistician.

**Results** 42 patients who underwent EBUS+/–EUS for mediastinal staging were found to have no evidence of N2/3 disease. In 3 cases subsequent mediastinoscopy was performed as a high degree of suspicion for mediastinal disease persisted. However, in all cases surgical staging correlated with endosonographic staging. At thoracotomy, 3 (other) patients were upstaged to N2 disease. In two cases, micrometastatic disease was present in a station 7 node and one case had positive station 5/6 not accessible at EBUS/EUS. Overall the NPV of EBUS+/–EUS was 93% (95% CI, 80%–98%). In 22 of 42 patients, the same nodal stations sampled on EBUS/EUS were removed at surgery. In this subset, EBUS/EUS had a NPV of 91% (95% CI, 71% to 99%).

**Conclusion** We have shown that in an experienced centre, mediastinal staging by EBUS+/–EUS can have a high NPV. In these circumstances, surgical staging following negative endosonography is probably not warranted unless a high degree of clinical suspicion remains following MDT discussion. Regular audit of NPV is recommended to ensure performance standards are maintained.

**REFERENCES**
1 Annema et al, JAMA 2010;304:2245
2 NICE guidelines, 2011, Lung Cancer, CG121
Introduction Endobronchial ultrasound and transbronchial needle aspiration (EBUS-TBNA) has been embraced as a breakthrough in the diagnosis and mediastinal staging of lung cancer. However, its utility in determining a diagnosis of lymphoma is not well defined, and is currently not recommended by the British Thoracic Society.

Aim Evaluate the role of EBUS-TBNA in the diagnosis and subtyping of haematological malignancies.

Method Patients referred with mediastinal lymphadenopathy for EBUS-TBNA in whom lymphoma was suspected, were identified retrospectively in 3 tertiary centres in the UK between 2008 and 2013. EBUS was performed using a linear array ultrasonic bronchoscope and specimens taken with a 21 or 22 gauge needle.

The diagnostic accuracy, avoidance of mediastinoscopy and surgical biopsy in cases of primary and relapsing haematological malignancy was recorded. Where EBUS-TBNA was negative, patients subsequently underwent surgical biopsy or clinical and radiological surveillance.

Results Twenty-four patients (10 female and 14 male) with a mean age of 55.5 years underwent EBUS-TBNA for evaluation of mediastinal lymphadenopathy. Clinical and radiological diagnosis was of either, isolated mediastinal lymphadenopathy of unknown cause (n = 15) or suspected mediastinal recurrence of lymphoma (n = 8). Five patients (62.5%) were found to have a relapse of their haematological malignancy, whilst a new diagnosis of lymphoma was made in 11 cases (73.3%) where the presentation was of isolated mediastinal lymphadenopathy. One patient in this group was found to have tuberculosis. Tissue obtained from nodal aspiration was sufficient to subtype the disease in detail in 14 patients with immunohistochemistry. Overall, 17 patients (70%) were prevented from having mediastinoscopy and other biopsies, and the diagnostic accuracy and sensitivity of EBUS-TBNA in primary and relapsing lymphoma was 74%.

Conclusion EBUS-TBNA is a safe and important approach to mediastinal lymphadenopathy in suspected lymphoma, whereby detection of either primary or relapsing haematological malignancy prevents need for other invasive biopsies.

**P221** THE USE OF CYTOLOGICAL SPECIMENS TO DETERMINE EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) MUTATION STATUS IN NON-SMALL CELL LUNG CANCERS (NSCLC)

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Introduction Treatments for patients with advanced NSCLC are improving, including the use of drugs which act on those cancers that express EGFR mutations. However, determination of EGFR status requires an adequate sample for analysis and national guidelines indicate that this is best obtained by tissue biopsy. Unfortunately, in this ill patient group tissue biopsy may be problematic and a diagnosis is often made through cytology alone. There are few published studies on the utility of cytological specimens for EGFR analysis and we wished to study this further.

Methods We reviewed all lung cancer samples that had been sent from our large cancer unit since EGFR mutation analysis became available 35 months ago, comparing the yield from cytology and formal tissue biopsy.

Results Of 330 cases sent for EGFR analysis, cytology was the only sample available in 92 cases (28%) – as might be expected this group contained individuals with poor lung function and high rates of metastatic disease (Mean FEV1 0.76 L, Median stage=4). Samples were most commonly obtained from EBUS (59%), bronchial brushings/washings (23%), or pleural aspiration (11%), and 64 (70%) of these were deemed adequate for mutation analysis.

Although formal histological samples were more likely to provide sufficient material for EGFR analysis than cytological methods [84% vs. 70%], those acquired through EBUS or pleural aspiration gave comparable rates [81% and 88% respectively]. Overall, 34 cases (10%) were EGFR positive, and 4 of these (12%) were based on cytology samples alone.

Conclusions Our data show that most cytopathological specimens, especially when obtained by EBUS or pleural aspiration, will provide adequate material for EGFR analysis and increase the identification of patients eligible to receive targeted therapy. As cytology specimens can often be obtained through relatively non-invasive means our findings further underline the importance of attempting a tissue diagnosis even in patients who may otherwise be regarded as too unwell for more intensive investigations.

**P222** SHORT AND LONG-TERM CONSEQUENCES OF PNEUMOTHORAX FOLLOWING CT-GUIDED LUNG BIOPSY FOR LUNG MALIGNANCY

E Johnson, A MacKenzie, S Tsim, K G Blyth. Department of Respiratory Medicine, Southern General Hospital, Glasgow, UK

Introduction and objectives Pneumothorax (PTX) is a common complication of Computed Tomography-guided lung biopsy (CTLB). We sought to quantify the short and long-term consequences of post-CTLB PTX in patients with lung malignancy.

Methods We retrospectively reviewed case records and imaging of all who underwent CTLB in NHS Greater Glasgow and Clyde between August 2011 and August 2012. Patient characteristics (including diagnosis, lung function and blood results), biopsy characteristics, 30-day mortality, PTX management and survival were recorded. Lesion size, depth and maximum PTX depth were directly measured on digitally-stored PACS images.

Patients were classified into no PTX, non-significant PTX (nsPTX) and significant PTX (sPTX), which was defined as any PTX which required pleural intervention. Differences in patient and biopsy characteristics between groups were identified by ANOVA and quantified by Tukey’s Multiple Comparisons Test. Kaplan-Meier curves were plotted and differences quantified by log-rank, log-rank for trend and Hazard Ratios. Results are mean (±SD).

Results 324 CTLB were performed. Malignancy was confirmed in 285/324 (88%). Mean age was 70(±11) years. 84/285 (29%) developed a PTX. 17/285 (6%) developed a sPTX. There were
Abstract P223 Figure 1  (A) Lesion size by PTX group, (B) Lesion Depth by PTX group, (C) Survival by PTX group and (D) Survival in patients with a peripheral NSCLC

no deaths related to CTGLB (30-day mortality: 100% in all groups).

SPTX were larger than nsPTX (34(±6) mm vs. 19(±6) mm, p = 0.0003). Other factors associated with sPTX were lesion size and depth (see Figure 1 (a and b), larger needle gauge (p < 0.0001), higher FEV1 (p = 0.01) and lower DLco (p = 0.049).

Length of stay (LoS) was longer in sPTX (5.8(±5.9) days, p < 0.0001) and nsPTX (1.7(±2.3) days, p < 0.0001) than No PTX (0.7(±0.9) days), but long-term survival was better (see Figure 1 (c and d)). This survival difference was pronounced in a sub-group of patients with a peripheral non-small cell lung cancer (defined as a lesion depth ≤ 0 mm, n = 53).

Conclusions CTGLB was associated with a low rate of sPTX (6%) and no short-term mortality, sPTX was associated with lung function indicative of emphysema and smaller, deeper lesions. The latter association likely explains the apparent survival advantage found in PTX patients but any long-term survival disadvantage seems unlikely. Post-CTLB PTX may be a positive sign in peripheral NSCLC, possibly inferring resectability.

P223    CONSENT FOR MEDICAL THORACOSCOPY: THE TRUTH, THE WHOLE TRUTH AND NOTHING BUT THE TRUTH?

S.J Jafri, K Ramsay, PA Beckett, RJ Berg. Royal Derby Hospital, Derby, UK 10.1136/thoraxjnl-2014-206260.351

Introduction Failure to provide adequate information for valid informed consent may impact negatively on patient satisfaction and trust, and is a common cause of medical litigation. Some professional societies produce standardised consent forms in an attempt to reduce variation in quality of consent. There is no published national guideline standard for consent for medical thoracoscopy. We reviewed the quality of consents for medical thoracoscopy in a unit performing an average of 40 medical thoracoscopies per year.

Methods Case records of 80 patients who had undergone medical thoracoscopy were retrospectively reviewed. Consent forms were assessed for mention of potential complications, and grade and competency at thoracoscopy of consent-takers. We analysed the consistency between consents taken by the same individuals at different times, and numbers of patients experiencing complications for which they were not consented.

Results Consent was taken by 19 individuals. Consultant thoracoscopists took 54% of consents; non-thoracoscopist consultants took 15% and trainees 31%. Potential complications consented for were: bleeding (100%), ‘infection’ (99%), persistent pneumothorax/trapped lung (81%), pain (73%), Empyema (46%), damage to underlying organs (28%), respiratory distress (28%), non-diagnostic procedure (20%), (talc related) fever (16%), cardiac complications (15%) and haemothorax (10%).

Consultant thoracoscopists were significantly more likely than other consent-takers to consent patients for empyema; 72% vs 16% of consents, p < 0.001, and pain; 93% vs 49%, p < 0.001.

Consistency with which consent-takers omitted or mentioned complications varied by individual and complication. For example, those individuals who consented at least once for empyema (7/19 consent-takers) did so collectively on 80% of their consents (individual range 5%-100%), whereas those who took consent for damage to underlying organs (10/19 consent-takers) did so on only 35% of their consents (range 5%-100%).

Empyema occurred in 5% of patients, all of whom had been consented for this complication. 38/80 patients (48%) experienced significant pain, of whom 34% were not consented for this.

Conclusion Information provided on thoracoscopy consent forms is inconsistent, both for common minor and serious complications. Even experienced thoracoscopists may fail to clarify significant complications. Introduction of a standardised consent form could reduce variation and consequent potential for patient distress and medico-legal risk.

P224    LYMPH NODE ASSESSMENT IN SURGICAL RESECTION OF NON-SMALL CELL LUNG CANCER (NSCLC): ARE WE HITTING THE TARGET?

AC McKay, H Ewan, G Beattie, AJB Kirk, M Asif. Thoracic Surgery, Golden Jubilee National Hospital, Glasgow, UK 10.1136/thoraxjnl-2014-206260.352

Introduction Guidelines from the British Thoracic Society (BTS) and the National Institute for Health and Care Excellence (NICE) recommend that nodal assessment be performed in all patients who have anatomical lung resection for NSCLC.

Nodal status is one of the major determinants of outcome and most multidisciplinary teams now record adequacy of nodal assessment. N1 nodes are removed with the specimen perforce; therefore, a better indicator of surgical performance is the number of N2 nodal stations sampled.

This paper describes a continual audit cycle of lymph node sampling performance data in relation to N2 nodes.

Methods A retrospective analysis of patients who underwent anatomical lung resection for NSCLC in the calendar years 2009, 2010, 2012 and 2013 was undertaken. Lymph node sampling data was taken from pathology reports. The number of different stations sampled, rather than number of individual lymph nodes, was counted. Basic patient demographics were also collected.

After each audit cycle individual results were tracked and presented at open local, regional and national forums.

Results A total of 937 patients were audited after anatomic lung resection for NSCLC during the study periods. Pathology of NSCLC resections were as follows: 52% adenocarcinoma,
33.9% squamous cell carcinoma, 7.3% large cell carcinoma, 6.1% other. The data is summarised in the table below:

**Conclusion**
- Audit over the past 3 years shown steady improvement in lymph node assessment performance.
- Continuous auditing and presentation of individual surgeon data at local, regional and national forums has contributed to the increasing compliance to the guideline targets.
- There remains scope for further improvement and consultant engagement.
- Re-auditing will be essential to further improve compliance with guidelines.

### Revised BTS Guidelines for Securing Cancer Diagnosis at Bronchoscopy – A Higher Recommended Yield is Realistic and Achievable

**AE Stanton, CI Mackinlay, Department of Respiratory Medicine, Great Western Hospitals NHS Foundation Trust, Swindon, UK**

**Poster sessions**

**P225**

**REVISED BTS GUIDELINES FOR SECURING CANCER DIAGNOSIS AT BRONCHOSCOPY – A HIGHER RECOMMENDED YIELD IS REALISTIC AND ACHIEVABLE**

*Introduction* The recently updated BTS guidelines on bronchoscopy recommend that a diagnostic level of 85% should be attainable when definite endobronchial tumour is visible, an increase from previous recommendation of 80%. We investigated whether this higher level was achievable.

**Methods** All patients undergoing bronchoscopy for suspected lung cancer were prospectively entered into a departmental database from April 2010, with performance analysed annually. The following specific data were entered: level of tumour presence (none seen / possible / definite tumour); diagnostic specimens taken (biopsy, brush, wash, TBNA); result of each diagnostic specimen (tumour present / not present, with reports “suspicious or suggestive” of tumour classified as “not present” unless there was a specific MDT decision to give a cancer diagnosis), and whether bronchoscopy was diagnostic of lung cancer overall. Finally clinical records were reviewed in patients without a bronchoscopic diagnosis of cancer to determine their final diagnosis. Results In the 4 full years since commencement of data collection, 356 bronchoscopies were performed for suspected lung cancer, with confirmed cancer diagnosis in 301. Table 1 summarises diagnostic sensitivity for endobronchial biopsy, brush, wash and overall sensitivity for lung cancer diagnosis at bronchoscopy in patients with bronchoscopically definite tumour seen. In 3/4 years our overall diagnostic sensitivity has reached the level recommended (86.4–91.7%), with first year performance just below the new standard (84.4%).

**Conclusions** The revised level of recommended diagnostic rate at bronchoscopy for definite tumour appears to be realistic and achievable. This should remain as the standard of care for patients undergoing bronchoscopy for suspected lung cancer.

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of Bronchs – Suspected LC</th>
<th>No. with confirmed LC</th>
<th>No. of bronchs – definite tumour seen</th>
<th>Biopsy sensitivity (%)</th>
<th>Brushing sensitivity (%)</th>
<th>Washing sensitivity (%)</th>
<th>Overall sensitivity when definite tumour seen (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010–11</td>
<td>92</td>
<td>72</td>
<td>33</td>
<td>67.7</td>
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<td>87</td>
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<td>41</td>
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<td>60.7</td>
<td>27.8</td>
<td>86.4</td>
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<tr>
<td>2012–13</td>
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<td>55.8</td>
<td>30.6</td>
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<tr>
<td>2013–14</td>
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<td>36</td>
<td>80</td>
<td>71.4</td>
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</table>

**REFERENCE**

BTS Guideline for diagnostic flexible bronchoscopy in adults. Thorax 2013;68(Suppl 1)

**P226**

WITHDRAWN

### Asthma Treatments

**P227**

EFFICACY AND SAFETY OF BUDENSONIDE–FORMOTEROL (BF SPIROMAX®) IN ADULTS AND ADOLESCENTS WITH ASTHMA: RANDOMISED COMPARISON WITH BF TURBUHALER®

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**Background** DuoResp Spiromax® (Teva Pharmaceuticals) is a dry-powder inhaler designed to deliver budesonide and formoterol fumarate (BF Spiromax®) with maximum ease of use. Pharmacokinetic studies have shown bioequivalence of BF Turbuhaler®. This study compared the efficacy and safety of these devices in patients with asthma.

**Methods** This was a 12-week, multicentre, double-blind, randomised, controlled trial (N=605). Eligible patients (≥12 years old) had persistent asthma with FEV1 ≥ 80% predicted, had used a SABA and ICS for ≥8 weeks before screening and were maintained on stable-dose ICS for 4 weeks. The primary objective was to demonstrate non-inferiority of twice-daily BF Spiromax® 160/4.5mcg to BF Turbuhaler® 200/6mcg, with respect to change from baseline in weekly average of daily trough morning PEF.

**Results** This analysis was based on the per protocol population (N=290 and N=284 for BF Spiromax® and BF Turbuhaler® groups, respectively). The least squares mean change from baseline to Week 12 in morning PEF was 18.8 L/min with BF Spiromax® and 21.796 L/min with BF Turbuhaler®. Non-inferiority of BF Spiromax® vs BF Turbuhaler® was demonstrated, as the lower limit of the 95% two-sided CI (~9.02 L/min) is greater than −15 L/min. Similarly, no significant between-group differences were observed in secondary efficacy endpoints. Both devices were well tolerated, with no significant differences in the incidence of adverse events or asthma exacerbations.

**Conclusions** This study has demonstrated the non-inferiority of BF Spiromax® vs BF Turbuhaler® in adults and adolescents with asthma. Further data are required to confirm whether BF Spiromax® can be used as an alternative to BF Turbuhaler® in other indications.

**Sponsor:** Teva Pharmaceuticals.
Background Fluticasone propionate (FP) and formoterol (FORM) have been combined in a single inhaler (FP/FORM; fluticason- 
formoterol®) for the treatment of adolescents and adults with asthma. This study assessed the efficacy and safety of FP/FORM 
in paediatric asthma patients.

Methods A total of 512 patients aged 5 to <12yrs were randomised 1:1:1 to 12 weeks of treatment with either FP/FORM 
(100/10 µg BID), FP (100 µg BID) or fluticasone propionate/sal-
meterol (FP/SAL) (100/50 µg BID) in a double-blind, parallel 
group, multicentre study. The objectives were to determine superiority of FP/FORM to FP and non-inferiority to FP/SAL. 
The primary endpoint was the change from predose FEV1 at baseline to 2-hour postdose FEV1 over the 12 weeks. The two key secondary endpoints were FEV1 AUC0–4h at Week 12 and change from pre-dose FEV1 over the 12 weeks.

Results FP/FORM was superior to FP for change from predose FEV1 at baseline to 2-hour postdose FEV1 (treatment difference = 0.07 L; 95% CI: 0.03, 0.11; p < 0.001) and FEV1 AUCO–4h at Week 12 (treatment difference = 0.09 L; 95% CI: 0.04, 0.13; p < 0.001). FP/FORM was non-inferior to FP/SAL for change from predose FEV1 at baseline to 2-hour postdose FEV1 (treatment difference = -0.00 L; 95% CI: -0.04, 0.04; p < 0.001). AUCO–4h at Week 12 (treatment difference = 0.01 L; 95% CI: -0.03, 0.06; p < 0.001) and change from predose FEV1 (treatment difference = -0.02 L; 95% CI: -0.06, 0.02; p < 0.001). The safety and tolerability profiles of all treatments were similar. Conclusion In children 5 to <12yrs with asthma, FP/FORM was superior to FP and non-inferior to FP/SAL for improvements in lung function, with a similar tolerability profile to both FP and FP/SAL.

Conclusion Once-daily tiotropium Respimat® as add-on to ICS or ICS + LABA in patients with moderate to severe symptomatic asthma reduces airflow obstruction, apparently independent of their atopic and/or allergic status.

ONCE-DAILY TIOTROPIUM RESPIMAT® IMPROVES LUNG FUNCTION IN PATIENTS WITH SEVERE SYMPTOMATIC ASTHMA INDEPENDENT OF LEUKOTRIENE MODIFIER USE

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10.1136/thoraxjnl-2014-206260.359

Background Once-daily tiotropium Respimat®, a long-acting anticholinergic bronchodilator, has been shown in a Phase III programme to improve lung function and reduce severe exacerbation risk in patients with severe asthma who remain symptomatic despite using inhaled corticosteroids (ICS) + long-acting β2-agonist (LABA). Use of pre-trial leukotriene receptor antagonists (LTRAs) was not restricted; we analysed whether pre-screening LTRA use affected tiotropium Respimat® efficacy.

Methods In two Phase III, replicate, randomised, double-blind, placebo-controlled, parallel-group trials (PrimoTinA-asthma®: NCT00772538, NCT00776984), symptomatic patients received high-dose ICS + LABA and once-daily tiotropium 5 μg or placebo (both delivered via the Respimat® SoftMist™ inhaler). LTRAs were permitted during run-in and treatment. Co-primary end points were peak and trough forced expiratory volume in 1 second (FEV₁) responses (difference from baseline) at 24 weeks. Subgroups were defined by pre-screening LTRA use: ‘Yes’/‘No’.

Results Of 912 randomised patients, 205 reported pre-screening LTRA use: peak FEV₁ was 99 ± 50 mL (p = 0.049) in the LTRA ‘Yes’ group and 113 ± 28 mL (p < 0.001) in the LTRA ‘No’ group (peak FEV₁ improvements independent of concomitant LTRA use [interaction p value = 0.6742]). Trough FEV₁ (difference from placebo) was 90 ± 46 mL (p = 0.052) in the LTRA ‘Yes’ group and 93 ± 25 mL (p < 0.001) in the LTRA ‘No’ group (trend FEV₁ improvements independent of concomitant LTRA use [interaction p value = 0.5218]).

Conclusion Once-daily tiotropium Respimat® added to ICS + LABA improves lung function in patients with severe symptomatic asthma, independent of initial LTRA use.

ONCE-DAILY TIOTROPIUM RESPIMAT®: SAFETY AND TOLERABILITY RESULTS FROM FIVE PHASE III TRIALS IN ADULTS WITH SYMPTOMATIC ASTHMA

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10.1136/thoraxjnl-2014-206260.360

Background Tiotropium Respimat®, a once-daily long-acting anticholinergic agent, is effective as add-on to inhaled corticosteroids (ICS) ± a long-acting β2-agonist (LABA) in adults with symptomatic asthma. Safety and tolerability are key issues in the development of new therapies or established therapies in new disease areas. We present key safety data from five Phase III, randomised, double-blind, parallel-group trials that evaluated the efficacy and safety of once-daily tiotropium Respimat® versus placebo in adults with symptomatic asthma. Methods: Two 48-week trials of tiotropium Respimat® 5 μg (PrimoTinA-asthma®: NCT00776984, NCT00772538) in patients on high-dose ICS (≥800 μg budesonide or equivalent) + LABA; two 24-week trials of tiotropium Respimat® 5 μg and 2.5 μg (MezzoTinA-asthma®: NCT01172808, NCT01172821) in patients on moderate-dose ICS (400–800 μg budesonide or equivalent); one 12-week trial of tiotropium Respimat® 5 μg and 2.5 μg (GraziaTinA-asthma®: NCT01316380) in patients on low-dose ICS (200–400 μg budesonide or equivalent). All tiotropium doses were delivered via the Respimat® SoftMist™ inhaler. Results:

Abstract P231 Table 1

<table>
<thead>
<tr>
<th>Tiotropium Respimat®</th>
<th>Placebo Respimat®</th>
<th>Tiotropium Respimat®</th>
<th>Placebo Respimat®</th>
<th>Salmeterol</th>
<th>Placebo</th>
<th>Tiotropium Respimat®</th>
<th>Placebo</th>
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<tr>
<td>5 μg QD (n = 456)</td>
<td>5 μg QD (n = 456)</td>
<td>2.5 μg QD (n = 519)</td>
<td>2.5 μg QD (n = 519)</td>
<td>50 μg BID</td>
<td>50 μg BID</td>
<td>5 μg QD (n = 155)</td>
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<tr>
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<td>8.8</td>
<td>2.1</td>
<td>2.2</td>
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<td>2.7</td>
<td>0.6</td>
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<tr>
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<td>50.9</td>
<td>21.5</td>
<td>15.5</td>
<td>19.4</td>
<td>23.0</td>
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<td>Decreased peak expiratory flow rate</td>
<td>20.4</td>
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<tr>
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<td>Nasopharyngitis</td>
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<td>7.8</td>
<td>4.5</td>
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*Placebo Respimat® QD + placebo hydrofluoroalkane metered-dose inhaler BID BID, twice-daily; QD, once-daily.
TREATMENT OF ALLERGIC RHINITIS WITH LONG-TERM IMPACT OF INHALED CORTICOSTEROIDS

Background Allergic rhinitis and Asthma are considered as ‘one airway disease’. Theophylline has been used as a bronchodilator in asthma for decades but more recently its anti-inflammatory properties have been identified. We hypothesise that treatment with low dose theophylline in patients with persistent allergic rhinitis is likely to improve the total nasal symptom scores and there by demonstrate a clinically meaningful difference.

Methods This was a single centre double- blind, randomised, placebo-controlled cross-over study of the effects of theophylline (one capsule of Theophylline 200 mgs as Uniphyllin continus twice a day for 4 weeks) in 21 patients with persistent allergic rhinitis in Norwich, U. K. Reference: NCT0113278. Primary outcome was Total Nasal Symptom Score (TNSS) after each intervention period. Secondary endpoint measures were differences in the domiciliary average total nasal symptom score, differences in nasal peak inspiratory flow (PNIF), differences in domiciliary nasal peak inspiratory flow and difference in Sino-Nasal Outcome Test (SNOT)-22.

Results Primary Endpoint
There was no significant (p = 0.276) difference in Total Nasal Symptoms scores during Theophylline treatment period and placebo period, mean (SD) (Table). The intention-to-treat analysis results were in keeping with the per protocol analysis.

Secondary End points
PNIF in the Theophylline period was 112.38(±43.49) compared to the placebo period 122.86(±33.77), p = 0.171 (Table). There was no change in SNOT-22 (p = 0.867) between treatment periods but there was a non-significant improvement with Theophylline (39.00 ± 19.78) compared to placebo (38.00 ± 19.63) treatment period. There was a non-significant improvement in the domiciliary total nasal symptom scores (TNSS) between Theophylline (3.53 ± 2.35) and placebo (2.81 ± 2.46). Nasal scrape samples were stained with HDAC2 antibodies and the signals were very weak.

Conclusion This is the first study evaluating Theophylline in persistent rhinitis. Low-dose Theophylline had no significant effects on Total nasal Symptom scores; Rhinosinusitis symptoms and nasal patency assessed using peak nasal inspiratory flow. There was a non-significant improvement in the total nasal symptom scores and sino-nasal outcome test and domiciliary nasal scores.

P234 IMPACT OF INHALED CORTICOSTEROIDS ON GROWTH IN CHILDREN WITH ASTHMA: SYSTEMATIC REVIEW AND META-ANALYSIS

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10.1136/thoraxjnl-2014-206260.363

Background A recent meta-analysis of 16 randomised controlled trials (RCTs) and 7 observational studies demonstrated a modest but statistically significant increase in fracture risk with inhaled corticosteroid (ICS) use in chronic obstructive pulmonary disease. However, it is not clear whether ICS use has similar skeletal adverse effects in patients with asthma. We aimed to evaluate the association between ICS and fractures and changes in bone mineral density when used for >12 months in asthma.

Methods We initially searched MEDLINE and EMBASE in July 2013, and performed an updated PubMed search in June 2014. We used a combination of search terms involving drug name and adverse effects of interest, and we also hand-searched reference lists of existing systematic reviews and trial reports. We selected RCTs and controlled observational studies of any ICS vs non-ICS control treatment for asthma (at least 52 weeks duration). Meta-analysis of odds ratios was conducted using RevMan 5.3 with the primary outcome measure being fracture events. We also analysed mean differences in bone mineral density (gram per cm squared) using inverse variance method. Heterogeneity was assessed using the I2 statistic.

Results We selected nine RCTs and 11 observational studies for the meta-analysis. There was no significant association between ICS and fractures in children in one RCT, or in a pooled analysis of two observational studies, (OR 1.02, 95% CI 0.94–1.10). No significant fracture risk in adults was reported in 4 observational studies (pooled OR 1.09, 95% CI 0.45–2.62). Meta-analysis of bone mineral density at the lumbar spine did not show significant reductions with ICS use in children (three RCTs and three observational studies), or in adults (three RCTs and four observational studies). Similarly, meta-analysis of bone mineral density at the neck of femur in adults did not demonstrate significant reductions compared to control (three RCTs and four observational studies).

Conclusion In our systematic review of 20 studies, use of ICS for >12 months in patients with asthma was not associated with statistically significant adverse effects on bone mineral density or fractures.
Background There are major concerns and uncertainty regarding a possible reduction in growth velocity and final height of children with asthma who are long-term users of inhaled corticosteroids (ICS). We aimed to evaluate the association between ICS use of >12 months and growth.

Methods We initially searched MEDLINE and EMBASE in July 2013, followed by a PubMed search updated to June 2014. We used a combination of search terms involving drug names and adverse effects of interest (such as growth or height), and we also hand-searched reference lists of existing systematic reviews and trial reports. We selected RCTs and controlled observational studies of any ICS vs non-ICS control treatment in patients with asthma (treatment duration of at least 52 weeks). Meta-analysis of continuous outcomes (growth velocity in cm/year or final height in cm) was conducted using RevMan 5.3. We analysed mean differences using inverse variance method, random effects model. Heterogeneity was assessed using the I² statistic.

Results We found 21 relevant studies (seventeen RCTs and four observational studies) after screening 1876 hits from the search. Meta-analysis of 16 RCTs showed a significant association between ICS use and reduction in growth velocity compared to controls (pooled Mean Difference -0.35 cm/year, 95% CI -0.54 to -0.18). No significant reduction in growth velocity with ICS was reported in two observational studies of lower quality (pooled Mean Difference 0.03 cm/year, 95% CI -0.61 to 0.67). Analysis of final adult height showed a mean reduction of -1.20 cm (95% CI -1.90 cm to -0.50 cm) with budesonide versus placebo in a high quality RCT. Meta-analysis of two lower quality observational studies found a non-statistically significant pooled mean reduction in final adult height of -0.85 cm (95% CI -3.35 to 1.65).

Conclusion Use of ICS for 12 months or more in children with asthma has a limited impact on annual growth velocity, with a slight reduction in final adult height. When interpreted in the context of the typical final adult height in the UK, ICS users may experience less than 0.7% reduction in height compared to non-ICS users.

**P235** PREDNISOLONE/CORTISOL SPOT TEST OF NON-ADHERENCE IN CORTICOSTEROID-DEPENDENT ASTHMA

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Background About 40% of severe asthmatics require maintenance oral corticosteroids (OCS) for disease control. However, significant proportion of these patients continues to have poor disease control due to OCS unresponsiveness or non-adherence (Gamble 2009).

Methods We conducted a validation study where we used a validated in-house developed liquid chromatography/mass tandem spectrometry (LC/MSMS) method for the spot measurement of serum prednisolone, prednisone and cortisol in 111 patients attending our severe asthma clinic over a 12 months period. Patients not on maintenance OCS comprised the control group. Suppressed cortisol (20nmol/l), were considered as compatible with adherence to OCS, whilst unsuppressed cortisol and undetectable prednisolone were considered as non-adherent. For validation purposes the test was repeated multiple times in few cases.

Results The prednisolone/cortisol spot test was conducted on 111 patients (79% females) with 44 (40%) on regular OCS (control group) and 67 (60%) on maintenance OCS. The test was conducted on 27/67 (40%) for non-ICS users. The prednisolone/cortisol spot test revealed non-adherence in 27/67 (40%) of patients and adherence in 40/67 (60%) of patients. The prednisolone/prednisone/cortisol assays were similar in non-adherent group and non-OCS group (figure). The mean daily prednisolone dose was 16.3, 20.1, and 0.0 mg dose in the adherent, non-adherent and non-OCS groups respectively. Non-adherent patients had lower BMI, and higher exacerbations frequency, blood eosinophil count, and fraction exhaled nitric oxide than OCS adherent group. The non-adherent group resembled more the non-OCS group with regard to aforementioned parameters.

Conclusion We conclude that this prednisolone/cortisol spot test is reproducible and diagnostic of non-adherence to OCS in 40% of patients on maintenance OCS, and should be routinely measured in severe asthma clinics to improve patients management.

**P236** RELATIONSHIP BETWEEN BONE MINERAL DENSITY AND BONE TURNOVER MARKERS IN SEVERE ASTHMA PATIENTS ON SYSTEMIC CORTICOSTEROIDS

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Background Severe asthma often requires regular SCS use. SCS cause several adverse effects including reduced bone metabolism; resorption is increased and formation is decreased resulting in osteoporosis. DXA scans monitor BMD in the hip and spine every 3–5 years. BMD decrease is treated with bone sparing medication (BSM), but treatment is retrospective and response takes years to assess. BTM represent markers of systemic bone metabolism and may offer a more efficient alternative. CTX is a resorption marker, PINP and BSALP are formation markers.

Methods We measured BTM in Manchester severe asthma patients with two or more DXA scans identified from case files. We used BMD in Manchester severe asthma patients.
and a control group of Manchester severe asthma patients requiring less than 3 courses of steroids per year. Using case files we collected data including DXA scan results, SCS use and osteoporosis risk factors.

Results BMD change and BTM did not correlate overall (patients n = 78, controls n = 18) but correlated negatively in patients where the most recent DXA was

Conclusion This study has confirmed that BTM may be potentially used as a surrogate for BMD measurement; however a more a prospective study where BTM are measured at the time of two DXA scans which are years apart is required.

Objectives To determine whether Mycophenolate mofetil (MMF) is an effective steroid sparing agent in a single centre cohort of severe asthma patients.

Background MMF is a powerful inhibitor of purine and pyrimidine synthesis via the de novo pathway, upon which lymphocyte production is dependent. It is currently licensed for use in transplant rejection prophylaxis. Other immunosuppressant therapies have been used off licence in difficult-to-treat asthma patients under specialist supervision in an effort to reduce corticosteroid use. MMF is currently a third line immunosuppressant after methotrexate and azathioprine at the North West Lung Centre.

Methods A retrospective data analysis was performed including all patients under specialist asthma care at UHSM that were previously or currently treated with MMF. Annualised average daily steroid dose was calculated from the available data in patient case notes. This was calculated for 12 months prior to commencing any immunosuppressant therapy and during MMF treatment. Exacerbation and hospital admission rates were also recorded.

Results A total of 34 patients were identified as being on MMF for severe asthma for at least 8 weeks. 11 did not tolerate MMF or had no response and subsequently stopped. The primary analysis was carried out on 23 patients and a secondary post hoc analysis was performed on all patients who had been on treatment for a minimum of 6 months at the time of the study (N=12). The average yearly steroid sparing impact of MMF was 5.9 mg per day, (p < 0.005), 74% had an overall reduction and 33% achieved a reduction of 10 mg or more. This value was lower in those who had been on treatment for >6 months (Δ 3.9 p = 0.20). There was no statistically significant reduction in admission or exacerbation rates.

Conclusion MMF has shown a small steroid sparing effect in this retrospective analysis, although the effect appeared less positive in the sub-group of those analysed after being on treatment for at least 6 months further analysis of the potential benefits of MMF in this patient population is required.

Rationale Although the guidance for using a pMDI is to inhale ‘slow and deeply’, many patients inhale fast over a short duration. The ERS/ISAM Task Force suggested ‘slowly’ equates to inhaling over 4–5 seconds (s) for adults, a much clearer instruction. This study therefore examined the influence of inhalation time on total lung deposition (TLD) using Functional Respiratory Imaging (FRI).

Methods Three-dimensional airway models of 6 asthma patients (mean FEV1 83%), treated with an ICS/LABA combination, were included. The lung deposition characteristics of an HFA-based pMDI (MMAD ~3.0 µm; fine particle fraction (FPF) ~40%) were assessed using FRI. Simulations were performed on 3 different inhalation profiles matched for the same inspiratory volume (3 L) with durations of 1s, 3s and 5s and actuation at start of inhalation.

Results For the 1s, 3s and 5s profiles, the TLD values were 22.81 ± 3.71%, 36.13 ± 2.51% and 41.61 ± 3.11% of nominal dose respectively, and were predicted using a concave down quadratic model (R2 = 0.87, p < 0.001). The central to peripheral deposition ratios were 1.58, 0.81 and 0.57 respectively.

Conclusions A 5 s inhalation led to highest TLD with greatest peripheral deposition. Increased deposition with longer times mainly reflected increased peripheral deposition, central deposition was less affected by flow rate. These data support ERS/ISAM guidance for inhaling over 4–5 sec to optimise deposition, although similar TLD were achieved with 3s. These data also suggest that high FPF pMDIs can achieve reasonable deposition even with short, fast inhalations.

REFERENCES

1 Laube BL, et al. ERS 2011;37(6):1308-417

**P239** EFFECT OF INHALED CORTICOSTEROID (ICS) PARTICLE SIZE ON ASTHMA EFFICACY AND SAFETY OUTCOMES: A SYSTEMATIC LITERATURE REVIEW

*E Suarez, S Fang, J Abraham, RL DiSantostefano, DA Stempel, LF Frith, NC Barnes.*

New England Research Institutes, Inc., Watertown, MA, USA; GlaxoSmithKline, Uxbridge, UK.

10.1136/thoraxjnl-2014-206260.368

Introduction and objectives ICS of differing particle size, due both to the formulation and propellant, may impact patient outcomes. This systematic review of randomised controlled trials compared asthma efficacy and safety outcomes from the use of fluticasone propionate (FP)-containing medications and alternative smaller particle ICS.

Methods English language published peer-reviewed literature (Jan 1, 1998-Feb 13, 2014) with FP-containing medications, yielded 1,655 potentially-relevant articles: 1,575 were excluded, 80 full-text articles were reviewed, and 25 were extracted for data with treatment comparisons (FP- vs. small particle ICS-containing medicines). Efficacy measures included lung function, asthma exacerbations, and rescue medication use. Safety endpoints included adverse events, growth and bone measures, and cortisol. Benefit-risk interval plots of risk differences with 95% confidence intervals were produced for FP vs. comparators.

Results Ten controlled trials compared the efficacy of FP with beclomethasone dipropionate (BDP-HFA). Six studies found no appreciable differences in efficacy while four trials identified improvement in lung function with FP vs. BDP-HFA. Ten randomised trials comparing the efficacy of ciclesonide (CIC) with FP. CIC was found to be non-inferior or not statistically different from FP on numerous efficacy endpoints in the majority of the studies. Most safety assessments across nine trials did not differ between treatments. Results were similar for fixed dose combination therapies that contained FP and BDP-HFA (n = 3 trials).

Conclusions This systematic review suggests no differences in efficacy or safety between FP-containing medications and small particle size ICS medications for the treatment of asthma.

(GSK-funded, LS2270)

**P240** SMARTINHALERS – A NEW APPROACH TO ASSESSING ADHERENCE IN DIFFICULT ASTHMA


10.1136/thoraxjnl-2014-206260.369

**Introduction** Poor adherence is one of the key determinants of sub-optimal asthma control in children. Correctly identifying children with poor adherence can avoid unnecessary escalation of treatment and enable a targeted adherence intervention.

**Objective** To use electronic monitoring devices (Smartinhalers) to measure adherence to inhaled corticosteroids (ICS) in children with problematic severe asthma (PSA) and compare the data with prescription uptake and symptoms during the monitoring period.

**Methods** Smartinhalers were issued to patients for a 6–8 week study period as part of an established nurse led assessment in a tertiary referral centre. Advice regarding adherence and the purpose of the Smartinhalers was explained to all children and their parents. Lung function, bronchodilator reversibility, exhaled nitric oxide (FENO), mini paediatric asthma quality of life questionnaire (mPAQLQ), and asthma control test (ACT) were recorded at baseline and follow up. Wilcoxon signed ranks was used to compare visit 1 and visit 2 data. GP prescription uptake for ICS and number of salbutamol canisters issued in past year were obtained.

**Results** 33 children (21 male), median age 13 (5–17) years were issued with Smartinhalers. 15 had adherence >80%, 14 between 50–80% and 4 < 50%. ACT and mPAQLQ improved significantly over the monitoring period (Figures 1 and 2). Children with a prescription uptake of <80% had a significant improvement in ACT compared to those with pick up of ≥80% (median change 3.5 (IQR 0.75–7.25) vs 0 (4–3)) and a non-significant trend towards improvements in FEV1 and BDR.

**Conclusion** Even when children know they are being monitored over half used <80% of the prescribed dose. Improvements in objective markers of asthma control during the monitoring period can help to identify those who were previously poorly adherent. Smartinhalers are useful tools in the assessment of adherence in conjunction with GP prescriptions and clinical observations.
cough and 10 = worst cough) significantly improved from a baseline mean of 7.3 (SD=1.9) to 2.6 (SD=3) at 3 months and 3.9 (SD=3.1) long term (Figure 1). In the asthma group we also observed an improvement in the mean HRCQ (0 = no reflux, 70 = worst reflux) from 49.2 (SD 13.8) at baseline to 22 (SD 13.9) long-term, without corresponding improvement in FEV1.

**Conclusion** Anti-reflux surgery provides sustainable long-term benefit to patients with significant GORD and poorly controlled asthma or chronic cough. These data require further confirmation in controlled trials.

**Transplantation advances**

**P242 PIRFENIDONE AS A BRIDGE TO LUNG TRANSPLANTATION IN PATIENTS WITH PROGRESSIVE IPF**

P Riddell, P Minnis, P Ging, JJ Egan. Mater Misericordiae University Hospital, Dublin, Ireland

10.1136/thoraxjnl-2014-206260.371

**Introduction and objectives** Lung transplantation provides a significant survival benefit to patients with advanced idiopathic pulmonary fibrosis (IPF). However, at this time, the transplant community is unable to meet the requirements on it services due to donor organ shortages. This results in an increased length of time spent on the waiting list and an increased risk of death prior to transplantation.

Pirfenidone has been reported to reduce the rate of disease progression in patients with IPF. It may therefore prolong the length of time that patients are able to spend on the transplant waiting list and an increased risk of death prior to transplantation.

Pirfenidone has been reported to reduce disease progression in IPF. However, at this time, the transplant community is unable to meet the requirements on it services due to donor organ shortages. This results in an increased length of time spent on the waiting list and an increased risk of death prior to transplantation.

**Methods** We retrospectively reviewed the medical records of all patients who had undergone lung transplantation for IPF from 2012–14 at our institution. Three patients who had been prescribed Pirfenidone prior to transplantation were identified. Each patient continued Pirfenidone until the day of transplantation. Patient demographics, lung function and post transplant data were collated.

**Results** Prior to the commencement of Pirfenidone the mean decline in forced vital capacity (FVC) was 52.2ml per month. Following Pirfenidone therapy, the mean decline in FVC was 29.2ml per month. The mean length of time from commencing Pirfenidone to transplantation was 419 days (range 190–768 days). The mean length of time spent on the transplant waiting list was 144 days (range 35–271 days).

With a mean follow up of 1.45 years, no episodes of acute or chronic rejection have occurred. Post-transplant survival is 100%. No adjustment in immunosuppressant induction or post-transplant therapy was necessitated. In the post-transplant period, Pirfenidone therapy was not linked to any adverse events.

**Conclusion** Pirfenidone has been reported to reduce disease progression in IPF. However, despite this, lung transplantation remains necessary in the management of this condition. For patients with IPF, in whom the transplant window is short, Pirfenidone may allow for valuable added time on the lung transplant waiting list.

**P243 A RETROSPECTIVE OBSERVATIONAL STUDY OF 20 YEAR LUNG TRANSPLANT SURVIVORS – A SINGLE CENTRE EXPERIENCE**

S Sithamparanathan, L Thirugnanasothy, AJ Fisher, J Lordan, G Meachery, JH Dark, A Hasan, SC Clark, K Gould, GA MacGowan, G Parry, PA Corris. Cardiopulmonary Transplantation, Institute of Transplantation, Freeman Hospital, Newcastle Upon Tyne, UK; Institute of Cellular Medicine, Newcastle University; Cardiopulmonary Transplantation, Institute of Transplantation, Freeman Hospital, Newcastle Upon Tyne, UK; Department of Paediatric Cardiac Surgery, Freeman Hospital, Newcastle Upon Tyne, UK; Institute of Genetic Medicine, Newcastle University, Newcastle Upon Tyne, UK; Departments of Cardiothoracic Surgery and Cardiopulmonary Transplantation, Freeman Hospital, Newcastle Upon Tyne, UK

10.1136/thoraxjnl-2014-206260.372

**Introduction and objectives** Lung transplant patients have a reduced survival rate compared to other solid organ recipients. Chronic lung allograft dysfunction (CLAD) remains the main factor in limiting longevity in lung transplant patients, with 50% of recipients developing Bronchiolitis Obliterans Syndrome (BOS) by 5.6 years. There is a lack of published data on the
CHARACTERISTICS AND OUTCOMES IN LUNG TRANSPLANT RECIPIENTS AGED 65 AND OVER

S Isse, R Hackett, D Thomas, P Catarino, S Tsui, JS Parmar. Papworth Hospital NHS Foundation Trust, Cambridge, UK

10.1136/thoraxjnl-2014-206260.373

Abstracts P244 Figure 1 Survival Functions

The indication for transplantation was COPD and IPF in all. The cause of death was BOS in 9/14, malignancy in 2/14 and pulmonary embolism, stroke and bleeding in the others. When compared with 50 single lung transplant recipients aged 60–64, we did not find any statistically significant differences in survival (p value 0.138) (see figure 1), cause of death and reason for transplantation.

P245 EVALUATION OF OUTCOMES OF ORAL RIBAVIRIN IN THE TREATMENT OF VIRAL LOWER RESPIRATORY TRACT INFECTION IN LUNG TRANSPLANT PATIENTS

RJ Hackett, S Isse, J Parmar, D Thomas. Papworth Hospital, Cambridge, UK

10.1136/thoraxjnl-2014-206260.374

Introduction Viral lower respiratory tract infections are common in lung transplant patients and contribute to the development of chronic rejection. Studies have highlighted the improvement in lung function and reduction in relative risk of chronic rejection in patients who are treated with appropriate anti-virals. Our study aimed to investigate the efficacy of three different routes of administration in patients with symptomatic declines in lung function and positive viral cultures.

Method Retrospective cohort study of viral respiratory tract infections treated with Ribavirin over a 5 year period was performed. Patients were divided in to 3 groups dependent on route of administration – Oral, Nebulised or Intravenous. Data was collected on patient demographics along with the indication for transplant, time since transplantation, pre and post treatment (6–8 weeks) lung function, viral cultures and details of any confounding factors such as prior rejection or concomitant bacterial infection were recorded.
Introduction and objectives Lung transplantation significantly improves the survival of patients with advanced idiopathic pulmonary fibrosis (IPF). Concurrent coronary artery disease (CAD) is a relative contraindication to transplantation and can limit access to this therapy. This is particularly relevant as it implies a high prevalence of CAD has been reported in patients with IPF.1 We sought to determine whether the presence of asymptomatic CAD impacted upon post-transplant survival.

Methods This retrospective study reviewed all patients who had undergone single lung transplantation for IPF at our centre, between May 2005 to April 2014. We compared post-surgical outcomes for patients with IPF who had an abnormal coronary angiogram (at the time of transplant listing), to those with normal angiography. Kaplan-Meier curves were created to study survival and univarate analysis performed using the Log-Rank score.

Results In this timeframe, 39 patients underwent lung transplantation for IPF, of which 22 patients (56.4%) had abnormal coronary angiography. Eight of these patients had minor disease, 5 had 10–30% stenosis and 5 had 30–50% stenosis. One patient required coronary artery stenting prior to transplantation, but 3 patients with ≥70% stenosis had no inducible ischaemia on dobutamine stress testing and were managed conservatively. All patients had normal pre-operative left ventricular function.

The post-transplant survival of patients with IPF and CAD was 95.7% at 1 year and 70.1% at 5 years. There was no significant difference in survival (p = 0.32) between the cohort with CAD and those with normal pre-operative coronary angiograms. Of note, 1 patient required coronary artery stenting 18 months after transplantation (this patient had 30% LAD stenosis at time of listing). No patients developed chronic arrhythmias, and no patients died as a result of cardiovascular disease.

Conclusion Although CAD remains a relative contraindication to transplantation, the effects of previous PCI or minor CAD are unknown and may be overstated. This finding is particularly relevant for patients with IPF, who may have an increased prevalence of CAD.

REFERENCE

Poster sessions

Abstract P245 Table 1

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<th>Nebulised Ribavirin</th>
<th>Intravenous Ribavirin</th>
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<tr>
<td>n</td>
<td>11</td>
<td>13</td>
<td>10</td>
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<tr>
<td>Mean Age</td>
<td>52</td>
<td>48</td>
<td>47</td>
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<tr>
<td>Type of transplant</td>
<td>4 Bilateral Lung, 4 Single Lung, 3 Heart Lung</td>
<td>9 Bilateral Lung, 1 Single Lung, 3 Heart Lung</td>
<td>7 Bilateral Lung, 1 Single Lung, 2 Heart Lung</td>
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<tr>
<td>Gender</td>
<td>7M 4F</td>
<td>7M 6F</td>
<td>5M SF</td>
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<tr>
<td>Mean time since Transplantation (months)</td>
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<td>24.4</td>
<td>54.4</td>
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<tr>
<td>Percentage change in FEV1±SD</td>
<td>96.4% ± 9.9</td>
<td>92.8±14.9</td>
<td>93.7±10.5</td>
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<tr>
<td>95% Confidence interval</td>
<td>5.84 (90.656/102.24)</td>
<td>8.11 (84.769/100.991)</td>
<td>6.50(86.899/89.8)</td>
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</tbody>
</table>

Abstract P246

Lung Transplantation for Patients with Idiopathic Pulmonary Fibrosis and Asymptomatic Coronary Artery Disease

P Riddell, K Redmond, D Eaton, L Nolke, SH Javadpour, D Healy, J McCarthy, JJ Egan. Mater Misericordiae University Hospital, Dublin, Ireland

10.1136/thoraxjnl-2014-206260.375

Introduction and objectives Lung transplantation significantly improves the survival of patients with advanced idiopathic pulmonary fibrosis (IPF). Concurrent coronary artery disease (CAD) is a relative contraindication to transplantation and can limit access to this therapy. This is particularly relevant as it implies a high prevalence of CAD has been reported in patients with IPF.1 We sought to determine whether the presence of asymptomatic CAD impacted upon post-transplant survival.

Methods This retrospective study reviewed all patients who had undergone single lung transplantation for IPF at our centre, between May 2005 to April 2014. We compared post-surgical outcomes for patients with IPF who had an abnormal coronary angiogram (at the time of transplant listing), to those with normal angiography. Kaplan-Meier curves were created to study survival and univarate analysis performed using the Log-Rank score.

Results In this timeframe, 39 patients underwent lung transplantation for IPF, of which 22 patients (56.4%) had abnormal coronary angiography. Eight of these patients had minor disease, 5 had 10–30% stenosis and 5 had 30–50% stenosis. One patient required coronary artery stenting prior to transplantation, but 3 patients with ≥70% stenosis had no inducible ischaemia on dobutamine stress testing and were managed conservatively. All patients had normal pre-operative left ventricular function.

The post-transplant survival of patients with IPF and CAD was 95.7% at 1 year and 70.1% at 5 years. There was no significant difference in survival (p = 0.32) between the cohort with CAD and those with normal pre-operative coronary angiograms.

Of note, 1 patient required coronary artery stenting 18 months after transplantation (this patient had 30% LAD stenosis at time of listing). No patients developed chronic arrhythmias, and no patients died as a result of cardiovascular disease.

Conclusion Although CAD remains a relative contraindication to transplantation, the effects of previous PCI or minor CAD are unknown and may be overstated. This finding is particularly relevant for patients with IPF, who may have an increased prevalence of CAD.

REFERENCE

Abstract P247 Table 1

<table>
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<tr>
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<th>Biodegradable stents</th>
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<td>Mean of bronchoscopes after stent insertion</td>
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<tr>
<td>Difference in FEV1</td>
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<td>Mean follow up after stent insertion (months)</td>
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<td>Mean survival after transplantation (months)</td>
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<td>54.7</td>
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</tbody>
</table>

Abstract P247

Management of Airway Stenosis and Bronchomalacia with Biodegradable Stents after Lung Transplantation. Single Institution Experience

P247

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10.1136/thoraxjnl-2014-206260.376

Introduction Although the rate of airway stenosis following lung transplantation (LT) has reduced dramatically, it is still a significant cause of morbidity and mortality. Traditional self expanding metallic stents (SEMS) carry a high risk of bleeding and hyperplastic granulation tissue formation. Biodegradable stents (BS) present a potential alternative approach that could reduce these complications, though little is currently known about their effectiveness and safety.

Methods A retrospective analysis of our institutions use of 7 BS (polidioxanone) placed in 6 patients who presented bronchial stenoses after LT between December 2011 and January 2013. 2 patients with single (1 right and 1 left) and 4 with bilateral LT. The indications for placing the stents were anastomotic bronchomalacia in 3 cases and bronchial stenoses in 4. The outcomes from these stents were compared with the last 10 patients who have SEMS.

Results Re-stenoses recurred in 3 cases, after 10, 6 and 4 months respectively; 2 responded to balloon dilatation and cryotherapy but 1 patient needed repeat stenting for restenosis. Stent migration occurred in 2 cases. No bleeding was reported. One patient died of obliterative bronchiolitis. The mean increase in FEV1 following treatment was a 312ml increase. Patients were treated with Oral medication, 13 with Nebulised and 10 with Intravenous.
Improving patient therapies in COPD

**CURRENT COPD DISEASE BURDEN ASSOCIATED WITH MAINTENANCE MONOTHERAPY IN THE UK**

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Introduction and objectives National Institute for Health and Care Excellence (NICE) recommends long-acting bronchodilators, including β2-agonists (LABAs) or muscarinic antagonists (LAMAs) as first line maintenance treatment for patients with COPD. The aim of this descriptive study was to characterise a cohort of COPD patients who were on maintenance bronchodilator monotherapy for at least six months to establish their disease burden, measured by healthcare utilisation.

Methods Data were extracted from the UK Clinical Practice Research Datalink (CPRD) which also linked to Hospital Episode Statistics (HES). The monotherapy period spanned the first prescription of a LABA or LAMA until the end of the study period (31/12/2013) or until step-up to dual/triple therapy; for example the addition of another long acting bronchodilator, an ICS or ICS/LABA. A minimum of four consecutive prescriptions and six months on continuous monotherapy were required for study entry. Patients <50 years old at time of first COPD diagnosis or with another significant respiratory disease prior to the start of monotherapy were excluded. Disease burden was evaluated by measuring patients’ rate of consultations with a healthcare professional (HCP), COPD-related exacerbations, hospitalisations and referrals to key specialities.

Results A cohort of 8,811 COPD patients (94% GOLD stage A or B) on maintenance monotherapy was identified between 2002 and 2013; 45% (N=3,947) of these patients were still on monotherapy by the end of the study period. The median time from first COPD diagnosis to first monotherapy prescription was 56 days while the median time on maintenance bronchodilator monotherapy was 748 days. The median number of prescriptions during this period was 14. Patients had a median of 19 HCP consultations and a mean of 0.1 (95% CI 0.1, 0.2, N=8,811) COPD exacerbations and 0.02 (95% CI 0.01, 0.02, N=4,848) COPD hospitalisations per year.

Conclusion In summary, COPD patients who are on maintenance bronchodilator monotherapy for at least six months appear to remain on this therapy for over two years despite having a disease burden that requires healthcare resources, particularly HCP consultations, at a cost to the NHS.

**EFFECT SIZE OF OPEN-LABEL VERSUS DOUBLE-BLIND ADMINISTRATION OF TIOTROPIUM IN TRIALS INVESTIGATING HEALTH-RELATED QUALITY OF LIFE IN COPD**

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Introduction Effects of interventions on patient-reported outcomes may be subjective and moderated by patients’ expectations regarding treatment efficacy. The ‘gold standard’ for minimising such biases are double-blind randomised controlled trials. We analysed the effects of tiotropium on health-related quality of life in chronic obstructive pulmonary disease (COPD) in placebo-controlled trials and assessed whether trial design (double-blind versus open-label) is a relevant modifier of the effects of tiotropium.

Methods Trials of ≥6 months’ duration investigating the effect of tiotropium versus placebo on health-related quality of life in COPD (assessed using St George’s Respiratory Questionnaire [SGRQ]) were identified from the Boehringer Ingelheim clinical trial database and by a systematic literature search in MEDLINE, with a cut-off date of 30 November 2011. As a clinical end point, the mean difference between treatment groups in SGRQ total score was assessed. Trials were grouped according to double-blind or open-label design. We performed a network meta-analysis including standard methodology to test for interaction to evaluate whether trial design is a potential modifier of effect size or its direction.

Results We identified 12 trials in which tiotropium had been administered double-blind and three trials with open-label application. The overall effect for mean difference versus placebo in SGRQ total score was -2.98 units (95% confidence interval [CI]: -3.49, -2.47). For the double-blind trial subgroup, mean difference versus placebo was -3.20 (95% CI: -3.75, -2.65) compared to -1.67 (95% CI: -3.02, -0.32) for open-label trials. The p-value for interaction between subgroup and effect on SGRQ total score was 0.04.

Conclusions In patients with COPD, trial design (double-blind versus open-label) was a statistically significant modifier of the effect of inhaled tiotropium on health-related quality of life. The modification was quantitative, resulting in a substantial underestimation of the effect of tiotropium on SGRQ total score when the administration had been open-label compared to the ‘gold standard’ double-blind. A subjective end point such as quality of life is particularly susceptible to bias due to patients’ expectations towards the efficacy of an intervention. Therefore, the validity of studies using non-blind designs to investigate such end points must be questioned.
Background Both tiotropium (T) and olodaterol (O) monotherapies improve exercise endurance in patients with chronic obstructive pulmonary disease (COPD).

Objective To evaluate the effects of T+O fixed-dose combination on exercise endurance in patients with Global initiative for Chronic Obstructive Lung Disease (GOLD) 2–3 COPD after 12 weeks.

Methods TORRACTO (NCT01525615) was a 12-week, double-blind, parallel-group, placebo-controlled, Phase III study. Patients with GOLD 2–3 COPD received T+O fixed-dose combination of indacaterol acetate and mometasone furoate via the Breezhaler® device for once daily maintenance treatment of asthma and COPD. This double-blind, 12-week study compared QMF149 (150/160µg) o.d. with salmeterol 50µg/fluticasone 500µg, (Serevent®; SFC) b.i.d. in patients with moderate to very severe COPD.

Objectives Primary objective of the study was to demonstrate the non-inferiority of QMF149 vs SFC in terms of trough FEV₁ at Week 12. Main secondary objectives were to compare the efficacy of QMF149 vs SFC in terms of dyspnoea via Transition Dyspnoea Index (TDI), health status via St. George Respiratory Questionnaire (SGRQ), rescue medication, exacerbations and safety during the treatment period.

Results 629 patients (mean FEV₁, 46.51% predicted) were randomised. The primary objective was met. QMF149 showed significant improvement in trough FEV₁ vs SFC (LSM treatment difference [LSMTD] 56mL; p < 0.001). QMF149 improved significantly TDI (LSMTD 0.5; p < 0.026) and numerically SGRQ (-1.66, p = 0.093) vs SFC. QMF149 significantly prolonged the time to first moderate or severe exacerbation with a 49% reduction in hazard ratio (hazard ratio [HR] 0.51; CI 0.298, 0.855; p = 0.011) and was associated with 44% reduction in the number of moderate or severe exacerbations (rate ratio [RR] 0.56; CI 0.331, 0.937; p = 0.028). A significantly greater percentage of days with no rescue medication (LSMTD 6.26%; p = 0.007) and significantly fewer rescue medication use was observed with QMF149 (daily number of puffs LSMTD -0.47; p = 0.003). Both treatments were well tolerated with low incidence of AEs.

Conclusion When compared with SFC, QMF149 significantly improves trough FEV₁ and dyspnoea, reduces exacerbations and rescue medication use in patients with moderate to very severe COPD.
care and office based chest medicine clinics. A convenience sample of 500 was selected.

Results We report the characteristics of the first 250 COPD patients from our ongoing 500 patient survey.

Basic demographics 55% Male, 45% Female. Mean age patients 68 ± 12 yrs, all patients were previous smokers with 56 ± 10 pkt/yr smoking history. 34% remain current smokers.

Mean FEV1 48% ± 10%, Mean FEV1/FVC ratio 49% ± 10. Median mMRC dyspnea score 2. Mean CAT score 18 ± 10 (Range 0–38).

GOLD Stage Classification 13% GOLD Stage A, 67% GOLD Stage B, 1% GOLD Stage C and 19% GOLD Stage D.

Current treatment LAMA (long-acting muscarinic antagonist) was prescribed to over 90% of all patients in groups B, C and D whereas monotherapy with LABA (long acting beta-agonist) or dual bronchodilatation with LABA/LAMA therapy was prescribed to less than 5%.

There was significant overtreatment with ICS/LABA in all categories with high dose ICS (inhaled corticosteroid) being preferred. 20% of patients in GOLD Stage A where receiving Triple therapy (LAMA + ICS/LABA) and a further 20% where receiving monotherapy with ICS/LABA, yet had no history of exacerbations.

30% of patients in GOLD Stage B where receiving Triple therapy (LAMA + ICS/LABA) yet had no history of exacerbations.

Conclusion Current Canadian Guidelines and the GOLD strategy focus on symptom relief and striving to prevent exacerbations with step-wise prescription of short and long-acting bronchodilators with individual or combinations of LAMA, LABA, LAMA/LABA or ICS/LABA inhalers. Patients in GOLD Group C are rare. Current prescription choices in our survey does not reflect current evidence or guidelines. We report a heavy reliance on ICS/LABA along with over prescription of triple therapy at all stages of disease.

P254 ONCE-DAILY TIOTROPIUM AND OLODATEROL FIXED-DOSE COMBINATION VIA THE RESPIMAT® IMPROVES OUTCOMES VERSUS MONO-COMPONENTS IN COPD IN TWO 1-YEAR STUDIES

R Buhl, E Derom, G Ferguson, E Pizzichini, I Reid, H Watz, G Gröcke, A Hamilton, K Tetzlaff, I Korducki, H Husman, W Sibbering, F Maltais. Pulmonary Department, Mainz University Hospital, Mainz, Germany; Ghent University Hospital, Ghent, Belgium; Pulmonary Research Institute of Northeast Ohio, Cleveland, USA; Boehringer Ingelheim Pharma GmBH and Co, KG, Ingelheim, Germany; Boehringer Ingelheim, Burlington, Ontario, Canada; Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, Connecticut, USA; Boehringer Ingelheim B. V., Alkmaar, The Netherlands; 11Centre de Recherche, Institut Universitaire de Cardiologie Et de Pneumologie de Québec, Québec, Canada

Introduction Tiotropium (T), a once-daily long-acting muscarinic antagonist, is a well-established first-line maintenance treatment in chronic obstructive pulmonary disease (COPD); olodaterol (O) is a once-daily long-acting β2-agonist that has recently gained approval in several countries. Two Phase III replicate pivotal studies assessed the efficacy and safety of fixed-dose combinations of T and O (T+O) delivered via Respimat® Soft Mist® inhaler in patients with GOLD 2–4 COPD.

Methods Two 52-week, double-blind, parallel-group studies randomised 5162 patients to O 5 µg, T 2.5 µg, T 5 µg, T+O 2.5/5 µg or T+O 5/5 µg. Primary efficacy end points were trough forced expiratory volume in 1 second (FEV1) response (ie change from baseline), FEV1 area under the curve from 0–3 h and St George’s Respiratory Questionnaire (SGRQ) total score after 24 weeks. Pooled data from the two studies are presented here; lung function from the individual studies will subsequently be provided.

Results A total of two articles met the end criteria. Outcome shows improvement in exercise time (treadmill test) at 95% CI, with statistically significant benefit with mean difference of 335.18 [253.93, 416.43] favouring Pravastatin group. The studies show inconclusive results for Pravastatin in improving FEV1 (%) with 95% CI with mean difference of 0.05 [-4.61, 4.7]. The outcome in total lung capacity shows inconclusive results but shows a trend toward benefit with 95% CI with mean difference of -0.08 [-0.46, 0.30]. Inspiratory capacity results at 95% CI with mean difference of 0.13 [-0.06, 0.32] showed an inconclusive outcome but has a trend toward benefit. Improvement in the Borg dyspnea score at 95% CI, showing statistically significant benefit with mean difference of -2.91 [-3.19, -2.63] favouring the Pravastatin group.

Conclusions Statins already have an established role in treating cardiovascular patients because of their cholesterol-lowering ability, but also have anti-inflammatory and immunomodulatory effects that are beneficial in airway inflammation in COPD. Statin administration to COPD patients showed amelioration in exercise tolerance, improvement in dyspnea scores and augmentation in pulmonary function indices. Thus, statins may be useful as adjuvant to currently available therapies as well as improvement in lipid status.
Once-daily tiotropium Respimat® add-on to at least ICS maintenance therapy reduces exacerbation risk in patients with uncontrolled symptomatic asthma

Background A reduction in asthma exacerbation risk may provide improvements in clinical burden, patient experience and healthcare costs. In Phase III trials, once-daily tiotropium (delivered via the Respimat® SoftMist™ inhaler) added on to at least inhaled corticosteroids (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 as add-on to at least ICS maintenance therapy (Table). 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 forced expiratory volume in 1 second, seven-question Asthma Control Questionnaire score and ICS dose (μg) were: 56.0 ± 13.1, 2.6 ± 0.7, 1198 ± 539 (PrimoTinA-asthma®); 75.1 ± 11.5, 2.2 ± 0.5, 660 ± 213 (MezzoTinA-asthma®); 77.7 ± 11.9, 2.1 ± 0.4, 381 ± 78 (GraziaTinA-asthma®). Tiotropium Respimat® 5 μg and provided symptomatic benefit over O 5 μg and T 5 μg, differences between T+O 5/5 μg and O 5 μg and T 5 μg were statistically significant (p < 0.05).

Conclusions T+O 5/5 μg significantly improved lung function and provided symptomatic benefit over O 5 μg and T 5 μg.

Conclusion Once-daily tiotropium Respimat® 5 μg add-on to at least ICS maintenance therapy consistently reduced exacerbations across asthma severities and may be a beneficial add-on option to reduce current and future exacerbation risk.

Abstract P255 Table 1

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<td></td>
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<tr>
<td>PrimoTinA-asthma® (≥800 μg budesonide or equivalent)</td>
<td>122/453</td>
<td>1198/454 (32.8)</td>
<td>0.78</td>
<td>0.034</td>
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<tr>
<td>(T+O)</td>
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<tr>
<td>MezzoTinA-asthma® (ICS 400–800 μg)</td>
<td>31/513</td>
<td>43/518</td>
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Abstract P256 Table 1

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<td>5 μg</td>
</tr>
<tr>
<td>T+O 2.5/5 μg</td>
</tr>
<tr>
<td>T+O 5/5 μg</td>
</tr>
</tbody>
</table>

| n = 1038 | n = 1032 | n = 1033 | n = 1030 | n = 1029 |

| Total AEs   | 76.6 | 73.4 | 73.3 | 74.7 | 74.0 |
| Serious AEs | 17.4 | 15.1 | 16.7 | 16.3 | 16.4 |
| Fatal AEs   | 1.2  | 1.2  | 1.6  | 1.4  | 1.7  |
| Cardiac disorders* | 5.7 | 5.8 | 5.3 | 5.8 | 4.5 |
| Respiratory, thoracic and mediastinal disorders* | 43.5 | 43.9 | 42.7 | 38.2 | 39.4 |

*MedDRA SOC
Conclusions T+O FDCs were safe and well tolerated. In comparison to the individual components, there was no notable increase in AEs with T+O FDCs.

**Poster sessions**

**P257**

**SUB-OPTIMAL INHALER TECHNIQUE IN PATIENTS AGED OVER 75 YEARS**

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10.1136/thoraxjnl-2014-206260.386

Introduction and objectives NICE guidelines highlight the importance of adequate inhaler technique to ensure sufficient drug delivery in asthma and C. O. P. D. Whilst adequate inhaler technique can be a problem for patients of any age, the delivery of inhaled medication continues to be a particular problem for elderly patients. Despite the existence of pressurised metered-dose inhalers and breath-actuated inhalers, physical and cognitive impairment continues to make the use of hand-held inhalers difficult in the elderly. It is therefore likely that inhaler use in the elderly is suboptimal, regardless of device used.

Methods We assessed 50 consecutive patients aged over 75 years with C. O. P. D or asthma at our centre (mean age 78.24 ± 7.32). All had inhaler therapy prescribed prior to examination. Two observers assessed inhaler technique against guidelines adapted from the National Asthma Council of Australia1 (see Table). Patients used either an Evohaler (pressurised metered-dose inhaler) or Accuhaler (breath-actuated inhaler) according to their choice.

Results In the Evohaler group (25 patients), the average age was 78 (±5.5) with an average score of 6.6 (±1.81) / 10. In the Accuhaler group (23 patients), average age was 77 (±6.4) with an average score of 7.2 (±2.0) /10. ‘Crucial’ steps to adequate inhaler technique were also assessed.2 The score in the Evohaler group was 4.4 (±1.2) /6, and in the Accuhaler group was 4.3 (±1.0) /6.

Conclusion This study shows that despite the availability of both Evohaler (pressurised metered-dose inhaler) and Accuhaler (breath-actuated inhaler) effective use by the elderly is still suboptimal. The very elderly need extra support when considering and prescribing inhalers. Whilst many centres have ‘good inhaler technique’ as a pillar of their COPD care bundle, it may be the case that specialist services, including the use of specialist devices, directed at the elderly may help to alleviate the problems of physical and cognitive impairment when using inhalers.

Abstract P257 Table 1

<table>
<thead>
<tr>
<th>Step</th>
<th>EVOHALER</th>
<th>ACCUHALER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Remove cap</td>
<td>Open using thumb grip</td>
</tr>
<tr>
<td>2</td>
<td>Hold inhaler upright and shake</td>
<td>Load dose by sliding lever until it clicks</td>
</tr>
<tr>
<td>3</td>
<td>Breathe out</td>
<td>Breathe out</td>
</tr>
<tr>
<td>4</td>
<td>Put mouthpiece between lips, close lips to form seal</td>
<td>Put mouthpiece between lips, close lips to form seal</td>
</tr>
<tr>
<td>5</td>
<td>Breathe in and press down</td>
<td>Breathe in steadily</td>
</tr>
<tr>
<td>6</td>
<td>Continue to breathe in</td>
<td>Continue to breathe in</td>
</tr>
<tr>
<td>7</td>
<td>Hold breath 10 secs</td>
<td>Hold breath 10 secs</td>
</tr>
<tr>
<td>8</td>
<td>Remove inhaler</td>
<td>Remove inhaler</td>
</tr>
<tr>
<td>9</td>
<td>Breathe out</td>
<td>Breathe out</td>
</tr>
<tr>
<td>10</td>
<td>Replace cap</td>
<td>Close cover</td>
</tr>
</tbody>
</table>

**REFERENCES**

1 National Asthma Council Australia. Inhaler technique in adults with asthma or COPD. Melbourne: National Asthma Council Australia, 2008

**P258**

**THE 24-HOUR LUNG FUNCTION PROFILE OF ONCE-DAILY TIOTROPIUM AND OLODATEROL FIXED-DOSE COMBINATION COMPARED WITH PLACEBO AND MONOTHERAPIES IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE**

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10.1136/thoraxjnl-2014-206260.387

Introduction Tiotropium (T), a once-daily long-acting muscarinic antagonist, is a well-established first-line maintenance treatment in chronic obstructive pulmonary disease (COPD). Olodaterol (O) is a once-daily long-acting β2-agonist, recently approved in several EU countries. This study investigated the 24-hour bronchodilator profile of once-daily fixed-dose combinations (FDCs) of T and O delivered via the Respimat® Soft Mist™ inhaler in patients with Global initiative for chronic Obstructive Lung Disease 2–4 COPD.

Methods This double-blind, placebo-controlled, Phase III, incomplete crossover study randomised 219 patients to receive four of the following treatments for 6 weeks (with a 3-week washout period in between): placebo, O 5 μg, T 2.5 μg, T 5 μg, T+O FDC 2.5/5 μg, T+O FDC 5/5 μg. The primary end point was forced expiratory volume in 1 second (FEV1) area under the curve from 0–24 h (AUC0–24) after 6 weeks. Secondary end points included additional spirometric parameters over 24 h and body plethysmography parameters in a sub-set of patients (2:30 and 22:30 h post-dose).

Results The 24-hour time profiles for both FDCs were similar, with clear, consistent increases in FEV1 compared to placebo and monotherapies. For FEV1 AUC0–24, both FDCs were significantly superior to placebo (T+O 5/5 μg: 0.280 L, p < 0.0001; T+O 2.5/5 μg: 0.277 L, p < 0.0001) and monotherapies (T+O 5/5 μg: 0.110–0.127 L, p < 0.0001; T+O 2.5/5 μg: 0.107–0.124 L, p < 0.0001). There were significantly greater increases in trough FEV1 with both FDCs compared to placebo (0.201–0.207 L, p < 0.0001) and monotherapies (T+O 5/5 μg: 0.079–0.107 L, p < 0.0001; T+O 2.5/5 μg: 0.073–0.101 L, p < 0.0001). In the body plethysmography sub-study, both FDC doses separated from

Abstract P258 Figure 1 Adjusted mean Fev1 over 24 h post dose after 6 weeks of treatment (full analysis set)
Tiotropium treatment, given via HandiHaler® or Respimat®, in patients with COPD.

Conclusions The results from this safety review do not indicate an increased overall risk for fatal or cardiovascular events during tiotropium treatment, given via HandiHaler® or Respimat®, in patients with COPD.

P259  Tiotropium HandiHaler® and Respimat® in COPD: A Safety Analysis on Pooled Data

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Rationale: Tiotropium has been approved and marketed via HandiHaler® (18 μg once daily [qd]) since 2002 and via Respimat® (5 μg qd) since 2007. The recent TIOSPIR™ (TIOtropium Safety and Performance In Respimat) study demonstrated that both products had comparable safety profiles; the objective of this analysis was to provide an updated safety evaluation of tiotropium in both formulations.

Methods Analysis of pooled adverse events (AEs) from randomised, double-blind, parallel-group, placebo-controlled clinical trials of ≥4 weeks’ duration where either tiotropium HandiHaler® 18 μg or tiotropium Respimat® 5 μg was indicated for chronic obstructive pulmonary disease (COPD). Rate ratios (RRs), incidence rates (IRs) and 95% confidence intervals (CIs) were determined for HandiHaler® and Respimat® trials together and separately.

Results This analysis of 28 HandiHaler® and seven Respimat® studies provided 14,909 (12,469 and 2440 with HandiHaler® and Respimat®, respectively) patient-years’ exposure to tiotropium. Mean age was 65 years and mean forced expiratory volume in 1 second was 1.16 L (41% predicted). The risk (RR [95% CI]) of AEs (0.90 [0.87, 0.93]) and serious AEs (0.94 [0.89, 0.99]) was significantly lower than with a numerically lower risk of death (0.90 [0.79, 1.01]) in the tiotropium group (pooled results) (Table). When separated by side of AEs and serious AEs remained lower in the tiotropium groups than placebo: RR 0.88 and 0.94 for HandiHaler® and 0.94 and 0.94 for Respimat® for serious AEs and serious serious AEs, respectively. Risks for cardiac events (0.93 [0.85, 1.02]) and major adverse cardiovascular events (MACE) (0.87 [0.73, 1.01]) were numerically lower and risk for respiratory, thoracic and mediastinal disorders (0.76 [0.61, 0.96]) was significantly reduced in the tiotropium group. The typical anticholinergic effects of dry mouth (2.39 [2.01, 2.84]), constipation (1.28 [1.06, 1.54]), intestinal obstruction (3.80 [1.42, 10.12]), dysuria (2.16 [1.31, 3.57]) and urinary retention (1.93 [1.21, 3.09]) were higher in the tiotropium group.

Conclusion The results from this safety review do not indicate an increased overall risk for fatal or cardiovascular events during tiotropium treatment, given via HandiHaler® or Respimat®, in patients with COPD.

Abstract P259 Table 1

<table>
<thead>
<tr>
<th>Placebo (n = 11,626)</th>
<th>Tiotropium (n = 12,929)</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs</td>
<td>7619 (65.5)</td>
<td>152.85</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>2654 (22.8)</td>
<td>23.08</td>
</tr>
<tr>
<td>Fatal AEs</td>
<td>523 (4.5)</td>
<td>3.71</td>
</tr>
<tr>
<td>MACE</td>
<td>358 (3.1)</td>
<td>2.56</td>
</tr>
<tr>
<td>Fatal MACE†</td>
<td>192 (1.7)</td>
<td>1.35</td>
</tr>
</tbody>
</table>

*Significantly different to 1; †including death unknown, IR per 100 patient-years

P260  Tiotropium Respimat® Add-on to Inhaled Corticosteroids Improves Lung Function in Patients with Symptomatic Mild Asthma: Results from a Phase III Trial

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Background Despite currently available therapies and detailed guidelines, many people with mild asthma remain symptomatic; it is important to establish the efficacy and safety of new treatments in this group.

Methods A Phase III, randomised, double-blind, parallel-group trial (GraziaTina-asthma®; NCT01316380) evaluated the efficacy and safety of once-daily tiotropium 5 μg or 2.5 μg versus placebo (all delivered via the Respimat® SoftMist™ inhaler) for 12 weeks in patients with symptomatic asthma on low-dose inhaled corticosteroids (200–400 μg budesonide or equivalent). The primary end point was peak forced expiratory volume in 1 second (FEV1) within 3 h of dosing (0–3h) response (change from baseline) at 12 weeks. Secondary end points were trough FEV1, FEV1 area under the curve (AUC0–3h) and peak expiratory flow responses (measured with the AM2+™ device) and seven-question Asthma Control Questionnaire (ACQ-7) score.

Results Of 464 treated patients, 155 received tiotropium Respimat® 5 μg, 154 received tiotropium Respimat® 2.5 μg and 155 received placebo Respimat®. Both tiotropium Respimat® doses were superior to placebo Respimat® in peak FEV1(0–3h) response (adjusted mean difference: 5 μg, 128 mL; 2.5 μg, 159 mL; both p < 0.001) and trough FEV1 response (adjusted mean difference: 5 μg, 122 mL, p = 0.001; 2.5 μg, 110 mL, p = 0.003). FEV1 AUC0–3h response at each visit, versus placebo Respimat®, significantly favoured tiotropium Respimat® 5 μg (p = 0.009 to p < 0.001) and 2.5 μg (all p < 0.001, except Day 1). Adjusted mean morning and evening peak expiratory flow responses, versus placebo Respimat®, each week, all favoured tiotropium Respimat® 5 μg (all p < 0.001) and 2.5 μg (all p < 0.003). Adjusted mean ACQ-7 score was similar across all arms (tiotropium Respimat® 5 μg, 1.391; tiotropium Respimat® 2.5 μg, 1.438; placebo Respimat®, 1.377). Adverse events were predominantly mild or moderate and were balanced between treatment groups.

Conclusion Tiotropium Respimat® was effective and well tolerated in patients with symptomatic mild asthma despite low-dose inhaled corticosteroid treatment.
**P261**

**TIOTROPIUM SAFETY AND PERFORMANCE IN RESPIMAT® (TIOSPIR™): SAFETY AND EFFICACY IN PATIENTS NAIVE TO TREATMENT WITH ANTAGONISMERS**

1R Wise, 2D Calverley, 3R Dahl, 4D Ducoy, 5N Metzdorf, 6A Mueller, 7A Fowler, 8A Anzueto, 9Johns Hopkins University School of Medicine, Baltimore, MD, USA; 10Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK; 11Odense University Hospital, Odense, Denmark; 12Service de Pneumologie Hôpital Cochin, AP-HP, Université Paris Descartes, Sorbonne Paris Cité, Paris, France; 13Boehringer Ingelheim Pharma GmbH and Co KG, Ingelheim, Germany; 14Boehringer Ingelheim Pharma GmbH and Co KG, Biberach, Germany; 15Boehringer Ingelheim Pharma Ltd, Bracknell, UK; 16Pulmonary Critical Care Center, San Antonio, TX, USA

Introduction The TIOSPIR™ trial showed similar safety and exacerbation efficacy profiles for tiotropium Respimat® and HandiHaler® in patients with chronic obstructive pulmonary disease (COPD). We present here the results for patients who were naïve to anticholinergic treatment at baseline.

Methods TIOSPIR™ (n = 17,135), a 2–3-year, randomised, double-blind, parallel-group, event-driven trial, compared safety and efficacy of once-daily tiotropium Respimat® 5 and 2.5 µg with HandiHaler® 18 µg in patients with COPD. Primary endpoints were time to death (non-inferiority of Respimat® 5 or 2.5 µg versus HandiHaler®) and time to first COPD exacerbation (superiority of Respimat® 5 µg versus HandiHaler®). Safety, including cardiovascular safety, was assessed.

Results Overall, 6966 patients from TIOSPIR™, naïve to anticholinergic treatment at baseline, were randomised and treated (n = 2345, n = 2312 and n = 2309 for tiotropium Respimat® 2.5 and 5 µg and HandiHaler® 18 µg). There was similar risk of death (vital status follow up) (measured as time to death) for the Respimat® groups versus HandiHaler® (Respimat® 5 µg: hazard ratio [HR], 0.93; 95% confidence interval [CI], 0.75–1.17; Respimat® 2.5 µg: HR, 1.05; 95% CI, 0.84–1.30) with similar results for the on-treatment sensitivity analysis (Respimat® 5 µg: HR, 0.91; 95% CI, 0.71–1.17; Respimat® 2.5 µg: HR, 1.11; 95% CI, 0.87–1.40). Risk of exacerbation was also similar for the Respimat® groups versus HandiHaler® (measured as time to first exacerbation) (Respimat® 5 µg: HR, 0.99; 95% CI, 0.90–1.08; Respimat® 2.5 µg: HR, 1.04; 95% CI, 0.95–1.14). Risk of major adverse cardiovascular event (MACE) or fatal MACE were similar for the Respimat® groups versus HandiHaler® (MACE: Respimat® 5 µg: HR, 1.20; 95% CI, 0.88–1.63; Respimat® 2.5 µg: HR, 1.11; 95% CI, 0.81–1.51; fatal MACE: Respimat® 5 µg: HR, 1.14; 95% CI, 0.75–1.71; Respimat® 2.5 µg: HR, 1.12; 95% CI, 0.75–1.69).

Conclusions Analogous to the global analysis, patients naïve to anticholinergic treatment and treated with tiotropium Respimat® 2.5 or 5 µg or HandiHaler® in the TIOSPIR™ trial exhibited similar safety and exacerbation efficacy profiles.

**P262**

**TIOTROPIUM SAFETY AND PERFORMANCE IN RESPIMAT® (TIOSPIR™): SAFETY AND EFFICACY IN PATIENTS WITH TIOTROPIUM HANDIHALER® USE AT BASELINE**

1P Calverley, 8A Anzueto, 3R Dahl, 4A Mueller, 7A Fowler, 5N Metzdorf, 6R Wise, 9D Dusser. 1Institute of Ageing and Chronic Disease, University of Liverpool, Liverpool, UK; 2Pulmonary Critical Care Center, San Antonio, TX, USA; 3Odense University Hospital, Odense, Denmark; 4Boehringer Ingelheim Pharma GmbH and Co KG, Biberach, Germany; 5Boehringer Ingelheim Pharma Ltd, Bracknell, UK; 6Boehringer Ingelheim Pharma GmbH and Co KG, Ingelheim, Germany; 7Johns Hopkins University School of Medicine, Baltimore, MD, USA; 8Service de Pneumologie Hôpital Cochin, AP-HP, Université Paris Descartes, Sorbonne Paris Cité, Paris, France

Introduction The TIOSPIR™ trial showed that tiotropium Respimat® and HandiHaler® have similar safety and exacerbation efficacy profiles in patients with chronic obstructive pulmonary disease (COPD). We present here results for patients from the United States (US) using tiotropium HandiHaler® at baseline.

Methods TIOSPIR™ (n = 17,135), a 2–3-year, randomised, double-blind, parallel-group, event-driven trial, compared safety and efficacy of once-daily tiotropium Respimat® 5 and 2.5 µg with once-daily HandiHaler® 18 µg in patients with COPD. Primary endpoints were time to death and time to first COPD exacerbation. Safety, including cardiovascular safety, was assessed. Tiotropium Respimat® was unavailable in the US (baseline tiotropium HandiHaler® use only), therefore this subgroup was analysed.

Results Overall, 1779 patients from TIOSPIR™ treated with tiotropium HandiHaler® 18 µg at baseline in the US were randomised and treated (n = 572, n = 602 and n = 605 for tiotropium Respimat® 2.5 and 5 µg and HandiHaler® 18 µg). A numerically lower time to death was observed for patients within the Respimat® groups versus HandiHaler® (vital status follow up: Respimat® 5 µg: hazard ratio [HR], 0.77; 95% confidence interval [CI], 0.53–1.12; Respimat® 2.5 µg: HR, 0.76; 95% CI, 0.52–1.12). Risk of major adverse cardiovascular event (MACE) and fatal MACE was numerically lower for the Respimat® groups versus HandiHaler® (MACE: Respimat® 5 µg: HR, 0.69; 95% CI, 0.41–1.18; Respimat® 2.5 µg: HR, 0.83; 95% CI, 0.50–1.39; fatal MACE: HR, 0.60; 95% CI, 0.26–1.37; Respimat® 2.5 µg: HR, 0.42; 95% CI, 0.16–1.09). Overall incidence of a fatal event (on-treatment) was lower in the Respimat® groups versus HandiHaler® (Respimat® 5 µg: HR, 0.60; 95% CI, 0.39–0.92; Respimat® 2.5 µg: HR, 0.67; 95% CI, 0.44–1.02). Time to first exacerbation was similar across groups (Respimat® 5 µg versus HandiHaler®: HR, 0.94; 95% CI, 0.82–1.08).

Conclusions Patients treated with tiotropium HandiHaler® 18 µg at baseline, and who were randomised and subsequently received tiotropium Respimat® 2.5 or 5 µg, had a similar risk of exacerbation as patients who continued to be treated with tiotropium HandiHaler® 18 µg. In this subgroup of patients, all-cause mortality was similar between tiotropium Respimat® and HandiHaler® 18 µg.

Abstracts M263 to M272 are found on page A218–A223.

**ILD: diagnosis, co-morbidities and treatment**

**P273**

**ASSESSMENT OF LUNG MICROSTRUCTURE IN INTERSTITIAL LUNG DISEASE WITH HYPERPOLARISED GAS MRI**

1NI Stewart, 2G Norquay, 3PR Parra-Robles, 4KH Marshall, 5G Leung, 6PS Murphy, 7RF Schulte, 8CA Elliott, 9R Cordiﬀe, 10CG Billings, 11SM Smith, 12PO Griffiths, 13JS Wolber, 14MK White, 15DG Kielty, 16JM Wild. 1University of Sheffield, Sheffield, UK; 2GlasgowKillearn, Bredington, UK; 3GE Global Research, Garching, Germany; 4Royal Hallamshire Hospital, Sheffield, UK; 5GE Healthcare, Amersham, UK

Introduction and objectives Magnetic resonance (MR) imaging of the hyperpolarised noble gases 3He and 129Xe provides...
Anti-synthetase syndrome (ASS) is characterised by interstitial lung disease (ILD), myositis, arthropathy, fever, Raynaud’s, and mechanic’s hands associated with anti-synthetase antibodies (including Jo-1, PL-7 and PL-12). ASS is a non-specific condition, and a histological diagnosis can only be achieved in 50% of cases. ANA is commonly used to screen for autoimmune diseases. If negative, in many centres extractable nuclear antigens (ENAs) are not tested. This study aims to highlight the inadequacy of this approach.

Method
We retrospectively examined consecutive patients in the Oxford ILD and Rheumatology services with ASS-ILD between 2009–2014. CT scans were reviewed to identify the pattern of ILD. Immunology, lung function and medication were identified from patient records.

Results
24 patients were identified with ASS-ILD: age 33–78 years (mean 54); 9 male, 15 female. Disease severity was assessed by lung function at presentation: FVC 42–118% (mean 77.9%) predicted, TLco 10–99% (mean 56%) predicted.

Only 1 of 24 (4.2%) were ANA positive (titre 1:80). 18 of 24 (75%) had a positive ENA screen (ELISA): 13 Jo-1; 4 Jo-1 and Ro-52; and 1 Ro, 6 (25%) patients had a negative ENA screen. 5 of these had a positive myositis blot (1 Jo-1, 3 PL-7, 1 PL-12) and 1 was negative for all 3 autoantibodies. Of 7 patients who were Jo-1 positive on ENA screen, 4 had a negative Jo-1 myositis blot.

CT patterns of disease: organising pneumonia (OP; n = 7), non-specific interstitial pneumonia (NSIP; n = 7), OP/NSIP overlap (n = 9), acute interstitial pneumonia (AIP; n = 1). There was no relationship between anti-synthetase antibody and CT pattern.

The identification of an ASS antibody significantly changed management in most patients; 17 were treated with (iv) cyclophosphamide and rituximab was added to 8 cases.
Conclusion The identification of an anti-synthetase antibody is central to diagnosis and significantly impacts on patient management. This data demonstrates that ANA is an inadequate screening test. If ASS is clinically suspected, ENA testing should be performed despite a negative ANA result. The data also demonstrate that either an ENA screen or a myositis blot used in isolation lack the required sensitivity. These tests need to be used in combination to avoid false negative results.

P275  EBUS OR EUS IN THE DIAGNOSIS OF SARCOIDOSIS?

1ADL Marshall, 2I MacPherson, 3GP Currie, 4GW Chalmers. 1Department of Respiratory Medicine, Glasgow Royal Infirmary, Glasgow, UK; 2Chest Clinic C, Aberdeen Royal Infirmary, Aberdeen, UK

Introduction The utility of endoscopic ultrasonography in the diagnosis of sarcoidosis was shown in the GRANULOMA trial.1 However, in the study, two thirds of samples were obtained using Endoscopic Ultrasound (EUS) via the gastrointestinal tract, and one third by Endobronchial Ultrasound (EBUS). Since this does not reflect typical practice in many areas, we assessed the diagnostic sensitivity of EBUS in suspected sarcoidosis and whether sampling nodes not accessible by EUS confers benefit.

Methods We retrospectively collected data relating to 128 consecutive patients in two separate experienced centres, who underwent EBUS over a 3 year period (2011–2013) with a pre-test differential diagnosis of sarcoidosis. Final diagnosis was based on decision at subsequent clinic review.

Results 129 EBUS procedures were performed in 128 patients (57% male, mean (range) age 49 (22–129) years. 221 nodal stations were sampled (median 9.0 ng/ml (range 0–3); p = 0.02. Bile salt concentrations were comparable in the two groups. To date, none of these patients have undergone fundoplication.

Discussion Oesophageal physiology and BAL assays may be combined to investigate reflux and aspiration in IPF. Our data suggest that acid reflux and weakly acid reflux is common and frequently asymptomatic. Our study suggests the need for carefully integrated assessments to inform potential treatment of reflux in IPF. High levels of oesophageal dysmotility and patient complexity support a cautious approach to antireflux surgery, which may be facilitated by multidisciplinary review.

REFERENCE
**Abstract P277** Figure 1  Cumulative incidence of lung cancer in people with IPF, CTD-PF and matched controls

**P277**  
**THE INCIDENCE OF LUNG CANCER IN PEOPLE WITH IDIOPATHIC PULMONARY FIBROSIS AND CONNECTIVE TISSUE DISEASE ASSOCIATED PULMONARY FIBROSIS IN THE UK: A POPULATION BASED STUDY**

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10.1136/thoraxjnl-2014-206260.396

**Introduction** Studies have suggested that lung cancer is more common in people with idiopathic pulmonary fibrosis (IPF). However, there is limited information on the risk of lung cancer in individuals with connective tissue disease associated pulmonary fibrosis (CTD-PF). The aim of this study was to compare the incidence of lung cancer in people with IPF and CTD-PF with that of the general population.

**Methods** Using electronic primary care records from The Health Improvement Network (THIN), we identified incident cases of IPF and CTD-PF between 2000 and 2011. For every case of IPF or CTD-PF, up to 4 general population controls matched on age, sex and general practice were randomly selected. We conducted a matched cohort analysis to estimate rate ratios for lung cancer in cases of IPF and CTD-PF compared with matched controls, adjusting for smoking habit.

**Results** Our study population consisted of 3266 incident cases of IPF, 494 cases of CTD-PF and 14,463 matched general population controls. The majority (64.1%) of people with IPF were male, while most (55.3%) of those with CTD-PF were female. Individuals with CTD-PF were also younger at time of diagnosis compared to people with IPF (mean age at diagnosis 69.0 vs. 74.2 years; p < 0.001). The median follow up time for our study population was 3.1 years (Interquartile range [IQR] 1.3 to 5.6). During this time 80 (2.5%) individuals with IPF, 9 (1.8%) with CTD-PF and 149 (1.0%) controls were diagnosed with lung cancer. After adjusting for smoking and the matching factors, the incidence of lung cancer was higher in people with IPF (Rate Ratio [RR] 3.61, 95% Confidence Interval [CI] 2.44 to 5.34) and CTD-PF (RR 2.35, 95% CI 0.78 to 7.09; p value for trend=0.013) compared to the controls (see Figure 1).

**Conclusion** Individuals with IPF and CTD-PF are at an increased risk of lung cancer, which cannot be fully explained by smoking habit. With the increasing use of new therapies that may prolong the median survival in individuals with lung fibrosis, our findings raise the possibility these patients may represent a suitable population for lung cancer screening.

---

**Abstract P278 Table 1**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age (years)</th>
<th>Diagnosis</th>
<th>Lung Injury Score</th>
<th>Duration MV before referral (days)</th>
<th>Respiratory support (duration in days)</th>
<th>ECMO complications</th>
<th>Treatment</th>
<th>Predicted ICU mortality (APACHE II)</th>
<th>ICU survival (LOS in days)</th>
<th>6 month survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>73</td>
<td>GPA</td>
<td>1</td>
<td>VV-ECMO (8)</td>
<td>Nil</td>
<td>PEX, MEP, HD, CYC</td>
<td>53.3%</td>
<td>Yes (17)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Male</td>
<td>61</td>
<td>GPA</td>
<td>3.5</td>
<td>VV-ECMO (8)</td>
<td>Nil</td>
<td>PEX, MEP, CYC</td>
<td>29.2%</td>
<td>Yes (14)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Female</td>
<td>21</td>
<td>MPA</td>
<td>TBC</td>
<td>VV-ECMO (6)</td>
<td>Nil</td>
<td>PEX, MEP, Rtx</td>
<td>35.5%</td>
<td>Yes (15)</td>
<td>TBC</td>
<td>TBC</td>
</tr>
<tr>
<td>Male</td>
<td>46</td>
<td>GPA</td>
<td>3.25</td>
<td>VV-ECMO (5)</td>
<td>Nil</td>
<td>PEX, MEP, HD, CYC</td>
<td>35.5%</td>
<td>Yes (21)</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

MV, mechanical ventilation; LOS, length of stay; GPA, Granulomatosis and Polyangiitis (Wegener’s Granulomatosis); MPA, Microscopic Polyangiitis; PEx, Plasma exchange; MEP, methylprednisolone; HD, Continuous veno-venous haemodialysis; CYC, Cyclophosphamide; Rtx, Rituximab; TBC, to be confirmed.
Poster sessions

ELSO The ELSO database contains 78 patients (adult, 59; paediatric, 19) with pulmonary vasculitides who received ECMO. 43 had a diagnosis of Granulomatosis and Polyangiitis (GPA), whereas the remaining diagnoses included hypersensitivity angitis, Goodpasture’s syndrome and thrombotic microangiopathy. The median age was 23 yrs (IQR 16–47). The median duration of ECMO was 190hrs (IQR 146–282) and ICU survival was 82%. Twelve patients (15%) were reported to have thrombotic ECMO circuit complications.

Conclusion In this case series, ECMO offers an excellent survival rate in SRF due to ANCA-associated DAH. ELSO registry data supports this, suggesting that ECMO should be considered as supportive therapy in DAH with SRF not responsive to conventional therapy.

P279 REDUCTION IN DISEASE PROGRESSION WITH NINTEDANIB IN THE INPULSIS™ TRIALS

Cottin, Taniguchi, Collard, Richeldi, Stowasser, Tscheppe, Schlenker-Herag, Raghi, Louis Pradel Hospital, University of Lyon, Lyon, France; Tosei General Hospital, Aichi, Japan; University of California San Francisco, San Francisco, California, USA; University of Southampton, Southampton, UK; Boehringer Ingelheim Pharma GmbH and Co. KG, Ingelheim Am Rhein, Germany; Boehringer Ingelheim France S. A. S., Reims, France; Boehringer Ingelheim Pharmaceuticals Inc., Ridgefield, Connecticut, USA; University of Washington, Seattle, Washington, USA

Background Nintedanib, an intracellular inhibitor of tyrosine kinases, is in development for the treatment of idiopathic pulmonary fibrosis (IPF). The INPULSIS™ trials were two replicate 52-week, randomised, double-blind, placebo-controlled Phase III trials that investigated the efficacy and safety of nintedanib 150 mg twice daily in 1066 patients with IPF. Declines in forced vital capacity (FVC)% predicted of >5% and >10% in patients with IPF have been proposed as indicators of disease progression and have been associated with reduced survival.

Aim To determine the effect of nintedanib on changes in FVC% predicted in the INPULSIS™ trials.

Methods The proportions of patients with absolute and relative declines in FVC% predicted of >5% and >10% at week 52 in each INPULSIS™ trial were determined in a post-hoc analysis.

Results In each trial, a significantly greater proportion of patients in the placebo group had an absolute decline in FVC% predicted of >5% compared with the nintedanib group. In INPULSIS™-1, a significantly greater proportion of patients in the placebo group had an absolute decline in FVC% predicted of >10% compared with the nintedanib group; the difference between groups in INPULSIS™-2 was numerically in favour of nintedanib but did not reach statistical significance. In each trial, significantly greater proportions of patients in the placebo group had relative declines in FVC% predicted of >5% and >10% compared with the nintedanib group.

Conclusion In the INPULSIS™ trials, nintedanib reduced the proportion of patients with IPF who experienced disease progression as measured by categorical FVC decline.

P280 EXTENDED CLINICAL EXPERIENCE WITH PIRFENIDONE DURING A NAMED PATIENT PROGRAMME FOR IDIOPATHIC PULMONARY FIBROSIS (IPF): INTERIM RESULTS

Panfrey, Chaudhuri, Gibbons, Anning, Balkin, Cooper, Dew, Maher. Papworth Hospital NHS Foundation Trust, Cambridge, UK; Royal Devon and Exeter NHS Foundation Trust, Exeter, UK; Royal Brompton and Harefield NHS Foundation Trust, London, UK; pH Associates Ltd, Marlow, UK; University of South Manchester NHS Foundation Trust, Manchester, UK

Introduction and objectives From September 2011 to May 2013, pirfenidone was available in the UK in a named patient programme (NPP). We present results from an extension to a previous real-world study (Parfrey et al. Abstract S98, BTS Winter Conference 2012) now including longer follow-up and all patients enrolled in the pirfenidone NPP from 4 centres.

Methods Four centre, retrospective, cohort review of patient outcomes in the 24 months following pirfenidone initiation in the NPP. Discontinuation data were separately collected for all patients prescribed pirfenidone at the Brompton between Sept 2011 and May 2014.

Results Two hundred and eighteen eligible patients have been identified. Demographic data have been collected for 124 patients (79% male) and outcome data at 12 months from 58 patients. Mean (± S. D.) age at diagnosis was 67.1 (± 8.1) years. Mean time from diagnosis to pirfenidone initiation was 27.7 (± 30.6) months. At pirfenidone initiation, mean FVC was 69.3 (± 18.9)% predicted (with 27 (22.0%) patients having FVC >80% predicted); DLco was 40.3 (± 13.8)% predicted. Following a 14-day titration period, 53 (93%) patients were receiving the recommended dose of 2403 mg/day pirfenidone. At 6 and 12 months; 47 (81%) and 44 (76%) patients continued to receive pirfenidone.

187 patients have been prescribed pirfenidone at the Brompton since Sept 2011. At 10 months following initiation 18.5% of these have discontinued pirfenidone with no further discontinuations beyond this time. For patients in the NPP with available paired baseline and 6 or 12 month FVC, mean decline in FVC% predicted over first 6 months of pirfenidone treatment was 3.2 (± 7.9)%; over first 12 months 1.6 (±12.0)%

Conclusions The high proportion of patients remaining on pirfenidone at 12 months suggests it is well tolerated and any tolerability issues tend to occur early in treatment. Lung function is largely preserved at 12 months following pirfenidone initiation. Longer-term observation of lung function and clinical outcomes will continue to determine the real-world benefits of pirfenidone.

Smoking detection and cessation and non tobacco products

P281 SMOKING PREVALENCE AND STOP SMOKING INTERVENTIONS FOR PATIENTS ADMITTED TO AN EMERGENCY DEPARTMENT (ED) IN A BUSY, INNER CITY HOSPITAL

Thomas, Warden, Stern. University of London Medical School, London, UK; Department Respiratory Medicine, Whittington Health, London, UK

Introduction ED admissions are ‘teachable moments’ to offer cessation advice to smokers. In this study, smoking prevalence and stop smoking interventions were investigated in patients

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10.1136/thoraxjnl-2014-206260.400
admitted to ED in a busy inner London hospital. The views of ED doctors on the value/appropriateness of offering smoking cessation advice in ED were canvassed with the aim of defining barriers to implementation of ‘right care’ for sick smokers.

Methods Proforma questionnaires guided interviews of ED patients and doctors. Patient demographics, smoking history (pack years, quit attempts, motivation to quit, smoking cessation advice/referral in ED) were documented. Doctors were asked about their views on ascertaining smoking status, offering brief advice and referral to quit smoking services to smokers in ED. All patients and staff were given an information sheet explaining the purpose of the questionnaires.

Results 101 patients were interviewed. 24/101(23%) were current smokers (3/24 12.5% also smoked cannabis), 39/101(39%) were ex-smokers and 38/101(37%) were lifelong non-smokers. Table 1 demonstrates that smokers were younger and never-smokers, never-smokers were predominantly female and 17/24 (71%) smokers had had multiple attempts to give up. In comparison, 36/39 (92%) ex-smokers gave up on their first attempt, with 33/39(85%) quitting without assistance. 13/24 (54%) smokers expressed a desire to quit yet only 4(17%) were asked/given advice about smoking by a doctor. 14 doctors (6 FYs, 4 CMT/SPRs, 4 consultants, 8/14 had had Stop Smoking training) were questioned. 14/14 agreed that smoking cessation was important; 8/14(57%) felt that ED was not an appropriate place to offer advice.

Conclusion 1/4 of patients attending A+E are smokers. Over 1/2 are motivated to quit but are not offered smoking-cessation advice during admission. Despite ED staff regarding Stop Smoking as valuable treatment, there is a perception that ED is an inappropriate setting to broach the issue of quitting. Smokers tended to be younger and had multiple unsuccessful attempts to quit compared to older ex-smokers who mainly quit on the first attempt. Offering support to quit during the first attempt is the most effective way to achieve permanent cessation. ED attendance should therefore be prioritised for targeted stop smoking interventions.

P281

Abstract P281 Table 1 Patient demographics and smoking characteristics

<table>
<thead>
<tr>
<th></th>
<th>Current Smokers</th>
<th>Ex Smokers</th>
<th>Never Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 24</td>
<td>n = 39</td>
<td>n = 38</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean±SD years</td>
<td>46.5 ± 17.5</td>
<td>55.5 ± 23.5</td>
<td>59.7 ± 22.3</td>
</tr>
<tr>
<td>Male/Female</td>
<td>13:11</td>
<td>21:18</td>
<td>11:27</td>
</tr>
<tr>
<td>Pack years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mean±SD (range)</td>
<td>28.5 ± 25.4 (5–96)</td>
<td>17.9 ± 22.7 (5–90)</td>
<td>12.5%</td>
</tr>
<tr>
<td>Cannabis (% of total)</td>
<td>12.5%</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Means±SD Number (range)</td>
<td>2.4 ± 2.3 (1–10)</td>
<td>1.1 ± 0.5 range 1–3</td>
<td></td>
</tr>
</tbody>
</table>

with tuberculosis

Background Smoking is an independent risk factor for tuberculosis infection, disease and mortality. It is therefore important that clinicians can identify patients who are actively smoking in order to provide optimal care. The reliability of self-reported smoking habits is often questioned but the development of biochemical assays that measure the nicotine metabolite cotinine, allow for an objective assessment of smoking status. Here we assess the accuracy of self-reported smoking habits in patients with tuberculosis by comparing these with urinary cotinine levels.

Methods Patients were recruited from two London tuberculosis clinics. Self-reported smoking habits were obtained from an interviewer administered questionnaire. Urinary cotinine levels were measured using a SmokeScreen® test kit (GFC Diagnostics, Oxfordshire, UK), a semi-quantitative colorimetric assay.

Results One hundred patients attending clinic for treatment of active tuberculosis or latent tuberculosis infection completed the study (Table 1). Nineteen reported using tobacco and had either smoked or chewed tobacco the day before testing, the quantity of which was representative of a standard day’s consumption. Duration of smoking ranged from 3 to 40 years with a mean of 13.4±10.5 and a median of 10.0. Eight further patients reported stopping smoking between a few days and 6 years prior to testing, with a mean cessation period of 2.0±2.1 years. Two of these had later started chewing tobacco.

Although nineteen patients reported either smoking or chewing tobacco, a further six patients’ urine tested positive for cotinine, i.e. 24% of tobacco users failed to report its use (Table 1). Furthermore, nine patients produced the colour change indicating heavy smoking (11–15/day) and ten patients produced a result indicating very heavy smoking (>16/day), although only two reported smoking 11–15 cigarettes the previous day and a further two must have chewed an equivalent amount of tobacco. This corresponds to 79% of heavy to very heavy tobacco users under-reporting its use.

Conclusion Discrepancies exist between objective and subjective assessments of smoking habits amongst patients with TB which may be attributable to an under-reporting of tobacco use, suggesting further avenues of research in this patient cohort.

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CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) CASE-FINDING AND TOBACCO DEPENDENCE ON LONG STAY PSYCHIATRIC WARDS


Introduction and objectives 42% of UK tobacco smoked is consumed by people with mental disorders. Smoking prevalence, and the proportion of highly-dependent smokers, are increased in patients with severe mental illness (SMI) and smoking is the main cause of high premature mortality in this group. The prevalence of COPD, a disease with >85% smoking-attributable deaths, in psychiatric in-patients is unknown and patients with SMI are less likely to have physical-health-checks and treatment. We hypothesised that COPD is under-diagnosed and under-treated in in-patients with SMI.

Methods Case notes review and a structured smoking/respiratory assessment, using NICE COPD guidance with spirometry/oximetry, were performed for in-patients with SMI over 1 month on three long-term psychiatric wards in an inner-city mental health trust.

Results Patient demographics are shown in the Table.

Poster sessions
34/41 (83%) were confirmed current tobacco smokers with mean (SD) 34 (28) pack-years; 5 were non-smokers and 2 ex-smokers. 24/41 (59%) were previous/current cannabis smokers. Quit Smoking Support (QSS) was offered to 25/34 (74%) tobacco smokers with medication prescribed for 9/34 (26%). Median (range) self-assessed MRC-breathlessness score was 1 (1–2); (n = 16 and 18 did not engage). Mean (SD) oxygen saturation was 96.6 (2.4)% (n = 21; 13 did not engage). Three smokers (9%) had an existing diagnosis of COPD. 18/28 eligible patients had spirometry; 10 (36%) did not engage. Mean (SD) FEV1 was 2.41 (1.01) L; 4/18 (22%) were obstructive. 3/6 (50%) smokers with COPD (1 ex-smoker) were offered QSS and 2 were referred for respiratory input.

Conclusions COPD prevalence was 17% in this in-patient group, over half of whom were undiagnosed. A third of patients declined spirometry, reflecting challenges of engagement in SMI. Nevertheless 2 in 9 tests resulted in new COPD diagnoses. Smoking prevalence was high at 83% but 1 in 5 smokers were not offered QSS, including half of those with COPD. These results support the case for respiratory-mental health collaborations during long psychiatric admissions.

REFERENCES
1 No health without mental health. Department of Health. 2011
2 NICE clinical guideline 101. Chronic obstructive pulmonary disease. 2010
A QUESTIONNAIRE STUDY OF ELECTRONIC CIGARETTE USAGE IN PATIENTS ATTENDING RESPIRATORY CLINICS IN A DISTRICT GENERAL HOSPITAL

AD Macfoy, E Crawford, K Srinivasan, H Moudgil. University of Keele Medical School, Staffordshire and Shrewsbury and Telford Hospitals NHS Trust, Shropshire

Background/objectives In the UK there are now more than two million users and more than 400 variations on electronic cigarettes (e-cigarettes) based on nicotine strength, flavours, devices etc. Despite the exponential rise in the use of e-cigarettes primarily as an adjunct to quit smoking strategies, the drive has predominantly been patient led and industry marketed with medical profession reluctant to engage, citing potential toxic effects as yet uncertain. Reporting from semi-rural community and focusing on respiratory patients attending respiratory clinics, objectives were to (1) document the current smoking pattern of our patients, (2) investigate their prior health seeking behaviour with respect to quit smoking, and (3) more specifically with respect to e-cigarettes address some of the questions raised with respect to where the medical profession may still have a role.

Methods Prospective, self-completed, questionnaire based survey of patients (>75%) attending respiratory clinic first three weeks July 2014.

Results Of 78 patients, mean (range) age was 63 (17–91) years with 49% male. Of these, 17 were smokers, 32 ex-smokers, and 29 never smokers. 42/49 (86%) had previously attempted to quit smoking; 26/42 had used no outside support, two had used nicotine gum or patches, three used drug therapies including Zyban or Champix, seven had used a combination, and four had used other unspecified techniques. 11/49 (22.4%) of those who had ever smoked had tried e-cigarettes: average set up was £23.33 with purchase on-line for three, specialist shops for four, market stalls for two, supermarket for one, and for one patient it was a gift. Only one patient had prior concerns about harmful effects, with two others asking and two others specifically being told by their retailer. Similarly, only two were given advice about suitable dosing based on baseline nicotine use, and two others about how to plan use and weaning.

Conclusions Although based on a small number of patients, the high use of e-cigarettes is recognised as is the intention to quit smoking. Importantly, the survey identifies a need for patient education about use and potential for harm and it is important that we now actively engage.

P285 ASSESSING THE IMPACT OF VARENICLINE INITIATION DURING ACUTE HOSPITAL ADMISSION FOR CURRENT SMOKERS WITH RESPIRATORY DISEASES: 18-MONTH EXPERIENCE FROM AN INNER CITY DISTRICT TEACHING HOSPITAL

A Ariley, E Pang, B Coleman, M Stern, L Restrick. Department of Respiratory Medicine, Whittington Health NHS Trust, London, UK

Introduction Smoking is a significant cause of respiratory disease and risk factor for chronic obstructive pulmonary disease (COPD) and asthma admissions. 70% of smokers admitted to hospital want to quit and quit smoking interventions during acute admission are NICE recommended.1 Many patients with respiratory disease are highly nicotine-dependent and varenicline is an effective treatment2-3 but is not routinely initiated during admission.

Method We retrospectively reviewed the notes of all patients prescribed varenicline during in-patient stay on the respiratory ward over 18 months (August 2012–January 2014). Baseline data included demographics, disease details (diagnosis, spirometry) and smoking history (tobacco/cannabis use, pack/joint-years). The primary outcomes were carbon monoxide (CO) validated quit rates at 4-weeks and self-reported quit rates at 6-months and 1-year.

All patients were seen on the ward by a smoking cessation advisor and after discharge as per NICE guidance.1 Nicotine withdrawal during varenicline initiation was treated with standard combination nicotine replacement therapy.1

Results 44 patients (17M:27F) were prescribed varenicline during admission. Mean (range) age was 61 (23–81) years with median (range) 50 (8–180) pack-years. 8/44 (18%) also smoked cannabis. 29 (66%) had COPD, 7 (16%) asthma, and 8 (18%) had both. Mean (SD) FEV1 was 1.18 (0.52)L (n = 40) with FEV1/predicted 47 (21%) (n = 26). 7 patients (16%) died; all from smoking-related diseases, within 18 months of admission with mean (range) age at death 71 (61–78) years. 2 were lost to follow-up. CO-validated 4-week quit rate was 48% (21/44). Self-reported 6-month and 1-year quit rates were 41% (18/44) and 20% (9/44) respectively. Only 4/44 (9%) stopped varenicline early due to side-effects (nausea/fever). Varenicline was safe and well-tolerated when initiated in hospital. The 4-week 48% quit rate for these ‘sick’ smokers was almost as high as the 52% national target for ‘well’ smokers. Self-reported 6-month quit rates were almost as good as the best published rates with intensive support in COPD (41% cf 49%).2 Varenicline should be used as a treatment for smokers admitted with respiratory disease.1


P286 RECOMMENDATIONS FOR SMOKING CESSION SERVICE Provision FOR Smokers WITH COPD WITH MULTIPLE COMPLEX NEEDS: FINDINGS FROM A PILOT STUDY

SY Yap, E Pang, S Lunn, C Croft, M Stern. Whittington Health, London, UK

Introduction Smokers with COPD are highly nicotine addicted and often have additional complex needs. Quit rates are poor and there is little evidence-based guidance on specific cessation interventions for these patients. This pilot study aimed to identify barriers to smoking cessation for this patient group.

Method Smokers with COPD were offered up to 12 individual sessions with a clinical psychologist in addition to standard smoking cessation counselling and pharmacotherapy. The psychological intervention included an initial assessment and formulation on factors maintaining smoking which informed an individualised psychological intervention targeting barriers to smoking cessation.

Results 37 patients (moderate COPD, high prevalence of complex physical and psychological comorbidities) were included in the study.2 (Table 1). 20/57 (35%) patients attended >2 sessions (mean=5, range 2–12). 7/20 had already quit (relapse prevention referrals), 13 were smokers. 22/57 (39%) patients never engaged. 15/57 (26%) were lost to follow-up. 6/7 (86%) of the relapse prevention group maintained their quit. 2/13 (15%) of
the current smoker group maintained a 28 day quit and 4/13 (31%) reduced tobacco intake. Psychological barriers to quitting were identified including smoking as a means of emotion regulation.

Conclusions For COPD smokers with a heavy smoking history and multiple quit attempts, and complex needs, additional psychological intervention alongside traditional quit smoking support may aid in preventing relapse, although further research is needed. For current smokers, the hypothesis was not supported, although the study did illuminate common themes regarding obstacles to quitting for this complex group who present a challenge to traditional quit smoking services.

It is clear that the current ‘one size fits all’ approach to smoking cessation does not meet the needs of these smokers who require more focused specific interventions to support smoking cessation including:

- Pre-quit support
- ‘Cut down to quit’ approach
- Long-term, intensive follow up
- Assertive outreach
- Multi-agency working

The above recommendations may provide a starting point for future service design.

### Abstract P286 Table 1 Patient demographics and morbidity

<table>
<thead>
<tr>
<th>Age (mean years±SD)</th>
<th>59 ± 10 (n = 57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M:F</td>
<td>27:32</td>
</tr>
<tr>
<td>FEV1 (mean litres±SD)</td>
<td>1.59 ± 0.8 (n = 37)</td>
</tr>
<tr>
<td>MRC Dyspnoea Score (mean±SD)</td>
<td>2.28 ± 1 (n = 37)</td>
</tr>
<tr>
<td>Consisting physical health problem e.g. arthritis, diabetes</td>
<td>79% (n = 29)</td>
</tr>
<tr>
<td>Consisting mental health problem e.g. depression, anxiety</td>
<td>64% (n = 28)</td>
</tr>
<tr>
<td>% with at least one psychosocial issue e.g. housing problems</td>
<td>67% (n = 30)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>57% (n = 35)</td>
</tr>
<tr>
<td>Pack Year History (mean±SD)</td>
<td>41 ± 22</td>
</tr>
<tr>
<td>No. of previous quit attempts</td>
<td>3 ± 2</td>
</tr>
</tbody>
</table>

**P287 MEASURING THE ACUTE CARDIOVASCULAR EFFECTS OF SHISHA SMOKING: A CROSS-SECTIONAL STUDY**

MK Kadhum, AEJ Jaffery, AH Haq, JB Bacon, BM Madden. St. George’s University of London, London, UK

**Objectives** To investigate the acute cardiovascular effects of smoking shisha.

**Design** A cross-sectional study was carried out in six shisha cafes. Participants smoked shisha for a period between 45 min (minimum) and 90 min (maximum). The same brand of tobacco and coal was used.

**Setting** London, UK.

**Participants** Participants were those who had ordered a shisha to smoke and consented to have their blood pressure, heart rate and carbon monoxide levels measured. Excluded subjects were those who had smoked shisha in the previous 24 h, who smoke cigarettes or who suffered from cardiopulmonary problems.

**Main outcome measures** Blood pressure was measured using a sphygmomanometer. Pulse was measured by palpation of the radial artery. Carbon monoxide levels were obtained via a carbon monoxide monitor. These indices were measured before the participants began to smoke shisha and after they finished or when the maximum 90 min time period was reached.

**Results** Mean arterial blood pressure increased from 96 mmHg to 108 mmHg (p < 0.001). Heart rate increased from 77 and 91 bpm (p < 0.001). Carbon monoxide increased from an average of 3 to 35 ppm (p < 0.001). A correlation analysis showed no relationship between carbon monoxide and the other indices measured.

**Conclusion** The acute heart rate, blood pressure and carbon monoxide levels were seen to rise significantly after smoking shisha. The weak correlation between carbon monoxide levels and the other variables suggests that carbon monoxide levels had not contributed to their significant increase.

**Introduction and objectives** Graphic Health Warning Labels (GHWL) assist in primary and secondary smoking prevention. A lack of evidence exists regarding their desensitisation with increased exposure. Investigating knowledge and attitudes around GHWL may allow better implementation of future public health policies. Singapore introduced GHWL in 2004, five years before they were introduced in the UK; this study aims to investigate any potential desensitisation effect by direct comparison.

**Methods** Data were collected from 266 smokers and non-smokers, 163 from London (54.6% smokers, 54.0% male, mean age 52.4 (17.8)) and 103 from Singapore (47.6% smokers, 77.7% male, mean age 57.7 (14.5)) between 2011 and 2013. A structured interview with fifty items, showing ten different GHWL, recorded demographics, smoking history, plans to quit and knowledge about the health-related consequences of smoking, as well as the emotional response, processing and impact of GHWL on behaviour. Participants further ranked hypothetical conditions that they could develop in terms of prevention and treatment.

**Results** The London cohort experienced significantly higher levels of ‘disgust’ when viewing GHWL than their Singapore counterparts (smokers 74.1% vs 49.0%, p = 0.003; non-smokers 83.8% vs 57.4%, p < 0.001), and felt GHWLs were a sufficient deterrent (smokers 33.7% vs 16.3%, p = 0.029; non-smokers 71.6% vs 50.0%, p = 0.013). London non-smokers had a higher awareness of heart disease (82.4% vs 32.0%, p = 0.007), stroke (72.3% vs 28.2%, p = 0.02), mouth and throat cancer (95.6% vs 35.0%, p < 0.001) and lung cancer (98.7% vs 35.0%, p < 0.001) as smoking-related diseases. London smokers reported an increased motivation to quit if they hypothetically developed smoking-related disease (85.2% vs 72.7%, p = 0.001). Blindness was the least well-known consequence overall (27.8%), despite provoking the highest levels of fear amongst Singaporeans.

**Conclusion** A desensitisation effect of GHWL is observed in cohorts with an increased length of exposure, both in smokers and non-smokers.
and non-smokers. The socio-cultural background needs to be considered when running public health campaigns due to differences in perception and responses to GHWL. Investigating the awareness of risks such as blindness, that have a low knowledge score but a high deterring impact, provides the chance to create a tailored approach when addressing this desensitisation.

In the largest group, those with drug or alcohol poisoning, smoking history was of poorer quality – pack-years could only be estimated in one case. Most had underlying mental health problems. None were referred to SSS.

Conclusions 1. Patients with COHb levels >2.0% are usually tobacco smokers.
2. Multiple substance dependence is common. Most have mental health problems and are rarely referred to SSS – a missed opportunity to improve life expectancy in this vulnerable population.
3. Carboxyhaemoglobin levels must be included in a systematic approach to identify people needing intensive support to quit smoking.

### Screening and treating sleep apnoea

**P290** **VALIDATION OF PREOPERATIVE SCREENING ALGORITHM FOR OBSTRUCTIVE SLEEP APNOEA**

VM Macavei, J Mitic, M Berger, OE Mohr, TC O'Shaughnessy, Newham University Hospital, Barts Health NHS Trust, London, UK

10.1136/thoraxjnl-2014-206260.409

Background Obstructive sleep apnoea (OSA) has been previously reported as a major risk factor for perioperative adverse events. Identifying patients with undiagnosed OSA can potentially have an impact on co morbidities and hospitalisation costs.

Aim To validate a previously reported screening tool for surgical patients suspected of having OSA.

Method A prospective study was performed in a university hospital between 1st Dec 2013 and 1st June 2014. An easy to use screening tool (STOP BANG) has been addressed to all patients prior to overnight oximetry sleep study during chest clinic assessment. The STOP BANG questionnaire incorporated 8 questions related to Snoring, Tiredness, Observed apnoeas, high blood Pressure, BMI >30 kg/m², Age >50, Neck size >15” and male Gender. Each affirmative answer was marked with 1 point. OSA was defined as dip rate ≥ 10 events per hour associated with an oxygen desaturation ≥ 4% below baseline value.

Results A total of 102 patients have been included, 57 males (55.8%) and average age 50.8 ± 14 years. 52 patients (50.9%) have been diagnosed with OSA out of which 29 patients (28.4%) had severe OSA (defined as dip rate ≥30 events per hour).

Using logistic regression analysis, a STOP BANG score of ≥ 3 had a sensitivity of 94.2% and specificity 72% with a positive predictive value of 77.8% and a negative predictive value of 92.3% in detecting OSA patients.

Conclusion We have identified a high incidence of OSA of 50.9% in our sleep study population. We have validated STOP BANG questionnaire to be a useful predictor of OSA with a sensitivity of 94.2% and specificity of 72%. This can be used during pre anaesthetic assessment indicating the requirement of chest clinic referral for sleep study at a score of ≥3.

REFERENCES
Introduction A recent meta-analysis shows obstructive sleep apnoea (OSA) increases the incidence of postoperative desaturation, respiratory failure, cardiac events, and ICU transfers (Kaw, R., et al., 2012). A study in gastrointestinal endoscopy showed no increased risk of cardiopulmonary complications in OSA screening positive patients (Mador, M. J., et al., 2012). There are no published studies in patients with OSA undergoing bronchoscopy, as far as we are aware. It has been suggested that patients should be screened for OSA prior to endoscopy and bronchoscopy.

Methods Nursing staff in the bronchoscopy suite used a validated OSA screening tool STOP-BANG score prior to the procedure. The physician performing the procedure was unaware of the score. The amount of sedation used during the procedure is recorded. Sedation score, Respiratory Rate (RR), Oxygen Saturation (SpO2), were documented 0, 30, 60, 120 min post procedure. The physician performing the procedure was unaware of the score. The amount of sedation used during the procedure is recorded. Sedation score, Respiratory Rate (RR), Oxygen Saturation (SpO2) were documented 0, 30, 60, 120 min post procedure. The physician performing the procedure was unaware of the score. The amount of sedation used during the procedure is recorded. Sedation score, Respiratory Rate (RR), Oxygen Saturation (SpO2) were documented 0, 30, 60, 120 min post procedure. The physician performing the procedure was unaware of the score. The amount of sedation used during the procedure is recorded. Sedation score, Respiratory Rate (RR), Oxygen Saturation (SpO2) were documented 0, 30, 60, 120 min post procedure.

Results Procedures were performed in 57 patients: diagnostic bronchoscopy 28, EBUS 29. Twenty-three patients (40.3%) were identified high risk for OSA (STOP-BANG score 3 or above). The mean age was 64 +/- 15. Male 29 (50.8%). There was no statistically significant difference in: amount of sedation used (midazolam, fentanyl or both), lignocaine use, initial sedation score, RR, SpO2, between high and low risk group. (Table 1). There was no correlation between initial sedation score with STOP-BANG score. There was no evidence of deeper sedation, drop in RR or SpO2 noticed in the post procedure observation period in the high risk group. Median length of observation was same in both groups. There were no complications or emergency admissions.

Conclusion In this small study there is no evidence of increased cardio respiratory complications in patients at high risk for OSA undergoing bronchoscopy under conscious sedation.

REFERENCES

P291 OBSTRUCTIVE SLEEP APNOEA SCREENING FOR PATIENTS UNDERGOING BRONCHOSCOPY – IS IT REQUIRED?
V Palissey, D Ghosh, MW Elliott. St James’s University Hospital, Leeds, UK
10.1136/thoraxjnl-2014-206260.410

Abstract P291 Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>High Risk Group (N=23)</th>
<th>Low Risk Group (N=34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>62 ± 3.6</td>
<td>66 ± 2.4</td>
<td>0.3149</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>85 ± 3.0</td>
<td>62 ± 2.2</td>
<td>-0.0001</td>
</tr>
<tr>
<td>Midazolam dose (mg)</td>
<td>5.2 ± 0.45</td>
<td>4.0 ± 0.36</td>
<td>0.0344</td>
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<tr>
<td>Fentanyl dose (mcg)</td>
<td>43 ± 9.5</td>
<td>36 ± 7.5</td>
<td>0.4951</td>
</tr>
<tr>
<td>Lignocaine dose (ml)</td>
<td>13 ± 0.34</td>
<td>14 ± 0.63</td>
<td>0.794</td>
</tr>
<tr>
<td>Sedation score (DAASS) immediate post procedure (1-4)</td>
<td>2.2 ± 0.14</td>
<td>2.3 ± 0.11</td>
<td>0.794</td>
</tr>
<tr>
<td>Deeper sedation score in post procedure observation</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>RR immediately post procedure</td>
<td>17 ± 0.69</td>
<td>18 ± 0.69</td>
<td>0.737</td>
</tr>
<tr>
<td>Oxygen Saturation</td>
<td>95 ± 0.50</td>
<td>95 ± 0.43</td>
<td>0.2866</td>
</tr>
<tr>
<td>Patients required observation beyond 2 h (number and percentage)</td>
<td>1 (4.3%)</td>
<td>1 (2.9%)</td>
<td>NS</td>
</tr>
<tr>
<td>RR &lt;8</td>
<td>0</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>RR 25% drop from baseline</td>
<td>2 (8.6%)</td>
<td>1 (2.9%)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Abstract P292 Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Sleep Apnoea</th>
<th>No Sleep Apnoea</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Number</td>
<td>36</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>62.2 (8.5)</td>
<td>62.1 (10.6)</td>
<td>0.9571</td>
</tr>
<tr>
<td>BMI</td>
<td>32.3 (5.3)</td>
<td>28.9 (5.8)</td>
<td>0.0052</td>
</tr>
<tr>
<td>ESS</td>
<td>8.9 (5.2)</td>
<td>7.8 (4.3)</td>
<td>0.2897</td>
</tr>
<tr>
<td>Males</td>
<td>25 (69.4%)</td>
<td>31 (47.7%)</td>
<td></td>
</tr>
<tr>
<td>Desaturation index</td>
<td>10.2 (9.9)</td>
<td>2.7 (1.2)</td>
<td></td>
</tr>
</tbody>
</table>

Categorical variables presented as frequency and continuous variables presented as mean (SD)
IS OBSTRUCTIVE SLEEP APNOEA A RISK FACTOR FOR CHRONIC KIDNEY DISEASE?

Thorax 2014; 4:1; doi:10.1136/thoraxjnl-2014-206260.412

Background Obstructive sleep apnoea (OSA) is associated with intermittent hypoxaemia which leads to activation of a number of pathways including oxidative stress, sympathetic nervous system, endothelial dysfunction and inflammation. These in turn lead to hypertension and atherosclerosis. There is some evidence that the same process may predispose to renal dysfunction. In this retrospective study, we compared a group people with hypertension and OSA on continuous positive airways pressure therapy (CPAP) with matched control group not known to have OSA.

Method Patients with known OSA and controls matched for age, sex and BMI were selected retrospectively from a hypertension clinic database. The two groups were compared using the following parameters: mean 24-hour systolic blood pressure (SBP, mmHg), mean serum creatinine (micromol/l) and mean urine albumin/creatinine ratio (ACR, mg/mmol).

Results Forty-nine patients were identified with confirmed OSA on CPAP. 6 were excluded due to insufficient data. Of the 43 remaining patients 35 were male, the mean age was 53.5 years and the mean BMI was 34.6 kg/m². The mean SBP was 143 in patients versus 135 in controls (p = 0.04). The mean serum creatinine was 94.0 in patients versus 93.4 in controls (p = 0.45). The mean ACR was 2.50 in patients versus 0.63 in controls (p = 0.031).

Conclusion This retrospective case-control study shows a higher prevalence of hypertension and proteinuria in patients with treated OSA when compared with controls matched for age, sex and BMI. OSA in the patients may not have been adequately treated. There may have been undiagnosed OSA in the controls. Patients’ higher proteinuria may have been caused by their more severe hypertension. Causation is not proven. However this study raises the possibility that OSA might predispose to chronic kidney disease. A larger, prospective study might confirm this finding and provide information on causation.

Factors Affecting CPAP Compliance

JA Stockley, S Huq, S Madathil, JA Hunt, BG Cooper. Queen Elizabeth Hospital, Birmingham, UK

Poster sessions

10.1136/thoraxjnl-2014-206260.413

Rationale Due to the nature and sensation of CPAP, not all patients comply with the treatment. Factors such as age, degree of sleepiness, health status, BMI and sleep apnoea severity may influence CPAP adherence. We sought to determine if these and other factors, particularly socioeconomic status, influence CPAP compliance of our patients.

Methods Demographic data (including age, sex, race and BMI), Epworth Sleepiness Score, Oxygen Desaturation Index (ODI; Desaturations/hour >4% SpO₂) and prescribed CPAP were retrospectively collected from all patients who had been issued CPAP between 2009 and 2013. In addition, the Index of Multiple Deprivation (IMD) Score and Rank were retrieved from the www.neighbourhood.statistics.gov.uk website. These parameters were then compared between CPAP “compliers” (≥4 hrs/night and ≥4 nights/week) and “non-compliers” (<4 hrs/night or <4 nights/week).

Results We obtained complete data from 407 patients over the four years period. Compliance was achieved in 70.5% of patients. CPAP compliers had significantly worse sleep apnoea (ODI), degree of sleepiness (Epworth) and a higher BMI (Table 1);

Conclusions Our data show a good level of compliance compared to previous reports (Shapiro et al. Sleep Breath 2010; 14: 323–25) and patient adherence at 12 months is better than previously reported (Bollig. Respir Care 2010; 55: 1230–9). Although ODI, Epworth and BMI were significantly higher in the CPAP compliers, the differences were only modest. Among the demographics tested, none seem to have a major influence on CPAP compliance in our cohort of patients.

Abstract P294 Table 1 Statistical comparisons between CPAP compliers and non-compliers. A better socioeconomic status is indicated by a lower IMD Score and a higher IMD Rank value. Age is presented as the median (range), sex and race are presented as% dominant trait and all other data are presented as median (IQR)

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Compliers (n = 287)</th>
<th>Non-Compliers (N=120)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>51 (20–84)</td>
<td>52 (24–76)</td>
<td>ns</td>
</tr>
<tr>
<td>% Male</td>
<td>80.5</td>
<td>72.5</td>
<td>ns</td>
</tr>
<tr>
<td>% Caucasian</td>
<td>82.2</td>
<td>82.5</td>
<td>ns</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>37.2 (32.2, 42.1)</td>
<td>34.6 (29.9, 40.2)</td>
<td>0.02</td>
</tr>
<tr>
<td>Epworth</td>
<td>14 (11, 17)</td>
<td>12 (9, 17)</td>
<td>0.02</td>
</tr>
<tr>
<td>ODI</td>
<td>20.9 (16.1, 57.8)</td>
<td>19.9 (10.8, 45.2)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>CPAP (cmH₂O)</td>
<td>12 (10, 12)</td>
<td>11 (10, 12)</td>
<td>ns</td>
</tr>
<tr>
<td>IMD Score</td>
<td>25.2 (15.3, 44.2)</td>
<td>29.2 (17.6, 47.9)</td>
<td>ns</td>
</tr>
<tr>
<td>IMD Rank</td>
<td>10527 (1344, 17818)</td>
<td>8695 (2594, 15936)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Patients’ Preference of Established and Emerging Treatments for Obstructive Sleep Apnoea

JA Stockley, S Huq, S Madathil, JA Hunt, BG Cooper. Queen Elizabeth Hospital, Birmingham, UK

Poster sessions

10.1136/thoraxjnl-2014-206260.414

Background Obstructive sleep apnoea (OSA) is the most common form of sleep-disordered breathing, and the standard treatment is continuous positive airway pressure (CPAP). Emerging treatments for OSA, including electrical hypoglossal nerve stimulation (HNS) and non-invasive electrical stimulation (nES), are currently being developed. To involve patients in the development of research projects, we evaluated patients’ preference for different treatments of OSA using a short survey.

Patients and methods We recorded patients’ age, gender, body-mass-index (BMI), Epworth Sleepiness Scale (ESS), Functional Outcomes of Sleep Questionnaire (FOSQ10), severity of OSA, and current treatment. We showed pictures of existing (CPAP, mandibular advancement device (MAD)) and emerging treatments (HNS and nES). We then asked 1) whether they were
interested in further information about HNS/nES, 2) if they would be willing to try HNS/nES, and 3) if they were to choose only one of the four listed treatments, which one would they prefer to use every night.

**Results** 162 patients completed the survey (81 males, mean age 52 (12) years, BMI 34 (7.3) kg/m², ESS 10.2 (6.0) points, FOSQ10 28.5 (8.1) points). The majority of the respondents (89.5%) had been diagnosed with OSA, with 95.4% of those being treated with CPAP. 91.3% of the respondents were interested in more information and were willing to try HNS/nES. Most respondents preferred the potential use of nES (56.7%), while 21.7% chose HNS, 17.8% CPAP, and 3.8% the MAD. There were no differences in the characteristics of the patients who preferred nES compared to those who preferred other treatments; however, a regression analysis showed that a low ESS score was a predictor of patients choosing nES (p < 0.05).

**Conclusion** Although the CPAP is the established treatment for OSA, most patients would prefer alternatives for long-term treatment. The majority of the respondents were interested in emerging technologies, with less sleepy patients more likely to choose less invasive treatment options.

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**Poster sessions**

**P296 EFFECTIVENESS OF ADAPTIVE SERVO VENTILATION IN THE TREATMENT OF CENTRAL SLEEP APNEA**

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10.1136/thoraxjnl-2014-206260.415

**Background** Adaptive Servo Ventilation (ASV) was developed to treat Central Sleep Apnea in patients with heart failure, which is usually associated with a low or normal PaCO2. The aim of ASV is to stabilise rather than increase overall ventilation. Evidence is limited regarding the use of ASV not only in heart failure patients but central sleep apnea of other aetiologies. The current study therefore explored this therapy in a regional sleep centre in the UK.

**Method** A retrospective review of the outcomes of 42 patients who were treated with ASV between January 2012 and December 2013, either following conventional positive airway pressure (PAP) or as an initial therapy. Measurements included the Apnea Hypopnea Index (AHI), compliance (measured by hours of machine use/night) and subjective sleep quality, pre and post ASV.

**Results** All patients demonstrated evidence of central sleep apnea with a reduced or normal transcutaneous CO2 during daytime spontaneous ventilation. Seven patients (16%) met the criteria for complex sleep apnea. 16 (38%) had evidence of heart failure whilst opioids were in use in six patients (14%). The majority of patients, (n = 36, 86%), were on PAP prior to ASV (mean duration 2.4 years), 22 patients (53%) were on Bi-level and 14 (33%) were on CPAP. Six patients (14%) had ASV as an initial therapy. The mean AHI improved from 31.7/h (range 2–84/h) to 5.1/h (Range 0–50/h) with ASV (Figure 1). Compliance improved from 5.2 h/night to 6.4 h/night with ASV. 22 patients (52%) reported a subjective improvement in their sleep quality using ASV.

**Conclusion** ASV appeared superior to traditional PAP in improving AHI, compliance and sleep quality for patients with central sleep apnea of various aetiologies.

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**From hospital to home: NIV in clinical practice**

**P297 EFFECT OF BTS-RECOMMENDED MEDICAL LEADERSHIP ON THE "DOOR-TO-MASK" TIME OF ACUTE NON-INVASIVE VENTILATION (NIV) SET UPS**

1H Boryslawskyj, 1T Ralp, 2B Beauchamp, 3A Oakes, 2N Santana-Vaz, 2B Chakraborty, 2R Mukheeje. 1School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, UK; 2Birmingham Heartlands Hospital, Birmingham, UK; 3School of Mathematics, University of Birmingham, Birmingham, UK

10.1136/thoraxjnl-2014-206260.416

**Introduction** NIV is now part of standard acute care in the UK. "Door-to-mask" time has been discussed as a performance/quality indicator of acute NIV services [Mandal S et al. Thorax, 66(4), A117]. We compare the 'Door-to-mask' time by analysing the "% of patients receiving NIV within 3 h" of diagnosis of acute hypercapnic respiratory failure (AHRF) at two acute hospitals in central England: Hospital A, which appointed a Lead NIV consultant in 2009–10 as per BTS recommendations and Hospital B without a Lead consultant. Both hospitals are run by the same Trust and on call physiotherapy teams, with comparable acute catchment sizes.

**Methods** The survey was approved as an audit by the Trust’s Clinical Standards Committee. Data was taken from the acute NIV database, maintained continuously since 2004 at HospitalA and since 2009 Hospital B as part of a drive to maintain built-in quality. All acute NIV episodes between 01/10/2010–01/04/2011 (period 1) and 01/10/2012–01/04/2013 (period 2) were included: 458 episodes (27 excluded – incomplete data).

**Results** In period1, the "% of patients receiving NIV within 3 h" of diagnosis of AHRF were 69.9% at Hospital A and 69.49% at Hospital B. In period2, Hospital A improved to 82% with Hospital B at 71.1%. The most significant improvement, however, was in the reduction of variance around the median "Door-to-mask" time of 1.55 h at Hospital A and 1.83 h at HospitalB on the Probability Density curves, also seen over other periods outside the ones studied.

**Conclusions** The service at Hospital B did not show any measurable improvement in 'door-to-mask time' between periods1 and 2 but Hospital A did. As there were no significant differences like the demography, work load, frequency of on calls or number/grades of staff between the periods 1 and 2, this improvement could be a reflection on the role of a Lead NIV consultant at Hospital A as per BTS recommendations. Furthermore, reduction of variance around the median "Door-to-mask" time is observed to be a consistent feature of the improvement, which
needs evaluation as an independent performance/quality indicator of acute NIV services.

**P298** REFERRAL PATTERNS AND MORTALITY IN A NON-INVASIVE VENTILATION (NIV) UNIT IN A TERTIARY UNIVERSITY HOSPITAL IN THE UK

K Aldridge, S Bikmalla, A Thomas. University Hospital of North Staffordshire, Stoke-on-Trent, UK

10.1136/thoraxjnl-2014-206260.417

Introduction NIV for acute hypercapnic respiratory failure (AHRF) in COPD and restrictive lung disease has become widespread in the UK. Early institution of NIV in appropriate patients gives the best outcome.

Methods We retrospectively examined referral patterns to our tertiary 12 bedded NIV unit during a 12 month period from November 2012 to October 2013. Admission criteria to the unit is standardised and through the NIV consultant or senior nursing staff. Site of referral was noted and mortality rate was calculated.

Results 612 referrals were made to the dedicated NIV unit in the 12 months. 125 were elective admissions for setting up domiciliary NIV and were excluded from the mortality analysis as there was no mortality in this group. The overall mortality for the rest of the cohort was 15.2% of the remaining 487 patients acutely admitted to the unit. The source of referrals to the unit was varied and as shown in Figure 1. The mortality rate for admissions from the acute portals (A and E) and the Acute Medical unit were significantly lower (10.4%) than from the medical wards (23%). This reflects the fact that even with a well selected cohort the timing of the respiratory failure in the course of illness plays an important part in determining mortality. We know that uncorrected respiratory acidosis after 4 h of NIV is a strong determinant of mortality. The highest mortality (64.5%) was seen of referrals from the Frail elderly unit. This also shows that general constitution plays an important role in mortality.

Conclusion Early referral for NIV support in AHRF improves outcomes. Delayed hypercapnic respiratory failure and frailty are important factors determining poorer outcomes.

**P299** THE ROLE OF A MULTIDISCIPLINARY RESPIRATORY HUB IN IMPROVING POST-DISCHARGE FOLLOW UP OF PATIENTS RECEIVING ACUTE NON-INVASIVE VENTILATION (NIV)

1F Ral, 1A Oakes, 1Y Khan, 1T Stuart, 1B Chakraborty, 1AM Turner, 1R Mukherjee.
2Birmingham Heartlands Hospital, Birmingham, UK; 3School of Mathematics, University of Birmingham, Birmingham, UK; 4College of Medical and Dental Sciences, University of Birmingham, Birmingham, UK

10.1136/thoraxjnl-2014-206260.418

Introduction Post-discharge follow up rate is a national audit metric for acute NIV services in the UK [Davies M. Adult NIV Audir report. BTS Reports 2012. 4 (3): 9–10.]. Appropriate respiratory follow up reduces the number of re-admissions [Turner AM et al. Prim Care Respir J 2013; 22(1):72–78.] In order to improve post-discharge follow up, a rapid access one-stop multidisciplinary respiratory outpatient Hub was created at our 709-bedded acute hospital in October 2011.

Methods From the acute NIV database maintained continuously since 2004, we analysed the proportion of discharges that were offered respiratory follow up within 6 months of discharge after Acute NIV during the calendar year 2009 (pre-Hub) and first 6 months of 2013 (post-Hub). Chi-squared test was performed for statistical significance of the observed differences.

Results The proportion of unique discharges offered a follow up appointment at the time of discharge improved from 57% (62/107) pre-Hub to 80% (36/45) post-Hub: p = 0.009. The proportion of patients attending follow-up appointments increased from 40% (42/107) pre-Hub to 58% (26/45) post-Hub: p = 0.036, confirming a statistically significant improvement. The number of acute NIV re-admissions dropped between 2009 and 2013 but expectedly not statistically significant, as only 6 months’ data from the post-Hub period was analysed against 12 months of data from the pre-Hub period.

Conclusions The increase in the number of patients attending post-discharge NIV follow up correlates with the direct increase in the number being offered follow up, an improvement most obviously measuring the impact of the multidisciplinary ‘Hub’. The Hub would also be the most plausible explanation for the drop in acute NIV re-admissions between the 2 periods, not the least because apart from a ‘routine’ follow-up, it supports community teams and provides an alternative to ambulance calls to people with complex respiratory needs in a responsive fashion. Further longitudinal evaluation of the Multidisciplinary Hub is necessary to fully understand its impact on the quality and safety of complex respiratory care.

**P300** THE CLINICAL EFFECTIVENESS OF DOMICILIARY NON-INVASIVE VENTILATION (NIV) IN PATIENTS WITH END-STAGE COPD

1J Dretke, 2C Dave, 3D Blissett, 4R Mukherjee, 5M Price, 5S Bayliss, 4K Wu, 4R Jordan, 5S Jovell, 1D Moore, 1AM Turner. 1University of Birmingham, Birmingham, UK; 2Heart of England NHS Foundation Trust, Birmingham, UK

10.1136/thoraxjnl-2014-206260.419

Background NIV is very effective when used acutely in hospital during acute exacerbations of COPD. However, evidence supporting its use in a home setting for more stable COPD patients is limited. In the UK domiciliary NIV is considered by many
clinicians on health economic grounds in patients after three hospital admissions for acute hypercapnic respiratory failure. Previous systematic reviews of domiciliary NIV have been limited in scope and required updating.

**Methods** Standard systematic review methods were used for identifying relevant clinical and cost-effectiveness studies of any appropriate design assessing NIV compared to usual care, or comparing different types of NIV. Risk of bias was assessed and checked. Primary effectiveness outcomes (mortality, hospitalisations, exacerbations and quality-of-life) were combined using random effects meta-analysis. Results were grouped into patients given NIV within 6 weeks of a hospital admission requiring inpatient NIV and those given NIV when stable.

**Results** Thirty controlled effectiveness studies were identified reporting a variety of outcomes, together with 65 uncontrolled studies. Benefit from NIV in terms of survival and hospital admissions in controlled studies was variable, and where present appeared most marked in post-hospital patients (based on limited evidence). For more stable patients, a modest volume of evidence found no benefit from NIV for survival and some non-significant beneficial trends for hospitalisations and quality-of-life. No conclusions could be drawn regarding potential benefit from different types of NIV due to limited study sizes and heterogeneity.

**Conclusions** Domiciliary NIV has greatest effect when used after a hypercapnic exacerbation and might improve hospitalisation rates and mortality in this group of patients. There is no benefit if used in stable, normocapnic patients.

This abstract summarises independent research funded by the National Institute for Health Research (NIHR) under its HTA Programme (Ref 11/27/01). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

**P301**

**A LARGE RETROSPECTIVE EVALUATION OF DOMICILIARY AND OUTPATIENT INITIATION OF HOME MECHANICAL VENTILATION**

**Introduction and objectives** Home Mechanical Ventilation (HMV) for patients with chronic ventilatory failure (CVF) often requires hospital admission for initiation of treatment. There are limited data evaluating the efficacy, efficiency and safety of initiating HMV in the domiciliary setting. Our centre has undertaken over 200 ‘home set-ups’ and we have evaluated outcomes in these patients.

**Methods** Patients with CVF who had HMV initiated in the domiciliary or outpatient setting were identified from our hospital database and data were retrospectively collected from their hospital records.

**Results** 214 patients with CVF were set-up at home between 2004 to 2013. Notes were available for 193 (90%) patients, mean (SD) age 59 (14) years, 63% male. The majority of patients had Motor Neuron Disease (MND)(30%) or obesity related respiratory failure (23%). Baseline lung function and arterial blood gas parameters are shown in Table 1.

178 (92%) patients had HMV initiated in their home; 15 attended the outpatient clinic for set-up. Three patients subsequently required hospital admission to support adaptation to HMV.

Following initiation, 135 (70%) patients were assessed as compliant with HMV, defined as >4 h self-reported use each night. Patients with MND had the lowest compliance rate with only 30 (52%) achieving this usage. If those with MND are excluded, overall compliance was 77% which is similar to our inpatient initiated HMV compliance rate of 83% (n = 224) and to case series reported by other centres.

Patients with few symptoms of nocturnal hypventilation had a lower compliance rate (55%) than more symptomatic patients (71%).

In patients who were compliant with HMV, mean (SD) time until >4 h use per night was 27 (60) days, but 33 (17%) patients achieved this usage after the first night. Those who became compliant with HMV had a mean of 2.9 (3.2) home visits and 1.4 (1.8) phone calls each.

**Conclusion** Establishing HMV in the domiciliary and outpatient setting can be effectively and safely achieved, even in patients with marked nocturnal hypventilation. Apart from patients with MND or those who are minimally symptomatic, ‘home set-up’ of HMV does not appear to affect compliance significantly.

**Abstract P301 Table 1**

<table>
<thead>
<tr>
<th><strong>Baseline Lung Function and Arterial Blood Gas Parameters in Patients receiving Domiciliary or Outpatient Initiation of HMV</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Parameter</strong></td>
</tr>
<tr>
<td>VATal Capacity (L)</td>
</tr>
<tr>
<td>pH</td>
</tr>
<tr>
<td>Arterial pCO2 (kPa)</td>
</tr>
<tr>
<td>Arterial pO2 (kPa)</td>
</tr>
<tr>
<td>Bicarbonate (mmol/L)</td>
</tr>
</tbody>
</table>

**P302**

**HOME MECHANICAL VENTILATION: HAS VENTILATOR TECHNOLOGY SURPASSED OUR ABILITY TO CARE FOR SOME PATIENTS IN A COMMUNITY SETTING?**

**Introduction** Home mechanical ventilation (HMV) for patients with chronic respiratory failure is a growing therapeutic modality that can reduce morbidity and mortality.1 HMV may be complex to establish and requires a clear care pathway from acute to community services. The aim was to ascertain factors influencing inpatient length of stay (LoS) and mortality in individuals requiring HMV who were unable to use the device independently.

All HMV was initiated in a respiratory high dependency unit (RHDU) in a university hospital.

**Method** A retrospective analysis of medical notes was conducted for all patients initiated on HMV between September 2012 and September 2013. Patients who were unable to manage the device independently were identified. Data collected included: admission data, social history, primary diagnosis, date deemed medically fit, readmission to RHDU, bed days post medically fit (section 5), reasons for delayed discharge and outcome.

LoS and bed day cost were calculated based on trust finance data for level 1 and 2 beds.
Introduction

Most people with motor neurone disease (MND) die from respiratory failure and non-invasive ventilation (NIV) can improve survival. The median survival of patients with good bulbar function not treated with NIV was just 11 days in one RCT (1). We wished to establish whether our 3 monthly follow-up regime, following NICE guidance (2), ensures all patients have an established care network pre-discharge with an increased LoS and higher mortality. The current Continuing Healthcare process and Social Services structure is not robust enough to meet these patients’ needs.

Results

Twelve patients were identified and separated into 2 groups according to LoS: less than 5 days (group 1; n = 5) or greater than 5 days (group 2; n = 7).

Various primary diagnoses were represented in each group. The main variable separating groups was pre-admission social status. Patients with a live-in carer, willing spouse or established 24-hour care were discharged back to their original home within 4 days of being declared medically fit. Those without such care had an average LoS of 27.4 days (17–51), with a large increase in associated cost and mortality. (Table 1). All patients in Group 1 survived and were successfully discharged. The in-hospital mortality for patients in Group 2 was 86%.

Discussion

HMV is a complex modality requiring specialist training to facilitate home use. Patients unable to manage HMV independently have significant care needs. This study showed that patients who do not have an established care network pre-discharge have an increased LoS and higher mortality. The current Continuing Healthcare process and Social Services structure is not robust enough to meet these patients’ needs.

References


P303 DOES REGULAR SURVEILLANCE ENSURE THE OPPORTUNITY OF NON-INVASIVE VENTILATION TO PATIENTS WITH MOTOR NEURONE DISEASE?

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Int. 10.1136/thoraxjnl-2014-206260.422

Introduction

Most people with motor neurone disease (MND) die from respiratory failure and non-invasive ventilation (NIV) can improve survival. The median survival of patients with good bulbar function not treated with NIV was just 11 days in one RCT (1). We wished to establish whether our 3 monthly follow-up regime, following NICE guidance (2), ensures all patients are offered NIV or whether many are dying without this treatment opportunity.

Aim

Establish what proportion of patients died before NIV was offered while under our follow up.

Method

A retrospective analysis of case notes of patients who died during the calendar year 2013. Survival was calculated as days (d) from starting of NIV until death.

Results

Of the 4 patients who died before NIV was offered, 2 had severe bulbar dysfunction and 1 patient was on CPAP for treatment of obstructive sleep apnoea. Pneumonia was reported as the cause of death in 2 of these patients. Details of the mode of dying of the other 2 patients could not be established (certified as MND).

Discussion

Most patients dying with MND had been offered NIV. 83% were compliant with treatment and survival was at least as good as published results. 4 died before NIV was offered but in 2, death was precipitant due to pneumonia, not ventilatory failure. As a default, 3 monthly review seems a reasonably safe interval for ventilatory surveillance in people with MND balancing intrusive hospital visits with the risk of missing the opportunity to try NIV at the end of life.

References

2. NICE guidelines (CG105). 2010. Use of NIV in the management of MND
Methods We conducted a prospective observational study of tracheostomy tube changes for patients admitted to home and those weaning from invasive ventilation in our unit. Data were collected from February to May 2014.

Results Eighteen patients receiving domiciliary tracheostomy ventilation attended during the study period. Eight patients had silver tubes, 7 had plastic cuffed tubes with inner cannulae and 1 had a plastic uncuffed tube with inner cannula. Two weaning patients were included and underwent five tracheostomy changes between them.

Data were obtained for 34 tube changes during the study period. Thirty were routine tube changes and 4 were expedited for reasons including stomal leak and partial dislodgement. Plastic tubes with inner cannulae were changed in accordance with the European Economic Community directive (1), with a mean of 28 days between tube changes. Sixteen (47%) were undertaken by consultant and 18 (53%) by trainee physician.

There were no complications in 31 (91%) tube changes. Three had minor complications such as minor bleeding and one patient who receives 24 hr home tracheostomy ventilation needed bagging and suction to clear secretions. Bronchoscopy was performed in 30 (88%) following tube change to clear respiratory secretions, check tube position and sometimes in response to a difficult tube insertion.

Conclusion No major complications occurred during the study period. This is probably because the procedure is undertaken by experienced personnel in a controlled environment. The threshold for post procedure bronchoscopy appears to be low and we are currently reviewing this aspect of our practice.

Tackling tuberculosis

M35 ADVERSE EFFECTS OF LATENT TUBERCULOSIS TREATMENT IN MIGRANTS

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Background Most cases of tuberculosis (TB) in the UK occur in migrants. The majority develop active TB within 5 years of arriving in the UK, usually due to reactivation from latent tuberculosis infection (LTBI). Therefore identifying and treating LTBI in migrants who are at risk of reactivation, is critical to reduce rates of active TB. It is, however, unclear, unless migrants develop any significant adverse effects from chemoprophylaxis (Rifampicin and Isoniazid), which subsequently affects adherence.

Aim To assess the type and frequency of adverse effects on migrants on treatment for LTBI.

Methods A retrospective study was conducted within our Trust between 1st January 2007 and 31st December 2012. Records of patients between the ages of 16–35, who had lived in the country for less than 5 years and received chemoprophylaxis, were examined.

Results 472 patients treated for LTBI were included. Mean age was 30.4 ± 7.4 years and 54.8%(259) were males. Ethnic origin included: Indian subcontinent 327(69.3%), African 113(24%), Caucasian 14(3%) and other 18(3.8%). Hepatitis B was detected in 5 cases (1%), hepatitis C in 2 cases (0.4%) and HIV was present in 1 case (0.2%). 19(4%) patients experienced adverse effects. 13(2.7%) reported gastrointestinal symptoms (nausea, vomiting), 4(0.8%) developed a skin rash and there was 1(0.2%) case of thrombocytopenia. Three of the 4 cases who developed a skin rash stopped ATT, and all three patients developed active TB two to four years later. One patient developed peripheral neuropathy due to Isoniazid. Drug induced hepatitis with a rise in ALT greater than three times the upper limit of normal was present in 15 patients (3.1%). An increase in bilirubin level greater than two times normal was recorded in 5 patients (1%). One patient who had concurrent hepatitis B was hospitalised due to hepatotoxicity.

Conclusion Treatment for LTBI in migrants below the age of 35 is safe, associated with a low risk of hepatotoxicity and should be feasible in primary care. Adverse effects should be managed promptly to ensure treatment adherence and prevention of progression to active TB.

EVALUATING AEROSOL ADMINISTRATION OF A CANDIDATE TB VACCINE MVA85A

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There is an urgent need for a better vaccine against TB than BCG, which confers variable protection against pulmonary TB, the main source of TB transmission.

Heterologous prime-boost vaccination regimens using virally vectored vaccines induce strong cellular immune responses and are a leading strategy for TB vaccine development. Boosting BCG with MVA85A, a recombinant viral vector expressing antigen 85A, can enhance BCG induced protection in animal models. MVA85A in humans is safe and immunogenic when administered systemically.

Animal data suggests delivering a vaccine to the respiratory mucosa may be the most protective route. We recently completed the first trial where a virally-vectored vaccine, MVA85A, was delivered to humans by aerosol; and was found to be safe and highly immunogenic. This route also has potential for dose-sparing.

A limitation of virally vectored vaccines is anti-vector immunity, which limits use and re-use.

Non-human primate data with aerosolised MVA85A suggests that aerosol vaccination induces less systemic anti-vector immunity than systemic routes. We have demonstrated this is also true in humans in our first aerosol trial, where humoral anti-vector immunity to MVA was induced by volunteers vaccinated by the systemic route but not the aerosol route.

An on-going trial now addresses the question, if alternating routes of vaccination can abrogate anti-vector immunity, by immunising twice with MVA85A by heterologous routes one month apart.

This would be an important development for the development of aerosolised TB vaccines but also for new vectored vaccines for RSV, universal influenza and a range of bacterial respiratory pathogens.
Background HIV infection is the strongest single risk factor for the development of active tuberculosis (TB) in individuals with latent TB infection (LTBI). NICE guidelines recommend screening HIV-positive patients for LTBI with an Interferon Gamma Release Assay (IGRA), plus a Tuberculin Skin Test (TST) in patients with a CD4 count <200 cells/mm³ if IGRA negative.

Method We began screening HIV-positive patients for LTBI in July 2011; this prospective study reports our 3 year data. Patients had an IGRA (T-SPOT. TB®), and a TST was performed in those with a negative result and a CD4 count <200 cells/mm³.

Results 116 HIV-positive patients were screened (Table 1): CD4 Count ≥200 Group Of 88 patients, 4 (5%) had a history of previous TB infection and were excluded. 70/84 (83%) had a negative IGRA, 9/84 (11%) had a positive IGRA (3 had active TB and 6 LTBI) and 5/84 (6%) had inconclusive IGRA results. Of these, 4/5 had a repeat IGRA (2 positive, 1 negative, 1 awaited) and I was lost to follow up.

CD4 Count <200 Group Of 28 patients, 1 (4%) had a history of previous TB infection and was excluded. 24/27 (89%) had a negative IGRA and were referred to TB clinic for a TST. Of these, 18/24 (75%) had a negative TST, 3/24 (12.5%) did not attend and 3/24 (12.5%) are awaiting appointments. 2/27 (7%) had a positive IGRA and were treated for LTBI. One (4%) had an inconclusive IGRA result but did not attend follow up.

Conclusions Screening for TB in HIV is worthwhile, with a 12% detection rate in our cohort. Performing a TST did not detect any additional cases of TB infection in the CD4 <200 group. Performing this test is time-consuming, costly and inconvenient, and we suggest that screening should be with an IGRA alone. The detection rate of TB infection was lower in those with more advanced immunocompromise, which raises concern about the sensitivity of the screening tests.

Abstract M37 Table 1

| Male sex | 60 (52%) |
| Median age | 40 years (range 22–79) |
| Ethnicity | |
| Black African | 69 (60%) |
| White UK | 28 (24%) |
| White other | 10 (8.5%) |
| Asian | 6 (5%) |
| Black Caribbean | 3 (2.5%) |
| Median CD4 count | 370 cells/mm³ (range 10–980) |
| No. with CD4 count ≥200 cells/mm³ | 88 (76%) |
| Median CD4 count | 430 cells/mm³ |
| Range (CD4 count) | 200–980 cells/mm³ |
| No. with CD4 count <200 cells/mm³ | 28 (24%) |
| Median CD4 count | 100 cells/mm³ |
| Range (CD4 count) | 10–190 cells/mm³ |

References

1 Treatment of latent tuberculosis infection in HIV infected persons. Akola C, Adetifa I et al. Cochrane Database of Systematic Reviews 2010, Issue 1
SCREENING FOR TUBERCULOMAS IN PATIENTS WITH MILIARY TUBERCULOSIS – WHAT MODALITY OF Imaging SHOULD WE BE USING?

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Introduction and objectives NICE guidance advises neuroradiology to investigate CNS signs in patients with miliary tuberculosis (TB). The aims of our study were to describe our population of patients with tuberculomas in the presence of miliary disease and identify any clues to the best radiological modality.

Methods The radiology and clinical history was retrospectively reviewed for all patients treated for miliary tuberculosis at one centre between 01/01/2009 and 31/12/2013.

Results 53/1650 (3.2%) of patients during this period were diagnosed with miliary (disseminated) tuberculosis. 27/53 (50.9%) underwent further neuroimaging. 10/53 (18.9%) miliary TB patients had evidence of tuberculomas on neuroimaging (M:F 6:4, age range 22-81). 2/10 had evidence of tuberculomas on both CT (2/2 with contrast) and MRI, 5/10 had a negative CT (2/5 with contrast) but an MRI result which revealed tuberculomas. 3 patients did not have a CT scan (MRI only). All 10 patients were HIV negative and had fully sensitive TB, 9/10 had neurological signs which warranted the subsequent neuroimaging.

Conclusion Tuberculomas are seen in a fifth of patients with miliary tuberculosis. Based on our findings, guidelines should be adapted to suggest that both use of contrast and MRI should be utilised preferentially.

TACKLING POOR ATTENDANCE TO TUBERCULOSIS CLINIC – WHO, WHY AND WHAT CAN BE DONE


Introduction Despite efforts to improve Tuberculosis (TB) services, disease rates remain high (UK national average 14.4 per 100,000). We believe one of the ongoing challenges is engaging patients in attending outpatient clinics for care. However, there is no current UK data evaluating poor attendance to TB clinic.

Aim To identify reasons for patient’s non-attending TB clinic, in order to implement service improvements and increase patient engagement.

Methods We conducted a prospective study reviewing the number of Did Not Attends (DNAs) to our TB clinic over a six-week period (April to June 2014). We evaluated data, usually obtained from patients who are contacted after they DNA, and cross referenced this with the trust electronic database. Data obtained included patient demographics, stage of TB treatment, route of referral, reasons for non-attendance and accessibility to clinic.

Results 63 of 385 patients (16% · 42 males, 21 females) did not attend their TB clinic appointments compared to 15% for non-TB respiratory appointments in this time. 64% were contactable (25 males, 15 females). Median age was 32 (range 17–78 years), which included 16 ethnicities and seven languages. 62.5% were follow-up appointments and 37.5% were new. 27.5% had TB previously. Stage of TB treatment included: completed (17.5%), current (25%), none (57.5%). Referral route included GP (40%), hospital (32.5%) and contact tracing (27.5%). 59% were aware of their appointment but were unable to attend due to other engagements. 41% stated they had not received a letter informing them of their appointment, 13% of these patients had relocated to another area and not updated their address. 8% of patients highlighted problems with transport leading to difficulties accessing the clinic.

Conclusions Communication to inform patients about appointments needs to be improved by both the referring and TB service. Utilising information technology and community links may improve patient education and therefore engagement with services. Experiencing the patient’s journey will highlight further areas for development.

RECURRENT TUBERCULOSIS AND ITS RISK FACTORS IN THE UK’S LARGEST TB CENTRE

K Avery, R Ghani, J Buckley, L John, RN Davidson. Department of Tropical Medicine and Infectious Diseases, Northwick Park Hospital, North West London Hospitals NHS Trust, London, UK

Objective To describe tuberculosis (TB) relapse/recurrence in patients treated at the UK’s largest TB centre and identify characteristic which predicted recurrence.

Design Retrospective observational cohort study.

Methods All patients treated at our centre between 1st Jan 2002–31st Dec 2013 were identified from the local TB register. We excluded patients who died due to TB or whose outcome was unknown. Details of patients with more than one notification episode of TB were obtained from patient records.

Results In total, 3534 patients were treated for TB during the 12-yr period. After exclusions, 3515 patients were included in the study. Of these, 42 patients had two notifications of TB; none were treated more than twice.

Of these 42, we considered 14 to be true relapses/recurrences. 28 patients were considered on review not to have had a true relapse/recurrence: of these, 11 had their first treatment episode at a different centre; 9 were re-starts of treatment because of non-adherence during the first TB episode; 2 had intracranial tuberculomas diagnosed within 12 months of initial episode; 6 were errors in notification.

Of 14 patients considered to be true relapses/recurrence, 6 were microbiologically confirmed on relapse/recurrence and a further 8 were re-treated on clinical grounds. None exhibited drug resistance and 2 were HIV positive. The 14 true relapse/
recurrence patients had mean age = 42 yrs (range 18–83 yrs) and 6 were males. The sites of relapse were; pulmonary in 6 cases, 3 patients had intracranial tuberculomas, 2 patients had bony TB, 3 patients had TB lymphadenitis. The mean time to relapse/recurrence was 41 months (range 2–96 mo). All 14 patients responded favourably to re-treatment.

The true relapse rate of TB treated at the centre was 0.4%. The age, gender and ethnicity of the relapse cases were similar to the overall TB case-mix.

Conclusions Our true relapse/recurrence rate of TB is very low, and had no obvious risk factors. We cannot determine retrospectively whether these were recurrence or reinfection, but strain typing (DNA fingerprinting) could differentiate these.

M42 INCREASING COMPLEXITY OF TREATING TB IN OLDER PATIENTS

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10.1136/thoraxjnl-2014-206260.431

Introduction Older adults remain an important reservoir of tuberculosis (TB) infection in the UK. Waning cellular immune responses, more frequent co-morbidities such as diabetes and malignancy, and increased polypharmacy may all modulate clinical presentation, treatment tolerability and ultimately outcomes when compared to younger individuals with TB. We sought to investigate this in our population.

Methods Retrospective study of all adults over 60 diagnosed with TB during a five year period at one hospital trust. Case-note and electronic record review established baseline disease features, co-morbidities, pre-morbid immune suppression including HIV status, TB-related outcomes and death. A randomly selected control group of identical size, containing adults aged 16–59 who were treated for TB during the same period, was used for comparison.

Results Forty-eight cases aged >60 years at TB diagnosis were identified. The case and control groups are described in the Table. Multi-lobar pulmonary disease was significantly more common in the >60 year old, as was diabetes, other significant co-morbidities and non-HIV immune suppression. Whilst treatment regimen discontinuation or alteration was more common in the >60 year old group (7 (14%) versus 3 (6%) if 60 years old but none (0%) of the younger group; whilst deaths after completion of TB treatment have been observed in 8 (17%) and 1 (2%) of cases respectively (no post-treatment death was related to TB in either group).

COPD: co-morbidities, deficiencies and interventions

M137 CAN STEROID INSSENSITIVITY IN COPD PATIENTS BE RESTORED USING VITAMIN D?

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10.1136/thoraxjnl-2014-206260.433

Background NICE guidelines for TB diagnosis recommend that sputum is obtained for culture for all suspected cases of pulmonary TB, and biopsies for all cases extrapulmonary TB. As results can take 6 weeks, treatment initiation decisions are frequently made without microbiological confirmation.

Aim This study set out to examine the accuracy of clinical diagnoses in a high incidence area, and the basis for these decisions.

Methods The data entered onto the national TB database was used to obtain a list of patients for whom no culture results had been recorded. Clinic letters, laboratory records and imaging were examined to determine whether samples had been sent for culture, how diagnoses were made in the event of negative results, and if alternative diagnoses were concluded.

Results Of 323 patients on the database, 7% had no samples sent for culture. There were 109 culture negative patients, of whom 13 (4% all cases) had alternative diagnoses. A combination of relevant history and imaging was the most commonly used method of diagnosis when culture was negative (47%). Histology was used in 17% patients and Mantoux or IGRA testing supported initiating treatment in 39% cases. The database was missing positive culture results for 102 patients, of which four were MDR TB.

Conclusions In this study, we found accurate initial clinical diagnoses, with only 4% patients subsequently obtaining alternative diagnoses. Most diagnoses were made on the basis of relevant history and imaging. Of concern are the 7% patients for whom tissue was never sent for culture. This is likely to be an underestimate when including all patients initially suspected of TB, raising the possibility of missed diagnoses. The utility of Mantoux and IGRA testing in active disease is now disputed. It is hoped with inter-specialty education regarding the importance of culture and futility of immunological based assays, the proportion of patients with suspected TB who have sputum or tissue sent for culture increases. Accurate recording of MDR-TB on the national TB database needs to be improved, to enable efficient monitoring of intervention programmes.
Introduction In many chronic diseases vitamin D has been proposed as an adjunctive anti-inflammatory therapy. Vitamin D up-regulates MKP1, thereby downregulating p38 phosphorylation and the NFκB inflammatory cascade (Zhang et al, J Immunol. 2012;188(5):2127–35). Steroids exert anti-inflammatory effects via this cascade, and exhibit synergy with vitamin D for some effects (Yu et al, Journal of the National Cancer Institute. 1998;90(2):134–41). Patients with COPD have chronic pulmonary inflammation, with upregulation of NFκB, yet do not exhibit a good response to steroids. Vitamin D therapy has been trialled in COPD patients, albeit with disappointing results (Lehouck et al, Annals of internal medicine. 2012;156(2):105–14). We hypothesised that COPD patients’ inflammatory response would differ from health, and that vitamin D would exhibit synergy with steroids in vitro to improve this.

Methods PBMCs isolated from 10 COPD patients and 10 healthy control subjects were incubated with LPS, vitamin D, dexamethasone, a p38 MAPK inhibitor or combinations of these agents. Supernatants were harvested for TNF and IL6 measurements (ELISA).

Results LPS caused a marked rise in IL6 in both healthy controls (p = 0.044) and COPD patients (p = 0.008). IL6 reduction with vitamin D was only seen in health. IL6 reduction with addition of dexamethasone was not statistically significant (p = 0.636) in COPD. Combinations of agents failed to produce any additional benefit in both health and COPD.

The response to vitamin D was heterogeneous; half of healthy subjects showed an anti-inflammatory response but in COPD only 12.5% of patients exhibited this. The difference in response rate was not significant (p = 0.120, Fishers exact test), though this may be due to low power. Similarly reduced response rate to dexamethasone was seen in COPD.

Conclusion Vitamin D does not enhance the anti-inflammatory effect of steroids. The anti-inflammatory effects of vitamin D are no different between COPD and health; variability of response may be one reason for lack of effect of vitamin D in clinical trials to date in COPD patients.

INTRODUCTION

Patients with COPD have increased risk of cardiovascular (CV) disease compared to smokers without COPD,1 with over 25% of deaths CV related.2 Several CV risk calculators for the general population exist but it is unclear whether they are applicable for COPD.

Hypothesis

Standard CV risk calculators do not identify the increased risk in patients with COPD.

Methods Subjects with a smoking history >10 pack years, with and without COPD, were assessed at clinical stability. COPD n = 191 and controls n = 106. Post-bronchodilator spirometry and blood pressure were performed, blood taken for lipids and self-reported medical and smoking history recorded. In those without documented established CV disease or diabetes (COPD n = 135 and controls n = 88), 10 year CV risk was calculated using ACC/AHA1 and NHLBI[4] calculators.

Results Both groups were well matched for gender and mean arterial blood pressure (MAP), with the COPD group slightly older, Table 1. Mean CV risk scores were similar between patients with COPD and controls, Table 1, ACC/AHA p = 0.16 and NHLBI p = 0.59. When using an established cut-off point of 20% for high 10 year CV risk, similar proportions were identified as high risk: the ACC/AHA calculator - 37% of the patients with COPD and 33% of controls; and with the NHLBI calculator 15% of the patients with COPD and 10% of controls were identified as high-risk.

Discussion Although nearly double the proportion of patients with COPD compared to controls with a smoking history have current CV disease or diabetes in this cross-sectional study, the increased risk of future incident CV disease in patients with COPD was not identified using standard calculators.

Supported by a NIHR BRF Fellowship.

REFERENCES

3 ACC/AHA Available from: http://my.americanheart.org/professional/StatementsGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp
4 NHLBI Available from: http://cvdrisk.nhlbi.nih.gov/

M138 DO STANDARD CARDIOVASCULAR RISK SCORES IDENTIFY RISK IN PATIENTS WITH COPD?

ME John, S Hussain, M Al Haddad, CE Bolton. University of Nottingham, Nottingham, UK

Introduction Patients with COPD have increased risk of cardiovascular (CV) disease compared to smokers without COPD,1 with over 25% of deaths CV related.2 Several CV risk calculators for the general population exist but it is unclear whether they are applicable for COPD.

Hypothesis

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Supported by a NIHR BRF Fellowship.

REFERENCES

3 ACC/AHA Available from: http://my.americanheart.org/professional/StatementsGuidelines/Prevention-Guidelines_UCM_457698_SubHomePage.jsp
4 NHLBI Available from: http://cvdrisk.nhlbi.nih.gov/

M139 FRAILTY AND PREMATURE CARDIOVASCULAR AGING IN COPD

AM Albarrat, NS Gale, S Enright, M Munnery, I Munnery, S Sakiya, JR Cockcroft, DJ Shale. Cardiorespiratory Medicine, Wales Heart Institute, Cardiff University, Cardiff, UK

10.1136/thoraxjnl-2014-206260.435

Background Presence of comorbidities in chronic obstructive pulmonary disease (COPD) parallels the accumulation of multiple system deficits associated with ageing and assessed as frailty. An important association of frailty in the elderly is increased cardiovascular disease, which is also a major cause of mortality in COPD.1 However, frailty has not been extensively studied in COPD. We hypothesised that frailty in COPD would be associated with biomarkers of greater systemic involvement including cardiovascular and indicating premareur cardiovascular aging.

Methods Frailty was determined as a Frailty Index (FI) using the 61-element comprehensive geriatric assessment questionnaire in 500 patients with stable COPD, confirmed with spirometry, and 150 non-COPD comparators. This cross-sectional study was taken from within the ARCADE study. Other assessments included body composition; handgrip strength (HGS); aortic pulse wave velocity (PWV); cardiac haemodynamics; 6 min walk distance (6MWD); Timed Up and Go (TUG) test; St George’s Respiratory Questionnaire (SGRQ) and C-reactive protein (CRP). The FI was calculated by dividing the number of deficits that the patient had by the maximum, 61

Results Patients and comparators were similar for age, BMI and gender proportion. The FI was greater in the COPD group;
mean (95% CI), 0.15 (0.14–0.16) than in comparators, 0.05 (0.03–0.05), independent of age, p

Conclusion Patients with COPD were frail compared with the comparator group of current or ex-smokers, independent of age. Frailty status in the patients was associated with a greater severity of the extra-pulmonary involvement including cardiovascular risk based on greater aortic PWV. Increased aortic PWV in frail patients was independent of blood pressure. These findings are consistent with premature cardiovascular ageing in COPD.

REFERENCE

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<td>FVC (%)</td>
<td>55.4</td>
</tr>
<tr>
<td>FEV/FVC</td>
<td>(7.6)</td>
</tr>
<tr>
<td>IC (L)</td>
<td>(0.55)</td>
</tr>
<tr>
<td>RV (L)</td>
<td>(0.06)</td>
</tr>
<tr>
<td>TLC (L)</td>
<td>(1.28)</td>
</tr>
<tr>
<td>DLco (L/mmHg)</td>
<td>7.51</td>
</tr>
<tr>
<td>DLco (%)</td>
<td>5.92</td>
</tr>
<tr>
<td>Kco</td>
<td>(2.24)</td>
</tr>
<tr>
<td>Raw</td>
<td>73.1</td>
</tr>
<tr>
<td>sRaw</td>
<td>(24.4)</td>
</tr>
<tr>
<td>IC</td>
<td>1.06</td>
</tr>
<tr>
<td>RV</td>
<td>(0.47)</td>
</tr>
<tr>
<td>TLC</td>
<td>12.89</td>
</tr>
<tr>
<td>sTLC</td>
<td>(3.25)</td>
</tr>
<tr>
<td>sRaw</td>
<td>0.09</td>
</tr>
<tr>
<td>sTLC</td>
<td>(0.02)</td>
</tr>
</tbody>
</table>

M140 EFFECT OF BETA-BLOCKADE ON LUNG FUNCTION IN A POPULATION WITH ARTERIAL VASCULAR DISEASE WITH AND WITHOUT COPD

A Key, M West, M Pary, F Tonella, S Jack, N Duffy, PP Walker. University Hospital Aintree, Liverpool, UK

10.1136/thoraxjnl-2014-206260.436

Introduction Patients are frequently prescribed β-blockers for heart failure, ischaemic heart disease and peri-operatively, especially for vascular surgery. However, β-blockers remain under prescribed in patients with COPD despite epidemiological evidence indicating little negative impact. This reluctance to use β-blockers is due to concerns about increased airway hyper-responsiveness and bronchoconstriction. As part of a study of peri-operative β-blockade in patients with abdominal aortic aneurysm (AAA) we examined the effect of β-blockers on lung function.

Methods We prospectively recruited 55 AAA patients with no selection bias for COPD or β-blocker use. Thirty eight patients successfully completed detailed lung function testing (PFT) measured by body plethysmography both on and off β-blockers. Subjects already taking β-blockers continued usual treatment while others were prescribed weight adjusted bisoprolol for 48 h.

Results Mean age was 70 (5) years and 33 (77%) subjects were male. 16/38 (42%) were already taking β-blockers and 5 people (13%) were diagnosed with COPD although 15 (39%) had COPD based on spirometry. Ten (26%) were current smokers and 19 (50%) ex-smokers. The lung function results are shown in the table. Beta-blockade had no significant impact on most lung function measures in both COPD and non-COPD subjects. Specific airways resistance (sRaw) was significantly higher when subjects were taking β-blockers but this effect did not differ between COPD and non-COPD subjects (Δ sRaw: whole group p = 0.004, COPD p = 0.025, non-COPD p = 0.031).

Discussion β-blockers had little effect on static lung function including FEV1 and specific conductance. The small change in resistance was seen in subjects with and without COPD. In this population there appears to be no reason for not using a cardio-selective β-blocker both in this peri-operative setting and for cardiac indications.

M141 IMPACT OF BETA-BLOCKADE ON EXERCISE CAPACITY AND DYNAMIC HYPERINFLATION IN PEOPLE WITH AND WITHOUT COPD AWAITING VASCULAR SURGERY

A Key, M Pary, M West, S Jack, F Tonella, N Duffy, PP Walker. University Hospital Aintree, Liverpool, UK

10.1136/thoraxjnl-2014-206260.437

Beta-blockers have a key role in the management of heart failure but have been under-utilised in people with COPD due to fear of bronchoconstriction and its impact on symptoms and function. Beta-blockers are also used peri-operatively in people undergoing vascular surgery due to improved cardiac function though this practice is contentious due to a risk of post-operative complications, particularly stroke. As part of a study looking at
the impact of beta-blockade in people under abdominal aortic aneurysm surveillance we examined the impact of beta-blockade on CPET variables and dynamic hyperinflation at peak exercise.

55 subjects were recruited though only 46 completed incremental CPET off and on beta-blockers. Mean age was 70 (6 years and 42 (91%) were male. IHD or heart failure was diagnosed in 13 people and COPD diagnosed in 7. However, 24/46 (52%) had post-bronchodilator airflow obstruction consistent with COPD (10 mild, 10 moderate and 4 severe). 18 were routinely prescribed beta-blockers (mainly bisoprolol). Those taking beta-blockers stopped treatment for the second CPET and other subjects commenced weight-adjusted bisoprolol before the second CPET.

The 25 COPD subjects had a mean FEV1 of 2.14 (0.62) L, FEV1 predicted 76 (20)% and FEV1/FVC 0.54 (0.11). The main results are shown in the table. Compared with the subjects without COPD at peak exercise the COPD subjects had slightly lower VO2, work and ventilatory equivalents but these did not differ significantly. When beta-blocked both COPD and non-COPD subjects had a lower heart rate (p < 0.001) and consequently oxygen pulse (p < 0.001) but there was a minimal effect on other variables. The COPD patients showed a greater fall in IC (p = 0.02) but the addition of a beta-blocker did not have any additional effect. The 7 subjects already diagnosed with COPD did not differ from the whole COPD group.

In an unselected clinic population with arterial vascular disease a majority of people had, mostly undiagnosed, COPD albeit predominantly mild to moderate. Continuation or commencement of beta-blockers had little effect on level of peak exercise or degree of dynamic hyperinflation. This supports the use of beta-blockers in this COPD population, both in a peri-operative setting and for a cardiac indication.

### Abstract M141 Table 1 Change in peak CPET variables and inspiratory capacity at isotime with and without beta-blockade in 46 subjects with and without COPD

<table>
<thead>
<tr>
<th>COPD (n = 25)</th>
<th>No COPD (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-blocker</td>
<td></td>
</tr>
<tr>
<td>ON</td>
<td>OFF</td>
</tr>
<tr>
<td>ON</td>
<td>OFF</td>
</tr>
<tr>
<td>Peak VO2</td>
<td></td>
</tr>
<tr>
<td>17.4</td>
<td>17.8</td>
</tr>
<tr>
<td>(3.5)</td>
<td>(3.5)</td>
</tr>
<tr>
<td>1.43</td>
<td>1.46</td>
</tr>
<tr>
<td>(0.31)</td>
<td>(0.32)</td>
</tr>
<tr>
<td>Peak VO2/kg</td>
<td></td>
</tr>
<tr>
<td>102#</td>
<td>106#</td>
</tr>
<tr>
<td>113</td>
<td>110</td>
</tr>
<tr>
<td>Peak Work</td>
<td></td>
</tr>
<tr>
<td>(2.7)</td>
<td>(2.7)</td>
</tr>
<tr>
<td>(30)</td>
<td>(30)</td>
</tr>
<tr>
<td>Peak VE/VO2</td>
<td></td>
</tr>
<tr>
<td>(3.9)</td>
<td>(3.9)</td>
</tr>
<tr>
<td>(3.8)</td>
<td>(3.8)</td>
</tr>
<tr>
<td>Peak VE/VCO2</td>
<td></td>
</tr>
<tr>
<td>(3.3)</td>
<td>(3.3)</td>
</tr>
<tr>
<td>Peak O2 Pulse</td>
<td></td>
</tr>
<tr>
<td>(2.6)</td>
<td>(2.4)</td>
</tr>
<tr>
<td>(3.7)</td>
<td>(3.7)</td>
</tr>
<tr>
<td>Peak HR</td>
<td></td>
</tr>
<tr>
<td>(15)</td>
<td>(17)</td>
</tr>
<tr>
<td>(25)</td>
<td>(19)</td>
</tr>
<tr>
<td>Δ IC isotime (mL)</td>
<td></td>
</tr>
<tr>
<td>-142 ~</td>
<td>-188 ~</td>
</tr>
<tr>
<td>-15 ~</td>
<td>-16</td>
</tr>
</tbody>
</table>

- p < 0.05 COPD vs. no COPD, # p < 0.05 on vs. off beta-blockers and ### p < 0.01 on vs. off beta-blockers

### Introduction and objectives
COPD patients have been shown to have a higher incidence of MI and stroke, than the general.2 There is also evidence that the risk of MI and stroke, in COPD patients, increases following an exacerbation.2 However, the association appears stronger between COPD exacerbations and MI, than it does between COPD exacerbations and stroke.1,2 We hypothesise that COPD patients, who are frequent exacerbators, have a higher stroke risk, than those who are infrequent exacerbators, even when stable.

### Methods
COPD patients, with a first stroke between 2004 and 2013, were identified in the UK CPRD database, as cases. Controls, were COPD patients, registered in the CPRD database, matched 1:1, to cases on age, sex and GP practice. We defined “frequent exacerbators” as COPD patients, with ≥ 2 exacerbations, resulting in treatment, per year and “infrequent exacerbators” as ≤1 exacerbation, per year. We also grouped exposure into four levels; 0, 1, 2 or ≥ 3 exacerbations, per year, to allow an analysis for trend between exacerbation number and stroke. A subgroup analysis of the association between exacerbation frequency and stroke type (ischaemic/ haemorrhagic or TIA) was also carried out. Conditional logistic regression was used for the analyses.

### Results
There were 6,441 cases and 19,523 controls. No difference was found in odds of stroke, comparing frequent and infrequent exacerbators (adjusted OR 0.95, 95% CI 0.89–1.01, p = 0.09), or in the odds for stroke of any type. However, there was a reduction in odds of stroke associated with increased number of exacerbations, per year, with evidence for a linear trend (p = 0.002) (see Table 1).

### Conclusion
These findings do not support the hypothesis that exacerbations in COPD are associated with increased stroke risk and warrant further investigation.

### Adjusted for age, sex, general practice, smoking status, family history, hypertension, heart failure, CABG, angina, B-blocker and Calcium channel blocker.

### REFERENCES

### M143 PROGRESSION OF CENTRAL ARTERIAL STIFFNESS IN COPD AFTER 2 YEARS OF OBSERVATION

1 GS Gale, 1AM AlBarrati, 1MM Munney, 1C Munney, 1RM Tal-Singer, 1JR Cockcroft, 1Di Shale. 1Wales Heart Research Institute, Cardiff University, Cardiff, UK; 2GlaxoSmithKline R and D, King of Prussia, Pennsylvania, USA

10.1136/thoraxjnl-2014-206260.439

### Background
COPD is a systemic disease with associated comorbidities including cardiovascular disease which have significant impact on morbidity and mortality. The heterogeneity of COPD has led to the concept of phenotypes; one of which may describe patients at greater cardiovascular risk. Aortic pulse wave velocity (aPWV) is a validated measure of arterial stiffness and an independent predictor of cardiovascular outcomes, and has been shown to be elevated in patients with COPD.1 We hypothesised that a subgroup of patients (progressors) would demonstrate increased aPWV over 2 years.

### Methods
The ARCADE study is a longitudinal study of cardiovascular risk and other comorbidities. Assessments include sphygmometry, BMI, aPWV and blood pressure, (BP), mean arterial

### M142 THE ASSOCIATION BETWEEN EXACERBATION FREQUENCY AND STROKE RISK, IN PATIENTS WITH COPD: A MATCHED CASE-CONTROL STUDY

CL Windsor, E Herrett, L Smeeth, J Quint. London School of Hygiene and Tropical Medicine, London, UK

10.1136/thoraxjnl-2014-206260.438

### The Association between Exacerbation Frequency and Stroke Risk, in Patients with COPD: A Matched Case-Control Study

CL Windsor, E Herrett, L Smeeth, J Quint. London School of Hygiene and Tropical Medicine, London, UK

10.1136/thoraxjnl-2014-206260.438
Abstract M143 Table 1  Baseline characteristics of patients (expressed as mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>Progressors n = 97</th>
<th>Non-progressors n = 103</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male/female)</td>
<td>48:49</td>
<td>46:57</td>
<td>0.294</td>
</tr>
<tr>
<td>Age (years)</td>
<td>66.5 ± 7.5</td>
<td>66.9 ± 6.5</td>
<td>0.669</td>
</tr>
<tr>
<td>FEV1 (L)</td>
<td>1.30 ± 0.59</td>
<td>1.33 ± 0.53</td>
<td>0.776</td>
</tr>
<tr>
<td>FVC (L)</td>
<td>2.53 ± 0.89</td>
<td>2.47 ± 0.75</td>
<td>0.614</td>
</tr>
<tr>
<td>FEV1/FVC (L)</td>
<td>0.49 ± 0.11</td>
<td>0.53 ± 0.12</td>
<td>0.044</td>
</tr>
<tr>
<td>FEV1% predicted</td>
<td>52 ± 17</td>
<td>57 ± 21</td>
<td>0.071</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>28 ± 6</td>
<td>28 ± 5</td>
<td>0.281</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>144 ± 17</td>
<td>149 ± 18</td>
<td>0.091</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>81 ± 12</td>
<td>83 ± 9</td>
<td>0.168</td>
</tr>
<tr>
<td>Mean arterial pressure (mmHg)</td>
<td>102 ± 12</td>
<td>106 ± 11</td>
<td>0.036</td>
</tr>
<tr>
<td>aPWV (m/s)</td>
<td>9.5 ± 2.2</td>
<td>10.4 ± 2.4</td>
<td>0.004</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>74 ± 11</td>
<td>76 ± 11</td>
<td>0.350</td>
</tr>
<tr>
<td>6MWT (m)</td>
<td>300 ± 98</td>
<td>309 ± 110</td>
<td>0.563</td>
</tr>
</tbody>
</table>

REFERENCES

M144 ACUTE DIETARY NITRATE SUPPLEMENTATION REDUCES THE OXYGEN COST OF SUBMAXIMAL EXERCISE IN COPD

1KJ Curtis, 1R Tanner, 2K O’Brien, 3MI Polkey, 1LM Edwards, 1NS Hopkinson. 1NIHR Respiratory Biomedical Research Unit, Royal Brompton and Harefield NHS Trust and Imperial College, London, UK; 2Centre of Human and Aerospace Physiological Sciences, King’s College, London, UK; 3Fibrosis Discovery Performance Unit, GSK Medicines Research Centre, Stevenage, UK

Introduction: The recognised link between plasma nitrite levels and exercise performance suggests a role for the nitrate-nitrite-nitric oxide pathway in facilitating exercise. Research in healthy individuals has demonstrated a reduction in the oxygen cost of exercise at submaximal workloads following nitrate supplementation. Dietary nitrate administration has been associated with reductions in blood pressure and augmented exercise performance. The effect of acute nitrate dosing on performance and metabolic parameters during cardiopulmonary exercise testing in COPD has not previously been investigated.

Objectives: To investigate the hypotheses that acute nitrate dosing would improve exercise performance, reduce the oxygen cost of submaximal exercise performance and lower arterial blood pressure in COPD patients (GOLD stage II-IV).

Methods: We performed a randomised, double-blind, placebo-controlled cross-over study comparing the effect of 140 ml of beetroot juice (containing 12.9 mmol nitrate) with a matched placebo of nitrate-depleted beetroot juice in COPD patients not receiving oral nitrates. Subjects were randomised to consume beetroot juice (BR) or placebo (PL) 3 h prior to endurance cycle ergometry, performed at 70% maximal workload assessed by a baseline incremental maximal, symptom-limited test. Blood pressure measurements were taken at baseline and immediately prior to the exercise test. After a washout period of a minimum of 7 days the protocol was repeated with the crossover beverage.

Results: 25 COPD patients were recruited of whom 21 successfully completed the study (age 68 ± 7 years; BMI 25.2 ± 5.5 kg/m²; FEV1 percentage predicted 50.1 ± 21.6%; peak VO2 during incremental cycle ergometry 18.0 ± 5.9 ml/min/kg). Diastolic blood pressure was significantly lowered by nitrate supplementation (-6.9 ± 7.8 BR vs. -1.4 ± 8.4 mmHg PL, p = 0.008). Nitrate supplementation significantly reduced oxygen consumption during equivalent isotime exercise (60–70% isotime 16.6 ± 5.6 BR vs. 17.1 ± 5.9 ml/min/kg PL, p = 0.017; 70–80% isotime 16.7 ± 5.7 BR vs. 17.2 ± 5.3 ml/min/kg PL, p = 0.010; 80–90% isotime 16.8 ± 5.7 BR, vs. 17.3 ± 5.7 ml/min/kg PL, p = 0.004). The endurance time was not significantly different between the groups (5.65 (3.90–10.40) BR vs. 6.40 (4.01–9.67) minutes PL, p = 0.50).

Conclusion: The acute administration of nitrate reduces oxygen consumption and diastolic blood pressure during equivalent exercise in COPD patients.

M145 PREVALENCE AND DETERMINANTS OF VITAMIN D DEFICIENCY IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

1DA Jolliffe, 1AR Martineau, 1WYJ James, 1KI Islam, 1CAM Mein, 1PMT Timms, 1RW Walton, 1CG Griffiths. 1Queen Mary University of London, London, UK; 2Hammersmith University Hospital, London, UK

10.1136/thoraxjnl-2014-206260.441

Background: Vitamin D deficiency may be a risk factor for exacerbations of chronic obstructive pulmonary disease (COPD). Studies investigating the prevalence and determinants of vitamin D deficiency among COPD patients in the UK are lacking.

Methods: We conducted a cross-sectional study in 278 COPD patients aged 40–85 years screened for eligibility to participate in a clinical trial of vitamin D supplementation. Lifestyle and demographic data were collected by questionnaire and a blood sample was collected for analysis of serum 25-hydroxyvitamin D (25[OH]D) concentration and DNA extraction. Serum 25(OH)D concentration was determined by liquid chromatography – tandem mass spectrometry. Thirty-seven single nucleotide polymorphisms (SNP) in 13 vitamin D-related genes (DBP, DHCRC7, CUBN, LRP2, CRTAM, LTA4 H, CYP2R1, CYP3A4, CYP27A1, CYP27B1, CYP24A1, VDR, RXRA) were typed using Taqman allelic discrimination assays. Logistic regression was used to

Moderated posters
identify environmental and genetic factors associated with risk of vitamin D deficiency (25(OH)D concentration < 50 nmol/L).

Results Mean serum 25(OH)D concentration was 45.4 nmol/L (SD 25.3); 171/278 (61.5%) participants were deficient. The following factors independently associated with increased risk of vitamin D deficiency: BMI >30 kg/m² (OR 1.87, p = 0.04) and blood draw during winter and spring seasons (OR 3.00, p < 0.01; OR 2.50, p < 0.01, respectively). The following factors independently associated with reduced risk of deficiency: consumption of a vitamin D supplement, 100–400 IU/day (OR 0.42, p < 0.01); and a sunny holiday abroad no more than 2 months prior to blood draw (OR 0.27, p = 0.02). None of the 37 SNP investigated independently associated with vitamin D deficiency.

Conclusions Vitamin D deficiency was highly prevalent among COPD patients in this study. Obesity and winter and spring sampling were risk factors for deficiency. Recent travel to a sunny country and consumption of vitamin D supplements were protective. Genetic variants in the vitamin D pathway that have previously been shown to associate with risk of vitamin D deficiency in healthy adult populations were not associated with deficiency in this patient group.

M146 VALIDATION OF FIVE NON-INVASIVE RESPIRATORY RATE MONITORS IN PATIENTS WITH COPD IN A LABORATORY SETTING

Noah Rubio, Brian McKinstry, Richard Parker, Hilary Pinnock, Christopher Weir, Janet Hanley, Claire Yerramau, Leandro Cruz-Mantoani, William Mackie, Roberto A. Rabinovich. Edinburgh Lung and the Environment Group Initiative (ELEGI), Centre for Inflammation and Research, Queens Medical Research Institute, Edinburgh, Edinburgh, UK; Centre for Population Health Sciences University of Edinburgh, Edinburgh, Edinburgh, UK; Edinburgh Clinical Trial Unit, University of Edinburgh, Edinburgh, UK; Centre for Wellbeing and Healthcare, Edinburgh Napier University, Edinburgh, UK.

Introduction There is a need of innovative models of care for patients with severe COPD and frequent AECOPD, and Telehealth (TH) is part of these programs. But current systems are limited by the parameters feasibly monitored in a domestic setting and lack of a reliable method of predicting exacerbations. Evidence from hospital based studies show that breathlessness increases during exacerbations. If respiratory rate (RR) could be reliably monitored remotely it may provide a significant advance in predicting and identifying COPD exacerbations and monitoring recovery. The aim of this study is to validate five non-invasive RR monitors (M1 to M5) in patients with COPD in a laboratory setting against a gold standard measurement of RR.

Methods and results Five RR monitors identified in the literature were selected for validation against RR measured with a gold standard method (Oxycon mobile, Carefusion) in 23 patients with COPD (13 males, age 70 ± 8.3 years, FEV1 58.3 ± 17.1% pred) during a 52 min protocol of a total of 19 activities of daily living (i.e sitting, standing, walking at different speeds, climbing stairs, lifting objects and sweeping the floor). Patients wore simultaneously the five monitors and the Oxycon mobile. RR was recorded breath by breath and averaged by minute. One minute of each activity was selected for analysis using Bland and Altman plots. Bias and limit of agreement (LoA) was established for each monitor (Figure 1). Bias and LoA for the five monitors were the following (M1 2.15 (-17.9 to 22.2), M2 3.1 (-8.7 to 14.9), M3 2.2 (-12.12 to 16.6), M4 -2.5 (-11.7 to 6.8) and M5 -1.9 (-10.8 to 6.9). Patients were compliant with the use of the five monitors.

Conclusions Monitoring RR is feasible and non-intrusive in patients with COPD. We have identified two monitors (M4 and M5) with the lowest bias and the narrower LoA. These monitors will be further investigated in a home setting.

Funded by the Chief Scientific Office, CZH/4/826.

M147 FEASIBILITY OF DELIVERING AN OCCUPATIONAL HEALTH INTERVENTION AIMED AT IMPROVING WORK PRODUCTIVITY, AMONG WORKING COPD PATIENTS

K. Kalirai, P Adab, R Jordan, JG Ayres, S Sadhra. The University of Birmingham, Birmingham, UK.

Introduction There is evidence that workplace productivity may be impaired among working patients with COPD. Occupational health (OH) interventions have been effective in improving work productivity in other chronic conditions. However, little is known about the feasibility and acceptability of such interventions among those with COPD.

Aim To assess feasibility and acceptability of an OH intervention in working COPD patients.

Methods Nested within a primary care COPD cohort (n = 1870), the study included all those who were in work (n = 309). Eligible patients were invited for an interview and assessment with an OH practitioner. The aim was to explore and identify workplace factors that may contribute to their work performance or exacerbate their condition, and to suggest approaches to minimise any respiratory symptoms and improve work capability. Recommendations are sent to the patient, and with their permission, to their GP and employer. The acceptability of the intervention to employers will be explored as a separate part of the study.

Results Of those eligible, 43 (13.9%) agreed to take part and 107 (34.6%) declined. The most common reasons for declining
investigated the feasibility of involving the employer will be further explored. were assessed. The acceptability of recommendations and feasibility factors in the work environment that could improve their symptoms and condition were identified for the majority who deliver an OH intervention to patients with COPD working in diverse occupations. Although uptake rates were low, modifying factors in the work environment that could improve their symptoms and condition were identified for the majority who were assessed. The acceptability of recommendations and feasibility of involving the employer will be further explored.

Conclusions This is the first study to assess the feasibility of delivering an OH intervention to patients with COPD working in diverse occupations. Although uptake rates were low, modifiable factors in the work environment that could improve their symptoms and condition were identified for the majority who were assessed. The acceptability of recommendations and feasibility of involving the employer will be further explored.

Abstract M148 Table 1  Table of themes

<table>
<thead>
<tr>
<th>Sub-themes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased motivation for self-management behaviours</td>
<td>Physical activity, healthy eating and quitting smoking. Raised awareness of healthy options and of current behaviours and habits, and introducing new behaviours, e.g. replacing some foods in the diet.</td>
</tr>
<tr>
<td>Use of self-management skills</td>
<td>Use of goal setting and pacing techniques to aid in behaviour change.</td>
</tr>
<tr>
<td>Increased access to information resources</td>
<td>Links to other external sources of information, providing further information on a wide range of subjects related to healthy lifestyles and COPD.</td>
</tr>
<tr>
<td>Enhanced understanding of lifestyle risk factors</td>
<td>How factors such as weight can impact on health.</td>
</tr>
</tbody>
</table>

Facilitators to gaining benefits

<table>
<thead>
<tr>
<th>Sub-themes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of action plans in TPP</td>
<td>Patients were able to register and self-monitor their progress towards goals and gain support and supervision from the nurse coach. The greatest benefit from action plans was gained where patients were motivated and committed towards a specific goal, such as losing weight or quitting smoking, but did not have a self-management strategy to implement the change.</td>
</tr>
<tr>
<td>Nurse coach contact</td>
<td>Ongoing contact through email, phone or visits provided progress checking and support for action programmes and behaviour change. The email function within TPP was used frequently by patients to support them in their use of TPP. The nurse coach was a driving force for patients’ motivation and involvement in the action programmes, improving their self-management skills and quitting tobacco. For some, this was more important than the TPP website.</td>
</tr>
<tr>
<td>Health Risk Assessment</td>
<td>Completing the HRA was beneficial for patients who had not attended PR or who had little awareness of their lifestyle risk factors.</td>
</tr>
<tr>
<td>Hand-held Personal Health Plan</td>
<td>Some patients found it more convenient and user-friendly to use the book rather than the website.</td>
</tr>
<tr>
<td>Patient’s own motivation</td>
<td>Self-motivation to make a change.</td>
</tr>
</tbody>
</table>

Barriers to gaining benefits

<table>
<thead>
<tr>
<th>Sub-themes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lack of personal contact</td>
<td>Despite the nurse support some self-motivation was required on the part of the patient to use the website, including the action plans. Some patients, particularly those who had attended Pulmonary Rehabilitation in the past, preferred the more interactive approach in PR with the opportunity to observe others doing things, rather than having to rely to a great extent on their own self-motivation and the impersonal nature of a web programme.</td>
</tr>
<tr>
<td>Lack of tailoring of information</td>
<td>Content was insufficiently tailored in terms of: overlap between information provided in TPP and that provided in other rehabilitation programmes which patients had attended; difficulty finding ways to information that was personally relevant; poor fit between patients who regard themselves as having a high level of self-management skill and the level of support provided by TPP.</td>
</tr>
<tr>
<td>Lack of user-friendliness</td>
<td>Navigation was difficult for some patients, especially through a large amount of information, making them opt for other alternatives or stop using the programme out of frustration.</td>
</tr>
<tr>
<td>Technical problems on the website</td>
<td>Problems such as links being unavailable slowed patients’ progress and caused frustration.</td>
</tr>
<tr>
<td>Physical discomfort</td>
<td>Physical discomfort sitting at a computer and poor eyesight.</td>
</tr>
</tbody>
</table>
Method Nineteen patients were recruited in two waves from May 2012–January 2013. Key selection criteria included for group 1 FEV₁ < 50% predicted and for group 2 FEV₁ <75% predicted.

Semi-structured interviews were scheduled for one month and three months after recruitment and were focused around experiences of the programme, benefits and self-management behaviours.

Qualitative data were imported into NVivo 10 and analysed through thematic content analysis. Two researchers discussed the themes and subthemes to ensure non-redundant categorization.

Results Fifteen patients were interviewed. Key benefits: increased motivation for self-management, use of self-management skills, increased access to resources and enhanced understanding of lifestyle risk factors. Benefits were facilitated by use of action plans within TPP, nurse coach support to on-going motivation and completion of a health risk assessment by those with little awareness of lifestyle risks. Barriers to gaining benefit included preference for one-to-one contact, insufficient tailoring of website content and difficulties with website navigation.

Patients most likely to benefit were those who: wanted to change but had no behavioural strategy; had little previous disease education; had an autonomous sense of self-determination.

Conclusions The programme provided good support for the action phase of behaviour change, but less so for the motivational phase. Patients who were ready to change but did not have knowledge, skills or strategies benefited the most. When implementing a behaviour change programme providers should identify whether it addresses motivation and/or behaviour and assess potential participants accordingly. People who are not ready or able to change may derive little benefit from a behavioural programme.

IPF: education, information and health status

A QUARTER OF IPF PATIENTS NOT ELIGIBLE FOR PIRFENIDONE TREATMENT DUE TO THE NICE CRITERIA SIGNIFICANTLY DECLINE OVER TIME

N Chaudhuri, CT Leonard. University Hospital of South Manchester, Manchester, UK

Introduction Pirfenidone has NICE approval and is recommended for patients with IPF if the FVC is 50–80%. We hypothesised that this would disadvantage a significant cohort of IPF patients who have moderate reduction in transfer factor despite preserved FVC.

Methods We present longitudinal data capturing 38 IPF patients who had FVC greater than 80% and not eligible for pirfenidone treatment.

Results Since NICE approval in July 2013, 43 patients were eligible for pirfenidone as per the NICE criteria and 38 (47%) patients were outside the NICE criteria. Of those outside the NICE criteria, the average FVC was 98% (81–145) and average DLCO was 58% (21–88). Sixteen (42%) patients had a DLCO <55%, nine (24%) had DLCO of 56–70% and nine (24%) with DLCO above 70%. Only nine (24%) had CT evidence of emphysema. We had one or more serial lung function results for 17 (49%) patients. A total of 9/38 (24%) patients demonstrated an absolute decline in FVC of over 10% and one patient had an absolute DLCO decline of over 15%. Only one of these patients became eligible for pirfenidone treatment.

This retrospective data demonstrates that the sole use of FVC in the NICE criteria for treating IPF disadvantages patients who demonstrate a significant reduction in transfer factor despite FVC greater than 80%. In this study this reduced transfer factor and preserved FVC can only be attributed to the presence of coexisting emphysema in 9/38 (24%) of patients. Ten (26%) IPF patients not treated with pirfenidone because they did not meet the NICE criteria demonstrate a clinically significant decline in their lung function. Despite this the majority are still not eligible for treatment with pirfenidone.

We would therefore advocate following our European partner countries and using both FVC and DLCO as per the CAPACITY criteria when assessing patient suitability for pirfenidone treatment for IPF, as the use of FVC alone with an upper limit of 80% excludes a substantial cohort of IPF patients who have preserved FVC, moderately reduced DLCO with or without the presence of coexisting emphysema and over time a quarter of these patients demonstrate lung function decline.

REFERENCES
Based on an annual unit cost of £22, 245.96 for pirfenidone (without undisclosed discount). To date 96 patients have been treated for a total of 876 months at a total cost of £1,623,955 in two and a half years.

Conclusion This study highlights both the health and economic impacts of pirfenidone over a two and a half year period of prescribing.

REFERENCES

M265 DAILY ACTIVITY MONITORING IN IDIOPATHIC PULMONARY FIBROSIS
MG Crooks, SP Hart. Hull York Medical School, Hull, UK
10.1136/thoraxjnl-2014-206260.447

Introduction Idiopathic pulmonary fibrosis (IPF) is an incurable chronic progressive lung disease with a poor prognosis. Decline in forced vital capacity (FVC) is the primary outcome measure in most clinical trials. However, slowing lung function decline does not translate into patients feeling better. We investigated the acceptability of activity monitoring as a patient centred outcome measure in IPF and correlated results with lung function and quality of life (QoL) measures.

Methods IPF Subjects underwent activity monitoring 23 h a day for a minimum of 8 days using the SenseWear armband (Bodymedia, Philadelphia). Monitoring data from the first and last 4 days were discarded to prevent clinic visits impacting the results. Participants completed the St George’s Respiratory Questionnaire (SGRQ) as a QoL measure. Lung function measurements performed within 3 months were collected and correlations assessed using Pearson’s correlation coefficient. Data are presented as mean±SD.

Results 17 IPF subjects (Age 76 ± 6.3, 82% males, FVC% predicted 82.3 ± 16.1%, TLCO% predicted 48.3 ± 13.3%) were monitored. There was excellent compliance – armbands were worn for an average of 23 h and 9 min per day (range: 22 h and 10 min to 24 h) for 6.2 ± 0.6 complete days. Activity levels measured in METs were 1.25 ± 0.2 with a daily step count of 3,364 ± 2504. IPF subjects were physically active (METs >3) for 83.8 ± 57.4 min per day. Mean daily METs inversely correlated with SGRQ score (r=-0.64, p = <0.01). Mean daily METs correlated with FVC (% predicted) (r = 0.50, p = 0.04) but there was no correlation with TLCO (% predicted) (r = 0.39, p = 0.13). Conversely TLCO inversely correlated with SGRQ score (r=-0.55, p = 0.03) but FVC did not (r=-0.29, p = 0.26).

Conclusion Activity monitoring is an acceptable, well tolerated means of measuring functional status in IPF patients. Mean daily activity level correlates well with QoL measures and FVC. Neither individual lung function measurement performed as well in terms of correlation with QoL and activity level. A larger longitudinal study is required to further evaluate the role of activity monitoring in IPF and identify its utility in prognostication.
HEALTH STATUS AND QUALITY OF LIFE IN IDIOPATHIC PULMONARY FIBROSIS

Although there was a trend towards a higher frequency of severe fatigue in sarcoidosis, no measures of dyspnoea or disease severity (spirometry abnormality, immunosuppression use or extrapulmonary disease) were associated with fatigue scores. In IPF increasing dyspnoea scores were associated with increased fatigue scores (p < 0.001).

Conclusions

Both sarcoidosis and IPF patients suffer with high levels of fatigue, although the sarcoidosis cohort showed a trend towards greater frequency of severe fatigue compared with IPF. In IPF patients increasing fatigue was associated with worsening dyspnoea, suggesting an association with disease progression, but no similar relationship was seen in sarcoidosis. This suggests that fatigue in sarcoidosis occurs independently of common markers of disease activity, whereas it occurs as a sequelae of progressive disease in IPF.

Discussion

This methodological approach to item generation will enhance the content validity of the IPF-PROM instrument. Items generated to date will be modified further by 80 patients from 4 UK centres and 20 ILD physicians participating in 3 rounds of a Qualtrics Delphi survey. This study is ongoing.


Abstract M266 Table 1

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*Key descriptors defined by focus group participants (n=4) added in Round 2

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M267 HEALTH STATUS AND QUALITY OF LIFE IN IDIOPATHIC PULMONARY FIBROSIS AND SARCOIDOSIS: EFFECT OF FATIGUE

CP Atkins, D Gilbert, C Brockwell, S Robinson, AM Wilson. Norfolk and Norwich University Hospital, Norwich, Norfolk

Introduction and Objective

Sarcoidosis and Idiopathic Pulmonary Fibrosis (IPF) are two common forms of interstitial lung disease. Sarcoidosis frequently causes extra-pulmonary disease whereas IPF specifically affects the lungs. Fatigue is a common feature of sarcoidosis, but an association between fatigue and IPF has not been investigated. We investigated the frequency and severity of fatigue in sarcoidosis and IPF, how it correlates with quality of life (QOL) scores, and whether fatigue is affected by disease severity.

Methods

This was a cross-sectional questionnaire study of patients with sarcoidosis and IPF. Questionnaire data was analysed to investigate health status, QOL, and symptom prevalence (fatigue, depression and sleepiness). Comparison of scores between groups, and an analysis of the effect of markers of disease severity on fatigue, was undertaken.

Results

Questionnaires were administered to 235 participants; 82 healthy volunteers, 76 sarcoidosis patients and 77 IPF patients. IPF patients had statistically higher St George’s Respiratory Questionnaire (p = 0.034) and Epworth Sleepiness Scale scores (p = 0.003) than sarcoidosis patients, but there was no difference in mean fatigue scores. When stratified by questionnaire scores (Table 1), including pathological fatigue levels, no statistical difference was seen between IPF and sarcoidosis, although there was a trend towards a higher frequency of severe ‘fatigue’ in sarcoidosis. Fatigue scores correlated strongly with quality of life scores (King’s Brief Interstitial Lung Disease score and St George’s Respiratory Questionnaire) in both IPF (r=-0.615 and 0.659 respectively) and sarcoidosis (r=-0.529 and 0.502).

In sarcoidosis, no measures of dyspnoea or disease severity (spirometry abnormality, immunosuppression use or extrapulmonary disease) were associated with fatigue scores. In IPF increasing dyspnoea scores were associated with increased fatigue scores (p < 0.001).

Conclusions

Both sarcoidosis and IPF patients suffer with high levels of fatigue, although the sarcoidosis cohort showed a trend towards greater frequency of severe fatigue compared with IPF. In IPF patients increasing fatigue was associated with worsening dyspnoea, suggesting an association with disease progression, but no similar relationship was seen in sarcoidosis. This suggests that fatigue in sarcoidosis occurs independently of common markers of disease activity, whereas it occurs as a sequelae of progressive disease in IPF.

Discussion

This methodological approach to item generation will enhance the content validity of the IPF-PROM instrument. Items generated to date will be modified further by 80 patients from 4 UK centres and 20 ILD physicians participating in 3 rounds of a Qualtrics Delphi survey. This study is ongoing.


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taking oxygen therapy. Patients may be left with feelings of anger at missed opportunities and concern for lost years of intervention and appropriate palliative care support.

Conclusions The diagnosis of IPF is a devastating one, which can be challenging to manage. Carers, patient groups and expert support at diagnosis were found to be invaluable to patients during this time.

M269 THE EMOTIONAL TURMOIL OF IPF
1Y Wilberley, 2Y Ochiai, 2R Pitt, 2N Mathieson. 1British Lung Foundation, London, UK; 2Boehringer Ingelheim Ltd UK, Bracknell, Berkshire, UK

10.1136/thoraxjnl-2014-206260.451

Background Our aim was to understand the emotions patients experience in IPF, from initial symptoms to IPF specialist management.

Methods Market research was conducted with an independent agency. Patients with IPF were asked to record a personal account of their experience on a hand-held camera. Face to face interviews with patients were conducted in their home. Carers were also interviewed to add an alternative perspective.

Results The sample included 13 male and 3 female patients with IPF. Patients with lung function impairment of all severities were included, five patients were treated with oxygen therapy and another had received a lung transplant.

Many patients had a very active lifestyle before developing IPF, leading to a high degree of frustration with the limitations imposed on their physical ability. A protracted time to diagnosis of a rare lung disease while symptoms progressed often led to distrust with their primary healthcare physician. Lack of expert knowledge about the condition often resulted in variable handling of the situation, with patients often finding themselves involved in a type of ‘role-reversal’ whereby they informed their primary healthcare physician about their own condition.

IPF specialists were perceived as their ‘guardian angels’. Despite being given a terminal diagnosis, patients felt reassured that they were receiving appropriate management for their condition. This stemmed from the perception that specialists treating them had appropriate knowledge and a feeling they were supported by the specialist team.

Conclusions As with other rare diseases, patients appear to gain most reassurance from HCP’s with a clear understanding of their condition. This highlights the benefit of expert multidisciplinary teams for IPF.

M270 OBTAINING INFORMATION WHEN YOU HAVE A RARE DISEASE – THE POTENTIAL FOR IPF SUPPORT GROUPS
5Y Wilberley, 1Y Ochiai, 2R Pitt, 2N Mathieson. 1British Lung Foundation, London, UK; 2Boehringer Ingelheim Ltd UK, Bracknell, Berkshire, UK

10.1136/thoraxjnl-2014-206260.452

Background The aim was to explore the ways in which patients with IPF obtain information about their condition.

Methods Market research was conducted with an independent agency. Patients with IPF were asked to record a personal account of their experience on a hand-held camera. Face to face interviews with patients were conducted in their home. Carers were also interviewed to add an alternative perspective.

Results The sample included 13 male and 3 female patients with IPF. Patients with lung function impairment of all severities were included, five patients were treated with oxygen therapy and another had received a lung transplant.

Patients reported finding information from a variety of sources, including primary healthcare professionals, patient information leaflets, the internet, district nurses and support groups. Most valued sources of information were IPF physicians, nurse specialists and patient support groups.

Gaps identified by patients were the need for high quality information including, 1) accurate and complete information about IPF, 2) clarity on the difficulty of predicting life expectancy, 3) how to access services and benefits, 4) how palliative care can help, 5) why support groups are beneficial, 6) how to modify lifestyle as capabilities change, 7) how to live and travel with oxygen and 8) how to explain oxygen to others.

Conclusions Support groups are under-developed, with great potential to help patients and their carers. Support groups are well placed to provide advice for everyday living that the healthcare community may be unable to offer. There is also a need to improve the standard of written information currently available for patients with IPF.

M271 A SURVEY OF TRAINEE EXPERIENCES IN INTERSTITIAL LUNG DISEASE
1C Sharp, 2M Gibbons. 1British Lung Foundation, London, UK; 2Royal Devon and Exeter NHS Foundation Trust, Exeter, UK

10.1136/thoraxjnl-2014-206260.453

Interstitial lung disease (ILD) is a major area of respiratory medicine. It is important that trainees gain competence and confidence in this area.

Methods A survey of BTS trainee members was conducted in November 2013 to examine training provision in ILD, including trainee’s opportunities, experience and confidence in aspects of ILD.

Results There were 104 respondents out of a possible 574.

33% of respondents were not expecting any subspecialty clinics in ILD in the course of their training. 42% of trainees expect to spend 3 months or less attending specialist clinics. Trainee attendance at MDTs is far from guaranteed, with 45% expecting to attend less than half during their period in these hospitals.

The majority of trainees are trained in performing BAL for cell differential analysis (73%), transbronchial biopsies (84%), however only 48% are confident performing transbronchial biopsies. Confidence interpreting investigation results increases with the frequency these are performed.

The self rated knowledge in a range of subject areas was also assessed and demonstrated that most areas were moderately well understood, however knowledge of the less frequently encountered IIPs was rated lower.

54% of trainees felt their ILD training was inadequate for SCE preparation. 94% would value a BTS Short Course on ILD to improve their knowledge and confidence.

Discussion This survey highlights areas where there are clear opportunities to enhance the training of registrars in ILDs. It is worth noting that some of the data is in conflict with previous BTS surveys in this area and there is the possibility of self-selection bias in the response population.

Whilst most trainees are trained in performing relevant procedures, their confidence interpreting the results of common investigations in ILD is low. To give evidence of training and
Abstract M271 Figure 1

Background Idiopathic Pulmonary Fibrosis (IPF) is an increasingly important respiratory illness in the UK. Rising prevalence of disease, emerging treatments, development of clinical guidelines for diagnosis and management and a NHS England service specification increase demands on healthcare providers who are required to enhance capacity or reconfigure services to manage patients.

Aims Estimate the patient care pathways across service providers in England compared with pathways recommended by NICE guidelines and the NHS England Service Specification; in terms of time and cost per patient by ‘diagnosis’, ‘management’ and ‘monitoring’, and then levels of reimbursement to providers for current levels of care and those recommended.

Methods Structured interviews with clinicians and coders ascertained current levels of service provision, excluding drug costs, by 14 NHS specialist ILD providers. Data were analysed utilising a bottom-up costing approach to estimate the total pathway costs. Comparison with services and costs as recommended by NICE guidelines and service specification allowed estimation of NHS providers’ profit or loss.

Results The estimated mean cost per patient for the first year of diagnosis, management and monitoring was £1,414, which is approximately £418 (42%) more than is reimbursed by the PBR tariff. By comparison, the equivalent cost of the NICE/service specification pathway is approximately £477 (41%) more than reimbursed by the tariff. In particular, it was noted that significant staff time is required for MDT discussion, but that this is not reimbursed.

Conclusions Results suggest that current NHS tariffs for ILD are insufficient to support current service provision. This is true for current levels of care as well as for the levels of care required to enhance capacity or reconfigure services to manage patients.
recommended by NICE. The risks of failure to amend the NHS tariff are:

1. Incomprehensive diagnosis and management may adversely impact patient care and outcomes, at a time when services are under increasing scrutiny and disease prevalence is rising
2. Adverse impact on the financial viability of specialist ILD providers

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Abstract M272 Figure 1. Mean cost and reimbursement for 9 providers included in this study (range as black bars), and for the cost recommended by NICE guidelines and draft NHS England Service Specification.
The number next to the author indicates the page number, not the abstract number.

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Professor Louise Donnelly  Dr Nick Hopkinson  Dr Tom Wilkinson
Dr Iolo Doull  Dr Gisli Jenkins  Dr Duncan Wilson
Dr Neil Greening  Professor Simon Johnson

The Society’s Specialist Advisory Groups also provided suggestions for symposia content.

Topic Leaders, who organised the symposia, were:

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