Objectives of this session

1. To review the **global epidemiology** of bronchiectasis

2. To review the current evidence for treatments

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4. To explore the **future** for patients with bronchiectasis
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Vicious Cycle

**AIRWAY DYSFUNCTION**
- Mucus inspissation, retention and plugging
- Impaired mucociliary clearance
- Innate & adaptive immune deficits

**INFECTION**
- Chronic infection
- Exacerbations
- Inflammation
- Clinical symptoms
- Changes in pulmonary physiology

**INFLAMMATION**
- Microorganism acquisition, colonisation & infection
- Neutrophil-mediated inflammation & neutrophil derived proteases (e.g. NE)

**STRUCTURAL DAMAGE**
- Anatomical distortion
- Lung injury – Bronchi & Parenchyma
- Loss of cilia & mucociliary function
- Destruction of the bronchial wall
- Mucus retention

Some causes have been known for centuries...

**TUBERCULOSIS**

**2400 BC**
Egyptian mummies reveal skeletal deformities typical of TB

**TUBERCULOSIS**

**~2000 BC**
First documented descriptions of TB (ancient Babylonian, Chinese and Indian texts)

**PERTUSSIS**

**1819**
Rene Laennec used his invention (stethoscope) to describe a 3 year old who died after pertussis
BRONCHIECTASIS
1880s
William Osler described clinical features of bronchiectasis and died of it

PRIMARY CILIARY DYSKINESIA
1904
First description of PCD by A. K. Zivert; first report published on the subject in 1933 by Manes Kartagener

ABPA + CVID
1950s
Initial reports by Dr Hinson and Dr Janeway on allergic bronchopulmonary aspergillosis (ABPA) and CVID respectively
CFTR

1989

Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene identified by geneticist Lap-Chee Tsui and colleagues

PCD GENES

2010

Identification of causative mutations in primary ciliary dyskinesia by Gaëlle Pennarun and colleagues
Registries - an international view

| registries are the state of the art |
Aetiology - an international view
Australian Bronchiectasis Registry

Patient registrations

- 0.5%
- 6%
- 27%
- 28%
- 38%

1297+ Patients

23 Sites

(New Zealand 7+ sites)

Sites per state

- 2
- 3
- 3
- 4
- 7
- 0

Never smokers: 66.4%
Ever smokers: 12.9%
Pack years >10: 8.5%
Unknown: 20.7%
Rhinosinusitis: 21%
Asthma: 27%
COPD: 10%
Cancer: 8%
Aetiology

- Other
- CTD
- PCD
- ABPA
- COPD
- Asthma
- Immunodeficiency
- Post-infective
- Idiopathic

Gao et al. Respirology 2016
Severity Scores

**BSI - Bronchiectasis Severity Index**

- **FEV1** % predicted
- Age
- **Colonisation** with other microorganisms
- **Exacerbations** in previous year
- MRC **Dyspnoea** score
- Hospital admission in previous year
- Pseudomonas aeruginosa colonization
- Radiological severity
- Body mass index (BMI)

**FACED**

- **F** - **FEV1**
- **A** - Age
- **C** - **Colonisation**
- **E** - **Exacerbation**
- **D** - **Dyspnoea**
## BSI and outcomes

<table>
<thead>
<tr>
<th>Severity Marker</th>
<th>HR (95% CI) for Hospital Admissions during Follow-up</th>
<th>HR (95% CI) for Mortality</th>
<th>Score Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50-69</td>
<td>1.38 (0.73-2.56)</td>
<td>2.21 (0.28-17.5)</td>
<td>2</td>
</tr>
<tr>
<td>70-79</td>
<td>1.56 (0.70-3.82)</td>
<td>8.57 (1.15-63.83)</td>
<td>4</td>
</tr>
<tr>
<td>80+</td>
<td>1.76 (0.89-3.50)</td>
<td>23.16 (3.09-173.7)</td>
<td>6</td>
</tr>
<tr>
<td>BMI</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;18.5</td>
<td>1.23 (0.73-2.08)</td>
<td>2.25 (1.09-4.67)</td>
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</tr>
<tr>
<td>18.5-25</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>2</td>
</tr>
<tr>
<td>26-29</td>
<td>0.90 (0.62-1.30)</td>
<td>0.91 (0.46-1.81)</td>
<td>0</td>
</tr>
<tr>
<td>≥30</td>
<td>1.14 (0.76-1.70)</td>
<td>1.38 (0.68-2.81)</td>
<td>0</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;80</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>0</td>
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<tr>
<td>50-80</td>
<td>1.17 (0.74-1.85)</td>
<td>1.34 (0.67-2.67)</td>
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</tr>
<tr>
<td>30-49</td>
<td>1.40 (0.68-2.85)</td>
<td>1.58 (0.72-3.46)</td>
<td>2</td>
</tr>
<tr>
<td>&lt;30</td>
<td>1.52 (1.03-2.25)</td>
<td>4.47 (1.60-12.53)</td>
<td>3</td>
</tr>
<tr>
<td>Hospital admission before study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>13.5 (9.40-19.46)</td>
<td>2.43 (1.30-4.53)</td>
<td>5</td>
</tr>
<tr>
<td>Exacerbations before the study</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>0</td>
</tr>
<tr>
<td>1-2</td>
<td>1.67 (0.78-3.58)</td>
<td>1.78 (0.80-3.98)</td>
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</tr>
<tr>
<td>3 or more</td>
<td>2.25 (0.89-5.70)</td>
<td>2.03 (1.02-4.03)</td>
<td>2</td>
</tr>
<tr>
<td>MRC dyspnea score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>2.42 (1.66-3.52)</td>
<td>1.05 (0.50-2.20)</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>2.69 (1.59-4.53)</td>
<td>1.15 (0.50-2.63)</td>
<td>3</td>
</tr>
<tr>
<td>Pseudomonas colonization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>2.16 (1.36-3.43)</td>
<td>1.58 (0.75-3.34)</td>
<td>3</td>
</tr>
<tr>
<td>Colonization with other organisms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>0</td>
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<tr>
<td>Yes</td>
<td>1.66 (1.12-2.44)</td>
<td>1.10 (0.54-2.24)</td>
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<tr>
<td>Radiological severity: ≥3 lobes involved or cystic bronchiectasis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1.0 (reference)</td>
<td>1.0 (reference)</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>1.48 (1.02-2.15)</td>
<td>1.05 (0.57-1.94)</td>
<td>1</td>
</tr>
</tbody>
</table>

### BSI and outcomes

<table>
<thead>
<tr>
<th>Severity Marker</th>
<th>Score Points</th>
</tr>
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<tbody>
<tr>
<td>Age, yr</td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>0</td>
</tr>
<tr>
<td>50-69</td>
<td>2</td>
</tr>
<tr>
<td>70-79</td>
<td>4</td>
</tr>
<tr>
<td>80+</td>
<td>6</td>
</tr>
<tr>
<td>BMI &lt;18.5</td>
<td>0</td>
</tr>
<tr>
<td>18.5-25</td>
<td>2</td>
</tr>
<tr>
<td>26-29</td>
<td>0</td>
</tr>
<tr>
<td>30 or more</td>
<td>2</td>
</tr>
<tr>
<td>FEV₁ % predicted ≥80</td>
<td>0</td>
</tr>
<tr>
<td>50-80</td>
<td>1</td>
</tr>
<tr>
<td>30-49</td>
<td>2</td>
</tr>
<tr>
<td>&lt;30</td>
<td>0</td>
</tr>
<tr>
<td>Hospital admission</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>2</td>
</tr>
<tr>
<td>Exacerbations before</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1-2</td>
<td>5</td>
</tr>
<tr>
<td>3 or more</td>
<td>0</td>
</tr>
<tr>
<td>MRC dyspnea score</td>
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</tr>
<tr>
<td>1-3</td>
<td>0</td>
</tr>
<tr>
<td>4, 5</td>
<td>0</td>
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<tr>
<td>Pseudomonas colonization</td>
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</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
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<td>Colonization with other organisms</td>
<td></td>
</tr>
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<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>3</td>
</tr>
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<td></td>
</tr>
<tr>
<td>cystic bronchiectasis</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>0</td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
</tr>
</tbody>
</table>

**0 - 4 Mild Bronchiectasis**
- 1 year outcomes: 0 – 2.8 % mortality rate, 0 – 3.4 % hospitalisation rate
- 4 year outcomes: 0 – 5.3 % mortality rate, 0 – 9.2 % hospitalisation rate

**5 – 8 Moderate Bronchiectasis**
- 1 year outcomes: 0.8 – 4.8 % mortality rate, 1.0 – 7.2 % hospitalisation rate
- 4 year outcomes: 4 % – 11.3 % mortality rate, 9.9 – 19.4 % hospitalisation rate

**9 + Severe Bronchiectasis**
- 1 year outcomes: 7.6 % – 10.5 % mortality rate, 16.7 – 52.6 % hospitalisation rate
- 4 year outcomes: 9.9 – 29.2 % mortality, 41.2 – 80.4 % hospitalisation rate
Disease Severity - ABR

- **FACED**
  - MILD: 41%
  - MODERATE: 42%
  - SEVERE: 17%
  - Faced: n=310

- **BSI**
  - MILD: 16%
  - MODERATE: 26%
  - SEVERE: 58%
  - BSI: n=290

- Restrictive Pattern: 21%
- Airflow Obstruction: 60%
- Normal Spirometry: 19%
- Other 4%
  - Restrictive Pattern: 20%
  - Airflow Obstruction: 40%
  - Normal Spirometry: 36%
Evidence-based approach

Stepwise Management Approach

- **Airway clearance techniques**
- **Long-term antibiotic therapy**
- **Anti-inflammatory therapy**
- **Therapies in advanced disease**

General management (applies at all stages of disease):
- Vaccination against influenza and pneumococcus
- Manage co-morbidities and underlying cause
- Pulmonary rehabilitation
- Prompt treatment of exacerbations
- Sputum surveillance of *Pseudomonas aeruginosa* and non-tuberculous *Mycobacteria*

**Mild severity**

- **Daily physiotherapy**

**Moderate severity or persistent symptoms despite standard care**

- Consider macrolides for patients with frequent exacerbations
- **Regular physiotherapy+adjuncts (devices/hyperosmolar agents)**

**Long-term oxygen therapy, lung transplantation, surgery**

- Inhaled corticosteroids in selected patients
- Macrolides for patients with frequent exacerbations
- Inhaled antibiotics particular with *Pseudomonas aeruginosa* colonisation

**Severe bronchiectasis or persistent symptoms despite standard care**

- **Regular physiotherapy+adjuncts (devices/hyperosmolar agents)**
Stepwise management

Antibiotics are used to treat exacerbations that present with an acute deterioration (usually over several days) with worsening local symptoms (cough, increased sputum volume or change of viscosity, increased sputum purulence with or without increasing wheeze, breathlessness, haemoptysis) and/or systemic upset. The flow diagram refers to three or more annual exacerbations.
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3. To review the value of a **treatable traits** approach to managing the individual patient with bronchiectasis

4. To explore the **future** for patients with bronchiectasis
Treatment strategies with high level evidence of effect for bronchiectasis are limited by heterogeneity

1. Macrolides for frequent exacerbations
2. Exercise and airway clearance
3. Vaccination Flu and pneumococcal disease
Macrolides reduce exacerbations

A significant reduction in the number of participants with exacerbations in the long-term macrolides group compared with control group.

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Macrolides</th>
<th>Control</th>
<th>Risk Ratio</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events</td>
<td>Total</td>
<td>Weight</td>
<td>M-H, Fixed, 95% CI</td>
</tr>
<tr>
<td>Altenburg 2013</td>
<td>20</td>
<td>43</td>
<td>22.1%</td>
<td>0.58 (0.41–0.83)</td>
</tr>
<tr>
<td>Cymbala 2005</td>
<td>2</td>
<td>11</td>
<td>5.3%</td>
<td>0.25 (0.07–0.92)</td>
</tr>
<tr>
<td>Koh 1997</td>
<td>0</td>
<td>13</td>
<td>1.7%</td>
<td>0.19 (0.01–3.52)</td>
</tr>
<tr>
<td>Liu 2012</td>
<td>1</td>
<td>24</td>
<td>2.1%</td>
<td>0.31 (0.03–2.72)</td>
</tr>
<tr>
<td>Serisier 2013</td>
<td>39</td>
<td>59</td>
<td>28.2%</td>
<td>0.91 (0.72–1.16)</td>
</tr>
<tr>
<td>Tsang 1999</td>
<td>0</td>
<td>11</td>
<td>1.7%</td>
<td>0.18 (0.01–3.41)</td>
</tr>
<tr>
<td>Wong 2012</td>
<td>44</td>
<td>71</td>
<td>38.9%</td>
<td>0.75 (0.61–0.92)</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>232</td>
<td>223</td>
<td>100.0%</td>
<td>0.70 (0.60–0.82)</td>
</tr>
<tr>
<td>Total events</td>
<td>106</td>
<td>147</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 10.48, df = 6 (P = 0.11); I² = 43%
Test for overall effect: Z = 4.63 (P < 0.00001)

Pulmonary Rehabilitation in Individuals With Non—Cystic Fibrosis Bronchiectasis: A Systematic Review

A CRM | Archives of Physical Medicine and Rehabilitation
Journal homepage: www.archives-pmr.org
Archives of Physical Medicine and Rehabilitation 2012;93:774-82

REVIEW ARTICLE (META-ANALYSIS)

Pulmonary Rehabilitation in Individuals With Non—Cystic Fibrosis Bronchiectasis: A Systematic Review

Annemarie L. Lee, PhD,1,4,5 Catherine J. Hill, PhD,1,6 Christine F. McDonald, PhD,1,6 Anne E. Holland, PhD1,6

From the 1West Park Rehabilitation Centre, Toronto, Ontario, Canada; 2Department of Physical Therapy, University of Toronto, Toronto, Ontario, Canada; 3Institute for Breathing and Sleep, and Departments of 4Physiotherapy and 5Respiratory and Sleep Medicine, Austin Health, Heidelberg, Victoria, Australia; 6Department of Physiotherapy, Alfred Health, Melbourne, Victoria, Australia, and 7Physiotherapy, Department of Rehabilitation, Nutrition and Sport, La Trobe University, Melbourne, Victoria, Australia.
Recent trials

Some disappointing results for inhaled therapies:

- **RESPIRE-** inhaled DPI Ciplox
  - BPAExac ++
  - Chosen trait was airway infection
  - 4 trial arms- inconsistent results

- **AIRBX-** aztreonam
  - 2 replicate trials
  - Chosen trait airway infection
  - Inconsistent results

- **Bronchitol-** dry powder mannitol
  - RCT
  - Chosen trait was retained secretions
  - Failed to reduce exacerbations (primary end point)
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Overlap with Asthma

Clear overlap with suggestion of causality for Bx/asthma

- 7% General population
- >25% Bronchiectasis clinic
- 40% radiological BX
- 20% clinically significant BX
- 8% Pulmonary trait SAWD

Difficult to treat asthma

McDonald et al Respirology 2019
Gupta et al Chest 2009
Overlap with COPD

Clear overlap with plausible causality for Bx/ COPD

Severe COPD

Bronchiectasis

Bx 60%

Airflow obstruction 40%

Overlap with COPD (cont’d)

COPD and bronchiectasis has increased mortality

--- COPD without bronchiectasis (n=86; 8 deaths)
- - - - COPD with bronchiectasis (n=115; 43 deaths)
Overlap with COPD (cont’d)

<table>
<thead>
<tr>
<th>Study</th>
<th>ID</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garcia-Vidal C (2009)</td>
<td></td>
<td>1.27 (0.99, 1.64)</td>
<td>18.45</td>
</tr>
<tr>
<td>Bafadhel M (2011)</td>
<td></td>
<td>0.97 (0.93, 1.02)</td>
<td>27.51</td>
</tr>
<tr>
<td>Martinez-Garcia MA (2011)</td>
<td></td>
<td>3.87 (1.38, 10.50)</td>
<td>2.99</td>
</tr>
<tr>
<td>Eman O. Arram (2012)</td>
<td></td>
<td>3.61 (1.33, 9.83)</td>
<td>3.07</td>
</tr>
<tr>
<td>Stewart JI/ (2012)</td>
<td></td>
<td>1.13 (1.06, 1.25)</td>
<td>26.52</td>
</tr>
<tr>
<td>Tulek B (2013)</td>
<td></td>
<td>1.77 (1.26, 2.53)</td>
<td>14.09</td>
</tr>
<tr>
<td>Sadigov AS (2014)</td>
<td></td>
<td>1.80 (1.00, 3.24)</td>
<td>7.36</td>
</tr>
<tr>
<td>Overall (I-squared = 84.7%, p = 0.000)</td>
<td></td>
<td>1.31 (1.09, 1.58)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis

| Bronchiectasis plus COPD predicts severe airflow obstruction |
Overlap (COPD)

| Bronchiectasis plus COPD predicts severe airflow obstruction |
### Overlap (COPD)

**Bronchiectasis plus COPD predicts exacerbations**

<table>
<thead>
<tr>
<th>Study ID</th>
<th>ES (95% CI)</th>
<th>% Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martinez-Garcia MA (2011)</td>
<td>3.07 (1.07, 8.77)</td>
<td>8.98</td>
</tr>
<tr>
<td>Eman O. Arram (2012)</td>
<td>4.75 (1.67, 13.52)</td>
<td>9.04</td>
</tr>
<tr>
<td>Stewart JI (2012)</td>
<td>1.04 (1.01, 1.30)</td>
<td>20.13</td>
</tr>
<tr>
<td>Martine-Garcia MA (2013)</td>
<td>2.34 (1.36, 4.01)</td>
<td>15.31</td>
</tr>
<tr>
<td>Tulek B (2013)</td>
<td>2.08 (1.20, 3.60)</td>
<td>15.19</td>
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<tr>
<td>Sadigoy AS (2014)</td>
<td>2.20 (1.31, 3.70)</td>
<td>15.62</td>
</tr>
<tr>
<td>Jairam PM (2015)</td>
<td>1.50 (0.90, 2.50)</td>
<td>15.74</td>
</tr>
<tr>
<td><strong>Overall</strong> (I-squared = 80.2%, p = 0.000)</td>
<td>1.97 (1.29, 3.00)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**NOTE:** Weights are from random effects analysis.

Fig 2. Odd ratios for the association between comorbid bronchiectasis and risk for COPD exacerbations.
Overlap (COPD)

Bronchiectasis plus COPD predicts pathogenic microorganism

Fig 3. Odd ratios for the association between comorbid bronchiectasis and risk for isolation of a potentially pathogenic microorganism.
Identification of traits helps...
Frequent exacerbator phenotype

- NTM
- Connective Tissue Disease
- Post Infective
- P. aeruginosa
- Obstruction
- Severe Exacerbation
- Functional impairment

- A1ATD
- ABPA
- Cystic
- Neutrophilic
- Sputum colour
- Eosinophilic

- IBD
- COPD
- Idiopathic
- PCD
- Increased Mortality

- Underlying Disorders
- Unknown Outcomes

- Linked to clinical outcomes
- Exercise intolerance
- Immuno-deficiency

- Frequent exacerbator phenotype
Exercise Intolerance

Linked to clinical outcomes

Underlying Disorders

Increased Mortality

Unknown Outcomes

Idiopathic

COPD

Obstruction

Post Infective

PCD

Cystic

Neutrophilic

Eosinophilic

Sputum colour

P. aeruginosa

Frequent Exacerbation

Connective Tissue Disease

Functional impairment

Severe Exacerbation

Exercise Intolerance

A1ATD

Immunodeficiency

IBD

NTM

Frequent Exacerbation

Post Infective

Infective

COPD

Obstruction

Unknown Outcomes

Idiopathic

PCD

Cystic

Neutrophilic

Eosinophilic

Sputum colour

P. aeruginosa

Frequent Exacerbation

Connective Tissue Disease

Functional impairment

Severe Exacerbation

Exercise Intolerance

A1ATD

Immunodeficiency
Treatable traits

Tweetable abstract @ERSpublications

A discussion of the concept of “treatable traits” as a way towards precision medicine of chronic airway diseases http://ow.ly/UbJAm

I cannot say whether things will get better if we change; what I can say is they must change if they are to get better.

“G.C. Lichtenberg (quoted in [1])”
Treatale traits: toward precision medicine of chronic airway diseases

Alvar Agusi1, Elisabeth Bel2, Mike Thomas3, Claus Vogelmeier4, Guy Brusselle5,6, Stephen Holgate7, Marc Humbert8, Paul Jones9, Peter G. Gibson10, Jørgen Vestbo11, Richard Beasley12 and Ian D. Pavord13
Treatable traits

Some important traits that could be treated:

- Airflow obstruction
- Eosinophilia
- Frequent exacerbators
- CTD
Treatable traits

P. aeruginosa infection is associated with worse clinical outcomes in bronchiectasis

- Increased exacerbation frequency
- Increased hospitalisation (OR 6.6)
- Worse quality of life
- Increased mortality (OR 2.9)

P. aeruginosa and mortality
Long-term benefits of airway clearance in bronchiectasis: a randomised placebo-controlled trial

Gerard Muñoz, Javier de Gracia, María Buxó, Antonio Alvarez, Montserrat Vendrell
European Respiratory Journal 2018 51: 1701926; DOI: 10.1183/13993003.01926-2017

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Macrolides</th>
<th>Control</th>
<th>M-H. Ratio</th>
<th>Risk Ratio</th>
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<td>Koh 1997</td>
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<td>Liu 2012</td>
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<td>Tsang 1999</td>
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<td>Wong 2012</td>
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<td>Total (95% CI)</td>
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<td>Total events</td>
<td>106</td>
<td>147</td>
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</table>

Heterogeneity: Chi² = 10.48, df = 6 (P = 0.11); I² = 43%
Test for overall effect: Z = 4.63 (P < 0.00001)
Long-term macrolides for non-cystic fibrosis bronchiectasis: A systematic review and meta-analysis

<table>
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<tr>
<td>Wong 2012</td>
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<td>46</td>
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<td>Total (95% CI)</td>
<td>19</td>
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</table>

Heterogeneity: Chi² = 1.14, df = 1 (P = 0.29); I² = 12%
Test for overall effect: Z = 0.51 (P = 0.61)
5 Approach to the management of stable bronchiectasis in adults

High sputum burden/difficulty expectorating*
Mucoactive agents

Frequent or severe exacerbations*
Macrolides and/or inhaled antibiotics

Concomitant asthma/COPD*
ICS/LABD†

New Pseudomonas aeruginosa*
Antibiotics for eradication

Treatable underlying cause*
Treat

Key management strategies
- Airway clearance
- Smoking cessation
- Vaccination
- Sputum cultures
- Consider pulmonary rehabilitation

COPD = chronic obstructive pulmonary disease; ICS = inhaled corticosteroid; LABD = long-acting bronchodilator. * Specialist referral recommended. † ICS/LABD should not be routinely prescribed in patients with bronchiectasis unless they have underlying asthma or COPD.
Bronchiectasis is common and burdensome

There is a subgroup at highest risk for poor outcomes

- Frequent exacerbators

Best chance of improving outcomes for those at highest risk for poor outcomes

- Identify treatable traits
- Treat treatable traits
- Precision medicine
Objectives of this session

1. To review the **global epidemiology** of bronchiectasis

2. To review the current evidence for treatments

3. To review the value of a **treatable traits** approach to managing the individual patient with bronchiectasis

4. To explore the future for patients with bronchiectasis
Where do we go from here?

The Future

NEXT EXIT
What organism is the strongest predictor of bad outcomes for patients with Bronchiectasis?

A) H influenzae  
B) H1N1  
C) Pseudomonas sp  
D) Staph Sp
What organism predicts bad outcomes for patients with Bronchiectasis?

A) H influenzae
B) H1N1
C) Pseudomonas sp
D) Staph Sp
Which treatments are currently best practice for the “Frequent Exacerbator” with bronchiectasis?

- A) airway clearance
- B) ICS/LABA and airway clearance
- C) long term macrolides and airway clearance
- D) long term macrolides and mucolytics
Which treatment are currently best practice for the “Frequent Exacerbator” with bronchiectasis?

A) airway clearance
B) ICS/LABA and airway clearance
C) long term macrolides and airway clearance
D) long term macrolides and mucolytics
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Learn More: athens.chestnet.org
## Minimum Tests

<table>
<thead>
<tr>
<th>Investigation*</th>
<th>Significance</th>
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</thead>
<tbody>
<tr>
<td>Full blood count and differential white cell count</td>
<td>Neutropenia/lymphopenia/lymphocytosis may suggest immune deficiency; eosinophilia suggests asthma or ABPA</td>
</tr>
<tr>
<td>Serum total IgE, specific IgG and IgE to <em>Aspergillus</em> (± <em>Aspergillus</em> skin prick testing)</td>
<td>Total IgE &gt; 1000 IU/mL and positive <em>Aspergillus</em> serology is consistent with ABPA</td>
</tr>
<tr>
<td>Serum IgG, IgM, IgA</td>
<td>Low immunoglobulin levels suggest a primary (eg, CVID) or secondary immunodeficiency state</td>
</tr>
<tr>
<td>Sputum MCS and AFB</td>
<td>To document microbiology and direct future antibiotic treatment</td>
</tr>
<tr>
<td>Spirometry</td>
<td>To document baseline lung function and allow monitoring</td>
</tr>
<tr>
<td>Oximetry</td>
<td>To document baseline oxygen saturations, allow monitoring, guide further tests (eg arterial blood gas) and guide treatment</td>
</tr>
</tbody>
</table>