EUROPEAN RESPIRATORY SOCIETY
ERS INTERNATIONAL CONGRESS 2015
AMSTERDAM netherlands, 26–30 september

Symposium: Bronchiectasis in Europe: an update from the European Bronchiectasis Network (EMBARC)

Understanding the heterogeneity of the disease

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Health Science Department
University of Milan Bicocca, Milan, Italy

Bronchiectasis
as a radiological diagnosis

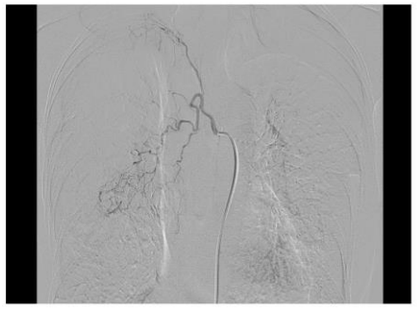
Bronchiectasis
as a DISEASE

Chronic cough **Purulent sputum** **Recurrent LRTI**

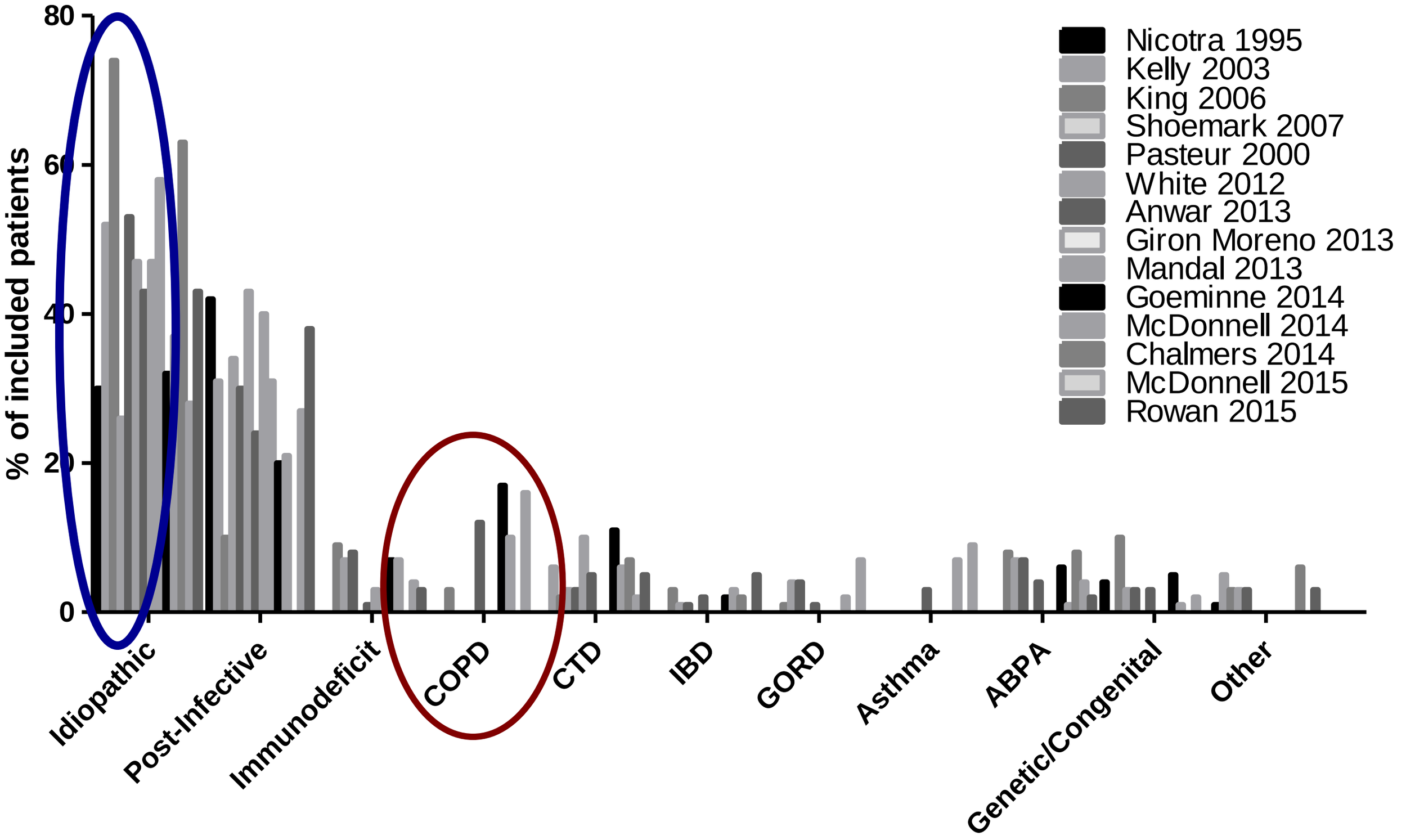
Haemoptysis **Wheeze** **Tiredness**

LRTI: low respiratory tract infections

The heterogeneity of bronchiectasis

Radiology						
Signs Symptoms	Chronic Productive cough	Recurrent Exacerbations	Recurrent pneumonia	Haemoptysis	Wheeze	Very mild S/S
Pulmonary Function	Completely normal	FEV_1 50-80%	FEV_1 35-50%	FEV_1 < 35%		
Etiology						

Disorders predisposing to bronchiectasis



CTD: connective tissue diseases; IBD: inflammatory bowel disease; GORD: gastro-oesophageal reflux disease, ABPA: allergic bronchopulmonary aspergillosis

Disorders predisposing to bronchiectasis

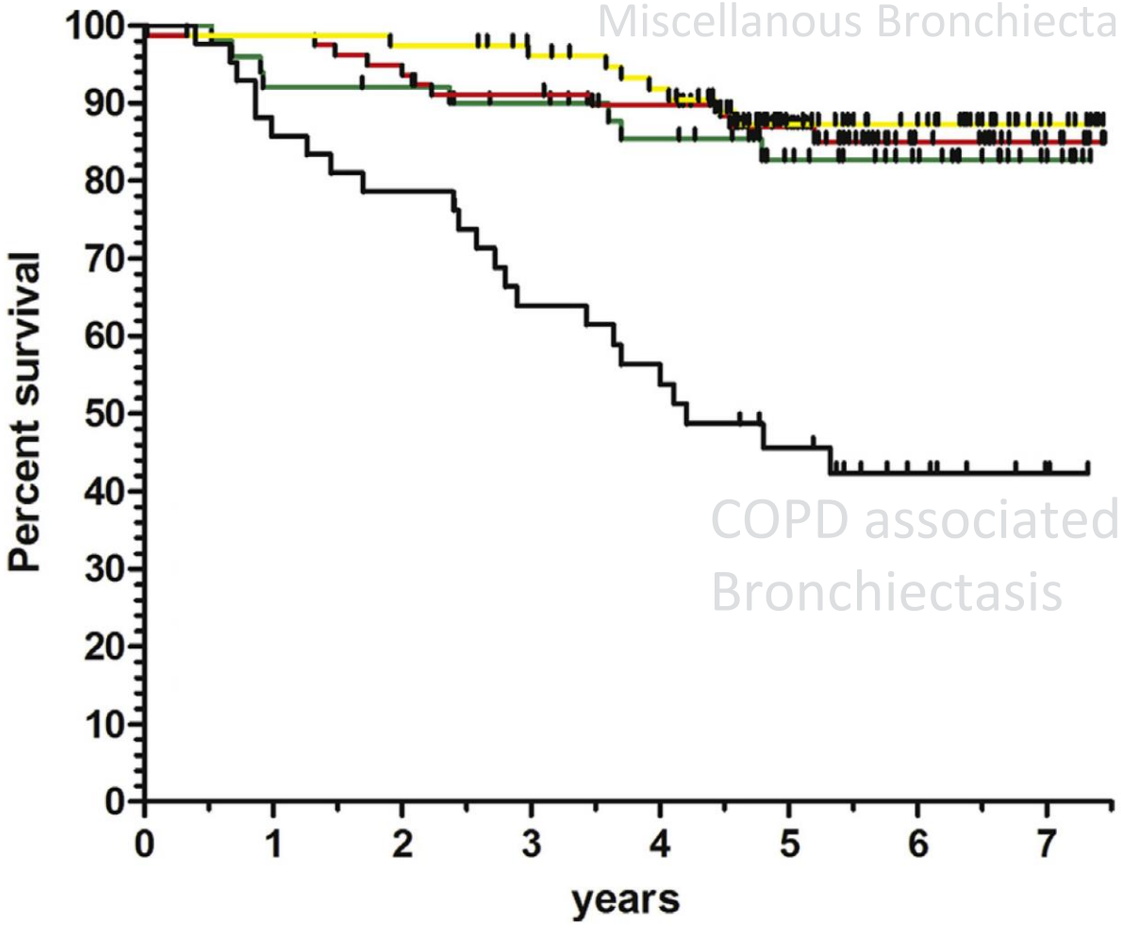
	Dundee (UK) 286 pts	Newcastle (UK) 110 pts	Leuven (Belgium) 253 pts	Galway (Ireland) 208 pts	Monza (Italy) 205 pts	Athens (Greece) 113 pts	Barcelona (Spain) 83 pts
Post-infective	18%	5%	19%	20%	25%	43%	15%
COPD	2%	12%	16%	13%	15%	5%	7%
CTD	9%	10%	13%	21%	2%	6%	3%
Immunodeficiency	6%	8%	7%	6%	4%	5%	5%
Asthma	0	7%	0	10%	2%	2%	7%
ABPA	11%	1%	6%	2%	2%	0	1%
Ciliary dysfunction	0.3%	1%	3%	3%	0.5%	2%	2%
IBD	2%	2%	2%	2%	3%	0	0
Aspiration/GORD	0	0	0	4%	0	0	0
Other	0.7%	1%	2%	2%	0.5%	0.9%	1%
Idiopathic	51%	54%	31%	18%	44%	37%	58%

CTD: connective tissue diseases; IBD: inflammatory bowel disease; GORD: gastro-oesophageal reflux disease, ABPA: allergic bronchopulmonary aspergillosis

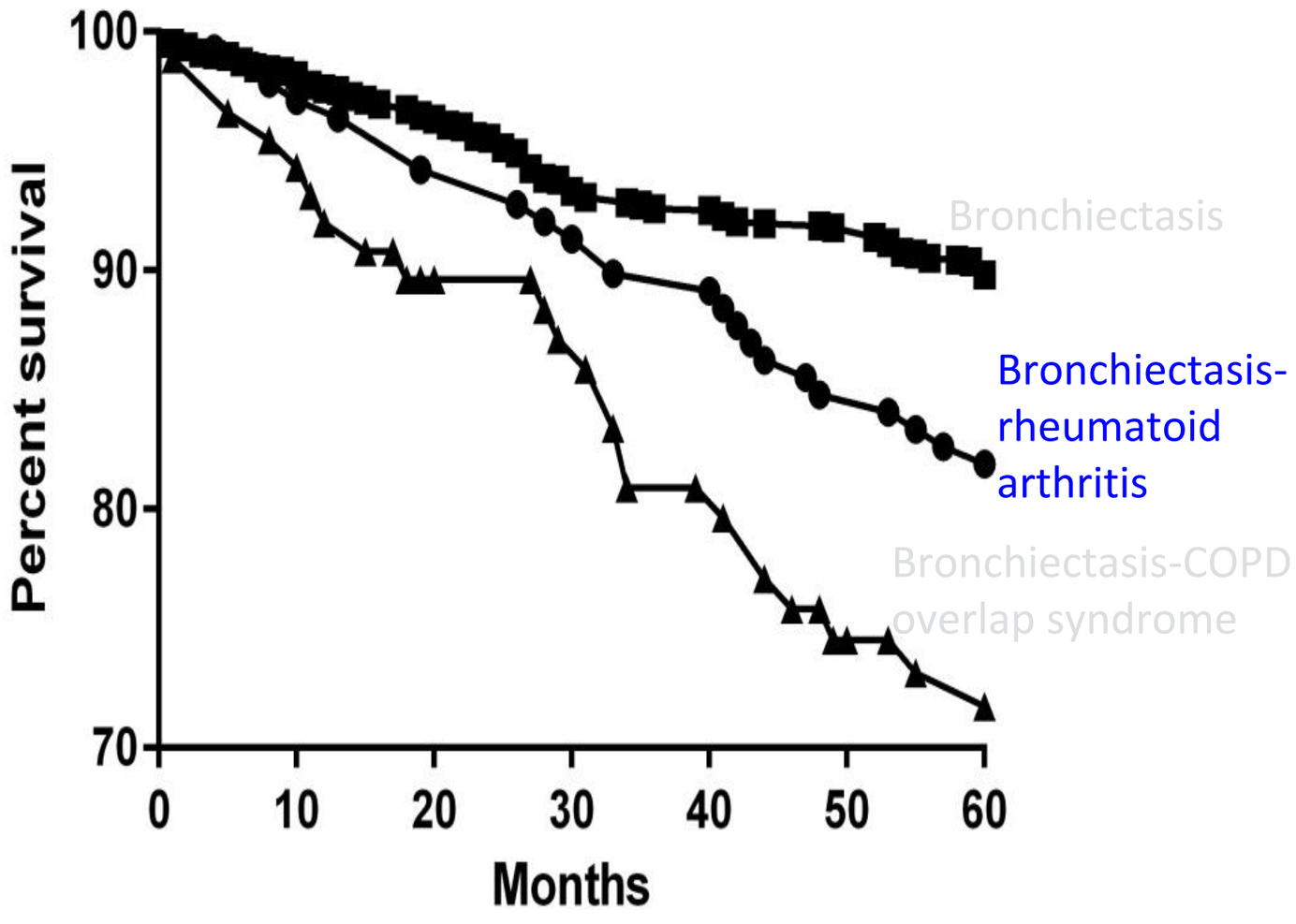
Lonni S et al. Submitted

Disorders predisposing to bronchiectasis

Impact on outcomes



Goeminne PC et al. Respir Med 2014;108:287



De Soyza A et al *Submitted*

Disorders predisposing to bronchiectasis

Concerns

1) Different definitions across literature and across centers

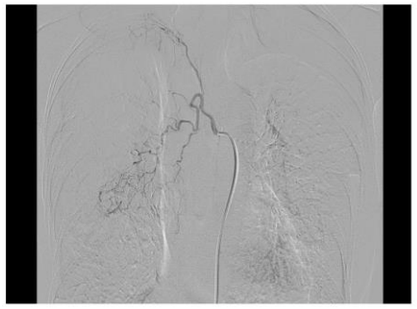
1) Long-term retrospective recall

1) Sometimes, more than one predisposing factor may be identified

1) Even where the underlying cause is identified, the reasons why certain individuals develop bronchiectasis in association with these disorders are largely unknown

The heterogeneity of bronchiectasis

Radiology



Signs Symptoms

Chronic Productive cough

Recurrent Exacerbations

Recurrent pneumonia

Haemoptysis

Wheeze

Very mild S/S

Pulmonary Function

Completely normal

FEV_1 50-80%

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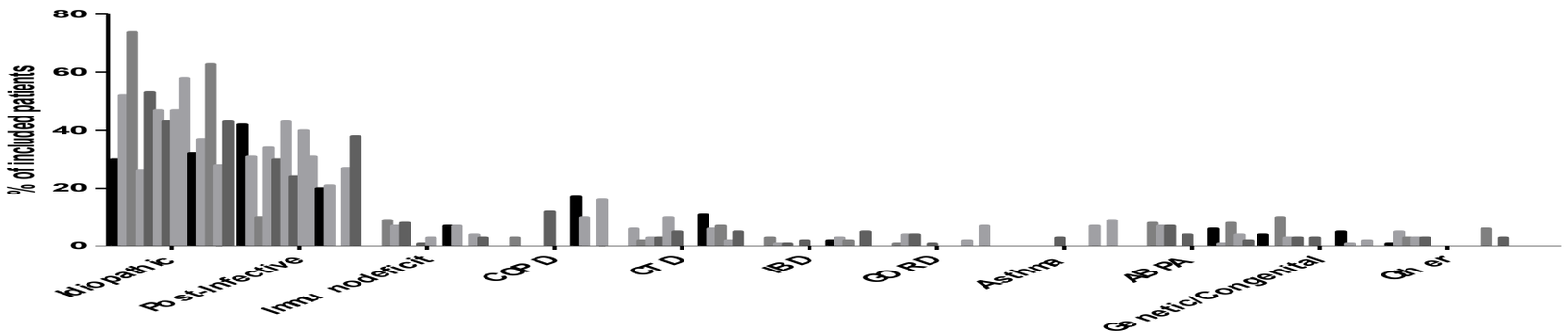
Etiology



Microbiology

Chronic infection

What we know

- *H. influenzae* (14-52%)*, P. aeruginosa*(12-58%) *S. pneumoniae* (7-37%)*, M. catarrhalis* (8-27%%)
- Despite the presence of purulent sputum, 18–40% of specimens will fail to grow any pathogens

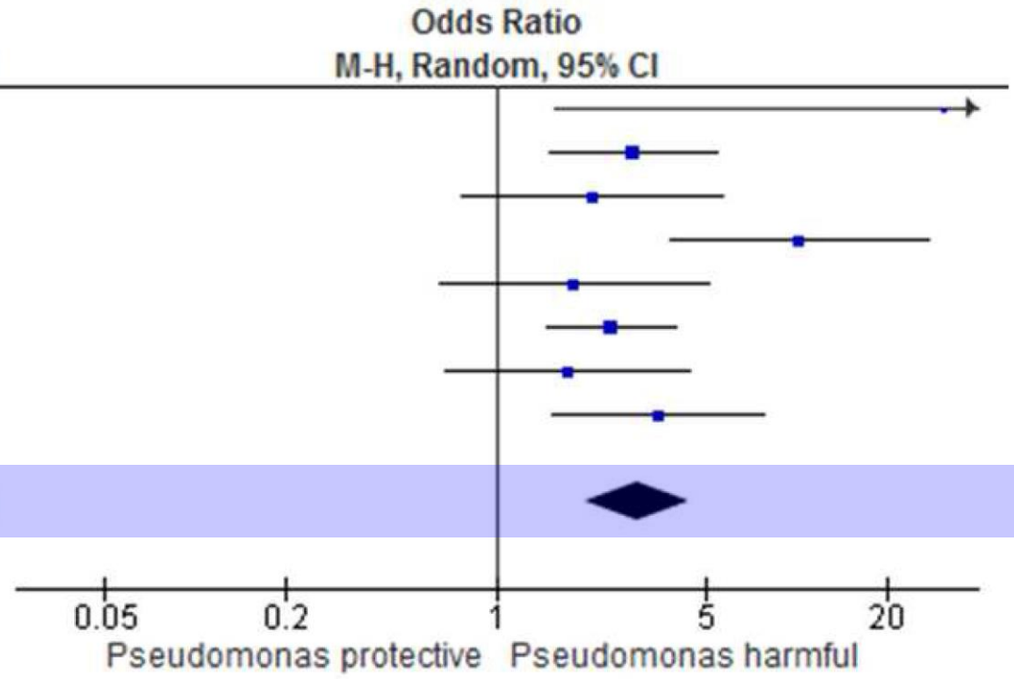
McShane PJ et al Am J Respir Crit Care Med 2013; 188:647

Mortality

Study or Subgroup	Pseudomonas Events	Pseudomonas Total	Non-Pseudomonas Events	Non-Pseudomonas Total	Weight	Odds Ratio M-H, Random, 95% CI
Aliberti 2014	3	39	0	162	1.7%	31.16 [1.58, 616.55]
Chalmers 2014	15	70	47	538	17.9%	2.85 [1.50, 5.43]
Chalmers 2015	6	44	17	242	11.0%	2.09 [0.77, 5.64]
Goeminne 2014	10	20	20	225	11.0%	10.25 [3.81, 27.57]
Loebinger 2009	8	20	19	71	10.3%	1.82 [0.65, 5.15]
Martinez-Garcia 2014	38	126	41	271	21.8%	2.42 [1.46, 4.01]
McDonnell 2014	9	47	13	108	12.0%	1.73 [0.68, 4.38]
McDonnell 2015	13	34	27	178	14.3%	3.46 [1.55, 7.73]
Total (95% CI)		**400**		**1795**	**100.0%**	**2.95 [1.98, 4.40]**
Total events	102		184			

Heterogeneity: Tau² = 0.13; Chi² = 11.72, df = 7 (P = 0.11); I² = 40%

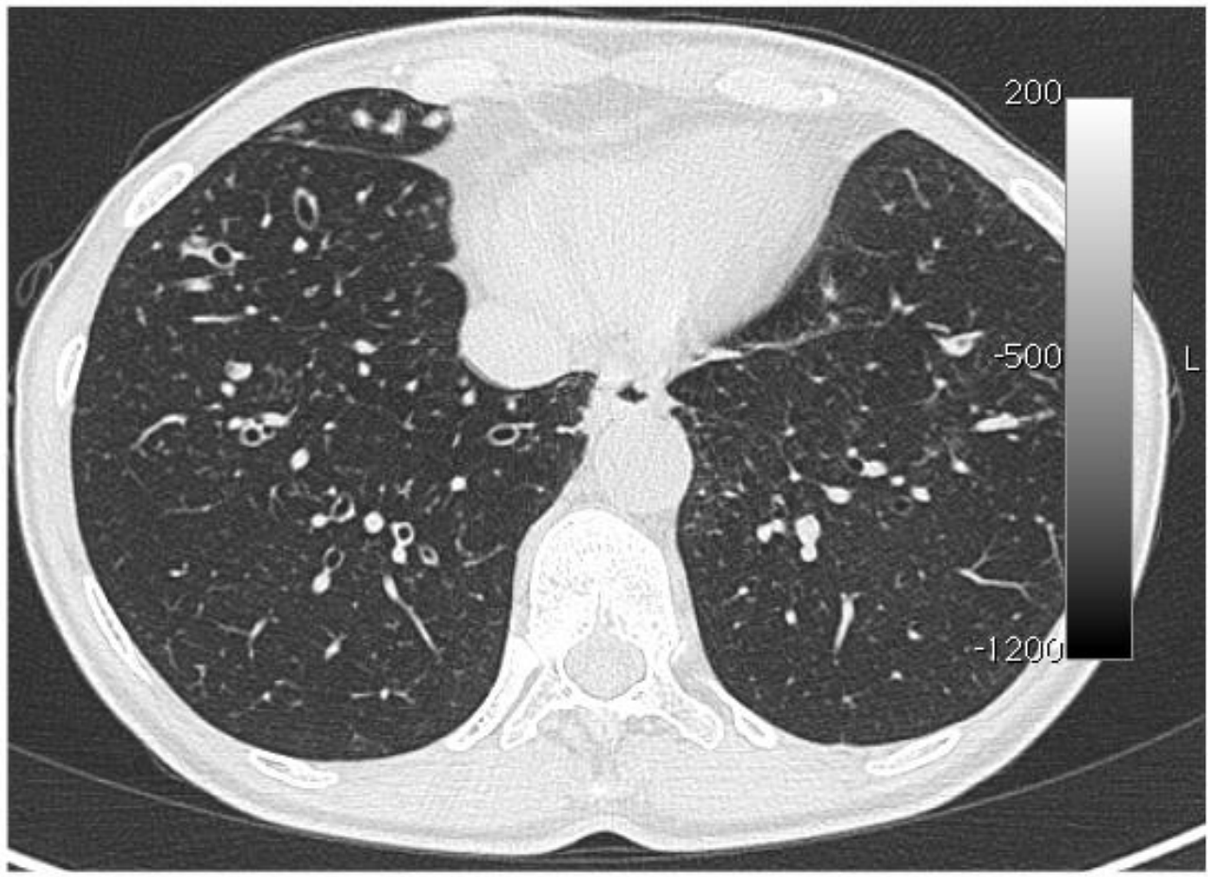
Test for overall effect: Z = 5.29 (P < 0.00001)



Finch S et al. Ann Am Thorac Soc. 2015 Sep 10

Chronic infection

What we know: NTM



Overall prevalence of 9.3%

MAC (up to 53%), *M. abscessus* (39%), *M. kansasii* (3-28%), *M. fortuitum* (1-3%), *M. chelonae* (1%), *M. malmoense* (1%)

Co-infection with *P. aeruginosa* (up to 52%)

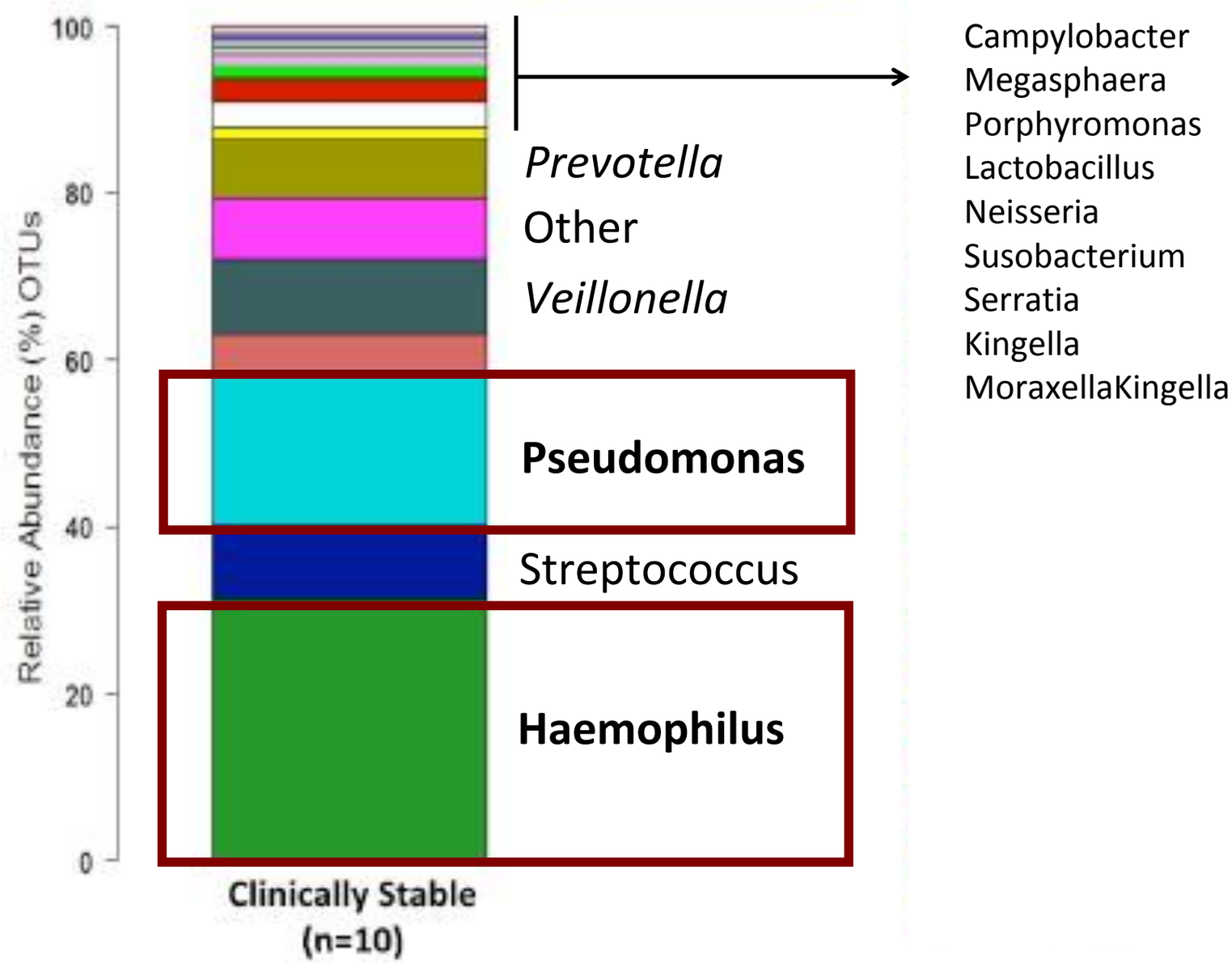
Usually, no frequent exacerbators

Ad hoc criteria for treatment in bronchiectasis

Bonaiti G et al Biomed Res Int. 2015;2015:197950

Chronic infection

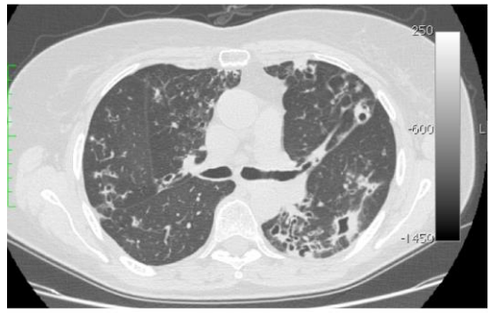
What we are learning

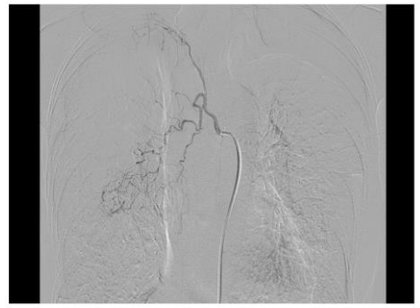


Tunney MM. Am J Respir Crit Care Med. 2013

The heterogeneity of bronchiectasis

Radiology





Signs Symptoms

Chronic Productive cough

Recurrent Exacerbations

Recurrent pneumonia

Haemoptysis

Wheeze

Very mild S/S

Pulmonary Function

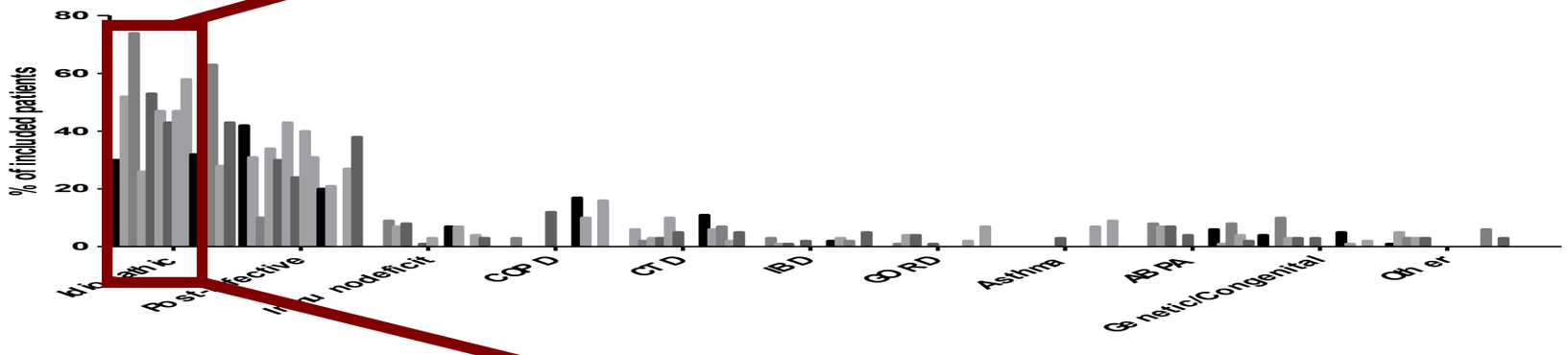
Completely normal

FEV_1 50-80%

FEV_1 35-50%

FEV_1 < 35%

Etiology



Microbiology

Pseudomonas dominant

Haemophilus dominant

Other pathogens dominant

Non-tuberculous mycobacteria

Viruses? Fungi?

The heterogeneity of bronchiectasis

Radiology					
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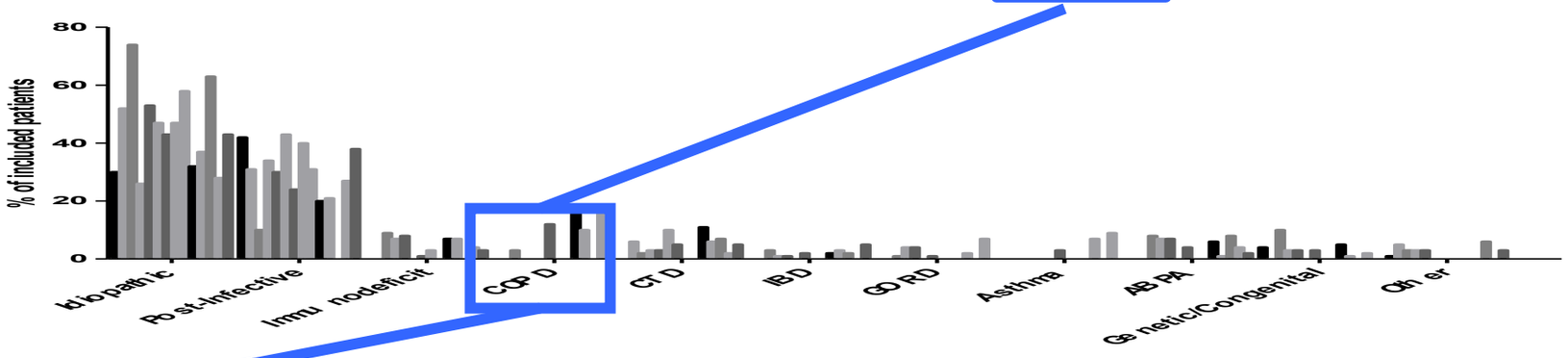
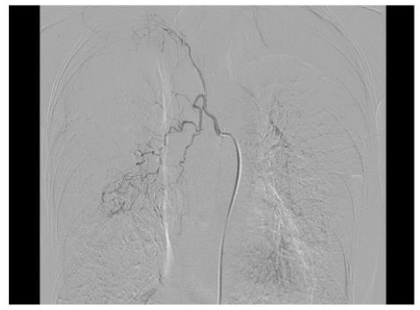
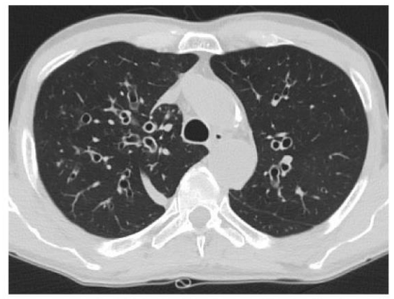
Microbiology	Pseudomonas dominant	Haemophilus dominant	Other pathogens dominant	Non-tuberculous mycobacteria	Viruses? Fungi?



1. Stratification according to severity

Radiology						
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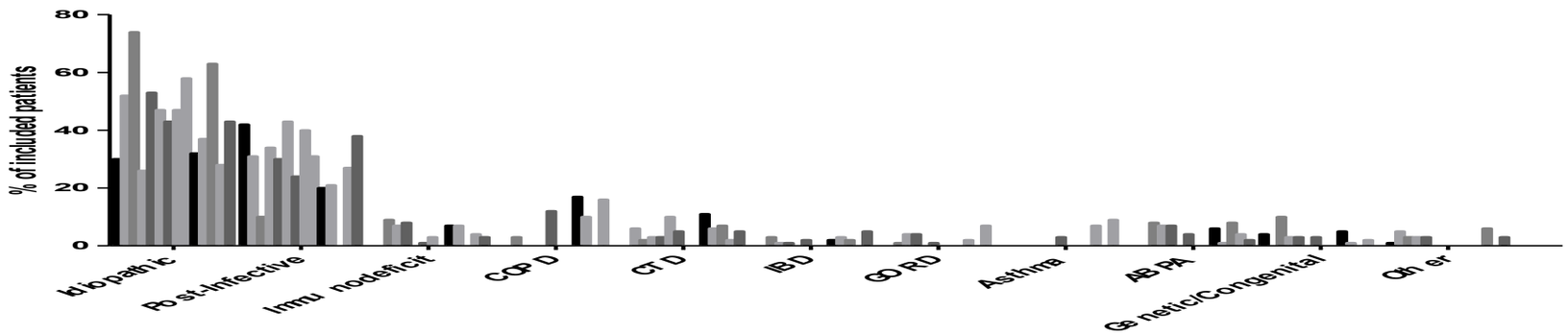
Etiology						
Microbiology	Pseudomonas dominant	Haemophilus dominant	Other pathogens dominant	Non-tuberculous mycobacteria	Viruses? Fungi?	

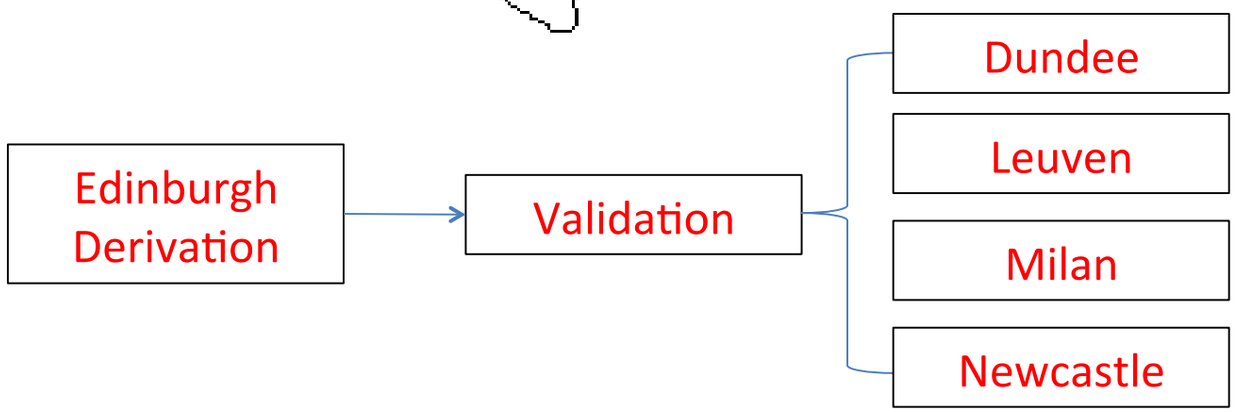
1. Stratification according to severity

The Bronchiectasis Severity Index

<u>5 European Centres</u>

- Dundee
- Edinburgh
- Leuven
- Milan
- Newcastle

<u>Total study population 1310</u>



Chalmers JD et al. Am J Respir Crit Care Med 2014;189:576

1. Stratification according to severity

The Bronchiectasis Severity Index

www.bronchiectasisseverity.com

Age, yr	
<50	0
50–69	2
70–79	4
80+	6
BMI	
<18.5	2
18.5–25	0
26–29	0
30 or more	0
FEV_1 % predicted	
>80	0
50–80	1
30–49	2
<30	3
Hospital admission before study	
No	0
Yes	5
Exacerbations before the study	
0	0
1–2	0
3 or more	2
MRC dyspnea score	
1–3	0
4	2
5	3
Pseudomonas colonization	
No	0
Yes	3
Colonization with other organisms	
No	0
Yes	1
Radiological severity: ⩾3 lobes involved or cystic bronchiectasis	
No	0
Yes	1

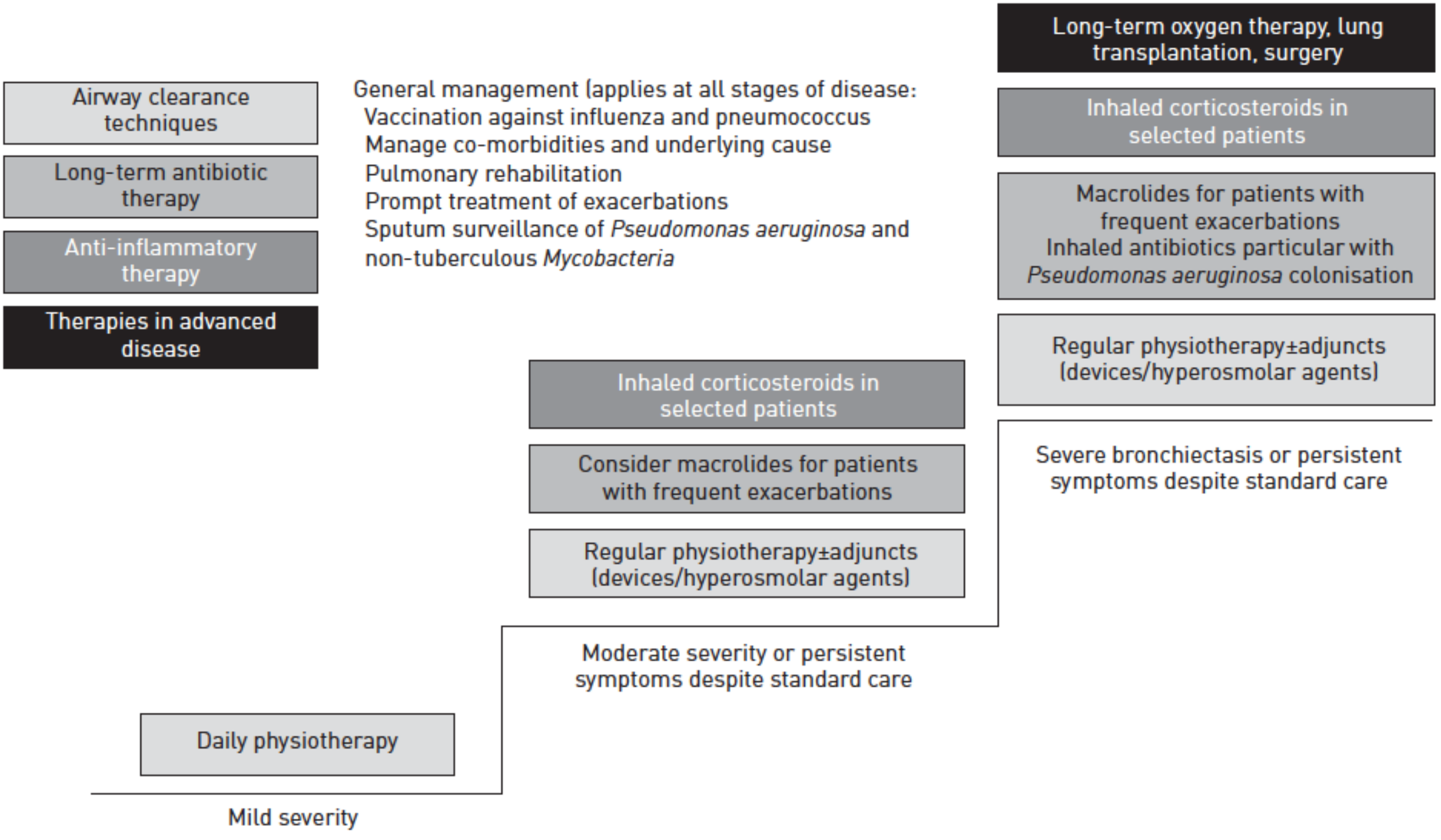
BSI Risk Classes

- Mild = 0-4
- Moderate = 4-8
- Severe = 9+

(Range = 0-25)

Chalmers JD et al. Am J Respir Crit Care Med 2014;189:576

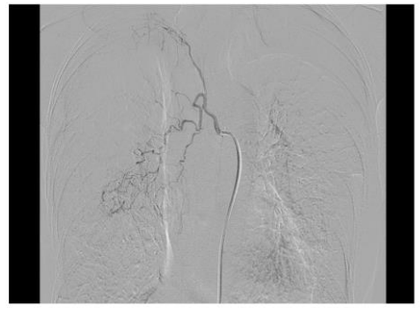
1. Stratification according to severity



Chalmers JD et al. Eur Respir J 2015;45:1446

The heterogeneity of bronchiectasis

Radiology



Signs Symptoms

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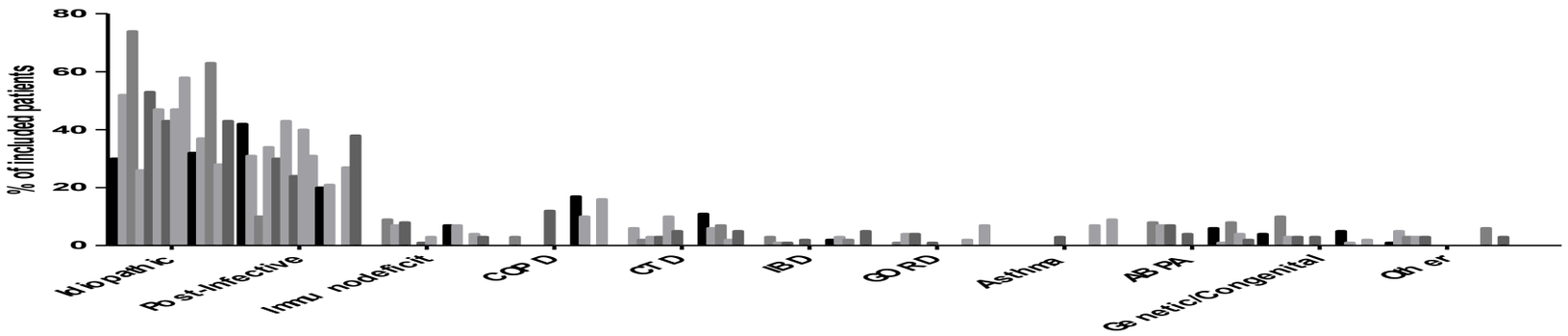


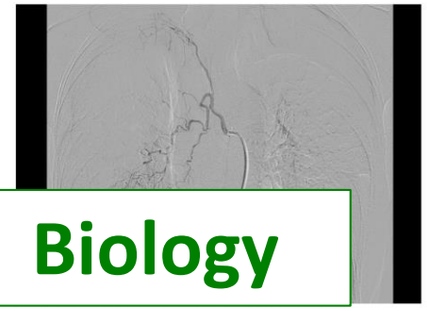
Microbiology

Pseudomonas dominant	Haemophilus dominant	Other pathogens dominant	Non-tuberculous mycobacteria	Viruses? Fungi?

2. Identification of clinical phenotypes

Biology

Radiology



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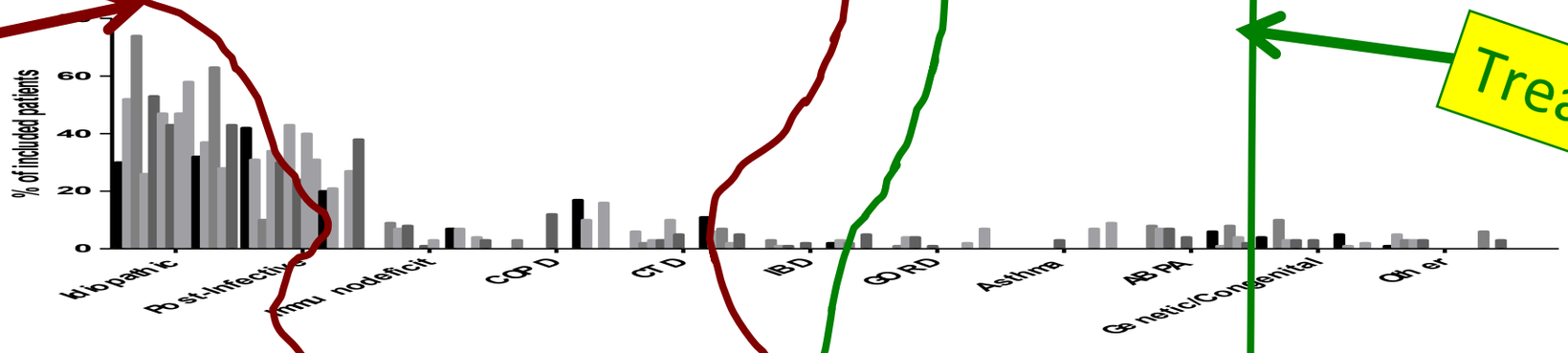
Treatment



Treatment

Etiology

Microbiology

Pseudomonas dominant

Haemophilus dominant

Other pathogens dominant

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Viruses? Fungi?

Outcomes

Outcomes

2. Clusters in bronchiectasis

1,145 adults with bronchiectasis

- Monza (Italy)
- Dundee (UK)
- Leuven (Belgium)
- Athens (Greece)
- Galway (Ireland)

1. Spearman correlation
2. Principal component analysis
3. Hierarchical analysis
4. Cluster analysis

1. Age
2. Radiological Severity (Reiff score)
3. Daily cough
4. Daily sputum
5. Dyspnea (Medical Research Council)
6. Long-term oxygen therapy
7. Exacerbations in the previous year
8. Hospitalization in the previous year
9. FEV_1
10. Chronic infection with *Pseudomonas aeruginosa*
11. Chronic infection with other pathogens
12. Charlson Comorbidity Index

Unpublished data from the EMBARC Network

2. Clusters in bronchiectasis

Variables		Severe Pseudomonas 19%	Others Chronic Infections 24%	Daily Sputum 33%	Mild-to-Moderate 24%	Overall p-value
Age, years	median (IQR)	67 (56-75)	65 (56-73)	67 (57-74)	66 (55-74)	0.52
Male	n.(%)	81 (45)	112 (41)	148 (40)	109 (36)	0.19
Body Mass Index	median (IQR)	25 (21-27)	25 (22-28)	25 (22-28)	25 (21-28)	0.47
Smoker or ex	n.(%)	56 (31)	90 (33)	165 (44)	121 (39)	0.005
Charlson Comorbidities Index>1	n.(%)	53 (30)	101 (37)	113 (30)	106 (35)	0.20
Reiff score	median (IQR)	6 (4-9)	4 (2-6)	3 (2-6)	3 (2-6)	0.0001
Daily cough	n.(%)	170 (95)	241 (88)	322 (86)	154 (50)	<0.0001
Daily sputum	n.(%)	166 (93)	204 (75)	362 (97)	0 (0)	<0.0001
Haemoptysis	n.(%)	42 (24)	36 (13)	80 (22)	43 (14)	0.002
MRC	median (IQR)	3 (2-5)	2 (1-3)	2 (1-3)	1 (1-2)	0.0001
Exacerbations in the previous year	median (IQR)	3 (2-4)	2 (1-3)	2 (1-3)	2 (1-3)	0.0001
FEV1 (% predicted)	median (IQR)	59 (46-78)	71 (55-93)	77 (57-95)	84 (68-101)	0.0001
Pseudomonas	n.(%)	179 (100)	0 (0)	0 (0)	0 (0)	<0.0001
Other pathogens	n.(%)	0 (0)	273 (100)	0 (0)	0 (0)	<0.0001
CRP, mg/L	median (IQR)	10.7 (4.0-36.0)	5.0 (3.7-9.0)	4.5 (2.0-7.7)	3.0 (1.2-7.2)	0.0001

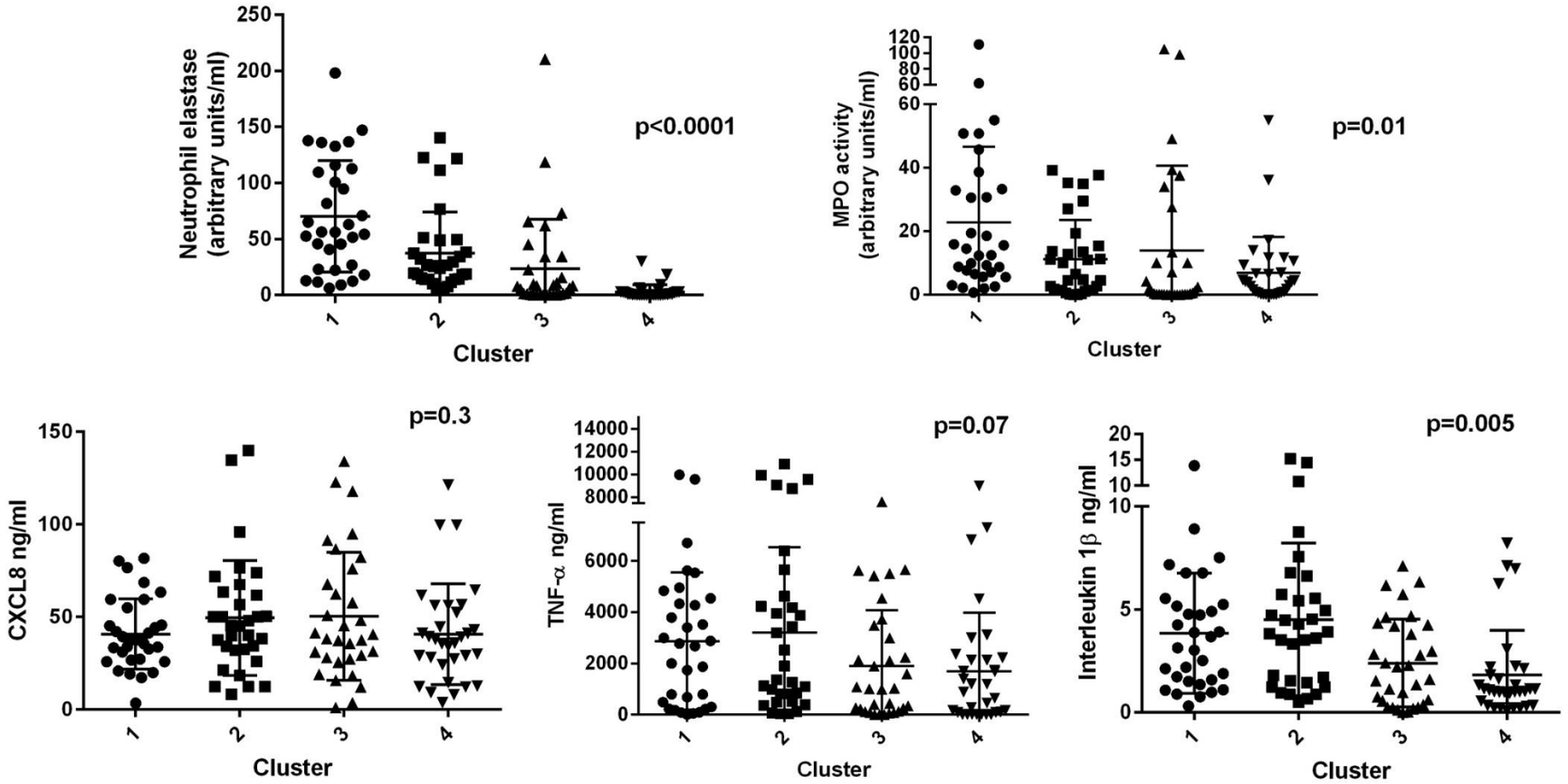
MRC: Medical Research Council; CRP: C-reactive protein

Unpublished data from the EMBARC Network

2. Clinical phenotypes in bronchiectasis

		Severe Pseudomonas 19%	Others Chronic Infections 24%	Daily Sputum 33%	Mild-to-Moderate 24%	
Quality of life						
SGRQ	median (IQR)	58 (34-72)	43 (27-61)	39 (27-55)	29 (12-40)	<0.001
Outcomes						
Exacerbations during one-year follow-up	median (IQR)	2 (1-3)	2 (1-2)	1 (0-2)	1 (0-2)	0.0001

SGRQ: St. George's Respiratory Questionnaire



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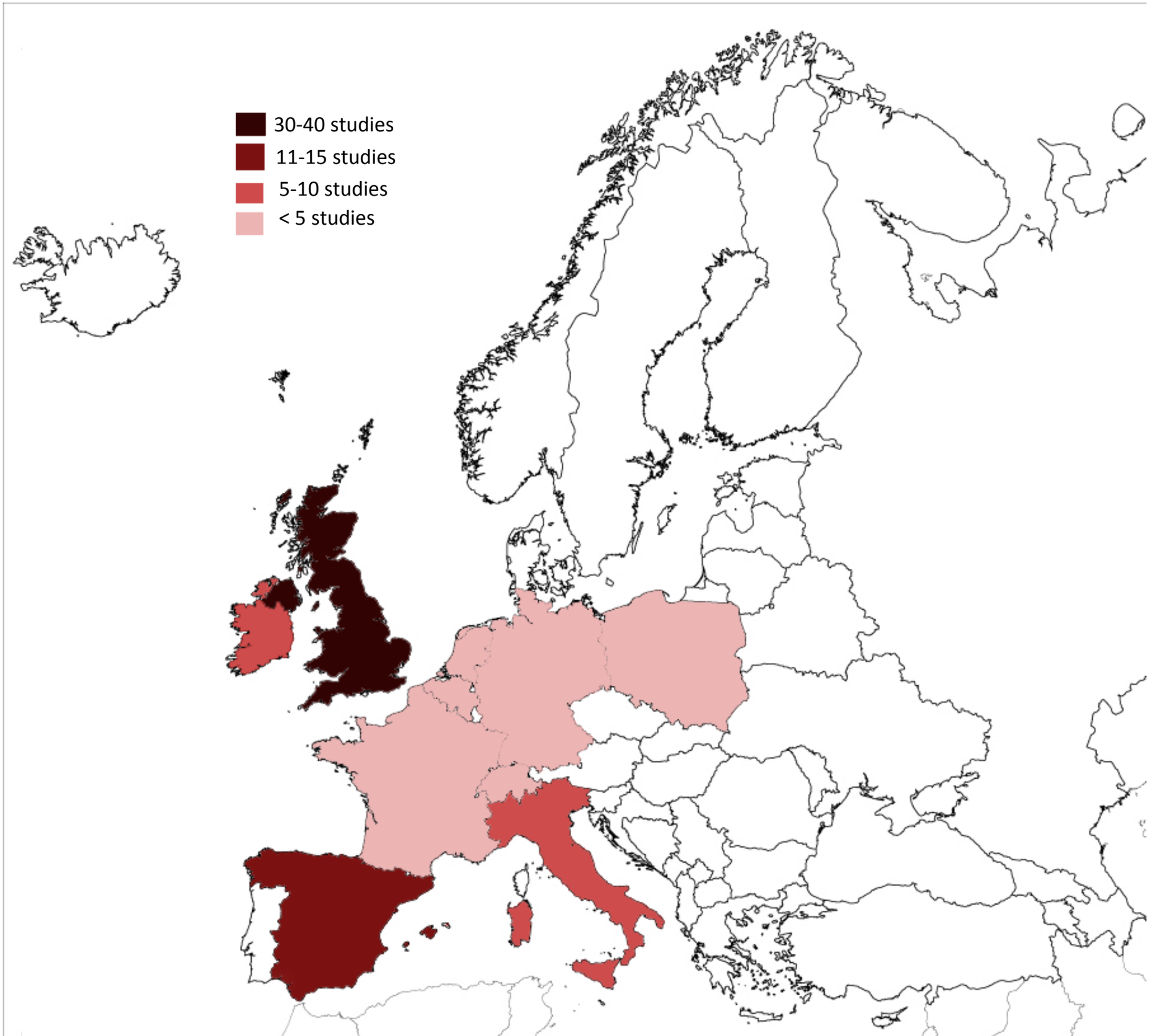
The heterogeneity in research

2000-2015; adults; original papers on bronchiectasis



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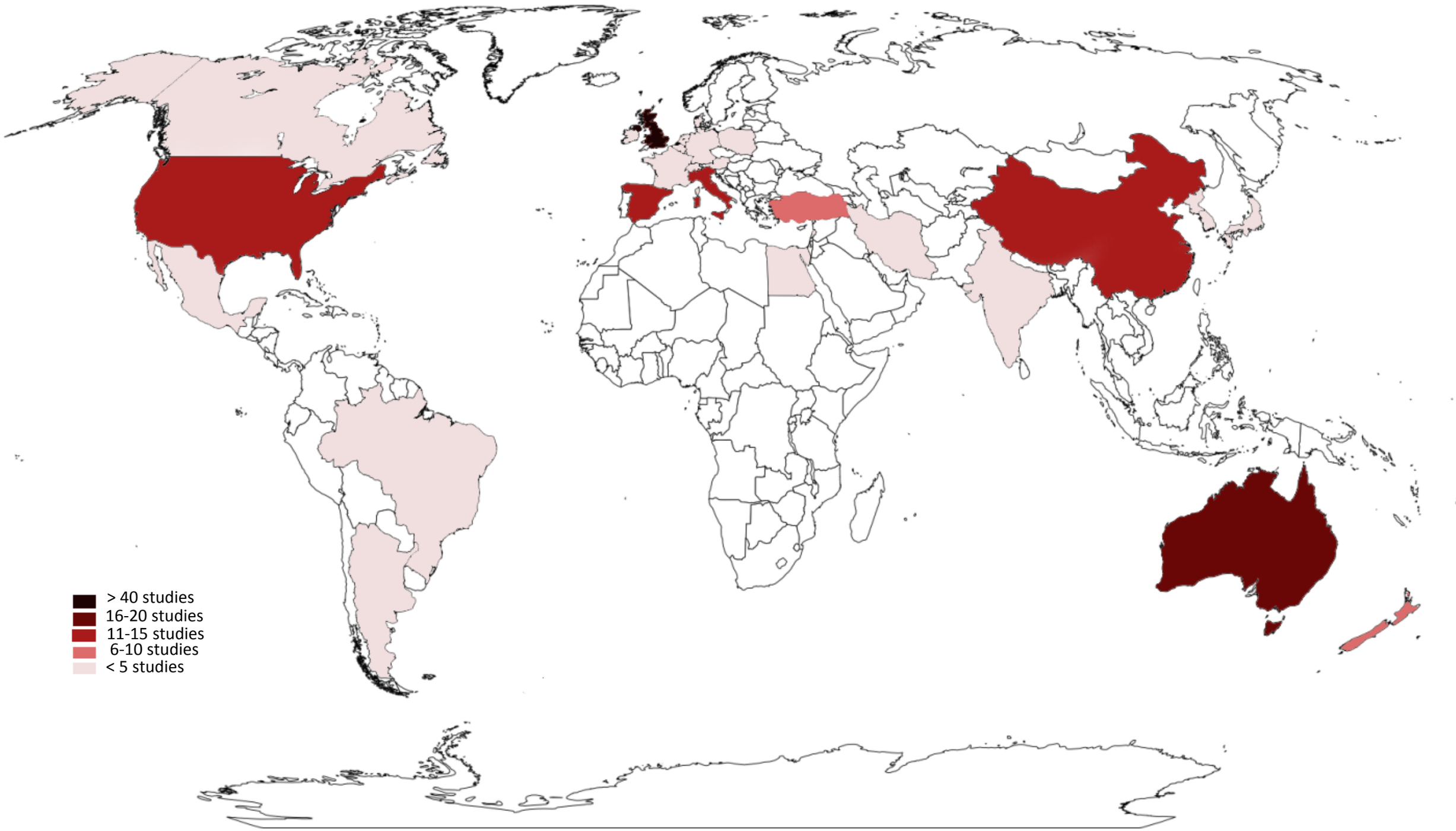
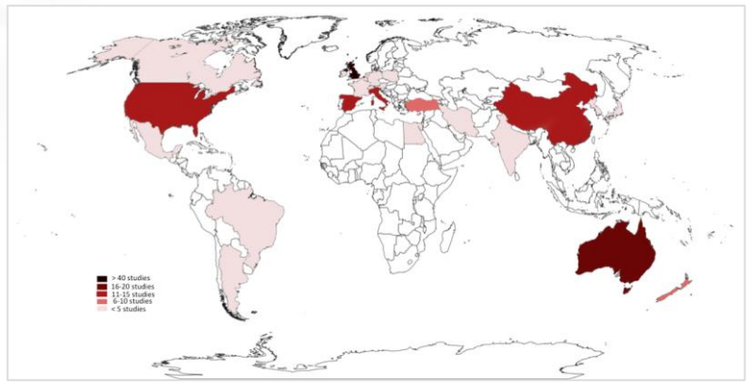


The burden of bronchiectasis



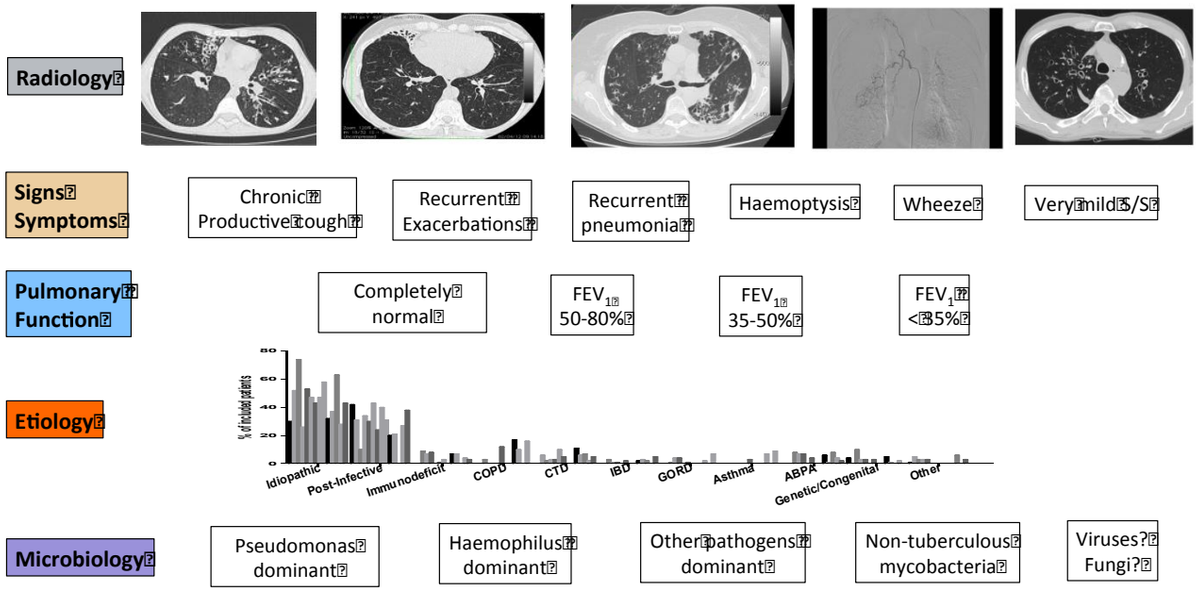
Prevalence data
67/100.000 Germany
52/100.000 USA

Mild-to-moderate patients with bronchiectasis
(Secondary Care and Primary Care)

Patients with Signs / Symptoms without a radiological diagnosis of bronchiectasis
(COPD)

Asymptomatic patients with
a radiological diagnosis

Conclusions



The Bronchiectasis Severity Index

www.bronchiectasisseverity.com

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BMI	
<18.5	2
18.5–25	0
26–29	0
30 or more	0
FEV_1 % predicted	
>80	0
50–80	1
30–49	2
<30	3
Hospital admission before study	
No	0
Yes	5
Exacerbations before the study	
0	0
1–2	0
3 or more	2
MRC dyspnea score	
1–3	0
4	2
5	3
Pseudomonas colonization	
No	0
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Colonization with other organisms	
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Radiological severity: ⩾3 lobes involved or cystic bronchiectasis	
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BSI Risk Classes

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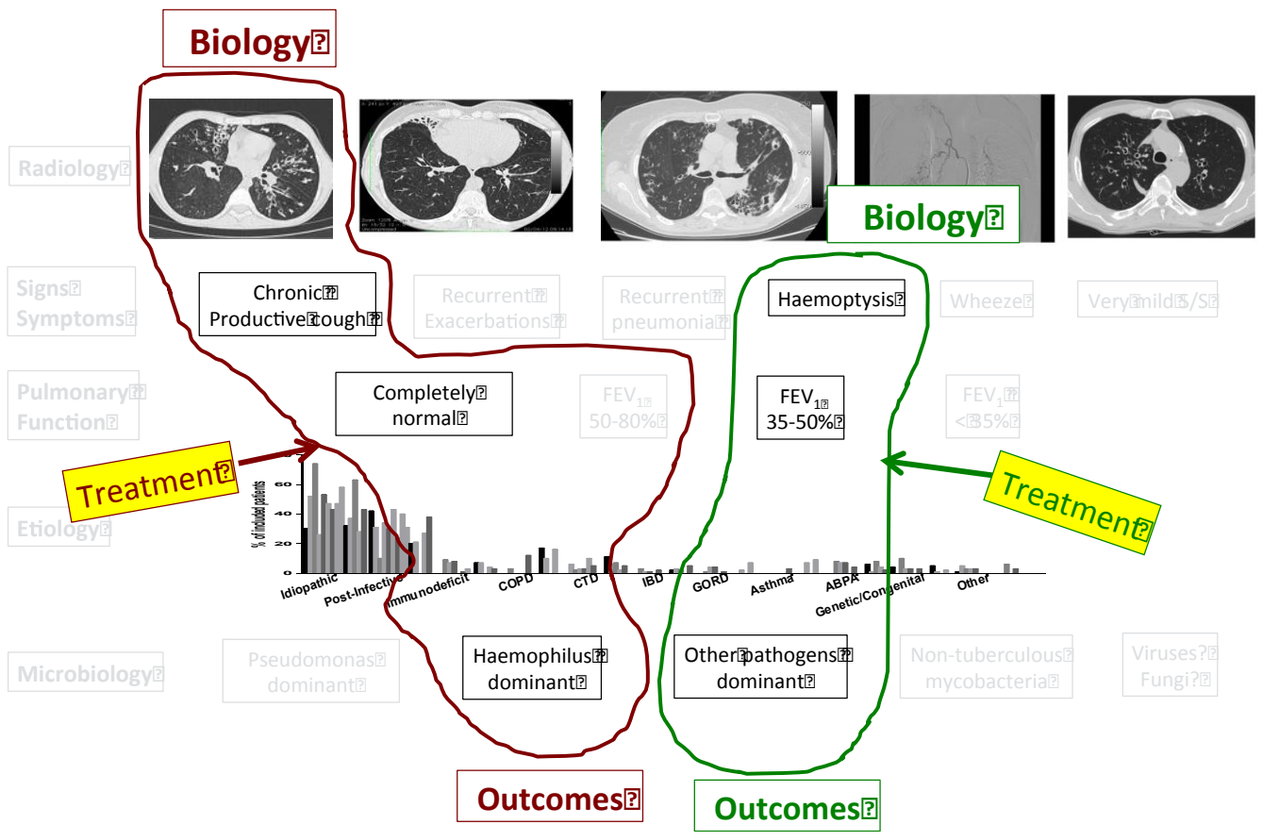

Acknowledgements

Executive committee
James Chalmers
Eva Polverino

Scientific Committee
Anthony De Soyza
Felix Ringshausen
Marlene Murris
Montserrat Vendrell
Wim Boersma
Stefano Aliberti

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Antoni Torres
Tobias Welte
Diana Bilton
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Gernot Rohde
Michael Loebinger
Katerina Dimakou
Stuart Elborn

ERS EUROPEAN RESPIRATORY SOCIETY
every breath counts

UNIVERSITY OF DUNDEE

wellcome trust

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NHS National Institute for Health Research

BRONCHIECTASIS RESEARCH REGISTRY
A COPD FOUNDATION INITIATIVE

EMBARC
The European Bronchiectasis Registry

www.bronchiectasis.eu