

WP5- European Registry for Bronchiectasis

iABC General Assembly

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EMBARC

The European Bronchiectasis Registry



ERS

EUROPEAN
RESPIRATORY
SOCIETY

every breath counts

Objectives

- Create a pan-European Bronchiectasis Registry
- Generate data describing the natural history of bronchiectasis
- Contribute to evidence based guidelines
- Develop strategies to make the registry sustainable

What is EMBARC?



International Bronchiectasis Registry Network

Europe
United States
India
Australia



Bronchiectasis biobank and translational research “hub”



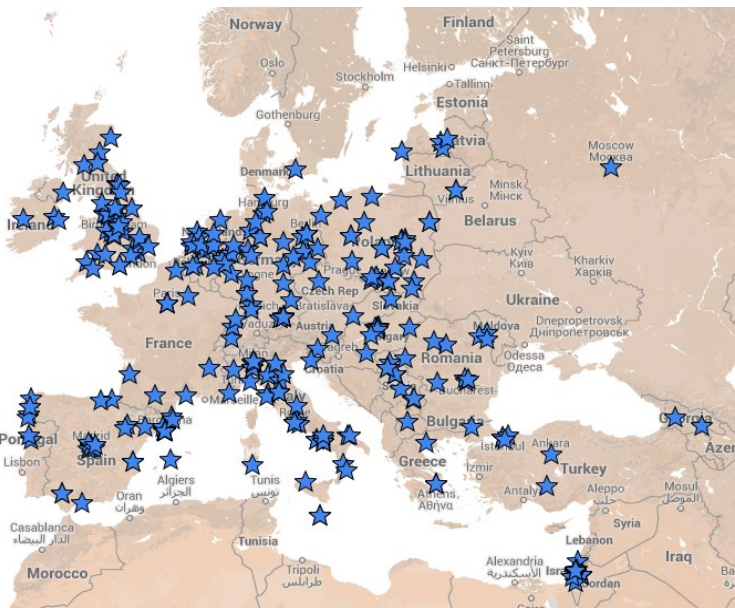
Clinical Trials Network





Registry data update

- 14,265 patients registered
- 27,502 unique records
- Nearly 80% eligible 1 year follow-up recording
- >60% eligible 2 year follow-up recording



Patients enrolled: 11204
from **27 countries**

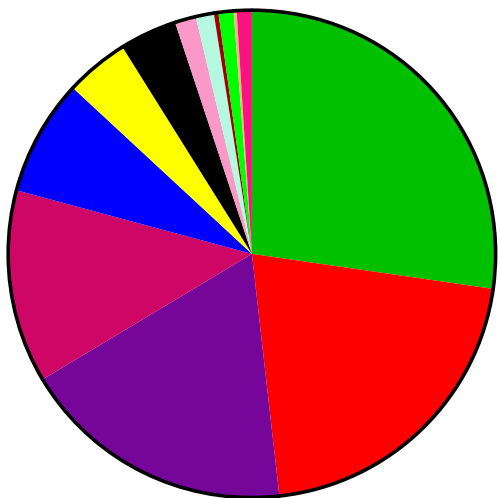
Demographics

58% female

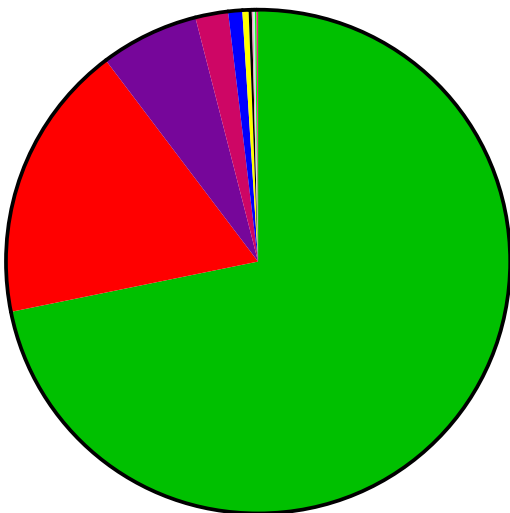
Median age= 68 years
(IQR 58-75)

Never smoked =55.9%

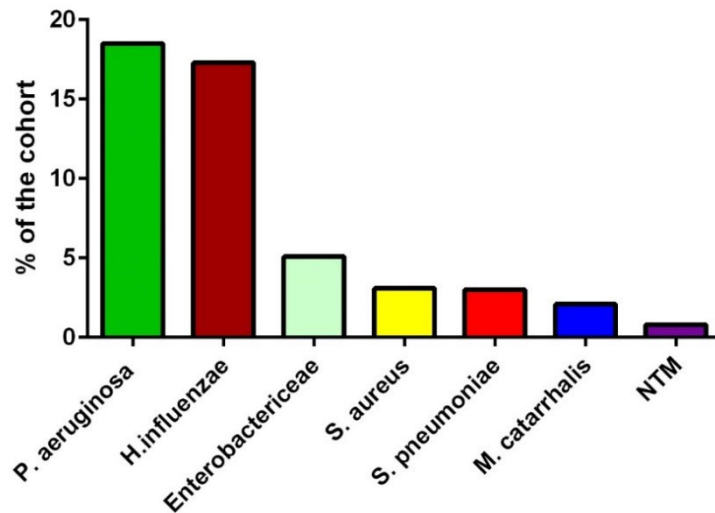
Ex smoker= 38.3%



Exacerbations
requiring oral
antibiotics per year

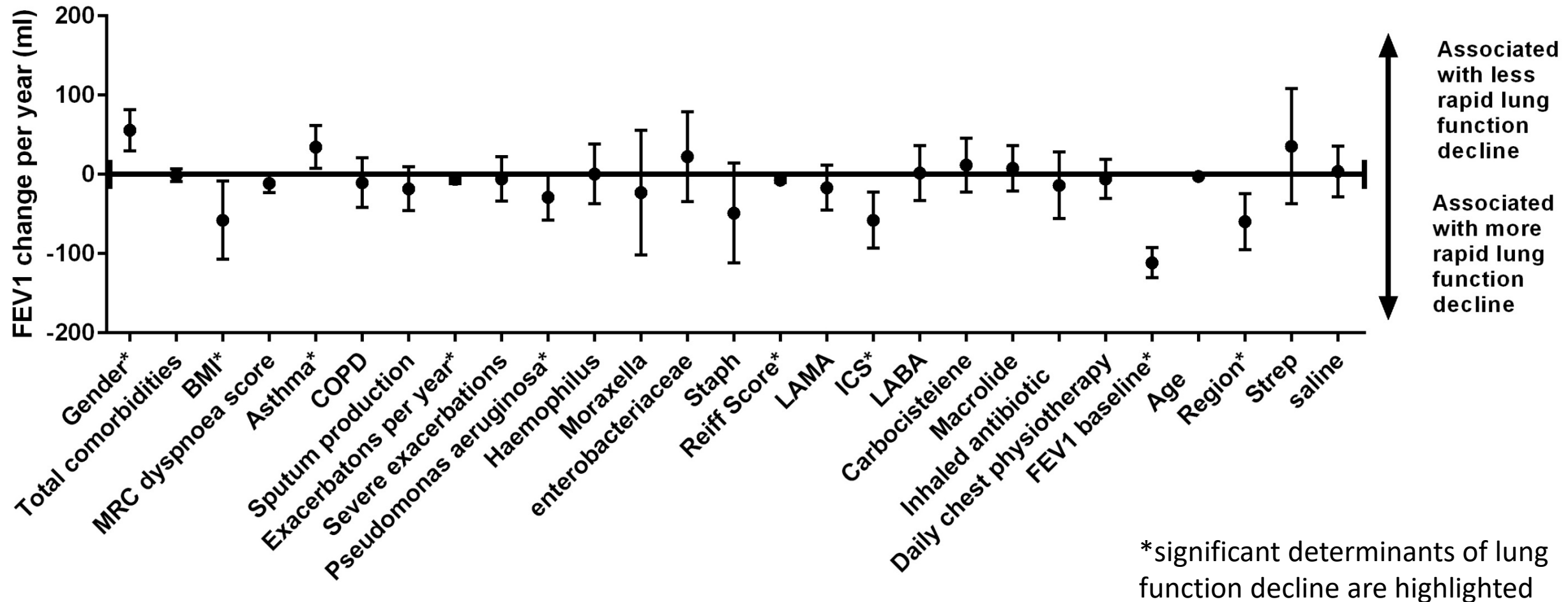


Exacerbations
requiring hospitalization
antibiotics per year





Results- independent predictors of lung function decline





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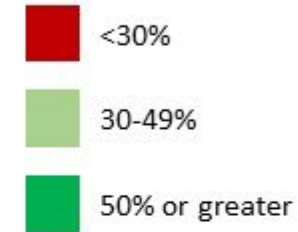
Inhaled Antibiotics in
Bronchiectasis and
Cystic Fibrosis



Innovative Medicines Initiative



% of patients infected with *P. aeruginosa*



Large variation in microbiology of patients across Europe

H. Influenzae most common in Northern Europe

P. aeruginosa most common in Southern and Eastern Europe

Registry activities at congress

Sunday 16th

Session 56 08:30—10:30

Poster discussion: The global impact of bronchiectasis and nontuberculous mycobacteria (NTM)

PA348: Characteristics of patients with pulmonary non-tuberculous Mycobacterial infection in bronchiectasis: Data from the EMBARC registry

PA350: Rhinosinusitis is associated with increased symptoms and more frequent exacerbations among patients with bronchiectasis- data from the EMBARC registry

PA356: Validity of COPD diagnosis in Bronchiectasis patients: data from the EMBARC registry

PA359: Primary ciliary dyskinesia in adults with bronchiectasis: Data from the EMBARC registry

Monday 17th

Session 256 10:45—12:45

Poster discussion: Respiratory epidemiology: from COPD to factors that associate with lung function and infections

PA2282: Sex differences in bronchiectasis patient characteristics: an analysis of the EMBARC cohort

Session 281 12:50—14:40

Thematic poster: Improving the quality of life of patients with bronchiectasis

PA2676: The heterogeneity of bronchiectasis patient characteristics, management and outcomes across Europe: Data from the EMBARC registry

PA2678: Impact of Inflammatory bowel disease in bronchiectasis (IBD-BR) data from the EMBARC registry

Session 285 12:50—14:40

Thematic poster: Pulmonary tuberculosis: long term complications, rehabilitation and challenges

PA2748: Post-Tuberculosis Bronchiectasis in India: Outcomes of the Indian EMBARC Registry

Tuesday 18th

Session 449 14:45—16:45

Oral presentation: Bronchiectasis: phenotypes, endotypes and new therapies

OA4951: Determinants of quality of life in bronchiectasis using the quality of life bronchiectasis (QOL-B) questionnaire: data from the EMBARC registry

OA4952: Phenotypes in Bronchiectasis from the EMBARC India Registry

Wednesday 19th

Session 532 08:30—10:30

Oral presentation: Latest advances in pulmonary rehabilitation assessment and content

OA5201: Variability in access and referral to pulmonary rehabilitation in European bronchiectasis patients enrolled in the EMBARC registry

EMBARC Projects - Update



The European NTM Registry

The first patients have been recruited to the NTM registry and invites for participation are being sent to more sites. A great number of sites across 10 countries have contacted us expressing their interest in taking part in this sub-study of EMBARC. We will be in touch with more information as further approvals are issued.



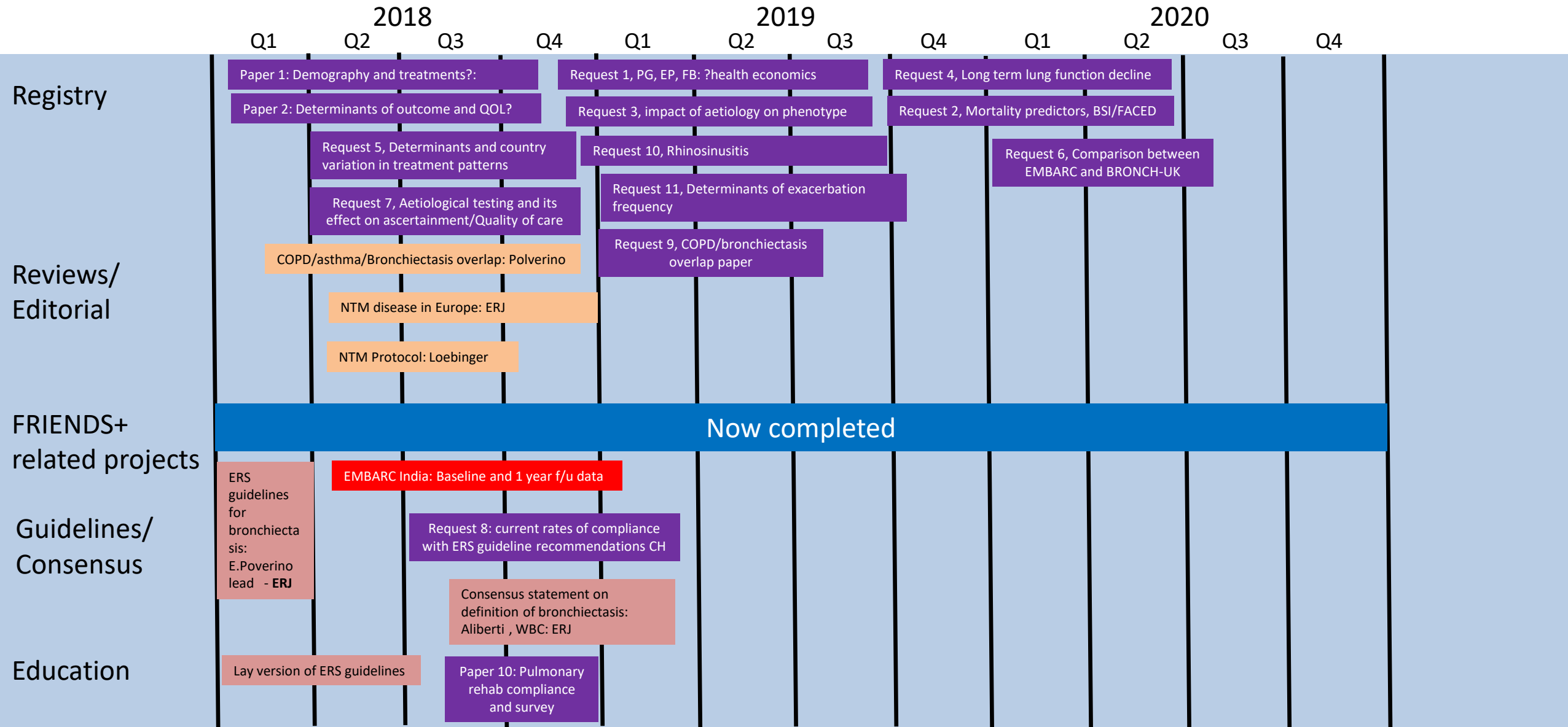
The interaction between airways disease and bronchiectasis - An initiative of the EMBARC and SHARP CRC's -

The EMBARC and SHARP (Severe Heterogenous Asthma Research collaboration, Patient-centered) clinical research collaborations have come together in organising a two day seminar which will discuss and debate respiratory overlap syndromes. This two day event will be held in Barcelona 7-8th February 2019. This research seminar will bring together key groups in asthma, bronchiectasis, and additional respiratory conditions to examine the knowledge and gaps regarding disease "overlap syndromes" with the goal of generating new collaborations and shared learning.

There are a limited number of spaces available for attending this seminar. If you are interested in attending, registration must be completed by 30th November 2018.

For more information on the seminar, registration or poster submission please follow this [link](#)

Publication strategy
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EMBARC 2 description of work

EMBARC2 Work Packages

1. Project management and governance
2. The European Bronchiectasis Registry
3. The EMBARC-BRIDGE study
4. Bronchiectasis and airways disease “overlap”
5. Clinical trials support and feasibility
6. Patient engagement activities
7. Engagement with the European Respiratory Society
8. Scientific Committee
9. Promotion and dissemination
10. Education

Registry becomes WP2

Arrangements in the registry are unchanged

EMBARC registry SC remains in place with current constitution

Data access unchanged

Consistent with current contractual arrangements



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The European Bronchiectasis Registry

N=10,000, 23 countries (by project start in 2018)



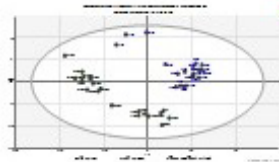
EMBARC-BRIDGE study
Representative cohort, 8 countries, N=1000

Sputum/nasal

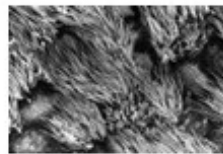
Blood



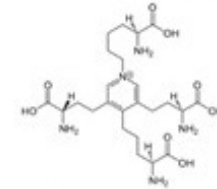
Microbiome
(N=800 stable, 160
exacerbation)



Proteomics
N=120 stable, 80
exacerbation



Cilia substudy
N=200 stable only



Desmosine
n=800 stable and
N=160 exacerbation



Serum markers
N=800 stable and
N=160 exacerbation

Exacerbation sub-cohort N=160

Bioinformatic analysis

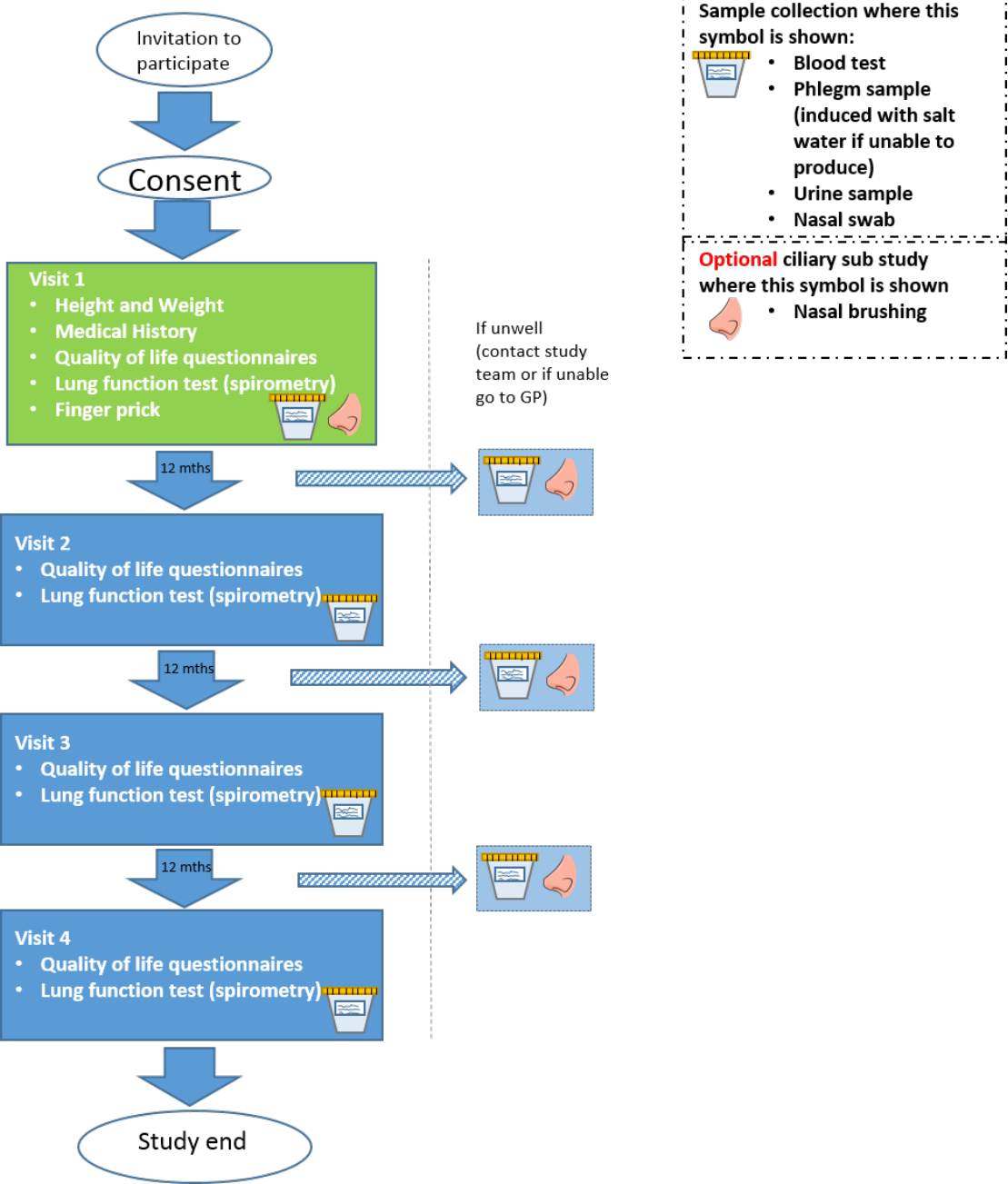
- Stable endotypes
- Exacerbation endotypes

Internal validity

- ELISA/western blot
- qPCR, standard microbiology
- Bronchoscopic substudy (N=30)

External validity

Study protocol



BRIDGE pilot study

- 3 centres – Milan, Barcelona, Dundee n=299
- Blood and soluble sputum
- Stable patients
- EMBARC registry data

Assays

Examples of the data

Blood and sputum

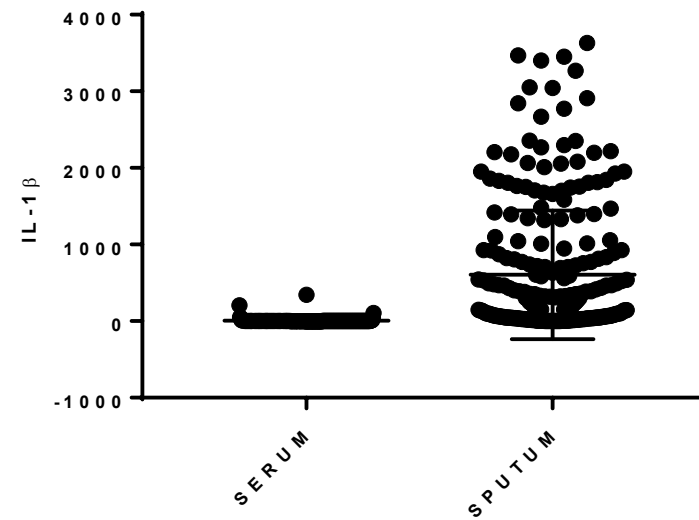
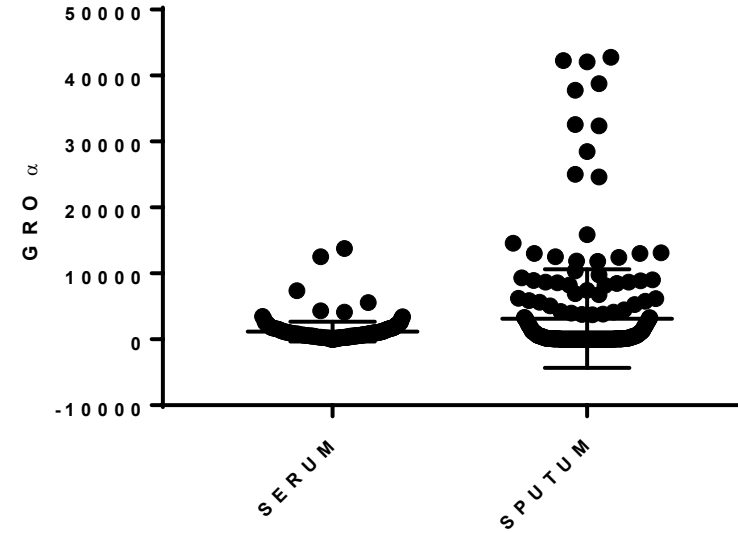


Multiplex

GM-CSF
Gro-alpha
IFN- γ
IL-10
IL-13
IL-17
IL-1 β
IL-5
IL-6
MCP-1
TNF- α
TSLP
VEGF

Single ELISAs

IL-8
IL-4
IL-2



Assays

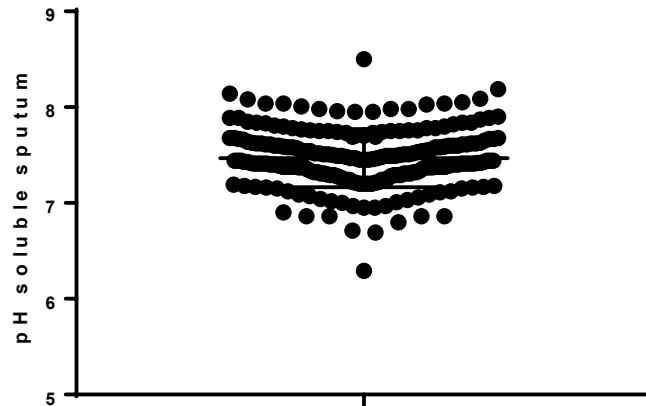
Sputum only

Neutrophil Elastase (ELISA and NEATstiks)

MPO

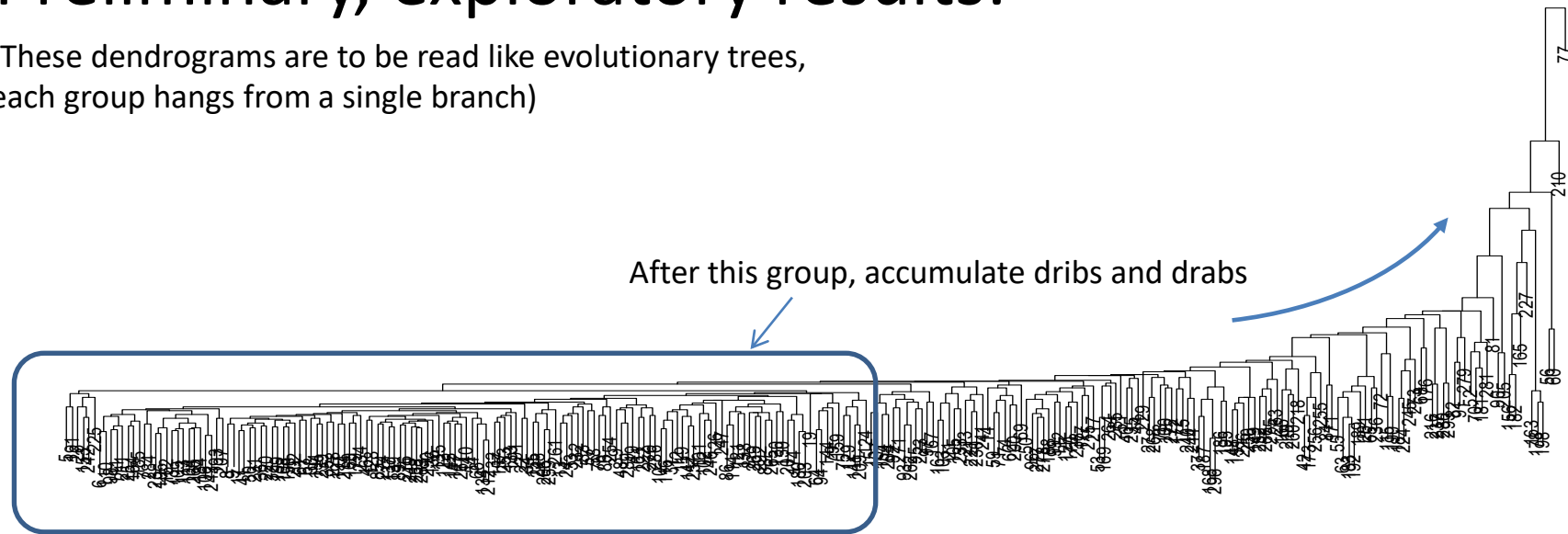
pH

Range of soluble sputum pH

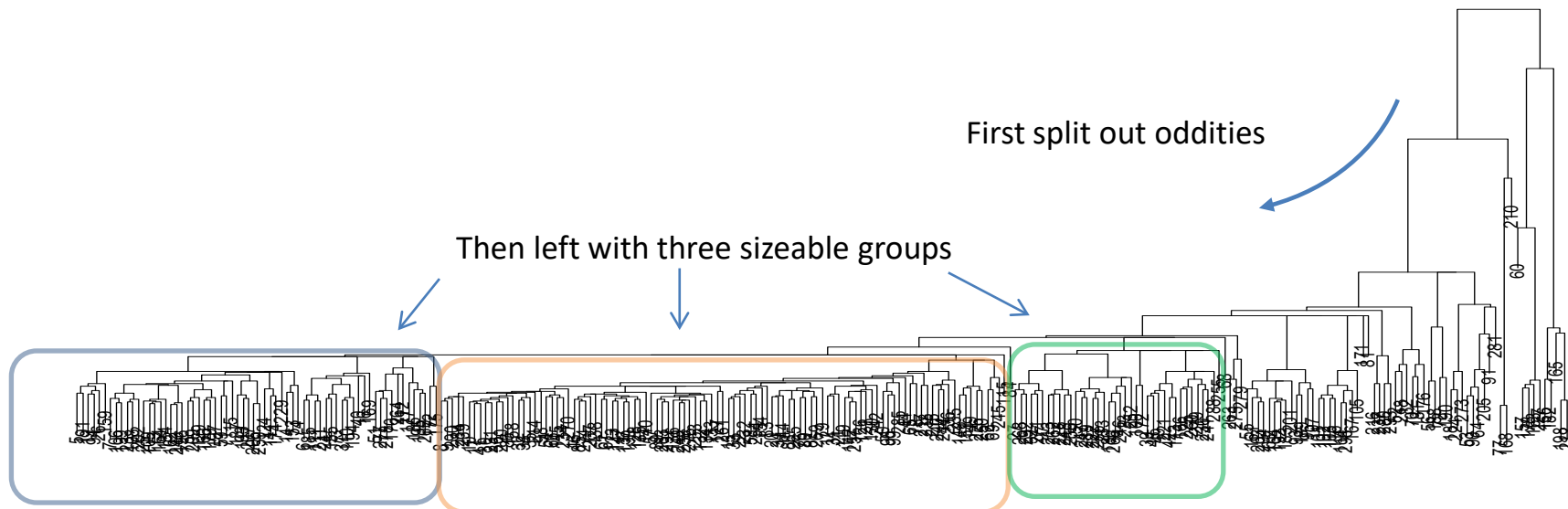


Preliminary, exploratory results:

(These dendrograms are to be read like evolutionary trees, each group hangs from a single branch)



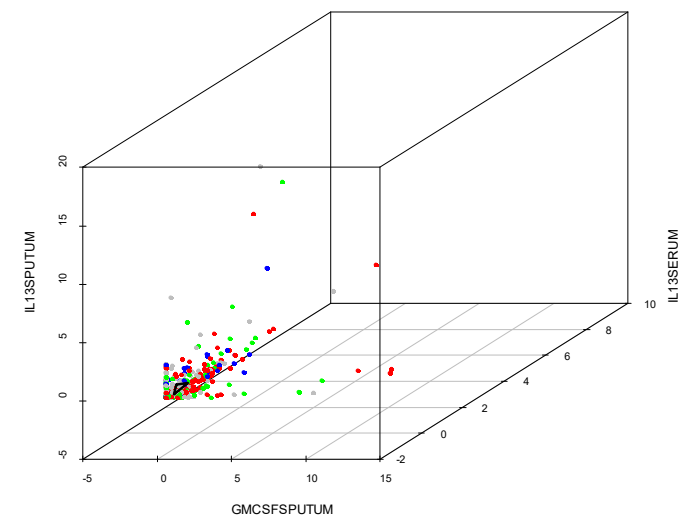
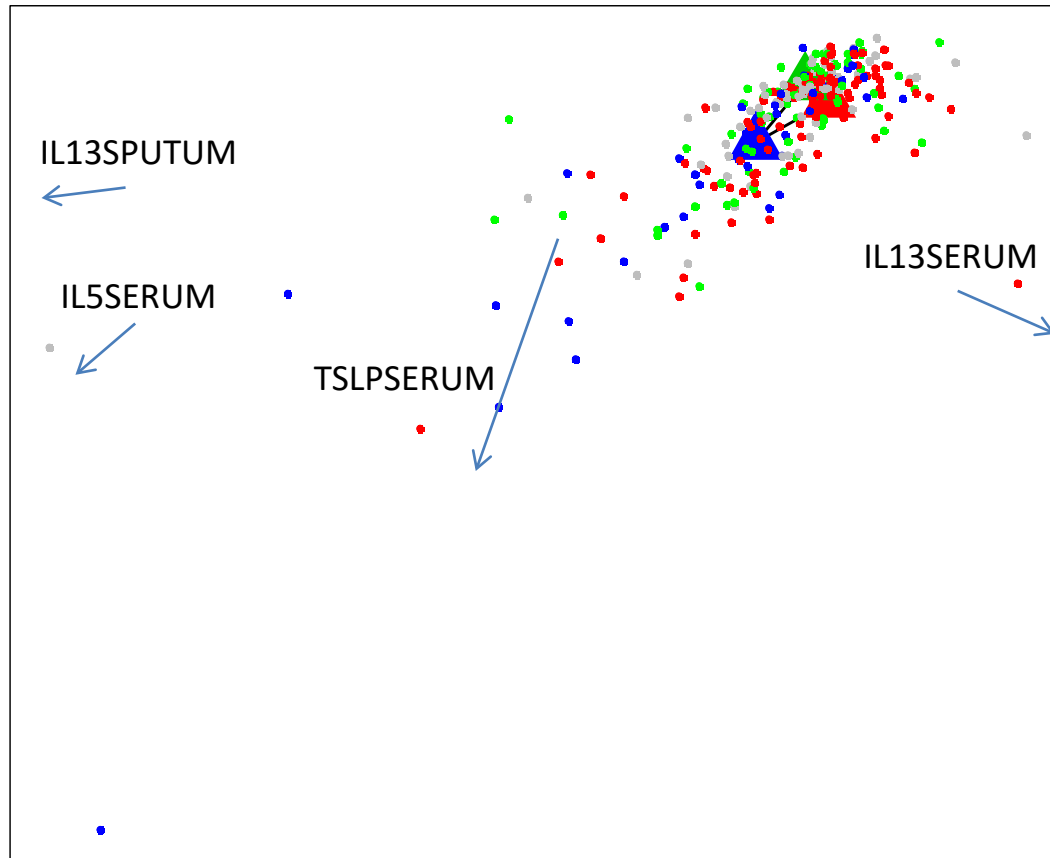
Agglomerative (joining) method



Divisive (splitting) method

Plotting the clusters:

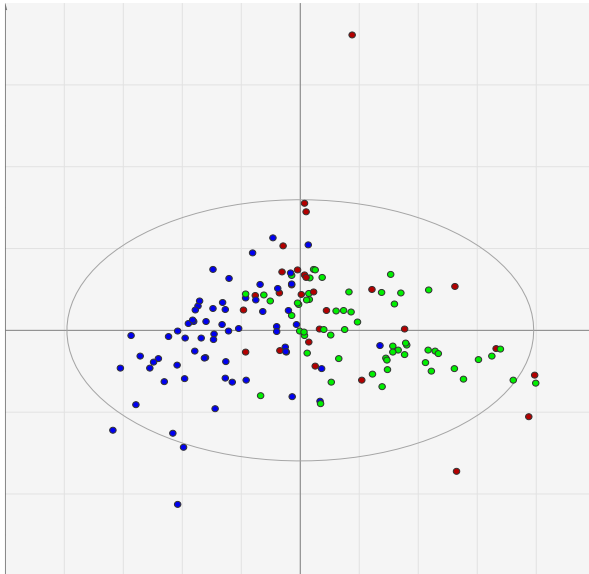
We have 35 dimensions, so most plots of the clusters are uninteresting, one of the better views comes from looking down onto the plane that connects the centres (medians) of the three clusters (shown as triangles). Arrows point in direction of increase of variables, and indicate rough size of effect.



So, this pilot does seem to identify some structure, but we need to further develop and refine our clustering methods.

Proteomics

2018-09-13_BMDA153 and GP-89 with clinical data_for SIMCA v1.M2 (PCA-X)
Colored according to classes in M2



Proteobacteria associated features

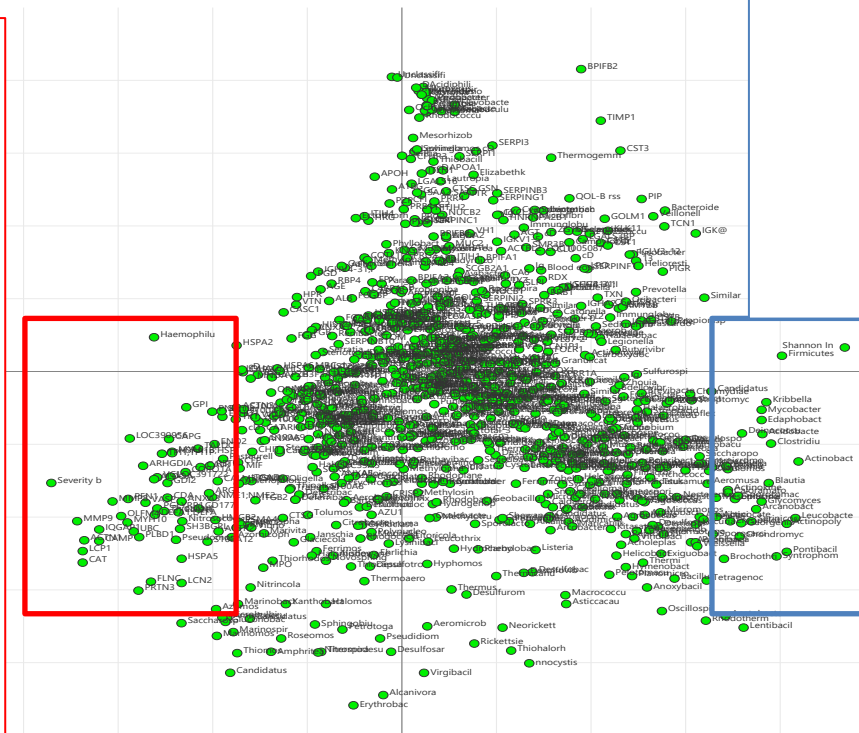
Proteome

- MMP9
- MMP8
- ACTN1
- LCP1
- CAT
- CAMP
- IQGAP1
- OLFM4
- PFN1
- VASP
- DEFA1
- ELANE
- TP11
- CD177
- RETN
- etc

Microbiome

- Saccharospirillum
- Pseudomonas
- Haemophilus
- Thioalkalivibrio
- Nitrosococcus

2018-09-13_BMDA153 and GP-89 with clinical data_for SIMCA v1.M2 (PCA-X)
Colored according to model terms



Firmicutes associated features

Proteome

- IG
- PIGR
- CST4
- TCN1
- PIP
- CST3

Microbiome

- Shannon Index
- Actinobacteria
- Leucobacter
- Actinopolymopha
- Pontibacillus
- Syntrophomos
- Firmicutes
- Clostridium
- Blautia
- Kribbella
- Mycobacterium
- Edaphobacter
- Acidobacteria
- Glycomyces
- etc

- Patients with the specific “proteobacteria” type of microbiome displayed sputum proteome profiles known to associate with worse outcome.



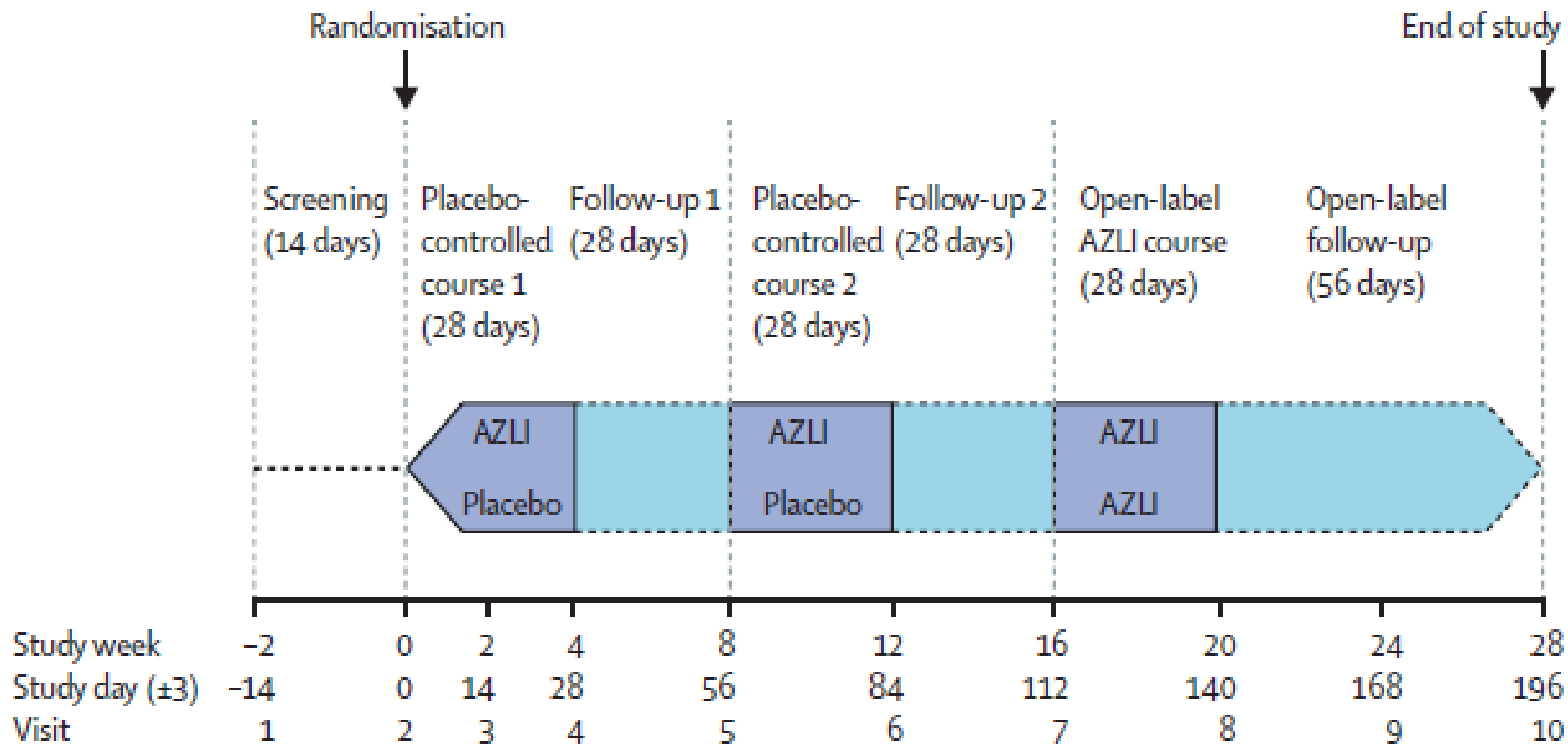
EMBARC

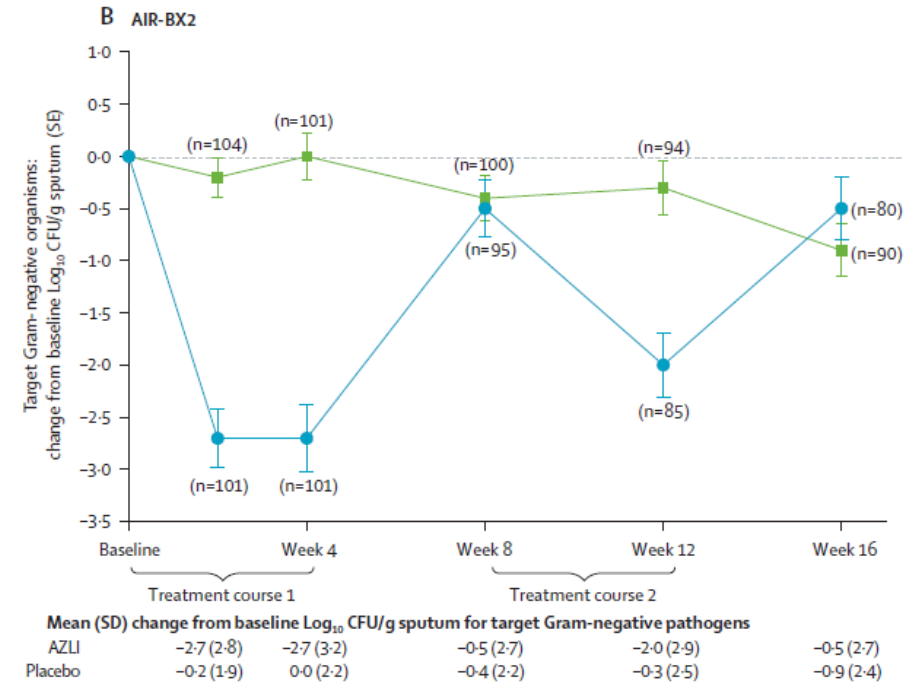
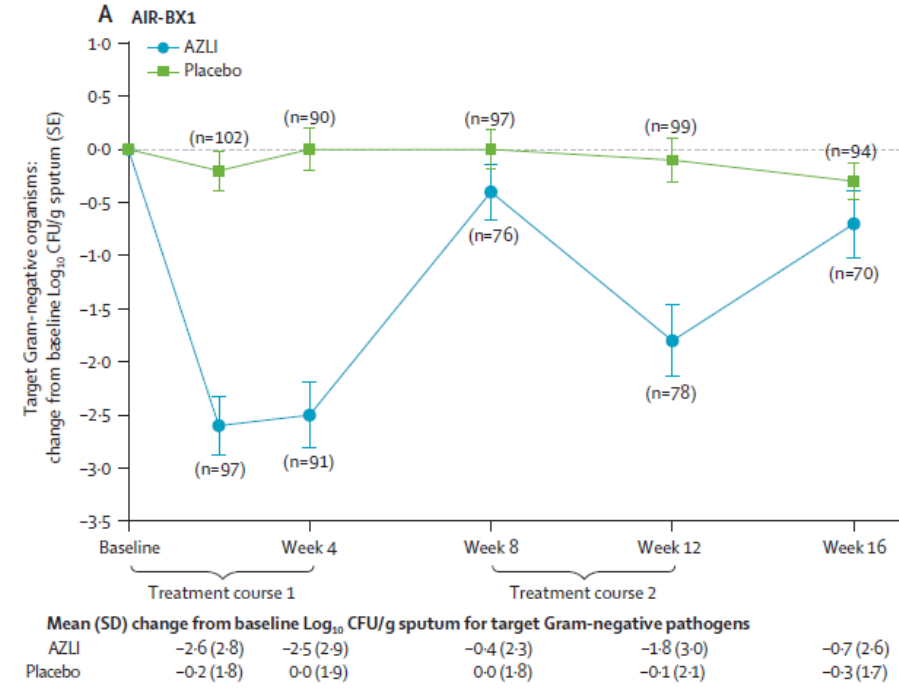
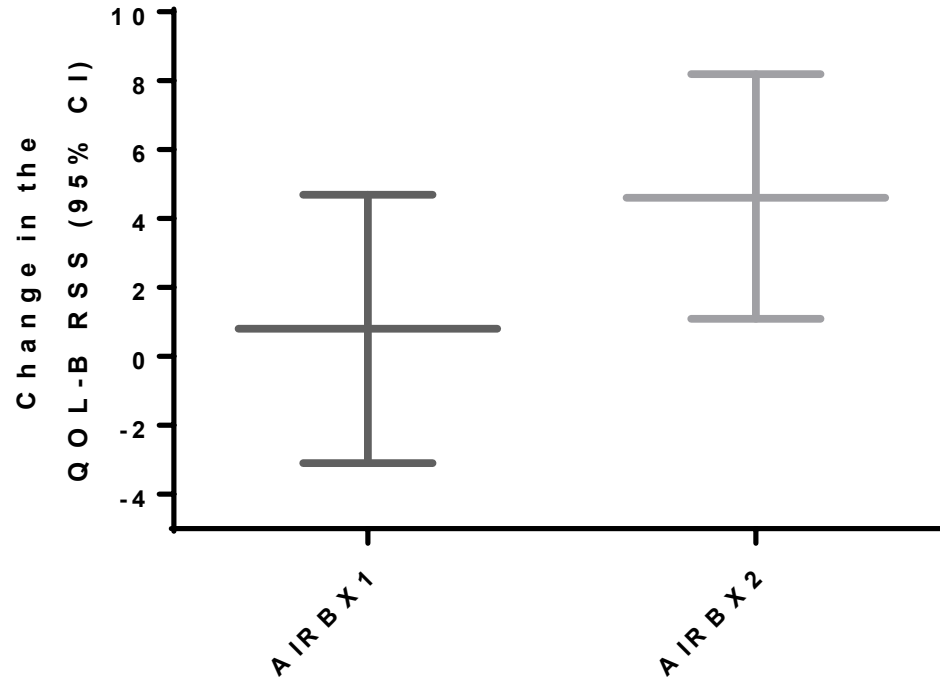
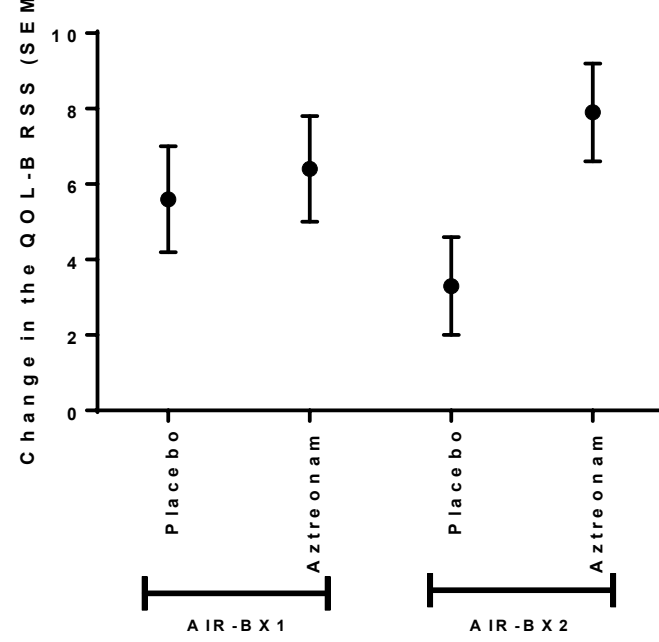
The European Bronchiectasis Registry



University
of Dundee

The AIR-BX studies- Randomized controlled trials of inhaled aztreonam







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The European Bronchiectasis Registry

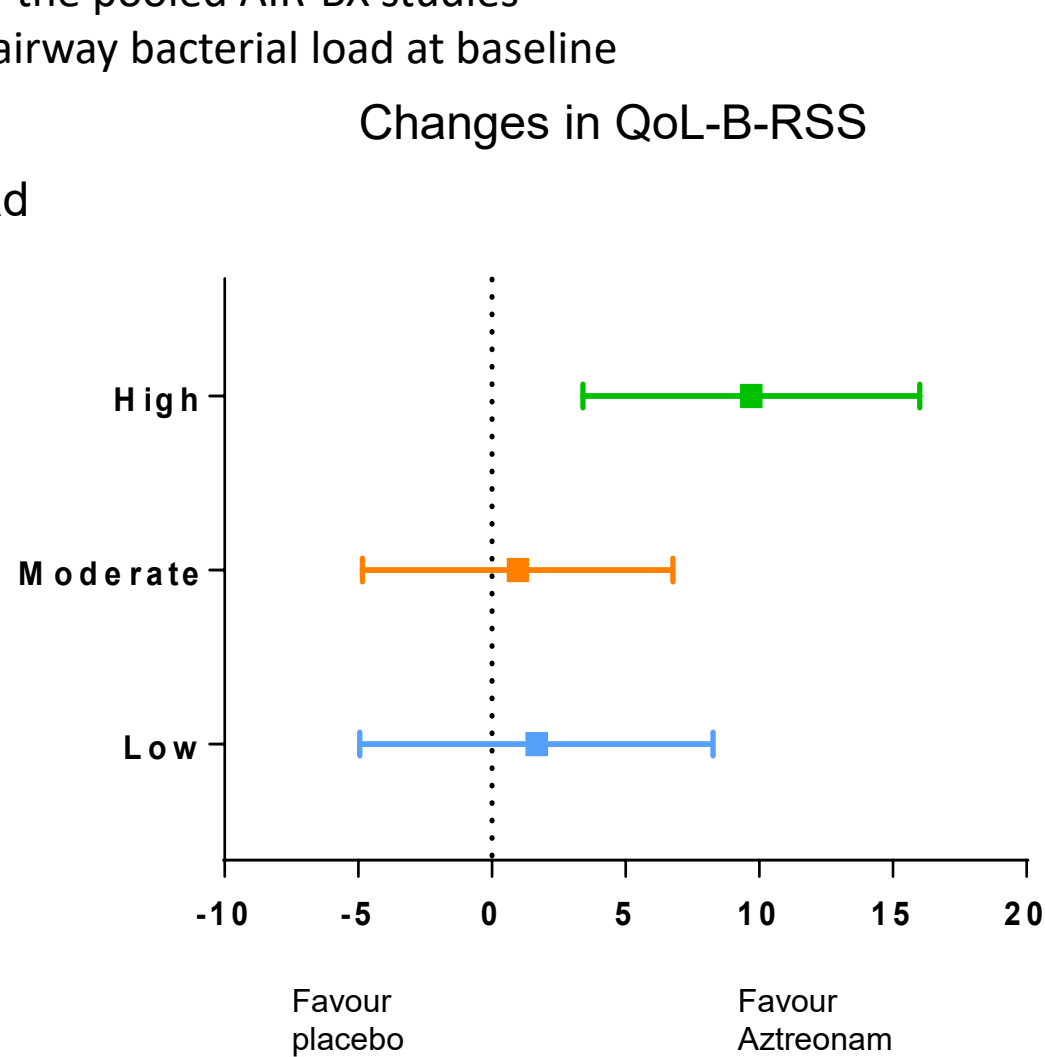


University
of Dundee

Re-analysis of the pooled AIR-BX studies
stratified for airway bacterial load at baseline

Changes in QoL-B-RSS

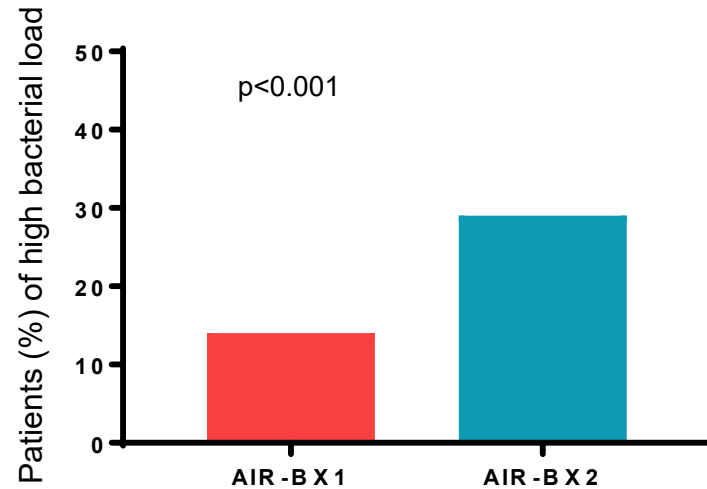
Bacterial load



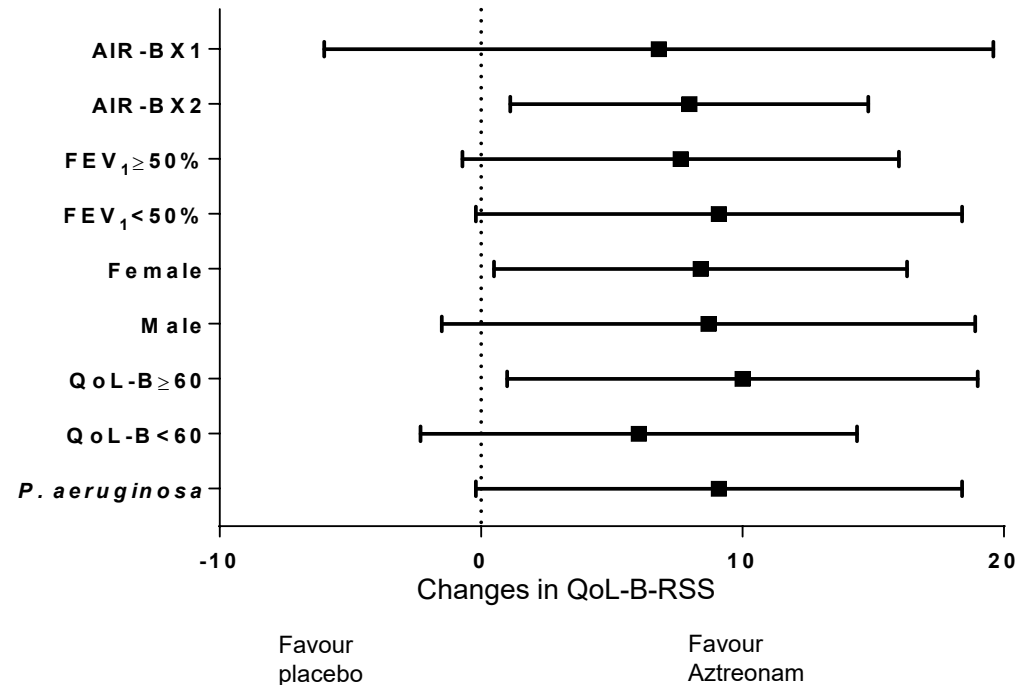


Consistent treatment benefit among patients with high bacterial loads

AIR-BX1 (negative study) had fewer “responders” than AIR-BX2 (positive study)



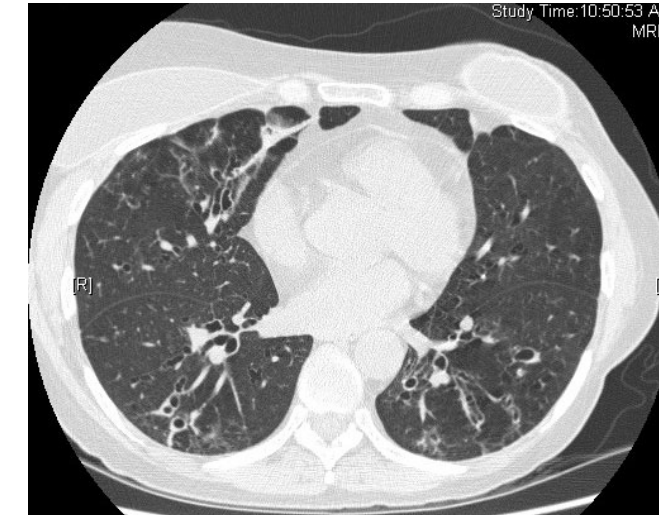
Treatment response among subgroups only in those with high bacterial load





Summary

- WP5 has met its objectives including sustainability
- Publications are planned for late 2018 and 2019 and we hope will be “landmark”
- The question for the consortium now is how to take this to the next level
- Observational data can underpin
 - Re-analysis of prior RCTs
 - Prospective studies embedded within the registry
 - Translational research



Acknowledgements

Executive group

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Eva Polverino

iABC co-ordinator

Stuart Elborn

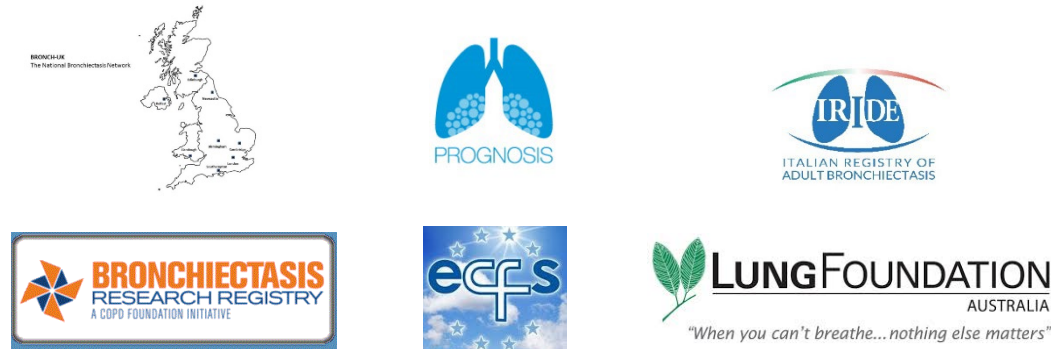
Steering committee

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Montserrat Vendrell
Tobias Welte
Robert Wilson

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Partners



Partners



www.bronchiectasis.eu

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