1st World Bronchiectasis Conference

"Joining forces for a breakthrough in bronchiectasis"

Abstract Book

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EMBARC
The European Bronchiectasis Registry

PROGNOSIS

DZL Deutsches Zentrum für Lungenforschung

BREATH HANNOVER

Dear Colleagues and Friends,

On behalf of the organizing committee and the EMBARC steering committee I extend a warm welcome to Hannover for the first World Bronchiectasis Conference.

After many years of describing bronchiectasis as an orphan or neglected disease, this conference is an opportunity to reflect on the progress we have made and to look forward to the opportunities and challenges that lie ahead. There is no more potent symbol of the progress that we have made together in the field of bronchiectasis, that we can gather together representatives from more than a dozen countries representing every continent and every major network, including EMBARC, the United States Bronchiectasis and NTM registry, the Australian Lung Foundation, ERS, ELF and our patient advisory group among many others.

We are extremely grateful to our friends in Hannover for their organization of this year's meeting and to the organizing committee. Their hard work and dedication has ensured this conference will be a success and we hope it will grow to become an annual event.

2016 has seen the completion of several large international clinical trials, the birth of large scale registries in Europe, Australia, Asia and beyond, the publication of cutting edge science and the first contributions from a generation of young clinicians and academics with bronchiectasis as their chosen field. It is the challenge for everyone at this year's conference to ensure that this is not the peak for our field, but rather a staging post towards even greater things to come.

We hope you have an enjoyable and stimulating 3 days in Hannover. We look forward to learning from you, and working with you towards a better future for all of our patients.

Yours, James D Chalmers

James Chalmers
EMBARC Chair
Member of PROGNOSIS' International Advisory Board

Dear Friends and Colleagues,

Dear Bronchiectasis Community,

For many centuries, bronchiectasis had been a well-known disease, well described in the literature. Although patients with bronchiectasis suffer severely and their quality of life decreases substantially, the disease has faded into obscurity for many years. This is manifested in today's glaring lack of data and randomized studies.

In recent years, however, bronchiectasis has regained attention. The First World Bronchiectasis Conference will therefore bring together physicians, scientists, patients and industry representatives to jointly discuss how research should be fostered and structured in the coming years.

The history of bronchiectasis astonishingly mirrors the history of the Herrenhausen Palace. While it saw glorious times during the reign of the kings of Hannover (and, for some time, even England), it was completely destroyed during the Second World War, and was almost forgotten in the following years. It took 70 years until it was rebuilt in 2013 by the Volkswagen Foundation according to the original plans. From the outside it today impresses with its historical appearance, while inside it is Hannover's most modern and architecturally striking conference venue.

We cordially invite you to visit the historical baroque gardens of the Palace while attending our meeting, adding a remarkable cultural experience to our scientific conference.

Welcome to Hannover!

Yours, Tobias Welte

Tobias Welte
(Congress Chair 2016)
Member of the EMBARC Steering Committee,
Director of BREATH, a site of the German Center for Lung Research

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Abstracts of oral presentations

OP I: The Past – The Renaissance of Bronchiectasis

Robert Wilson [1]

[1] Consultant Physician, NHS, UK

Bronchiectasis is the pathological end result of a number of heterogeneous disease processes. The vicious circle hypothesis proposes that impaired host defences lead to persistent bacterial infection which stimulates chronic neutrophilic inflammation, which together with bacterial products damages lung tissue, further impairing the defences, and perpetuating the circle. This may lead to spread of disease to normal bystander lung. I will examine the evidence for this hypothesis, and explore how it has guided management of patients. However, the hypothesis does not satisfactorily explain why some patients achieve relative stability and fair health status, whereas others do not, and this latter group drive healthcare costs, and have reduced life expectancy. I will speculate why this might be, and hope to set the scene for the rest of the conference

OP II: Inhaled antibiotics: potential and pitfalls

Alan F. Barker [1]

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The administration of inhaled antibiotics represents two somewhat baffling and contradictory directions in bronchiectasis. Inhaled antibiotics have a strong appeal for the treatment of lower respiratory tract infections because they directly target the lower airways, allow high local drug concentrations well above bacterial microbe MICs, have demonstrated efficacy in cystic fibrosis, and avoid high systemic absorption and toxicities. Yet, in spite of many years of careful investigation, no inhaled antibiotic has shown proof-of-concept in pivotal Phase 3 clinical trials nor been approved by regulatory authorities in any country.

The modern consideration of inhaled antibiotics in the 1990s included the exploratory trial of TSI in bronchiectasis that demonstrated highly efficient Pseudomonas killing. Subsequent clinical trials failed to demonstrate clinical efficacy and were accompanied by bothersome cough and hoarseness. Gentamicin administered by nebulizer has demonstrated antimicrobial and clinical efficacy in a small single blinded randomized trial. Aztreonam delivered by a convenient e-flow nebulizer demonstrated antimicrobial effectiveness, but failed to meet a patient reported outcome primary endpoint. Most recently colistin by nebulization failed to significantly reduce time to a first exacerbation although several secondary endpoints were favorable. Excitement has been building with the completion in 2016 of trials of 2 formulations of inhaled ciprofloxacin, both with favorable Phase 2 results.

In summary, inhaled antibiotics are effective to prevent exacerbations and reduce the decline in pulmonary function in cystic fibrosis. Large clinical trials (250 to 500 subjects) in bronchiectasis can be accomplished in a reasonable period of time. Virtually all trials have shown excellent microbial killing of virulent and often resistant organisms including Pseudomonas. Adverse events including cough, sore throat, and hoarseness occur but can be controlled and seem tolerable. Stabilization of FEV1 does not occur and may not be an appropriate endpoint in bronchiectasis. Future trials may need to better identify appropriate patients for study and evaluate a combination of desirable endpoints such as reduction in exacerbations, lowering of systemic and airway inflammatory mediators, and patient reported outcomes.

OP III: Macrolides: known knowns, and known unknowns

Conroy Wong [1]

[1] Middlemore Hospital in Auckland, New Zealand

Recent randomised controlled trials of macrolide therapy have increased our knowledge about how to treat our patients with bronchiectasis. However, many aspects of macrolide therapy remain unclear.

Macrolide antibiotics possess anti-inflammatory and immunomodulatory properties in addition to their antibacterial properties. Multiple mechanisms of action have been described.

Four major randomised, placebo-controlled trials have recently shown that prolonged treatment with azithromycin (EMBRACE, BAT, and BIS studies) or erythromycin (BLESS study) significantly decreased the frequency of pulmonary exacerbations in patients with bronchiectasis. Modest improvements in lung function and quality of life were also seen.

Many questions remain about macrolide therapy. These include concerns about hearing loss, risk of cardiac arrhythmia, and antimicrobial resistance. Furthermore, which patients should have long term macrolide therapy, what is the best macrolide and how long should patients be treated for? Do macrolides increase the risk of developing non-tuberculous mycobacterial infections and what are the effects on the microbiome?

Prolonged macrolide treatment is effective in preventing pulmonary exacerbations. The challenge for clinicians at present is how to use macrolides optimally whilst minimizing the risks to the individual and the community.

OP IV: The relationship between serum- and sputum levels of azithromycin and clinical endpoints in bronchiectasis patients in bronchiectasis patients using maintenance treatment

Josje Altenburg [1,*], *Erik Wilms* [2], and *Wim Boersma* [1]

[1]Alkmaar Medical Centre

[2]The Hague Hospital Pharmacy

*Presenting author

Background
Azithromycin (AZM) is a macrolide antibiotic with distinct pharmacokinetic properties and is increasingly used as maintenance treatment in patients with bronchiectasis in order to reduce infectious exacerbations and improve pulmonary symptoms. The exact mechanism of action is not known and the relation between azithromycin dose level, local and systemic drug levels and clinical effect however, has not been extensively studied yet.

Objectives
To explore the relation between AZM serum and sputum concentrations, clinical effect parameters and side effects.

Methods
Azithromycin concentrations were measured in serum and sputum samples of bronchiectasis patients receiving one year of AZM treatment (250mg OD) enrolled in the Bronchiectasis and Azithromycin Treatment (BAT) trial, a double blind, randomised placebo-controlled trial. Results were correlated with data on AZM dose level, exacerbation frequency, lung function (forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC), quality of life and symptoms collected within the same year.

Results
83 sputum samples from 31 patients and 151 serum samples from 43 patients were available for analysis. Mean AZM dose-level ranged from 18.8 to 39.8 mg/kg body weight/ week, generating mean AZM concentrations of 7.57 mg/L (SD 9.49) in sputum and 0.11 mg/L (SD 0.085) in serum. No correlation was found between side

effects and AZM dose level, sputum- or serum concentrations. Significant correlation was found between AZM sputum concentration and CRP-level (r= -0.6).

Conclusions
High and stable AZM sputum levels were reached during long term treatment, as opposed to low AZM levels in serum. Apart from CRP-levels to AZM sputum concentration, no other outcome parameter showed significant correlation to AZM serum- or sputum levels. AZM dose- or exposure levels were not predictive for the occurrence of side effects.

OP V: Quality of life as an outcome measure in clinical trials

Alexandra Quittner [1]

[1] Miami College of Arts and Science, USA

TheQualityofLife-Bronchiectasis(QOL-B), is a new, self-administered, patient-reported outcome measure assessing symptoms, functioning and health-related quality of life for patients with non-cystic fibrosis (CF) bronchiectasis. It was developed using the FDA Guidance on Patient-Reported Outcomes (FDA, 2009) and with consultations from the FDA. Thus, it can be used as a primary or secondary endpoint in clinical trials of new medications. It contains 37 items on 8 scales (Respiratory Symptoms, Physical, Role, Emotional and Social Functioning, Vitality, Health Perceptions and Treatment Burden). Psychometric analyses of the QOL-B V.3.0 indicated is has excellent internal consistency (Cronbach's $\alpha \geq 0.70$) and 2-week test–retest reliability (intraclass correlation coefficients ≥ 0.72), as well as convergent validity with the 6 min walk test and the SGRQ. It has demonstrated good discriminant validity between patients, based on baseline FEV_1% predicted. The QOL-B has been translated into over 40 languages and is being utilized in several international clinical trials.

OP VI: Lost in translation? Therapeutic contrasts in CF and non-CF bronchiectasis

Lieven Dupont [1]

[1] Department of Respiratory Medicine, University of Leuven, Belgium

Non–cystic fibrosis bronchiectasis is a significant cause of morbidity and mortality and its prevalence is increasing. Unlike CF, non–cystic fibrosis bronchiectasis (NCFB) is a heterogeneous disease, with a variety of predisposing factors and disease mechanisms implicated in its pathogenesis. However, the "vicious cycle" hypothesis is the generally accepted explanation for the evolution of bronchiectasis, both in CF as in NCFB.

Pharmacologic and nonpharmacologic therapies are used in CF and NCFB with varying success. The routine use of bronchodilator therapies or steroids in CF and NCFB is not recommended except when there is airflow reversibility or allergic bronchopulmonary aspergillosis. Long-term azithromycin consistently shows a reduction in exacerbations and as a consequence is widely used in patients with both CF and NCFB and is recommended for use in patients with and without Pseudomonas aeruginosa (PA) infection. The use of antibiotics in patients with NCFB is driven mostly by studies in patients with CF. In CF and NCFB, exacerbation frequency, lung function, and disease extent are worse in patients infected with PA. As in CF, eradication of PA in NFCB should be attempted, especially following initial colonization. Inhaled antibiotics reduce airway bacterial load and associated airway inflammation in NCFB. Unlike data in the CF population, where inhaled antibiotics have been shown to reduce exacerbations and hospital admissions, studies in NCFB did not persuasively demonstrate a reduction in exacerbation frequency. Hypertonic saline benefits patients with CF by improving quality of life, reducing pulmonary exacerbations and improving lung function. Although there are no strong data or recommendations

for routine use of hypertonic saline in NCFB, some patients seem to benefit from this therapy. Aerosolized dornase alpha reduces mucus viscosity, improves lung function, and reduces hospitalizations in patients with CF but in NCFB was found to cause greater reductions in FEV1.

Many aspects of the management of bronchiectasis in patients with no CF have thus been based on the experience gained from and the more extensive research studies performed in CF. However, therapies for NCFB cannot simply be extrapolated from CF, and some treatments, such as the use of inhaled DNase, may actually result in harm. The differences in efficacy likely result from differences in pathophysiology and patient demographics. Clinical studies that specifically target patients with NCFB are sorely needed.

OP VII: Risk factors for bronchiectasis exacerbations caused by multidrug-resistant microorganisms

Rosario Menéndez [1,*], *Eva Polverino* [2], *Raúl Méndez* [1], *Edmundo Rosales-Mayor* [2], *Isabel Amara-Elori* [1], *Tomás Posadas* [1], and *Antoni Torres* [2]

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*Presenting author

Rationale and aim.
Non cystic-fibrosis bronchiectasis (BE) is a chronic structural lung condition characterized by exacerbations mainly caused by bacteria and in some cases by multidrug-resistant (MDR).
The aim of the study was to investigate risk factors associated with exacerbation due to MDR pathogens.

Methods.
Prospective observational study performed in two tertiary-care hospital with specific BE clinic. We included patients treated as outpatient and or hospitalized due to exacerbation. MDR aetiologies were considered MDR Pseudomonas, MRSA, ESBL Enterobacteriaceae, Stenotrophomonas.

Results.
245 exacerbations were included in the cohort and aetiology was found in 173 exacerbations of which 39 were due to MDR pathogens. Overall, 48 patients were treated as outpatients while 125 were hospitalized. Main demographic characteristics of the patients, comorbidities, usual treatment and severity scores are depicted in the Table. No differences were found regarding usual treatment (bronchodilator, corticosteroids) excepting prior use of antibiotics and oxygen therapy that were more frequent in MDR. The multivariate regression analysis for MDR showed the following independent factors: FACED (OR: 3.05 95%CI 1.16-7.99), chronic renal disease (OR: 7.01, 1.77-27.65), hospitalization last year (OR: 3.62, 1.26-10.38) and prior colonization by MDR microorganism (OR: 5.67, 2.16-14.85).

Conclusions.
MDR pathogens are responsible of 22.5% BE exacerbations and most of them required hospitalization. The most frequent MDR aetiologies were Pseudomonas, MRSA and ESBL+. A high FACED score, hospitalization during last year, chronic renal disease and prior colonization by MDR microorganism are independent risk factors for MDR aetiology. That information may assist clinicians in choosing empirical antibiotic in BE exacerbations.

Funding: Beca SEPAR (Sociedad Española de Neumología y Cirugía Torácica) 106/2012 and CIBERES (Centro de investigación en red de enfermedades respiratorias).

OP VIII: Introducing the microbiome, lessons from the healthy lung and CF

Michael G Surette [1]

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The microbiome of the upper respiratory tract (URT), including the nasopharyngeal and oropharyngeal microbiota, is a dynamic community of microorganisms as diverse as the gastrointestinal microbiome. Until recently, the lower airways of healthy individuals were considered to be effectively sterile. This has been challenged by recent studies, and the best evidence suggest the lungs of healthy individuals are transiently colonized by microbes of the URT. In cystic fibrosis the chronic colonization of the lower airways by bacterial pathogens is the leading cause of morbidity and mortality. It is now well established that the lower airways in CF patients are colonized by a more complex polymicrobial community comprised primarily of bacteria found in the URT along with the traditional pathogens associated with CF airway disease. This community may include pathogens missed by conventional CF microbiology and organisms that can act synergistically with *P. aeruginosa*. These observations now guide disease management in some patients and are being applied to other respiratory diseases. Considering respiratory infections as polymicrobial diseases offers new avenues to for treatment and possible new directions for developing new therapies. The CF airways have been the focus of molecular microbiome studies, however, there remain many challenges that must be overcome if microbiome profiling is going to inform clinical practice.

OP IX: Pseudomonas aeruginosa diversity and adaptation in the non-Cystic Fibrosis bronchiectasis lung

Yasman Hilliam [1], *Matthew Moore* [1], *Ian Lamont* [1], *Charles S. Haworth3* [2], *Juliet Foweraker* [3], *Diana Bilton* [4], *Martin Walshaw* [5], *Jo Fothergill* [1], *Anthony De Soyza* [6,*], and *Craig Winstanley* [1]

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INTRO:
In contrast to many studies using phenotyping and genomic analyses to characterise the evolution and adaptation of Pseudomonas aeruginosa populations during chronic lung infections of cystic fibrosis (CF) patients, the study of such infections in non-CF bronchiectasis (BE) is much less well advanced.

METHODS:
We used whole genome sequencing to (i) assess the diversity of P. aeruginosa strains causing infections in BE in the UK, (ii) assess the prevalence of multi-lineage (strain) infections, (iii) look for evidence for cross-infection or common source acquisition and (iv) characterise both adaptive mutations and within-population heterogeneity during P. aeruginosa chronic lung infections of BE patients.
Using the Illumina platform, a total of 189 isolates were genome sequenced, obtained from 93 patients attending 16 adult UK BE centres. Genomic data was used to extract multilocus sequence type (MLST) profiles, perform core genome SNP phylogenetic analysis, and analyse genomic variations (such as large deletions and

adaptive mutations).

RESULTS:
The BE isolates were widespread when analysed within the wider P. aeruginosa population structure, with the most widespread lineages being the known common lineages ST-253 (PA14-like) and ST-179 (Clone C).
Of 23 patients from whose samples multiple isolates were examined, there were six examples of multi-lineage infections.

In one patient there were three co-existing lineages (strains). SNP phylogeny revealed examples of more than one patient attending the same centre being infected with a common lineage.
There were common loss of function mutations in genes identified previously as being commonly mutated in CF, including mucA (mucoidy) and lasR (quorum sensing), as well as deletions in a genomic region encoding pyoverdine, psl polysaccharide and type VI secretion genes.
As in CF, we observed within-patient heterogeneity in the infecting P. aeruginosa populations.

FUNDING:
Funding from the UK Medical Research Council in support of the BRONCH-UK network.

OP X: Microbiota composition and disease severity in bronchiectasis

Geraint Rogers [1]

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The microbes present in the lower airways are strongly implicated in the development, progression, and severity of many types of chronic lung disease. Complex and bidirectional relationships exist between the airway environment, the composition of the lung microbiota, and rate and nature of accumulated damage. Understanding these interactions, and their implications for bronchiectasis, is challenging. The development of local immune regulation in early life, and the effects of host mutations, such as those affecting mucin properties, both influence airway microbiology. As disease develops, there is a divergence from healthy airway microbiology, while in later disease, changes in the physicochemical characteristics of the lungs due to inflammation and remodelling, as well as exposure to antibiotics and other therapies, are central in defining more marked changes in airway microbiology. Throughout this process, the impact of altered airway microbiology of respiratory health is influenced by both the behaviour and immune-modulatory traits of pathogenic taxa, and the interactions of these key species with the wider airway microbiota. Recent technological advances present opportunities for detailed characterisation of the airway microbiome, allowing us to dissect the relationships between airway microbiology and respiratory health. The ways in which this basic research can help to provide mechanistic insight, prognostic information, and a basis for improved clinical care, will be discussed.

OP XI: Molecular diagnosis of infection and resistance

J Stuart Elborn [1]

[1]Queen's University Belfast

The identification of bacteria in sputum has traditionally relied on wet culture of bacteria and other micro organisms on agar plates. This approach is geared to identify specific pathogens and it has become clear that this approach only identifies a narrow group of pathogenic bacteria. Next generation sequencing (NGS) and other molecular methods, particularly 16srDNA, have identified a much wider range of bacteria though many of these are in low abundance and may not be important clinically. In addition, it is apparent from culture based methodologies that the assessment of microbial resistance using culture based techniques has significant limitations and does not predict clinical outcomes. New technologies in bacterial identification such as MALDI-TOF and the application of NGS in the clinical context is increasing our capacity to identify bacteria and potentially mutations associated with resistance. How this diagnostic information can be used to improve treatment is an area which will require further research.

OP XII: Prevalence of Nontuberculous Mycobacterial Pulmonary Disease, Germany, 2009–2014

Felix C. Ringshausen [1], *Dirk Wagner* [2], *Andrés de Roux* [3], *Roland Diel* [4], *David Hohmann* [5], *Lennart Hickstein* [6], *Tobias Welte* [1], and *Jessica Rademacher* [7*]

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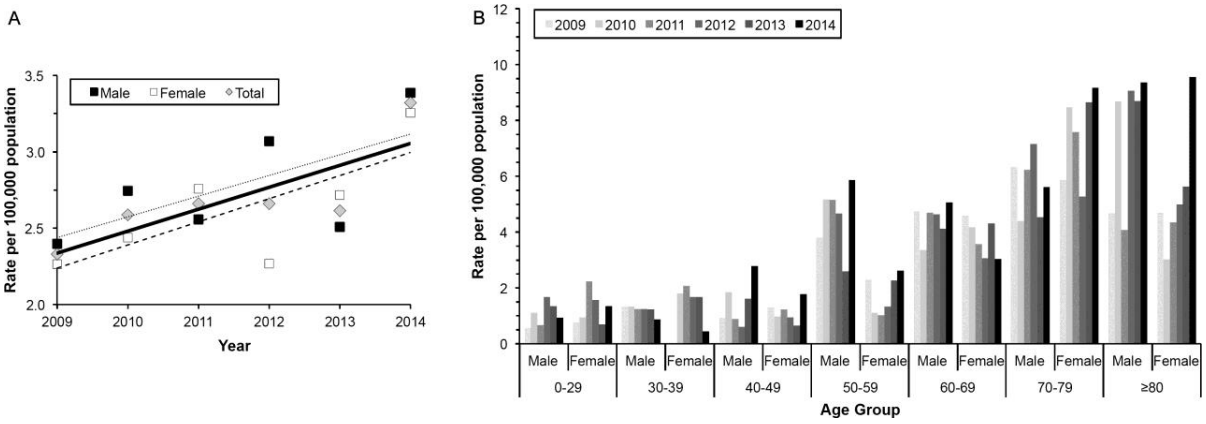
[5]HGC GesundheitsConsult, Düsseldorf
[6]Health Risk Institute, Berlin
[7]Hannover Medical School
*Presenting author

We could recently demonstrate that the burden of nontuberculous mycobacterial pulmonary disease (NTM-PD) is steadily increasing in Germany, as in many other countries [1]. However, population-based data on the epidemiology of NTM-PD are still scarce.
We analyzed representative samples of German routine statutory health insurance (SHI) claim data regarding the annual prevalence rates of NTM-PD (ICD-10 diagnosis code A31.0) over a six-year period and the distribution of age and sex, the site of health care provision as well as concomitant conditions.

Overall, from 2009 to 2014 we identified between 85 and 126 subjects with NTM-PD per year, with a balanced sex distribution. Mean age was not significantly different between males and females, except in 2013. The majority of subjects were managed in outpatient care (76–87%). Notably, the most frequent concomitant diagnosis was COPD/emphysema (ICD-10 codes J43–J44) in 62–79% of subjects. Between 6.6 and 18.3% of subjects had bronchiectasis. Annual prevalence rates increased from 2.3 (95% CI 1.87–2.87) to 3.3 (95% CI 2.78–3.94) cases per 100,000 population between 2009 and 2014, while the corresponding projected total number of subjects with NTM-PD in Germany increased from 1,907 to 2697 (Figure 1A). Overall, annual rates did not differ significantly between males and females. We observed the highest prevalence rates among subjects aged ≥50 years, in particular among males and females aged ≥80 years in 2014 (9.4 (95% CI 4.35–17.78) and 9.6 (95% CI 5.44–15.65) per 100,000, respectively; Figure 1B).

In conclusion, the annual prevalence rate of NTM-PD in Germany increased between 2009 and 2014. NTM-PD showed a strong association with advanced age and chronic airway diseases. Further reliable data on the epidemiology of NTM-PD are urgently needed and could become available if NTM-PD became a notifiable disease or comprehensive disease-specific registries were established [2].



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OP XIII: The Present: Bronchiectasis in 2016

Anne E. O'Donnell [1]

[1] Georgetown University Medical Center Washington DC, USA

In this presentation Anne O'Donnell will review the current best practices for the evaluation and treatment of patients with bronchiectasis and will discuss controversies/unsettled issues in this disease.

OP XIV: Non-CF bronchiectasis: a spectrum of CFTR (and ENaC) dysfunction?

Felix C. Ringshausen [1] *(Hannover, Germany)*

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Disorders of the respiratory epithelium's ion conductance result in abnormal airway surface liquid hydration, defective mucociliary clearance and impaired host defense and may contribute to the pathogenesis of bronchiectasis. This may affect either the amiloride-sensitive epithelial sodium channel (ENaC) or the chloride channel cystic fibrosis transmembrane conductance regulator (CFTR). The most prominent channelopathy associated with bronchiectasis is cystic fibrosis (CF), an autosomal recessive disease caused by mutations in the CFTR gene, which encodes the chloride CFTR channel. The diagnosis of a defective ion conductance is difficult

and the most important diagnostic tool for subjects with bronchiectasis, the measurement of the nasal transepithelial potential difference (nPD), is not readily available in most centers. Nevertheless, the efficient and exact diagnosis of underlying CFTR or ENaC dysfunction is an issue of increasing relevance as targeted treatment options like specific modulators of CFTR or specific inhibitors of ENaC function have already become available or may enter clinical routine as a mucolytic approach in the near future.

This presentation will summarize the current knowledge, introduce a fascinating diagnostic technique and will postulate a novel diagnostic pathway for subjects with idiopathic bronchiectasis based on unique original data.

OP XV: Bronchiectasis with upper airways symptoms is associated with allergic features and frequent exacerbations

Michal Shteinberg [1,*], *Najwan Nasrallah* [2], *Evgenia Gerbeshian* [3], and *Yochai Adir* [4]

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*Presenting author

Background
The association of bronchiectasis with upper airway symptoms (UAS) has been previously reported (1). However, apart from primary ciliary dyskinesia (PCD) and cystic fibrosis (CF), predisposing conditions have not been established. The aim of our study was to evaluate whether patients with BE and UAS have unique etiologic, laboratory and clinical features and whether presence of UAS has implications on severity.

Methods
We retrospectively reviewed the charts of adult patients with non CF, non PCD related bronchiectasis. The presence of UAS was defined as nasal discharge in most days of the year, sinusitis or nasal polyps. Patients with a discrepancy between symptoms and sinus CT findings were excluded. Laboratory data including IgG, total IgE, blood eosinophils, sputum bacteriology, as well as lung function, were recorded. CT scoring of bronchiectasis (Reiff score) and sino- nasal pathology (Lund- McKay score) (2) was performed by a radiologist blinded to UAS presence. Data regarding exacerbations were collected from patients' files and antibiotic prescription records.

Results
163 patients out of 220 screened were included in the study. 59 (36%) had UAS. Patients with UAS had an earlier age of onset (34±24 vs. 45±24, p=0.007) and the duration of disease was longer (26±20 vs. 19±19 years, p=0.02) than patients without UAS, with similar current age. Patients with UAS had higher blood eosinophils (median, 290 vs. 200/ml, p=0.002) and total IgE (median, 100 vs. 42 IU/ml, p=0.066). These patients had significantly more exacerbations (3.4±2.5 vs. 2.63±2.4, p=0.016), and less were free from exacerbations (3.4% vs. 14%, p=0.034). No differences in gender, lung function, hospitalizations, Reiff CT score, colonization with bacteria, or IgG levels were found.

Conclusion
Patients with UAS had an earlier onset, with features suggestive of allergic diathesis and higher rate of exacerbations. This may implicate a higher disease burden in patients with UAS.

	No UAS (104)	UAS (59)	P value
Sex (% female)	61.5%	67.8%	0.424
Onset age (y), median (mean±SD)	30 (45±24)	50 (34±24)	**0.007**
Age at diagnosis (y), median (mean±SD)	65.5 (64±15)	63.1 (59±18)	0.201
Time from onset to diagnosis (y) median (mean±SD)	12.9 (18.9±18.7)	23.8 (25.9±20)	**0.02**
Presence of asthma, no. (%)	5 (4.8)	7 (11.9)	0.122
Idiopathic etiology, no. (%)	50 (48.1)	31 (52.5)	0.584
Post infectious etiology, no (%)	31 (29.8)	7 (11.9)	**0.009**
Eosinophils /µl, median (mean±SD)	200 (216±174)	290 (249±399)	**0.002**
IgE (IU/ml), median (mean±SD)	42 (139±240)	100 (375±878)	0.066
IgG (IU/ml), median (mean±SD)	1169 (1198±318)	1184 (1210±383)	0.747
FEV_1 (% of predicted) mean±SD	81±26	81±26	0.905
Reiff score, median (mean±SD)	7 (8.13±4.2)	6 (8±4.4)	0.632
Lund – McKay score, median (mean±SD)	0.5 (.87±1) N=38	11.5 (10.6±3.8) N=34	**<0.0001**
Exacerbations/ year, median (mean±SD)	2 (2.63±2.4)	3 (3.36±2.5)	**0.016**
Occurrence of exacerbation in previous year, no. (%)	60 (86 %)	56 (96.6%)	**0.034**

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OP XVI: Omics approaches to understand airway inflammation in bronchiectasis

James D Chalmers [1]

[1] University of Dundee, UK

Bronchiectasis is characterised by chronic airway inflammation, leading to progressive lung damage. The inflammation is predominantly characterised by neutrophils, although the epithelium, macrophages and T cells also clearly contribute to the microenvironment. Bronchiectasis is heterogeneous, but the reported profiles of cytokines/chemokines and inflammatory mediators in bronchiectasis are surprisingly consistent and unaffected by aetiology. Bacterial infection has been demonstrated to be the key driver of neutrophil recruitment, with data also suggesting that bacterial clearance can achieve resolution of inflammation.

This talk will review published and unpublished data on the nature of inflammation in bronchiectasis. "Omics" technologies are providing a broader and in some cases surprising view of the drivers of the development and progression of bronchiectasis. GenOMICS: we will review published data on genetic modifiers of disease severity and what the genetic susceptibility factors of bronchiectasis tell us about airway inflammation. ProteOMICS: we will review the protein biomarkers identified as modifiers of disease severity in bronchiectasis, with a focus on those that can be used for disease phenotyping, MetabolOMICS: small molecules and metabolites that can detect bacterial infection or inflammatory patterns.

Development of new treatments, and targeting of current treatments to the appropriate patients, requires a better understanding of the nature of airway inflammation and disease phenotypes. This talk will aim to review how close we are to understanding the role of the new technologies and new markers in bronchiectasis.

OP XVII: Pneumonic vs. non-pneumonic exacerbations in bronchiectasis

Edmundo Rosales-Mayor [1,*], *Victoria Alcaraz-Serrano* [1], *Rosario Menendez* [2], *Emilio Ansotegui* [2], *Beatriz Montull* [2], *Rosa María Girón* [3], *Carolina Cisneros* [3], *Montserrat Vendrell* [4], *Gerard Muñoz* [4], *María Angeles Marcos* [5], *Eva Polverino* [1], and *Antoni Torres* [1]

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*Presenting author

Rationale: Exacerbations are relevant in bronchiectasis (BE) but little is known regarding microbiology and outcomes of pneumonic (CAP) vs. non-pneumonic (EXAC) exacerbations.

Objective: To compare clinical and microbiological characteristics of CAP vs. EXAC in adult patients with BE.

Methods: Multicentre prospective observational study of consecutive cases from 4 Spanish hospitals.

Results: We recruited 144 patients: 91 EXAC (63%) and 53 CAP (37%); 89% required hospitalization (CAP 94%, EXAC 86%). Demographics, vaccines, bronchiectasis aetiology and severity, and lung function were similar in both groups. CAP group showed more males and COPD but less chronic bronchial infection, previous exacerbations and macrolides than EXAC group. Clinical presentation was similar excepting higher values of creatinine, C-reactive protein, glucose and leukocytes in CAP. S.pneumoniae and P.aeruginosa were the first cause of CAP and EXAC, respectively. Most patients with P.aeruginosa already had a chronic infection by the same microorganism prior to CAP (71%) or EXAC (81%). Nevertheless, numerous patients with previous chronic P.aeruginosa had a new infection in our study (19% of EXAC, 58% of CAP). CAP showed more atrial fibrillation but similar outcomes (hospital stay, mortality, etc.) than EXAC. Chronic bronchial infection and previous exacerbations≥2/year were protective factors for CAP at multivariate analysis.

Conclusions: CAP and EXAC in patients with BE have similar clinical presentation.An initial antibiotic treatment should cover S.pneumoniae in CAP and P.aeruginosa in EXAC, particularly in case of previous chronic infection, however a complete microbiological research is recommended. Pneumococcal vaccination should be considered in BE

OP XVIII: Anti-Pseudomonas aeruginosa IgG Antibodies and Chronic Airway Infection in Non-Cystic Fibrosis bronchiectasis

Guillermo Suarez-Cuartin [1,*], *Oriol Sibila* [1], *Alex Smith* [2], *Hani Abo-Leyah* [2], *Ana Rodrigo-Troyano* [1], *Silvia Vidal* [1], *Vicente Plaza* [1], *Thomas C Fardon* [2], and *James D Chalmers* [2]

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Rationale: Identification of Pseudomonas aeuginosa (PA) infection status is important in the management of non-cystic fibrosis bronchiectasis. Serum anti-PA IgG antibodies have been proposed to diagnose chronic PA infection.

Methods: Clinically stable bronchiectasis patients were studied prospectively. Chronic PA infection was defined as 2 or more positive sputum samples at least 3 months apart and/or failure to clear PA following eradication treatment. Baseline serum samples were assayed for anti-PA IgG by a validated ELISA kit. The cut-off value for a

positive ELISA Unit/10 result was 2.96.

Results: 361 patients were included. Fifty-four (14.9%) of them had chronic PA infection. Patients with chronic PA infection had significant more severe bronchiectasis (BSI score mean 14 vs 7, p<0.0001) and more frequent exacerbations (mean 4 vs 2, p<0.0001). Patients with chronic PA infection had higher baseline PA IgG levels (median 8.1 vs 1.4, p<0.00001). Significant correlations were found between IgG levels and frequency of exacerbations (p=0.005), BSI score (p<0.0001) and neutrophil elastase in sputum (p=0.004). All patients with chronic PA infection had a positive IgG, giving a sensitivity of 100%, specificity of 75.3% and area under the ROC curve (AUROC) of 0.95. During the study, 38 patients had a new isolation of PA. Eradication at 12 months was achieved in 15.8% of patients with a positive antibody test (n=3) and 89.5% of patients with a negative IgG test.

Conclusions: The accuracy of anti-PA IgG test to detect chronic PA infection in bronchiectasis patients is very high. PA IgG is not sufficiently sensitive or specific to guide the decision to eradicate PA but may be a marker of severity of disease and treatment response.

OP XIX: COPD and bronchiectasis - a real phenotype?

John Hurst [1]

[1] Centre for Inflammation and Tissue Repair, University College London

Bronchiectasis is an anatomical diagnosis, arising from a diverse range of mechanisms conceptualised as a 'vicious cycle' and ultimately resulting in permanently dilated airways. COPD is a physiological diagnosis – the end result of a susceptible individual being exposed to sufficient airborne environmental toxin. Confusion between COPD and bronchiectasis arises because of the potential for a similar clinical presentation. However, when extensive, bronchiectasis can result in fixed airflow obstruction that meets the physiological definition for COPD and conversely, some patients with COPD have airway wall changes – typically airway wall thickening rather than dilation – which is commonly labelled as 'bronchiectasis'. Cue confusion, and talk of 'BCOS' – a bronchiectasis-COPD overlap syndrome. Whether you accept this or not, it is important to note that fixed airflow obstruction is associated with poor outcomes in bronchiectasis (FEV_1 is a component of BSI and FACED), and airway wall changes have been associated with poor outcomes in COPD. Therapy differs significantly between COPD and bronchiectasis: this presentation will therefore argue that it IS important to distinguish the primary pathology.

OP XX: Translating treatments between COPD and bronchiectasis

Menno van der Eerden [1]

[1] Erasmus MC Rotterdam, The Netherlands

Treatment with Long-acting bronchodilators in patients with COPD is mainly directed at improving symptoms and quality of life, furthermore long-acting bronchodilators and inhalation corticosteroids can prevent COPD exacerbations. The use of these medications in bronchiectasis is not clear. To date there is not sufficient evidence to recommend routine use of these medications in patients with bronchiectasis. This presentation will discuss the current evidence of these treatments in bronchiectasis. For now it is recommend to use these medications when COPD is the underlying cause of bronchiectasis. Furthermore it could be suggested to perform a spirometry for assessing the presence of reversibility of airway obstruction.

OP XXI: The Future: what is next in bronchiectasis?

Anthony de Soyza [1]

[1] Newcastle University

In this lecture Dr. De Soyza will draw upon the progress made in bronchiectasis to date and provide a (rose tinted) view of where we want to be in 5 years and then 10 years. The talk aims to be light hearted but covers what advances in understanding the pathophysiology, basic science, clinical trials and day-day management of bronchiectasis we hope for and what steps to meet these are currently underway. The talk will aim to pull in what other fields within respiratory medicine have learned in these achieving their goals to discovery and better treatments entering the clinic.

Poster Abstracts

Clinical Trials

P01: Study of population of patients with non-cystic bronchiectasis treated in the University Hospital of Olomouc, Czech Republic

Denisa Rozsivalova [1,*], *Vitezslav Kolek* [1], *Petr Jakubec* [1], *Jaromir Zatloukal* [1], and *Petra Smickova* [1]

[1]The Faculty of medicine and dentistry, The Palacky University and The University Hospital of Olomouc
*Presenting author

Introduction:
Bronchiectasis (BE) is a chronic disease, characterised by irreversible dilatation of bronchi. It is commonly associated with chronic productive cough, bronchial obstruction, and recurrent infections. BE (non-cystic) are often localised in the lower pulmonary lobes. The treatment of BE is focused on the successful management of the acute and chronic infection, and on the easing of the obstruction of the airways.

Description:
Currently we collected data from the 64 patients with BE, who were examined and treated in our hospital in the past three years. Out of this number two patients died of cardiorespiratory failure. Patients with cystic fibrosis and pneumooncological disease were not included. Ratio of women to men was 4: 1, 79% were nonsmokers. The median age was 63 years. In comparison with common population, patients with BMI in normal weight range predominated. Congenital BE were diagnosed in 19%. Acquired BE thus prevailed and most common types were postinfectious BE and BE connected with obstruction. The most frequent sign of BE in stable phase was expectoration of light sputum, it was coloured sputum during exacerbation. The most frequent microbial finding was Haemophilus influenzae, Streptococcus spp., Pseudomonas aeruginosa and Klebsiela spp. Chronic colonization with Pseudomonas aerigunosa was found in 7 patients, 27 patients needed hospitalization during exacerbation. The localisation of BE assessed by the HRCT examination was in 53% bilateral, 39% was unilobar and the rest was multilobar or unilateral. The immunological and ventilation parameters, type of treatment were evaluated. The data of the series are continuously updated and prognostic value of various laboratory parameters are tested.

Conclusion:
BE could be very variable in clinical and laboratory findings, which could be the reason why BE are commonly underdiagnosed. Modern diagnostic methods and especially better awareness of this disease can help in early diagnosis and treatment.

P02: 12-Month Follow-up From Phase 2 Trial of Liposomal Amikacin for Inhalation (LAI) in Patients With Nontuberculous Mycobacterial (NTM) Lung Infection

Kenneth Olivier [1], *David Griffith* [2,*], *Kevin Winthrop* [3], *Barbara Brown-Elliott* [2], *Gina Eagle* [4], *John McGinnis* [4], and *Richard Wallace* [2]

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[2]University of Texas Health Science Center
[3]Oregon Health & Science University
[4]Insmed Incorporated
*Presenting author

Introduction:
TR02-112 enrolled adult patients with NTM lung infection due to MAC and/or Mycobacterium abscessus refractory to a multi-drug regimen for ≥6 months. The randomized, placebo-controlled study evaluated efficacy, safety, and tolerability of LAI 590 mg administered once daily added to multi-drug regimen for 84 days (Double-blind). Patients continuing in the Open-label phase received LAI added to multi-drug regimen for 84 additional days. Here we report long term safety and efficacy data collected for patients in the 12-months after the last dose of LAI.

Methods:
The follow-up period was included to allow long term LAI safety and efficacy assessments 12 months after the last dose of LAI.

Data collected included a review of medical conditions and hospitalizations, current medications, vital signs, physician's assessment, and sputum samples for microbiology.

Results:
Sixty-five patients entered the long-term follow-up. Fifty-seven patients completed the 12-month follow up visit. Seven patients died during the follow-up period. Only 1 of these patients achieved culture conversion (3 consecutive negative sputum cultures) during the treatment phase. 'Pulmonary exacerbations' were the most frequent medical condition at the follow-up visit. No clinically meaningful changes from baseline in vital signs or physical examination were observed. Among patients with available follow-up data, those who culture-converted during either treatment phase were more likely to demonstrate negative sputum cultures at the 12-month follow-up vs. those who did not (14/17; 82.5% vs. 6/28; 21.4%, respectively).

Conclusion:
For many patients achieving culture conversion after 3-6 months of add-on LAI treatment resulted in sustained negative sputum cultures 12 months after LAI was discontinued. Study findings confirm the durability of LAI treatment response and continue to support the potential role of LAI as a viable add-on treatment to standard multi-drug regimens for NTM lung infections in patients' refractory to previous regimens.

P03: Looking for Right Management for Patients Severe COPD associated with NON-CF Bronchiectasis:Where Is Rifht Way to GO?

Alizaman Sadigov [1,*]

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*Presenting author

Recognition of Bronchiectasis among patients with COPD is important because its presence is associated with worse outcomes.Specifically,outpatients with comorbidities and COPD suffer more freguent respiratory exacerbations,higher rates of potentially pathogenetic microorganisms isolated in their sputum,and increased mortality.Intubated intensive care unit(ICU) patients with overlaping bronchiectasis and COPD experience prolonged courses of mechanical ventilation,extended ICU and hospital-of stay,and increased rates of ventilator associated pneumonia.

In addition to prognostication and risk startification,diagnosis of bronchiectasis may also carry therpeutic relevance regarding the approach to microorganisms isolated in sputum,the role for bronchial hygiene ,and the possibility of targeted pulmonary resection.In nonCF related bronchiectasis,colonization with Pseudomonas aeruginosa has been associated both with disease progression ,defined by forced expiratory volume in 1 second decline ,and mortality.Anti-pseudomonal treatment treatment is recommended for non-CF patients with evidence of chronic colonization with Pseudomonas aeruginosa and also may have a role those with freguent exacerbations.Application of macrolikdes for prevention of exacerbations in both non-CF related bronchiectasis and COPD has been approved ,however,this application is not yet approved in patients with comorbidities :bronchiectasis and COPD.
Long-term nocturnal non-invasive ventilation(NIV) only recently has been showed benefits for patients with COPD.However there is not suggestions application of long-term use of NIV in patients with non-CF related bronchiectasis associated with chronic hypercapnic respiratory failure and also the use of nocturnal long-term NIV in patients with comorbidities bronchiectasdis and COPD not approved yet.

In summary,bronchiectasis is prevalent among patients with advanced COPD and may represent a distinct phenotype that warrants targeted therapy.

Allison A.Lambert,Mark T.Dansfield.COPD and Bronchiectasis.JCOPD F.2015:3(ISSUENUMBER):459-465.doi:HTTP://DX.DOI.ORG/10.15326/JCOPD.3.1.2015.0176.
Centers for Disease Control and Prevention.Chronic Obstructive Pulmonary Disease.Centers for Disease Control and Prevention website.HTTP://WWW.CDC.GOV/COPD/INDEX,HTML. Published March 2015.Assessed December 20,2015

P04: Combination of non CF-bronchiectasis and calcifications: a hallmark of high burden TB country

Victor Botnaru [1,*], *Oxana Munteanu* [1], and *Doina Rusu* [1]

[1]State University of Medicine and Pharmacy "Nicolae Testemitanu"
*Presenting author

Aims:
To analise imaging, functional and microbiological features of non CF-bronchiectasis in a large cohort of adult patients from a high burden TB setting.

Methods:
Prospectively colected chest HRCT images, pulmonary function tests and microbiological data of patients with non-CF bronchiectasis were corelated with history of treated TB, presence and distribution of calcifications (considered very suggestive for TB etiology in a high burden country), TB microbiology tests and severity of bronchiectasis disease.
Results: Among the 178 enrolled patients (mean age 56.48±14.07; 56% men) with bronchiectasis (87 diagnosed for the first time), the etiology could be established in 60% (107/178) cases. History of treated TB was found in 20% (36/178) of cases. One third of subjects had cystic bronchiectasis at least in one lobe with no preferences for distribution by lobes. More than three exacerbations during the last year were experienced by 40% of subjects and severe BSI score (9+) was found in 62% cases. P.aeruginosa was the most common pathogen in sputum cultures followed by S.aureus and H.influenzae. Active TB was confirmed in 9 cases: sputum and bronchial washings AFB smear and Gene-X-pert or by Lowenstein-Jensen media culture.

Association of bronchiectasis with calcifications was attested 54% (97/178) of patients (calcifications in bronchial walls 33% cases, lung parenchyma 25%, chest lymph nodes 25%, liver and spleen 12% of cases). Patients with pulmonary calcifications and no history of treated TB had a more severe respiratory symptoms and pulmonary function tests decline than those with pulmonary calcification and past TB treatment.

Conclusions:
Calcifications as a possible imaging marker of "spontaneous recovery" of a non treated TB is common in patients with bronchiectasis in high burden TB country. That suggests a TB underdiagnoses in these settings. Effective programatic detection and treatment of active TB disease may ensure less pulmonary sequela in recovered subjects.

P05: A Phase 3 Study Design of Pulmaquin® in Non-Cystic Fibrosis Bronchiectasis (NCFBE) Patients Chronically Colonized with Pseudomonas aeruginosa (PA)

Anne O'Donnell [1,*], *Diana Bilton* [2], *David Serisier* [3], *Adam Wanner* [4], *Juergen Froehlich* [5], *Paul Bruinenberg* [6], and *Igor Gonda* [7]

[1]Georgetown University
[2]Imperial College, Royal Brompton Hospital
[3]Mater Health Services - South Brisbane
[4]University of Miami School of Medicine
[5]Aradigm Corporation
[6]Biotrack
[7]Aradigm Corporation
*Presenting author

Introduction:
Bronchiectasis is a neglected disease in respiratory medicine. In adult NCFBE patients, PA infections are associated with an increased risk of death, hospital admissions and exacerbations. There is no approved treatment to prevent pulmonary exacerbations (PE) in bronchiectasis.

Methods:
Pulmaquin, a once-a-day inhaled dual-release formulation composed of both liposome encapsulated and unencapsulated ciprofloxacin, is being evaluated in two Phase 3 trials in patients with CT-scan documented NCFBE who have chronic lung infections with PA. The subjects must have had at least 2 PEs in the 12 months prior to enrollment, and a positive sputum sample with at least one PA isolate nonresistant to ciprofloxacin. Each trial has a 48-week double blind period of 6 cycles of 28 days on and 28 days off treatment comparing Pulmaquin against placebo, followed by a 28-day open label extension with Pulmaquin. The primary endpoint is time to first PE during the double blind period and key secondary endpoints are the number of PEs, severe PEs and quality of life. Microbiology assessments (PA density, ciprofloxacin MIC for PA, isolation and quantification of other selected pathogens, PA sensitivity testing to selected antibiotics), ciprofloxacin serum levels, 6 minute walk test and productivity questions are conducted. Spirometry and DLCO are monitored as safety indicators. PEs are assessed based on protocol specified symptoms, signs, or laboratory findings.

Results:
1046 subjects were screened in the U.S., Canada, Australia, New Zealand, Israel, South Korea, Taiwan, South Africa, U.K., Germany, France, Spain, Italy, Ireland, Georgia, Serbia, Poland, Romania, Latvia and Peru. Both studies completed enrollment with a total of 584 subjects randomized and dosed.

Conclusion:
The two well-controlled clinical trials will provide a large database of well-defined NCFBE subjects with chronic PA colonization to investigate the effect of Pulmaquin on the prevention of PEs using a rigorous definition of exacerbation.

P06: Living your life with bronchiectasis. Qualitative interviews inform the development and evaluation of a novel information resource.

Katy Hester [1,*], *Tim Rapley* [2], *Julia Newton* [2], and *Anthony De Soyza* [1]

[1]Newcastle University and The Freeman Hospital
[2]Newcastle University
*Presenting author

Introduction:

Bronchiectasis is a chronic lung condition, about which there is relatively little high-quality patient information. Information and education could, however, support patients to become "expert patients" thereby aiding self-management and optimising engagement with treatment.

Aims:

1. To develop an information resource based on the identification and understanding of patient and carers' needs.
2. To undertake a pilot trial of using the novel information resource as an intervention.

Methods & Results:

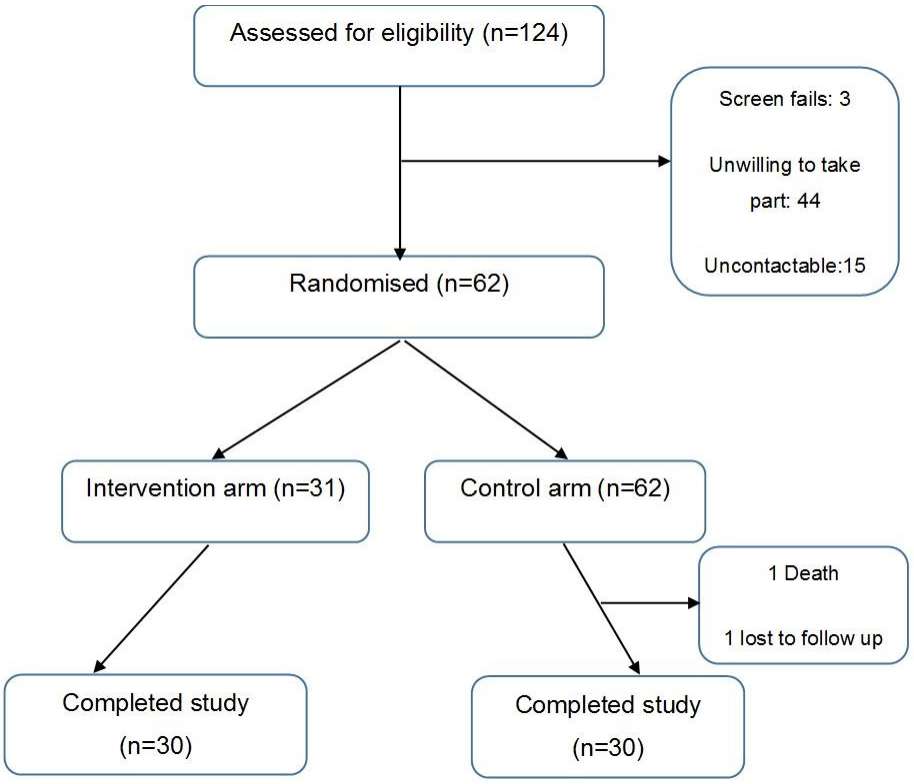
Qualitative interviews with 26 people (17 with bronchiectasis and 9 carers) were conducted. We sampled newly-diagnosed patients and those with an established diagnosis (age range 33-78 years). The focus of the interviews was to identify, explore and understand their information needs. However, a core mediating issue emerged: 'What it means to learn to live your life with bronchiectasis'. Embedded within this were issues around developing support and coping mechanisms, learning to connect with information and how people start to take back control and develop, new, active partnerships with the medical team.

Understanding these issues and the biographical disruptions that bronchiectasis imposes has advanced our understanding of patients' and carers' information needs and how these could be met. This qualitative work, and user workshops, were fundamental in the co-development of a novel web-based information resource and booklet.

The resource was evaluated in a feasibility study [1] determining feasibility of conducting a future RCT. Outcome measures included website access analytics, questionnaires about the resource, symptoms, and quality of life; spirometry and exacerbation frequency. 62 participants were randomised (Figure). Focus group feedback about the resource and study process has been positive. Full details of the trial results are expected by June 2016.

Conclusions:

Patients are engaged with developing reliable information sources. The pilot trial suggests larger, definitive studies in improving compliance and self-management are warranted.


Assessed for eligibility (n=124)
Screen fails: 3
Unwilling to take part: 44
Uncontactable:15
Randomised (n=62)
Intervention arm (n=31)
Control arm (n=62)
1 Death
1 lost to follow up
Completed study (n=30)
Completed study (n=30)

P07: Sensitization to Aspergillus fumigatus in COPD patients with and without bronchiectasis

Stephanie Everaerts [1,*], *Kristina Vermeersch* [1], *Erna Van Hoeyveld* [2], *Bart Vanaudenaerde* [1], *Xavier Bossuyt* [1], *Katrien Lagrou* [1], *Lieven Dupont* [1], and *Wim Janssens* [1]

[1]Catholic university of Leuven
[2]Catholic University of Leuven
*Presenting author

The clinical impact of sensitization to Aspergillus fumigatus (Aspf) and its role in the development of bronchiectasis (BRECT) in COPD is not well understood. We scored computer tomography of the thorax for BRECT using the modified Reiff score in 300 patients with COPD. This score assesses the number of involved lobes (the lingula considered separately) and degree of dilatation (1=tubular, 2=varicose and 3= cystic). Consequently 0 is the minimum and 18 is the maximum score. Furthermore we measured concentrations of total IgE, Aspf IgE (including Aspf recombinants rAsp f1-f4 and f6) and Aspf IgG by ImmunoCap fluorenzyme-immunoassay. 99 patients of our COPD patient cohort had a modified Reiff score of ≥2, which we considered clinical relevant. These patients differed in age (69,2 years versus 66,6 years, p=0.0114), BMI (23,5 versus 25,2, p=0.0053), diffusion capacity (44,8% of predicted versus 50,2% of predicted, p=0.0094) and significantly more patients had ≥2 exacerbations per year (53,5% versus 38,3%, p=0.0123). There was no significant difference in total IgE, FEV1 and gender between patients with and without BRECT. Sensitization to Aspf (crude extract or one of the available recombinant antigens >0,35 Ua/mL) was significantly more prevalent in the COPD subjects with BRECT; 25,3% versus 14,9%, p=0.0297. Presence of Aspf IgG wasn't different between groups (28,3% versus 20,4%, p=0.1270). We conclude that sensitization to Aspf is more prevalent in COPD patients with BRECT compared to COPD patients without BRECT. Furthermore COPD patients with BRECT are older, had lower BMI, lower diffusion capacity and more exacerbations.

Characteristics of COPD patients with and without bronchiectasis (modified Reiff score ≥ 2)

	COPD-BRECT	COPD+BRECT	p-value
Number (%)	201 (67)	99 (33)	
Men (%)	137 (68.2)	78 (78.8)	0.0547
Age, years	66.6 (±8,3)	69.2 (±8,7)	0.0114
BMI	25.2 (±5,8)	23.5 (±4,4)	0.0053
FEV1, % of predicted	47.5 (±18,3)	45.3 (±17,6)	0.3180
DLCO, % of predicted	50.2 (±17,8)	44.8 (±15,0)	0.0094
Log (1+Total IgE)	1.8 (±0,7)	1.8 (±0,8)	0.9873
Sensitization (%) (Aspf IgE or recombinant >0.35 Ua/mL)	30 (14.9)	25 (25.3)	0.0297
Aspf IgG > 50mg/L (%)	41 (20.4)	28 (28.3)	0.1270

Results are presented as number (percentage) and mean +- standard deviation

P08: Baseline therapies for Bronchiectasis (non-CF etiology) vary by country- data from the RESPIRE1 trial of Ciprofloxacin Dry Powder for Inhalation (DPI)

Anthony De Soyza [1,*], *Timothy Aksamit* [2], *Tiemo-Joerg Bandel* [3], *Margarita Criollo* [4], *J. Stuart Elborn* [5], *Elisabeth Operschall* [3], *Eva Polverino* [6], *Kevin Winthrop* [7], and *Robert Wilson* [8]

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[6]Fundacio Clinic, IDIBAPS, CIBERES
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[8]Royal Brompton Hospital
*Presenting author

Background:
RESPIRE 1, an international Phase III trial, aimed to evaluate if Ciprofloxacin DPI as long-term, intermittent therapy in bronchiectasis patients (non-CF etiology) with ≥2 exacerbations (prior 12 months) and respiratory pathogens reduces exacerbations and improves quality-of-life (QoL). We investigated concomitant treatment use at baseline in different countries.

Methods:
We analysed preliminary baseline demographics, disease characteristics, and treatment use of subjects randomised in RESPIRE1 by country. Countries that contributed >1% of the full cohort were evaluated for numerical differences in the sub-analysis.

Results:
416 subjects enrolled in 14 countries were analysed. Six countries enrolled 11–13% subjects each (Australia/Germany/Spain/Israel/New Zealand/US), three contributed 5–8% each (UK/Italy/Japan) and three enrolled 1–4% (Argentina/France/Latvia), while two randomised <1% (Denmark/Slovakia). Baseline data for the full cohort are reported in Table 1. Mean (range) patient age in the full cohort was 64.7 (51.5–70.4) years. Patients from the US/Israel/France/Argentina reported poorer QoL (total St Georges Respiratory Questionnaire (SGRQ) score >4 points above full cohort mean [44.9 vs 51.8/54.4/57.9/58.6, respectively]). Patients in UK/New Zealand/Spain had the highest rates of ICS use, including ICS/LABA combination (66.7%/52.9%/46.9%, respectively) while Germany/Latvia/Japan had the lowest (21.3%/18.8%/15.2%, respectively). Patients in Japan had comparatively high usage rates of long-term macrolides (69.7%) and mucolytics (75.8%). Lower macrolide usage rates of 0%/5.9%/8.5% were observed in Israel/New Zealand/Germany, respectively. Long-acting bronchodilator use in Spain was high (LABA, 40.8%; LAMA, 24.5%) and low in US patients (LABA, 15.9%; LAMA, 9.1%) although SABA use in US patients was high (68.2%).

Conclusions:
Between countries, demographics of patients enrolled in RESPIRE 1 were generally similar. Numerical differences in baseline concomitant therapy may result from low patient numbers and center effect, or reflect inter-country management differences and lack of international treatment guidelines.

Characteristic	Value
N (%)	416 (100)
Female n (%)	285 (68.5)
Age, mean [SD]	64.7 [12.9]
FEV1 % predicted, mean [SD]	62.4 [16.8]
SGRQ total score, mean [SD]	44.9 [19.9]
Concomitant medication (reported use >5% of patients), n (%)	
Short-acting beta-agonist bronchodilators (SABA)	172 (41.3)
Inhaled corticosteroids and ICS combinations (ICS)	153 (36.8)
Long acting beta-agonist bronchodilators (LABA)	112 (26.9)
Long-acting muscarinic antagonists (LAMA)	80 (19.2)
Mucolytics	78 (18.8)
Long-term macrolides	66 (15.9)
Short-acting muscarinic antagonists (SAMA))	23 (5.5)

TABLE 1: Preliminary baseline demographics and patient characteristics in RESPIRE 1 (full cohort)

P09: Effects of long term ToBrAmycin InhalaTion SoluTion (TIS) once daiLy on Exacerbation rate in patients with non-cystic fibrosis bronchiectasis. A doubleblind, randomized, placebo controlled trial. The BATTLE study.

Lotte Terpstra [1,*], *Josje Altenburg* [1], and *Wim Boersma* [1]

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*Presenting author

Rationale:
Patients with bronchiectasis often have exacerbations of their disease. These exacerbations influence the quality of life. In patients with cystic fibrosis (CF) inhaled antibiotics lower the bacterial load in bronchial secretions and have a positive effect on the number of exacerbations, lung function and quality of life (QoL). In patients with non-CF bronchiectasis colonized with *Pseudomonas aeruginosa*, studies with tobramycin inhalation solution (TIS) are limited. In present study the value of TIS will be investigated in patients with non-CF bronchiectasis colonized by Gram-negative bacteria and/or *Staphylococcus aureus* in sputum.

Methods:
In this multicenter, double-blind, randomized, placebo controlled study, TIS 300mg OD will be compared to placebo OD during 12 months. Patients will be randomized 1:1. Patients are included who are aged ≥ 18-year-old with confirmed bronchiectasis by (HR)CT and at least two exacerbations during the previous 12 months. For the study schedule see figure 1.

Results:
The hypothesis of the study is a 50% reduction in exacerbation rate in patients with prolonged treatment of tobramycin (OD) in a patient group with 2 or more exacerbations per year. This reduction represents clinical relevance and is based on the assumption that maintenance treatment with TIS will be comparable to that of systemic azithromycin treatment. This assumption is derived from data of the BAT trial. In order to determine a statistical difference of $p < 0.05$, with a power of 0.80, and a drop-out percentage of 30%, 26 patients will be allocated on each treatment arm. Secondary outcome parameters are lung function (FEV1, FVC), QoL (QOL-B, LTRI-VAS, Leicester cough score), bacterial load in sputum and tobramycin resistant pathogens.

Conclusions:
The primary outcome of the study is a 50% reduction in exacerbation rate in patients with non-CF bronchiectasis using TIS (OD) compared to placebo. A total number of 52 patients will be included.

This study design was earlier presented at the ATS, San Francisco, May 2016.

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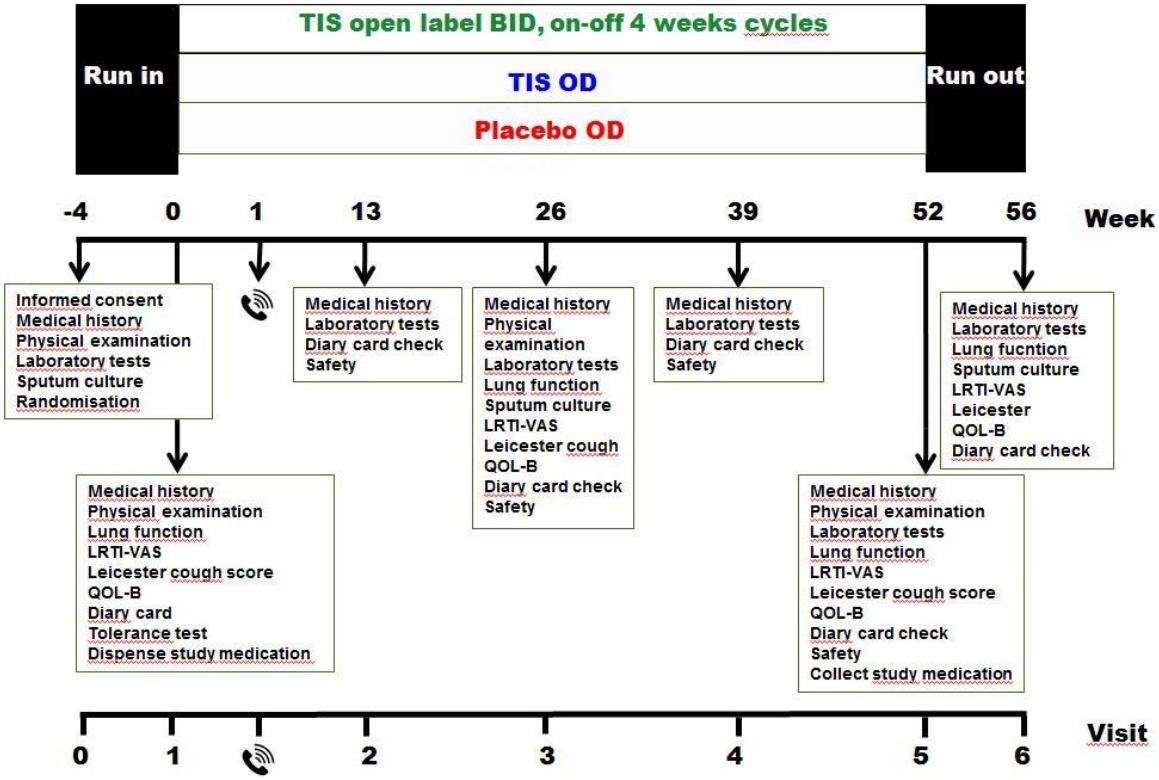
Figure 1: Study schedule



LRTI-VAS=Lower Respiratory Tract Infections- Visual Analogue Scale; QOL-B=Quality of Life-Bronchiectasis

P10: Frequency and severity of chronic rhinosinusitis exacerbations in patients with bronchiectasis

Saso Stoleski [1,*], *Jordan Minov* [1], *Jovanka Karadzinska Bislimovska* [1], and *Dragan Mijakoski* [1]

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*Presenting author

Introduction:
Patients with bronchiectasis commonly have sinonasal disease, which is thought to have the same aetiology and pathophysiology as the chronic lung disease.

Objective:
To evaluate the frequency and severity of chronic rhinosinusitis exacerbations in patients with bronchiectasis.

Methods:
The study recruited 69 subjects with chronic rhinosinusitis exacerbations treated in the last 12 months on outpatient basis, diagnosed according to the actual EPOS recommendations. The participants were divided in two groups. The first group included 35 patients with bronchiectasis diagnosed by high-resolution computed tomography (HRCT). In addition, clinical findings from 34 patients without confirmed presence of bronchiectasis were taken as controls.

Results:
The results showed higher mean number of rhinosinusitis exacerbations during the last 12 months in patients with bronchiectasis (3.9 ± 1.3) as compared to their mean number in controls (3.5 ± 1.1), but the difference was yet not statistically significant ($P = 0.172$). The mean period of chronic sinusitis exacerbations, measured by the mean number of days for reaching complete symptoms resolution or their return to the baseline severity, was significantly longer in patients with bronchiectasis as compared to controls (5.8 ± 1.9 vs. 4.7 ± 1.6; $P = 0.011$).

Conclusion:
Our findings indicate that presence of bronchiectasis probably has an influence on the frequency and severity of chronic sinonasal disease among these patients.

Microbiome

P11: Lobar Distribution in Non-Cystic Fibrosis Bronchiectasis Predicts Bacteriologic Pathogen Treatment

Shimon Izhakian [1], *Walter Wasser* [2], *Leonardo Fuks* [1], *Baruch Vainshelboim* [1], *Benjamin Fox* [1], *Oren Fruchter* [1], and *Mordechai Kramer* [1]

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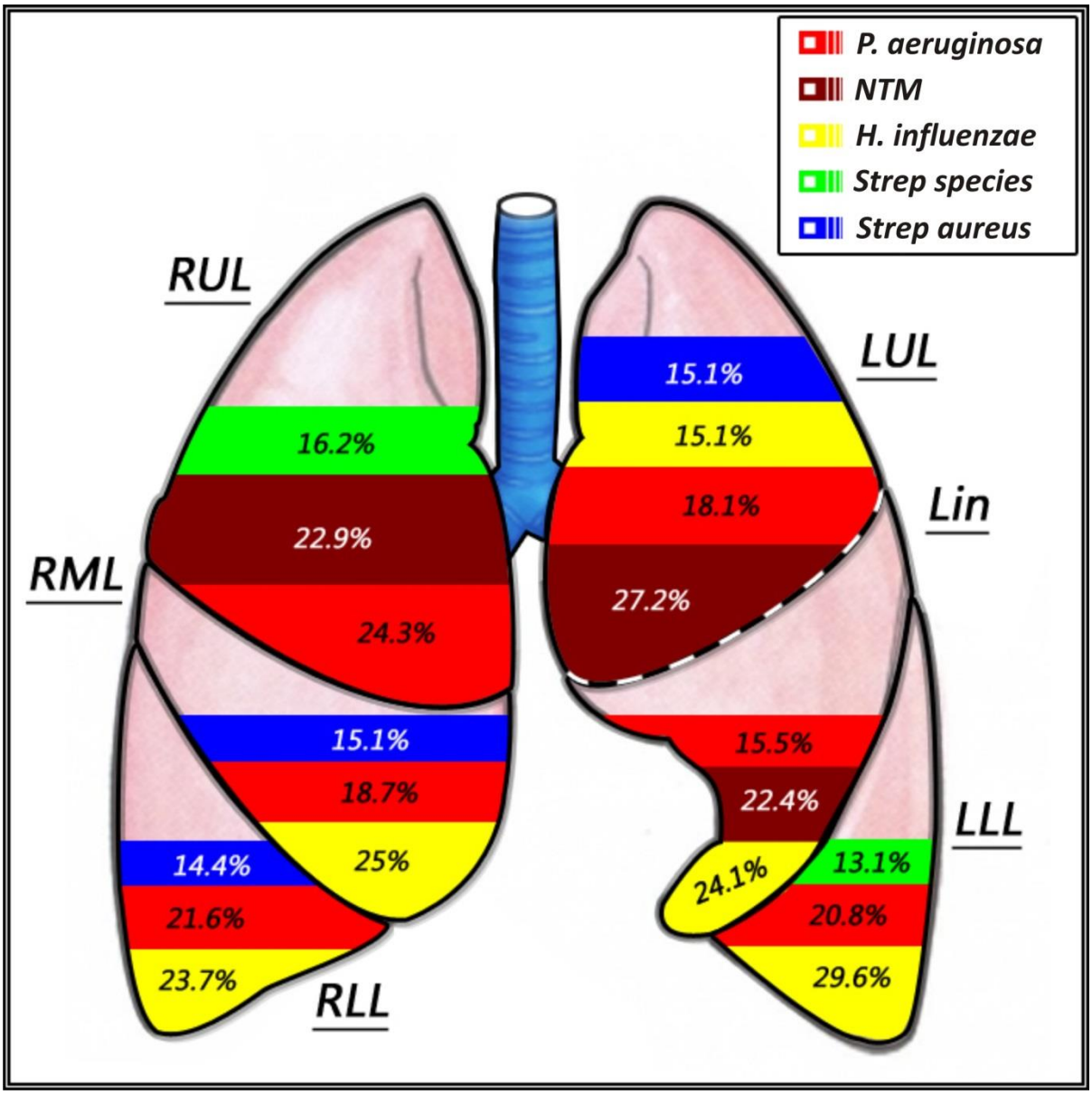
[2]and Rambam Health Care Campus, Haifa, Israel

Purpose:
Non-cystic fibrosis bronchiectasis (NCFBr) is a major cause of morbidity due to frequent infectious exacerbations. We analyzed the influence of patient age and bronchiectasis location on the bacterial profile of patients with NCFBr.

Methods:
This retrospective cohort study included 339 subjects diagnosed with an infectious exacerbation of NCFBr during the 9-year period between January 2006 and December 2014. Bronchoalveolar lavage (BAL) cultures and high-resolution computed tomography scans (HRCT) were utilized to characterize the location of the bronchiectasis and bacteriologic pathogenic profile.
Results: In univariate logistic regression, the frequency of Haemophilus influenzae was higher in patients aged ≤64 years (OR=0.969, p<0.0001, 95% CI 0.954-0.983), whereas the frequency of Pseudomonas aeruginosa (OR=1.027, p=0.008, 95% CI 1.007-1.048) and Enterobacteriaceae (OR=1.039, p=0.01, 95% CI 1.009-1.069) were significantly higher in patients aged >64 years.

The lobar distribution of bronchiectasis in the subjects was 25.9% in the right middle lobe (RML), 20.7% in the right lower lobe (RLL), 20.4% in the left lower lobe (LLL), 13.8% in the lingula, 13% in the right upper lobe (RUL), and 6.2% in the left upper lobe (LUL). In the lower lobes, H. influenzae was the dominant species isolated, whereas in the RUL it was P. aeruginosa and in the LUL it was non- tuberculous mycobacterium (NTM).

Conclusions:
H. influenzae was more prevalent in younger patients, whereas P. aeruginosa, Enterobacteriaceae and NTM predominated in older patients. Different pathogens were associated with different lobar distributions. The RML, RLL and LLL showed a greater tendency to develop bronchiectasis than other lobes.


P. aeruginosa
NTM
H. influenzae
Strep species
Strep aureus
RUL
16.2%
22.9%
24.3%
RML
15.1%
18.7%
25%
14.4%
21.6%
23.7%
RLL
LUL
15.1%
15.1%
18.1%
Lin
27.2%
15.5%
22.4%
LLL
24.1%
13.1%
20.8%
29.6%

P12: Non-tuberculous mycobacteria in patients with non-cystic fibrosis bronchiectasis – a prospective analysis

David Araújo [1,*], *Adelina Amorim* [1], *Teresa Carvalho* [1], *Angélica Ramos* [1], *Margarida Redondo* [1] and *Manuela Ribeiro* [1]

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*Presenting author

Background:
The role of non-tuberculous mycobacteria (NTM) in patients with non-cystic fibrosis bronchiectasis (BE) is not yet completely understood, in terms of prevalence, risk factors, prognostic value and other factors.

Methods:
A prospective analysis of a group of patients followed in a specialized BE outpatient clinic was made. Inclusion criteria were: >18 years old, HRCT scan documented BE, a minimum of 1 year follow-up. Clinical and demographical data were collected, lung function test performed annualy and a sputum bacterial culture was requested at each appointment. Only those with at least two mycobacterial sputum culture were included in this study.

Results:
A total of 140 patients met the inclusion criteria. The mean follow-up time was 3.7 years. A total of 968 mycobacterial sputum cultures were assessed with an average of 2.1 exams per year for each patient. Patients were divided in two groups: bronchiectasis with NTM isolates (n=23 – 16.4%) and bronchiectasis without NTM isolates (n=117 – 83.6%). The first group had a higher mean age (59.4 vs 54.3years), a higher female predominance (78.0% vs 59.8%) and a lower incidence of tobacco exposure (8.7% vs 22.2%). No difference was seen in terms of body mass index and prevalence of chest wall or spinal deformities. A higher percentage of chronic bacterial infection (persistence of the same microorganism in 3 sputum samples in 12 months with a minimum interval of one month) was seen in the NTM group (47.8% vs 37.3%). The most frequent NTM isolates were M. gordonae (n=7), M. spp. (n=7) and M. avium (n=6). In 5 patients the ATS criteria for NTM lung disease were present and treatment was performed.

Conclusions:
A significant percentage of NTM isolates was shown in this bronchiectasis population, due to a routine based screening, although only a small part had NTM lung disease.

Understanding inflammation and anti-inflammatory approaches

P13: Anti-Pseudomonas aeruginosa IgG Antibodies and Chronic Airway Infection in Non-Cystic Fibrosis Bronchiectasis

Guillermo Suarez-Cuartin [1,*], *Oriol Sibila* [1], *Alex Smith* [2], *Hani Abo-Leyah* [2], *Ana Rodrigo-Troyano* [1], *Silvia Vidal* [1], *Vicente Plaza* [1], *Thomas C Fardon* [2], and *James D Chalmers* [2]

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*Presenting author

Rationale:
Identification of Pseudomonas aeuginosa (PA) infection status is important in the management of non-cystic fibrosis bronchiectasis. Serum anti-PA IgG antibodies have been proposed to diagnose chronic PA infection.

Methods:
Clinically stable bronchiectasis patients were studied prospectively. Chronic PA infection was defined as 2 or more positive sputum samples at least 3 months apart and/or failure to clear PA following eradication treatment. Baseline serum samples were assayed for anti-PA IgG by a validated ELISA kit. The cut-off value for a positive ELISA Unit/10 result was 2.96.

Results:
361 patients were included. Fifty-four (14.9%) of them had chronic PA infection. Patients with chronic PA infection had significant more severe bronchiectasis (BSI score mean 14 vs 7, $p<0.0001$) and more frequent exacerbations (mean 4 vs 2, $p<0.0001$). Patients with chronic PA infection had higher baseline PA IgG levels (median 8.1 vs 1.4, $p<0.00001$). Significant correlations were found between IgG levels and frequency of exacerbations ($p=0.005$), BSI score ($p<0.0001$) and neutrophil elastase in sputum ($p=0.004$). All patients with chronic PA infection had a positive IgG, giving a sensitivity of 100%, specificity of 75.3% and area under the ROC curve (AUROC) of 0.95. During the study, 38 patients had a new isolation of PA. Eradication at 12 months was achieved in 15.8% of patients with a positive antibody test (n=3) and 89.5% of patients with a negative IgG test.

Conclusions:
The accuracy of anti-PA IgG test to detect chronic PA infection in bronchiectasis patients is very high. PA IgG is not sufficiently sensitive or specific to guide the decision to eradicate PA but may be a marker of severity of disease and treatment response.

P14: Bronchiectasis with upper airways symptoms is associated with allergic features and frequent exacerbations

Michal Shteinberg [1,*], *Najwan Nasrallah* [2], *Evgenia Gerbeshian* [3], and *Yochai Adir* [4]

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[2]Radiology department, Carmel Medical Center, Technion- B. Rappaport Faculty of Medicine
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[4]Pulmonology Institute, Carmel Medical Center, Technion- B. Rappaport Faculty of Medicine
*Presenting author

Background
The association of bronchiectasis with upper airway symptoms (UAS) has been previously reported (1). However, apart from primary ciliary dyskinesia (PCD) and cystic fibrosis (CF), predisposing conditions have not been established. The aim of our study was to evaluate whether patients with BE and UAS have unique etiologic, laboratory and clinical features and whether presence of UAS has implications on severity.

Methods
We retrospectively reviewed the charts of adult patients with non CF, non PCD related bronchiectasis. The presence of UAS was defined as nasal discharge in most days of the year, sinusitis or nasal polyps. Patients with a discrepancy between symptoms and sinus CT findings were excluded. Laboratory data including IgG, total IgE, blood eosinophils, sputum bacteriology, as well as lung function, were recorded. CT scoring of bronchiectasis (Reiff score) and sino- nasal pathology (Lund- McKay score) (2) was performed by a radiologist blinded to UAS presence. Data regarding exacerbations were collected from patients' files and antibiotic prescription records.

Results
163 patients out of 220 screened were included in the study. 59 (36%) had UAS. Patients with UAS had an earlier age of onset (34±24 vs. 45±24, p=0.007) and the duration of disease was longer (26±20 vs. 19±19 years, p=0.02) than patients without UAS, with similar current age. Patients with UAS had higher blood eosinophils (median, 290 vs. 200/ml, p=0.002) and total IgE (median, 100 vs. 42 IU/ml, p=0.066). These patients had significantly more exacerbations (3.4±2.5 vs. 2.63±2.4, p=0.016), and less were free from exacerbations (3.4% vs. 14%, p=0.034). No differences in gender, lung function, hospitalizations, Reiff CT score, colonization with bacteria, or IgG levels were found.

Conclusion
Patients with UAS had an earlier onset, with features suggestive of allergic diathesis and higher rate of exacerbations. This may implicate a higher disease burden in patients with UAS.

	No UAS (104)	UAS (59)	P value
Sex (% female)	61.5%	67.8%	0.424
Onset age (y), median (mean±SD)	30 (45±24)	50 (34±24)	**0.007**
Age at diagnosis (y), median (mean±SD)	65.5 (64±15)	63.1 (59±18)	0.201
Time from onset to diagnosis (y) median (mean±SD)	12.9 (18.9±18.7)	23.8 (25.9±20)	**0.02**
Presence of asthma, no. (%)	5 (4.8)	7 (11.9)	0.122
Idiopathic etiology, no. (%)	50 (48.1)	31 (52.5)	0.584
Post infectious etiology, no (%)	31 (29.8)	7 (11.9)	**0.009**
Eosinophils /µl, median (mean±SD)	200 (216±174)	290 (249±399)	**0.002**
IgE (IU/ml), median (mean±SD)	42 (139±240)	100 (375±878)	0.066
IgG (IU/ml), median (mean±SD)	1169 (1198±318)	1184 (1210±383)	0.747
FEV_1 (% of predicted) mean±SD	81±26	81±26	0.905
Reiff score, median (mean±SD)	7 (8.13±4.2)	6 (8±4.4)	0.632
Lund – McKay score, median (mean±SD)	0.5 (.87±1) N=38	11.5 (10.6±3.8) N=34	**<0.0001**
Exacerbations/ year, median (mean±SD)	2 (2.63±2.4)	3 (3.36±2.5)	**0.016**
Occurrence of exacerbation in previous year, no. (%)	60 (86 %)	56 (96.6%)	**0.034**

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P15: STAT3-gain of function mutation as a cause of severe bronchiectasis and multi-organ autoimmunity; A case report

Tawfik Khoury [1], *Rottem Kuint* [1,*], *Vered Molho-Pessach* [1], *Yuval Ramot* [1], *Ayman Abu Rmeileh* [1], *Orly Elpeleg* [1], *Neville Berkman* [1], *Abraham Zlotogorski* [1], and *Yaron Ilan* [1]

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*Presenting author

Background: Signal transducer and activator of transcription 3 (STAT3) is a member of a family of proteins involved in the regulation of inflammation, differentiation, proliferation and survival. Loss or gain-of-function mutations in STAT3 lead to infectious and autoimmune complications. Recently, STAT3 gain-of-function mutations have been associated with the development of a multi-organ autoimmune syndrome. Case presentation: Here, we describe a 38-year-old male who presented with severe diffuse bronchiectasis in addition to gastrointestinal, dermatological, and malignant manifestations. Following negative workup, whole exome sequencing, validated by Sanger sequencing, revealed a heterozygous missense mutation in the STAT3 gene, c.1261G>A (p.G421R). FACS analysis of peripheral T lymphocytes revealed low levels of CD4+CD25+FoxP3 and CD8+CD25+FoxP3 regulatory T cells (Tregs). Following treatment with two cycles of tocilizumab, an interleukin-6 receptor antibody, a significant increase in the level of Tregs was observed, accompanied by clinical improvement. Conclusion: This case sheds light on the emerging role of STAT3 gain of function mutation in the pathogenesis of autoimmune diseases and development of bronchiectasis, and further addresses the therapeutic role of IL-6 blocker treatment in this syndrome.

P16: The incidence of metabolic syndrome in patients with non-CF bronchiectasis and chronic obstructive pulmonary disease

Dusan Skrbic [1,*], *Djordje Povazan* [1], *Edita Stokic* [2], *Mirna Djuric* [1], *Tatjana Boskovic* [1], and *Dusanka Obradovic* [1]

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[2]2. Clinical Centre of Vojvodina, Novi Sad
*Presenting author

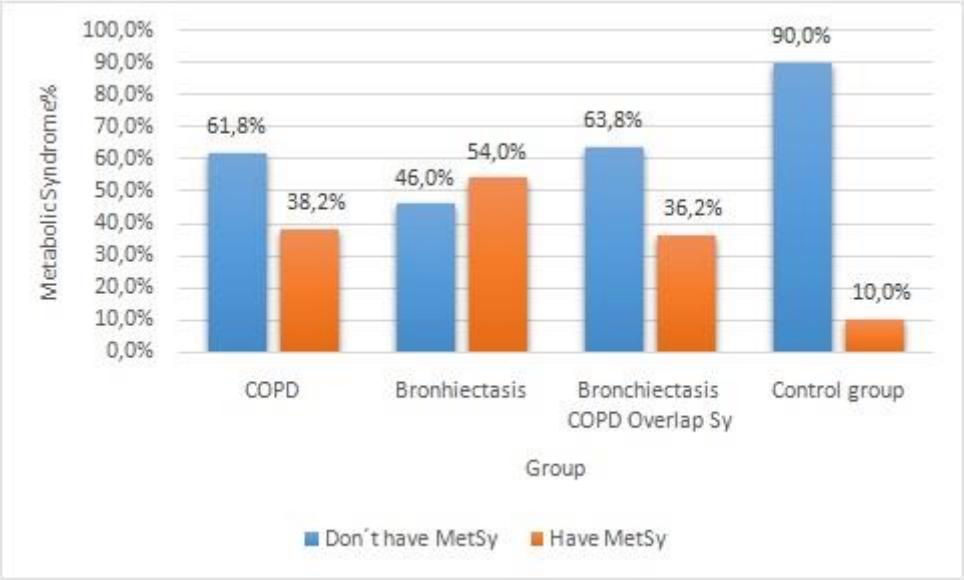
Background:
Bronchiectases and COPD are inflammatory airway diseases that have some clinical similarities and differences. The 2011 „GOLD" update lists the comorbidities that every COPD patient should be evaluated for: cardiovascular diseases, skeletal muscle dysfunction, metabolic syndrome, osteoporosis, depression and lung cancer. The metabolic syndrome is a group of metabolic disorders which increase the risk of cardiovascular diseases and type 2 diabetes. In our investigation, we utilized the NCEP-ATPIII definition based on the presence of three of five components: abdominal obesity, elevated triglyceride levels (>1.7 mmol/l), reduced HDL cholesterol, elevated systolic and/or diastolic blood pressure (>130/>85 mmHg), elevated glucose levels (>5.6 mmol/l), or history of treated hyperlipoproteinemia, hypertension or type 2 diabetes mellitus.

Aims:
1) establishing the frequency of the metabolic syndrome and its components among the patients with bronchiectases and COPD;
2) analyze and compare the frequency of metabolic syndrome in the examined groups related to the patients' sex and age

Methods:
The study included 193 subjects, classified into four groups: COPD (n=55), bronchiectases (n=50), and patients with concurrent bronchiectases and COPD (n=58). The control group included 30 subjects without bronchiectases and COPD.

Results:
The metabolic syndrome was more frequent in the patients with bronchiectases and/or COPD than in the control group. It was confirmed in 38.2% of COPD patients, 54% of the patients with bronchiectases, and in 36.2% of the patients with concomitant COPD and bronchiectases. The metabolic syndrome components were neither more frequent, nor statistically higher in the patients with concomitant COPD and bronchiectases as compared to the patients with a single presence of any of the two diseases.

Conclusions:
We conclude that COPD and bronchiectases are the conditions with a higher cardiometobolic risk. Among the patients with bronchiectases and/or COPD, no correlation was observed between the metabolic syndrome frequency and the patients' sex or age.



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P17: CHI25243, a novel potent inhaled inhibitor of neutrophil elastase for the treatment of bronchiectasis and other chronic inflammatory lung disease

Chiara Carnini [1], *Daniela Miglietta* [1], *Veronica Puviani* [1], *Maria Adelaide Calderazzo* [1], *Harry Finch* [2], *Craig Fox* [2], *Mary Fitzgerald* [2], *Riccardo Patacchini* [1], *Maurizio Civelli* [1], and *Gino Villetti* [1]

[1]Chiesi Farmaceutici
[2]Pulmagen Therapeutics

Neutrophil elastase (NE) is a key proteolytic enzyme implicated in the pathogenesis and progression of chronic neutrophil-driven inflammatory lung diseases, including bronchiectasis, cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD). A number of clinical observations indicate that targeting NE might be beneficial for treating such inflammatory lung diseases. Here we studied the pharmacological profile of CHI25243, a novel inhaled NE inhibitor designed for inhaled treatment of neutrophil-driven inflammatory lung diseases such as bronchiectasis.

In in vitro assays, CHI25243 shows a high potency in inhibiting human NE (IC50=0.2nM) conserved across species (rat, IC50=4.1nM; dog, IC50=7.9nM; cynomolgus monkey, IC50=2.3nM), with a significant selectivity (more than 100-fold) toward NE compared to other serine proteases. The in vivo effect of CHI25243 in inhibiting NE in the lungs was assessed in two rat models: human NE-induced lung injury and LPS-fMLP models. When administered intratracheally (i.t.), CHI25243 prevents human NE-induced lung injury, measured as lung haemorrhage with an ED50 of 74µg/kg, while in the LPS/fMLP model CHI25243 significantly reduces endogenous elastase activity at 3µg/kg reaching a maximal effect at 300µg/kg. The protective effect observed with CHI25243 in the LPS-fMLP model is maintained up to 24h post-treatment, with 30µg/kg being the minimum dose providing 24h efficacy. In addition, CHI25243 was tested in the rat lung infection model which mimicks the persistent Pseudomonas aeruginosa infection experienced by patients with CF and bronchiectasis. Here, when administered i.t. for 7 days, CHI25243 significantly reduces both lung tissue infection and inflammation with a MED between 30 and 100µg/kg.

CHI25243 is a novel, potent and selective inhaled NE inhibitor, which shows target inhibition in the lung and is capable of inhibiting both pulmonary inflammation and infection in various preclinical animal models, suggesting the potential for the treatment of bronchiectasis and other chronic inflammatory lung diseases.

P18: Plasmapheresis as rescue therapy in severe bronchiectasis with blocking anti pseudomonas antibodies

Anthony De Soyza [1,*], *Timothy J Wells* [2], *John Davison* [3], *Emma Sheehan* [4], *Suren Kanagasundaram* [5], *Gavin Spickett* [1], *Gareth Davies* [6], *Calman A MacLennan* [4], *Rob Stockley* [7], and *Ian Henderson* [4]

[1]Newcastle University
[2]Birmingham University, UK
[3]Freeman Hospital, Newcastle, UK
[4]Birmingham University
[5]Freeman Hospital
[6]William Leech Centre for Lung research
[7]Lung investigation unit
*Presenting author

Rationale:
There are few salvage therapies for advanced bronchiectasis. Recently, we identified a subset of patients with non-cystic fibrosis bronchiectasis and chronic Pseudomonas aeruginosa infection (1). These patients had an excess of IgG2 specific to the bacterial O-antigen. This IgG2 inhibited immune killing of the infecting strain. Patients with inhibitory antibody had worse lung disease (1).

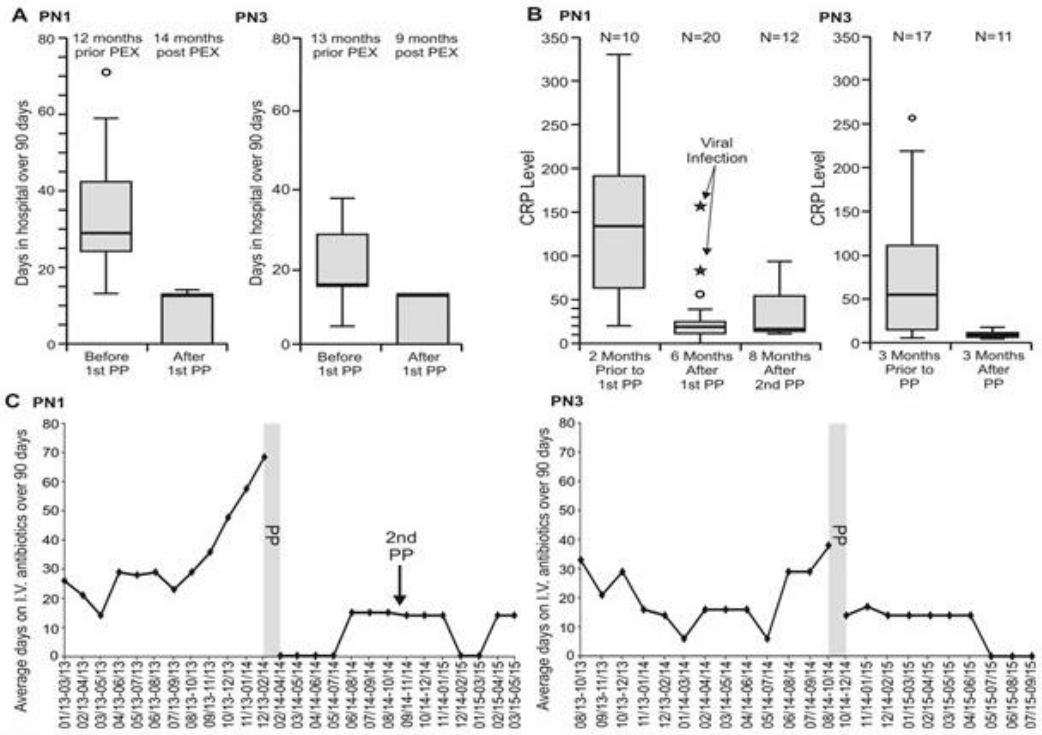
Here we describe the treatment of two critically ill patients with non-cystic fibrosis bronchiectasis. Each patient had inhibitory antibodies, chronic Pseudomonas infection and had experienced clinical decline despite optimal conventional therapy.

Objectives:
To determine if removing inhibitory antibody from two critically ill patients would result in improved health.

Methods:
Inhibitory antibodies were removed by plasmapheresis (Pex). Blocking antibody levels were assessed longitudinally as (1).

Measurements and Main Results:
Post-plasmapheresis both patients had a significant and sustained drop in intravenous antibiotic use, days in hospital and CRP levels. Both patients also became Pseudomonas negative immediately after treatment. Over time the levels of anti-O-antigen IgG2 rose in both patients such that it reached titres equivalent to those measured before plasmapheresis. The return of high IgG2 titres correlated with the appearance of Pseudomonas in the sputum and worsening disease.

Conclusion:
Plasmapheresis of these two patients led to an immediate improvement in health and reduced clinical intervention. To our knowledge this is the first time plasmapheresis has been successfully used to treat respiratory infections. More cross sectional studies to define the rates of "blocking antibodies" are needed. Longitudinal studies are also needed to understand if these can be suppressed, at an earlier stage, by other less invasive means than plasmapheresis.



Clinical data for patient's pre and post-treatment. (A) Box and whisker plot and mean of days spent in hospital over 90 days for PN1 or PN3, recalculated monthly. (B) Box and whisker plot and mean of CRP levels taken on different days in the months prior to and after the plasmapheresis treatments for PN1 or PN3. N is the number of CRP measurements used to make each box and whisker plot. (C) Moving average of i.v. use over 90 days, recalculated monthly for PN1 or PN3. Plasmapheresis indicated by PP.

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P19: Why do some adults with PiMZ alpha1-antitrypin develop bronchiectasis?

Nupur Aggarwal [1], *Beatriz Martinez Delgado Delgado* [2], *Sandeep Salipalli* [1], *Nerea Matamala* [2], *Jessica Rademacher* [1], *Nicolaus Schwerk* [1], *Tobias Welte* [1], *Sabina Janciauskiene* [1], and *Felix C. Ringshausen* [1,*]

[1]Hannover Medical School
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*Presenting author

Several reports indicate an association among inherited alpha-1-antitrypsin deficiency (A1ATD), pulmonary infections and bronchiectasis. Most reported A1ATD cases with bronchiectasis are elderly homozygous PiZZ (Glu342Lys) smokers with emphysema. Whether there is an increased risk of pulmonary diseases, including bronchiectasis, in heterozygous PiMZ A1ATD carriers is debated.

We describe an 18-year old, non-smoking male who had neonatal hyperbilirubinemia and suffered from productive cough, chronic rhinosinusitis and recurrent otitis since early childhood. A high-resolution CT scan of the chest revealed bronchiectasis in both lower lobes with thickening of bronchial walls and additional tree-in-bud sign, indicating bronchiolitis and mucus plugging, but no emphysema. Analysis of the serum A1AT and phenotyping revealed that this patient had reduced A1AT levels of 0.78 g/L (normal is 0.9-2.0g/L) associated with an intermediate PiMZ A1ATD. To elucidate a possible link between PiMZ A1ATD and bronchiectasis, we asked whether blood neutrophils and A1AT protein isolated from our PiMZ patient differ from healthy PiMM donors. At a baseline and in response to inflammatory stimuli PiMZ neutrophils expressed more elastase and IL-1β and less A1AT than PiMM neutrophils. Moreover, affinity purified MZ A1AT protein had lower ability to inhibit endotoxin-induced TNFα and IL-1β expression than MM A1AT. Our findings in a young patient highlight the quantitative and qualitative deficiency of MZ A1AT, which offers an explanation for the early-age airways infections and early-age onset of bronchiectasis.

Respiratory physiotherapie

P20: Long-term randomized controlled trial to evaluate the efficacy of low expiration with the open glottis in the lateral posture in bronchiectasis

Gerard Muñoz [1,*], *Javier de Gracia* [2], *Maria Buxó* [1], *Antoni Alvarez* [2], *Gladis Sabater* [3], *Eric Rojas* [3], and *Montserrat Vendrell* [3]

[1]Biomedical Researche Institute of Girona
[2]Vall Hebron University Hospital
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*Presenting author

No placebo controlled clinical trials evaluating airway clearance techniques have been performed in BC. We evaluate short and long-term efficacy of ELTGOL in BC in a randomized control trial with placebo (Clinical Trial Registration NCT01578681). Non-cystic fibrosis BC adult patients in stable state with >10ml sputum/day not practising regular chest physiotherapy were randomized to perform ELTGOL or a placebo exercise twice daily. Patients were assessed at 7 visits (V) over one year. Primary endpoint: sputum volume during the procedure at V2 and 24-h post treatment. Secondary endpoints: sputum volume during the procedure at V7 and 24-h post treatment; Leicester Cough Questionnaire (LCQ), Saint George's Respiratory Questionnaire (SGRQ). Results: 44 patients were randomized (22 ELTGOL group and 22 placebo group; mean age 63.04±13.48 and 67.72±9.08). Sputum volume during the procedure at V2 and 24-h post treatment were higher in the ELTGOL group (12.27±11.92ml vs. 0ml and 47.75±31.6ml vs. 12.04±9.86ml, $p<0.001$). At V7 sputum volume during the procedure and 24-h post treatment were higher in the ELTGOL group (11.07±5.60ml vs. 0ml and 45.71±26.30ml vs. 13.43±7.46ml, $p<0.001$). The ELTGOL group showed a significant improvement in the SGRQ ($p<0.001$) andthe LCQ ($p<0.002$). Conclusions: The ELTGOL technique is effective in airway clearance both in the short and long term, improves quality of life and reduces the impact of daily cough in non-cystic fibrosis BC adult patients.

Funding: SEPAR, SOCAP, CFC, ACMG, Fiss PI12/01551

P21: Effects of hypertonic saline on sputum clearance in patients with bronchiectasis

Alcaraz-Serrano Victoria [1], *Herrero-Cortina Beatriz* [2], *Vilaró-Casamiitjana Jordi* [3], *Rosales-Mayor Edmundo* [4,*], *Torres-Marti Antoni* [5], and *Polverino Eva* [1]

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[2]Universidad de San Jorge, Zaragoza
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*Presenting author

Hypertonic saline (HS) has been largely approved in cystic fibrosis to increase airways clearance while little evidence is available in bronchiectasis (BE)

Aim:
To compare 3 inhaled solutions (7%HS; 0.1%Hialuronic Acid [HA] + 7%HS and 0.9%Isotonic Saline [IS]) in terms of: expectoration, cough severity, lung function and safety.

Methods:
Was conducted a double-blind, randomized, crossover trial in BE patients. Patients inhaled each solution during 4 consecutive days, followed by a physiotherapy session (apart from 3rd day). A 7-day washout period was used between treatments. Safety was analyzed using an adverse events' score. In each treatment arm, lung function and cough severity (Leicester questionnaire, LCQ) were measured. For statistical analysis a mixed model was used (significant $p<0.05$).

Results:
24 patients were included with a mean age of 62.6 (17.6[SD]). HS was the worst tolerated solution. HS and HA+HS induced greater expectoration during inhalation than IS ([HSvsIS] 9.9g vs 3.9g ($p<0.001$); [HA+HS vs IS] 8.1g vs 3.9g ($p<0.001$). Sputum obtained during physiotherapy period (1,2,4 day) was similar ($p\geq0.6$) regardless of inhaled solution. However, this amount was always greater than the 3rd day without physiotherapy. No differences were observed in 24h post-session sputum collection ($p\geq0.05$) for days 1,2,and 4,while it was higher for day 3 (15.9 vs 21.9,$p<0.001$). There were no significant differences in LCQ or in lung function. Most patients (45%) selected HA+HS as the preferred inhaled solution (IS:29.2%; HS:25%).

Conclusions:
This is the first study demonstrating that HA+HS and HS are more effective on sputum clearance than IS, being HA+HS better tolerated than HS. The combination HA+HS and physiotherapy was even more effective in reducing daily expectoration.

P22: Effect of professional physiotherapy on patients with non CF bronchiectasis – a preliminary study.

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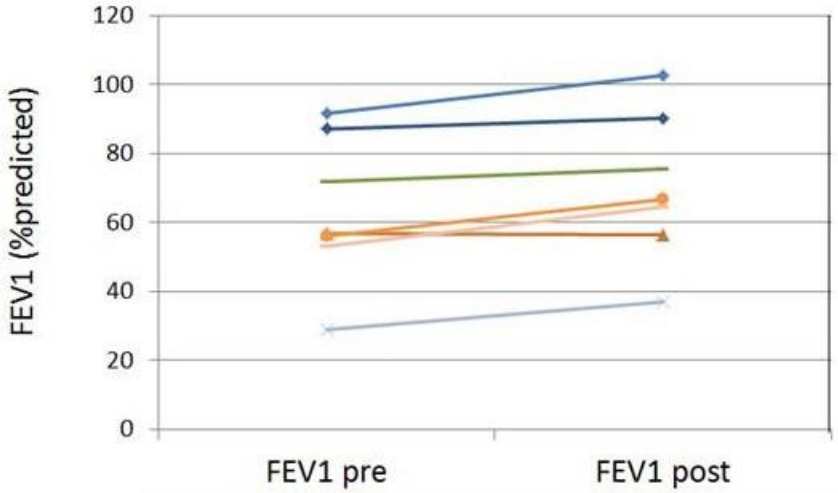
Introduction:
Non CF bronchiectasis is a rising entity around the world with developing diagnostics and evolving treatments being researched in the past few years. It is a pathological final common pathway of different etiologies and a thorough evaluation of the patients should be sought to establish a specific diagnosis. The aim of our study was to evaluate the efficacy of professional respiratory physiotherapy on the patients in which a specific diagnosis was not established.

Method:
Eight young patients with bronchiectasis who are under follow up at our pulmonary center in Tel Hashomer were evaluated. Specific diagnoses such as Cystic Fibrosis, Primary Ciliary Dyskinesis and immunodeficiencies (in which physiotherapy is known to be mandatory) were excluded. We examined the pulmonary function tests of these patients before and after one year of individually tailored professional physiotherapy at our institution three times per week in addition to independent physiotherapy at home using incentive resistance devices such as TRI-GYM .

Results:
Mean age of the patients at time of referral was 17.9 years (+/- 6.2). Mean FEV1 before starting physiotherapy was 63.6% predicted (+/- 21.7%) and after a year of treatment 70.4% predicted (+/- 21.8%), $P<0.01$ (see table & figure).

Conclusion:
We showed a significant improvement in pulmonary function tests which we assume are due to the individually tailored physiotherapy these patients received. Since most other therapies such as inhaled antibiotics, Azithromycin, mucolytic agents and inhaled corticosteroids were also used before referral to our center; the change in FEV1 can probably not be attributed to their use. This assumption should be investigated further.

Lung function 1-year post regular respiratory physiotherapy



	Baseline PFT	1 year post regular physiotherapy (x3/week)	P value
FVC	75.3 ±19.4	79.4 ±19.1	0.1835
FEV1	63.6 ±21.7	70.4 ±21.8	0.0088
FEV1/FVC	83.9 ±17.3	88.1 ±14.9	0.1381
FEF25-75	52.1 ±83.9	56.2 ±27.0	0.3145

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P23: Intrapulmonary percussive ventilation, indication, clinical experience and patient opinion

Wolfram Meister [1], *Nils Meyne* [1], *Michael Hamm* [1,*], and *Gerhard Müller* [2]

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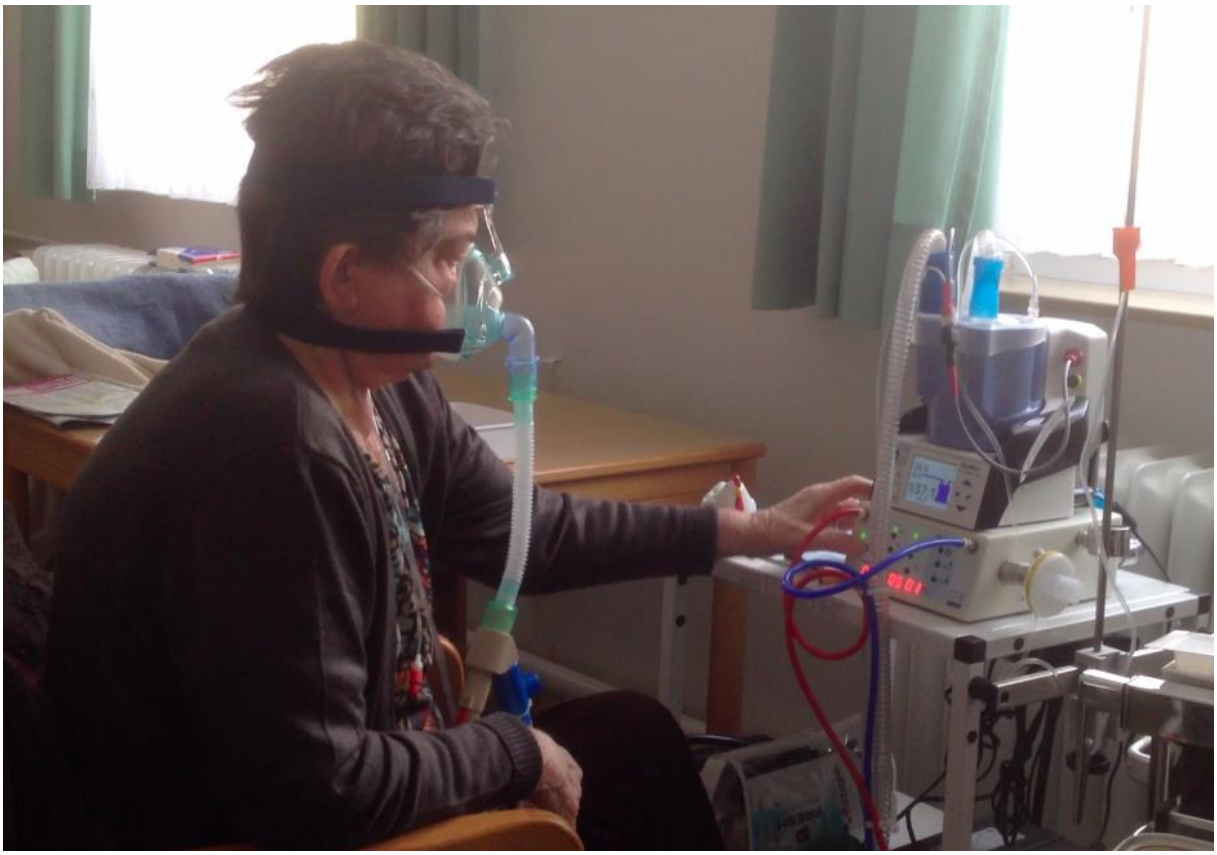
In the United States Intrapulmonary Percussive Ventilation (IPV) is a well-established treatment to support airway clearance in patients with severe airway obstruction from tenacious sputum. It is used in patients with bronchiectasis as well as in COPD or neuromuscular disease. Despite the known benefits IPV is rarely applied in Germany because of the high technical and personnel expenditure . On the basis of ten cases we present the indications, the clinical effects and the patients experience. These preliminary results support the addition of IPV to the standard therapy of bronchiectasis as a very effective method to increase the quality of life of our patients.



Prof. T. Welte, Hanover
Prof. T. Bauer, Berlin

Others

P24: An interactive educational website for the management of bronchiectasis: The Bronchiectasis Toolbox

Caroline Nicolson [1,*], *Anne Holland* [2], and *Annemarie Lee* [3]

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*Presenting author

Background:
The aim of the Bronchiectasis Toolbox is to provide health professionals with a multidisciplinary resource of current evidence based practice on the management of people with bronchiectasis. With the health burden of bronchiectasis increasing world-wide, there is a need to ensure this information is readily accessible to clinicians. It is well documented that e-learning enhances and enables effective learning for a digital generation.

Methods:
Funding for the project was via a competitive grant from the Australian Physiotherapy Association and several unrestricted educational grants. The content, developed by a team of clinicians with extensive experience in bronchiectasis, was based on the current national and international guidelines.
A web designer was employed to develop the branding of the site. The design was based on the Wordpress Management System with a responsive HTML5 front end which enables viewing on all platforms, including mobile phones.
Instructional videos of physiotherapy airway clearance techniques were developed and added to the website via Vimeo.
Experienced clinicians and students provided peer review of the website which was updated following their feedback.

Results:
The Bronchiectasis Toolbox was live in December 2015 at www.bronchiectasis.com.au
In three months the site had 3,628 hits with 2,500 unique users. The average time spent on the site per user was 4 .5 minutes. Twenty four countries accessed the website including Australia (49.2%), the United Kingdom (15.1%), the USA (6.5 %) and Canada (2.1%). The educational videos had 1,119 plays and were accessed by 21 countries.

Conclusion:
The Bronchiectasis Toolbox is a unique solution to a pressing need which has been accessed and utilised by clinicians' worldwide. Future evaluation of the website will assist with the continuing inclusion of relevant evidence based updates.

P25: Antibiotic use in treatment of non-CF Bronchiectasis: A retrospective analysis

Mohummad Shaan Goonoo [1,*], *Safina Kausar* [1], and *Saifudin Khalid* [1]

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*Presenting author

Background:

The British Thoracic Society (BTS) guidelines recommend obtaining sputum cultures when patients are stable and before administering antibiotics during an exacerbation of bronchiectasis. Additionally, criteria are described for Outpatient Parenteral Antibiotic Therapy (OPAT) services use.

Aims:
To assess use of antibiotics, ensure we are following BTS and trust guidelines and evaluate OPAT services use.

Materials and Methods:
A retrospective review of patients, admitted with acute exacerbation of non-cystic fibrosis bronchiectasis between August 2014 and August 2015, was done using clinical coding (n=58). The following were compared to guidelines: sputum bacteriology culture, use of empirical antibiotics, involvement of microbiologists, objective evaluation of parenteral antibiotics and OPAT services use.

Results:
55% had sputum sent for culture and sensitivity (C&S) by their General Practitioner when stable. 83% had no sputum sent for C&S on admission before starting antibiotics. Microbiology discussion took place in only 7 cases. 12 patients' sputum grew pseudomonas species. Out of 20 patients receiving IV antibiotics for more than 3 days, 65% received Piperacillin/Tazobactam. Most patients were evaluated using CRP measurements but none had spirometry. Only 3 patients were provided with OPAT services.

Discussion:
Discussion with microbiologists and attempts at objectively measuring response to parenteral antibiotics were inadequate. OPAT services were not always provided to patients appearing to be eligible for them; reasons for this were unclear. One explanation might be that antibiotics which require administration three times a day are often prescribed while local OPAT services currently only cater for up to twice daily administration.

Conclusions:
Management of acute exacerbations was often not in line with guidelines. This can potentially result in lack of antibiotic efficacy or antibiotic resistance. We suggest greater involvement of microbiologists and using C&S to aid antimicrobial selection. Greater investment in the OPAT services will promote care closer to home and fewer hospital stays.

https://www.brit-thoracic.org.uk/document-library/clinical-information/bronchiectasis/bts-guideline-for-non-cf-bronchiectasis/
ELHT anti-microbial guidelines

P26: The existence of asthma increases bronchiectasis exacerbation

Jin-Fu Xu [1,*], *Bei Mao* [1], *Jia-Wei Yang* [1], and *Hai-Wen Lu* [1]

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Background:
Bronchiectasis and asthma are common respiratory diseases worldwide. However, the influence of asthma on bronchiectasis remains unclear. The objective of this study is to analyze the effects of asthma on bronchiectasis exacerbation.

Methods:
Data from inpatients diagnosed with bronchiectasis with or without asthma at Shanghai Pulmonary Hospital between January 2013 and December 2014 was retrospectively collected and analyzed. 249 patients with only bronchiectasis and 214 patients with both bronchiectasis and asthma were included in the study. Follow-up records were used to evaluate exacerbations due to bronchiectasis and the effect of asthma on bronchiectasis.

Results:
The variables found to be independently associated with hospitalization due to bronchiectasis exacerbations were age (OR, 1.07; $P < 0.001$), duration of symptom (OR, 1.06; $P < 0.001$), the presence of asthma (OR, 2.6; $P = 0.021$), forced expiration volume at 1 second (FEV1) < 50% of the predicted value (OR, 4.03; $P = 0.001$), isolation of Pseudomonas aeruginosa (PA) in the patient's sputum (OR, 2.41; $P = 0.05$), and lung lesion extension > 2 lobes (OR, 2.73; $P = 0.022$).

Conclusion:
The existence of asthma was associated with an independent increase in risk of bronchiectasis exacerbation.

P27: Bronchiectasis in China: Present Situations and Challenges

Jin-Fu Xu [1,*], *Jie-lu Lin* [1], and *Jie-Ming Qu* [2]

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Bronchiectasis is a common but long-neglected disease in China, causing great burden both to the patients and to the society. The object of this article is to review and estimate the present status of bronchiectasis in China and the challenges on it, with the aim of bringing more attention to the disease. We review the available studies of bronchiectasis in China – encompassing data on prevalence, causes and related diseases, diagnosis and management – with a focus on the present situation and associated challenges of the disease, and comparing them with those of western countries. The overall prevalence of physician-diagnosed bronchiectasis in people aged ≥40 years was 1.2% and trended upwards with increasing age according to an urban population-based, cross-sectional survey of bronchiectasis in China. The exact etiology cannot be identified in more than 70% of patients in China, with pneumonia and tuberculosis still the most common causes of acquired bronchiectasis. NTM, COPD and asthma were also found and analyzed in bronchiectasis patients. The comprehensive evaluation of the severity of bronchiectasis relies on clinicians' subjective judgments, not according to the multidimensional grading systems such as FACED or BSI. Available treatment statement in China was first established in 2012, through expert consensus on the diagnosis and treatment of adult bronchiectasis, which was mainly in accord with British Thoracic Society (BTS) guideline on bronchiectasis. The majority of clinical work for respiratory physicians in China is treating patients who have severe exacerbations. However, treatment of stable bronchiectasis is ignored and should receive more attention.

P28: Pulmonary Nocardiosis in a Non-Immuncompromised Patient with Bronchiectasis

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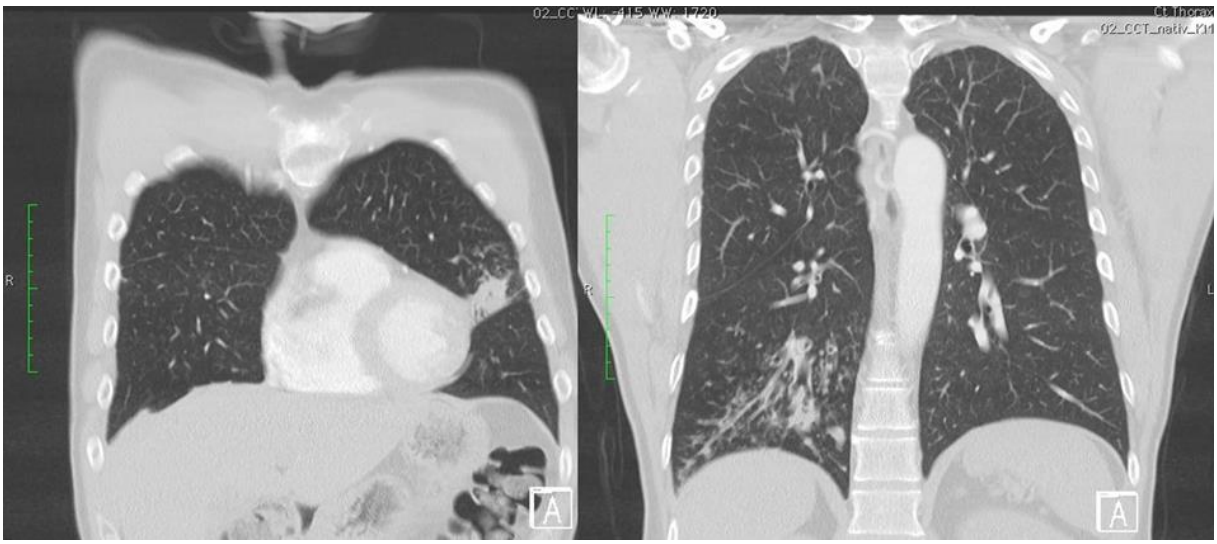
Introduction: Nocardia spp are found worldwide ubiquitous in the environment, forming part of the usual microbiota of soil and water as saprophytes. About 25 species are causing human infections. Nocardia spp belong to the aerobic actinomycetes group of bacteria which are gram-positive and weakly acid-fast bacilli showing branching filamentous ("fungal") pattern. Human infections are infrequent, most of the patients are immunocompromised (1). Inhalation of the bacteria can result in pulmonary nocardiosis, i.e. pneumonia, lung abscess, and cavitary lesions. Contact of the bacteria with abraded skin causes cutaneous nocardiosis and consequent hematogenous spread is possible. Nocardiosis is a neurotropic infection often disseminating to the brain. Frequent manifestations include the abdomen, nosocomial infections and surgical implants.

Case report: In 1992 after a "common cold" the 1954 born German male patient started with late onset non-atopic infect-triggered asthma. 11 years later he suffered from a community acquired pneumonia. On CT right lower lobe bronchiectasis was detected. Thereafter he had a few infective asthma exacerbations and needed antibiotics and sometimes intermittent inhaled corticosteroid/long acting bronchodilator treatment. Otherwise the patient remained free of symptoms, but starting with the fall/winter season 2011 3-4 yearly exacerbations emerged. After May 2015 continuously subfebrile despite targeted antibiotic courses; Haemophilus influenzae, Streptococcus agalctiae were detected. In December 2015 intractable cough, malaise, night sweats and mild reversible bronchial obstruction emerged. CT scan showed marked bronchiectasis, coin lesion-like mucoid impaction, mostly peribronchial infiltrates (figure 1). From sputum and bronchial lavage Nocardia cyriacigeorgica was isolated and also proven histologically in transbronchial biopsies (figure 2). Targeted sequential iv and oral antibiotic treatment was introduced. After 1 month we registered good clinical and radiological treatment success.



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P29: Characterization of bronchiectasis in the elderly

Giuseppe Bellelli [1], *James D Chalmers* [2], *Giovanni Sotgiu* [3], *Simone Dore* [3], *Melissa J McDonnell* [4], *Pieter C Goeminne* [5], *Katerina Dimakou* [6], *Dusan Skrbic* [7], *Andrea Lombi* [8], *Federico Pane* [8], *Dusanka Obradovic* [7], *Thomas C Fardon* [2], *Robert M Rutherford* [4], *Alberto Pesci* [8], and *Stefano Aliberti* [8,*]

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*Presenting author

Background:
Although bronchiectasis particularly affects people ≥65 years of age, data describing clinical characteristics of the disease in this population are lacking. This study aimed at evaluating bronchiectasis features in older adults and elderly, along with their clinical outcomes.
Methods. This was a secondary analysis of six European databases of prospectively enrolled adult outpatients with bronchiectasis. Bronchiectasis characteristics were compared across three study groups: younger adults (18-65 years), older adults (66-75 years), and elderly (and >76 years). 3-year mortality was the primary study outcome.

Results:
Among 1,258 patients enrolled (median age: 66 years; 42.5% males), 50.9% were >65 years and 19.1 >75 years old. Elderly patients were more comorbid, had worse quality of life and died more frequently than the others. Differences were detected among the three study groups with regard to neither the etiology nor the severity of bronchiectasis, nor the prevalence of chronic infection with P. aeruginosa. In multivariate regression model, age (Odds Ratio, O.R: 1.04, 95%Confidence Intervals [CI]:1.01-1.07), low BMI (OR: 2.48, 95% CI:1.14-5.39), previous hospitalizations (OR: 1.97, 95% CI:1.18-3.30), low FEV1 (OR: 1.02, 95% CI:1.01-1.03) and COPD (OR: 1.98, 95%CI:1.10-3.58) were independent predictors of 3-year mortality, after adjustment for covariates.

Conclusions:
Bronchiectasis does not substantially differ across age groups. Poor outcomes in elderly patients with bronchiectasis might be directly related to individual's frailty that should be further investigated in clinical studies.

P30: Pneumonic vs. non-pneumonic exacerbations in bronchiectasis

Edmundo Rosales-Mayor [1,*], *Victoria Alcaraz-Serrano* [1], *Rosario Menendez* [2], *Emilio Ansotegui* [2], *Beatriz Montull* [2], *Rosa María Girón* [3], *Carolina Cisneros* [3], *Montserrat Vendrell* [4], *Gerard Muñoz* [4], *María Angeles Marcos* [5], *Eva Polverino* [1], and *Antoni Torres* [1]

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Rationale:
Exacerbations are relevant in bronchiectasis (BE) but little is known regarding microbiology and outcomes of pneumonic (CAP) vs. non-pneumonic (EXAC) exacerbations.

Objective:
To compare clinical and microbiological characteristics of CAP vs. EXAC in adult patients with BE.

Methods:
Multicentre prospective observational study of consecutive cases from 4 Spanish hospitals.

Results:
We recruited 144 patients: 91 EXAC (63%) and 53 CAP (37%); 89% required hospitalization (CAP 94%, EXAC 86%). Demographics, vaccines, bronchiectasis aetiology and severity, and lung function were similar in both groups. CAP group showed more males and COPD but less chronic bronchial infection, previous exacerbations and macrolides than EXAC group. Clinical presentation was similar excepting higher values of creatinine, C-reactive protein, glucose and leukocytes in CAP. S.pneumoniae and P.aeruginosa were the first cause of CAP and EXAC, respectively. Most patients with P.aeruginosa already had a chronic infection by the same microorganism prior to CAP (71%) or EXAC (81%). Nevertheless, numerous patients with previous chronic P.aeruginosa had a new infection in our study (19% of EXAC, 58% of CAP). CAP showed more atrial fibrillation but similar outcomes (hospital stay, mortality, etc.) than EXAC. Chronic bronchial infection and previous exacerbations≥2/year were protective factors for CAP at multivariate analysis.

Conclusions:
CAP and EXAC in patients with BE have similar clinical presentation.An initial antibiotic treatment should cover S.pneumoniae in CAP and P.aeruginosa in EXAC, particularly in case of previous chronic infection, however a complete microbiological research is recommended. Pneumococcal vaccination should be considered in BE

P31: Computed tomography features in patients with non- cystic fibrosis bronchiectasis and COPD – one Institution experience

Tatjana Boskovic [1,*], *Dusan Skrbic* [1], *Slobodanka Pena Karan* [1], *Dragan Dragisic* [1], *Djordje Povazan* [1], and *Mirna Djuric* [1]

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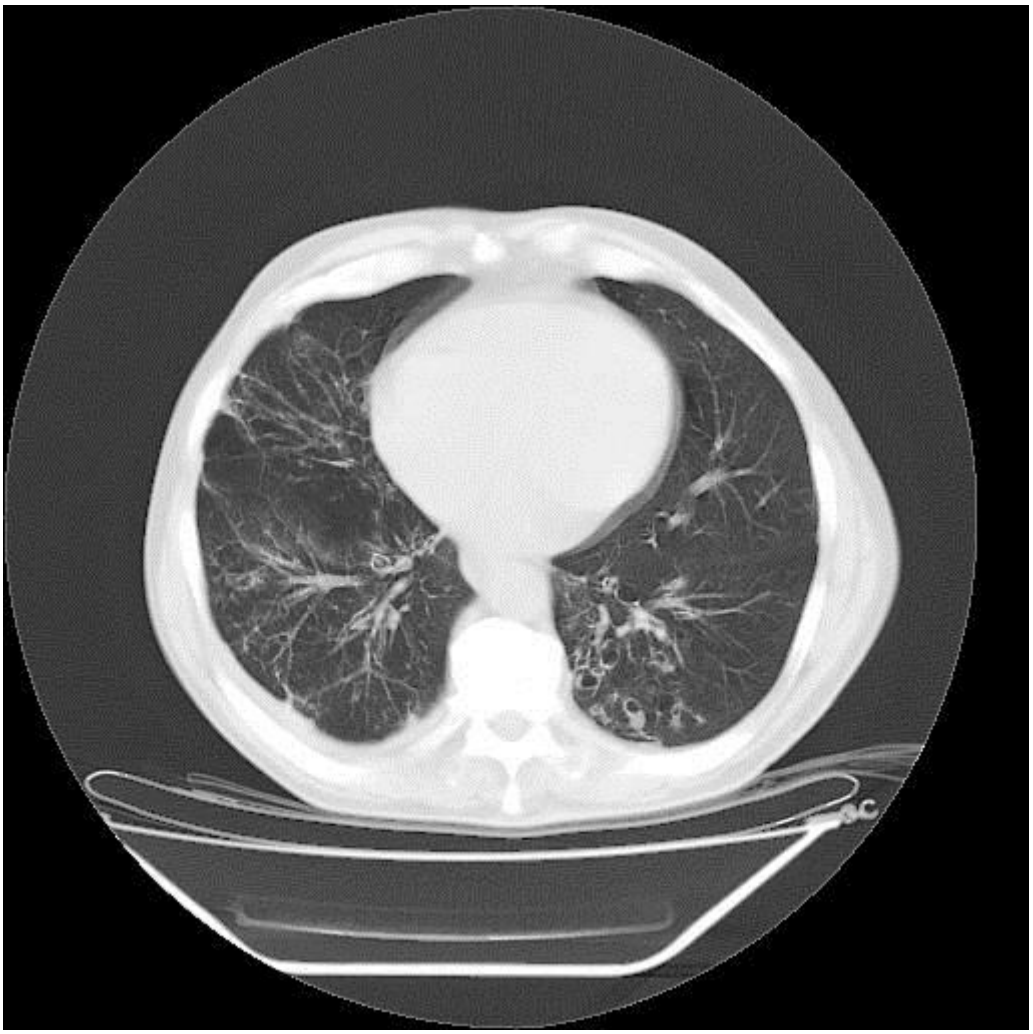
Introduction:
Non-cystic fibrosis bronchiectasis is a progressive respiratory disease of permanent dilatation of bronchi. Radiologically, they are divided into groups: cylindrical, varicose or cystic. Most commonly used radiological score for evaluation of bronchiectasis is Reiff score (0-18) which is believed to have impact on severity and outcome of disease.

Methods:
There was 108 patients in this retrospective study who previously had the diagnosis of non-cystic fibrosis bronchiectasis in their medical data, all hospitalized in our Institution in the past three years. After reviewing their CT/HRCT examinations, 102 patients were involved in this study.

Aim:
It was to evaluate radiological features in these patients with emphasis on correlation with COPD, the Reiff score and emphysema.

Results:
In our study, over two thirds of patients were male (73/102) and 29 female, with the average age of 62 years. Half of patients (53/102) did not have clinical signs of emphysema. From the medical data, patients were categorized in two groups, one who had only bronchiectasis (46 pt), and who had combined bronchiectasis and COPD (56/102 patients). Average number of hospitalizations was 1 (in 67 pts), with the maximum number of 9 in 1 patient. Upon CT/HRCT reviews, we concluded that 63 patients had radiological signs of emphysema, of which 34 had mild emphysema, 20 moderate and 9 severe form. Average Reiff score was 4.78 (23 pt), with the maximum of 17 (in one patient), only three patients had score of 1. Score was higher in group with combined bronchiectasis/COPD (4.98:4.63).

Conclusion: In patients previously diagnosed with emphysema and bronchiectasis, CT average Reiff score was 4.78, and only three patients had score over 10. More than half of patients had CT signs of emphysema. In correlation, all patients who had 4 or more hospitalizations did not have the average Reiff score over 7.



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P32: Prevalence of Nontuberculous Mycobacterial Pulmonary Disease, Germany, 2009–2014

Felix C. Ringshausen [1,*], *Dirk Wagner* [2], *Andrés de Roux* [3], *Roland Diel* [4], *David Hohmann* [5], *Lennart Hickstein* [6], *Tobias Welte* [1], and *Jessica Rademacher* [7]

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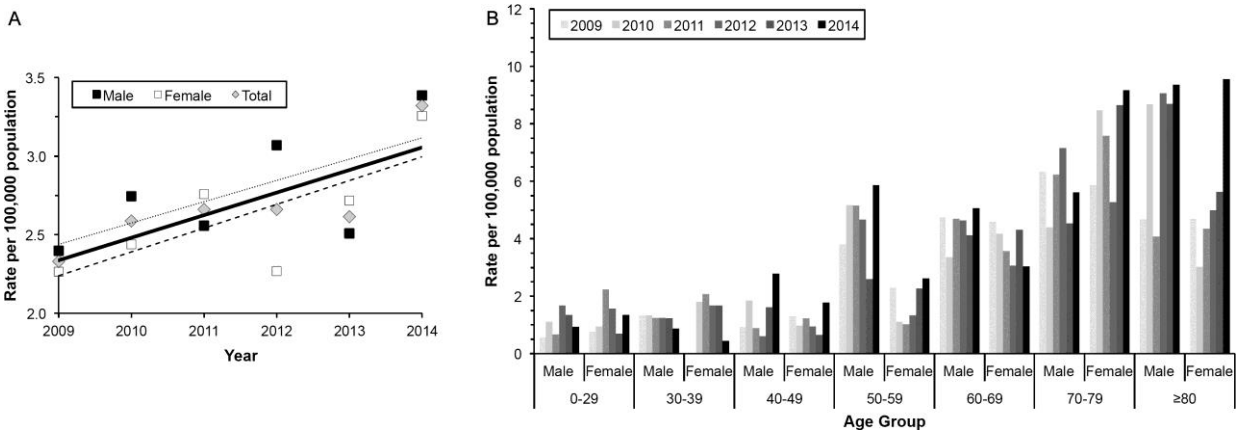
We could recently demonstrate that the burden of nontuberculous mycobacterial pulmonary disease (NTM-PD) is steadily increasing in Germany, as in many other countries [1]. However, population-based data on the epidemiology of NTM-PD are still scarce.
We analyzed representative samples of German routine statutory health insurance (SHI) claim data regarding the annual prevalence rates of NTM-PD (ICD-10 diagnosis code A31.0) over a six-year period and the distribution of age and sex, the site of health care provision as well as concomitant conditions.

Overall, from 2009 to 2014 we identified between 85 and 126 subjects with NTM-PD per year, with a balanced sex distribution. Mean age was not significantly different between males and females, except in 2013. The majority of subjects were managed in outpatient care (76–87%). Notably, the most frequent concomitant diagnosis was COPD/emphysema (ICD-10 codes J43–J44) in 62–79% of subjects. Between 6.6 and 18.3% of subjects had bronchiectasis. Annual prevalence rates increased from 2.3 (95% CI 1.87–2.87) to 3.3 (95% CI 2.78–3.94) cases per 100,000 population between 2009 and 2014, while the corresponding projected total number of subjects with NTM-PD in Germany increased from 1,907 to 2697 (Figure 1A). Overall, annual rates did not differ significantly between males and females. We observed the highest prevalence rates among subjects aged ≥50 years, in particular among males and females aged ≥80 years in 2014 (9.4 (95% CI 4.35–17.78) and 9.6 (95% CI 5.44–15.65) per 100,000, respectively; Figure 1B).

In conclusion, the annual prevalence rate of NTM-PD in Germany increased between 2009 and 2014. NTM-PD showed a strong association with advanced age and chronic airway diseases. Further reliable data on the epidemiology of NTM-PD are urgently needed and could become available if NTM-PD became a notifiable disease or comprehensive disease-specific registries were established [2].



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P33: PROGNOSIS - the German Bronchiectasis Registry

Felix C. Ringshausen [1,*], *Andrés de Roux* [2], *Roland Diel* [3], *Grit Barten* [4], *Annegret Zurawski* [5], *Tobias Welte* [1], and *Jessica Rademacher* [6]

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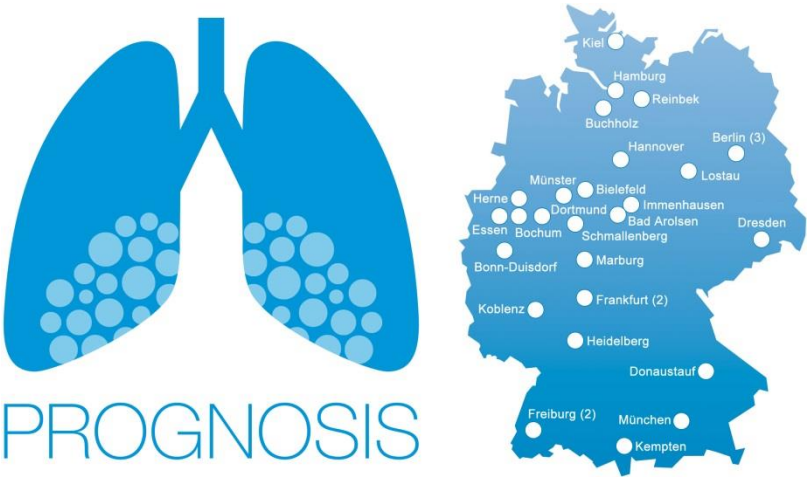
Impressively, biomedical research and resulting innovations have improved the prognosis of patients with cystic fibrosis (CF) over the past decades. While bronchiectasis is the hallmark of CF lung manifestation, there is still no approved pharmacotherapy available for the treatment of bronchiectasis not associated with CF. Consequently, bronchiectasis is considered one of the most neglected diseases in respiratory medicine, with a great lack of research and an urgent need to determine the optimal management strategies.
Recently, we provided first epidemiological evidence on the burden and the prevalence of bronchiectasis in Germany, clearly demonstrating that bronchiectasis is not an orphan disease and that it is associated with increasing healthcare unsafe [1, 2].
In order to advance research in the field of bronchiectasis we proposed the German Bronchiectasis Registry PROGNOSIS, which is aligned and collaborating with EMBARC, the European Bronchiectasis Registry.

The main objectives of PROGNOSIS are:
- To sustain and expand a national, representative, prospective, observational and longitudinal bronchiectasis database, recruiting a minimum of 750 patients from 25-35 centers from all levels of healthcare across Germany over a 3-year period
- To study the epidemiology of bronchiectasis and to provide an estimate of the distribution of bronchiectasis etiologies across different levels of healthcare
- To provide real-life data regarding the current management of bronchiectasis
- To perform observational research into bronchiectasis, particularly in areas where single center datasets are underpowered, such as in rare etiologies or determining markers of prognosis
- To promote collaborative clinical, basic and translational research in bronchiectasis
- To provide a registry of well phenotypes patients with bronchiectasis in clinical centers potentially eligible for enrollment into future clinical trials.

Currently, after having started recruitment in summer 2015 PROGNOSIS is well inline with the projected milestone of 250 recruited patients within the first year, with 30 centers actively participating.



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P34: A Novel Combination of Tobramycin with a Potentiator for the Treatment of Chronic Pseudomonas aeruginosa Infections

Martina Koeva [1], *Alina Gutu* [2], *Fred Ausubel* [2], and *Diane Joseph-McCarthy* [1]

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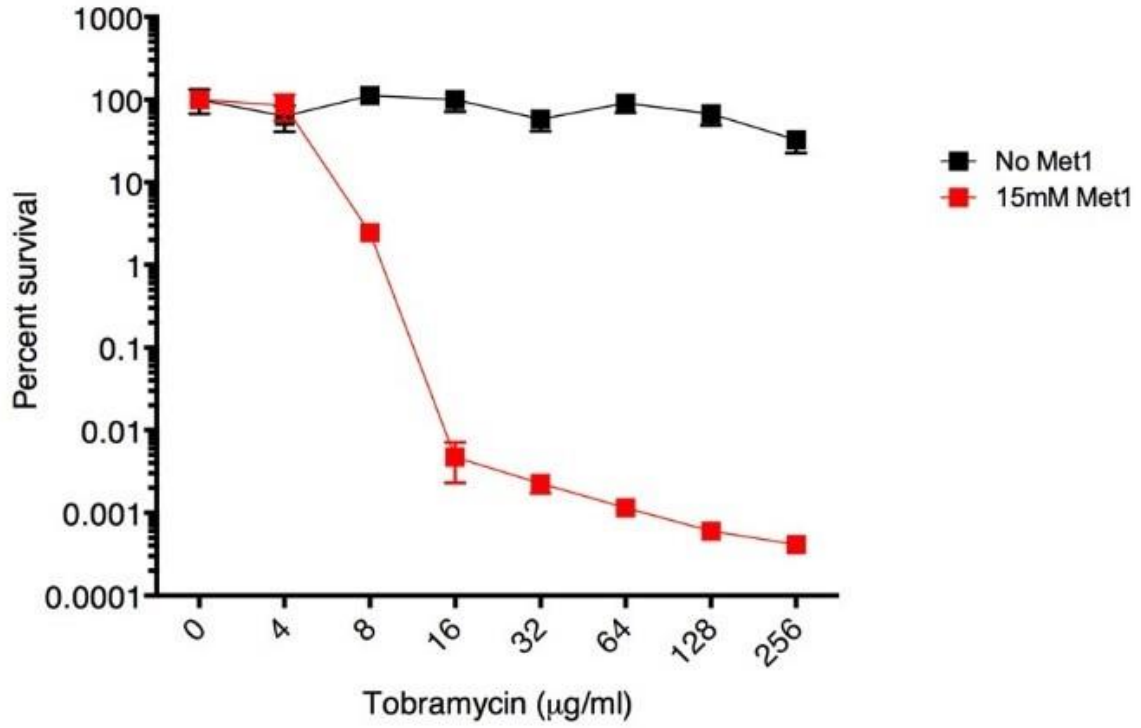
EBX-001, a combination of tobramycin with a bacterial metabolite as a potentiator, is being developed for the treatment of chronic P. aeruginosa infections in Cystic Fibrosis, non-CF bronchiectasis, and COPD patients. The combination utilizes an anti-persisters strategy and is aimed at reducing recurrent infections. P. aeruginosa cultures in planktonic stationary phase (PSP) were used to select for bacterial persisters, bacteria in a quasi-dormant state. In these PSP experiments, a range of tobramycin concentrations was tested with a range of metabolite concentrations to determine the potentiation effect of the metabolite under a variety of conditions. MICs were also determined for a variety of CF and COPD clinical isolates to select a diverse set of strains for inclusion in the study. Enhanced killing of up to 6 orders of magnitude of P. aeruginosa persisters for a range of strains was observed; see example for a mucoid CF isolate in the figure below. A combination of tobramycin with a potentiator remains an attractive therapeutic option for eliminating recurrent P. aeruginosa infections through the eradication of bacterial persisters, whether in CF, non-CF bronchiectasis, or COPD.



P35: Exacerbations by Pseudomonas aeruginosa in patients with bronchiectasis

Edmundo Rosales-Mayor [1,*], *Victoria Alcaraz-Serrano* [1], *Laura Raguer* [2], *Rosario Menendez* [3], *Emilio Ansotegui* [3], *Beatriz Montull* [3], *Rosa María Girón* [4], *Carolina Cisneros* [4], *Montserral Vendrell* [5], *Gerard Muñoz* [5], *María Angeles Marcos* [6], *Eva Polverino* [1], and *Antoni Torres* [1]

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*Presenting author

Rationale:
Chronic infection with Pseudomonas aeruginosa (PA) in patients with bronchiectasis (BE) is related with poor prognosis. Little is known about acute exacerbation by PA in these patients.

Objective:
To compare clinical characteristics and prognosis of exacerbations cause by PA or not in patients with BE.

Methods:
Multicentre prospective observational study of consecutive cases from 4 Spanish hospitals. Patients with negative or different isolation instead of PA were classified as not having an PA exacerbation.

Results:
We recruited 143 exacerbations; 53(37%) were pneumonia; 127(89%) required hospitalization; 38(27%) has a PA exacerbation. Demographics, vaccines, bronchiectasis aetiology and lung function were similar in both groups. Patients with PA exacerbation showed more bronchial chronic infection, exacerbations, macrolides, inhaled antibiotics and oxygen therapy, and higher FACED score than for other aetiologies. However their clinical presentation was characterized by less fever and pneumonia, lower C-RP and creatinine, but increased thrombocytosis and arterial carbon dioxide. Polymicrobial infection was detected more frequent in the PA group (39% vs. 19%;p=0.012). Short (during episode, day 30 and 90) and long term (1 year) mortality or relapse rates were similar between both groups but a non-significant trend to increased 1-year mortality was observed in the PA group. Factors associated with PA exacerbation at multivariate analysis were: previous neoplastic disease (OR 4.6), frequent exacerbations ≥2/year (OR 3.2) and PA bronchial chronic infection (OR 18.4), while fever (OR 0.3) was protective. Fever in patients with PA chronic infection was associated with a new (non pseudomonic) infection (72% vs. 33%;p=0.009)

Conclusions:
Patients with PA infection seemed to have more severe bronchiectasis although clinical presentation and final outcomes were similar. History of PA chronic bronchial infection supports the use of an initial empiric anti-pseudomonic treatment in an acute exacerbation of BE; however in these patients the presence of fever may indicate a new infection.

P36: Pneumococcal vaccination in bronchiectasis- an area for improvement?

Eve Palmer [1], *Nicholas Lane* [1], *John Davison* [1,*], *Donna McEvoy* [1], and *Anthony De Soyza* [2]

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*Presenting author

Patients with Bronchiectasis(BE) are "at risk" of pneumococcal disease. UK National guidelines recommend routine pneumococcal vaccination (PV) in all with respiratory disease or those 65yrs+ (1). Pneumococcal vaccination is also recommended in the BTS 2010 guidelines. Our experience is that re-vaccination advice has varied and recall programs are not routine (1). Patients unsure of their vaccination schedules may miss vaccination risking pneumococcal disease, some patients may expect re-vaccination based on prior advice.

Hypothesis:
1) Patients with bronchiectasis may not be receiving revaccination according to the current guidelines.
2) Bronchiectasis patients are at a higher risk of pneumonia

Methods:
Single-centre prospective questionnaire study of vaccination, pneumonia rates and patient knowledge of pneumococcal vaccine at a UK specialist centre for adult bronchiectasis patients.

Results:
Data on the first 81 patients recruited are presented. Mean age was 67 yrs (M:F ratio was 29:52). 95% received PV; only 3 patients hadn't received PV with 2 additional patients unsure of PV status.

Only 6 patients (7% of cohort) reported having received written information on PV or revaccination. 28 pts were either not told revaccination schedules or could not recall being told anything. 15 patients reported being told vaccination was once per lifespan, 23 were told revaccinate every 10yrs, 12 pts were told every 5 years, remainder included yearly or 3 yearly.

Only 12% reported an expected PV revaccination date.
43 patients self-reported a prior episode of pneumonia. We confirmed pneumonia from secondary care radiology in 8 patients (9.9%). Primary care records were provided in 20 of 62 requests to date.

Conclusions: Self-reported and confirmed episodes of pneumonia are common in BE.
Pneumococcal vaccination (PV) is frequently administered in bronchiectasis patients but patients receive limited written information and are unclear about re-vaccination. Clear guidance/ Automated scheduling may help improve this.

Funding: Unrestricted grant Pfizer

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/263318/Green-Book-Chapter-25-v5_2.pdf

P37: Pulmonary targeted antibiotics in bronchiectasis; inhalers vs. nebulisers. A qualitative and quantitative assessment of patients' attitudes.

John Davison [1,*], *Tony De Soyza* [1], *Richard Lee* [2], *Tim Rapley* [2], and *Donna McEvoy* [1]

[1]Freeman Hospital
[2]Newcastle University
*Presenting author

Background:
Regular, twice daily nebulised antibiotics are useful in managing bronchiectasis with 10-20% of patients receiving such therapy. This patient population typically has severe bronchiectasis requiring multiple other medications.

Methods:
90 adult bronchiectasis patients completed questionnaires. 16 patients and/or carers attended focus groups providing in-depth information of lived experience using inhaled antibiotics. Thematic data analysis (TA) allowed questionnaire development that was applied to the larger group.

Results:
TA of the focus group data identified that many patients found nebulised therapy an imposition on their daily routine that impaired adherence. Reducing treatment burden/ time administering therapy was important. Others however reported that nebulisation time was a period of rest, often incorporated into daily routines. The data from questionnaires showed although 70% currently taking nebulised antibiotics found them easy/very easy to administer, 10% found these hard/very hard to administer. 20% found taking the nebuliser in front of others "uncomfortable". When nebulising, 47% excluded themselves in a separate room on a daily basis. 53% stopped nebulised therapy during vacations.
If an inhaler was available, that was as effective as nebulised therapy at preventing exacerbations, 53% strongly agreed/agreed, they preferred an antibiotic delivered by an inhaler over a nebuliser. 16% stated a preference for nebulised. Notably, only 10% wished to remain on nebulised therapy.

Conclusions:
Bronchiectasis patients do not fully adhere with current treatments based upon treatment burden, life experience and lay knowledge. Health care professionals should recognise patient challenges to adherence and act in partnership with them to develop treatment regimens that facilitate adherence.

P38: MDCT severity score of bronchiectasis in correlation with pulmonary function tests

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Objectives:
To assess whether there is a correlation between a proposed MDCT severity score of bronchiectasis and pulmonary function tests.

Materials/Methods:
40 patients presented with clinically or CT known bronchiectasis evaluated clinicaly and with multidetector CT of the chest and relevant pulmonary function tests.

Results:
By correlating severity of airway obstruction represented by the FEV1 severity (decreased forced expiratory volume in one second) with our proposed CT score of bronchiectasis , we found that CT score correlate with the severity of PFTs, and airflow obstruction in bronchiectasis which is primarily linked to severity of extent of bronchiectasis, severity of bronchial wall thickening and the degree of mosaic attenuation (the extent of decreased attenuation of lung parenchyma) which implies an association of obliterative bronchitis with bronchiectasis. On the other hand there was no statistically significant relationship between the severity of bronchial dilatation and FEV1 (p value of 0.655). Also no statistically significant relationship between the extent of mucous plugging in relation to FEV1 severity (p value of 0.091).

Conclusions:
MDCT is sensitive for showing, detecting, scoring and evaluating bronchiectasis, and with the recent advances in MDCT, it become the modality of choice and the corner stone in the evaluation of bronchiectasis.

P39: Bronchiectasis mortality in New Zealand, 2003-2013

Braden Te Ao [1,*], *Alain Vandal* [1], and *Conroy Wong* [2]

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*Presenting author

Objectives:
There is limited literature available about the mortality associated with bronchiectasis. The aim of this study is to describe bronchiectasis mortality in New Zealand (NZ), including trends and variations between groups by age, gender, ethnicity and socioeconomic deprivation.

Methods:
National representative data for bronchiectasis deaths between 2003 and 2013 were extracted from the National Mortality Collection New Zealand Ministry of Health using International Classification of Disease code J47. Deaths were analysed by age, gender, ethnicity and socioeconomic deprivation (as a proxy for socio-economic status). Mortality rates were age-standardised by the direct method, with the World Health Organisation standard population as the reference.

Results:
A total of 890 deaths were recorded. The number of deaths from bronchiectasis in NZ increased at a rate of approximately 4.5% per year to 97 deaths in 2013. Age-adjusted mean mortality rates over the period were 34% higher for women than men, and 8.3 fold higher in Pacific peoples than for European and other ethnicities. Deaths were 4 times more frequent among those residing in highly deprived areas than those in least deprived areas.
Conclusion: Our results suggest an upward trend in bronchiectasis mortality in NZ between 2003 and 2013. Mortality rates were particularly high in Pacific patients and those residing in highly deprived areas. Further research on measures to improve equity of health outcomes across ethnic and socioeconomic groups in NZ is required.

P40: Bronchictasis and asthma-case report

Sabina Škrgat [1,*], *Jernej Sitar* [1], and *Franc Šifrer* [1]

[1]University clinic Golnik
*Presenting author

Allergic bronchopulmonary aspergillosis (ABPA) is an IgE mediated hypersensitivity response to A. fumigatus colonization of the tracheobronchial tree. It occurs most often in conjunction with asthma and cystic fibrosis. Clinically it presents with asthma-like exacerbations and can lead to irreparable lung damage such as bronchiectasis and fibrosis.
We present a case of a middle aged woman admitted to our ICU unit due to respiratory failure.

She had a history of asthma with fixed obstruction, fibrothorax due to empyema treatment 13 years ago. Despite maximal inhalatory therapy she had multiple asthma exacerbations requiring hospital treatment. Exacerbations were also attributed to her 30 pack/years of smoking and obesity. Additional diagnosis of obesity hypoventilation syndrome led to treatment with noninvasive mechanical ventilation. Despite treatment she developed chronic hypercapnic respiratory failure, supplemental oxygen was initiated in addition to noninvasive ventilation.

At admission to our ward mechanical ventilation was needed due to respiratory failure. Antibiotic treatment for infection with Pseudomonas aeruginosa, bronchodilation and bronchial secretion clearance led to slow, but unsatisfactory improvement.
Review of the patient history led to high suspicion for diagnosis of allergic bronchopulmonary aspergillosis. Review of CT scans revealed central bronchiectasis with thickened bronchial walls and mucoid impaction. Additional diagnostic tests were done. We managed to confirm positive specific IgE for Aspergilus fumigatus, elevated levels of cIgE, history of peripheral eosinophilia. We did not confirm positive test results for Aspergilus precipitins or Aspergilus species in the bronchial lavage culture .
Therapy with oral corticosteroid was initiated which led to fast clinical improvement. She was succesfully extubated.

We believe bronchial clearance, inhalatory antipseudomonal antibiotic and standard therapy for ABPA is the cornerstone treatment for this patient.

P41: Hyper IgE Syndrome : a rare cause of bronchiectasis

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*Presenting author

Introduction
Job's syndrome (Hyper IgE Syndrome - HIES) is a primary immunodeficiency characterized by raised levels of IgE, eczema and recurrent skin and lung infections in childhood , affecting fewer than 1 per million patients . Although defect in STAT3 protein plays a role , diagnosis is based on clinical and laboratory features. Therapy includes antibiotics , with Staph. Aureus being the most common pathogen . Pneumatoceles and bronchiectasis formed during the healing process predispose to Gram (-) and fungal infections. Finally, HIES is also associated with an increased risk of malignancy.

Aim
The presentation of a rare case of bronchiectasis due to HIES in a patient diagnosed in childhood , experiencing recurrent infections after a long asymptomatic period following bone marrow transplantation.

Methods
A 32-year-old man was admitted to our hospital complaining of productive cough since a week. He has a long history of bronchiectasis formed after pneumonias at early childhood. Eczema and a high title of IgE had established the diagnosis of HIES, while other diagnosis were excluded. He received intravenous immunoglobulin (IVIG) for 5 years. At the age of 14 he developed a non Hodgkin lymphoma and underwent bone marrow transplantation. For the next 15 years he remained asymptomatic. Nevertheless, the last 3 years his situation was deteriorated with annual infections treated with oral antibiotics.

Results
Physical examination revealed clubbing , eczema and pleuritic murmur . HRCT showed extensive bilateral bronchiectasis whereas sputum culture yielded multisensitive Klebsiella pneumoniae. The patient was administered Piperacillin-Tazobactam for 15 days and underwent respiratory physiotherapy. He rapidly improved and was discharged.

Conclusions
HIES constitutes a rare cause of bronchiectasis formed in childhood. Diagnosis is mainly clinical with treatment of infections being the mainstay . IVIG and bone marrow transplantation may be beneficial for some patients.

P42: Prevalence of bronchiectasis in four European countries

Marc Miravitlles [1], *Mònica Monteagudo* [2], *Teresa Rodríguez* [2], *Miriam Barrecheguren* [1], *Pere Simonet* [3], *María E. Sáez* [4], *Antonio González-Pérez* [4], *Luis A. García Rodríguez* [4], *Juha Mehtälä* [5], *Ilona Iso-Mustajärvi* [5], *Sebastian Braun* [6], *Jennifer Haas* [6], *Felix C. Ringshausen* [7], *Fabian Juelich* [8], *Gisela Korfmann* [8], and *Kiliana Suzart-Woischnik* [9,*]

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[2]Primary Care University Research Institute Jordi Gol (IDIAP Jordi Gol), Barcelona, Spain, Universitat Autònoma de Barcelona, Bellaterra (Cerdanyola del Vallès), Spain
[3]Family Physician, Director of the PCC Viladecans-2, Catalan Institute of Health, Barcelona, Spain
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[9]Bayer Pharma AG, Berlin, Germany
*Presenting author

Background
Bronchiectasis is a pulmonary disorder defined morphologically as permanent bronchial dilatation involving a vicious cycle of recurrent infection, inflammation and bronchial-wall damage. Despite its clinical importance, there is a lack of robust prevalence estimates of bronchiectasis especially for Europe.

Objectives
The primary objective of this research project was to estimate the prevalence of bronchiectasis not associated with cystic fibrosis in four European countries (Germany, Spain, Sweden and the United Kingdom [UK]). Furthermore, patient demographics and the clinical burden of illness were characterized.

Methods
Four observational studies were conducted using administrative databases. The study period included the calendar year 2013 in Germany and 2012 in the other three countries. Bronchiectasis subjects were identified via International Classification of Diseases (ICD, 9th or 10th revision) Codes or Read Codes, as applicable. Data on healthcare resource utilization were analysed to characterize the clinical burden of illness. Descriptive statistics were performed.

Results
The prevalence of bronchiectasis per 10,000 ranged from 6.6 in Germany to 7.9 in Sweden, 34.0 in the UK and 36.2 in Spain (see Table). The median age was above 60 years and women were more often affected (53-62 %) than men in all countries. More than half of patients studied (55% to 77%) received at least one course of antibiotics, except in Spain where only 4.9% of the patients received antibiotic treatment. Prescriptions for respiratory drugs (e.g. long-acting β2-agonists [LABAs], long-acting muscarinic antagonists [LAMA], inhaled corticosteroids [ICS]) ranged from 48% to 66% and bronchiectasis-related hospitalizations were identified in 13% to 27% of patients.

Conclusions
In Europe, bronchiectasis is a rarely documented disease with a broad range of prevalence estimates in different countries. However, it is unclear whether these ranges can be attributed to geographic differences or different coding behaviour. Overall, the documented health resource utilization indicates a high disease burden.

Table: Epidemiology of bronchiectasis in four European countries

	Germany	Spain	Sweden	UK
Data sources	Health Risk Institute research database	SIDIAP database	The National Patient Register of Sweden	The Health Improvement Database (THIN)
Sample/study size	3,785,076	5,800,000	9,600,379	3,559,726
Study period	2013	2012	2012	2012
Estimated prevalence/10,000	6.6	36.2	7.9	34.0
Median age group	65-69	65-99	61-70	60-79
Female gender, %	52	54	62	58
Respiratory drugs (e. g. LABA, LAMA, ICS), %	64	48	n. a.	66
Antibiotic treatment, %	63	4.9	58	77
Patients with at least one hospitalization related to bronchiectasis, %	13	14*	14	27

*Hospitalization due to bronchiectasis or other causes

P42: Presentation of Yellow Nail Syndrome in a two female patients Milenkovic B, Cvejic J, Dimic Janjic S

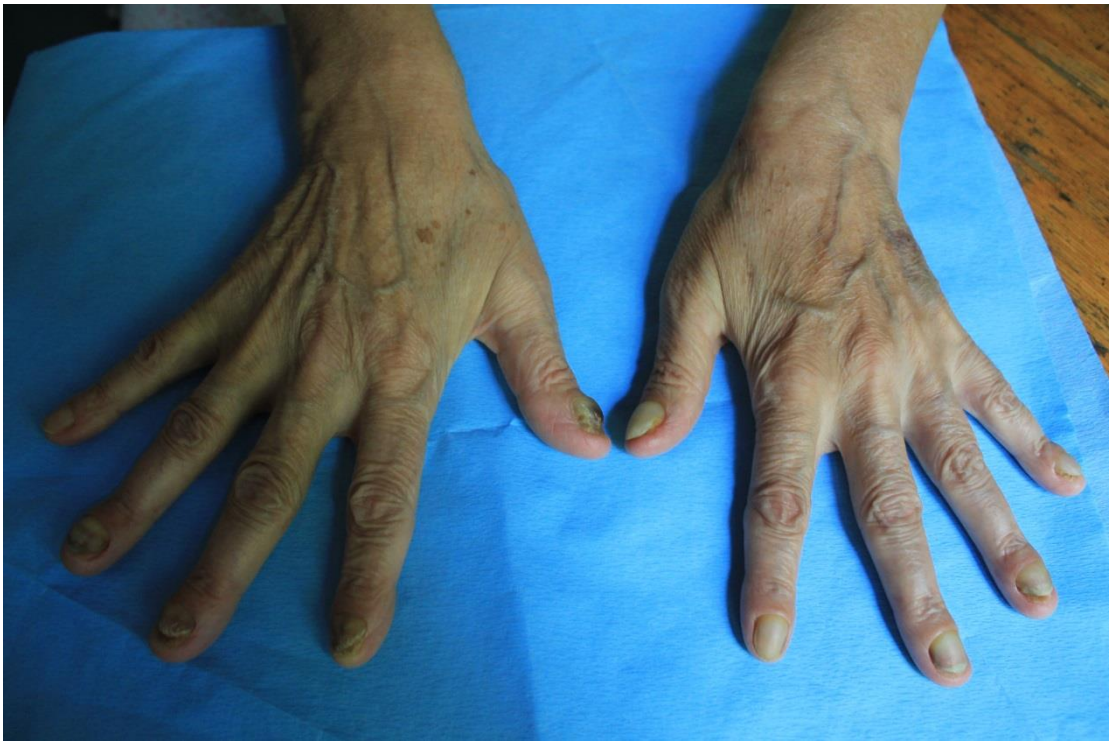
Branislava Milenkovic [1,*]

[1]Institute for Pulmonary Disease
*Presenting author

BACKGROUND:
Yellow nail syndrome (YNS) is a rare disorder characterized with a specific nail dystrophy (yellowish or green nails, transverse ridging, increased curvature with "a hump" and distal onycholysis), lymphoedema and respiratory tract involvement (mainly bronchial hyper-responsiveness, recurrentpneumonia, bronchiectasis and pleural effusion), with or without sinusitis. We report two adult cases.

PATIENTS:
A 50 year old women had 20 yellow nails, lymphedema of the lower limbs, pleural effusion on both sides, bronchiectasis, diagnosis of asthma and sinusitis, and pericardial effusion. A 67 year old women had yellow nails, giant saccular bronchiectasis and diagnosis of COPD. Both patients denide similar disorders in their family.

CONCLUSION:
Yellow nail syndrome is a rare cause of bronchiectasis



P44: The prevalence of non-cystic fibrosis bronchiectasis in the US

Christopher Blanchette [1,*], *Joshua Noone* [1], *Glenda Stone* [2], *Emily Zacherle* [1], *Michael C Runken* [3], *Reuben Howden* [1], and *Doug Mapel* [4]

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[2]Grifols
[3]Grifols
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*Presenting author

OBJECTIVES:
Non-cystic fibrosis bronchiectasis (NCFBE) is a rare, chronic lung disease characterized by bronchial inflammation and permanent airway dilation. Chronic infections with Pseudomonas aeruginosa (PA) have been linked to higher morbidity and mortality in NCFBE patients. Prevalence of PA among NCFBE have been reported in epidemiologic studies to be as high as 30%, however there has not been a large nationwide assessment of diagnostic patterns in the US. This study assessed the prevalence of PA diagnosis among US commercially insured NCFBE patients.

METHODS:
Using data from the 2007-2013 PharMetrics Plus administrative claims database, we identified bronchiectasis (ICD-9-CM: 494.xx) patients, then excluded those with cystic fibrosis (277.XX). Patients were stratified by evidence of PA (482.1 or 041.7). We compared patient demographics and comorbidities between NCFBE patients with and without PA infection. Frequencies and percentages were compared using bivariate statistics (e.g., chi-square test).

RESULTS:
Among a base population of 101,321,694, we identified 23,740 patients with NCFBE of which 2.5% (595) had evidence of PA. Patients were mostly over 50 years of age (82.7%) and female (61.7%). Patients with PA had higher comorbidity rates in numerous disease areas including cardiac arrhythmias (44.2% vs 24.1%, $p<0.0001$), CHF (28.0% vs 12.3%, $p<0.0001$), COPD (83.7% vs 60.9%, $p<0.0001$), coagulopathy (12.2% vs 5.5%, $p<0.0001$) and fluid and electrolyte disorders (34.7% vs 17.7%, $p<0.0001$).

CONCLUSIONS:
The prevalence of PA appears to be vastly under-reported in diagnostic healthcare data compared to epidemiologic studies, which may suggest a lack of diagnosis in routine healthcare practice. We also found PA patients to have much higher comorbidity rates. Greater emphasis on identifying NCFBE patients with PA is needed.

FUNDING SOURCE:
Grifols, RTP, NC

P45: Treatment patterns associated with pseudomonas aeruginosa among patients with non-cystic fibrosis bronchiectasis in the US

Christopher Blanchette [1,*], *Joshua Noone* [1], *Glenda Stone* [2], *Emily Zacherle* [1], *Michael C Runken* [2], *Reuben Howden* [1], and *Doug Mapel* [3]

[1]University of North Carolina at Charlotte
[2]Grifols
[3]Lovelace Clinic Foundation
*Presenting author

OBJECTIVES:
Non-cystic fibrosis bronchiectasis (NCFBE) is a rare, chronic lung disease characterized by bronchial inflammation and permanent airway dilation. Chronic infections with Pseudomonas aeruginosa (PA) have been linked to higher morbidity and mortality in NCFBE patients. We assessed treatment patterns for PA among NCFBE patients in a US commercially-insured database.

METHODS:
Using data from 2007-2013 PharMetrics Plus administrative claims, we included patients with >2 claims for bronchiectasis (ICD-9-CM: 494.xx); then excluded those with >1 claim for cystic fibrosis (277.xx). The prevalent cohort of NCFBE patients were indexed at first NCFBE claim and required to have at least 12 months post-index for assessment of treatment patterns. PA was defined by >1 claim for PA (482.1 or 041.7) during the study period. We evaluated all respiratory medications used by the entire cohort. The mean difference in treatment fills were compared between those with and without PA using paired t-tests.

RESULTS:
Of 36,350 patients with NCFBE, 1285 had a claim for PA. Patients with PA were similar to those without PA: mostly over age 50 (88% vs. 82.1%) and female (59.6% vs 63%). PA patients had significantly greater mean prescription fills per patient of ($p<0.05$) albuterol (187%, 1.66 vs. 0.88), budesonide (187%, 0.8 vs. 0.43), ciprofloxacin (463%, 1.24 vs. 0.27), fluticasone products (181%, 2.03 vs. 1.12), ipratropium (250%, 0.96 vs. 0.39), levalbuterol (266%, 0.34 vs. 0.13), methylprednisolone (195%, 0.27 vs. 0.14), prednisone (211%, 1.86 vs. 0.89), tiotropium (250%, 1.22 vs. 0.49) and tobramycin (2047%, 0.51 vs. 0.02).

CONCLUSIONS:
NCFBE patients with PA were treated with more antibiotics, steroids and respiratory medications compared to NCFBE patients without PA. However, health outcomes of those with PA have been reported in prior publications as comparatively poorer. Additional research is needed to establish better treatment management for these patients.

FUNDING SOURCE:
Grifols, RTP, NC

P46: Healthcare cost and utilization before and after diagnosis of pseudomonas aeruginosa among patients with non-cystic fibrosis bronchiectasis in the US

Christopher Blanchette [1], *Joshua Noone* [1], *Glenda Stone* [2], *Emily Zacherle* [1], *Michael C Runken* [2], *Reuben Howden* [1], and *Doug Mapel* [3]

[1]University of North Carolina at Charlotte
[2]Grifols
[3]Lovelace Clinic Foundation

OBJECTIVES:
Non-cystic fibrosis bronchiectasis (NCFBE) is a rare, chronic lung disease characterized by bronchial inflammation and permanent airway dilation. Chronic infections with Pseudomonas aeruginosa (PA) have been linked to higher morbidity and mortality in NCFBE patients. We assessed healthcare cost and utilization in the year before and after PA diagnosis among US commercially-insured NCFBE patients.

METHODS:
Using data from 2007-2013 PharMetrics Plus administrative claims, we included patients with >2 claims for bronchiectasis (ICD-9-CM: 494.xx) and >1 claim for PA (482.1 or 041.7); then excluded those with a claim for cystic fibrosis (277.xx). Patients were indexed at first claim for PA and were required to have >12 months before and after the index PA claim for assessment of healthcare cost and resource utilization. The mean difference in utilization and costs were assessed using paired t-test for statistical significance.

RESULTS:
Of 23,740 patients with NCFBE, 716 had PA. Patients with PA were mostly over age 50 (88.8%) and female (60.5%), had a high rate of cardiac arrhythmias (28.6%) and uncontrolled hypertension (49.6%). Total healthcare costs per patient in the year prior to PA diagnosis was $36,213 on average compared to $67,764 in the year following, for an increase of 87% or $31,551 ($p<0.0001$). Hospital cost represented the largest proportion of total healthcare cost after PA diagnosis (54%) and was associated with an 80% increase or $16,243 ($p=0.0004$), representing an increase of 4 hospitalizations per patient ($p<0.0001$).

CONCLUSIONS:
NCFBE patients with evidence of PA incur substantially greater healthcare costs and utilization after diagnosis of PA. While these patients may have had PA prior to diagnosis, they appear to consume greater healthcare services post-diagnosis. Future research should explore methods of earlier identification of NCFBE patients with PA, as this may lead to a reduction in US healthcare costs.

FUNDING SOURCE:
Grifols, RTP, NC

P47: Problems of diagnosis and treatment of bronchiectasis in Kyrgyz Republic in conditions of limited health care resources

Venera Eshenkulova [1,*], and *Talant Sooronbaev* [1]

[1]NCCIM
*Presenting author

Aim:
To examine the diagnosis and treatment of bronchiectasis in Kyrgyz Republic

Materials and Methods:
During 12 months in 2015, 1796 patients were observed in pulmonology department of National centre of cardiology and internal medicine. Distribution of patients by referral's from local doctors: bronchial asthma -557, 998 with COPD, bronchiectasis- 56, 185 -pneumonia. 176 participants were examined by CT, bronchiectasis were verified in 59 cases first time, 38 patients of them were directed with COPD. To all 115patients with bronchiectasis (34 men, 81 women), average age =48,5 ± 1,1, were determined frequency of exacerbations per year, using of antibacterial drugs, accordingly to diagnostical tests.

Results:
The analysis showed that there are serious problems with diagnosis and treatment. 71.6% of all patients did not have access to the CT, in 86.8% cases they can't afforded sputum culture. The frequency of exacerbations before the diagnosis and choosing of adequate therapy was defined as 3.4 ± 0.3 times per year in newly diagnosed patients. There were serious obstacles with drug supply and treatment. Analysis of the effectiveness of antibiotic presented that only 6.7% of patients received adequate therapy, and 93.3% inadequate. After the prescription of therapy by results of microbiological test the frequency of exacerbations per year was reduced to 2.2 times per year.

Conclusions:
1. The analysis showed that the possible causes of delayed diagnosis of BE in patients with various respiratory diseases are due to the lack of available simple survey techniques like CT, sputum culture, limited health care resources.
2. The reasons of the ineffectiveness of the therapy: the wrong choice of antibacterial drugs, problems with drug supply, which led to frequent exacerbations and the progression of the disease.

P48: Evaluation of two prognostic scores in adult patients with non-cystic fibrosis bronchiectasis

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Rationale:
Non-cystic fibrosis bronchiectasis (NCFBE) is a chronic and heterogeneous respiratory disease that requires a multidimensional scoring system to properly assess severity. Pseudomonas aeruginosa (PA) and exacerbations are important prognostic factors in this population.

Objective:
To compare the severity stratification by 2 validated scores (BSI and FACED) in a NCFBE cohort and to determine their predictive capacity for exacerbations or hospitalizations. Besides, we investigate a modified FACED score.

Methods:
Observational study including NCFBE patients. All patients were stratified according exacerbations (≥2/year). We modified FACED (E-FACED) by adding exacerbations and changing punctuation of PA chronic infection. ROC curves were performed to determine predictive capacity.

Results:
We studied 193 NCFBE patients (40% males; mean age 68.8 years). BSI classified most of our patients as severe (56.5%) or moderate (24.9%), while FACED mainly scored as mild (58.6%) or moderate (34.7%). BSI and FACED showed an area under ROC curve (AUC) for exacerbations (≥2/year) of 0.709 and 0.614; and for hospitalizations (≥1/year) of 0.859 and 0.748 respectively. E-FACED classified patients as mild 36.3%, moderate 30.0% and severe 33.7%, with a high AUC for exacerbations (0.845) and hospitalizations (0.857).

Conclusions:
Despite previous validations of BSI and FACED, they classify our patients very differently likely due to the different weight of exacerbations and PA chronic infection. As expected FACED showed poor prognostic capacity for exacerbations. We support the use of E-FACED that combine easiness of use in clinical practice and its ability to predict exacerbations, hospitalizations and mortality (as widely demonstrated for FACED). BSI is a multifactorial score that could probably better be used for research activity.

P49: TAp73 is a central transcriptional regulator of airway multiciliogenesis and protects bronchial function

Alice Nemajerova [1], *Daniela Kramer* [2], *Saul Siller* [1], *Christian Herr* [3], *Orr Shomroni* [4], *Tonatiuh Pena* [4], *Cristina Gallinas Suazo* [2], *Katharina Glaser* [2], *Merit Wildung* [2], *Henrik Steffen* [2], *Anusha Sriraman* [2], *Fabian Oberle* [2], *Magdalena Wienken* [2], *Magali Hennion* [4], *Ramon Vidal* [4], *Bettina Royen* [5], *Mihai Alevra* [5], *Detlev Schild* [5], *Robert Bals* [3], *Jürgen Dönitz* [5], *Dietmar Riedel* [6], *Stefan Bonn* [4], *Ken-Ichi Takemaru* [1], *Ute Moll* [1], and *Muriel Lizé* [2,*]

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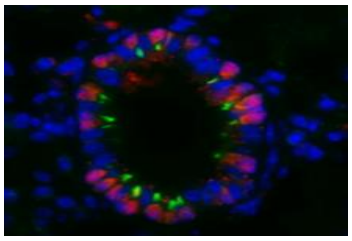
Motile multiciliated cells (MCCs) have critical roles in respiratory health and disease and are essential for cleaning inhaled pollutants and pathogens from airways. Mucociliary clearance defects can lead to chronic lung diseases such as bronchiectasis, Chronic Obstructive Pulmonary Disease (COPD) or Primary Ciliary Dyskinesia (PCD). Despite their significance for human disease, the transcriptional control that governs multiciliogenesis remains poorly understood.

Here we identify p73, a tumor suppressive p53 homolog whose transcriptionally active form is named TAp73, as governing the program for airway multiciliogenesis. Mice with TAp73 deficiency suffer from chronic respiratory tract infections due to profound defects in ciliogenesis and complete loss of mucociliary clearance, ultimately leading to a phenotype of COPD with secondary emphysema due to mucus hypersecretion, macrophage invasion and Mmp12 increase. Organotypic airway cultures pinpoint TAp73 as necessary and sufficient for basal body docking, axonemal extension, and motility during the differentiation of MCC progenitors.

Mechanistically, cross-species genomic analyses and complete ciliary rescue of knockout MCCs identify TAp73 as the conserved central transcriptional integrator of multiciliogenesis. TAp73 directly activates the key regulators FoxJ1, Rfx2, Rfx3, and miR34bc plus nearly 50 structural and functional ciliary genes, some of which are already associated with human ciliopathies.

Our results position TAp73 as a novel central regulator of MCC differentiation and as a guardian of bronchial function.



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