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ABSTRACT BOOK



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A08 [121] Population-based incidence and prevalence (2013-2015) of nontuberculous mycobacterial lung disease in incident cohorts of bronchiectasis and chronic obstructive pulmonary disease

Jennifer Adjemian¹; Quanwu Zhang²; Gina Eagle²; Xin Li³; Engels Chou²; Kenneth Olivier¹

¹National Institutes of Health, Bethesda, USA; ²Insmad Incorporated, Bridgewater, USA; ³KMK Consulting, Inc., Morristown, USA

Background: The incidence of nontuberculous mycobacterial lung disease (NTMLD) is increasing in the United States. Patients with NTMLD often have a history of bronchiectasis (BE) or chronic obstructive pulmonary disease (COPD).

Objective: This study was to estimate incidence and prevalence (2013-15) of NTMLD in incident cohorts of BE and COPD.

Methods: Individuals with ≥ 2 medical claims for BE or COPD between 2012 and 2015 were identified from a large US managed care database (2007-16). Individuals were retained in the incident cohort of BE (n=15,430) or COPD (n= 687,993) if they had 12 months (baseline) of continuous medical insurance with no COPD or NTMLD diagnosis before the first BE claim or no BE or NTMLD diagnosis before the first COPD claim at baseline. Yearly NTMLD incidence and prevalence were estimated by identifying patients with ≥ 2 medical claims ≥ 30 days apart in the BE and COPD cohorts. For incidence, prior 12-month medical insurance coverage was required for each yearly estimation. Overall rate of NTMLD per 1000 person-years was estimated from the BE and COPD cohorts using Poisson regression.

Results: Patients in the BE and COPD cohorts aged 66 and 62 years with 64% and 55% women, respectively. Charlson comorbidity score (standard deviation) was 1.35 (1.94) for BE and 0.97 (1.72) for COPD. The BE cohort vs. COPD appeared to have higher frequencies of asthma (18.9% vs. 10.6%), gastroesophageal reflux disease (21.3% vs. 13.7%), pneumonia (19.3% vs. 6.1%), rheumatoid disease (4.6% vs. 2.3%), immune system disorder (2.8% vs. 0.9%), hyperlipidemia (49.6% vs. 40.4%), and hypertension (51.3% vs. 45.8%). The COPD cohort vs. BE had a higher frequency of claims for current tobacco use (9.5% vs. 2.8%) and obesity (9% vs. 5.5%). NTMLD incidence was 7.1 in 2013 and 2014, and 10 in 2015 per 1000 patients with BE. NTMLD incidence was 0.22 in 2013, 0.18 in 2014, and 0.22 in 2015 per 1000 patients with COPD. NTMLD prevalence was 22.5 in 2013, 23.6 in 2014, and 25.1 in 2015 per 1000 patients with BE. NTMLD prevalence was 0.51 in 2013, 0.43 in 2014, and 0.53 in 2015 in 1000 patients with COPD. Overall rate of NTMLD between 2013 and 2015 was 11.22 per 1000 person-years in BE and 0.31 per 1000 person-years in COPD. For age-gender standardized incidence per 1000 patients in 2015, incidence in BE was 11.84 for women <65 years and 12.41 for women ≥ 65 years. Incidence in COPD was 0.16 for women <65 years and 0.32 for women ≥ 65 years. Standardized incidence rates for men were lower. Standardized prevalence rates were also higher in women than men.

Conclusions: This database study shows that NTMLD incidence and prevalence are substantially higher in the incident BE than COPD cohort, and event rates in BE appear to be increasing. On average, in the US managed care population, over 20 out of 1000 patients are likely to have NTMLD per year after diagnosis of BE. Further efforts on clinical intervention are needed to reduce NTMLD in patients with BE.

B15 [107] The variability of patient demographics and characteristics in international multicentre clinical studies

Timothy Aksamit¹; Tiemo-Joerg Bandel²; Anthony De Soyza³; J Stuart Elborn⁴; Elisabeth Operschall⁵; Eva Polverino⁶; Katrin Roth⁵; Kevin L Winthrop⁷; Robert Wilson⁸

¹Mayo Clinic, Pulmonary Disease and Critical Care Medicine, Rochester, MN, USA; ²Bayer AG, Wuppertal, Germany; ³Newcastle University and Freeman Hospital, Newcastle upon Tyne, United Kingdom; ⁴Royal Brompton Hospital, London, United Kingdom; ⁵Bayer AG, Berlin, Germany; ⁶Hospital Universitari Vall d'Hebron (HUVH), Institut de Recerca Vall d'Hebron (VHIR), Passeig Vall d'Hebron, Barcelona, Spain; ⁷Oregon Health & Science University, Portland, OR, USA; ⁸Host Defence Unit, Royal Brompton Hospital, London, United Kingdom

Background: Two international Phase III studies (RESPIRE 1 and RESPIRE 2) of the same design were conducted to assess the efficacy of Ciprofloxacin DPI in bronchiectasis.

Objective: We investigated the similarities and differences in baseline demographics by geography of RESPIRE 1 and 2.

Methods: Baseline demographics and characteristics of patients enrolled into the RESPIRE programme were descriptively analysed by predefined geographical territories and countries.

Results: RESPIRE 1 randomised 416 patients from 14 countries between May 2013 and February 2015; RESPIRE 2 randomised 521 patients from 24 countries between April 2014 and October 2015.

In RESPIRE 1, the top three recruiting countries were Australia (12.5%), Israel (12.7%) and New Zealand (12.3%), while in RESPIRE 2, these were Russia (11.5%), Bulgaria (10.4%) and Latvia (8.6%). Five countries (Germany, Latvia, US, Argentina, Australia) recruited for both trials. There was variation between RESPIRE 1 and 2 in the European countries recruiting patients (Table 1).

Patient demographics and characteristics differed between territories and between countries. Patients from Japan, which recruited patients only to RESPIRE 1, had the highest mean age (67.2), whereas patients from China, which recruited patients only to RESPIRE 2 had the lowest mean age (52.2).

Primary diagnosis of chronic obstructive pulmonary disease (COPD) was an exclusion criterion; however, a medical history of COPD was reported in 43.6% of patients in the Europe South 2 territory. The lowest rates of COPD were observed in patients from Japan (0%).

For Europe South 1 countries enrolling patients in RESPIRE 1, long-term macrolide use was reported in 11.4% of patients, whereas in Europe South 2 countries enrolling patients in RESPIRE 2, macrolide use was reported in 3.1% of patients overall.

Pseudomonas aeruginosa isolation at baseline ranged between 42.0% in patients from Europe North 2 and 88.0% in patients from Asia (excluding Japan and China). Ciprofloxacin-resistant pathogens at baseline were isolated in 21.7% of patients overall, ranging from 10.9% of patients from Europe North 2 to 36.4% of patients from Japan.

Inclusion criteria required a minimum of two documented exacerbations in the previous 12 months. Overall, 12.5% of patients from US 2 experienced three or more exacerbations in the 12 months prior to the study compared with 67.0% of patients from ROW 1.

Conclusion: Although the RESPIRE studies were of the same design and identical in their inclusion and exclusion criteria, the RESPIRE 1 and 2 patient cohorts differed in their clinical and demographic characteristics. Country composition differed markedly between the studies; this may help to explain some of the differences in clinical characteristics observed between patients in RESPIRE 1 and 2. These findings highlight the need for further investigation into the impact of regional recruitment variations on patient characteristics for international, multicentre clinical studies.

Table 1. Territories recruiting to the RESPIRE 1 and 2 studies

		RESPIRE 1 N=416 (100%)	RESPIRE 2 N=521 (100%)
Europe North 1	United Kingdom	27 (6.5%)	
	Slovakia	2 (0.5%)	
	Denmark	1 (0.2%)	
	Germany*	47 (11.3%)	19 (3.6%)
	Latvia*	16 (3.8%)	45 (8.6%)
Europe North 2	Russian Fed.		60 (11.5%)
	Poland		39 (7.5%)
	Netherlands		19 (3.6%)
	Lithuania		6 (1.2%)
	Czech Republic		4 (0.8%)
	Austria		1 (0.2%)
Europe South 1	Israel	53 (12.7%)	
	Spain	49 (11.8%)	
	Italy	21 (5.0%)	
	France	14 (3.4%)	
Europe South 2	Bulgaria		54 (10.4%)
	Serbia		33 (6.3%)
	Romania		32 (6.1%)
	Turkey		30 (5.8%)
	Portugal		14 (2.7%)
Japan	Japan	33 (7.9%)	
China	China		33 (6.3%)
Asia	South Korea		34 (6.5%)
	Thailand		13 (2.5%)
	Philippines		10 (1.9%)
	Hong Kong		9 (1.7%)
	Taiwan		9 (1.7%)
US 1/US 2	United states	44 (10.6%)	16 (3.1%)
Rest of world (ROW) 1	New Zealand	51 (12.3%)	
ROW 2	Australia [†]	52 (12.5%)	21 (4.0%)
	Argentina [†]	6 (1.4%)	13 (2.5%)
	Brazil		5 (1.0%)
	South Africa		2 (0.4%)

*Countries included in both EUROPE NORTH 1 and EUROPE NORTH 2 territories

[†]Countries included in both ROW 1 and ROW 2 territories

B01 [196] Prevalence and incidence of adult bronchiectasis in an Italian primary care setting

Stefano Aliberti¹; Francesco Lapi²; Giovanni Sotgiu³; Claudio Cricelli⁴; Francesco Blasi¹

¹*Department of Pathophysiology and Transplantation, University of Milan, Internal Medicine Department, Respiratory Unit and Cystic Fibrosis Adult Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy;* ²*Health Search, Italian College of General Practitioners and Primary Care, Florence, Italy;* ³*Clinical Epidemiology and Medical Statistics Unit, Dept of Biomedical Sciences, University of Sassari, Sassari, Italy;* ⁴*Italian College of General Practitioners and Primary Care, Florence, Italy*

Introduction: There are major deficits in our understanding of the epidemiology of bronchiectasis with very few data published worldwide. European prevalence data are mainly from UK, Germany and Spain, while no studies have been published from Italy. Main objectives of this research were to estimate the prevalence of adults with bronchiectasis, and the incidence of adults with bronchiectasis in 2015 on an overall basis and within age- and sex-specific subgroups.

Methods: Data from computer-based records contained in the Health Search IMS Health Longitudinal Patient Database (HSD) were used for this study. The HSD contained clinical records from 1996 to 2015; data are updated by general practitioners (GPs) uniformly distributed throughout the whole Italian territory. GPs voluntarily agreed to collect patients' information and attend training courses for data entry. In this study, data from 800 Italian GPs with the best data for epidemiological study were used. Diseases were classified according to the International ICD-9-CM. The population of HSD is comparable to that surveyed by the Italian National Institute of Statistics in terms of distribution by gender, age, and geographical location. Data concerning all patients with a diagnosis of bronchiectasis, from January, 1, 2002 to December 2015, were identified through the following ICD9CM codes: 494*; 011.5* excluding those diagnoses labelled as "suspected" by GPs.

Results: A total of 1,054,376 subjects were included in the database: 543,974 (52%) were females and 268,693 (25%) were over 65 years of age. A total of 1,775 patients were identified at 31.12.2015 with bronchiectasis (males: 56%; 1,166 (66%) subjects had 65 years of age or more). The overall prevalence of bronchiectasis was 168/100,000 subjects. Prevalence of bronchiectasis according to both age groups and sex is reported in Figure 1a. No gender differences were identified. The prevalence estimates increase with age, particularly among subjects aged 65 years or older. Prevalence of bronchiectasis among subjects with 65 years of age or more was 433/100,000. In 2015, the overall bronchiectasis incidence was 16,6 per 100,000 person-years. Incidence of bronchiectasis according to both age groups and sex is reported in Figure 1b. Incidence rates increased with age, especially in subjects aged 65 years or older (39.5 per 100,000 person-years), and was higher among men than women (19.7 vs. 13.6 per 100,000 person-years).

Conclusions: This study provides the first epidemiological assessment on bronchiectasis in Italy showing that this is not an uncommon disorder. Our data are in line with recent findings highlighting the need to design appropriate measures for the care and management of bronchiectasis also in general practice.

D01 [160] Thrombocytosis predicts mortality in adult bronchiectasis: results from the FRIENDS cohorts

Stefano Aliberti¹; Melissa McDonnell²; Simone Dore³; Eva Polverino⁴; Pieter Goeminne⁵; Katerina Dimakou⁶; Zucchetti Carlo Stefano⁷; Simonetta Edoardo⁷; Conio Valentina⁸; Fardon Thomas⁹; Rutherford Robert²; Torres Antoni¹⁰; Blasi Francesco¹; Sotgiu Giovanni³; Chalmers James⁹

¹*Department of Pathophysiology and Transplantation, University of Milan, Cardio-thoracic unit and Adult Cystic Fibrosis Center, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy;*
²*Department of Respiratory Medicine, Galway University Hospitals, Newcastle Road, Galway, Ireland;*
³*Clinical Epidemiology and Medical Statistics Unit, Department of Biomedical Sciences, University of Sassari - Research, Medical Education and Professional Development Unit, AOU Sassari, Sassari, Italy;*
⁴*Servei de Pneumologia, Hospital Universitari Vall d'Hebron, Institut de Recerca Vall d'Hebron, Barcelona, Spain;*
⁵*University Hospital Gasthuisberg, Respiratory Medicine, Department of Respiratory Medicine, UZ Leuven, Leuven, Belgium;*
⁶*5th Pulmonary Department, "Sotiria" Chest Hospital, Athens, Greece;*
⁷*Health Science Department, University of Milan Bicocca, AO San Gerardo, Milano, Italy;*
⁸*Pneumology Unit, Department of Internal Medicine and Medical Therapy, San Matteo Polyclinic and Institute for Scientific Research, University of Pavia, Pavia, Italy;*
⁹*Tayside Respiratory Research Group, University of Dundee, Dundee, Dundee, United Kingdom;*
¹⁰*Department of Pneumology, Institut Clínic Respiratori, Hospital Clinic of Barcelona, Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), University of Barcelona, Ciber de Enfermedades Respiratorias (CIBERES), Barcelona, Spain*

Platelets have been previously evaluated as key inflammatory mediator in several chronic respiratory diseases, but bronchiectasis. We hypothesised that abnormal platelet counts in stable bronchiectasis may be associated with both disease severity and short and long-term outcomes.

This study is part of the FRIENDS (Facilitating Research Into Existing National DataSet) project: a secondary analysis of seven databases of prospectively enrolled adult outpatients with bronchiectasis referred to bronchiectasis clinics in Monza and Pavia (Italy), Dundee (UK), Leuven (Belgium), Athens (Greece), Galway (Ireland) and Barcelona (Spain) was performed. All patients underwent the same comprehensive diagnostic work-up as recommended by the 2010 British Thoracic Society guidelines. According to their platelet count recorded during stable state, patients were categorised into three groups: normal range ($150\text{--}400\times 10^9/\text{L}$), thrombocytopenia ($<150\times 10^9/\text{L}$), and thrombocytosis ($>400\times 10^9/\text{L}$). The primary outcome was five-year mortality. Secondary outcomes included exacerbations, hospitalizations, and mortality at one-year, as well as mortality at two and three-year of follow-up.

A total of 1,333 patients (median age: 67 years; 39.9% males) were enrolled across the seven centres: 3.4% were thrombocytopenic and 8.0% had thrombocytosis. A significant higher Bronchiectasis Severity Index (BSI) was registered in the thrombocytosis group compared with the normal group. A significantly higher percentage of thrombocytosis was detected in patients with mild vs. moderate vs. severe disease according to the BSI score (20.6% vs. 29.0% vs. 50.5%, respectively, p-value: 0.02). Patients with thrombocytosis experienced significantly worse clinical outcomes at one, three and five-year follow-up in comparison with those with normal platelet count (see Table). After adjustment for centres, comorbidity, disease severity, and long-term macrolide treatment, thrombocytosis was significantly associated with 5-year mortality [OR (95% CI): 2.83 (1.56-5.12); p-value: 0.001].

These results suggest platelets might have an important inflammatory role in bronchiectasis. A deep analysis of the mechanisms behind these findings along with the evaluation of a possible role of

antiplatelet medications in decreasing mortality in bronchiectasis represent important research questions for the next future.

Table. Quality of life and clinical outcomes up to five-year follow-up in the three study groups.

Variables	Thrombocytopenia	Normal platelets	Thrombocytosis	p-value*	p-value#
n.	45	1,181	107		
One-year median (IQR) SGRQ	33.3 (13.8-48.5)	38.5 (25.2-57.5)	50.1 (32.3-71.0)	0.008	0.004
One-year median (IQR) follow-up exacerbations	2 (1-3)	1 (1-2)	2 (1-3)	0.03	0.007
One-year follow-up hospitalization, n (%)	14 (31.8)	231 (20.3)	34 (32.4)	0.004	0.004
One-year mortality, n (%)	5 (11.4)	35 (3.1)	7 (6.6)	0.004	0.05
Two-year mortality, n (%)	6 (13.6)	54 (4.8)	9 (8.5)	0.01	0.10
Three-year mortality, n (%)	7 (16.7)	81 (7.5)	21 (20.4)	<0.0001	<0.0001
Five-year mortality, n (%)	10 (30.3)	114 (15.9)	24 (33.8)	<0.0001	<0.0001

n: number; IQR: interquartile range 25-75; *across three study groups; #between normal platelets vs. thrombocytosis

C19 [137] PREDICTORS OF REQUIRING HOSPITAL ADMISSION IN BRONCHIECTASIS EXACERBATIONS

Isabel Amara¹; Raúl Méndez¹; Beatriz Montull¹; Soledad Reyes¹; Emilio Ansotegui¹; Alexandra Gimeno¹; Edmundo Rosales-Mayor²; Eva Polverino²; Antoni Torres²; Rosario Menéndez¹

¹*Pneumology Department. University and Politechnic Hospital La Fe, Valencia, Spain;* ²*Pneumology Department. Hospital Clínic, IDIBAPS, CIBERES., Barcelona, Spain*

Background: Bronchiectasis (BE) is a chronic structural lung disease with frequent exacerbations, some of which require hospital admission. We aimed to evaluate risk factors associated with hospitalization due to exacerbations during a 1-year follow-up period.

Objectives: We aimed to investigate risk factors associated with hospital admission in bronchiectasis exacerbations in a one-year follow-up period.

Methods: Prospective observational study performed in patients recruited from specialized BE clinics. We considered all exacerbations diagnosed and treated with antibiotics during a follow-up period of one year. The protocol recorded baseline variables, usual treatments, Bronchiectasis Severity Index (BSI) and FACED scores, comorbid conditions and prior hospitalizations.

Results: Two hundred and sixty-five patients were recruited, of whom 162 required hospital admission during the follow-up period. The mean age was 68.4 (65 years in outpatients vs 73 in inpatients), 159 were female and 106 male. Patients were stratified according to the FACED scale: 133 (50.2%) mild, 89 (33.6%) moderate, 43 (16.2%) severe, and to BSI scale 47 (17.71%) mild, 73 (27.5 %) moderate, 145 (54.7%) severe. Demographic data, comorbid condition, usual treatments, prior colonization and prognostic scales are described in table 1. Independent risk factors for hospital admission were hospitalization in the previous year (OR, 2.3), use of proton pump inhibitors (OR, 2.66), age-adjusted Charlson comorbidity index >5 (OR, 2.73), severe FACED (OR, 2.4) and severe BSI (OR: 6.05), whereas pneumococcal vaccination was a protective factor (OR, 0.28). The area under the receiver operator characteristic curve (AUC) was 0.881.

Conclusions: Hospitalization in the previous year, use of proton pump inhibitors, higher age-adjusted Charlson score and severe BE scores are risk factors for developing exacerbations that require hospitalization. Pneumococcal vaccination was protective.

Table 1. Univariate analysis

Patient characteristics	Hospitalization at 1- year		P-value
	NO	YES	
	103 (38,9)	162 (61,1)	
<u>Demographic data:</u>			
Age > 65 years	50 (48,5)	122 (75,3)	0,000
Male	27 (26,2)	79 (48,8)	0,000
Flu vaccine	75 (72,8)	109 (67,3)	0,341
Pneumococcal vaccine	59 (57,3)	64 (39,5)	0,005
<u>Comorbidity:</u>			
Dementia	3 (2,9)	6 (3,7)	0,729
COPD	11(10,7)	54 (33,3)	0,000
Diabetes mellitus	7 (6,8)	34 (21)	0,012
Congestive heart failure	3 (2,9)	31 (19,1)	0,000
Myocardial infarction	2 (1,9)	16 (9,9)	0,012
Age-adjusted Charlson comorbidity index (>5)	12(11,7)	79 (48,8)	0,000
P.aeruginosa colonization	34 (33)	66 (40,7)	0,206
<u>Treatment</u>			
Long-acting anticholinergic	40 (38,8)	100 (61,7)	0,000
Proton pump inhibitor	26(25,2)	100 (61,7)	0,000
Chronic oxygen therapy	4 (3,9)	25 (15,4)	0,013
<u>History of exacerbations:</u>			
Hospitalization last year	23(22,3)	97 (59,9)	0,000

C01 [180] Chronic infection in bronchiectasis patients - Comparative analysis between *Pseudomonas aeruginosa* and other pathogens

David Araujo¹; Leonor Meira¹; Margarida Redondo¹; Daniela Lazzara¹; Manuela Ribeiro¹; Adelina Amorim^{1,2}

¹Centro Hospitalar São João, Porto, Portugal; ²Faculty of Medicine, Universidade do Porto, Porto, Portugal

Background: Chronic infection in bronchiectasis patients is known to be associated with a worse outcome. *Pseudomonas aeruginosa* is the most well-known case, however, there are many pathogens responsible for this, and their role is yet to be clearly accessed.

Objective: To do a comparative analysis between *Pseudomonas aeruginosa* versus other pathogens, among a population of bronchiectasis patients with chronic infection.

Methods: A prospective analysis of a group of patients followed in a specialized bronchiectasis outpatient clinic was made. Inclusion criteria: >18 years old, HRCT scan documented bronchiectasis, minimum of 1 year follow-up. Patients with diagnosed cystic fibrosis or interstitial lung disease were excluded. The patients with criteria for chronic infection (isolation of potentially pathogenic bacteria in sputum culture on two or more occasions, at least 3 months apart over a 1-year period) were selected. Clinical and functional parameters were compared.

Results: A total of 101 patients met the criteria for chronic infection (41 patients with *P. aeruginosa* and 60 patients with other pathogens (some of them with more than one)). The most common pathogen identified on the latter group was *Haemophilus influenza* (n=44, 45.8%) followed by *Stenotrophomonas maltophilia* (n=8, 8.3%), *Staphylococcus aureus* (n=6, 6.3%), *Serratia marcescens* (n=5, 5.2%), *Streptococcus pneumoniae* (n=5, 5.2%), and *Achromobacter spp.* (n=4, 4.2%). The mean follow-up was 4.1 years (no significant differences were seen between the groups).

The *P. aeruginosa* group was older (mean age of 60,9 years vs 53,2y; p=0.025), had a higher level of dyspnea on the mMRC scale (p=0,025), more hemoptysis (61% vs 30%; p=0,002) and more patients with a daily sputum production (90,2% vs 68,3%; p=0,03). Also, the *P. aeruginosa* group had a significantly higher mean bronchiectasis severity index (10 vs 5; p<0,000) and worse pulmonary function tests (lower FVC% (79.7% vs 92.3%; p=0,03) and lower FEV1 (1,45L vs 1.95L; p=0,003)).

There were no significant differences in terms of smoking history, body mass index and Murray's sputum color chart.

In terms of aetiology, no significant differences were seen. In both groups, the most common were the idiopathic (41,5% in *P. aeruginosa* and 38,3% in other pathogen group) and post-infectious (34,1% and 25%). However, regarding the third most common cause a difference was seen - connective tissue disease in the *P. aeruginosa* group (4.9%) and immunodeficiency in the other (13,9%).

Although with a tendency to a higher number of exacerbations in the *P. aeruginosa* group no statistically significant differences were seen between the groups.

Conclusions: Chronic infection plays a key role in bronchiectasis patients, but not all pathogens have the same clinical consequences. *P. aeruginosa* chronic infection seems to be associated with a more severe disease even when only compared to chronic infection by other pathogens. The differences stated here between this two groups can help to understand more clearly how we can phenotype and treat better bronchiectasis patients. A future analysis of the clinical role of each chronic infection pathogen is the next step.

B03 [95] Epidemiological data of hospitalized patients with non-cystic fibrosis bronchiectasis (NCFB)

Zoran Arsovski¹; Biserka Jovkovska Kjaeva¹; Dejan Dokic¹; Gorica Breshkovska¹; Kiril Naumoski²

¹Clinic of Pulmonology and Allergy, Skopje, Macedonia; ²None, Skopje, Macedonia

Introduction: NCFB in recent years have been a field of interest.

Materials and methods: A retrospective study in patients with non-cystic fibrosis bronchiectasis (NCFB) that were hospitalized at the Clinic of Pulmonology and Allergy – Skopje was performed from July 2010, until December 2016. A total of 366 patients were analyzed.

Results: Of all patients, 53.6% were male, 46.4% were female. The patients in the study were between the ages of 16 and 89. Statistically significant and predominant age group were the patients above 60 years of age ($p=0.05$). Billateral bronchiectasis were present in 74.9% of the patients, but only 4.6% were bleeding. There was no statistically significant correlation between smoking and bleeding NCFB. Only one co-morbidity was registered in 202 (32.9%) of the patients, 144 had two. Six or more co-morbidities were found only in two patients. The majority of the patients were non-smokers (48.5%). Of the rest, 25.9% quit smoking, 25.6% were active smokers. Microbiological examination of sputum was conducted, *Candida albicans* was found in 62 cases, while *Pseudomonas aeruginosa* was found in 43. On average, the patients with NCFB were hospitalized 10.1 days, the minimum length of stay being 1, and the maximum 29 days. From all the patients, 265 or 72.5%, were hospitalized only once. Of the rest, 56 or 15.3% were re-hospitalized once, but only 3% had 5 or more hospitalizations.

Conclusion: The data which were analyzed at our Clinic of Pulmonology and Allergy – Skopje could contribute to a new insight of epidemiology and better understanding of NCFB.

D03 [130] Prognostic value of FACED and E-FACED scores for 5-year all-cause mortality according to underlying etiology of bronchiectasis

Rodrigo Athanazio¹; Monica Corso Pereira²; Georgina Gramblicka³; Fernando Cavalcanti-Lundgren⁴; Mara Fernandes de Figueiredo⁵; Francisco Arancibia⁶; Samia Rached¹; David de la Rosa⁷; Luis Máiz-Carro⁸; Rosa Girón⁹; Casilda Oliveira¹⁰; Concepción Prados¹¹; Javier de Gracia¹²; Montserrat Vendrell¹³; Miguel Angel Martinez-Garcia¹⁴

¹Pulmonary Division, Heart Institute (Incor), Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; ²Pneumology Service. State University of Campinas (Unicamp), Campinas, Brazil; ³Pneumology Service. Hospital del Tórax, Buenos Aires, Argentina; ⁴Pneumology Service. Hospital Octávio de Freitas, Recife, Brazil; ⁵Pneumology Service. Hospital de Messejana, Fortaleza, Brazil; ⁶Pneumology Service. Instituto Nacional del Tórax, Santiago, Chile; ⁷Pneumology Unit. Hospital Platón, Barcelona, Spain; ⁸Pneumology Service. Hospital Universitario Ramón y Cajal, Madrid, Spain; ⁹Pneumology Service. Hospital Universtario La Princesa, Madrid, Spain; ¹⁰Pneumology Service. Hospital General de Málaga, Malaga, Spain; ¹¹Pneumology Service. Hopital Universitario La Paz-Carlos III, Madrid, Spain; ¹²CIBER de Enfermedades Respiratorias, Madrid, Spain; ¹³Dr. Trueta University Hospital, Girona, Spain; ¹⁴Pneumology Service. Polytechnic and University La Fe Hospital, Valencia, Spain

Background: FACED and E-FACED scores are multidimensional tools to assess prognosis in bronchiectasis. Previous studies have already proven their ability to predict both mortality and future risk of exacerbations. Since bronchiectasis is a heterogeneous disease, it is crucial to understand whether these tools maintain their reliability in specific subgroups.

Objective: To investigate the ability of FACED and E-FACED scores to predict mortality in patients with bronchiectasis according to their underlying etiology.

Methods: Multicentric study of historical cohorts in 1451 consecutive patients (800 from Spain and 651 from six cohorts of three different countries in Latin America - Argentina, Brazil and Chile). The diagnosis of bronchiectasis was made by HRCT scan. Data were collected using the same standardized protocol in all centers (clinical, microbiological, functional and radiological variables). The vital status of all patients was determined at 5 years of follow-up, calculated from the date of radiological diagnosis of bronchiectasis. The area under ROC curve (AUC-ROC) was used to calculate the predictive power of FACED and E-FACED scores for all-cause mortality according to bronchiectasis underlying etiology.

Results: Patients were divided as follow: idiopathic (514 patients with 83 deaths), post-infectious (511 patients with 95 deaths), immunodeficiencies (115 patients with 15 deaths), COPD (52 patients with 10 deaths), primary ciliary dyskinesia (79 patients with 11 deaths), aspiraton (38 patients with 3 deaths), systemic inflammatory diseases (47 patients with 14 deaths), asthma-ABPA (24 patients with 1 death) and others (71 patients with 16 deaths). Since the number of deaths in patients with aspiration and asthma-ABPA was very low, it was not possible to evaluate these subgroups. The predictive capacity for all-cause mortality measured by the AUC-ROC was superior to 0.80 for both FACED and E-FACED scores despite underlying etiology. The best performance was observed in the subgroup of patients with primary ciliary diskinesia with an AUC-ROC for FACED score of 0.83 (0.68 – 0.99) and for E-FACED score of 0.88 (0.76 – 0.99).

Conclusions: FACED and E-FACED scores maintained an excellent predictive power for all-cause mortality independently of the underlying etiology of bronchiectasis.

Table: Prognostic value of FACED and E-FACED scores for 5-year all cause mortality related to different etiologies

Etiology	N	Deaths	Mean age (yrs)	AUC ROC FACED	AUC ROC EFACED
Idiopathic	514	83	53.9 (17.6)	0.83 (0.79-0.88)	0.83 (0.78-0.88)
Post-infectious	511	95	56.6 (16.9)	0.83 (0.79-0.87)	0.85 (0.81-0.88)
Immunodeficiencies	115	15	46.9 (17.9)	0.83 (0.72-0.94)	0.81 (0.65-0.92)
COPD	52	10	64.8 (12.8)	0.81 (0.65-0.96)	0.86 (0.73-0.98)
Primary ciliary dyskinesia	79	11	36.2 (14.1)	0.83 (0.68-0.99)	0.88 (0.76-0.99)
Aspiration	38	3	54.9 (14.3)	--	--
Systemic inflammatory diseases	47	14	58.9 (15.2)	0.80 (0.68-0.93)	0.84 (0.72-0.95)
ABPA-asthma	24	1	50.8 (16.1)	--	--
Others	71	16	57.7 (18.7)	0.83 (0.73-0.94)	0.82 (0.71-0.93)

C26 [135] FACED and E-FACED scores annual prognostic ability to predict mortality in patients with bronchiectasis



Rodrigo Athanazio¹; Monica Corso Pereira²; Georgina Grambicka³; Fernando Cavalcanti-Lundgren⁴; Mara Fernandes de Figueiredo⁵; Francisco Arancibia⁶; Samia Rached¹; David de la Rosa⁷; Luis Máiz-Carro⁸; Rosa Girón⁹; Casilda Oliveira¹⁰; Concepción Prados¹¹; Javier de Gracia¹²; Montserrat Vendrell¹³; Miguel Angel Martinez-Garcia¹⁴

¹Pulmonary Division, Heart Institute (Incor), Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; ²Pneumology Service. State University of Campinas (Unicamp), Campinas, Brazil; ³Pneumology Service. Hospital del Tórax, Buenos Aires, Argentina; ⁴Pneumology Service. Hospital Octávio de Freitas, Recife, Brazil; ⁵Pneumology Service. Hospital de Messejana, Fortaleza, Brazil; ⁶Pneumology Service. Instituto Nacional del Tórax, Santiago, Chile; ⁷Pneumology Unit. Hospital Platón, Barcelona, Spain; ⁸Pneumology Service. Hospital Universitario Ramón y Cajal, Madrid, Spain; ⁹Pneumology Service. Hospital Universitario La Princesa, Madrid, Spain; ¹⁰Pneumology Service. Hospital General de Málaga, MalHospital General de Málagaaga, Spain; ¹¹Pneumology Service. Hospital Universitario La Paz-Carlos III, Madrid, Spain; ¹²CIBER de Enfermedades Respiratorias, Madrid, Spain; ¹³Dr. Trueta University Hospital, Girona, Spain; ¹⁴Pneumology Service. Polytechnic and University La Fe Hospital, Valencia, Spain

Background: Both FACED and E-FACED are multidimensional scores that had already been proven to predict all-cause and respiratory mortality in five years of follow-up. Since new therapies are emerging to treat this disease, it is important to try to predict relevant clinical outcomes in a shorter period of time.

Objective: To investigate the ability of FACED and E-FACED scores to predict annual mortality in patients with bronchiectasis during a 5-years follow-up .

Methods: Multicentric study of historical cohorts in 1470 consecutive patients (819 from Spain and 651 from six cohorts of three different countries in Latin America - Argentina, Brazil and Chile). The diagnosis of bronchiectasis was made by HRCT scan. Data were collected using the same standardized protocol in all centers (clinical, microbiological, functional and radiological variables). The vital status of all patients was determined at 5 years of follow-up, calculated from the date of radiological diagnosis of bronchiectasis. The area under ROC curve (AUC-ROC) was used to calculate the predictive power of FACED and E-FACED scores for all-cause mortality each year of the follow-up.

Results: The mean (SD) age was 54.1 (17.7) with 39% of males. The mean FACED score was 2.35 (2.8) and E-FACED score was 3.02 (2.23). The prevalence of Pseudomonas aeruginosa colonization was 27.5%. During the 5-year follow up, 249 patients (16.9%) died, starting from 37 deaths (2.5%) in the first year, followed by 72 deaths (4.9%) in the second year, 128 deaths (8.8%) in the third year and 184 deaths (12.4%) in the fourth year. The AUC-ROC for all-cause mortality in the first year was 0.79 (0.71 – 0.86) for FACED and 0.81 (0.74 – 0.87) for E-FACED scores, maintaining similar values each year.

Conclusions: FACED and E-FACED scores maintained an excellent predictive power for all-cause mortality even in shorter periods of follow-up assessment.

Table: Annual AUC ROC for FACED and E-FACED scores during 5-year follow-up period.

	FACED	E-FACED
	AUC ROC	AUC ROC
First year	0.79 (0.71 - 0.86)	0.81 (0.74 - 0.87)
Second year	0.77 (0.72 - 0.82)	0.79 (0.71 - 0.84)
Third year	0.81 (0.77 - 0.85)	0.82 (0.79 - 0.85)
Fourth year	0.81 (0.78 - 0.84)	0.82 (0.79 - 0.85)
Fifth year	0.83 (0.80 - 0.86)	0.84 (0.82 - 0.87)

C21 [136] Exacerbator phenotype is associated with all-cause mortality independently of initial severity in bronchiectasis

Rodrigo Athanazio¹; Monica Corso Pereira²; Georgina Grambicka³; Fernando Cavalcanti-Lundgren⁴; Mara Fernandes de Figueiredo⁵; Francisco Arancibia⁶; Samia Rached¹; Miguel Angel Martinez-Garcia⁷

¹Pulmonary Division, Heart Institute (Incor), Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil; ²Pneumology Service. State University of Campinas (Unicamp), Campinas, Brazil; ³Pneumology Service. Hospital del Tórax, Buenos Aires, Argentina; ⁴Pneumology Service. Hospital Octávio de Freitas, Recife, Brazil; ⁵Pneumology Service. Hospital de Messejana, Fortaleza, Brazil; ⁶Pneumology Service. Instituto Nacional del Tórax, Santiago, Chile; ⁷Pneumology Service. Polytechnic and University La Fe Hospital, Valencia, Spain

Background: Exacerbation is a common and deleterious event in patients with bronchiectasis. Both E-FACED and BSI multidimensional scores had already proven that exacerbation in the previous year of diagnosis is an independent risk factor associated with mortality. Nevertheless, the impact of these events during follow-up remains unclear. Since the number of exacerbations may be a changeable risk factor and prevention of these events is a main goal in bronchiectasis management, it is important to investigate the behavior of patients with high rates of exacerbations.

Objective: To evaluate if an exacerbator phenotype is related to an increase in mortality in patients with bronchiectasis.

Methods: Retrospective and multicenter study conducted in six historical cohorts of patients from Latin America (Argentina, Brazil and Chile) including 651 patients with bronchiectasis with the diagnosis made by HRCT scan. Clinical, microbiological, functional, and radiological variables were collected following the same protocol. The vital status of all patients was determined in the fifth year of follow-up. Exacerbator phenotype was defined as a patient with at least 2 exacerbations/year or at least 1 hospitalization/year during the 5-year follow-up.

Results: The mean (SD) age was 48.2 (16) with 32.9% of males. The mean E-FACED score was 2.89 (2.09). During the follow up, 95 patients (14.6%) died (66% from respiratory causes). The prevalence of exacerbator phenotype was 23.3%. By Cox multivariate regression, exacerbator phenotype appeared as an independent and significant variable associated with all-cause mortality adjusted by baseline E-FACED (OR = 1.78 [1.06 – 2.98] – p = 0.027).

Conclusions: E-FACED had already been proven as an excellent initial severity score with good prognosis of all-cause mortality at 5 years, but the presence of an exacerbator phenotype adds new prognostic value as a longitudinal assessment in patients with bronchiectasis.

TABLE: Cox's survival analysis

	B	ET	Wald	df	Sig	OR	95% IC for OR	
							Lower	Upper
							E-FACED score (at diagnosis)	0.485
Exacerbator phenotype (follow-up)	0.581	0.262	4.911	1	0.027	1.788	1.069	2.988

D04 [96] Non invasive respiratory mechanics evaluation in adult patients affected by cystic fibrosis experiencing respiratory exacerbation.

Gian Piero Bandelli¹; Cristina Bena¹; Irene Bianchi¹; Barbara Messori¹; Giacomo Bonizzoni¹; Sara Demichelis²; Laura Maugeri²; Emiliano Gatti²; Carlo Gulotta²; Carlo Albera¹

¹University of Turin, Department of Clinical and Biological Sciences, Interstitial and Rare Lung Disease Unit, Adult Cystic Fibrosis Referral Centre, Turin, Italy; ²Respiratory Medicine Unit, AOU San Luigi Gonzaga, Orbassano, Italy

Background: Cystic fibrosis (CF) is a multisystem disorder with significantly shortened life expectancy. The major cause of mortality and morbidity is lung involvement. The most important pathological changes are bronchiectasis and bronchiolitis obliterans-like changes of the small airways. The primary aim of CF therapy is to prevent any structural damage and to conserve lung function. Adequate monitoring of CF lung disease is paramount to tailoring treatment to a patient's need. Therapeutic interventions for CF have improved significantly in the last two decades and now there are targeted therapies which may impact exacerbation frequency, symptoms and mortality due to lung disease. CF therapies can be resumed in the following list of interventions: potentiating and correcting mutant CFTR, gene and cell therapy, improving airway clearance, antibiotic treatment, exercise, lung transplantation. In addition it is important to manage all extrapulmonary manifestations. In CF the mucociliary clearance is impaired and techniques of airway clearance have the aim to compensate for this by promoting secretion clearance. Recent trials have identified the challenges related to using forced expiratory volume in 1 second (FEV1) as a primary outcome measure for airway clearance trials.

Objective: A pilot prospective study has been conducted in our centre with the aim to evaluate the possible use of forced oscillation technique (FOT) and diaphragm ultrasound in association with FEV1 serial measures to monitor the level of bronchial obstruction and respiratory mechanics in patients affected by CF hospitalized for respiratory exacerbation.

Methods: Eight patients, half males, mean age 31.25 years (27-44), mean FEV1 1276 cc (950-2120) have been enrolled in this study during a period of three months (February-April 2017). They all have been treated with airway clearance techniques, systemic antibiotics and inhaled drugs such as bronchodilators, DNase (pulmozyme) and 7% hypertonic saline. Each patient underwent spirometry (COSMED), FOT (Resmon Pro – Restech, Milano, Italy) and diaphragm ultrasound (Esaote) both at the beginning and at the end of the hospitalization period. The aim of right emi-diaphragm ultrasound was to calculate diaphragm thickening fraction (DTF, calculated as percentage from the following formula: thickness at end inspiration - thickness at end expiration / thickness at end expiration) in the apposition zone and M-MODE maximum excursion (ME), M-MODE index of obstruction (MIO) and M-MODE 1st second/maximum excursion ratio (ME ratio) in the subcostal projection.

Results: Preliminary results show a direct correlation between FEV1 and DTF. ME appears to be the same or better for all patients at the end of the study demonstrating an improvement in respiratory mechanics at the end of treatment in particular in all patients in which there is a progressive reduction of residual volume. There were no correlations between FEV1 and both MIO and ME ratio. FOT results are unclear and require further analysis.

Conclusions: DTF and ME could be a new non invasive, rapid and easy to obtain outcome measure to evaluate the efficacy of airway clearance in patients affected by CF. Further studies are needed to validate these findings.

D22 [113] Reduced quality of life in physically inactive bronchiectasis patients

Aslihan Cakmak¹; Deniz Inal-Ince¹; Hazal Sonbahar-Ulu¹; Cemile Bozdemir-Ozel¹; Ebru Calik-Kutukcu¹; Melda Saglam¹; Naciye Vardar-Yagli¹; Hulya Arikan¹; Lutfi Coplu²

¹Hacettepe University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Ankara, Turkey; ²Hacettepe University, Faculty of Medicine, Department of Chest Diseases, Ankara, Turkey

Purpose: Bronchiectasis is a chronic lung disease, causing reduced exercise tolerance, physical activity, and worsening of quality of life. In our study, we aimed to compare quality of life according to physical activity level in patients with bronchiectasis.

Methods: Thirty-four bronchiectasis patients (22F, 12M, mean age=37.97±17.58 years) were included in this study. Pulmonary function test was performed. Physical activity level was measured for seven consecutive days using SenseWear Armband. Patients were classified according to their daily step counts (<5000 steps/day as sedentary, 5000-7499 steps/day as low active, >7500 steps/day as active). Patients completed the Short Form SF-36v2 Health Survey to assess quality of life. Incremental shuttle walk test (ISWT) was performed to measure exercise tolerance.

Results: Physically inactive bronchiectasis patients (n=10) had significantly lower scores in role limitations due to physical health and emotional problems when compared with low active (n=13) and active patients (n=11) (p<0.05). There was no significant difference in pulmonary function, exercise tolerance and in other parameters of SF-36v2 Health Survey among the groups (p>0.05).

Conclusion: Bronchiectasis patients who are physically inactive reported that they have more role limitations due to physical health and emotional problems than physically active ones. These findings reinforce the recommendation of physical activity in treatment of bronchiectasis. Further studies with larger number of participants may reflect the effects of physical activity level on quality of life in patients with bronchiectasis in a wider perspective.

Keywords: Bronchiectasis, quality of life, physical activity

D02 [129] Association of systemic inflammation and oxidative stress with clinical and activity features in patients with bronchiectasis



Anderson Alves Camargo¹; Rejane Agnelo Castro¹; Cristiane Santos Oliveira¹; Rodolfo de Paula Vieira^{1,2}; Katia Angelis^{1,2}; Rodrigo Athanazio³; Samia Rached³; Alberto Cukier³; Rafael Stelmach³; Simone dal Corso¹

¹Post-graduate Program in Rehabilitation Sciences, Universidade Nove de Julho – UNINOVE, São Paulo, Brazil; ²Postgraduate Program in Medicine, Universidade Nove de Julho – UNINOVE, São Paulo, Brazil; ³Pulmonary Division, Heart Institute (Incor), Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

Background: Biomarkers of systemic inflammation and oxidative stress (OS) are raised in patients with bronchiectasis (BCT), but their association with exercise capacity and physical activity in daily life (PADL) has not been solidly investigated.

Objective: This study aimed to compare the inflammatory and OS state in patients with BCT and healthy controls. Inflammatory and OS levels were also correlated with exercise capacity and PADL.

Methods: Seventy-four patients (49 ± 15 years, FEV₁: 52.5 ± 25.6% of predicted) and 42 healthy (44 ± 17 years, FEV₁: 95.9 ± 14.0% of predicted) performed a cardiopulmonary exercise test, an incremental shuttle walking test (ISWT) and had the PADL measured. Inflammatory cytokines and OS were measured in the plasma.

Results: Compared to controls, IL-6 (p<0.001), IL-10 (p<0.001), carbonylated proteins (p=0.001), and superoxide anions (p=0.046) were significantly increased in BCT. Catalase activity (CA) was reduced in patients with BCT (p<0.001), and presented a weak correlation with PADL (r= 0.295, p= 0.011). VO₂ correlated with inflammatory markers (IL-1β: r= -0.408, IL-6: r= -0.308 and TNF-α: r= -0.207, respectively) and with oxidative stress (T-bars: r=-0.290 and carbonyls r= 0.379, respectively).

Conclusions: Patients with BCT presented with higher levels inflammation and OS which are related to worse aerobic capacity, functional capacity, and lower PADL

B04 [189] The independent contribution of *Pseudomonas aeruginosa* infection to clinical outcomes in bronchiectasis patients - data from the FRIENDS cohort

James Chalmers¹; Anthony De Soyza²; Michal Shteinberg³; Simon Finch¹; Adam Hill⁵; Thomas Fardon¹; Katerina Dimakou⁷; Eva Polverino⁸; Dusanka Obradovic⁹; Melissa McDonnell¹⁰; Stefano Aliberti¹¹; Pieter Goeminne¹²; Glenda Stone¹³; Angela Davis¹³; Marion Trautmann¹³

¹Scottish Centre for Respiratory Research, University of Dundee, Dundee, United Kingdom; ²Newcastle University, Newcastle upon Tyne, United Kingdom; ³Pulmonary Institute, Carmel Medical Center, Haifa, Israel; ⁵University of Edinburgh, Edinburgh, United Kingdom; ⁷"Sotiria" Chest Hospital, Athens, Greece; ⁸Hospital Clinic de Barcelona, Barcelona, Spain; ⁹Institute for Pulmonary Diseases of Vojvodina Sremska Kamenica, Sremska Kamenica, Serbia; ¹⁰Department of Respiratory Medicine, Galway University Hospitals, Galway, Ireland; ¹¹University of Milan Bicocca, Clinica Pneumologica, Monza, Italy; ¹²Dept of Respiratory Medicine, AZ Nikolaas, Sint-Niklaas, Belgium; ¹³Grifols, Research Triangle Park, USA

Introduction: Although *P. aeruginosa* has been associated with poor outcomes in bronchiectasis across a number of studies, patients with *P. aeruginosa* also tend to have more severe baseline disease. No studies have had long enough follow-up to examine the independent contribution of *P. aeruginosa* to outcomes.

Methods: Patients with HRCT confirmed bronchiectasis (BE) aged >18 years from 8 EU and EU affiliated countries were enrolled. Patients with cystic fibrosis were excluded. Patients were followed up for up to 5 years. Severe exacerbations were defined as those requiring hospital admissions. Quality of life (QoL) was measured using the St Georges Respiratory Questionnaire (SGRQ). *P. aeruginosa* chronic infection was defined as two isolates ≥ 3 months apart in 1 year prior to the study. Survival and future exacerbation frequency were analysed using Cox proportional hazards and zero inflated Poisson regression models, respectively.

Results: 2596 patients were included. Median age was 67 years (IQR 57-74). 61.1% were female. *P. aeruginosa* chronic infection was present in 389 patients (15%). Unadjusted mortality while higher in patients with *P. aeruginosa*, was not evident after adjusting for confounders (HR 0.88 95% CI 0.64-1.22). Subsequent analysis identified that patients with *P. aeruginosa* having ≥ 2 exacerbations per year had increased mortality (HR 2.03 95% CI 1.34-3.08) while patients with *P. aeruginosa* with < 2 exacerbations did not (HR 0.86 95% CI 0.37-2.00).

Independent associations between *P. aeruginosa* infection and severe exacerbations (OR 2.28 95% CI 1.69-3.08), exacerbation frequency (incidence rate ratio 1.14 95% CI 1.04-1.27) and QoL were demonstrated ($p=0.0001$ for correlation of *P. aeruginosa* and SGRQ total score).

Conclusions: *P. aeruginosa* is associated with an increase in adverse clinical outcomes. The relationship with mortality and other clinical outcomes was modified by exacerbation frequency. The hypothesis that exacerbation prevention may improve long term clinical outcomes and QoL should be tested in registries and long term clinical trials.

C03 [70] The impact of long-term erythromycin therapy on the oropharyngeal microbiota and associated resistome



Jocelyn Choo^{1,2}; Guy Abell²; Lucy Burr^{3,4}; Rachel Thompson⁵; Lucy Morgan⁶; Waterer Grant⁷; David Gordon^{8,9}; Steven Taylor²; Lex Leong^{1,2}; Geraint Rogers^{1,2}

¹Infection and Immunity Theme, South Australia Health and Medical Research Institute, Adelaide, Australia; ²SAHMRI Microbiome Research Laboratory, Flinders University School of Medicine, Adelaide, Australia; ³Immunity, Infection and Inflammation Program, Mater Research Institute - University of Queensland, Translational Research Institute, Queensland, Australia; ⁴Department of Respiratory Medicine, Mater Health Services, Queensland, Australia; ⁵Gallipoli Medical Research Centre, Greenslopes Private Hospital and University of Queensland, Queensland, Australia; ⁶Department of Respiratory Medicine, Concord Hospital Clinical School, University of Sydney, New South Wales, Australia; ⁷School of Medicine and Pharmacology Royal Perth Hospital Unit, The University of Western Australia, Perth, Australia; ⁸Department of Microbiology and Infectious Diseases, Flinders University, Adelaide, Australia; ⁹SA Pathology, Flinders Medical Centre, Adelaide, Australia

Background. Long-term macrolide therapy is effective in reducing pulmonary exacerbations in adults and children with bronchiectasis. However, concerns exist over the potential for macrolide therapy to substantially alter the composition of the oropharyngeal commensal microbiota, and to increase the carriage of transmissible antimicrobial resistance genes.

Objectives. Our aim was to determine the impact of long-term erythromycin therapy on the composition and resistance profile of the oropharyngeal microbiota.

Methods. Analysis was based on oropharyngeal swabs collected as part of the BLESS randomised controlled trial of twice-daily erythromycin ethylsuccinate (400 mg) in adults with non-cystic fibrosis bronchiectasis. Swabs collected at baseline and following 48 weeks of erythromycin (n=43) or placebo (n=41) were assessed directly by a combination of 16S rRNA gene amplicon sequencing and quantitative PCR assays for specific bacterial taxa and antibiotic resistance genes.

Results. Erythromycin treatment resulted in a significant change in oropharyngeal microbiome composition, compared with placebo (ANOSIM R=0.054, P=0.0003). The relative abundance of an operational taxonomic unit (OTU) assigned to *Streptococcus pseudopneumoniae* (a viridans streptococcus which commonly exhibits acquired resistance to macrolide antibiotics, and which has been associated with chronic lower airways infection) decreased significantly with treatment (log₂ fold change: -1.57 ± 0.41, FDR P=0.024). Significant decreases were also observed in the relative abundance of three *Actinomyces odontolyticus* OTUs (an opportunistic pathogen commonly isolated from the oral cavity) (-2.69 ± 0.75, -1.86 ± 0.55, -2.51 ± 0.69; FDR P<0.05) and a novel *Actinomyces* genus OTU (-2.06 ± 0.53, FDR P=0.024). Absolute levels of *Actinomyces* within the oropharynx also decreased significantly (P=0.046). In contrast, the relative abundance of two *Haemophilus parainfluenzae* related taxa increased significantly following erythromycin treatment (2.16 ± 0.61 and 1.65 ± 0.49, FDR P=0.027 and 0.04 respectively). Erythromycin treatment was not associated with a significant change in the proportion of individuals carrying specific macrolide resistance genes (*erm*(A), *erm*(B), *erm*(C), *msrA* and *mefA/E*). However, the number of *erm*(B) and *mefA/E* gene copies, normalised to bacterial load, increased in treated subjects: *erm*(B); (T1: median log₂ *erm*(B)/16S ratio: -4.03, IQR= -7.24 to -1.92; T8: median log₂ *erm*(B)/16S ratio= -2.93, IQR= -5.65 to -1.73; P=0.012); *mefA/E* (T1: median log₂ *mef*/16S ratio=-12.07, IQR= -13.15 to -11.65; T8: median log₂ *mef*/16S ratio=-11.67, IQR= -12.64 to -11.27; P=0.029). Notably, macrolide resistance genes were detected in subjects where no macrolide-resistant streptococci had been cultured, indicating the dispersal of resistance determinants beyond commonly

assessed populations. Assessment of resistance gene carriage in matched induced sputum samples indicated that oropharyngeal changes occurred independently of those in the lower airways.

Conclusions. Erythromycin treatment substantially altered the composition of the oropharyngeal microbiota, a commensal system that is known to influence susceptibility to a range of bacterial and viral infections. Significant changes were observed in the relative abundance of species capable of contributing directly to airways disease. The observed increase in oropharyngeal resistance gene carriage is unlikely to result in a reduction in treatment efficacy. However, it supports concerns about potential for onward transmission of resistant bacteria to vulnerable individuals, and highlights the capacity of the oropharyngeal microbiota to act as a reservoir for resistance carriage.

D05 [94] Telomere length in blood leukocytes of patients with bronchiectasis

Maria Cristina Colanardi¹; Grazia Pia Palladino¹; Giovanna Elisiana Carpagnano¹; Maria Pia Foschino Barbaro¹; Donato Lacedonia¹

¹Department of Surgical and Clinical Sciences – University of Foggia, Foggia, Italy

Background: Telomeres are considered a marker of biological age. Up to now a number of studies investigated their role in COPD where the accelerating ageing resulting in premature cell senescence contribute to the pathobiology. COPD patients have shorter leucocytes telomeres and, also, dysfunctional ones.

Objective: The aim of study is to investigate whether in patients with bronchiectasis is associated telomere shortening in blood leucocytes, as known in COPD.

Methods: Our study was performed on 53 patients, enrolled in our Centre: 34 had non CF bronchiectasis as demonstrated by HRCT (of whom 14 associated with COPD), 19 had COPD without bronchiectasis, matched for age and FEV₁; 23 healthy controls, without bronchiectasis and with normal lung function were also selected.

Results: Telomere length (T/S) was significantly lower in COPD than in patients with bronchiectasis, associated or not to COPD, and in control subjects (0.041 ± 0.026 vs 0.066 ± 0.04 vs 0.082 ± 0.04 and 0.098 ± 0.046 ; $p < 0.001$) (Fig. 1). We also investigated level of Mitochondrial DNA (mtDNA), as marker of oxidative stress. This was lower in patients with COPD (1.61 ± 0.37) and bronchiectasis COPD associated or not (1.58 ± 0.34 and 1.67 ± 0.32) respect to the controls (2.67 ± 0.47 ; $p < 0.001$) (Fig. 2). Analysis showed that telomere length directly correlates with FEV₁% and mtDNA ($p < 0.05$).

Conclusions: This study confirm that the telomere length, is markedly decreased in patient with COPD compared to the controls, while patients with bronchiectasis doesn't shows any difference in terms of telomere length. Moreover other interesting finding is that in both diseases, there is an alteration of Mitochondrial DNA which is correlate with telomere length. COPD and bronchiectasis are two distinct diseases that even if sometimes coexist, presents different biological mechanism.

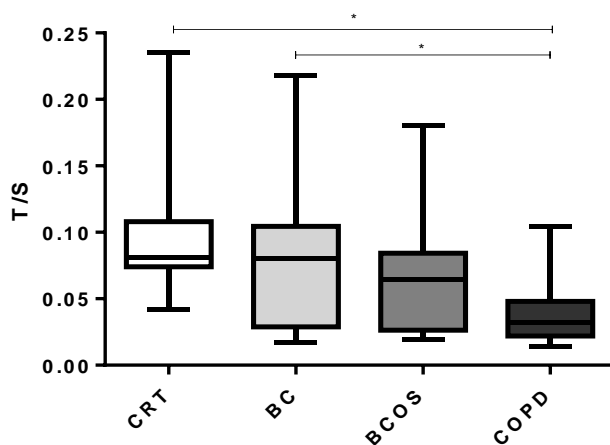


Figure 1 Difference between telomere length in different study groups.

CTR: controls; BC: non CF bronchiectasis; BCOS: bronchiectasis-COPD overlap syndrome

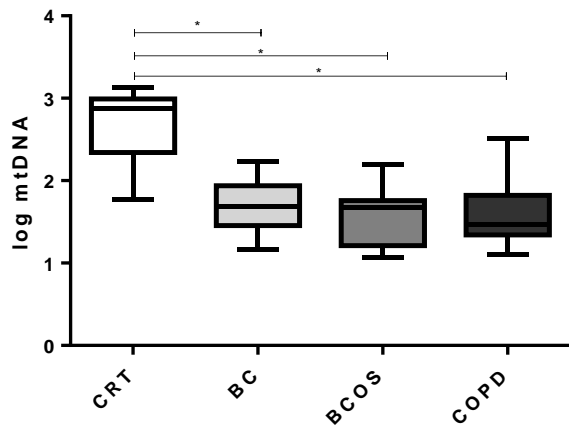


Figure 2 Difference between level of Mitochondrial DNA in different study groups.

D10 [101] Bronchiectasis disease relevant PAMPs stimulate VEGF and neutrophil elastase release from neutrophils

Christopher Cole¹; Sonya Carnell³; Kasim Jiwa⁴; Jodie Birch²; Katy Hester¹; Chris Ward¹; John Simpson¹; Anthony De Soya¹

¹*Institute of Cellular Medicine, Newcastle University, Newcastle Upon Tyne, United Kingdom*; ²*Institute for Cell & Molecular Biosciences, Newcastle Upon Tyne, United Kingdom*; ³*Newcastle Clinical Trials Unit, Newcastle Upon Tyne, United Kingdom*; ⁴*Sir William Leech Centre for Lung Research, Freeman Hospital, Newcastle Upon Tyne, United Kingdom*

Intro: Airway infection and inflammation drive bronchiectasis progression. Neutrophils are known for playing an important role in the disease and may promote airway remodelling by releasing elastase and vascular endothelial growth factor (VEGF).

Aims: To understand the role of neutrophils in bronchiectasis and determine if airway neovascularisation is present in bronchiectasis.

Methods: Peripheral blood neutrophils were isolated from healthy volunteers and bronchiectasis patients then stimulated with bronchiectasis relevant PAMPs (e.g. bacterial lysates, fMLP) for 4 hours with the supernatant being assessed for VEGF and elastase concentration by ELISA. An anti-CD31 antibody was used to visualise blood vessels in endobronchial biopsies from healthy and bronchiectasis airways allowing counts to be carried out. VEGF concentration in serum/sputum from bronchiectasis patients (n=115) and healthy serum (n=26) was determined by ELISA, after which results were categorised by bronchiectasis severity index score.

Results: Several stimuli (e.g. LPS, TNF- α) caused significantly ($p<0.05$) more VEGF to be released by neutrophils, elevated elastase secretion was seen in all stimulatory conditions. Bronchiectasis neutrophils secreted more VEGF, IL-6 and TNF- α than healthy. There were significantly ($p<0.05$) more blood vessels/mm of basement membrane in bronchiectasis airways than in healthy. Some individuals had elevated VEGF however no correlation was found between serum/sputum VEGF and disease severity.

Conclusion: The bronchiectasis airways present symptoms of hyper-vascularity suggestive of in vivo pro-angiogenic conditions. Disease severity does not correlate with serum/sputum VEGF. Neutrophils release elastase and VEGF in response to PAMPs that may be encountered in the bronchiectasis airway. Greater amounts of VEGF are secreted by bronchiectasis peripheral blood neutrophils in comparison to healthy. Neutrophils may contribute to the neovascularisation seen in bronchiectasis.

B05 [213] First analysis of the Italian Registry of Adult Bronchiectasis (IRIDE)

Valentina Conio¹; Stefano Aliberti²; Federico Dente³; Marialma Berlendis⁴; Salvatore Battaglia⁵; Emanuela De Juli⁷; Giovanni Sotgiu⁶; Francesco Blasi²

¹Cardiothoracic and Vascular Department, Pneumology Unit, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; ²Dept of Pathophysiology and Transplantation, Università degli Studi di Milano, IRCCS Fondazione Ca' Granda, Ospedale Maggiore Policlinico, Milano, Italy; ³Cardiothoracic and Vascular Department, University of Pisa, Pisa, Italy; ⁴UO Pneumologia, AO Spedali Civili di Brescia, Brescia, Italy; ⁵Dipartimento Biomedico di Medicina Interna e Specialistica (DiBiMIS), Sezione di Malattie Cardio-Respiratorie ed Endocrino-Metaboliche, University of Palermo, Palermo, Italy; ⁶Clinical Epidemiology and Medical Statistics Unit, Dept of Biomedical Sciences, University of Sassari, Sassari, Italy; ⁷Divisione di Pneumologia, Osp Niguarda Ca' Granda, Milano, Italy

Bronchiectasis is a heterogeneous, multidimensional disease with increasing prevalence and hospitalization rates. Patients' characteristics and response to treatment may vary from country to country. Data at national level are crucial to design appropriate processes of care for adult bronchiectasis. We aimed at evaluating characteristics of adult patients with bronchiectasis enrolled in the Italian registry of adult bronchiectasis (IRIDE).

IRIDE is a national registry of adult patients with non-CF bronchiectasis including a total of 13 centers. Patients are prospectively enrolled at the moment across 9 sites while the rest of the sites are still waiting for their IRB approval. Baseline demographic, clinical, functional, microbiological, and treatment data are entered into an electronic case report form (CRF). IRIDE is linked and supported by both the European registry of bronchiectasis (EMBARC) and the Italian Respiratory Society (IRS/SIP).

A total of 552 patients have been enrolled into the registry from October 2014 to May 2017. The majority of the patients are female (n= 374, 68%) and the median (interquartile range (IQR)) age is 69 (56–76) years.

A total of 170 (31%) patients are in BSI risk class mild, 232 (42%) patients moderate and 150 (27%) patients severe, the median (interquartile range (IQR)) is 6 (4-9).

The most common comorbidities include cardiovascular diseases (n=210, 38%), chronic rhino-sinusitis (n=129, 23%), neoplastic disease (n=77, 14%) and diabetes (n=38, 6.9%). Asthma is reported as a comorbidity in 118 patients (21%), while a diagnosis of COPD is present in 101 patients (18%). Etiology of bronchiectasis has been identified in 50% of cases (post-infective: 22.3%; immunodeficiencies: 10%; COPD: 7.8%; asthma: 2.4%; connective tissue disease: 2.5%; primary ciliary dyskinesia: 2.5%; inflammatory bowel disease: 1.9%). A total of 295 (53%) patients reported at least two exacerbations, 190 (34%) at least three exacerbations and 92 (17%) at least one severe exacerbation requiring hospital admission in the previous year. Median (IQR) predicted value of FEV1 is 84%. Pseudomonas has been isolated at least once in respiratory samples of 153 (28%) of the patients, while a chronic Pseudomonas infection has been reported in 15% of the patients. Other isolated pathogens include Haemophilus influenzae in 6.9% of the population and Staphylococcus aureus in 3.8%. A total of 49 (8.9%) patients are on long-term antiinflammatory/antibiotic treatment with an oral macrolide, while 1.6% of the patients are on long-term inhaled/ nebulised antibiotics.

Adult patients with bronchiectasis enrolled in IRIDE are described, with differences noted in demographic, clinical, microbiological, and treatment variables. These results might lead to a better care of patients with personalized treatment.

A10 [163] Epidemiological and clinical features of non tuberculous mycobacteria infection (NTM) in a five-year single centre experience

Valentina Conio¹; Alessandro Cascina¹; Laura Saracino²; Domenica Di Costanzo²; Claudio Valizia²; Rita Di Domenica¹; Angelo Guido Corsico^{1,2}

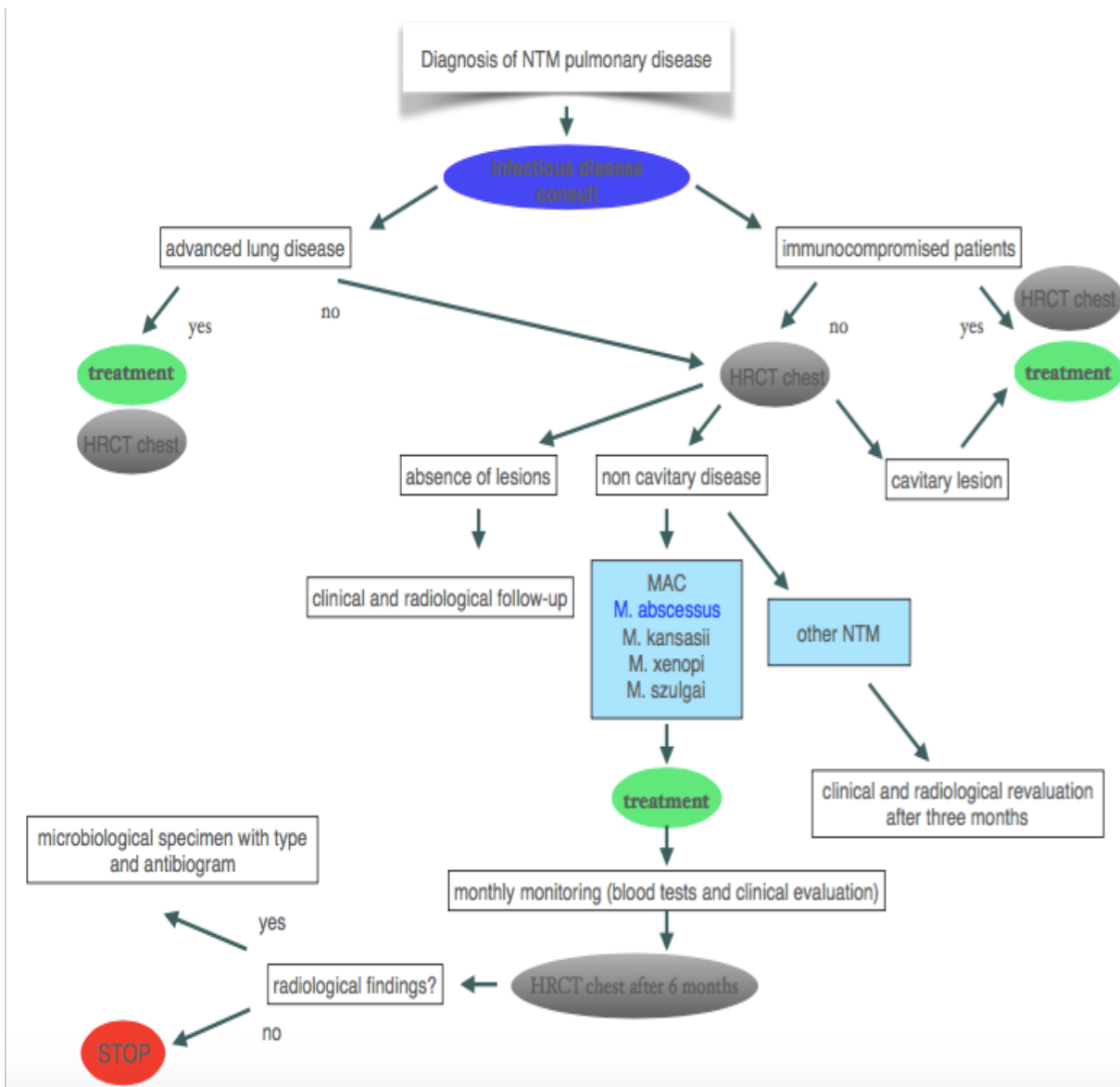
¹Cardiothoracic and Vascular Department, Pneumology Unit, IRCCS Policlinico San Matteo Foundation, Pavia, Italy; ²Department of Internal Medicine, Pneumology Unit, University of Pavia, Pavia, Italy

The incidence and prevalence of NTM disease are increasing globally. Previously NTM disease was more frequent in immunocompromised patients, but nowadays it also concerns patients apparently immunocompetent.

Patients from whom NTM were isolated from respiratory specimens such as sputum, bronchoalveolar lavage (BAL) fluid and lung biopsy between January 1, 2010 and January 1, 2015 at Fondazione IRCCS Policlinico S. Matteo, Pulmonology department, were included in the analysis. Hence, a total of 35 NTM isolated from 31 patients during the study period were analyzed retrospectively. We assessed the number of isolates in which a typing identification and an antibiogram were performed.

Demographic and comorbidities of the patients from whom NTM were isolated were reviewed. Demographic data including age, gender, and smoking habits; comorbidities (malignancy, diabetes mellitus, rheumatic disease, post-transplantation, primary immunodeficit) and underlying lung disease. We also consider previous treatment with corticosteroids. The characteristics of lung lesions were analyzed based on chest computed tomography (CT). The choice to start the treatment and the infectious consultation were reviewed. We analyze the duration of treatment. We also consider when the therapy was discontinued and clinical, microbiological and radiological follow-up. 35 NTM were isolated from 31 pts. Of those, 23 from bronchoalveolar lavage, 12 from other samples (bronchial aspirate, sputum, induced sputum and lung biopsy). 7/31 pts (22,5%) had no apparently known comorbidities/risk factors. The most common lung comorbidity was bronchiectasis (15/31 pts, 25,8%), while extra respiratory comorbidities were type 2 diabetes (7/31 pts, 22,5%) and cancer (6/31 pts, 19,3%). The most frequent chest CT alteration was "tree in bud" (14/31 pts, 40%).

Since low uniformity in identification of NTM patients deserving treatment was found, we designed the enclosed algorithm to guide future decisions. We found a high rate of NTM infections in subjects without risk factors. Multidisciplinary discussion is highly recommended.



C04 [169] Open label case-control study to assess Pidotimod efficacy in Non CF Bronchiectasis Disease: a pilot study

Maria D'Amato¹; Debora Paris²; Dominique J Melck²; Nunzia Sorrentino¹; Antonio Molino¹; Anna A Stanziola¹; Andrea Motta²

¹Department of Respiratory Medicine, A.O. dei Colli, Federico II University,, Naples, Italy; ²Institute of Biomolecular Chemistry, National Research Council, Pozzuoli ,, Naples, Italy

Background: Diagnosis and management of non CF bronchiectasis has been largely empirical and therapies other than antibiotics are subject of relatively few controlled clinical trials.

Methods: Patients selected were 20 adults affected from nCF Bronchiectasis in ≥ 2 lobes, history of frequent exacerbations (≥ 4 in the last year) and presented a moderate or severe obstructive airflow limitation. They were randomized to receive Pidotimod 800 mg OD for 20 days monthly (Group A) or nothing (Group B) for 6 months. All patients had a ICS+LABA inhalation therapy.

All patients underwent spirometry, FeNO measurement, assessment of exacerbations at baseline (T0), 3 months (T3), 6 months (T6).

Exhaled breath condensate (EBC) was also collected for NMR-based metabolomics studies.

Results: At T6 FeNO significantly improved in Group A ($\Delta = -57,20 \pm 7,43$ %) but worsened in Group B ($\Delta = +41,57 \pm 18,77$ %). No difference was observed in FVC, FEV₁ and IT.

At T6 Group A patients with number of mild or severe exacerbations ≤ 1 was significantly less than Group B (P=0.0003).

NMR profiles indicated that treated subjects present a respiratory metabolic phenotype that differs from that of untreated patients.

Conclusions: This study suggests that pidotimod may be able of preventing recurrent respiratory infections in adult nCF Bronchiectasis Disease. Pidotimod may contribute to reduce lower airway inflammation as assessed by FeNO measurement.

D06 [89] Non CF Bronchiectasis Clinic – Digging deep to find the etiology

Adi Dagan¹; Ori Efrati¹; Amir Onn²

¹*Pediatric Pulmonary Unit and the National Center for Cystic Fibrosis, Sheba Medical Center, Tel-Hashomer, affiliated to Sackler Medical School, Tel Aviv University, Ramat Gan, Israel;* ²*Lung institute, Sheba Medical Center, Tel-Hashomer, Ramat Gan, Israel*

Background and Objective: Non-CF bronchiectasis patients of all age were followed in our multidisciplinary center, in order to re-evaluate their diagnosis and optimize management.

Methods: Sixty three patients, 67% female, are under our surveillance. All underwent a physical examination and a specific etiology was sought by completion of laboratory and functional tests.

Sputum cultures (87%) and/or bronchoalveolar lavages (49%) were attained.

All patients were referred to our respiratory physiotherapy for evaluation.

Inhaled corticosteroids, hypertonic saline (3%), bronchial dilators, antibiotics (inhaled or systemic), or preventive azithromycin treatment were recommended in relation to basic disease.

Results: Age range is 3-84 years (median 35). 19% are under 18 years old, 37% are young adults, 18-40 years old, and 44% are above 40 years of age. 81% do not smoke and have not been exposed to cigarette smoke in the past.

84% of the patients have bilateral bronchiectatic lung disease. 11% have left side bronchiectasis, and 5% have right lung disease.

30% maintain normal pulmonary function tests with FEV1>80%, 46% show a mild obstructive disease (60 %<FEV1<80%), 11% have moderate disease (40 %< FEV1<60%), and 8% show severe end stage lung disease (FEV1<40%) – one of which underwent lung transplant recently.

Sputum and lung lavage yielded *Pseudomonas aeruginosa* in 30%, *Haemophilus influenza* in 27%, *Streptococcus pneumonia* in 13%, *Staphylococcus aureus* 11%. *Klebsiella pneumonia*, *E. coli*, *Achromobacter* and *Nocardia* species were found in sputum of few patients. *Mycobacterium* species was found in 21%.

24% suffer from post infectious bronchiectasis: 8% were diagnosed with bronchiolitis obliterans syndrome. 5% have a history of early childhood bilateral pneumonia with bronchiectasis as a probable complication. 5% suffered from severe bacterial pneumonia previous to their bronchiectatic disease. 6% show bilateral disease post *Mycobacterium* disease.

17% of our patients are diagnosed with PCD, 3 of them have complete Kartagener syndrome.

Four patients (6%) have immunodeficiency, 2 with lymphoma and 2 with Common Variable Immunodeficiency.

6% suffer from a rheumatologic disease. Two of them have Inflammatory Bowel Disease, one with Scleroderma and another has positive markers but a specific rheumatologic diagnosis is pending.

6% have anatomic malformations that were diagnosed after bronchoscopy.

Only two patients (3%) have COPD as the single cause for their bronchiectatic disease!

3% are highly suspected of Cystic Fibrosis.

Another patient is currently being diagnosed with asthma related Allergic Bronchopulmonary Aspergillosis.

32% in the clinic remain of unknown or idiopathic cause:

5% are proposed to have an undiagnosed genetic cause due to familial history of siblings with a similar disease.

8% have a single side bronchiectasis and bronchial stenosis – the cause could be either congenital versus acquired due to a post infectious cause.

19% are idiopathic, 6 of them are still completing their investigations.

Conclusion: A thorough investigation for the specific etiology of patients with bronchiectatic lung disease, especially those with bilateral disease, young age and no cigarettes exposure has a high yield for earlier diagnosis, which allows better management and quality of life.

D07 [201] Standardised classification of the aetiology of bronchiectasis across Europe using an objective algorithm

Araujo David¹; Aliberti Stefano²; Shteinberg Michal³; Goeminne Pieter⁴; Hill Adam⁵; Tom Fardon⁶; Obradovic Dusanka⁷; Dimakou Katerina⁸; Polverino Eva⁹; de Soya Anthony¹⁰; McDonnell Melissa¹¹; James Chalmers⁶

¹São João Hospital Center, Porto, Portugal; ²University of Milan, Milan, Italy; ³Carmel Medical Center, Haifa, Israel; ⁴AZ Nikolaas, AZ Nikolaas, Belgium; ⁵Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; ⁶University of Dundee, Dundee, United Kingdom; ⁷Institute for pulmonary diseases, Sremska Kamenica, Vojvodina, Serbia, University of Novi Sad, Faculty of Medicine, Novi Sad, Serbia; ⁸Sotiria Chest Hospital, Athens, Greece; ⁹University of Barcelona, Barcelona, Spain; ¹⁰Newcastle University, Newcastle, United Kingdom; ¹¹University of Galway, Galway, Ireland

Background: Bronchiectasis have multiple possible causes. Despite guideline recommended testing for aetiology, studies still show a considerable number of cases classified as idiopathic.

There is a lack of agreed definitions of concepts such as post-infectious bronchiectasis and no agreed method for assigning the aetiology of bronchiectasis, leading to variation across countries that may have more to do with testing methods and definitions than genuine disease heterogeneity.

Objectives: The aim of this study was to create a bronchiectasis aetiology classification algorithm that could be applied objectively to different healthcare settings.

Methods: A database covering 10 different bronchiectasis clinical centres was used (Dundee, Edinburgh, Newcastle– United Kingdom; Haifa-Israel; Galway - Ireland; Leuven - Belgium; Athens - Greece; Monza - Italy; Barcelona - Spain; Serbia). These patients had a diagnosis of bronchiectasis based on high-resolution computed tomographic scan. Patients with Cystic fibrosis or traction bronchiectasis due to pulmonary fibrosis were excluded. The aetiological algorithm was created having the British Thoracic Society Bronchiectasis guidelines from 2010 as a starting point, and classifying the several possible causes as “definitive diagnosis”, “possible diagnosis, association or complication” and “diagnosis of exclusion”.

Results: A total of 2502 patients were accessed. The clinicians made a diagnosis in 58.2% of the patients. The most common aetiology (excluding idiopathic) was post-infective (n=427, 17.7%) and COPD (n=235, 9.4%). After applying the aetiological algorithm, a significant reduction was seen in terms of idiopathic cases (41.8% vs 29.0%) and COPD was the most common aetiology (excluding idiopathic) with 373 patients (14.9%). The number of post-infective cases was also lower (n=427, 17.1% vs n=349, 13.9%). The other main differences were a higher number of diagnosis made of connective tissue disease associated bronchiectasis (n=157, 6.3% vs n=237, 9.5%) and gastroesophageal reflux disease / aspiration (n=15, 0.6% vs n=109, 4.4%). The number of patients with more than one possible diagnosis was also reduced after applying the algorithm (n=14, 0.6% vs n=8, 0.3%).

Conclusions: These results show that by applying the same structured aetiological algorithm to a bronchiectasis patient group the number of idiopathic cases can be lowered substantially. We demonstrate that clinicians frequently diagnose idiopathic bronchiectasis in the presence of disease associated with bronchiectasis suggesting the need for standardized aetiological categorization.

D08 [116] Factors associated with the formation and progression of bronchiectasis in patients with moderate to severe chronic obstructive pulmonary disease

David de la Rosa¹; Marta Ballester²; Pablo Catalan-Serra²; Juan-José Soler-Cataluña³; Marco Agramunt²; Javier Ballester²; María José Selma⁴; Gabriel Anguera⁴; Grace Oscullo⁴; José Daniel Gómez⁴; Yolanda Roca¹; Miguel Angel Martinez-Garcia⁴

¹Hospital Plató, Barcelona, Spain; ²Hospital General de Requena, Requena, Spain; ³Hospital Arnau de Vilanova, Valencia, Spain; ⁴Hospital La Fe, Valencia, Spain

Background: The strikingly high prevalence of bronchiectasis in patients with moderate to severe COPD has led to the hypothesis of a possible causal relationship between both conditions. However, no longitudinal studies have proved the development of bronchiectasis in patients with COPD.

Objective: To assess the long-term evolution of bronchiectasis in patients with moderate to severe COPD and to establish factors associated with it.

Methods: Prospective observational study of a cohort of patients diagnosed with moderate to severe COPD in two Pneumology outpatient clinics. Bronchiectasis was diagnosed by high-resolution computed tomography scan (HRCT), and its extent was evaluated according to the number and location of pulmonary lobes and segments affected. Cylindrical bronchiectasis observed in a single pulmonary segment was not considered. Several variables were collected on admission into the study and regularly during the follow-up (every 3–6 months): general data, smoking habit, systemic and respiratory clinical history, symptoms, treatments, spirometric values, blood levels of CRP and albumin, sputum microbiology and a detailed history of every acute COPD exacerbation. All patients had expectoration in varying degrees. A control HRCT was performed at least 5 years after the previous one, performing tomographic slices and measuring the morphological characteristics at the same level as in the previous HRCT. The development of new bronchiectasis, the increase in the number (emergence in 2 more segments) or size of existing bronchiectasis (an increase of $\geq 10\%$ in airway lumen diameter) was assessed.

Results: 201 patients were included. Bronchiectasis was present in 115 (57.2%) patients. During a follow-up of 8.5 years (median 102 months [interquartile range, 77–116]) 99 patients died (49.5%) and 35 withdraw from the follow-up. With the HRCTs performed in the final cohort, 4 groups were studied. The first had bronchiectasis at baseline and developed more or they increased (n=13); the second had no bronchiectasis and new ones appeared (n=15); the third showed no bronchiectasis in either the first or the second HRCT (n=21); the fourth had bronchiectasis that did not change during follow-up (n=28). Therefore, a group (28 patients, 36.7%) had radiological progression (new or larger bronchiectasis) while another group (49 patients, 63.3%) showed no formation of new or progression of existing bronchiectasis. In any case, other diseases were detected as a possible cause of bronchiectasis. In the logistic regression, three variables were independently associated with radiological progression in the fully-adjusted analysis by age, BMI, Charlson index, dyspnoea, CRP levels and FEV1%: the isolation of potentially pathogen microorganisms (HR 1.11; 95%CI 1.02-1.21), the number of severe exacerbations (HR 1.15; 95%CI 1.04-1.26) and the presence of chronic purulent sputum (HR 2.6; 95%CI 1.18-5.71). A COPD patient with all these three characteristics had a 5.7 fold higher probability of developing bronchiectasis than patients without them.

Conclusions: The natural course of patients with moderate or severe COPD may lead to the development of bronchiectasis in a third of them. Factors associated with this evolution are the isolation of potentially pathogenic microorganisms, a higher number of severe exacerbations and the presence of purulent sputum.

C22 [82] Cost of hospitalizations for exacerbation of bronchiectasis in Spain

David De la Rosa¹; Annie Navarro²; Marta Garcia-Clemente⁴; Oriol Sibila⁵; Rosa Maria Girón⁶; Concepción Prados⁷; Casilda Olveira⁸; Esther Quintana⁹; Alicia Padilla¹⁰; Beatriz Montull³; Antonio Ruiz¹¹; Eva Polverino¹²; Nuria Celorrio¹³; María Jesús Buendía¹⁴; Luis Máiz¹⁵; M^a Victoria Leal¹⁶; Juan Luis Rodríguez¹⁷; M^a Jesús Avilés¹⁸; M^a Carmen Abellán¹⁸; Ana Pando⁴; Marina Blanco¹⁹; Ainhoa Gomez²⁰; Rafael Golpe²¹; Patricia Minguez²²; Cristina Gómez²³; Ane Uranga²⁴; Ana Nuñez²⁵; Lorena López²⁷; Abel Jesús Martínez²⁶; Francisco Javier Michel²⁸; Raúl Godoy²⁹; Miguel Angel Martinez-Garcia³

¹Hospital Plató, Barcelona, Spain; ²Hospital Mutua de Terrassa, Barcelona, Spain; ³Hospital La Fe, Valencia, Spain; ⁴Hospital Central de Asturias, Oviedo, Spain; ⁵Hospital Santa Creu i Sant Pau, Barcelona, Spain; ⁶Hospital La Princesa, Madrid, Spain; ⁷Hospital La Paz, Madrid, Spain; ⁸Hospital Regional de Málaga, Malaga, Spain; ⁹Hospital Virgen del Rocío, Sevilla, Spain; ¹⁰Hospital Costa del Sol, Marbella, Spain; ¹¹Hospital Príncipe de Asturias, Alcalá de Henares, Spain; ¹²Hospital Clínic, Barcelona, Spain; ¹³Hospital Viladecans, Viladecans, Spain; ¹⁴Hospital Infanta Leonor, Madrid, Spain; ¹⁵Hospital Ramón y Cajal, Madrid, Spain; ¹⁶Hospital Basurto, Bilbao, Spain; ¹⁷Hospital Clínico San Carlos, Madrid, Spain; ¹⁸Hospital Reina Sofía, Murcia, Spain; ¹⁹Complejo Hospitalario A Coruña, La Coruña, Spain; ²⁰Hospital de Cruces, Baracaldo, Spain; ²¹Hospital Lucus Augustí, Lugo, Spain; ²²Hospital Puerta de Hierro, Madrid, Spain; ²³Hospital de la Defensa, Zaragoza, Spain; ²⁴Hospital de Galdakao, Usansolo, Spain; ²⁵Hospital General Universitario, Albacete, Spain; ²⁶Hospital de Hellín, Hellín, Spain; ²⁷Hospital de Santa Marina, Bilbao, Spain; ²⁸Hospital Universitario Donostia, San Sebastian, Spain; ²⁹Hospital Nuestra Señora del Perpetuo Socorro, Albacete, Spain

Background: Hospitalizations due to exacerbations are one of the factors with the greatest impact on the total annual cost of patients with bronchiectasis. However, the actual cost of an admission is unknown, and the only data available come from estimates through hospital discharge codes (approx.4000 €).

Objective: To establish the average cost of an admission due to exacerbation of bronchiectasis in Spain, and to evaluate the parameters associated with a higher cost of the hospitalization.

Methods: Adult patients hospitalized for bronchiectasis exacerbation were included in a prospective multicentre study. All expenditures were collected, from the moment of hospital admission to discharge, applying unit costs to each: pharmacological treatments (drugs catalogue 2016); oxygen therapy, complementary explorations, ambulances, rehabilitation and post-discharge convalescence (average rate of the participating autonomous communities); emergency room and hospitalization at home price of each hospital, as well as structural costs (70% of the price of bed per day). The costs of treatments during the two months pre- and post-admission were also collected.

Results: We included 222 patients (52.7% males, average 71.8 years) from 29 centres (44.6% second level hospitals and 55.4% tertiary hospitals). The most frequent etiologies of bronchiectasis were: COPD (24.3%), post-infectious (23.8%), idiopathic (22.1%) and post-tuberculous (20.3%). 54.5% of the patients had chronic bronchial infection, with *P. aeruginosa* being the most frequently isolated microorganism (84.3%). According to e-FACED score, 14.9% of the patients had mild bronchiectasis, 44.7% had moderate bronchiectasis and 40.4% had severe bronchiectasis. 66.2% of the patients required hospitalizations during the previous year, and 92.3% presented exacerbations. The mean duration of admission was 10.8 days. 8.7% of patients completed the inpatient treatment at home. 7.3% were readmitted before 2 months post-discharge. Mortality rate was 1.4%. Regarding the total emergency room cost, complementary examinations represented 35.4%, treatments 9.1%, while the

rest of the cost was due to other expenses and to the emergency rate of each hospital. Regarding the cost of inpatient hospitalization, 7.3% was due to complementary examinations, and 8.9% to treatments and 83.7% was due to the hospital's structural cost and other charges. The total cost of admission was $5,284.7 \pm 2,445.7$ €. A 10.1% of the total cost was due to outlay in the emergency room and 86.9% to expenditures in the hospitalization area. The variables associated with a higher cost were: bronchial colonization by *P. aeruginosa*, admission to a tertiary hospital and longer admission times. We found no significant relationship between the cost of admission and the severity or aetiology of bronchiectasis. In the multivariate analysis, the factors associated with a higher cost were bronchial colonization by *P. aeruginosa*, longer admission times and hospitalization at home. The cost of treatment in the 2 months post-discharge was significantly higher than in the previous 2 months, due to a greater use of systemic steroids, oral antibiotics and home oxygen therapy.

Conclusions: The average cost of hospitalization for exacerbation of bronchiectasis is higher than estimated by public agencies. It is mainly due to structural costs, and is higher in longer durations of admission, in patients with bronchial colonization by *P. aeruginosa*, and in those who end hospitalization at home. Strategies are needed to reduce hospitalizations, given the significant impact they have on the total expenditure in patients with bronchiectasis.

C35 [172] Unawareness, chronicity and misdiagnosis of Bronchiectasis. Association with disease severity.

Katerina Dimakou¹; Myrsini Melachroinou¹; George Hillas²; Maria Kaponi¹; Serafeim Chrysikos¹; Anna Gousiou³; Eleftheria Mizi²; Sotiria Macrodimitri⁴; Christina Triantafillidou⁴

¹5th Pulmonary Department, "Sotiria" Chest Hospital, Athens, Greece., Athens, Greece; ²Department of Critical Care and Pulmonary Services, University of Athens Medical School, Evangelismos Hospital, Athens, Greece, Athens, Greece; ³The American College of Greece, DERE, Athens, Greece; ⁴6th Pulmonary Department, "Sotiria" Chest Hospital, Athens, Greece., Athens, Greece

Introduction: Bronchiectasis (BE) is an underdiagnosed and underestimated condition. Delay of diagnosis may lead to disease progression without appropriate treatment.

Aim: To estimate the awareness and the delay of diagnosis in bronchiectasis patients in relation to the duration of symptoms and indices of severity.

Methods: We studied symptomatic patients with BE proven by HRCT. We recorded the patients' unawareness of the diagnosis of BE prior to our estimation and in that case the previous diagnosis known by patients. We also evaluated the time, in years, since initiation of symptoms (symptoms' duration), exacerbations, CT score according to Reiff scale, spirometry and microbiology.

Results: 261 patients were studied (159 women), mean age 60,3 years (18-87). The main symptoms were cough and mucopurulent sputum. Mean values (\pm SD): duration of symptoms 12.1 years (11.3), number of exacerbations during the last year 2.1 (1.43), number of hospitalizations during the last year 0.45 (0.5), Reiff CT score 4.9 (2.4), number of lobes with BE involved 2.2 (1.0), FEV1% of predictive value: 69.3(23.1), FVC% of predictive value: 80.7(18.9). 127 (49%) patients were colonized by pathogens and the predominant one was *Pseudomonas aeruginosa* (Pa) (33% of them).

162 patients (62%) knew their diagnosis of BE. 52% of them were colonized by pathogens and mainly by Pa. Unawareness of BE was reported by 99 patients (38%). The most common previous diagnoses were: none 37%, COPD 26%, chronic bronchitis 14%, asthma 10%. 40 /99 patients (40%) were colonized by pathogens, half of whom by Pa (20%). Symptoms' duration was related to the exacerbations ($p=0.001$), hospitalizations ($p=0.0016$), CT score ($p=0.001$), FEV1% ($p=0.0016$), while the number of lobes with BE in HRCT related to the exacerbations ($p=0.0001$), hospitalizations ($p=0.0001$), and FEV1% ($p=0.0001$).

Conclusion: Bronchiectasis often remains undiagnosed or misdiagnosed years after symptoms' initiation. This may lead to the disease progression and severity.

B06 [139] Microbial landscape of sputum in patients with non-cystic fibrosis bronchiectasis

Valeriia Dmytrychenko¹; Tetyana Pertseva¹; Kateryna Bogatska¹; Tetyana Kyreeva¹

¹SE "Dnipropetrovsk medical academy of Health Ministry of Ukraine", Dnipro, Ukraine

The airways of patients with bronchiectasis, even in the absence of cystic fibrosis become chronically infected by bacteria. Aim of the study was to determine the microbiological pathogens in sputum of patients with bronchiectasis without signs of cystic fibrosis in stable phase of cystic fibrosis.

Materials and methods: We examined 13 women who suffered from bronchiectasis, in all patients the presence of bronchiectasis confirmed by computed tomography. Isolation and identification of pathogens was carried by classical bacteriological methods of sowing on nutrient media, sensitivity to drugs was determined using disco-diffusion method according to CLSI guidelines.

Results: The average age of patients was 48.0 ± 3.0 years. 13 samples of sputum were obtained, which was distributed on purulent by nature – 3 (23.1 %), mucopurulent – 7 (53.8 %), mucosalivary – 3 (23.1 %). In 12 (92.3 %) samples the pathogen was detected. The combination of pathogens was in 2 (16.7 %) patients. The most common pathogen was *P. aeruginosa* – 12 (100 %) strains and its combination of with *M. catarrhalis* and with *A. fumigatus* 1 (8.3 %) sample. *P. aeruginosa* susceptibility profile was as follows: colistimethate sodium – 12 (100 %) strains were sensitive; ceftazidime: sensitive – 10 (83.3 %), resistant – 2 (16.7 %); ciprofloxacin: sensitive – 2 (33.3 %), medium sensitive – 4 (66.7 %), resistant – 1 (8.3 %); meropenem – sensitive 12 (100 %) strains; piperacillin/tazobactam: sensitive – 10 (83.3 %) resistant – 2 (16.7 %); tobramycin: sensitive 12 (100 %) strains. There are 2 (16.7 %) strains that were resistant to more than one group of drugs (piperacillin/tazobactam, ceftazidime and ciprofloxacin) and 3 (25.0 %) showed pathogen resistance to only one drug (ciprofloxacin).

Conclusions: The most generally accepted pathogen among patients with bronchiectasis in the stable phase is *P. aeruginosa*. 58.3 % selected strains were sensitive to all groups of drugs that have been studied. 100 % was recorded the sensitivity of colistimethate sodium. Almost 42 % of the strains have showed resistance to variety of antibiotics. Most frequently observed was the resistance to ciprofloxacin.

C27 [140] EXPERIENCE OF USING THE BRONCHIECTASIS SEVERITY INDEX IN THE PATIENTS WITH NON-CYSTIC FIBROSIS BRONCHIECTASIS

Valeriia Dmytrychenko¹; Tetyana Pertseva¹; Kateryna Bogatska¹; Tetyana Kyreeva¹

¹SE "Dnipropetrovsk medical academy of Health Ministry of Ukraine", Dnipro, Ukraine

Identifying the risk of exacerbations, hospital admissions, and mortality is vital for patients with non-cystic fibrosis bronchiectasis (BE).

Aim: to stratify the patients (pts) with BE in accordance with risk of unfavorable events by means of the Bronchiectasis Severity Index (BSI).

Materials and methods: 13 stable pts with BE were enrolled into a study. The diagnosis was confirmed by a clinical history consistent with BE and high-resolution computed tomography. Physical examination performed in all patients. Age, BMI (body mass index), FEV₁ (forced expiratory volume on first second) % predicted, hospital admission for 2 previous years, exacerbations in previous year, Medical Research Council (MRC) dyspnea score, Pseudomonas colonization, colonization with other organisms and radiological severity(>3 lobes involved or cystic bronchiectasis) were evaluated for BSI calculation. BSI calculation present in table 1.

Table 1

BSI

Severity marker	Score points	Severity marker	Score points
Age, year		Exacerbations previous year	
<50	0	0	0
50–69	2	1–2	0
70–79	4	≥3	2
≥80	6	MRC dyspnea score	
BMI, kg/m ²		1–3	0
<18,5	2	2	2
18,5–25	2	3	3
26–29	0	Pseudomonas colonization	
≥30	0	No	0
FEV1 % predicted		Yes	3
>80	0	Colonization with other organisms	
50–80	1	No	0
30–49	2	Yes	1
≤30	3		
Hospital admission 2 previous years		Radiological severity: >3 lobes involved or cystic bronchiectasis	
No	0	No	0
Yes	5	Yes	1

Results: We examined 13 women, mean age – 48.0 ± 3.0 years. In accordance with BSI: low risk (0–4 points) had 1(7.7 %) pt, intermediate (5 to 8 points) – 5 (38.5 %) pts and high (more than 9) – 7 (53.8 %) pts with BE.

Conclusions: In accordance with BSI more than 90 % stable pts with have intermediate and high risk of exacerbation, hospitalization and mortality. The most significant impact on prognosis severity had low BMI (less than 18.5), exacerbation and hospitalization rate and Pseudomonas colonization.

C28 [74] New opportunity of inhaled therapy for patients with non-CF bronchiectasis

Galina Ignatova¹; Vladimir Antonov¹; Olga Rodionova¹; Irina Grebneva¹; Elena Blinova¹; Maria Belsner¹

¹South Ural State Medical University, Chelyabinsk, Russian Federation

Background: Mucolytics used traditionally for treatment of non-cystic fibrosis (non-CF) bronchiectasis cannot be recommended widely and have some use limitations. Also they have lack of effectiveness regardless their good tolerability. 7% hypertonic saline (HS) has showed its effectiveness in improvement lung function and quality of life in non-CF bronchiectasis patients. Addition of 0.1% hyaluronic acid (HA) to 7% hypertonic saline has shown its improved tolerability in patients with cystic fibrosis and patients' adherence including patients with intolerance of 7% HS.

Objective: The aim of this observation was evaluation of effectiveness and safety of daily 7% HS and 0.1% HA fixed combination in patients with non-CF bronchiectasis.

Methods: There were 14 patients in our observation: 7 patients with post-infective bronchiectasis (mean age 47,23±4,18) and 7 patients with COPD associated bronchiectasis (mean age 58,35±5,14) all confirmed by computer tomography. Clinical examination and function tests were performed for all patients including pulmonary function and oxygen saturation assessment, 6 minute walk test, MRC dyspnoea scale measurement, evaluation of prognostic BODE index, SGRQ questionnaire analysis. Inhalations of 7% HS and 0.1% HA fixed combination (Hyaneb®) 5 ml twice daily were given by adding to standard therapy for 10-30 days by individual need. Period of observation was 2 months.

Results: After 2 months from the start of treatment general well being was improved in both groups confirmed by quality of life analysis with SGRQ questionnaire: significant decrease of scores was registered in all components by 4.2 units minimum including Total score (from 46.19 to 41.99). After first inhalations there was increase of sputum production from ~30 ml to 1.5 liters per day. This effect remained up to 10 days after inhalations stopped. Stabilizing of FEV₁ was shown without significant changes. Index BODE was significantly reduced to the second month of observation from 4.44 (3.91; 4.98) to 1.81 (1.32; 2.31). There were no adverse effects registered, no patient has refused treatment.

Conclusions: Daily 7% HS and 0.1% HA fixed combination inhalations with nebulizer are additional effective inhaled therapy tool in patients with bronchiectasis with different etiology. Use of 7% HS and 0.1% HA combination can be considered as "non invasive therapeutic bronchoscopy". 7% HS and 0.1% HA fixed combination has good tolerability and has shown no pronounced adverse effects.

B07 [194] Risk factors associated with non-fc bronchiectasis in 110 children

Andrea Farolfi¹; Emanuela Boselli¹; Lucia Cococcioni¹; Chiara Bersanini¹; Alessandra Zenga¹; Salvatore Zirpoli²; Anna Mandelli³; Gian Vincenzo Zuccotti⁴

¹*Pediatric Pulmonology, Pediatric Department, V. Buzzi Children's Hospital, University of Milan, Milan, Italy;* ²*Department of Radiology and Neuroradiology, V. Buzzi Children's Hospital, Milan, Italy;* ³*Department of Anesthesiology and Intensive Care Unit, V. Buzzi Children's Hospital, Milan, Italy;* ⁴*Pediatric Department, V. Buzzi Children's Hospital, University of Milan, Milan, Italy*

Background: Bronchiectasis is a disease defined by irreversible dilation and distortion of the conduction airways. Diagnosis is made by chest HRCT in children with chronic moist-sounding cough, recurrent wheezing and chest infections. These symptoms are common among children attending nurseries, but only few develop bronchiectasis (67/100.000 in the general population) implying individual susceptibility.

Non-CF bronchiectasis are associated with intrinsic or extrinsic airway's obstruction, ciliary dyskinesia, aspiration syndrome, impaired immune function, diffuse lung disease, various clinical syndromes and probably asthma. The majority of children with non-CF bronchiectasis have no documented underlying disease. The only consistent association is with lower respiratory infections, especially with the overall number of them.

Objective: To outline the risk factors associated with bronchiectasis in children.

Methods: A retrospective case-review of 110 pediatric patients with non-CF bronchiectasis from 1995 to 2017 at V. Buzzi Children's Hospital, Milan .

Results: In 30 patients (27%) an underlying predisposing condition was found: 6 had bronchopulmonary dysplasia, 4 IgA deficiency, 3 pulmonary sequestration, 3 tracheoesophageal fistula, 2 neurodevelopmental disorders, 2 bronchomalacia, 2 ciliary dyskinesia, 1 tracheomalacia, 1 diaphragmatic hernia, 1 extrinsic bronchial stenosis due to intrapulmonary mature teratoma, 1 right pulmonary aplasia, 1 rheumatoid arthritis, 1 Optiz syndrome, 1 Wolf-Hirshhorn syndrome, 1 Ellis-van Creveld syndrome (with transposition of the great arteries).

Three patients had received surgical treatment for isolated congenital cardiac anomalies: double outlet right ventricle, transposition of the great vessels with pulmonary valve stenosis, aortopulmonary window with interrupted aortic arch.

In 77 patients (70%) no susceptibility underlying condition was found; all of them had recurrent pulmonary infections and 9 (11%) with acute respiratory failure requiring Oxygen therapy or NIV. The mean age at diagnosis was 5.8 years old. In 27 (35%) patients the first symptoms occurred in the first year of life. The mean number of chest x-rays, before diagnosis (a proxy for the number of pneumonias) was 3.3.

Conclusions: Only a minority of our patients had an identified underlying condition for bronchiectasis. The overall number of pneumonias, rather than the severity or the site, was associated with bronchiectasis: in the vast majority of children no predisposing factor was found, other than early onset of pulmonary infections.

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C05 [212] *P. aeruginosa* resistance pattern and risk factors: a longitudinal observational cohort study

Paola Faverio¹; Elisa Franceschi²; Stefano Zucchetti¹; Francesco Amati²; Francesca D'Arcangelo¹; Angela Bellofiore²; Anna Stainer¹; Martina Contarini²; Francesco Blasi²; Stefano Aliberti²

¹Cardio-Thoracic-Vascular Department, University of Milan Bicocca, Respiratory Unit, San Gerardo Hospital, ASST di Monza, Via Pergolesi 33, 20900, Monza, Italy; ²Department of Pathophysiology and Transplantation, University of Milan, Internal Medicine Department, Respiratory Unit and Cystic Fibrosis Adult Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via Francesco Sforza 35, 20122, Milan, Italy

Background: Bronchiectasis represent a progressive respiratory disease characterized by abnormal chronic dilatation of bronchi that predisposes to impaired mucus clearance and chronic bacterial infection. *P. aeruginosa* is the most common pathogen in patients with bronchiectasis and defines a specific clinical phenotype associated with worse patients' outcomes, particularly in those with multi-drug resistant *P. aeruginosa*. Few studies have longitudinally assessed the development of antibiotic resistance in patients with a chronic *Pseudomonas* infection.

Objective: The aim of this study was to describe the frequency and risk factors for the development of antibiotic resistance in bronchiectasis patients with *Pseudomonas*.

Methods: This was an observational, prospective study of consecutive adult outpatients with bronchiectasis attending the Bronchiectasis Clinics at the San Gerardo University Hospital in Monza and the IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico in Milan, Italy, from 1st January 2013 to 30th April 2017. The Institutional Review Board of both Institutions approved the study and patients signed an informed consent. A complete medical history was recorded including previous antibiotic therapies, exacerbations and hospitalizations, and other bacterial colonization. Drug-Resistance (DR) was defined as acquired non-susceptibility to at least one agent in one antimicrobial category and Multi-Drug Resistance (MDR) was defined as acquired non-susceptibility to at least three different agents in three different antibiotic classes.

Results: Out of 480 patients with bronchiectasis, a total of 113 patients (median age 64 years; 35% males) presented at least 1 *Pseudomonas* isolation. Out of 113 initial *Pseudomonas* isolates, 20 (18%) were resistant to ciprofloxacin, 7 (10%) to piperacillin-tazobactam, 9 (8%) to ceftazidime, 7 (6%) to tobramycin, 6 (5%) to gentamicin, 3 (3%) to amikacin, 2 (2%) to colistin, and 2 (2%) to meropenem. 78 (72%) patients had pan-sensible *Pseudomonas*, 23 (21%) patients drug-resistant *Pseudomonas* and 7 (7%) multi-drug resistant *Pseudomonas*. When considering the 62 patients with at least 2 *Pseudomonas* isolates: 4 (8%) out of 50 that were initially sensible to ciprofloxacin developed resistance, 4 (7%) out of 54 that were initially sensible to piperacillin-tazobactam developed resistance, 6 (11%) out of 56 developed resistance to ceftazidime, 7 (11%) out of 61 developed resistance to amikacin, 7 (11%) out of 61 developed resistance to gentamicin, 3 (5%) out of 61 developed resistance to meropenem, 1 (2%) out of 60 developed resistance to tobramycin, 1 (2%) out of 61 developed resistance to colistin. Median [IQR] time between first and last isolate was 22 months [11-45].

Conclusions: in our population a considerable percentage of patients (18%) showed ciprofloxacin resistance since the first *Pseudomonas* isolation. The antibiotics to which resistance is most often developed are ceftazidime, amikacin and gentamicin (11% each). Future studies with longer follow up time may reveal higher percentages of resistance development.

C06 [179] The effectiveness of macrolide antibiotics in non-cystic bronchiectasis: Cochrane systematic review

Lambert Felix¹; Relph Nicola²; Kelly Carol³; Chalmers James⁴; Crossingham Iain⁵; Milan Stephen⁶; Spencer Sally¹

¹Postgraduate Medical Institute, Edge Hill University, Ormskirk, United Kingdom; ²Physical Activity and Sports, Edge Hill University, Ormskirk, United Kingdom; ³Faculty of Health and Social Care, Edge Hill University, Ormskirk, United Kingdom; ⁴University of Dundee, Ninewells Hospital and Medical School, Dundee, United Kingdom; ⁵Thoracic Medicine, Hemel Hempstead Hospital, Hemel Hempstead, United Kingdom; ⁶Lancaster Health Hub, Lancaster University, Lancaster, United Kingdom

Background : Bronchiectasis is a chronic respiratory disease characterised by abnormal and irreversible dilatation and distortion of the smaller airways (Chalmers 2015). Globally, it is estimated that the prevalence of bronchiectasis in adults will increase from approximately 2.4 million in 2012 to over 3 million by 2020 (Polverino 2014). Recent studies have highlighted an increase in the prevalence rate that could be partly attributable to better access to high quality CT scans thus improving the validity of diagnosis (Goeminne 2016; Quint 2016). This Cochrane systematic review of macrolide therapy is the first of a series of five systematic reviews of antibiotics for bronchiectasis, designed to address gaps in the evidence base in terms of the safety and effectiveness of therapy (Welsh 2015, Aliberti 2016, Kelly 2016;).

Objective: To determine the impact of macrolide antibiotics in the treatment of adults and children with non-cystic fibrosis bronchiectasis.

Methods: We included randomised controlled trials (RCTs) of at least four weeks duration. We also included cross-over studies, but only used data from the first pre-cross-over phase to eliminate potentially irreversible carry-over effects (e.g. antibiotic resistance). We included adults and children diagnosed with bronchiectasis by bronchography, plain film chest radiograph, or high-resolution computed tomography who reported daily sputum expectoration of at least three months duration. We excluded studies of mixed respiratory populations when the data for bronchiectasis patients was not reported separately. We included studies comparing macrolide antibiotics with placebo, standard care or non-macrolide antibiotics in the long-term management of stable bronchiectasis and each comparison was reported separately. We excluded studies looking at short-term macrolides for the treatment (as opposed to prevention) of exacerbations of bronchiectasis. Our primary outcomes were exacerbations, hospitalisations, and serious adverse events. Secondary outcomes included sputum volume and purulence; pulmonary function tests, systemic markers of infection, adverse events, mortality, antibiotic resistance, exercise capacity, and quality of life. We collected outcome data at a range of follow-up points that best reflected the available evidence from included studies, e.g. end of study, end of follow-up, change from baseline.

Results: As our team is currently analysing the results, we will provide an overview of the included trials and present full results at the conference.

The search identified sixteen trials, twelve with adults and four with children. The study sample sizes ranged from 20 to 141 participants. Eight trials were conducted in Asia, three each in Australia and Europe, and one each in Africa and North America. The type of macrolide was azithromycin in seven trials; roxithromycin in five, erythromycin in three; and clarithromycin in one trial. The comparator was placebo in eleven trials, and usual care or no intervention in the remaining five trials. Treatment duration was for a median of 3 months, with a range of 2 months to 24 months. The weekly dose for

children was between 15 and 30 mg/kg and in adults ranged from 750 to 1500 mg for azithromycin, 1050 to 2100 mg for roxithromycin, and 5600 - 7000 mg for erythromycin. Four trials were judged at low risk of bias for all criteria with the remainder having variable risk of bias across criteria. Three trials were only reported as abstracts and did not contain review outcome data.

Conclusions: Conclusions will be presented at the conference following completion of the analyses.

The protocol to the review can be accessed from:

(<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD012406/full>)

C23 [114] Bronchiectasis and Asthma: only a comorbidity or a new phenotype?

Sebastian Ferri¹; Teresa Augelletti¹; Ramona Sorrentino¹; Sabrina Genco¹; Raffaele Campisi¹; Enrico Heffler¹; Nunzio Crimi¹

¹*AOU Policlinico-Vittorio Emanuele, Catania, Italy*

Introduction: Bronchiectasis (BE) is a chronic disease associated with high morbidity e mortality. Several studies have enlightened pathophysiology, microbiology and epidemiology of the disease, but few is known about its phenotypes. We aimed to study the correlation between asthma and BE as a new phenotype.

Methods: We consecutively enrolled all adult patients with a CT diagnosis of noncystic fibrosis BE and treated asthma presenting to our Outpatients Clinic in a 6-months period. Patients with traction BE were excluded. All included patients underwent clinical and laboratory workup, lung function tests and microbiological analysis of sputum. Asthma control test (ACT) was submitted at the recruitment visit. We collected blood and sputum samples and skin prick tests were conducted in order to define asthma phenotype.

Results: 16 patients (6 males/10 females; 1 current smoker, 4 ex smokers and 11 non smokers) were enrolled into the study. BE were cylindric in 87% and both cystic and cylindric in only 2 cases. 50% patients had BE in 4 lobes, 30% in 6 lobes and 20% in 2 lobes. Radiologically, 11 and 5 patients were defined as mild and moderate respectively. None was found with severe BE. The main hallmark was frequent, non-seasonal exacerbations (mean 4,18/year), with productive cough and non purulent phlegm. Microbiological analysis was lead in sputum samples. Pseudomonas Aeruginosa was found in 4 patients while no pathogens were found in the remaining samples. All patients were negative for allergic bronchopulmonary aspergillosis (ABPA). Mean ACT was 14.2. 50% of patients had both peripheral and sputum eosinophilia. Lung function tests were normal or mildly obstructive in 81% of patients, only 3 were moderate.

Conclusions: Asthma/BE patients seems to have worse symptoms in spite of mild radiological and lung functional findings. We suppose that the association between Asthma and BE can play a role as a trigger for exacerbations and it may be a new phenotype for both diseases.

C29 [165] Inhaled Liposomal Ciprofloxacin In Patients With Non-Cystic Fibrosis Bronchiectasis (NCFBE) And Chronic Pseudomonas Aeruginosa Infection: Pharmacokinetics Of Once-Daily Inhaled ARD-3150

Juergen Froehlich¹; David Cipolla¹; Anthony De Soyza²; Glynn Morrish³; Igor Gonda¹

¹Aradigm Corporation, Hayward, CA, USA; ²Newcastle University and Freeman Hospital Adult bronchiectasis service, Newcastle, United Kingdom; ³Clinical Network Services, Toowong, Australia

Background: ARD-3150 is a combination of free (60mg/3mL) and liposome-encapsulated ciprofloxacin (150mg/3mL), providing immediate and slow release of ciprofloxacin to the respiratory tract and allowing once daily inhalation. In the double blind ORBIT-3 trial ARD-3150 was investigated in NCFBE patients with chronic lung infections with *Pseudomonas aeruginosa* (PA) (NCT01515007). Treatment with ARD-3150 or placebo consisted of 6 cycles of 28 days on/28 days off treatment, followed by a 28 day open label extension with once-daily ARD-3150 that included a PK sub-study.

Methods: Patients with NCFBE, documented chronic infection with PA, and ≥ 2 pulmonary exacerbations (PEs) requiring treatment with antibiotics in the preceding year, were enrolled (n=278) in ORBIT-3. In the open label extension, nebulized ARD-3150 was administered once-daily for 28 days with intensive PK sampling in 16 patients. In these, blood was collected pre-dose on Day 7, and at 15 min, 30 min, 1 h, 1.5 h, 2 h, 3 h, 4 h, 6 h and 8 h post-dose. Sputum samples were collected pre-dose on Day 7, and 15-30 min, 1-1.5 h, 2-2.5 h, 3-3.5 h, 4-4.5 h, 6-6.5 h, and 8-8.5 h post-dose. If possible, 12-hour samples of sputum and plasma were collected at the study site or at the subject's home. Additionally, sputum and blood samples were collected pre-dose and 2 hours post-dose on Days 8 and 28. Plasma and sputum ciprofloxacin PK parameters were determined using non-compartmental analysis methods. Accumulation of ciprofloxacin in plasma and sputum was evaluated by the ratio of Day 8 and Day 28 pre-dose and 2-hour post-dose concentrations.

Results: There were 223 plasma and 205 sputum concentrations available for ciprofloxacin analysis. After inhalation of ARD-3150, there was an early peak of free ciprofloxacin both in sputum (median $T_{max}=0.8$ h) and plasma (median $T_{max}=1.4$ h), followed by slow elimination. This profile represents the combined effect of immediate availability of free ciprofloxacin and slow release of the liposome-encapsulated ciprofloxacin from ARD-3150. Median sputum ciprofloxacin PK parameters were: $C_{max} = 1,530$, mcg/g; $C_{min} = 70.25$ mcg/g; and $AUC_{0-24} = 11,570$ (h*mcg/g). Median plasma ciprofloxacin PK parameters were: $C_{max}=180.0$ ng/mL; $C_{min}=26.0$ ng/mL; $AUC_{0-24} = 1481$ (h*ng/mL); and $t_{1/2}=9.3$ h. Median sputum C_{max} was 8,500 times greater than plasma C_{max} . There was no systematic trend of further increasing sputum ciprofloxacin concentrations from day 8 to day 28, indicating that high steady state levels were sustained.

Conclusions: Treatment with once-daily inhaled ARD-3150 is associated with high sputum ciprofloxacin concentrations throughout the 24 h dosing interval that are several orders of magnitude higher than plasma concentrations, are achieved early after initiation of treatment and remain above the minimum inhibitory concentration of typical PA strains during the 28-day on-treatment period. Systemic ciprofloxacin concentrations in plasma are at least an order of magnitude lower than plasma concentrations reported in the literature achieved with commonly used therapeutic doses of intravenously or orally administered ciprofloxacin.

C30 [166] Microbiological Results From Two Parallel, Randomized, Double-Blind, Placebo-Controlled Phase III Trials (ORBIT-4 and ORBIT-3) Of The Inhaled Antibiotic ARD-3150 In Patients With Non-Cystic Fibrosis Bronchiectasis And Chronic Pseudomonas aeruginosa Infection

Juergen Froehlich¹; Janice Dahms¹; David Cipolla¹; Donald VanDevanter²; Igor Gonda¹

¹Aradigm Corporation, Hayward, CA, USA; ²Case Western Reserve University School of Medicine, Cleveland, OH, USA

Background: In a Phase II study (ORBIT-2), once-daily inhaled ARD-3150 (liposome-encapsulated ciprofloxacin 150mg/3mL and free ciprofloxacin 60mg/3mL) showed promising clinical and microbiological responses, achieving the primary outcome of significant reduction in sputum *P aeruginosa* (PA) bacterial density in patients with non-cystic fibrosis bronchiectasis (NCFBE) and chronic PA infection. In the 2 identical, multi-national, randomized, double blind, placebo-controlled, phase 3 trials (ORBIT-4, NCT02104245; ORBIT-3, NCT01515007) of ARD-3150 in patients with NCFBE, reduction in sputum PA bacterial density and ciprofloxacin susceptibility were key secondary endpoints. We report these microbiologic results from both trials.

Methods: Patients with NCFBE, chronic infection with PA, and ≥ 2 pulmonary exacerbations (PEs) requiring treatment with antibiotics in the preceding year, were enrolled in either ORBIT-4 (n=304) or ORBIT-3 (n=278). Nebulized ARD-3150 or placebo was administered once-daily for six cycles of 28 days on treatment, separated by 28 days off treatment for a total of 48 weeks. In addition to the efficacy endpoints related to protocol-defined PEs, microbiological endpoints included reduction in colony forming units (CFU) in sputum PA density (\log_{10} CFU/g) and ciprofloxacin minimum inhibitory concentration (MIC) changes from baseline. Individual log changes were analyzed using a general linear model procedure with treatment as factor and stratification factors of sex and previous number of PE as covariates.

Results: ARD-3150 significantly reduced mean (\pm SE) sputum PA density more than placebo on day 28 of the first dosing period by $-1.80 \pm 0.37 \log_{10}$ and -1.87 ± 0.38 CFU/g in ORBIT-4 and Orbit-3, respectively ($p < 0.0001$ for both). With the exception of cycle 3 in ORBIT-3, significant reductions in sputum PA density compared with baseline ($p < 0.05$) were observed at the end of every on-treatment period throughout both trials demonstrating a persistent antipseudomonal effect with ARD-3150, but not with placebo. PA density increased returning to near baseline values during the off-treatment periods. Reductions in PA sputum density with ARD-3150 occurred regardless of susceptibility of PA isolates to ciprofloxacin at baseline or when PA isolates became more resistant (MIC > 4 mcg/mL) on treatment. There was a greater tendency for increasing ciprofloxacin MICs with ARD-3150 vs placebo during the on-treatment periods, and this increase subsided during the off-treatment periods. A small number of patients exhibited the emergence of PA strains with ciprofloxacin MIC ≥ 64 mcg/mL; however, these were often transient.

Conclusion: Cyclical treatment with once-daily inhaled ARD-3150 was associated with a significant reduction in sputum PA density, without attenuation of antibiotic activity, during each treatment cycle over the 48-week trial.

A02 [131] Non tuberculosis Mycobacteria and bronchiectasis among patients who underwent bronchoscopy.

Leonardo Fuks^{1,2}; Shimon Itzhakian^{1,2}; Mordechai R. Kramer^{1,2}

¹Lung institute Rabin medical center, Israel; ²Sackler faculty of medicine. Tel aviv university. Israel

Background and Objective: Several works showed a high prevalence of Non Tuberculosis Mycobacterium (NTM) among patients with bronchiectasis. The prevalence and particularities of the different subtypes of NTM and their connection to different bronchiectatic anatomic sites still need to be understood and researched. In our work we tried to identify those patients, the bronchiectasis localization and what kind of NTM grown from the Broncho alveolar lavage.

Methods: The retrospective study included 390 patients with known bronchiectasis and at least one exacerbation per year who underwent bronchoscopy and Broncho alveolar lavage in our center (Rabin Medical Center). We looked after the cultures positive to NTM and then scrutinized the results and the location of the bronchiectasis in those patients.

Results: 30 from the 390 patients had NTM positive cultures. 20 were females and 10 males. The mean age was 68.3 years old (from 42 to 90). All the patients had idiopathic bronchiectasis. 9 patients had previous history of sinusitis \rhinitis. The vast majority of the patients (18) had Right middle lobe (RML) bronchiectasis. 24 patients had bronchiectasis in more than one lung lobe and only 6 patients had bronchiectasis in one single lobe. 8 patients had mycobacterium Avium complex. 8 had intracellulare. 8 had Simiae. 3 had Fortuitum and 3 had Abscessus. 28 from the 30 patients were treated for their NTM with treatment durations ranging from 4 months to 16 months.

Conclusion: NTM associated to bronchiectasis was prevalent in 7.7% of our patients who underwent bronchiectasis. Most of the patients were female and had multilobular bronchiectasis. They were usually older than 65 year old but there were also Youngers.

Bronchiectasis associated NTM disease can be very symptomatic and associated with exacerbations and if specific data will be available, the better will be the understanding of the disease particularities and our capacity of treat it.

B14 [125] Bronchiectasis phenotypes in a group of french hospitalized patients.

Fabien Gayda¹; Marlene Murriss¹; Aurelie Le Borgne¹; Alain Didier¹

¹*Respiratory Unit. Adult cystic fibrosis Centre, Toulouse, France*

Bronchiectasis is now an increasingly recognized disease of renewed interest. There are few french epidemiological data. The aim of our study was to describe the clinical, functional, microbiological phenotypes and treatments of patients hospitalized for bronchiectasis in a respiratory department. It was a monocentric retrospective study, conducted between July 2012 and July 2015 in a university hospital.

319 patients have been included in the study, with a mean age of 61 years and a mean FEV1 of 72%. Idiopathic bronchiectasis represents the main etiology (31% of the admitted cases), followed by post-infectious 27%, COPD (11%), genetic diseases (10%), immune deficiency (8%), systemic disease (6%), asthma (5%) and others(2%). Hemoptysis was encountered in 16% of the cohort.

32.7% were infected with *Pseudomonas aeruginosa*. Infection with *Pseudomonas aeruginosa* was significantly associated with a more severe disease (dyspnea, FACED score, FEV1, frequency of exacerbations), macrolides and inhaled antibiotic prescriptions. 27% of the all population and 51.5% of the colonized patients received macrolides.

Our results confirmed already published data. Screening the etiology and the clinical phenotype may have a main impact on specific long term treatment.

B08 [151] Economic burden of bronchiectasis: known and unknown

Pieter C Goeminne¹; James D Chalmers²; Roland Diel³; Anna Filonenko⁴; Rebecca Germino⁵; Francisco Hernandez⁶; Fabian Juelich⁷; George M Solomon⁸; Alex Upton⁹; Kamonthip Wichmann⁴; Weiwei Xu⁶

¹*Department of Respiratory Diseases, AZ Nikolaas, Sint-Niklaas, Belgium and Department of Respiratory Diseases, UZ Leuven, Leuven, Belgium;* ²*Scottish Centre for Respiratory Research, University of Dundee, Dundee, United Kingdom;* ³*Institute of Epidemiology, University Hospital Schleswig Holstein, Kiel, Germany;* ⁴*Bayer AG, Berlin, Germany;* ⁵*Bayer US LLC, Whippany, NJ, USA;* ⁶*Pharmerit, Rotterdam, Netherlands;* ⁷*Bayer Vital GmbH, Leverkusen, Germany;* ⁸*University of Alabama at Birmingham, Birmingham, AL, USA;* ⁹*Bayer, Reading, United Kingdom*

Background: Patients with bronchiectasis experience daily respiratory symptoms and episodes of exacerbation, both of which require medical intervention. Given the increasing prevalence and recognition of bronchiectasis in clinical practice, a better understanding of the economic disease burden is needed.

Methods: A systematic search was conducted using Medline, Embase and Cochrane databases to identify publications (1 Jan 2001 to 31 Dec 2016) on the economic burden of bronchiectasis. Papers reporting costs, cost-savings, resource use and societal costs in adults with bronchiectasis were to be included.

Results: Thirty-two relevant publications were identified. Four studies reported mean annual age-adjusted hospitalisation rates for bronchiectasis as the primary diagnosis; rates ranged from 1.8–25.7 per 100,000 population. Six studies, all conducted over the past 15 years, reported increases in hospitalisation rates over time. Mean annual hospitalisation rate per patient ranged from 0.30–1.29 (6 publications). Average length of hospital stay (11 publications) ranged from 2 to 17 days and increased with the annual number of exacerbations, comorbidities and extent of lung damage. Patients with *Pseudomonas aeruginosa* infection had a higher risk of hospitalisation (5 publications) and a longer hospital stay (1 publication) compared with patients without *P. aeruginosa* infection. Mean annual cost ranged from €2,993 (mild disease according to FACED score) to €9999 (severe) and from €3,515 (primary diagnosis) and €4,559 (secondary diagnosis) from two Spanish studies. Two US studies reported the excess costs over controls to be US\$5,681 and US\$2,319.

Conclusions: The current literature is likely to substantially underestimate the true economic burden of bronchiectasis given that most studies were retrospective claims or hospital admissions analyses. In contrast, outpatient burden and costs are largely undocumented but are likely to be considerable as a major part of care is ambulatory. Furthermore, the analyses in the identified publications have methodological limitations such as inaccuracies in coding for bronchiectasis (versus other common respiratory conditions). A more comprehensive assessment of the burden of bronchiectasis is thus warranted to understand its true impact on individuals, healthcare systems and society.

Note regarding authorship: the authors unanimously decided to apply alphabetical order to all authors except the first author.

D11 [211] Assay development and comparison of assays for neutrophil elastase inhibition in sputum from cystic fibrosis patients

Yveline Hamon¹; Brice Korkmaz¹; Sylvain Marchand-Adam¹; Gwen Kennedy²; James Chalmers²; Eric Chevalier³; Odile Sellier-Kessler³; Johann Zimmermann³

¹INSERM U-1100, "Centre d'Etude des Pathologies Respiratoires CEPR" and Université François Rabelais, Tours, France; ²Immunoassay Biomarker Core Laboratory, School of Medicine, Ninewells Hospital & Medical School, Dundee, United Kingdom; ³Polyphor Ltd., Allschwil, Switzerland

Background: Neutrophil elastase (NE) - is a serine protease released by activated neutrophils involved in tissue degradation and inflammation of pulmonary neutrophilic diseases like bronchiectasis and cystic fibrosis (CF). NE levels present in sputum of those patients are considered to reflect the activity in lung tissue.

Objective: The aim of this study was to evaluate the levels of NE in CF sputa and to establish correlations between different assays and laboratories. In addition, the effect of the novel NE inhibitor POL6014, a medium-sized fully synthetic macrocycle, was evaluated in the different NE assays with human CF sputum.

Methods: Patients: CF patients enrolled were between 21-53 years old, the FEV₁ ranged from 28-104% and gender was distributed equally (9 male, 9 female). All patients gave their informed consent.

Sputum collection and processing: Freshly obtained spontaneously expectorated sputum was diluted with phosphate buffered saline (PBS) and the supernatant (also called PBS sputum) was collected by low-speed centrifugation. PBS sputa were stored until analysis at -80°C.

Assays: NE sputum levels were assessed by a standard ELISA, an enzymatic assay using the Fluorescence Resonance Energy Transfer (FRET)-based substrate, and the ProteaseTag[®] technology (ProAxis, Belfast).

Results: PBS sputum could be used in the three assay formats ELISA, FRET and ProteaseTag[®] to assess the NE levels. Different NE levels were found in PBS sputa. Levels of enzymatically active NE measured by the FRET assay were ranging from 0.9 – 32 microgramm/mL. There was a good correlation between NE FRET and NE ELISA ($R^2=0.79$), NE FRET and NE ProteaseTag[®] ($R^2=0.76$). The NE FRET assay was established independently in two laboratories (INSERM U-1100, CEPR, Tours and the Immunoassay Biomarker Core Laboratory at Ninewells Hospital & Medical School, Dundee) and identical frozen PBS sputa were tested in blinded mode. A very good inter-laboratory correlation of results was found ($R^2=0.92$).

In preparation to clinical samples measurements, POL6014 was spiked into PBS sputa to reach approximately 50 and 90% NE inhibition. *Ex-vivo* added POL6014 was able to inhibit NE efficiently in all PBS sputa. The inhibition by POL6014 remained unchanged when PBS sputa were stored for at least three months at -80°C and freeze-thaw cycles were avoided.

Conclusions: ELISA, FRET and ProteaseTag[®] assays are compatible with NE assessment in CF PBS sputa. Appropriate processing and storage conditions for sputum samples from clinical trials were identified. NE activity in PBS sputum is a suitable candidate biomarker to demonstrate NE inhibition by POL6014. These assays could be used in future clinical trials with POL6014 for the treatment of CF patients.

C31 [164] Inhaled Liposomal Ciprofloxacin In Patients With Bronchiectasis And Chronic Pseudomonas Aeruginosa Infection: Results From Two Parallel Phase III Trials (ORBIT-3 and ORBIT-4)

Charles Haworth¹; Adam Wanner²; Juergen Froehlich³; Tanya O'Neal³; Angela Davis⁴; Anne O'Donnell⁵

¹Papworth Hospital NHS Foundation Trust, Cambridge, United Kingdom; ²University of Miami School of Medicine, Miami, FL, USA; ³Aradigm Corporation, Hayward, CA, USA; ⁴Grifols, Research Triangle Park, NC, USA; ⁵Georgetown University, Washington, DC, USA

Background: Chronic airway infection with *Pseudomonas aeruginosa* (PA) in patients with non-cystic fibrosis bronchiectasis (NCFBE) is associated with more frequent pulmonary exacerbations (PEs), hospital admissions, reduced quality of life and higher mortality than in patients without PA infection. ARD-3150 is an inhaled antibiotic containing liposome-encapsulated ciprofloxacin 150mg/3mL and free ciprofloxacin 60mg/3mL which resulted in compelling microbiological and clinical outcomes in a Phase II study (ORBIT-2) of NCFBE patients with chronic PA infection.

Objectives: To evaluate the efficacy and safety of once daily ARD-3150 in 2 identical multi-national, randomized, double blind, placebo-controlled clinical trials (ORBIT-4, NCT02104245; ORBIT-3, NCT01515007).

Methods: 582 patients with NCFBE, chronic infection with PA, and ≥ 2 PEs requiring treatment with antibiotics in the preceding year were enrolled in ORBIT-4 (n=304) and ORBIT-3 (n=278). Nebulized ARD-3150 or placebo were administered once daily for six cycles of 28 days on treatment, separated by 28 days off treatment, for a total of 48 weeks. The key efficacy endpoints were the time to first protocol defined PE and the frequency of all and severe PEs (defined as requiring treatment with intravenous antibiotics and / or hospitalization).

Results: In both, ORBIT-4 and ORBIT-3 treatment with ARD-3150 compared to placebo was associated with an increase of >2 months in the median time to first PE. In ORBIT-4 this result was statistically significant in the log rank test with stratification for sex and prior PEs, while in ORBIT-3 it was not. ORBIT-4 also showed a statistically significant reduction in the frequency of all protocol defined PEs (regardless of whether antibiotic treatment was given) and all severe PEs compared to placebo. In ORBIT-3 the frequency of all and severe PEs was not statistically significantly reduced. Pooled analyses for PEs that required treatment with antibiotics resulted in statistically significant results for the prolongation of the median time to first PE of > 3 months and the reduction of the frequency of all and severe PEs. Pulmonary function tests (FEV1, FVC or DLCO) were not different between the ARD-3150 and placebo groups in each study. The rates of treatment-emergent adverse events (TEAEs) and serious TEAEs were also similar in both treatment groups.

Conclusion: In ORBIT-4, cyclical treatment with ARD-3150 resulted in statistically significant prolongation of the time to first PE and reductions in the annual frequency of all and severe PEs in patients with NCFBE and chronic lung infections with PA. ORBIT-3 did not show significant results for the key PE endpoints. The safety profile between ARD-3150 and placebo was similar.

D23 [100] Chest physiotherapy in European patients with bronchiectasis: Data from EMBARC registry



Beatriz Herrero-Cortina¹; Stefano Aliberti²; Blasi Francesco²; Vendrell Montserrat³; Elborn Stuart⁴; Loebinger Michael⁵; Menendez Rosario⁶; Torres Antoni⁷; Ringshausen Felix⁸; Welte Tobias⁸; Wilson Robert⁵; Chalmers James D⁹; Polverino Eva¹⁰

¹Universidad San Jorge, Zaragoza, Spain; ²Department of Pathophysiology and Transplantation, University of Milan, Cardiothoracic unit and Adult Cystic Fibrosis Center, Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Milan, Italy; ³Respiratory Disease Department, Hospital Trueta, Girona, Spain; ⁴Queen's University of Belfast, Belfast, United Kingdom; ⁵Host Defence Unit, Royal Brompton Hospital, London, United Kingdom; ⁶Respiratory Disease Department Hospital La Fe, Valencia, Spain; ⁷Fundación Clínic, Hospital Clínic de Barcelona, Universitat de Barcelona, IDIBAPS, CIBERES, Barcelona, Spain; ⁸Department of Respiratory Medicine, Hannover Medical School, Member of the German Centre for Lung Research, Hannover, Spain; ⁹College of Medicine, University of Dundee, Ninewells Hospital and Medical School, Dundee, United Kingdom; ¹⁰VHIR Respiratory Disease Department, Hospital Vall'Hebron, Barcelona, Spain

Introduction: Airway clearance is considered a key component of the management of patients with bronchiectasis. Evidence is limited and there is no standardised regimen or approach. We used the European Bronchiectasis Registry to explore the most frequently used treatments.

Methods: Multicentre prospective registry across 23 European Countries.

Results: 5750 patients were enrolled. Median (IQR) age was 68 years (58-75), 58% were female and 18.5% of patients were colonized with *Pseudomonas aeruginosa*. 50.5% of patients reported that they regularly performed chest physiotherapy (as opposed to it being recommended but not performed or only performed during exacerbations). The most popular technique was the active cycle of breathing technique (ACBT), followed by autogenic drainage and postural drainage. Also, chest physiotherapy devices were used by 43% of patients. Figure 1 shows the most popular regimes used. In a logistic regression model, independent predictors of chest physiotherapy were frequency of exacerbations OR 1.08 95% CI 1.04-1.12, $p < 0.0001$, *P. aeruginosa* infection OR 1.80 95% CI 1.46-2.21, $p < 0.0001$, *Haemophilus Influenzae* infection, OR 2.18 95% CI 1.79-2.64, $p < 0.0001$, co-treatment with macrolide OR 1.46 (1.21-1.75), $p < 0.0001$ and co-treatment with an inhaled antibiotic OR 1.76 95% CI 1.33-2.32, $p < 0.0001$. Factors associated with a significantly lower rate of chest physiotherapy use were enrolment from Eastern Europe OR 0.55 95% CI 0.46-0.66, $p < 0.0001$, and co-existing COPD OR 0.73 (0.61-0.88), $p = 0.001$.

Conclusion: Chest physiotherapy is underutilised in European practice, particularly in Eastern Europe and patients with co-existing COPD.

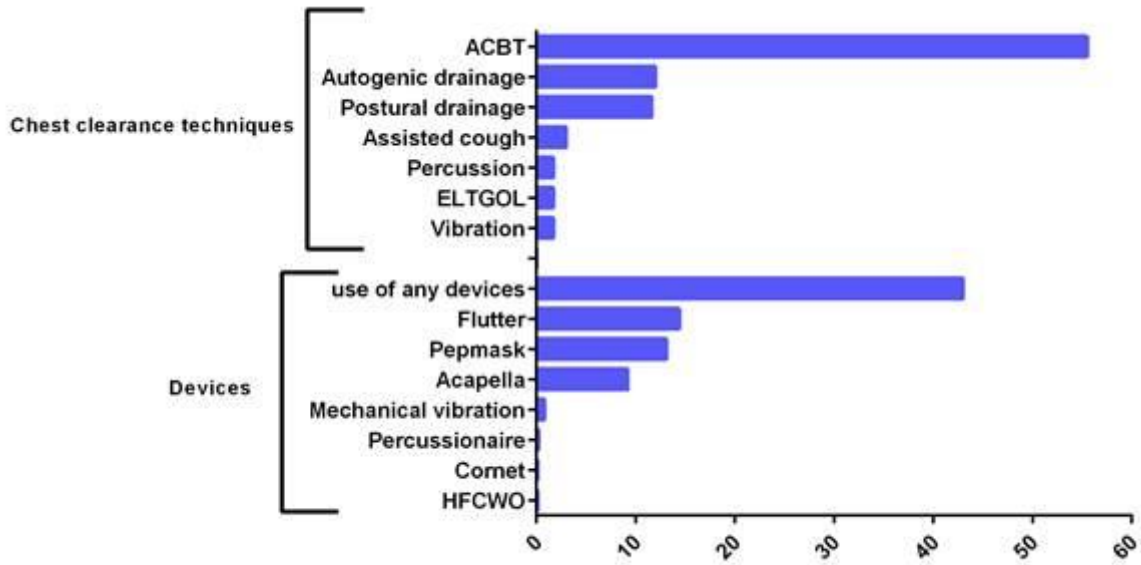


Figure 1. Frequency of airway clearance techniques used in Europe.

This work has received support from the EU/EFPIA Innovative Medicines Initiative Joint Undertaking iABC grant agreement n° 115721.

D25 [143] Effects of a home programme of airway clearance techniques on adventitious respiratory sounds in patients with bronchiectasis: a randomised controlled trial



Beatriz Herrero-Cortina¹; Oscar Membrado¹; Marta San Miguel-Pagola¹; Marina Francín-Gallego¹; Juan Antonio Saez-Pérez¹; Eva Polverino²

¹Universidad San Jorge, Zaragoza, Spain; ²VHIR Respiratory Disease Department, Hospital Vall'Hebron, Barcelona, Spain

Introduction: Computerised adventitious respiratory sounds (ARS), such as crackles and wheezes, have already used to analyse immediate effects of airway clearance techniques (ACTs) in patients with bronchiectasis. However, the use of this objective outcome measure to assess the accumulative effects of ACTs has not evaluated yet.

Design: a pilot, single-blind, randomised and controlled trial with concealed allocation and intention-to-treat analysis was conducted.

Participants: Adult outpatients with bronchiectasis and daily expectoration.

Intervention: The experimental group completed a 3-week home programme comprising ACTs (using an oscillatory positive expiratory pressure device and autogenic drainage technique) and bronchiectasis education. Participants performed at least one session per day (30 min) and received twice therapist-guided sessions per week. The control group completed 3 weeks of bronchiectasis education (once session per week) at home.

Outcome measures: Computerised ARS was registered at baseline (Week 0) and at the end of the programme (Week 3). The primary outcome was a between-group comparison of the change in the mean number of expiratory crackles. Secondary outcomes included: mean number of inspiratory crackles and mean number of wheezes during inspiratory and expiratory phases.

Results: In 12 participants [mean age 60.5(14.1), mean FEV₁ 2.11(0.8)], there was no significant between-group difference on expiratory crackles change, with a median difference of -0.04 (95%CI -1.38 to 1.47) at Week 3. Inspiratory crackles [-0.07 (95%CI -1.4 to 0.84)], inspiratory wheezes [-0.06 (95%CI -0.61 to 1.55)] and expiratory wheezes [-0.62 (95%CI -2.40 to 2.73)] did not show significant differences. The adherence rate was 100% to self-management sessions in the experimental group. No adverse events was observed throughout the study.

Conclusion: A home programme of ACTs does not impact on the ARS (crackles and wheezes). Arguably, a larger sample size is needed to detect any possible difference in ARS.

Trial registration: NCT02324855.

C32 [162] Information provision in bronchiectasis: an evaluation of online resources

Katy Hester^{1,2}; Anthony De Soyza^{1,2}; Tim Rapley¹; Julia Newton¹; Ryan Vicky¹

¹Newcastle University, Newcastle upon Tyne, United Kingdom; ²Adult Bronchiectasis Service, Freeman Hospital, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, United Kingdom

Background: Bronchiectasis causes symptoms including chronic productive cough, dyspnoea, and recurrent respiratory infections often requiring hospital admission. Fatigue and poorer quality of life are also reported. Patients often require multi-modal treatments that can be burdensome, leading to issues with adherence. Optimising self-management and improving training in symptom recognition could lead to measurable improvements in health outcomes. Qualitative work has established the unmet information needs of patients with bronchiectasis and their carers. Based upon this in depth understanding of the experiences and needs of those living with bronchiectasis, a novel information resource, www.bronchiectasis.me was developed. This resource was evaluated by patients, carers and professionals working within a specialist bronchiectasis service during a series of workshops and a feasibility study (Bronchiectasis Information and Education: Feasibility study and evaluation of a novel resource (BRIEF) Study ISRCTN84229105, REC 14/NE/011).

Aims: To report evaluations of the resources used within the BRIEF study and evaluate other available online bronchiectasis resources in keeping with identified user priorities.

Methods: Data from the BRIEF study relating to use or evaluation of the provided educational resource (booklet and online www.bronchiectasis.me) were reviewed. Other available online resources were also evaluated in keeping with the requirements identified by patients and carers within prior qualitative interviews. For the purposes of evaluation within this report, requirements were summarised as follows:-

- Information from a patients perspective
- Users have been involved with production
- Information on prognosis
- Advice on diet and lifestyle
- Advice on self-help and self-management
- Multi format information to include video
- No adverts on the page
- Markers of credibility (e.g. produced by recognised healthcare provider or charity)

Results: We identified 13 readily accessible, English language bronchiectasis patient information websites with a range of content using search engines. The text content ranged from 900 to 13,000 words. The majority did not state that they had been produced with patients. Two were produced by patients with some medical support but without clarity on the level of involvement. Version control and date of updates were not included in all sites but 9/13 were > 12 months since update. 1/13 had video content. 1 had audio content. 4/13 had adverts on the same page. 5/13 had information on the listed key topics, yet volume and clarity of this information varied. 8/13 were produced by a credible healthcare provider or charity. (See table)

Conclusions: Patients in the BRIEF study reported that the resource www.bronchiectasis.me met requirements, was easy to use, and felt their understanding of their condition improved. In comparison to other currently available online resources, this resource met the patients specified needs identified during prior qualitative work and was presented in a style and format that engaged users. It is the only resource with video content easily accessible to patients with bronchiectasis. For resource uptake to

be optimised, potential users' requirements must be established prior to development, and users must be involved in a co-development process. Further work is required to establish impact of such resources on self-management, patient understanding and health outcomes in bronchiectasis.

Resource	Provider	Description	User Co-production	Recognised healthcare provider or trusted charity?	Information in video format?	Adverts or other side sections unrelated to bronchiectasis on the pages	Patient stories	Content Includes self-management, prognosis and diet and lifestyle advice
1. http://www.bronchiectasis.scot.nhs.uk/	NHS Lothian and input from patients with bronchiectasis	Good online information with input from patients (Approximately 3,000 words plus written patient stories). Option to download PDF brochure. Last updated Jan 2015.	Yes. User input during development.	Yes	No	No	Yes	Yes
1. www.bronchiectasis.me	Produced by a multidisciplinary bronchiectasis team and patients and carers based at Newcastle University and Newcastle upon Tyne Hospitals NHS Foundation Trust	Content and format based upon findings of qualitative research with patients and carers. Comprehensive information in text (13,000 words yet all sub-sectioned so small, relevant portions of information visible at a time) plus images and multiple videos. Option to download PDF. Updated and available open access June 2017	Yes. Co-produced with patients and carers and based upon prior research.	Yes	Yes	No	Yes (and videos)	Yes
1. https://www.blf.org.uk/support-for-you/bronchiectasis	British Lung Foundation (BLF)	Online and booklet version available. Quite brief information about bronchiectasis (600 words). (Note this is due to be revised June 2017 to include more comprehensive information based upon the resources used in the BRIEF study (Master et al, 2016))	User reviewers	Yes	No	No	No, but will be in new revision	No (but revision will)
1. http://www.nhs.uk/Conditions/Bronchiectasis/Pages/Diagnosis.aspx	U.K. National Health Service	Online information (3,600 words). Lots of text on the page to scroll through plus extra items alongside. Last updated 2015	Not specified	Yes	No	yes	No	All in brief
1. http://patient.info/health/bronchiectasis-leaflet	Patient (patient and professional information provider)	Online text. Multiple adverts alongside. Includes discussion forum. Last Updated 2014	Not specified	No	No	Yes	No	Prognosis and exercise only
1. http://www.bronchiectasishelp.org.uk/	Written by a patient with bronchiectasis	Patient's perspective with input from professionals. Basic information. Not text-heavy. No Adverts.	Yes	No	No	No	Yes	Yes
1. https://www.nlm.nih.gov/health/health-topics/topics/brn	National Heart Lung and Blood Institute (USA)	Well organised sections. High volume of information and text (4,500 words). No Adverts. Last updated 2014	Not specified	Yes	No	No	No	Not prognosis
1. http://www.bronchiectasis.info/	Run by patients with bronchiectasis	Discussion forum and online community rather than an information resource.	Yes	No	No	No	Forum	no
1. https://en.wikipedia.org/wiki/Bronchiectasis	Wikipedia	Text and Images. Not always considered credible. Last edited April 2017	Not specified	No	No	No	No	no
1. http://medlineplus.gov/ency/article/000144.htm	US National Library of Medicine	Small amount of basic information (670 words). Review date of 2016 listed. Last updated April 2017.	Not specified	Yes	No	No	No	No, very brief
1. http://bestpractice.bmj.com/best-practice/pdf/patient-summary/531907.pdf	British Medical Journal	Concise information (1200 words) no adverts. All text format, no pictorial content. Last updated October 2015.	Not specified	Yes	No	No	No	yes
1. https://www.youtube.com/watch?v=7OOv6t1TYM	BLF online presentation and question and answers with consultant and physiotherapist.	YouTube video of presentation slides and audio. Patient questions and answers. Published 2012.	Not specified	Yes	Yes	Yes (within youtube only)	No	yes
1. http://www.webmd.boots.com/a-to-z-qa/qa/bronchiectasis	Boots, Pharmacy/ WebMD.	Online text information (1300 words). Lots of adverts on the page. Last reviewed July 2015.	Not specified	No (*)	No	Yes	No	no

D24 [155] Development of a Self-Management Action Plan app for bronchiectasis

Oonagh Hewitt¹; Judy Bradley²; Damian Downey¹; Andrew Ennis³; Joseph Rafferty³; Jonathan Synnott³; Christopher Nugent³; Denise Cosgrove⁴; Kathryn McDowell⁴; Brenda O'Neill⁵

¹Regional Respiratory Centre, Belfast Health and Social Care Trust, Belfast, United Kingdom; ²Centre of Experimental Medicine, Queen's University Belfast, Belfast, United Kingdom; ³School of Computing and Maths, University of Ulster, Belfast, United Kingdom; ⁴Northern Ireland Clinical Research Network, Belfast Health and Social Care Trust, Belfast, United Kingdom; ⁵School of Health Sciences, University of Ulster, Belfast, United Kingdom

Background: Self-management action plans support people with bronchiectasis to recognise exacerbations of their symptoms and guide them in the management of exacerbations

Objective: The objective of the project was to develop an action plan in the form of a software 'app' which will offer people with bronchiectasis an alternative to the paper-based plan to support self-reporting and self-management of symptoms.

Methods: The development of the content and format of the app involved an iterative process. The existing paper self-management action plan and the associated health professional guidelines in Northern Ireland were updated/revised. Revisions were informed by the current evidence base and BTS Bronchiectasis guidelines (2010). A software requirements specification was created based on the paper self-management action plan and health professional guidelines. This content was formatted into the app interface and function applied to the content within the app (Figure 1). The development process of the app was responsive and iterative, facilitating rapid feedback from the clinical team as new functionality was added. Distribution and testing of the app by the clinical team was facilitated through publication of the app on the Google Play Store (restricted access). The app then underwent a heuristic evaluation with 6 service users with bronchiectasis, 6 health care professionals (HCP) and an expert reviewer to explore usability, design and functionality.

Results: The app was acceptable, usable and functional from the perspective of service users with bronchiectasis and HCPs (Table 1). Most service users reported they would use the app frequently (n=4/6, 66%) and felt confident using it (n=5/6, 83%). The only service user who was less confident had not previously used smart phone apps. All HCPs would like to use the app frequently (n=6/6, 100%) and the majority thought that most patients would learn to use this app very quickly (n=5/6, 83%). One HCP reported that the age and the type of patient could influence use due to it being complex (n=1/6, 17%). Key amendments resulting from service users, HCPs and the expert reviewer included further aligning the content of the app with current guidelines and recent publications (e.g. aligning the warning signs with the British Thoracic Society Bronchiectasis quality standards' action plan (2012)); ensuring the content of the app was comprehensive (e.g. house hold activities that caused breathlessness were separated into light and vigorous) and ensuring appropriate medical oversight while supporting the patient to self-manage (e.g. ensuring the alerts in the red warning signs section provide correct advice). Other amendments included improvements to the app terminology. This included reducing ambiguity, optimising patient-friendliness and amending the symptoms review section to capture the potential change in symptoms for those patients who do not expectorate sputum when well or those who are unable to expectorate when they are exacerbating.

Conclusion: An Action Plan in the form of a smart phone app has been developed. The app received positive feedback from both service users and HCPs. Further work is in progress to establish if the app can be used in the same way as the paper action plan to monitor symptoms over time and modify

treatments when symptoms worsen. A web-based platform has been developed to enable HCPs to remotely monitor service users' use of the app and currently the functionality and use of this is being explored.

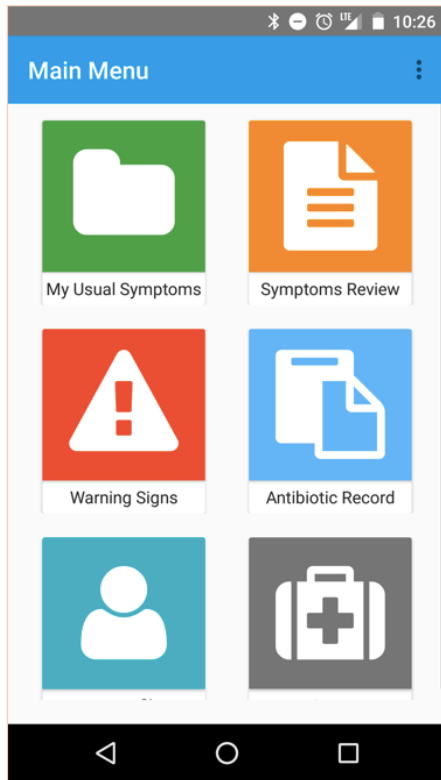


Fig./1: Screenshot of app home screen

Table 1: Service users and Health care professionals feedback

Function Tested	Service users (n=6)	HCP (n=6)
Look/colour	100%	100%
Easy to use	100%	100%
Learn to use very quickly	100%	83%
No support from technical person required	83%	100%
Confident using the app	83%	100%
Not complex	83%	83%
Well integrated/consistent and no significant errors	100%	100%
Would use the app frequently	66%	100%
Had used smart phones apps before	66%	100%

C07 [112] Nebulised gentamicin in bronchiectasis- safety, resistance and compliance data from a large observational cohort

Janice Higginson¹; Helen Groves¹; John Davison¹; Catriona Carmichael¹; Anthony Desoyza^{1,2}; Katherine Walton¹

¹Adult bronchiectasis service Freeman Hospital, Newcastle-Upon-Tyne, United Kingdom; ²Institute of Cellular medicine Newcastle University, Newcastle-Upon-Tyne, United Kingdom

Background: Nebulised antibiotics are recommended by the British Thoracic Society (BTS) for patients with non-cystic fibrosis bronchiectasis experiencing more than three exacerbations per year, especially those colonised with pseudomonas. Murray et al demonstrated a reduction in exacerbations over 12 months of gentamicin treatment in their single blind study which excluded patients with FEV1 <30% or co-existing COPD. Use of nebulised gentamicin remains 'off-label' in the United Kingdom and little real world data is available.

Objective: To assess tolerability and antibiotic resistance over 12 months of nebulised gentamicin treatment in an unselected cohort of non-CF bronchiectasis patients.

Methods: Single centre, prospective audit of nebulised gentamicin 80mg twice daily, prescribed where clinically indicated. Microbiology data were extracted from our lab systems: resistance rates to gentamicin 12 months prior to therapy and during 12 months of initiation were recorded. Respiratory cultures and identification of potential pathogens were performed using the UK standards for microbial investigations in an accredited laboratory; and antimicrobial susceptibility testing by disk susceptibility was carried out in accordance with the European Committee on Antimicrobial Susceptibility testing (EUCAST) method. Systemic breakpoints Pseudomonas R is MIC >4mg L gentamicin and for Enterobacteriaceae (coliforms) R is MIC >1 mg/L. Compliance was checked based on prescription rates and clinic letters and used 80% of prescribed drug to define compliance.

Results: We identified all patients who completed a successful gentamicin trial between 01/06/2014 and 31/12/2016. This gave 48 patients, aged 16-85 (median 63), female 71%, male 21%. Mean FEV1 at baseline was 1.55 litres (range 0.4 -4.0), mean percentage predicted 59.99% (range 17-111). The dominant pathogen in 12 months pre-gentamicin was pseudomonas for 15 patients (31%), haemophilus 10 patients (21%) and no documented pathogen in 11 patients (23%). Before gentamicin treatment 2 patients had one or more isolates resistant to gentamicin (4%), which increased to 6 patients in the 12 months following treatment (12%). In patients with positive sputum microbiology the pre-treatment gentamicin resistance was 5% and 29% post treatment. In the 12 months pre gentamicin trial 77% had positive sputum culture and this fell to 46% of patients had positive sputum samples in the 12 months after the gentamicin was initiated. Compliance data is incomplete but indicated that less than 50% of prescriptions were collected over a year.

Conclusion: Nebulised gentamicin was well tolerated acutely in this cohort with wide range of age and FEV1. Gentamicin resistance, as measured by systemic break points, did rise after gentamicin treatment but the absolute numbers remained low. These break points are likely many times lower than drug concentrations in the airways. The percentage of patients with positive sputum culture decreased after treatment suggesting an effect on bacterial load (or eradication). Nebulised gentamicin seems to have a therapeutic role in bronchiectasis patients but compliance and long term tolerability remains a challenge.

A03 [22] MYCOBACTERIES OTHER THAN MYCOBACTERIUM TUBERCULOSIS ISOLATED at the Tshikaji Hospital in Kananga / DR Congo

Jean Paul Ilunga Mulaja¹

¹*ONG Equilibre International, Kananga, Democratic Republic of Congo*

Context: The considerable increase in lung infections due to tuberculous bacilli other than tuberculosis complexes poses a real public health problem. Their strong responsibility in various human pathologies such as tuberculosis-like lung infections, extrapulmonary infections or those disseminated especially in immunocompromised patients deserves special attention.

Objective: Identify the Mycobacterium tuberculosis complex and other isolates using the DNA-STRIP molecular assay.

Methods: We carried out a study of 208 samples collected between January 2011 and June 2012. The samples received were decontaminated by the N acetyl cysteine sodium method and then seeded on automated liquid media and lowenstein Jensen. DNA extraction on the positive cultures obtained was performed by the chloroform method prior to identification with the mycobacterium CM genotype kit and by Maldi-TOF mass spectrometry.

Results: Our study population comprised 59.7% males and 39.5% females for an age range of 11 months to 87 years. New cases accounted for 93%, reprocessing (4%), relapse (1%), and mostly from services such as internal medicine, pneumology and pediatrics. Positive cultures for atypical mycobacteria accounted for 25.4% of the total crop versus 74.5% for mycobacteria of the tuberculosis complex. M.fortuitum was the most isolated atypical mycobacterial species (18.75%), followed by intracellular M. (12.5%). M. gordonae (5.6 per cent); M. abscessus (3.7%); M. intracellular (3.7%) and M. malmoense (1.8%). However, 39% of the atypical mycobacteria isolated could not be identified by the kit Genotype Mycobacterium CM used and by mass spectrometry. Intracellular M. was isolated in two HIV patients, Multi Resistance and aged over 60 years.

Conclusion: The diversity of strains of Mycobacteria isolated from hospitalized patients build a real warning sign of the involvement of these bacilli in certain pulmonary conditions. Their high resistance to antibiotics, combined with the complexity of their clinical presentation, hinders their treatment and consequently the optimal management of patients infected with these bacilli.

B09 [195] Clinical presentation of Japanese patients with Primary Ciliary Dyskinesia: Systematic review and meta-analysis

Atsushi Inaba^{1,2}; Kozo Morimoto³; Masanori Furuhashi^{1,4}; Mahbubur Rahman⁵; Osamu Takahashi⁵; Minako Hijikata¹; Naoto Keicho¹

¹Department of Pathophysiology and Host Defense, The Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Tokyo, Japan; ²Department of Respiratory Medicine, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; ³Fukujuji Hospital, Japan Anti-Tuberculosis Association, Respiratory Disease Center, Tokyo, Japan; ⁴Department of Pathology, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan; ⁵Center for Clinical Epidemiology, St. Luke's International University Graduate School of Public Health, Tokyo, Japan

Background: Diagnosis of primary ciliary dyskinesia (PCD) is not easily made, because PCD has no specific symptoms, clinicians are often unaware of it, and medical facilities for the specific diagnostic tests are limited particularly in non-Western countries.

Objective: The aim of this study is to attempt a systematic review and meta-analysis, and to reveal characteristics of all-reported cases of PCD in Japan.

Methods: We searched databases of MEDLINE, EMBASE, and Japana Centra Revuo Medicina (*Ichushi* in Japanese) for all accessible articles on Japanese patients with PCD, published between 1985 and 2015. Two investigators (A.I. and M.F.) of our team independently extracted the data from the articles and summarized them.

Results: Of 562 accessed, 329 articles including 316 patients (170 men and 146 women) met our eligibility criteria. Therein, information from the same patients was merged. Age at the diagnosis (mean 28.2 ± 22.0 , median 26 [0–83]) was older than in previous reports from other countries. Respiratory symptoms were often recognized in childhood or adolescent period (42.1%). The patients had family history of PCD in 6.6%, parents with consanguineous marriage 5.1%, history of tuberculosis 2.5%, and nontuberculous mycobacterial infection 0.9%. These proportions appeared to be higher than those in the general population, whereas otitis media and congenital heart disease were not frequently observed. Pulmonary function tests showed the obstructive (FEV1% $63.3 \pm 15.0\%$, median 65% [25–91%]) and restrictive (%VC $71.3 \pm 22.5\%$, median 65% [26–120%]) patterns, consistent with other reports. Sputum tests identified *Pseudomonas aeruginosa* most frequently. In 231 (73.1%) patients, electron microscopy (EM) had been used for confirmation of the diagnosis: 217 were tested only one time and 14 two times from different biopsy sites. 85 (26.9%) were diagnosed without specific tests. Although ultrastructural abnormalities of cilia from nasal and bronchial mucosae were similar, those of sperm were often inconsistent with findings obtained from airway cilia. In most of the PCD reports on EM findings, outer dynein arm (ODA) defects are more frequently observed than inner dynein arm (IDA) defects. In our review of Japanese PCD patients, however, IDA defects were more frequently reported than ODA defects (63 [29.4%] versus 14 [6.54%] respectively), and the combination of IDA and ODA defects were seen in 57 patients [26.6%]. Immunofluorescence (IF) tests and high-speed video microscopy (HSVM) were not performed in these reports, and genetic tests have rarely been done thus far.

Conclusions: Diagnosis of PCD is often delayed in Japan, and pediatric patients with otitis media, congenital heart disease, or other symptoms should be diagnosed in the earlier stage. We should also be aware of PCD as an infrequent cause of mycobacterium and *P. aeruginosa* infection. The reason for high frequency of IDA defect on EM should be investigated carefully. We should establish accurate and efficient PCD diagnostic system together with our own genetic database.

C33 [152] Non CF-bronchiectasis: Etiology, clinical, radiological and microbiological profile of patients presented in outpatient pulmonary clinic of a tertiary care center of Pakistan

Muhammad Irfan¹; Nousheen Iqbal¹; Kauser Jabeen²; Afshan Yasin¹; Ali Bin Sarwar Zubairi¹

¹Section of Pulmonary & Critical Care Medicine, Department of Medicine, Aga Khan University, Karachi, Pakistan; ²Department of Pathology & Microbiology, Aga Khan University, Karachi, Pakistan

Background: Non-Cystic Fibrosis (CF) bronchiectasis is very common in developing countries where tuberculosis is endemic. Little attention has been paid to the investigation of its etiology, clinical, radiological and microbiological profile. No data is available from the developing country like Pakistan.

Objective: To evaluate the clinical characteristics, etiology, radiological features and microbiological profile of Non CF-bronchiectasis patients presented in outpatient pulmonary clinic of tertiary care center of Pakistan.

Methods : It was an observational study from May 2015 to January 2017 in outpatient pulmonology clinics at Aga Khan University, Karachi-Pakistan. Patient's medical records with a principle diagnosis of bronchiectasis were reviewed and those who fulfill the radiological criteria were included. Clinical characteristics, etiology, radiological findings, spirometry and microbiological data were recorded in a preformed performa.

Results: Out of 250 records reviewed, 84 patients fulfill the criteria and were included. The mean age was 50.26± 19.9 years and 43 (51.1%) were females. Majority (>50%) have duration of illness of more than 5 years The commonest underlying cause of non-CF bronchiectasis was post tuberculosis (TB) in 46(54.76%) followed by allergic bronchopulmonary aspergillosis (ABPA) 12(14.28%). On HRCT bilateral extensive disease were present in 56 (66.7%) patients. The commonest organism identified was *Pseudomonas aeruginosa* in 34(40.4%) followed by *Hemophilus influenzae* 15(17.8%) and *Staphylococcus aureus* 5(6%). The most common complications were pneumonia 40(47.6%) and hemoptysis 9(11%).

Conclusion: Post TB bronchiectasis is the commonest form of non-CF bronchiectasis in our population with high burden of *Pseudomonas* infection and extensive disease. Further multicenter prospective studies are need for better understanding of the disease.

A04 [168] Clinical characteristics, radiological pattern and spectrum of non-tuberculous Mycobacterium in patients with non-cystic fibrosis bronchiectasis at a tertiary care center, Pakistan

Kauser Jabeen¹; Muhammad Irfan²; Joveria Farooqi¹; Nousheen Iqbal²; Safia Awan²; Rumina Hasan¹

¹Department of Pathology and Laboratory Medicine, Aga Khan University, Karachi, Pakistan; ²Section of Pulmonary & Critical Care Medicine, Department of Medicine, Aga Khan University, Karachi, Pakistan

Background: During the past decades, there is a growing interest in evaluating nontuberculous mycobacteria (NTM) in patients with non-cystic fibrosis (CF) bronchiectasis. Limited data is available on pulmonary NTM infections from developing countries in this group of patients.

Objective: We aimed at describing the clinical characteristics, radiological pattern and spectrum of NTM in patients with non CF-bronchiectasis.

Methods: An observational study was conducted from January 2013 to January 2017 at Aga Khan University Hospital, Karachi Pakistan. Bronchiectasis patients with clinically significant culture positive NTM infection were included.

Results: 23 patients with clinically significant NTM infection were identified. There were 16 (69.5%) male with mean age of 39.04 ± 21.63 years. Most common cause of bronchiectasis was previous tuberculosis. Two third of the patients have bilateral bronchiectasis on imaging. AFB smear was positive in 14 (60.8%). Most commonly isolated species was *Mycobacterium kansasii* 9 (39.13%) followed by *Mycobacterium avium* complex (MAC) 6 (26.08 %) and *Mycobacterium fortuitum* 2 (8.69%).

Conclusion: NTM infection seems to be a frequent event in bronchiectasis patients in our setting. Most common organism is *Mycobacterium kansasii* in our population. High clinical suspicion and good diagnostic facilities are required for proper diagnosis. Further multicenter prospective studies are need for better understanding of the disease spectrum.

C08 [147] Spectrum and resistance pattern of bacteria isolated from respiratory specimens in adult patients with acute exacerbation of bronchiectasis

Kauser Jabeen¹; Muhammad Irfan²; Joveria Farooqi¹; Nousheen Iqbal²; Rumina Hasan¹

¹Department of Pathology and Laboratory Medicine, Aga Khan University, Karachi, Pakistan; ²Section of Pulmonary & Critical Care Medicine, Department of Medicine, Aga Khan University, Karachi, Pakistan

Background: Bronchiectasis unrelated to cystic fibrosis (CF) is increasingly being recognized as a chronic respiratory illness in developing countries. Patients with bronchiectasis present with frequent respiratory infections and exacerbation of their illness. In such patients presence of certain bacteria has been associated with severe disease and frequent exacerbations. No data exists from Pakistan regarding the spectrum or antimicrobial resistance in bacteria isolated from the bronchiectasis patient population during an episode of exacerbation.

Objective: To study the bacterial agents as well as their antimicrobial resistance yielded from respiratory specimens of adult patients with acute exacerbation of non CF bronchiectasis presenting to Aga Khan University (AKU), Karachi, Pakistan.

Methods: This cross sectional study was performed from 2015-2016. List of respiratory specimens submitted from adult patients with acute exacerbation of non CF bronchiectasis presenting to AKU pulmonology clinics was identified from AKU laboratory database. Microbial cultures were performed in the AKU Laboratory that is accredited with the College of American Pathologists (CAP). All specimens were processed and reported using CAP standards. Susceptibility testing was performed and interpreted using Clinical Laboratory Standard Institute criteria.

Results: Positive respiratory specimens (total 100 from 67 patients) with acute exacerbation of bronchiectasis were evaluated. These specimens included; sputum (n=90), tracheal aspirate (n=5) and bronchoalveolar lavage (n=5). The most frequent organisms were *Pseudomonas aeruginosa* (n=57) followed by *Hemophilus influenzae* and *Hemophilus parainfluenzae* (n=22), *Streptococcus pneumoniae* (n=11) and *Klebsiella pneumoniae* (n=10). Proportion of *Pseudomonas aeruginosa* strains that were either resistant or showed intermediate resistance to antipseudomonal antibiotics was high; 24% against ciprofloxacin, 18% against cefipime, 14% against ceftazidime and gentamicin, 11% against amikacin, 10% against imipenem and 3.5% against piperacillin tazobactam. In *Hemophilus influenzae* 73% isolates were resistant to cotrimoxazole, 55% to ciprofloxacin and 22% to ampicillin.

Conclusion: *Pseudomonas aeruginosa* was the commonest organism isolated from our patients with non CF bronchiectasis during exacerbation. The high resistance against antipseudomonal 3rd generation cephalosporin and ciprofloxacin is a concern. Multicenter country wide study with large sample size is needed to further evaluate the bacterial etiology and resistance pattern in this population of patients.

D12 [59] Hypohidrotic ectodermal dysplasia syndrome : A rare cause of bronchiectasis

Maria Kaponi¹; Serafeim Chrysikos¹; Georgios Drivas¹; Konstantina Deskata¹; Myrsini Melachroinou¹; Katerina Dimakou¹

¹5th Pulmonary Department, "Sotiria" Chest Hospital, Athens, Greece

Background: HED syndrome is a rare congenital disease that affects several ectodermal structures, usually transmitted as a X-linked recessive trait and with a prevalence between 1:10000 and 1:100000. Manifestations of the disease usually involve teeth, skin, hair, nails and sweat glands.

Objective: Presentation of a case of bronchiectasis in a patient diagnosed with HED syndrome in infancy and then experiencing respiratory infections.

Methods: A 35-year-old man was admitted to our hospital complaining of chronic productive cough, pyrexia and malaise since the last two years. HED syndrome was diagnosed in childhood due to abnormal sweat production and facial characteristics. A long history of upper and lower airways infections was recorded.

Results: Physical examination revealed facial malformation, dry skin, finger clubbing and rhonchi. HRCT showed bilateral cylindrical bronchiectasis and tree-in bud lesions. Immunoglobulins were normal. The patient underwent bronchoscopy with purulent secretions that yielded *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Staphylococcus aureus* multisensitive. Ziehl-Neelsen stain was negative. The patient received ciprofloxacin for 15 days. Subsequent sputum cultures yielded the same pathogens, so he was prescribed inhaled colistin as eradication treatment. Clinical and radiological improvement was achieved after three months of therapy.

Conclusions: While infections have been reported at increased incidence in HED, most forms do not impact the immune system, with the exception of HED with immunodeficiency. Otherwise patients' susceptibility to respiratory infections and bronchiectasis, as it was in our case, may be related to abnormal epithelial barrier or mucus production.

D13 [197] Investigation into the intra- and inter- individual variation of total and active neutrophil elastase (NE) in sputum from patients with cystic fibrosis (CF) and non-cystic fibrosis bronchiectasis (NCFB) over 14 days.

Holly Keir¹; Megan Crichton¹; Philip Barth²; Eric Chevalier²; Gayle Scott¹; Gill Grady¹; Johann Zimmerman²; Piet LB Bruijnzeel²; Alison J Dicker¹; James Chalmers¹

¹University of Dundee, Dundee, United Kingdom; ²Polyphor AG, Basel, Switzerland

Introduction: NE inhibitors are currently in development for the treatment of patients with CF, NCFB and chronic obstructive pulmonary disease (COPD). NE activity and total protein levels in sputum samples may be used as a biomarker or may be used as an endpoint to demonstrate effectiveness of inhibitors.

Methods: intra- and inter individual variation of total and active NE levels in induced sputum from patients with CF or NCFB were monitored over a period of 14 days. Patients with established CF and NCFB (n=5 per group) were recruited. Induced sputum was collected on days 1, 3, 5, 7 and 14. Sputum handling after collection was fully standardised and under optimal conditions for elastase measurement. Sputum elastase was measured using three different methods: a total elastase ELISA, an activity based immunoassay from ProAxis Ltd and a FRET-based assay.

Results: All three assays showed a high day to day variability. The within subject coefficient of variation and the standard deviation of the measured NE sputum elastase levels was around 50% with a standard deviation between 20-60. Individual subjects showed co-efficient of variation ranging from 17-111% (total elastase ELISA), 0-223% (FRET) and 32-94% (Protease-TAG). Use of 24h sputum collection rather than single time point induced sputum did not reduce variability. Mean active sputum elastase levels in CF patients were generally higher than those in NCFB patients.

Active elastase measures by FRET and Protease Tag assay were correlated ($r=0.9, p<0.0001$).

Conclusion: Active elastase measurements in induced sputum of CF and NCFB patients are feasible but show a large inter-day and inter-individual variance. Such a variance should be taken into consideration when using sputum elastase as a biomarker or as a readout for testing NE-inhibition in clinical trials.

D14 [198] Neutrophil elastase inhibitors prevent neutrophil extracellular trap formation but do not reduce priming or phagocytic dysfunction in bronchiectasis and cystic fibrosis neutrophils

Holly R Keir¹; Megan Crichton¹; Philip Barth²; Eric Chevalier²; Gayle Scott¹; Gill Brady¹; Johann Zimmerman²; Piet LB Bruijnzeel²; Dicker Alison J¹; James Chalmers¹

¹University of Dundee, Dundee, United Kingdom; ²Polyphor AG, Basel, Switzerland

Background: Neutrophil elastase inhibitors (NEi) are currently in development for the treatment of patients with cystic fibrosis (CF), non-cystic fibrosis bronchiectasis(NCFB) and chronic obstructive pulmonary disease (COPD). Neutrophils from these disease have been shown to have phagocytic dysfunction and are primed to undergo neutrophil extracellular trap formation. NET formation requires intracellular activity of NE. While the ability of NEi to inhibit extracellular elastase activity in chronic lung disease has been demonstrated, their ability to impact NET formation and neutrophil priming have not been reported.

Methods: Induced sputum samples were collected from either CF or NCFB patients (n=5 per group). Neutrophils were isolated from peripheral blood and sputum. Autologous sputum (with and without NEi) was used to prime neutrophils followed by exposure to *P. aeruginosa* (for phagocytosis), or PMA (to stimulate NET formation). Neutrophil surface expression of CD11b, CD88, CD62L and CD35, neutrophil phagocytosis of FITC-labelled E-Coli, neutrophil apoptosis (caspase-3 staining) and NET formation were tested

Results: Increased neutrophil elastase in sputum was associated with reduced neutrophil phagocytosis of *P. aeruginosa* ex-vivo (p=0.008). BE and CF sputum primed neutrophils to undergo NET formation (p=0.01), suppressed neutrophil phagocytosis (p=0.02) and upregulated CD11b, a marker of neutrophil activation. NEi added during sputum exposure prevented surface cleavage of CD88 but did not reverse priming for NET formation or improve phagocytosis.

In contrast, NEi added for 4 hours during induction of NET formation with sputum or PMA prevented DNA and histone-elastase release independent of priming.

Conclusion: NEi prevent NET formation and surface CD88 receptor cleavage induced by BE and CF sputum,

C09 [182] Overtime diversity of *Pseudomonas aeruginosa* isolates from chronic non-cystic fibrosis bronchiectasis patients.

Daniela Lazzara¹; António Carlos Ferreira²; Miguel Soares³; Manuela Ribeiro¹; Adelina Amorim⁴

¹Clinical Pathology Department, São João Hospital Centre, Porto, Portugal; ²Laboratory of Support to Research in Molecular Medicine, Department of Biomedicine, Faculty of Medicine of the University of Porto, Porto, Portugal; ³Department of Biomedicine, Unit of Experimental Biology, Faculty of Medicine of the University of Porto, Porto, Portugal; ⁴Pulmonology Department, Faculty of Medicine of the University of Porto, Porto, Portugal

Background: The importance of chronic infection by *P. aeruginosa* in non-cystic fibrosis (CF) patients is well recognized but little is known about the diversity of sequential isolates in the same patient.

Objective: The aim of this study was to analyze the diversity of *P. aeruginosa* isolates from chronic non-cystic bronchiectasis patients overtime, using a molecular method.

Materials and Methods: *Pseudomonas aeruginosa* isolates from chronically infected non-CF bronchiectasis adult patients, attending the Bronchiectasis outpatient clinic, were typed.

All the samples collected were incubated during 48 hours in MacConkey agar in capnophilic atmosphere and then identified by Vitek[®] MS System. The susceptibility test was always performed. A PCR assay targeting *P. aeruginosa* species-specific *oprI* and *oprL* genes was performed. Molecular typing of *P. aeruginosa* was carried out by Enterobacterial Repetitive Intergenic Consensus (ERIC)-PCR and similarity analysis was performed by cluster analyses of similarity matrices generated using the unweighted pair group method using arithmetic mean (UPGMA) algorithm employing the Dice coefficient as similarity index.

Results: Thirty-two *P. aeruginosa* isolates cultured from sputum (81.25% mucoid strains) of 12 patients were included. The number of samples per patient vary from two to five. Five patients had identical strains overtime (14 samples) and the other seven had unrelated strains (18 samples) with average interval between them of 129 days (64-182,5): 74 days (31-127) for the identical strains and 179 days (134-647) for the unrelated strains.

The Bronchiectasis Severity Index (BSI) was used to classify the patient disease severity with a median of 11 (range 6-14).

Two patients (1 with unrelated and 1 with identical strains) were under inhaled antibiotic therapy and six (2 with unrelated and 4 with identical strains) with azithromycin.

Antimicrobial therapy was administered five times between the sputum collections in the identical strains group and 20 times (13 times in one patient) in the unrelated group with a median in both groups of 1/patient.

Many factors can contribute to this situation: antimicrobial therapy between the sputum collections, coinfection with different strains, adaptation of the *P. aeruginosa* strain to the patients' lung environment.

Conclusion: These preliminary results showed two different patterns: patients maintaining the same strain overtime and patient with constantly different strains. Although the causal factors for this situation still remain unclear, in the first group the interval between the sputum collection was short which suggest less opportunity of bacteria be influenced by intrinsic and extrinsic factors.

It will be important to include more samples during a longer period of time in order to identify which factors contribute to the appearance of these different chronic infection profiles and how they correlate with clinical outcomes.

B02 [142] Epidemiology and microbiology of Non-CF Bronchiectasis (NCFB) Patients in community based outpatient care

Ana Victoria López-Zertuche Ortiz¹; Ralf Stahlmann²; Felix Ringshausen³; Jessica Rademacher³; Tobias Welte³; Andres de Roux⁴

¹*Cand. med. Charité, Berlin, Germany;* ²*Institut für Klinische Pharmakologie und Toxikologie, Charité, Berlin, Germany;* ³*Medizinische Hochschule Hannover (MHH), Klinik für Pneumologie, Hannover, Germany;* ⁴*Pneumologische Praxis am Schloss Charlottenburg, Berlin, Germany*

Background: Non-cystic fibrosis bronchiectasis is a relevant disorder dealt with by pulmonologist in the outpatient setting. Our study center is a community based doctors office with a focus on respiratory and infectious diseases and part of the german bronchiectasis network (PROGNOSIS). Around 9000 patients with respiratory diseases are treated per year. The purpose of this study was to identify an outpatient cohort with the diagnosis of Non-CF Bronchiectasis. The set of variables are in accordance with the PROGNOSIS Database and have been described elsewhere.

Methods: 50 patients with an established diagnosis of NCFB treated between 2008 and 2017 in our center were included in the database. SPSS was used for data analysis. Demographic, clinical, epidemiological and microbiological data were recorded.

Results: The average age was 66 years (25-96 years), most patients were of german origin (84%) followed by Turkey 8%. The etiologies for the NCFB condition were: 44% idiopathic, 42% post infectious, 10% COPD, 2% immune defect, 2% others. 32% of the Patients had a pulmonary exacerbation within the last 12 months, 26% of these had two or more (6% two, 12% three, 8% four). Of those with a positive sputum microbiology within the last 12 months the isolated pathogens were *Pseudomonas aeruginosa* (PA) 33%, followed by *S. aureus* 11%, *H. influenza* 6%, *Mhoraxella* 6%, *Klebsiella* 6%, *E. coli* 6%. Patients with positive bacteriology for PA had an average FEV1 of 68% predicted (range 57-88%) vs. FEV1 87% pred. The risk for an exacerbation in the previous 12 months was much higher in those with PA (75% vs 10%). Most commonly affected were two lobes 42%, followed by one lobe 36%. Long-acting-beta-2-agonists (LABA) was the most often used long-term-therapy (54%), followed by short-acting-beta-2-agonists (SABA) 52%. 72% of patients received airway clearance therapy. 46% received oral antibiotics within the last 12 months, 10% were treated with inhaled antibiotics.

Conclusion: In a non specialized outpatient setting *P. aeruginosa* is the leading identified pathogen clearly associated with more exacerbations and poorer lung function.

B12 [115] The incidence, clinical features and cost of non-cystic fibrosis bronchiectasis: a multi-center clinical data analysis in China



Yanliang Ma¹; Daishun Liu²; Yingqun Ji³; Xuemei Wei⁴; Dianzhu Pan⁵; Fei Xu⁶; Qingguo Di⁷; Fengming Luo⁹; Jiujin Zhang¹⁰; Guiying Ou¹; Yan Zhang¹; Kaishu Li¹¹; Huijie He¹²; Wanping Wang¹³; Jinfu Xu¹⁴; Jianying Li¹⁵; Dan Zhu¹⁶; Feng Tian¹⁷; Manqi Fan¹⁸; Xiaoju Chen⁸

¹People's Hospital, Peking University, Beijing, China; ²The First People's Hospital of Zunyi City, Guizhou province, Zunyi, China; ³The First Affiliated Hospital of Dalian Medical University, Dalian, China; ⁴Affiliated Hospital of Xinjiang Medical University, Urumqi, China; ⁵The First Affiliated Hospital of Liaoning Medical College, Jinzhou, China; ⁶The First Affiliated Hospital of Nanchang University, Nanchang, China; ⁷Cang Zhou Central Hospital, Cangzhou, China; ⁸Affiliated Hospital of North Sichuan Medical College, Nanchong, China; ⁹West China Hospital of Sichuan University, Chengdu, China; ¹⁰Guangxi Yulin First People's Hospital, Yulin, China; ¹¹Binzhou People's Hospital, Binzhou, China; ¹²The First Affiliated Hospital of Baotou Medical College, Baotou, China; ¹³Changzhi people's Hospital of Shanxi, Changzhi, China; ¹⁴Shanghai Pulmonary Hospital, Shanghai, China; ¹⁵Xi'an Central Hospital, Xian, China; ¹⁶Jinhua Central Hospital of Zhejiang, Jinhua, China; ¹⁷Linyi People's Hospital, Shandong province, Linyi, China; ¹⁸Kunming General Hospital of Chengdu military command, Kunming, China

Background: Bronchiectasis is not an orphan disease in China which is associated with high healthcare system usage. However, little is known about economic burden of bronchiectasis, which may be important to guide the management of bronchiectasis and to allocate resources in healthcare. We undertook a multi-center retrospective cohort study cross China in order to investigate the clinical characteristic and economic burden of bronchiectasis.

Methods: The medical records of adult patients admitted to 18 tertiary hospitals from 2010 to 2014 with a diagnosis related "bronchiectasis" were reviewed retrospectively. Clinical data including the demographics, initial symptoms at admission, duration of symptoms, smoking history, physical examination findings, comorbidity and the use of antibiotics were extracted from the medical records. Length of stay, cost of hospitalization and the outcome at discharge were recorded. Multilevel linear model was used to analyze the risk factors associated with cost using MLwiN software.

Results: From 2010 to 2014, 5,469 subjects with bronchiectasis were identified, and they admitted to the respiratory departments of these 18 hospitals for 5915 times. Patients discharged with a diagnosis of bronchiectasis accounted for 3.13%±1.80% of the total discharged patients with any diagnosis in the same period. There was a preponderance of males (51.92%). 1,435 patients (26.24%) had a history of smoking. Cough (88.51%) and expectoration of purulent sputum (83.86%) were the most common symptoms on admission. COPD was the most common comorbidity disease (23.37%). Cultures of the sputum were done in 2,907 patients, the most frequent microorganisms were *Pseudomonas aeruginosa* isolated from 399 patients. In 2,163 patients, more than 3 lobes were involved according to the report of HRCT. The left upper lobe was the most common site (n=3,302). Most patients (96.04%) were treated with antibiotics, intravenous infusion (n=5,443) and combined therapy of more than 1 antibiotic (n=2,465) was common. The most commonly used antibiotic is cephalosporin (n=1,997), followed by penicillin/beta-lactamase inhibitor (n=1,664). 13 patients died at discharge. The average hospitalization cost was ¥14,828.47, equivalent to €1983.13. The difference of average costs of hospitalization among different hospitals was statistically significant, and other risk factors associated with costs of hospitalization included age at admission (>70 years old vs. <40 years old, OR=1.217, 95%CI 1.077–1.374; >80 years old vs. <40 years old, OR=1.266, 95%CI 1.102–1.455), smoking (≤15 packs/yr vs. non-smokers, OR=1.131, 95%CI 1–1.28), length of stay (OR=1.069, 95%CI

1.055–1.063), cough (without cough vs. cough, OR=0.844, 95%CI 0.74–0.962 and wheeze (without wheeze vs. wheeze OR=0.93, 95%CI 0.877–0.986), presence of *cor pulmonale* (OR=0.916, 95%CI 0.843–0.994), isolation of *Pseudomonas aeruginosa*(OR=1.101, 95%CI 1.026–1.181) and death(OR=1.829, 95%CI 1.136–2.946) .

Conclusions: Bronchiectasis was not a rare disease in china, which caused extensive application of antibiotics and heavy economic burdens. Age, smoking status, symptoms and comorbidity are important factors associated with the costs of hospitalization.

C34 [181] Personalising cardiovascular risk assesement in non cystic fibrosis bronchiectasis patients using a odd ratio table

Luis Magalhaes¹; Nuno Cortesao¹; Joao Neves²

¹Hospital Luz Arrábida, Vila Nova de Gaia, Portugal; ²Centro Hospitalar do Porto, Porto, Portugal

Recently, non cystic fibrosis bronchiectasis (NCFBQ) have been shown to be an independent risk factor for cardiovascular disease. NCFBQ patients are a heterogenous population with a large spectrum of clinical manifestations. We believe that there could be subpopulations with increased cardiovascular risk and that their identification could lead to a more personalized approach. We propose a conceptual idea how to identify these patients quickly during routine consultation using age, FEV1%, a known cardiovascular risk factor on COPD patients, and steady state sputum purulence as a surrogate marker of airway chronic inflammation.

EMBARC data from 81 patients from two northern Portugal centres were evaluated regarding the presence of any cardiovascular disease. 5 patients were excluded by lack of spirometry values. Patients were divided in 3 age groups (<65, >=65-<75 and >=75 yo), 2 FEV1% groups (<50% and >=50%) and 2 steady state sputum characteristics (no sputum/mucoid and mucopurulent/purulent).

An odd ratio (OR) table was obtained, taking as control group patients under 65 yo, FEV1% >=50% and no steady state sputum or mucoid. Depending of a predefined group OR, a colour was set (>= 5.0 - red, 3.0-4.9 - orange, 1.5-2.9 - yellow and 1-1,4 – green).

FEV1%	Age	No Sputum/mucoid	Mucopurulent/Purulent
	>=75	Not available	Not available
<50%	>=65-<75	1.83	3.67
	<65	Not available	1.80
>=50%	>=75	4.71	3.67
	>=65-<75	2.14	11.00
	<65	1.00	11.00

High cardiovascular disease prevalence (red) corresponded to patients with steady state mucopurulent/purulent sputum, FEV1% >= 50% and <65 and >=65-75 yo patients. Age increased risk for cardiovascular disease trough all groups of patients, with the exception of FEV1%>=50 and steady state mucopurulent/purulent sputum. Patients with FEV1%<50% were less likely to have cardiovascular disease comparing to patients with greater FEV1%, adjusting to age and steady state sputum characteristics. Not all groups had sufficient patients to allow OR analysis.

Extrapolation of the results is severely compromise due to a small population study and prevalence/OR statistical analysis. Also, other cardiovascular risk factors were not excluded has confounding factors.

Our results suggest that steady state sputum can be associated with and increased risk of cardiovascular disease. We believe that a survival bias may have resulted in lower OR of cardiovascular disease in patients over 75 yo with steady state mucopurulent/purulent sputum and in patients with FEV1%<50%, independently of sputum characteristics or age.

This is a conceptual idea that would benefit from a greater population with incidence/hazard ratio analysis.

[128] Prevalence of Dynamic Hyperinflation and Aerobic Capacity Assessment in Bronchiectasis Patients



Maria Cecília Maiorano-de Nucci¹; Frederico Fernandes¹; Rodrigo Athanazio¹; João Marcos Salge¹; Rafael Stelmach¹; Alberto Cukier¹

¹*Pulmonary Division, Heart Institute (Incor), Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil*

Background: Bronchiectasis (BCT) is characterized by abnormal and irreversible airway dilatation caused by a wide variety of conditions. Dynamic hyperinflation (DH) is characterized by progressive air trapping, which leads to increased lung volume at end expiration and decreased inspiratory capacity (IC) in situations where there is increased ventilation, such as exercise. The DH is one mechanism for dyspnea and reduced exercise tolerance in patients with expiratory flow limitation such as asthma and COPD. There are no studies evaluating the presence of DH in patients with BCT and there are few studies on the physiology of dyspnea in this population. DH may explain the dyspnea on exertion and decreased exercise capacity in patients with BCT.

Objective: To assess the prevalence of DH in patients with BCT and evaluate the aerobic capacity in this population.

Methods: Patients older than 18 years with BCT confirmed by chest CT scan were included. Patients were evaluated with the mMRC dyspnea scale, spirometry, whole body plethysmography and maximum incremental cardiopulmonary exercise test by bicycle ergometer with IC measurements each 2 minutes. Patients were divided in two groups based on their VO₂ (> or ≤ 20 ml/kg/min)

Results: Population characteristics are shown in table 1. Sixty-three patients were included. In this population, 87% of patients have obstructive lung disease, 1.5% restrictive disorder, 3.1% mixed obstruction-restriction and 7.9% had normal pulmonary function test. The prevalence of DH in this population is 66.6% and the medium maximal oxygen consumption (VO₂ máx) was 18,5 ml/kg/min. Patients with reduced aerobic capacity had lower FEV₁ values and increased air trapping at rest when compared to patients with normal aerobic capacity. There was no statistically significant association between DH and decreased aerobic capacity. Greater degree of dyspnea at the end of the exercise by Borg scale was not associated with worst aerobic capacity.

Conclusions: The prevalence of DH in bronchiectasis is high and the aerobic capacity is reduced in this population. Reduced FEV₁ and air trapping at rest are associated with reduced aerobic capacity.

Sex	22 Male / 41 Female
Age (years)	49 (22-75)
BMI (kg;m ²)	26,1 (13,97-46,2)
FEV1%	54 (25-119)
FEV1/FVC	60 (29-97)
RV/TLC	53 (28-77)
Work (Watts)	85 (24-227)
VO ₂ max%	77 (40-118)
VO ₂ ≤20ml/kg/min	FEV1 1,20 (1,01-1,63) p<0,001
VO ₂ >20ml/kg/min	FEV1 1,70 (1,64-2,11) p<0,001
VO ₂ ≤20ml/kg/min	RV/TLC 55 (48-60) p=0,005
VO ₂ >20ml/kg/min	RV/TLC 47 (41-50) p=0,005

A06 [68] Symptom burden among patients reporting nontuberculous mycobacteria (NTM): Findings from the COPD Foundation Survey

David Mannino¹; Vira Pravosud²; Radmila Choate²; Delia Prieto¹; Elisha Malanga¹; Quan Zhang³; Timothy Aksamit⁴

¹COPD Foundation, Washington, USA; ²University of Kentucky, Lexington, USA; ³Insmmed, Inc, Bridgewater, USA; ⁴Mayo Clinic, Rochester, USA

Background: The burden of symptoms that patients with nontuberculous mycobacterial lung disease (NTMLD) or infection can experience remains underreported. These data may contribute to design future investigations of individuals diagnosed with NTM infection or disease.

Objective: To determine the proportion of NTMLD patients with NTMLD who reported symptoms and quality of life impairments. We also sought to determine the proportion of patients reported being troubled by these symptoms or impairments.

Methods: The COPD Foundation developed the website BronchandNTM360social based on their COPD360 social community. The “Burden of NTM Survey” was developed by the COPD Foundation and posted on the website from September 12, 2016 through January 11, 2017. Respondents were limited to those patients reporting that they had been diagnosed with NTMLD. The survey participants were asked about experiencing twelve symptoms during the past two weeks including cough, cough up blood/phlegm/mucous, fatigue or lack of energy, sleep problems, feelings of sadness or depression related to illness, difficulty in walking 500 meters without stopping, difficulty in interacting with others, difficulty with sensitivity to cold or heat, difficulty with fever, chills, or night sweats, and experiencing body pain. The survey participants were also asked about taking any medication to treat their NTMLD, their age group, gender, residence, duration of living with NTMLD, and experiencing selected comorbidities.

The analysis was carried out using SAS 9.4.

Results: Data were available from 266 individuals reporting an NTMLD diagnosis. The majority (n=250, 95.06%) of respondents were aged 50 or older, of female gender (n=244, 93.1%), had an on-going NTM lung infection (n=190, 73.9%), were living with NTMLD for more than 5 years (n=142, 55.7%). The proportion of respondents reporting symptoms ranged from 35% (loss of appetite) to 81% (cough) for the various symptoms, and the proportion of patients troubled by symptoms often or daily ranged from 22% (fevers, chills) to 61% (fatigue) (Table 1). The Kruskal-Wallis H test indicated that there were no statistically significant differences between the medians of the number of self-reported symptoms neither between women and men ($\chi^2= 1.4436$, $p= 0.2296$) nor between two age groups of less than or equal/more than 50 years old ($\chi^2= 2.9870$, $p= 0.0839$). For the subsample of the U.S. patients only (n=235), statistically significant differences ($\chi^2= 8.7104$, $p= 0.0334$) among the medians of the number of self-reported symptoms were observed among four U.S. regions representing the place of residence. Also, those patients who were from the Midwest had reported a higher mean number of symptoms ($\mu=7.1$), followed by patients from the South region ($\mu=6.8$), the West ($\mu=6.5$), and finally from the Northeast region ($\mu=5.5$).

Conclusions: The findings of this study suggest that there were no significant gender or age differences in the medians for number of self-reported symptoms, whereas statistically significant differences were observed among the U.S. patients from different geographical regions. The symptom burden among patients is high, with many patients reporting symptoms that bother them frequently.

Funding Source: BronchandNTM360social was funded by an unrestricted grant from Insmmed.

Acknowledgement: The NTM survey was developed by the COPD Foundation with input from Amy Leitman and Susan Wisliceny from NTM Info & Research and from Insmmed.

Table 1. The burden of the self-reported symptoms.

# Responded	Symptom during the past 2 weeks	Reporting Any	Troubled Often or Daily
		(% of those who responded)	
251	<i>Cough</i>	80.9	61.0
252	<i>Cough up blood, phlegm, mucous</i>	59.5	45.2
250	<i>Shortness of breath, wheezing or other breathing difficulties</i>	68.8	51.2
249	<i>Fatigue or Lack of Energy</i>	81.1	60.6
247	<i>Loss of appetite</i>	34.8	23.9
246	<i>Sleep problems</i>	61.4	45.9
246	<i>Feelings of sadness or depression related to the illness</i>	55.3	31.3
247	<i>Difficulty in walking 500 meters without stopping</i>	40.5	32.0
245	<i>Difficulty in interacting with others</i>	39.6	26.1
242	<i>Difficulty with sensitivity to cold or heat</i>	64.1	41.3
245	<i>Difficulty with fever, chills, or night sweats</i>	37.6	22.4
243	<i>Experiencing pain in body</i>	49.4	37.0

A05 [99] Medication use as a measure of severity: Findings from the COPD Foundation NTM Social Survey

David Mannino^{1,2}; Vira Pravosud²; Radmila Choate²; Delia Prieto¹; Elisha Malanga¹; Quan Zhang³; Timothy Aksamit⁴

¹COPD Foundation, Washington, USA; ²University of Kentucky, Lexington, USA; ³Insmmed, Inc., Bridgewater, USA; ⁴Mayo Clinic, Rochester, USA

Background: Understanding how nontuberculous mycobacterial lung disease (NTMLD) can affect a patient remains under investigated. The information about the factors which may be associated with the burden of symptoms can be used for future development of interventions for NTMLD patients.

Objective: We hypothesize that among patients who report NTMLD, those currently on medication report a higher symptom burden and quality of life impairment than those not currently on medication.

Methods: The COPD Foundation developed the website BronchandNTM360social based on their COPD360 social community. The “Burden of NTM Survey” was developed by the COPD Foundation and posted on the website from September 12, 2016 through January 11, 2017. The analysis was limited to those patients reporting a diagnosis of NTMLD and compared those not on therapy to those currently on therapy. The survey participants were asked about experiencing different symptoms during the past two weeks (yes/no), taking any medication to treat their NTMLD (yes/no), their gender, duration of living with NTMLD (less than 1 year, 1 to less than 2 years, 2 to 5 years, more than 5 years), experiencing other lung illnesses or infection such as bronchiectasis, COPD/emphysema, cystic fibrosis, or asthma. The survey participants were divided into two age categories (<50 or ≥50).

The analysis was carried out using SAS 9.4. Based on the fact of being on or off medication to treat NTMLD, bivariate analyses, such as Pearson χ^2 tests, were conducted to identify differences in the number of individuals having reported such symptoms as cough, fatigue or lack of energy, sleep problems, feelings of sadness or depression related to illness, difficulty in walking 500 meters without stopping, difficulty in interacting with others. The multivariable logistic regression models were carried out with seven symptoms as separate outcomes of interest, and taking any medication to treat NTMLD as the main predictor.

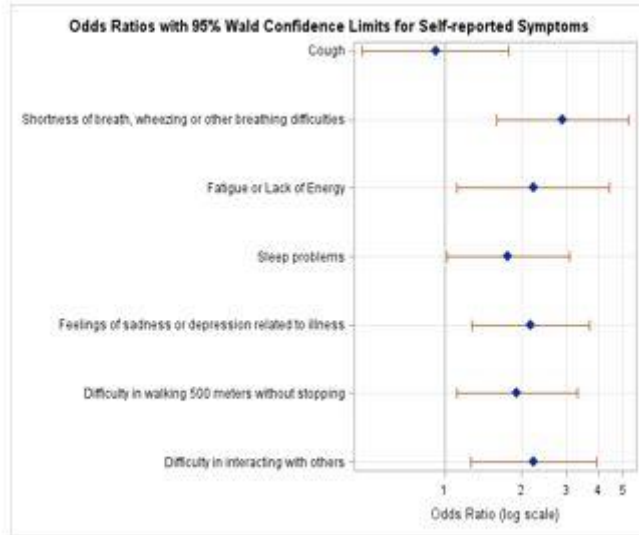
Results: Of the 266 patients reporting NTMLD, 129 were currently on medication and 129 were not on medication (8 did not answer this question). After adjusting for age, gender, duration of living with NTMLD, and comorbidities, patients on medication had statistically significantly larger odds of reporting of shortness of breath, wheezing or other difficulties (OR=2.9, 95% CI: 1.6-5.3), fatigue or lack of energy (OR=2.2, 95% CI: 1.1-4.5), sleep problems (OR=1.8, 95% CI: 1.01-3.1), feelings of sadness or depression related to illness (OR=2.2, 95% CI: 1.3-3.7), difficulty in walking 500 meter without stopping (OR=1.9, 95% CI: 1.1-3.3), and difficulty in interacting with others (OR=2.2, 95% CI: 1.3-3.9), as compared to those who were off medication (Figure 1). Cough was similar in the two groups.

Conclusions: In this database, patient currently on medication reported more symptoms, probably reflecting a higher disease severity among those requiring therapy.

Funding Source: BronchandNTM360social was funded by an unrestricted grant from Insmmed.

Acknowledgement: The NTM survey was developed by the COPD Foundation with input from Amy Leitman and Susan Wisliceny from NTM Info & Research and from Insmmed.

Figure 1. The odds of reporting symptoms when comparing patients on medication to those not on medication, adjusting for covariates.



C10 [183] Impact of chronic bacterial infection in patients with bronchiectasis

Leonor Meira¹; David Araújo¹; Margarida Torres Redondo¹; Daniela Lazzara²; Manuela Ribeiro²; Adelina Amorim^{1,3}

¹Pulmonology Department, Centro Hospitalar São João, Oporto, Portugal; ²Clinical Pathology Department, Centro Hospitalar São João, Oporto, Portugal; ³Faculty of Medicine of University of Porto, Oporto, Portugal

Introduction: Patients with bronchiectasis often have chronic bacterial infections (CBI) which maintain the vicious cycle of inflammation and progressive destruction of the airways. Most published data is based on *Pseudomonas aeruginosa* infection, and there is insufficient knowledge about the importance and impact of CBI by other agents.

Aims: To evaluate the characteristics and disease behaviour in patients with non-CF bronchiectasis, according to the presence of CBI.

Methods: A prospective analysis of adult patients (>18 years old) with non-CF bronchiectasis, confirmed by chest HRCT, followed for at least 1 year in the Bronchiectasis Clinic from a tertiary hospital in Portugal was made. The patients were divided in two groups: with CBI defined as having ≥two positive cultures for potentially pathogenic microorganisms at least 3 months apart in a 12 months period, and without CBI. Their characteristics such as demographic data, lung function, disease behaviour and severity were compared.

Results: 186 patients met the inclusion criteria, with minimum follow up of 12,4 months. Mean age was 54,7 (SD 16,2) years old, age at diagnosis was 41,0 (SD 19) and 60,8% were female. The most common known cause for bronchiectasis was postinfectious (31,7%), followed by primary immune deficiencies (11,3%) and in 30,1% no cause was identified.

BCI was present in 101 patients, with 18 different types of bacteria isolated, mostly *Haemophilus influenza* (33,3%) and *Pseudomonas aeruginosa* (31,1%).

Statistical significant differences were found between groups regarding aetiology ($p=0.021$): in the CBI group idiopathic was more common (39,6% vs. 18,8%) while in non CBI group was postinfectious (35,3% vs. 28,7%), and follow up time ($p=0.003$): 50,0 months in patients with CBI vs. 103,3 months. No differences were found concerning sex ($p=0.621$), age ($p=0.237$), age at diagnosis ($p=0.532$), BMI ($p=0.132$) or smoking habits ($p=0.118$).

The mean Bronchiectasis Severity Index was worse in CBI group (7 vs. 4, $p<0.001$) and according to mMRC scale, significant differences were also found ($p<0.003$), with 23,9% of CBI group presenting a score ≥ 2 .

Daily sputum production (77,2% vs. 56,7%), mean volume (30ml/24h vs. 16ml/24h) and presence of purulent sputum (80,4% vs. 53,9%) was found to be more common in those with CBI ($p=0.002$, $p<0.001$ and $p<0.001$, respectively).

Patients with CBI presented worse lung function: mean FEV1 1.75L, mean FEV1% 68,11% and RV 3.65L comparing to those without CBI: 2.03L, 76.51% and 2.84% ($p=0.049$, $p=0.008$ and $p=0.030$, respectively).

Although a higher tendency for exacerbations during follow up period was found in CBI group, both treated in outpatient or inpatient basis, it didn't reach statistical significance: outpatient 1,29 vs. 1,00 ($p=0.082$) and inpatient 0,36 vs. 0,33 ($p=1.00$).

Conclusion: This study highlights not only the diversity of chronic infection but also the importance of the frequent microbiological evaluation of the sputum, as it can lead to a different treatment approach, such as the eradication of other bacteria besides *Pseudomonas aeruginosa*, considering the impact on symptoms and disease behaviour caused by CBI.

C36 [98] Bronchiectasis and lung cancer: case report.

Maria Aurora Mendes¹; Inês Sanches¹; Eloísa Silva¹; Ivone Pascoal¹

¹Pulmonology Department, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal

Introduction: The relationship between pre-existing bronchiectasis (BE) and lung cancer risk is not well established. Controversy exists regarding the potential role of bronchial and systemic inflammation accompanying BE on lung cancer development.

We present a case of incidental finding of squamous cell lung carcinoma in a patient with extensive BE in the same lobe.

Clinical case: A 51-year-old man, retired (ex-printer), 15-pack-year ex-smoker with history of osteoporosis and depression, was followed in our Pulmonology department since 2004 for chronic obstructive pulmonary disease and post-tuberculosis BE with recurrent respiratory tract infections. He had two prolonged hospital admissions between February and June 2016 due to severe acute exacerbations of BE. During this period, *Pseudomonas aeruginosa* was first identified in repeated sputum cultures and an eradication strategy was adopted with nebulized colistin after a course of intravenous antibiotic therapy. Follow up chest computed tomography (CT; Figure 1) revealed right upper lobe predominant BE with a 40mm densification in the posterior segment, considered a fibroatelectasic area apparently stable comparing with previous chest CT (Figure 2). In October 2016, he presented to the emergency room with a 3 day history of purulent and hemoptoic sputum, fever and right-sided pleuritic chest pain. On pulmonary auscultation significant bilateral bronchospasm was heard. Blood test showed leucocytosis with neutrophilia and mild eosiphilia and elevated C-reactive protein. Chest X-ray revealed a right apical opacity. Empirical intravenous antibiotic and bronchodilator therapy were initiated. No infectious agent was identified on blood or sputum cultures. The clinico-radiological evolution was not satisfactory; despite defervescence and diminution in sputum production and purulence, he maintained a difficult to manage right-sided pleuritic chest pain and right apical opacity on chest X-ray. Bronchoscopy was performed and no endobronchial lesions or microbiological isolates (bacteria, mycobacteria or fungi) were found. However, bronchial aspirate cytology provided incidental evidence of squamous cell carcinoma. Chest CT (Figure 3) confirmed the progression of the lesion previously described, now with 77mm in length. Final staging showed a IIIA squamous cell carcinoma, and the patient was proposed for chemoradiotherapy.

Discussion: Bronchial bacterial colonization, recurrent infections and frequent interaction with other inflammatory comorbidities predispose BE patients to chronic inflammation and epithelial damage that could increase the risk of lung cancer. Despite limited scientific data on this topic, this case reminds us that clinicians should have a high index of clinical and radiological suspicion to a prompt lung cancer diagnosis in BE patients.

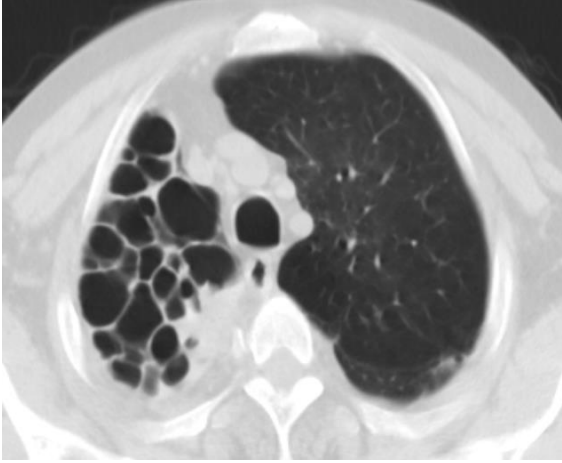


Figure 1



Figure 2

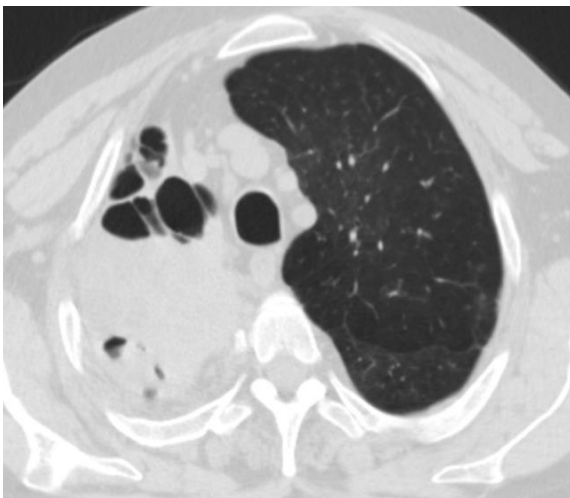


Figure 3

C11 [141] Inhaled antibiotic therapy in non-cystic fibrosis bronchiectasis: does it make the difference?

Maria Aurora Mendes¹; Inês Sanches¹; Regina Monteiro¹; Ivone Pascoal¹

¹*Pulmonology Department, Centro Hospitalar Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal*

Introduction: The majority of the literature on inhaled antibiotic therapy comes from studies on cystic fibrosis (CF). It has been hypothesized that similar outcomes would be seen to manage *Pseudomonas aeruginosa* eradication at first isolation and chronic bronchial infection in patients (pts) with non-CF bronchiectasis (BE).

Aim: To evaluate safety and efficacy of inhaled antibiotic therapy in non-CF BE.

Methods: Retrospective study of pts with non-CF BE that started inhaled antibiotic therapy in our Pulmonology department since December 2012. Among pts who completed one year of therapy, the Wilcoxon Signed-Rank Test was used to compare health outcomes between the year before and after beginning of therapy.

Results: Until March 2017, 16 pts started inhaled antibiotic therapy (8 male, median age 59 years-old, 3 ex-smokers). An etiology of non-CF BE was determined in 10 pts including tuberculosis (4 pts), alfa 1-antitrypsin deficiency (2 pts), chronic obstructive pulmonary disease (2 pts), immunodeficiency (1 pt) and primary ciliary dyskinesia (1 pt). 13 pts started inhaled antibiotic therapy due to chronic bronchial infection (10 pts with *Pseudomonas aeruginosa*) and 3 as an eradication strategy of *Pseudomonas aeruginosa* at first isolation. The inhaled antibiotics used were tobramycin (6 pts), colistin (6 pts), tobramycin and colistin (3 pts) and gentamicin (1 pt). 3 pts died during the therapy period due to causes not related with the inhaled antibiotic. 1 pt suspended tobramycin due to bronchospasm. Other significant adverse events were not reported. Eradication therapy was completed in 2 pts that remained *Pseudomonas*-free at their latest follow up (median 4.5 months). Among 10 pts who completed one year of therapy, the number of exacerbations reduced significantly (median year before vs. year after beginning of therapy: 3 vs. 2; p 0.027). No significant differences were found regarding the number of hospital admissions (median year before vs. year after beginning of therapy: 1 vs. 1; p 0.317), length of hospital stay (median year before vs. year after beginning of therapy: 11 vs. 15 days; p 0.440), forced expiratory volume in 1 second (median year before vs. year after beginning of therapy: 65% vs. 52%; p 0.327) or forced vital capacity (median year before vs. year after beginning of therapy: 79% vs. 67%; p 0.401).

Discussion: In our cohort, one year of inhaled antibiotic therapy significantly reduced the number of non-CF BE exacerbations. There were no significant adverse events. Despite the limited number of pts, our data suggests that inhaled antibiotic therapy could be a valuable and safe alternative to improve outcomes of pts with non-CF BE.

C02 [173] Intravenous Fosfomycin for treatment of pulmonary exacerbations in adult cystic fibrosis with chronic infection by multi-drug resistant *P. aeruginosa* and advanced lung disease.

Barbara Messore¹; Cristina Bena¹; Sara Demichelis¹; Carlotta Biglia¹; Gian Piero Bandelli¹; Giacomo Bonizzoni¹; Elvira Rizza¹; Cinzia Ferrero¹; Fabio Traversa¹; Carlo Albera¹

¹University of Turin, Department of Clinical and Biological Sciences, Interstitial and Rare Lung Disease Unit, Adult Cystic Fibrosis Referral Centre, Turin, Italy

Background: Fosfomycin (F) disodium is a broad spectrum bactericidal antibiotic chemically unrelated to other antimicrobial agent; it has a unique mode of action against *P. Aeruginosa* (PA) and may be efficacious in multidrug-resistant (MDR) pathogens. The concentration of F in lung tissues may be up to 50% of serum level 1 – 2 h after intravenous (IV) administration. F use may be an alternative to aminoglycoside in treating pulmonary exacerbations (PE) protecting patients from renal and ototoxic effects. However there is a little experience about F use in cystic fibrosis (CF) because it has not been licensed in Europe since long time.

Objective: Although F was not licensed for IV treatment in Italy until recently, the Pharmacy of our centre imported it from Japan to treat MDR infections in CF patients; this was allowed by following a standard procedure for off label treatments.

Methods: We report our two years experience (April 2015 – April 2017) with IV F in combination with other IV antibiotics in treating 14 PE in 7 CF patients (3 females, medium age 42.3 years, age range 30-60 years) with severe lung disease (medium FEV1% 35, FEV1% range 25 – 45%, 2 on waiting in active list for lung transplantation, 4 on long term oxygen therapy) with chronic respiratory infection with MDR PA and concomitant *Achromobacter spp.* in 2 patients, *S. Aureus meticillin resistant* in 2 patients, *Proteus mirabilis* in 1 patient only. All patients have pancreatic insufficiency, 2 fed with percutaneous enteral nutrition, 3 affected by insulin-treated diabetes. The median number of antibiotic courses for each patient is 2 (range 1-3).

Results: Patients were treated with IV therapy with F for a total period of 196 days (days/patient: medium, range 14.5, 10–23). F infusion was administered by using a central venous permanent catheter in 3 patients, a midline in 5 patients, a peripheral venous cannula in 4 patients. Average dose was 240 mg/kg (range 200-290) divided in 3 (7 cases) or 4 administrations/day (5 cases).

In all courses F was associated with another IV antibiotic (meropenem in 5 patients, imipenem-cilastatin in 1 patient, tobramycin in 3 patients, piperacillin-tazobactam in 2 patients, linezolid in 1 patient, ceftobiprole in 1 patient and colistin in 1 patient). All antibiotic courses have been administered in hospital, one has been completed at home with territorial nursing surveillance.

Therapy with F was generally well tolerated, with no impairment in renal function; only patient with PEG reported nausea solved with prokinetic and another one had transient asymptomatic elevation in transaminases (3xUNL, in this case F associated with piperacillin-tazobactam), promptly normalized after one week termination. All patients had respiratory and systemic benefit resulting from antibiotic treatment.

Conclusions: In our experience Fosfomycin disodium given IV in combination with other antibiotics for PE in CF patients infected by MDR *P. aeruginosa* (or even other gram negative pathogens) resulted in clinical improvement with a good safety profile.

C12 [192] Dose-finding study to assess the efficacy, safety and tolerability of tobramycin inhalation powder in patients with non-cystic fibrosis bronchiectasis and pulmonary *P. aeruginosa* infection (iBEST-1), ClinicalTrials.gov Identifier: NCT02712983

Loebinger Michael¹; Polverino Eva²; Blasi Francesco³; Elborn Stuart^{1,4}; Chalmers James D⁵; Tiddens Harm A.W.M.⁶; Goossens Hermann⁷; Tunney Michael⁴; Angyalosi Gerhild⁸; Hill Adam⁹; Haworth Charles¹⁰

¹Royal Brompton Hospital Trust, London, United Kingdom; ²Vall Hebron University Hospital, Barcelona, Spain; ³University of Milan, Milan, Italy; ⁴Queen's University Belfast, Belfast, United Kingdom; ⁵University of Dundee, Dundee, United Kingdom; ⁶Erasmus Medical Centrum Rotterdam, Rotterdam, Netherlands; ⁷University Hospital Antwerp, Antwerp, Belgium; ⁸Novartis Pharma AG, Basel, Switzerland; ⁹University of Edinburgh, Edinburgh, United Kingdom; ¹⁰Papworth Hospital Cambridge, London, United Kingdom

Rationale: Patients with bronchiectasis are frequently infected with Gram negative pathogens, in particular *P. aeruginosa*, which is difficult to treat and associated with lung function decline and more frequent pulmonary exacerbations. Several inhaled antibiotics are used in clinical practice as they directly target airway infection and have low systemic side effects; however, none are yet approved for this indication. Tobramycin inhalation powder (TIP) offers the added convenience of inhaler delivery, reducing the treatment time associated with nebulization and cleaning. The objective of this study is to select an efficient dose and regimen of TIP for bronchiectasis patients that is well tolerated. The study protocol has been developed and is executed as part of the in the iABC (inhaled antibiotics for bronchiectasis and cystic fibrosis) IMI project.

Methods: In this multicenter, double-blind, randomized, placebo controlled study, three different daily doses of TIP will be tested in continuous and cyclical regimens. The study protocol includes up to 4 weeks screening, 16 weeks double-blind treatment and 8 weeks of follow-up. Patients ≥18-year-old with confirmed bronchiectasis by CT scan, 2 or more pulmonary exacerbations treated with oral antibiotics or 1 or more pulmonary exacerbations requiring intravenous antibiotic treatment within 12 months prior to screening, and documented *P. aeruginosa* infection are being enrolled.

The primary endpoint is change in *P. aeruginosa* density in sputum from baseline. Key secondary objectives are improvements in clinical outcomes: number of protocol defined pulmonary exacerbations, use of systemic antipseudomonal antibiotics, serum and sputum tobramycin concentrations, patient reported outcomes including QOL-B. Exploratory endpoints include airway inflammatory biomarkers, CT-scans, and lung clearance index.

It is planned to recruit 180 patients from more than 40 centers in 8 European countries.

Conclusions: This phase II study will test three different daily doses and compare continuous versus cyclical treatment regimens, with the aim of selecting the optimal daily dose and regimen to be brought forward into phase III studies involving patients with bronchiectasis and chronic *P. aeruginosa* infection. The study will also inform about the utility of using novel endpoints in bronchiectasis and will contribute to biorepositories of respiratory isolates and sputum samples from patients with bronchiectasis.

Acknowledgements: This work has received support from the EU/EFPIA Innovative Medicines Initiative Joint Undertaking iABC grant agreement n° 115721.

D20 [146] Cystic Fibrosis males with genotype F508del/R75L can be fertile

Peter Middleton^{1,2}

¹Ludwig Engel Centre for Respiratory Research, Westmead Institute for Medical Research, Sydney, Australia; ²Cystic Fibrosis Unit, Department of Respiratory Medicine, Westmead Hospital, Sydney, Australia

Introduction: In men with Cystic Fibrosis (CF), azospermia is almost universally present through failure of the Vas Deferens to develop *in utero*, resulting in Congenital Bilateral Absence of the Vas Deferens (CBAVD). Having typical features of CF without CBAVD is extremely rare, so many clinicians use the presence of normal fertility in males with lung disease as an exclusion criterion for CF. This case of an adult male with mild CF lung disease, on a background of typical genetic and sweat test abnormalities, demonstrates that even the presence of normal sperm counts cannot be used to exclude CF.

Case: The diagnosis of CF was made at newborn screening. A sweat test at age 6 years showed a Cl⁻ concentration of 92 mM, diagnostic cut-off for CF >60mM. Genotype was recorded as F508del/----. The patient was managed through the paediatric CF clinic, where his lung function was always 110-115% predicted. As he resided 6 hours drive from clinic, he was seen on a yearly basis. At age 20 he grew *Staphylococcus aureus* which resolved with a course of oral antibiotics.

On yearly review as a 25 year old, the patient stated that his partner had become pregnant after unprotected sex for less than 6 months. Given the rarity of males with CF being fertile, a series of investigations were then undertaken. Firstly, to confirm the diagnosis, a repeat sweat test showed a chloride concentration of Cl⁻ 115 mM, sweat weight 168mg, typical for CF. Genetic analysis showed both the F508 del and R751L mutations. Lung function remains in the upper normal range, whilst chest CT showed mild small airways disease and borderline upper lobe bronchiectasis. He remains clinically pancreatic sufficient, without need for pancreatic supplements. Semen analysis showed a normal ejaculate volume, normal sperm count and normal sperm motility.

Discussion: This case of CF (F508del/R75L) with typical genetic and diagnostic features of CF yet normal fertility raises a number of important issues. Firstly CF physicians should not inform their male patients that they will be infertile, unless testing confirms azospermia. Furthermore, respiratory physicians outside the CF clinic should be aware that, in a male with bronchiectasis, the presence of children or normal sperm analysis does not exclude the possibility of CF.

A07 [93] NTM in BAL fluid – treat it or not: two cases and literature review

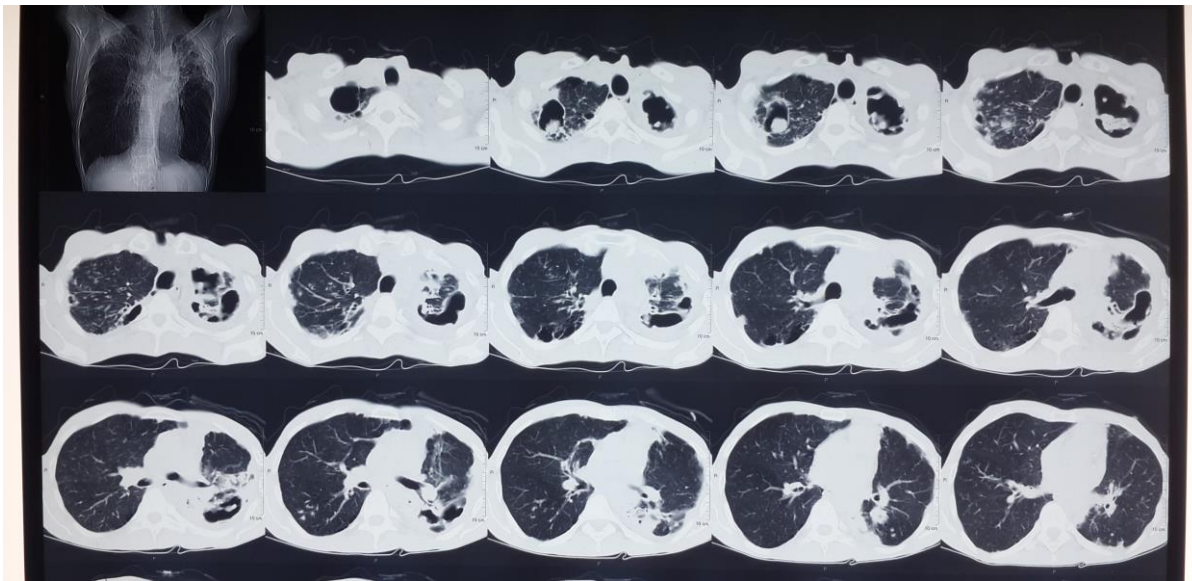
Mayank Mishra¹; Subodh Kumar²

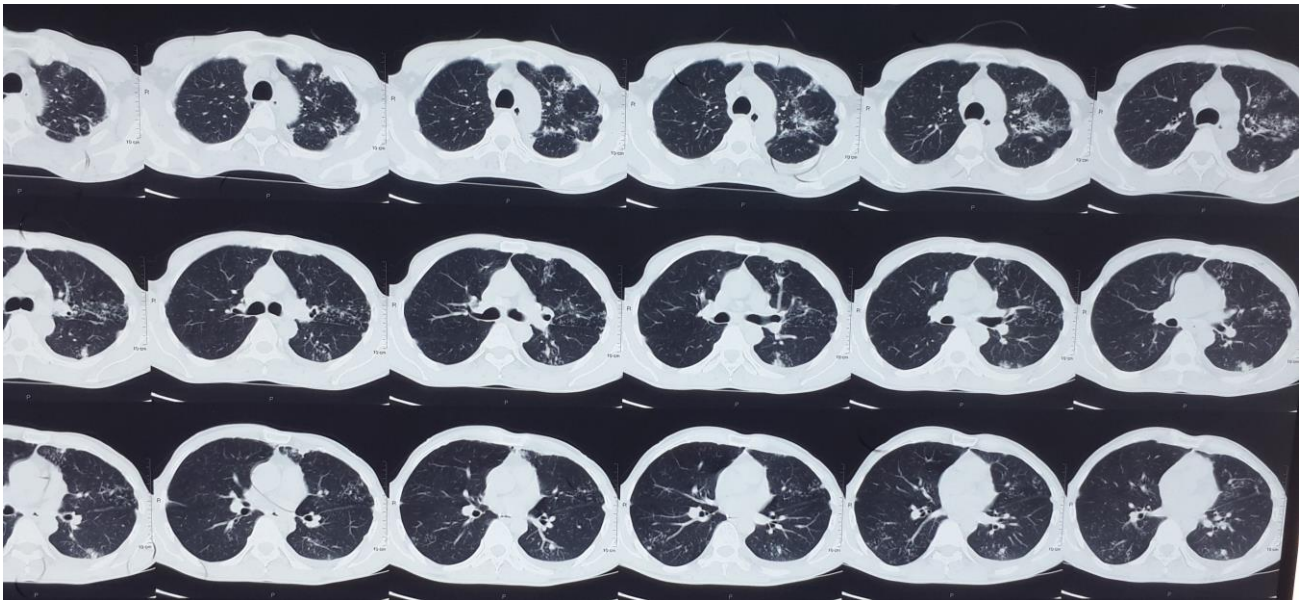
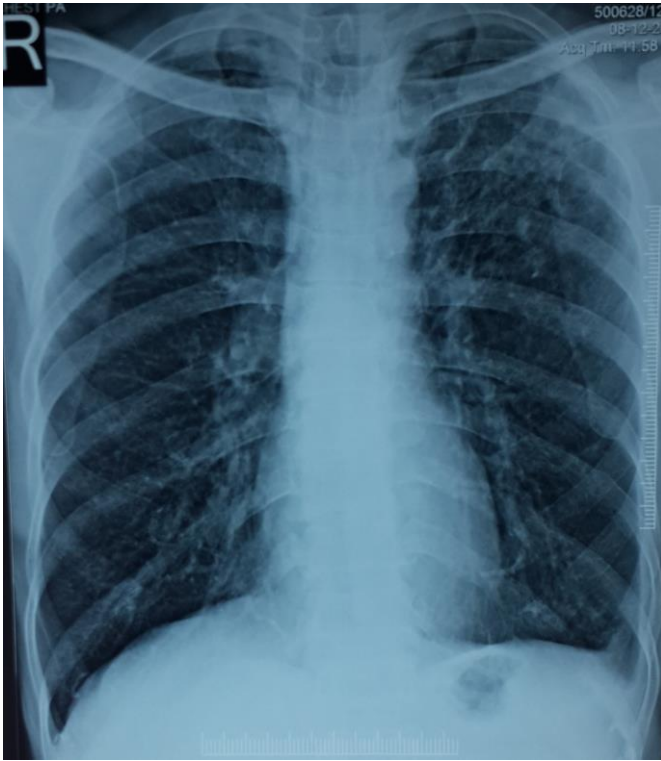
¹Assistant Professor, Department of Pulmonary Medicine, All India Institute of Medical Sciences, Rishikesh, Dehradun, India; ²Assistant Professor (Pulmonologist), Department of Trauma & Emergency, All India Institute of Medical Sciences, Rishikesh, Dehradun, India

Detection of non-tuberculous mycobacteria (NTM) on broncho-alveolar lavage (BAL) fluid analysis is not uncommon, either as a contaminant or as a true pathogen. The procedure is especially useful in cases where sputum production is not possible, inadequate, or inconclusive. Careful judgement about the decision to treat needs to be taken by the treating physician in light of available microbiological evidence in a relevant clinical background, especially in situations where clinical correlation is lacking.

We hereby report cases of two middle-aged unrelated men with a background illness of obstructive airway disease, presenting with prolonged fever and worsening of their baseline symptoms over a few months. Computed tomography revealed a predominantly fibro-cavitary radiographic pattern in one patient while fibro-infiltrative/nodular pattern in the other. Inconclusive sputum results prompted us to perform fiberoptic bronchoscopy and BAL analysis. The BAL fluid was subjected to Ziehl Neelson (ZN) staining and liquid culture and sensitivity testing. On ZN stain, one case had a positive result while the other was negative. However, both cases grew NTM on BAL culture – slow grower *M.chimaera* in one and rapid grower *M.abscessus* in the other. Both patients fulfilled the American Thoracic Society/Infectious Disease Society of America criteria (clinical, radiological and microbiological) for pulmonary NTM diagnosis, and were initiated on multidrug treatment regimen. Six months into the treatment both of them are asymptomatic and currently in our follow-up.

M.chimaera is a recent, infrequently described entity under the *Mycobacterium avium complex* group of slow growing NTMs, while *M.abscessus* is a well-known rapid growing NTM. The cases highlight the importance of BAL analysis in NTM detection, its relevance and interpretation in the correct clinical context, and further provides a short review of the available literature on the subject.





B11 [184] How common are respiratory viruses in the airways of patients with stable bronchiectasis?

Alicia Mitchell¹; Jackson Daniel²; Oliver Brian¹; Morgan Lucy³

¹University of Technology, Sydney, Sydney, Australia; ²Australian Bronchiectasis Registry, Sydney, Australia; ³Concord General Repatriation Hospital, Sydney, Australia

Introduction: Viral infections are accepted as being important precursors to the post-infectious aetiology of bronchiectasis, however information regarding their role in both exacerbations and progression of the underlying condition has been largely absent from the literature. Increased levels of both systemic and airway inflammation lead to recurrent respiratory infections in bronchiectasis patients, and the abundance of pathogenic bacterial species such as *Pseudomonas Aeruginosa* which have been shown to be associated with more severe disease. These conditions would also encourage viral infections. In other diseases such as cystic fibrosis and COPD, respiratory viruses have been commonly identified as causative factors in exacerbation, and play a role in progression of disease. Due to the lack of literature regarding viral presence in bronchiectasis, this study was designed as a pilot analysis to identify the incidence of respiratory virus detection in stable bronchiectasis patients.

Methods: Over a winter and summer season, patients with Bronchiectasis were recruited from an outpatient clinic. Based on physician's assessment of symptoms and spirometry, all patients were deemed to be stable at the time of sampling. A spontaneously expectorated sputum sample was collected for viral analysis. These samples were subjected to an RNA extraction, cDNA synthesis and multiple uniplex PCR assays for a panel of respiratory viruses (Human Rhinovirus (HRV), Respiratory Syncytial Virus (RSV), Influenza A and B, Parainfluenza virus (PIV) 1, 2, 3 and Human Metapneumovirus). All patients have been followed up until May 2017.

Results: A total of 27 patients with a diagnosis of bronchiectasis, were recruited over two distinct seasonal periods. During the winter period (May – September 2014) 12 patients were recruited, while over the summer period (December – March 2017) 15 patients were recruited. In the winter period, 11/12 patients were PCR positive for respiratory viruses, with multiple concurrent viruses being present in the majority of samples. RV, RSV, Influenza A and B were all detected concurrently in sputum in 7/12 patients, with RV and RSV being detected concurrently in 2, and RV and Influenza A detected concurrently in 1. At follow up, all patients were clinically stable with no reports of exacerbation in the month prior to, or after sampling. During the summer period, 5/15 patients were PCR positive for a respiratory virus, all with influenza A. Of these, 1 outpatient-managed exacerbation was recorded within the month following virus detection.

Discussion: In this small cohort of stable patients, respiratory viruses were frequently detected, particularly in the winter. This preliminary analysis suggests that some respiratory viral species may be part of the resident microbiome of the lungs alongside colonising bacterial species. This area requires further, longitudinal studies to characterise the role of respiratory viruses in bronchiectasis.

C13 [76] Bacterial community fingerprinting in a Bronchiectasis cohort

Philip Mitchelmore^{1,2}; Bull Matthew³; Sheldon Christopher¹; Mahenthiralingam Eshwar³; Withers Nicholas¹; Brown Alan⁴

¹Royal Devon & Exeter Hospital, Exeter, United Kingdom; ²University of Exeter Medical School, Exeter, United Kingdom; ³Cardiff University, Cardiff, United Kingdom; ⁴University of Exeter, Exeter, United Kingdom

Background: The complexity of the bacterial community of the bronchiectatic lung is far greater than that revealed by the culture techniques used in standard clinical practise. A rapid and cheap culture-independent bacterial profiling technique could potentially be useful in large research studies, clinical trials and everyday clinical decision making.

Objectives: Ribosomal Intergenic Spacer Analysis (RISA) is a PCR-based community fingerprinting technique commonly used in environmental research. Herein we investigate the utility of RISA when applied to sputum samples from a Non-cystic Fibrosis Bronchiectasis (NCFB) cohort, and compare it to the gold standard culture-independent technique, 16S rRNA sequencing.

Methods: Patients with radiologically-confirmed NCFB were prospectively recruited to donate sputum samples acquired through standard clinical care, with relevant clinical data concurrently collected. An aliquot of each sputum sample underwent independent standard microbiological investigation. In parallel, DNA extraction and RISA was performed on all samples. The PCR products were visualised by microfluidic amplicon separation on an Agilent Bioanalyser. Primary analysis involved cluster analysis and band counting. Bioanalyser-generated values for the number and concentration of visualised bands were used for potential estimates of diversity and evenness. A sub-set of samples is currently undergoing 16S rRNA sequencing analysis.

Results: Ninety-nine patients were recruited. The mean age was 65.5 years old and 64.6% were female. A wide range of disease severity was seen (Bronchiectasis Severity Index (BSI); mean 7.4, range 1-18). *Haemophilus influenzae* and *Pseudomonas aeruginosa* were the most commonly cultured pathogens (22.2% and 19.2% respectively). Overall 43.4% of samples were described as “culture negative”, where no putative bacterial pathogen was reported. RISA fragments were successfully generated from all samples, including culture negative samples.

The number of visualised bands per sample (a marker of richness) varied from 1-12, with a mean of 5.6. Cluster analysis divided the samples into three main groups: (1) had a high proportion of culture negative samples (16/22; 72.7%); (2) had a high proportion of *H. influenzae* culture-positive samples (14/25; 56%); and (3) had no dominant microbiological profile (n=46). Whilst *H. influenzae* culture-positive samples were associated with a characteristic RISA profile, RISA profiles associated with *P. aeruginosa* culture-positive samples were more diverse. Early indications from 16S rRNA sequencing suggests this may be due to *H. influenzae* having a higher relative abundance within samples. Other putative patterns were seen for samples which isolated *Moraxella catarrhalis* or *Stenotrophomonas maltophilia* by traditional culture methods. Cluster analysis did not illustrate a link between disease severity, as measured by the BSI, and community profiles. A positive correlation was however noted between FEV₁%predicted and the number of bands visualised (p=0.039). When compared with culture-positive samples, culture-negative samples had a higher evenness score (p=0.027), consistent with there being less dominance of single species.

Conclusion: Subject to our ongoing validation by 16S rRNA sequencing, RISA provides a cheap and rapid bacterial community profiling output that may have potential as an adjunct to traditional culture techniques. In this cohort, RISA has shown an association between lung function and community richness, highlighting the clinical relevance of community profiling in the bronchiectatic lung.

C37 [167] Bronchiectasis in PCD looks different to CF on CT scan

Lucy Morgan^{1,5}; Tadd Katlyn⁶; Susanto Clarissa¹; Rosenow Tim^{3,7}; Murray Connor^{3,7}; Schultz Andre^{3,7}; Robinson Phil^{2,6}

¹Sydney Medical School, University of Sydney, Sydney, Australia; ²Murdoch Children's Research Institute, Melbourne, Australia; ³School of Paediatrics and Child Health, The University of Western Australia, Perth, Australia; ⁴Department of Paediatrics, University of Melbourne, Melbourne, Australia; ⁵Department of Respiratory Medicine, Concord Hospital, Sydney, Australia; ⁶Departments of Respiratory Medicine, Royal Children's Hospital, Melbourne, Australia; ⁷Telethon Kids Institute, The University of Western Australia, Perth, Australia

Background: Primary Ciliary Dyskinesia (PCD) and Cystic Fibrosis (CF) are both inherited, progressive, incurable, respiratory conditions associated with the development of bronchiectasis. Each has different pathophysiology resulting in recurrent lower respiratory tract infections and plausibly a different pathoradiology. Scoring systems have been developed and validated to monitor the severity and progression of structural lung changes demonstrable on computed tomography (CT) for patients with CF. All studies to date describing lung damage in PCD use these CF-derived tools. We postulate that there may be PCD specific changes and set out to develop a PCD specific scoring system.

Methods: We retrospectively analysed 58 CT scans from 40 adult and paediatric patients with PCD. We used a standardised CF CT scoring system to assess the presence and extent of bronchiectasis, bronchial wall thickening, atelectasis, mucous plugging, and air trapping. In addition, an experienced respiratory radiologist reviewed all scans to look for the presence of any additional radiological abnormalities.

Results: Bronchial wall thickening was the most common abnormality, and air trapping the least common. All abnormalities were present significantly more often in the middle and lower lobes compared to the upper lobes, with all p values <0.001. When present, all abnormalities were significantly more extensive in the middle and lower lobes compared to the upper lobes. Bronchiectasis, mucus plugging, atelectasis (p<0.001) and air trapping (p=0.005) were all present significantly more often in the PCD cohort than the respective CF cohorts. The PCD-unique changes identified were dextrocardia, extensive tree-in-bud patterns, whole lobe atelectasis, and interlobar and interlobular septal thickening.

Table A-C Statistical analyses of findings in PC scans vs CF scans from original Brody and Bhalla descriptions: Multiple X² tests were used to compare parameters and populations. p values less than 0.05 were considered significant.

Table A: Presence of CT abnormalities in Upper vs Middle/Lower lobes in PCD

	Upper lobe changes (n)	Middle-/Lower lobe changes (n)	p value	95% confidence interval
Bronchiectasis	32/58	52/58	<0.001	0.195-0.495
Bronchial wall thickening	40/58	58/58	<0.001	0.191-0.429
Mucous Plugging	25/58	53/58	<0.001	0.336-0.610
Atelectasis	27/58	54/58	<0.001	0.322-0.610
Air trapping	21/52	41/52	<0.001	0.211-0.558

Table B: Extent (when present) of CT abnormalities in Upper vs Middle-Lower lobes in PCD

	Upper lobes with changes (n)	Upper lobes with severe change (n)	Middle-Lower lobes with changes (n)	Middle-Lower lobes with severe change (n)	p value	95% CI
Bronchiectasis	8	49	73	161	<0.001	0.0161-0.419
Bronchial wall thickening	4	70	62	189	<0.001	0.019-0.357
Mucous Plugging	1	35	56	147	<0.001	0.026-0.448
Atelectasis	0	41	44	168	<0.001	0.195-0.328
Air trapping	4	33	31	105	.0450	0.033-0.316

Table C: Presence of CT abnormalities in a PCD cohort vs CF Cohort (Brody*, Bhalla[†])

	PCD with change (n)	scans with any change (n)	Total scans (n)	PCD CF scans with any change (n)	Total scans (n)	CF p value	95% confidence interval
Bronchiectasis	51	58	58	35	60*	<0.001	0.0146-0.446
Bronchial wall thickening	58	58	58	13	14 ⁺	0.040	-0.635-0.206
Mucous Plugging	53	58	58	9	60*	<0.001	0.648-0.879
Atelectasis	55	58	58	2	14 ⁺	<0.001	0.614-0.997
Air trapping	45	52	52	38	60*	0.005	0.088-0.385

Conclusions: Significant structural changes were seen on CT scans in patients with PCD. Many of these changes are outside those describes using the CF specific CT scoring system. Our findings illustrate the need for development of a PCD-specific scoring system, which can function as a tool for the objective assessment of disease status, progression and efficacy of therapy.

B13 [127] Epidemiological Characteristics of Bronchiectasis: Comparison Study of Death Statistics Between Bronchiectasis and Nontuberculous Mycobacterial Pulmonary Disease from 1970 to 2015 in Japan

Kozo Morimoto^{1,2}; Yuka Sasaki¹; Kiyohiko Izumi²; Atsuyuki Kurashima¹; Takashi Yoshiyama¹; Kazuro Iwai²; Naoki Hasegawa³; Gen Goto¹

¹Fukujuji Hospital, Japan Anti-Tuberculosis Association, Tokyo, Japan; ²Research Institute of Tuberculosis, Japan Anti-Tuberculosis Association, Tokyo, Japan; ³Keio University, Tokyo, Japan

Background: Epidemiological characteristics of bronchiectasis (BE), which shows similar radiological presentation to nodular bronchiectatic (NB)-type nontuberculous mycobacterial pulmonary disease (NTM-PD), is unclear in Japan. The prevalence of NB-type NTM-PD is known to be increasing, especially in Asia-Pacific countries including Japan and US. Because BE is frequently complicated with NTM and also shows similar clinical presentation with NB-type NTM-PD, mortality of both diseases is likely to be interrelated. Therefore, comparison of death statistics of BE and NTM would be useful to understand the epidemiological characteristics of BE.

Methods: We analyzed the death statistics of BE (International Classification of Diseases 10th version code of J47) and NTM (A31) from 1970 to 2015 in Japan. The census data were used to analyze the age-adjusted mortality rate and regional differences in the standardized mortality ratio (SMR). The consecutive data for BE death cases in a tertiary hospital in the Tokyo area (Fukujuji Hospital, Japan Anti-Tuberculosis Association) were extracted to determine the history of the cases.

Results: The number of NTM-related deaths has remarkably increased from 3 cases (male, 2; female, 1) in 1970 to 1397 cases (male, 480; female, 917) in 2015. The mortality rates began to rise around the 1990s with female dominance. The age-adjusted mortality rate of NTM-PD among males remained constant since the 2000s, whereas that among females continued to increase during the study period. On the contrary, no remarkable changes were observed in the number of deaths caused by BE during the past 4 decades (1076 and 1021 in 1970 and 2015, respectively). However, these numbers decreased from 663 to 304 deaths among males but increased from 413 to 717 deaths among females. The number of BE deaths among females exceeded that of males around the mid-1990s, when the number of deaths due to NTM among the female remarkably increased. The age-adjusted mortality rate of BE decreased in both sexes, but that for females had started to slightly increase after 2005. Both the number of death and age-adjusted mortality rate of NTM exceeded those of BE among males and females in 2015 for the first time. In terms of regional differences in NTM, the southwestern part of the country displayed consistently higher SMR than the other areas as previously reported. However, no tendency was observed in the SMR of BE. Some prefectures showed similar SMR trends (e.g., both low or high SMR for NTM and BE), but other areas exhibited opposing data for the two diseases (low SMR for NTM but high SMR for BE). A BE death analysis conducted in Fukujuji Hospital demonstrated that approximately 20% of patients who died of BE had a history of NTM.

Conclusions: The epidemiological status of BE in Japan appears to be complicated and could be influenced by the NTM data, especially among females. Further study is desperately needed to comprehensively clarify the real figures of BE in Japan where cystic fibrosis is seldom observed, taking the relationship between BE and NTM-PD into consideration.

D21 [79] Lung Transplantation for Cystic Fibrosis: the Milan experience

Letizia Corinna Morlacchi¹; Valeria Rossetti¹; Sonia Henchi¹; Lorenzo Rosso²; Mario Nosotti²; Maria Pappalettera¹; Paolo Tarsia¹

¹Cardiothoracic Unit and Cystic Fibrosis Adult Centre, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano; Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Milan, Italy; ²U.O. Chirurgia Toracica e dei Trapianti di Polmone, IRCCS Fondazione Ca' Granda Ospedale Maggiore Policlinico di Milano; Università degli Studi di Milano, Milan, Italy

Background: Cystic Fibrosis (CF) currently accounts for almost 15% of lung transplant (LuTx) procedures worldwide and represents the third major diagnosis leading to indication for a LuTx for adults following emphysema and pulmonary fibrosis and the leading indication among paediatric candidates. LuTx is considered an established option for end stage CF patients with a statistically significant difference over all the other indications and a median survival of 8.5 years.

Objective: Aim of this study was to assess the results of our LuTx program for CF patients in terms of graft function and survival.

Methods: A retrospective study was conducted including all LuTx recipients performed in our hospital from January 2004 to December 2016. Two groups of patients were identified: CF and non-CF. Clinical data were collected and analysed. All data were statistically analysed with SPSS version 22 for Macintosh. Descriptive statistics were reported with continuous data expressed as median (IQR) and categorical data expressed as counts. Comparisons were performed using Mann-Whitney test and Chi Square test. Survival rates were measured by the Kaplan Meier estimator and compared with the log-rank test.

Results: A total of 157 primary LuTx were performed; of those, 67 (43%) grafts were allocated to CF recipients. Of note, 4 patients underwent re-transplantation; 2 of them died in the perioperative period, one died after 14 months and one is currently alive at 30 months from re-transplant date. Table 1 summarises our results.

Survival rates are shown in Figure 1. Significantly higher survival was observed for CF patients compared to those with other indication for LuTx ($p = 0.001$).

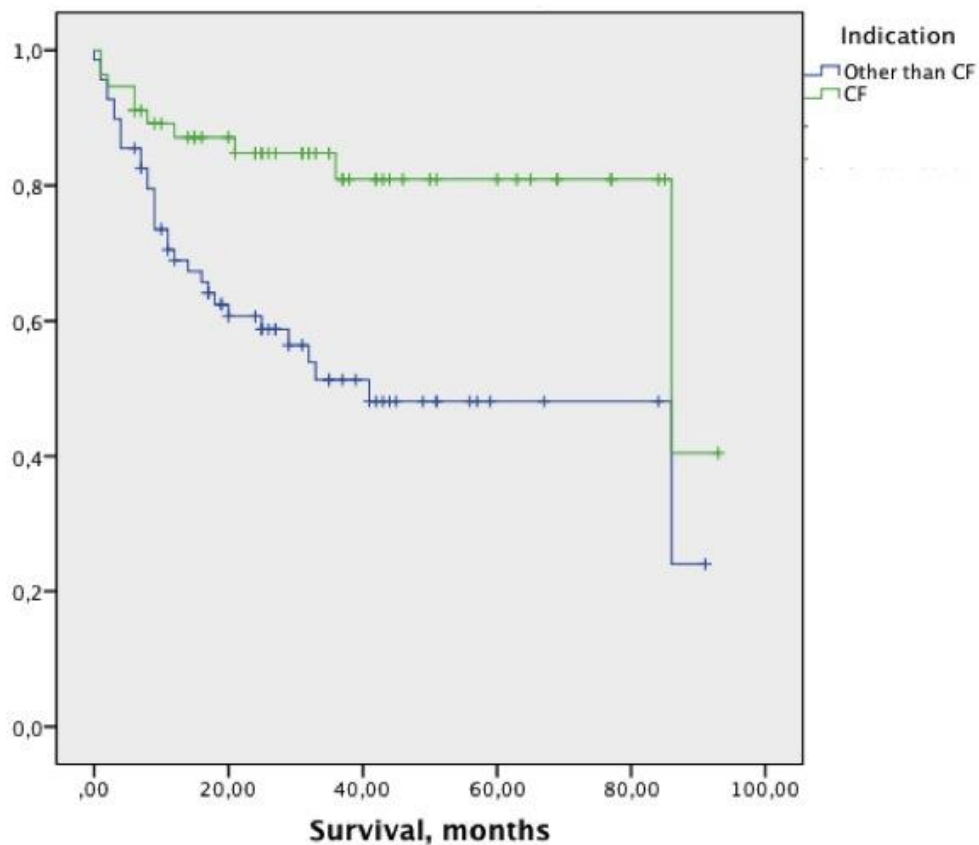
Conclusions: Despite the greater incidence of urgency code and cardiopulmonary bypass in CF recipients, LuTx was performed with acceptable morbidity. Our study seems to support the already existing evidence of a considerable survival advantage for CF recipients, making LuTx a treatment of choice for those individuals who develop end stage respiratory disease.

Table 1 - Recipient characteristics and outcomes

	CF recipients (67 pts)	Non CF recipients (90 pts)	p
Sex, males	26 (39%)	51 (57%)	0.062
Age at LuTx, years	32 (23; 37)	59 (47; 64)	0.001
Waiting List (time on), months	3 (1; 11)	4 (2; 9)	0.969
Lung allocation score	47 (37; 80)	49 (35; 68)	0.969
EVLP	7 (11%)	13 (14%)	0.788
ECMO bridge (urgent WL)	18 (27%)	8 (9%)	0.001
PGD within the first 72 hours	28 (42%)	45 (50%)	0.437
ALAD	8 (14%)	32 (36%)	0.003
CLAD	8 (15%)	23 (26%)	0.063
Survival after LuTx, months	88 (16; 155)	41 (17; 65)	0.001

Abbreviations: EVLP, *Ex vivo lung perfusion*; ECMO, *extracorporeal membrane oxygenation*; WL, *waiting list*; PGD, *primary graft dysfunction*; ALAD, *acute lung allograft dysfunction*; CLAD, *chronic lung allograft dysfunction*.

Figure 1 - Survival after LuTx



[145] The bacterial diversity of the Lung Microbiome of Children with Non-CF Bronchiectasis at diagnosis is similar to healthy controls-opportunities for preservation



Anna Mulholland¹; Alana Ainsworth¹; Naveen Pillariseti¹

¹Starship Children's Hospital, Auckland, New Zealand

Rationale: Non-CF bronchiectasis is a significant and increasing health problem in New Zealand and in many parts of the world. The pathophysiology of this disease is poorly understood, but bacterial infection and associated inflammation are presumed to be important contributors. Current understanding of the bacterial microbiome in suppurative lung disease suggests preservation of microbiome diversity in early disease and loss of diversity in advanced disease.

Aims: The aim of this study was to describe the lung microbiome in children with bronchiectasis at diagnosis compared to healthy controls.

Method: Children undergoing flexible bronchoscopy during clinical stability for investigation of suspected bronchiectasis were prospectively recruited (n=13). Following CT diagnosis of bronchiectasis, bronchoalveolar lavage (BAL) was performed from at least two affected lobes. BAL samples were obtained from healthy controls recruited from surgical lists. BAL samples were processed for microbiological culture and microbiome analyses. The latter involved Illumina MiSeq sequencing of PCR-amplified bacterial 16S ribosomal RNA genes (V3-V4 region) from extracted DNA. Quality processing and taxonomic classification was done using a bioinformatics pipeline employing USEARCH and QIIME. A minimum of 3000 sequences were obtained per sample. Bray-Curtis dissimilarity within and between patients and healthy controls was calculated.

Results: The median age of diagnosis of bronchiectasis in this study was three years (range 0.9 – 16). All 13 children had HRCT evidence of bilateral disease and 5/13 children had pan-lobar involvement. The median age of 12 healthy controls was 5.2 years (range 1.4-9.4).

A total of 26 BAL samples from 13 children with bronchiectasis were sequenced. The most abundant sequences were from the bacterial phylum Proteobacteria, followed by members of the Firmicutes, Bacteroidetes and Fusobacteria. Haemophilus was the most abundant genus (mean relative sequence abundance per patient of 24.3%), followed by Moraxella (19%) and Neisseria (13.5%); all of these were detected in every BAL sample. Streptococcus (13% of sequences) and Prevotella (7.7%) also featured frequently. While Pseudomonas was detected in 12/13 children, its contribution to total sequence number was invariably very low (0.01 to 0.12%). Similarly, Staphylococcus was detected in 11/13 children but comprised only 0.01 to 0.18% of total sequence reads. The mean relative sequence abundance of individual organisms in healthy controls was very similar to the bronchiectasis patients with Haemophilus (26.6%), Moraxella (12.4%), Neisseria (17.3%), Prevotella (9.3%) and Streptococcus (7.4%) present in all control BAL samples.

The mean microbiome dissimilarity within individual bronchiectasis patients was 44%, compared to 78% between patients. The mean microbiome dissimilarity among healthy controls was 80%. The alpha diversity of BAL from young children with bronchiectasis was similar to healthy controls.

Conclusion: Proteobacteria including Haemophilus, Moraxella and Neisseria dominate the lung microbiome in non-CF bronchiectasis at diagnosis. The bacterial diversity of the lung microbiome of healthy controls was very similar to that of children with bronchiectasis at the time of diagnosis.

B16 [159] Comorbidities and clinical characteristics associated with *Pseudomonas aeruginosa* among Medicare beneficiaries newly diagnosed with non-cystic fibrosis bronchiectasis in the United States

Joshua Noone^{1,2}; Christopher M Blanchette^{1,2}; Glenda Stone³; Emily Zacherle^{1,2}; Reuben Howden¹; Douglas Mapel⁴

¹University of North Carolina at Charlotte, Charlotte, NC, USA; ²Precision Health Economics, Davidson, NC, USA; ³Grifols, Research Triangle Park, NC, USA; ⁴Lovelace Clinic Foundation, Albuquerque, NM, USA

Background: 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.

Objective: Assess morbidity and healthcare utilization associated with PA among elderly incident NCFBE patients.

Methods: Using data from the 2011-2014 Medicare 5% Sample, we identified incident bronchiectasis (ICD-9-CM: 494.xx) patients, then excluded those with cystic fibrosis (277.XX). Patients were then stratified by PA (482.1 or 041.7) within the first year of bronchiectasis diagnosis. Patient demographics, comorbidities, and clinical characteristics were compared between NCFBE patients with and without PA infection. Chi-square tests were used for frequencies and percentages. Logistic regression was used to predict the odds of PA patients having an inpatient stay or ER visit.

Results: 4,876 newly diagnosed NCFBE patients were identified, of which 1.9% had a PA diagnosis within the first year of their NCFBE diagnosis. PA patients were more likely to have pulmonary complications including pulmonary circulation disorders (19.0% vs 10.3%, $p < 0.05$) and COPD (77.9% vs 66.4%, $p < 0.05$). Other comorbidities more likely to be found among PA patients included arrhythmia (48.4% vs 36.1%, $p < 0.05$), coagulopathy (12.6% vs 6.7%, $p < 0.05$), fluid and electrolyte disorders (34.7% vs 24.7%, $p < 0.05$), blood loss or deficiency anemia (27.4% vs 16.6%, $p < 0.05$), and depression (26.3% vs 20.2%, $p < 0.05$). The proportion of PA patients having all-cause ER visits (54.7% vs 38.4%; $p \leq 0.01$), or inpatient stays (79.0% vs 42.7%; $p \leq 0.01$) was significant. Lung-related inpatient stays (36.8% vs 10.4%; $p \leq 0.01$) were also significantly higher for PA patients, while there was no significant difference in lung-related ER visits. After adjusting for age, gender and Charlson Comorbidity Index (CCI) score, Medicare PA patients were found to be over four times more likely to have either an all-cause or lung-related inpatient stay [OR: 4.81 (2.90-7.98); $p \leq 0.01$] and [OR: 4.69 (3.04-7.25); $p \leq 0.01$], respectively. Medicare NCFBE patients with PA were also 77% more likely to have an all-cause ER visit and 65% more likely to have a lung-related ER visit, [OR: 1.77 (1.17-2.69); $p \leq 0.01$] and [OR: 1.65 (0.84-3.23); $p \leq 0.14$], respectively.

Conclusions: Many clinical characteristics along with the high prevalence of several comorbid conditions are known to burden the Medicare patient population. Though the percentage of identified patients with PA is low, this study suggests that PA imposes an additional burden on both patients and the healthcare system, as it is associated with substantial incremental morbidity and healthcare utilization among Medicare beneficiaries with newly diagnosed NCFBE. The limitations of the study include the possibility of inexact coding practices which could result in underestimates of the true percentage of incident NCFBE patients colonized with PA.

FUNDING SOURCE: Grifols, RTP, NC

B18 [175] Estimates of the Prevalence of Non-cystic Fibrosis Bronchiectasis in the United States

Joshua Noone^{1,2}; Glenda Stone³; Christopher M Blanchette^{1,2}; Emily Zacherle^{1,2}; Reuben Howden¹; Douglas Mapel⁴

¹University of North Carolina at Charlotte, Charlotte, NC, USA; ²Precision Health Economics, Davidson, NC, USA; ³Grifols, Research Triangle Park, NC, USA; ⁴Lovelace Clinic Foundation, Albuquerque, NM, USA

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 has been reported in clinical 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 among NCFBE patients across various US healthcare claims databases using two case definitions – one sensitive and the other specific.

Methods: Data from the 2011-2014 PharMetrics Plus administrative claims database, Medicare 5% claims and the Nationwide Inpatient Sample (NIS) were used. NCFBE patients were identified using both sensitive and specific measurement algorithms for determination of clinically verified NCFBE diagnoses. The sensitive measure, a measure typically attributed to fewer cases of disease being missed, included any patient with ≥ 1 hospitalization for BE or ≥ 2 claims ≥ 7 days apart or 1 outpatient BE w/bronchoscopy or CT scan ≥ 7 days prior. The specific measure, a measure designed to capture fewer false positive diagnoses, required 2 BE claims ≥ 90 days apart. Both measures excluded those with cystic fibrosis (277.XX). Patients were stratified by evidence of PA (482.1 or 041.7).

Results: Among base populations of 101,321,694 from PharMetrics representing the 272,900,000 commercially insured; 2,670,000 from the Medicare 5% sample representing the 46,000,000 Medicare fee-for-service beneficiaries; and applying hospitalization distributions from the National Inpatient Sample for others; we estimated the US prevalence of NCFBE. Using the specific measure 237,464 (42,537 commercial, 166,978 Medicare and 27,949 Medicaid/other) NCFBE patients were identified. With the sensitive measure, 431,585 (120,223 commercial, 247,091 Medicare and 27,991 Medicaid/other) were identified. Of the entire estimated US NCFBE population, we estimate 16,191(6.8%) (specific measure) and 27,991(6.5%) (sensitive measure) were also colonized with PA.

Conclusions: US prevalence estimates for NCFBE as well as NCFBE+PA are presented using two measurement methodologies, triangulated using three large US healthcare databases. Determining the size of the affected population is challenging because it is uncommon to find a decision rule that is both highly specific and highly sensitive. Usually it is a trade-off. The true US prevalence is probably between the high and low estimates presented here.

C20 [108] The impact of *Pseudomonas aeruginosa* on health care utilization and costs among newly diagnosed non-cystic fibrosis bronchiectasis patients in the United States

Joshua Noone^{1,2}; Christopher M Blanchette^{1,2}; Glenda Stone³; Emily Zacherle^{1,2}; Reuben Howden¹; Douglas Mapel⁴

¹University of North Carolina at Charlotte, Charlotte, NC, USA; ²Precision Health Economics, Davidson, NC, USA; ³Grifols, Research Triangle Park, NC, USA; ⁴Lovelace Clinic Foundation, Albuquerque, NM, USA

Background: 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, resulting in higher costs and rates of health care resource use.

Objective: Assess healthcare utilization and cost associated with PA among commercially managed, incident NCFBE patients.

Methods: Using data from the 2011-2014 PharMetrics Plus administrative claims database, we identified incident bronchiectasis (ICD-9-CM: 494.xx) patients, then excluded those with cystic fibrosis (277.XX). Patients were then stratified by PA (482.1 or 041.7) within the first year of bronchiectasis diagnosis. Patient demographics, comorbidities, healthcare costs and utilization were compared between NCFBE patients with and without PA infection. Chi-square tests were used for frequencies and percentages Logistic regression was used to predict the odds of PA patients having an inpatient stay or ER visit.

Results: 1,427 newly diagnosed NCFBE patients were identified, of which 4.8% were found to have PA within the first year of their NCFBE diagnosis. Mean total direct medical costs for PA patients were significantly higher (\$123,629±173,535 vs. \$31,579±63,875; $p \leq 0.01$) with mean lung related costs for PA patients of (\$46,893±108,627 vs \$7,222±27,508; $p \leq 0.01$), and mean NCFBE related costs for PA patients of (\$5,103±7,598 vs \$2,565±5,656; $p \leq 0.01$). The proportion of PA patients having all-cause ER visits (47.1% vs. 22.7%; $p \leq 0.01$) or inpatient stays (48.5% vs. 18.5%; $p \leq 0.01$) is significantly higher. The proportion of those having lung related ER visits (13.2% vs. 4.6%; $p \leq 0.01$) or inpatient stays (60.3% vs. 16.9%; $p \leq 0.01$) were also significantly higher for PA patients. After adjusting for treatment, age, gender and Charlson Comorbidity Index (CCI) score, U.S. commercially managed PA patients were over three times more likely to have an all-cause inpatient stay [OR: 3.82 (2.31-6.32); $p \leq 0.01$] and six times more likely to have a lung-related inpatient stay [OR: 6.57 (3.91–11.06); $p \leq 0.01$]. PA patients had similar significantly higher likelihoods of having either an all-cause or a lung-related ER visit [OR: 2.75 (1.67–4.53); $p \leq 0.01$] and [OR: 2.74 (1.29–5.86); $p \leq 0.01$], respectively.

Conclusions: The results of this study confirm the close association previously observed with PA and increases in health care utilization and costs among NCFBE patients. Additionally, these results suggest that the association between PA and health care utilization and costs, may be apparent within a year of diagnosis among newly diagnosed, commercially managed NCFBE patients in the U.S. The limitations of the study include the possibility of inexact coding practices which could result in underestimates of the true percentage of incident NCFBE patients colonized with PA.

FUNDING SOURCE: Grifols, RTP, NC

C38 [188] Creating a new Center for Bronchiectasis and NTM Care at an academic center in the USA.

Peadar G Noone¹; Mary LeighAnne Daniels¹; Kelli Sullivan¹; Sanniya Nanda¹; Michael R Knowles¹

¹University of North Carolina, Chapel Hill, USA

Background: Bronchiectasis and NTM lung diseases are common, yet are difficult and time consuming to diagnose and manage in a general clinical setting. There is increasing awareness of bronchiectasis and NTM Lung disease across the globe. Registries have been established and are growing in the US (n>2,000), Europe (>8,000), Australia (n>600), India and other countries, to facilitate disease characterization, translational research, and patient participation in clinical studies. Although there are little evidenced based data for treatment, there are consensus statements on optimal disease management. There are only a few centers in the US with a special interest in seeing patients with bronchiectasis and NTM lung disease.

Objective: We hypothesize that there is a need for Bronchiectasis Centers in the US, to evaluate and manage patients, including NTM, and help drive research into this hitherto neglected disease. We sought to set up such a center at UNC.

Methods: UNC has long had an interest in CF, PCD and Lung Transplantation for bronchiectasis, and multi-disciplinary team (MDT) care is well developed for these patients. We took advantage of a call for submissions for an “Innovation Request for Applications” at UNC to develop a proposal to set up a UNC Center for Bronchiectasis / NTM Care. At its core is an MDT of experienced physicians, a respiratory therapist, pharmacist, care management assistant, with the support of several sub-specialty clinicians (ENT, CT Surgery, Immunology, ID, Radiology, Lab Microbiology). Facilitation of research studies was also a focus.

Results: Clinical: The Center was set up in May 2016. A weekly half-day clinic has been established, staffed by two experienced clinicians, supported by an airway clearance expert, a nurse assistant and a pharmacist. A website has been built as an educational resource for patients and clinicians

(<http://www.med.unc.edu/medicine/pulmonary/bronchiectasis>). A “podcast” was posted as a simple overview of disease concepts. Clinician visits are combined with airway clearance assessments and pharmacy evaluations. Education leaflets and “dot” phrases (macros) for EMR after visit summaries were developed (simple definitions, images/videos and airway clearance techniques) for patient “homework”. An average of 1-2 new patients with bronchiectasis and / or NTM have been seen weekly, with an average of 2-4 monthly “urgent” (same week) referrals. N=351 patients with bronchiectasis have been logged into the local clinic registry; n=23 with NTM lung disease. Nationally / internationally (e.g. Brazil, Canada, Puerto Rico, Cayman Islands) there is increasing aware of the Center.

Research: A coordinator ensures full research access for all patients. Since center inception, n= 103 patients have been added to the US Registry (n=320 in total at UNC, #2 enrollment in the US), n=67 / n=12 patients respectively participated in expectorated / induced sputum research studies and n=13 for nasal NO measures.

Conclusions: With careful planning, networking, and using mainly existing resources, a visible, successful Center for Bronchiectasis / NTM Care Center can be set up, for excellence in clinical care as well as research activities. We will report more detailed patient outcomes after a two-year timeframe.

D15 [161] Is quality control for Multiple Breath Washout tests necessary in multicentre bronchiectasis studies? Experiences from the BronchUK Clinimetrics study

Katherine O'Neill¹; Gokul. R Lakshmiopathy¹; Mary Carrol²; James Chalmers³; Chris Johnson⁴; Adam. T Hill⁵; Michael Loebinger⁶; Ian Bradbury⁷; J. Stuart Elborn¹; Judy. M Bradley¹

¹Queen's University Belfast, Belfast, United Kingdom; ²Southampton University Hospital, Southampton, United Kingdom; ³Ninewells Hospital Dundee, Dundee, United Kingdom; ⁴Papworth Hospital, Papworth, United Kingdom; ⁵Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; ⁶Royal Brompton Hospital, London, United Kingdom; ⁷Frontier Science, Inverness-shire, United Kingdom

Introduction: Multiple Breath Washout (MBW) to measure lung clearance index (LCI) is increasingly used in multicentre bronchiectasis studies. The Belfast site have developed an innovative training and eLearning programme to train and certify sites in the BronchUK Clinimetrics study. In addition, data quality control or "over-reading" of LCI data is considered best practice to ensure data validity and quality. However, the over-reading process increases trial costs but its impact is unclear.

Objectives: To assess the change in LCI (no. turnovers), LCI coefficient of variation (CV%) and tidal volume (V_T) CV% after over-reading.

Methods: By January 2017, 93 patients from 5 trained and certified UK centres had performed 216 MBW tests in the BronchUK Clinimetrics study. Each MBW test was assessed for validity and quality by a trained "over-reader" at the Belfast over-reading centre, using pre-defined technical (signal misalignment, leak, did not meet end of test criteria, N_2 did not return to baseline between trials) and qualitative (repeatable testing session which reflects tidal breathing) criteria (1). A minimum of 2 technically valid and repeatable trials which represented tidal breathing were required for a successful MBW test. Test with ≥ 3 trials are required to calculate CV%. Values for LCI, LCI CV% and V_T CV% before and after over-reading, were compared using paired t-tests and p-value < 0.05 = significant.

Results: 40/216 (19%) tests were excluded because the subject being unable to complete/tolerate the procedure (15/40; 37%), for technical reasons (21/40; 53%) and qualitative reasons (4/40; 10%). 176 tests were used for analysis of LCI. 138 tests (i.e. those tests containing ≥ 3 trials) were used for analysis of LCI CV% and V_T CV%. LCI and V_T CV% did not change significantly after over-reading (MD [95% CI] = 0.003 [-0.08 to 0.09], $p=0.95$) and 4.6 [-4.2 to 13.5], $p=0.31$). LCI CV% was significantly lower after over reading 0.28 [0.03 to 0.53], $p=0.03$).

Conclusion: Over-reading is important in this study as it resulted in the exclusion of 12% of tests due to technical or quality issues. Furthermore, over-reading resulted in a reduction in LCI variability (CV%) which impacts the precision of data in clinical trials as well as sample size calculations for future trials. Our training programme successfully trained and certified BronchUK sites, however ongoing quality control of MBW data was required to ensure data validity.

References:(1) Jensen R, Stanojevic S, Klingel M, Pizarro ME, Hall GL, Ramsey K, et al. A Systematic Approach to Multiple Breath Nitrogen Washout Test Quality. PLoS ONE 2016 06/15;11(6):e0157523.

D09 [122] Relative risk of all-cause mortality associated with incident cohorts of bronchiectasis and chronic obstructive pulmonary disease in a national US managed care insurance plan

Kenneth Olivier¹; Quanwu Zhang²; Engels Chou²; Carlos Fernandez²; Raymond Zhang³; Jennifer Adjemian¹

¹National Institutes of Health, Bethesda, USA; ²Insmmed Incorporated, Bidgewater, USA; ³Orbis Data Solutions, Woburn, USA

Background: Comparative risk of mortality between bronchiectasis (BE) and chronic obstructive pulmonary disease (COPD) is rarely reported.

Objective: This study was to evaluate the relative risk of all-cause mortality between patients with incident BE and COPD.

Methods: Individuals with ≥ 2 medical claims for BE or COPD between 2008 and 2015 were identified in a large US managed care insurance plan. Individuals were retained in the incident cohort of BE (n=15,238) or COPD (n=562,136) if they had 12 months (baseline) of medical insurance coverage and had no diagnosis of COPD or nontuberculous mycobacterial lung disease (NTMLD) before the first BE claim or no BE or NTMLD diagnosis before the first COPD claim at baseline. Mortality data originated from the Social Security Death Master File. The number of mortality records after 2011 were reduced by about 30% following local court decisions. However, these decisions were unlikely related to BE or COPD resulting in biased estimation of relative risk of mortality. Cox proportional hazard methods were used to compare all-cause mortality between the cohorts, adjusting for demographic factors and baseline comorbidities.

Results Mean age was 64 vs 58 years with 63% and 55% women in BE and COPD cohort, respectively. Charlson comorbidity score (standard deviation) was 1.52 (2.2) vs. 0.89 (1.7) for BE vs. COPD. More baseline medical claims were recorded in the BE vs. COPD cohort for asthma (18.4% vs. 11%), cancer (17.5% vs. 7.7%), cystic fibrosis (2.0% vs. 0.01%), gastroesophageal reflux disease (GERD) (21.4% vs. 12.9%), valve disease (12.2% vs. 7.2%), hyperlipidemia (48.7% vs. 38.9%), hypertension (50.7% vs. 43.2%), immunosuppressant use (36.5% vs. 24.7%), organ transplant (0.6% vs. 0.2%), pneumonia (19.9% vs. 6.2%), and rheumatoid disease (4.8% vs. 2.2%). Claims for current tobacco use were 9.4% for COPD vs. 3.9% for BE. Observed mortality was 15.1 vs. 10.6 events per 1000 patient-years for BE vs. COPD (rate ratio=1.4, 95% CI: 1.3-1.5). BE vs. COPD was associated with a slightly higher risk of mortality after adjustment (hazard ratio (HR)=1.09, 1.02-1.17). Relative risk of mortality increased by 94% (HR=1.94, 1.78-2.12) with every additional 20 years of age in BE relative to 160% (2.66, 2.61-2.71) in COPD. Relative mortality risk in the entire sample increased with male gender (1.31, 1.28-1.35), congestive heart failure (1.45, 1.4-1.5), cystic fibrosis (3.69, 2.22-6.13), immune system disease (1.13, 1.02-1.25), mental disorder (1.41, 1.37-1.45), metastatic carcinoma (1.28, 1.18-1.39), moderate or severe liver disease (1.29, 1.14-1.46), and tobacco use (1.24, 1.19-1.30). Baseline immunosuppressant use was associated with a slight lower mortality risk (0.92, 0.89-0.95). Each additional point in Charlson comorbidity index was associated with 19% additional mortality risk (1.19, 1.18-1.2).

Conclusions Incident BE cohort is associated with a 40% higher relative risk for all-cause mortality compared with the COPD cohort. A portion of the incremental mortality risk is explained by a higher comorbidity burden in BE patients and the relative risk is attenuated to 9% after multivariable adjustment. This finding suggests that an effective intervention for BE comorbidities may improve risk for all-cause mortality.

A09 [123] Risk factors and diagnosis of nontuberculous mycobacterial lung disease in incident cohorts of bronchiectasis and chronic obstructive pulmonary disease in a national US managed care insurance plan

Kenneth Olivier¹; Jennifer Adjemian¹; Engels Chou²; Gina Eagle²; Raymond Zhang³; Quanwu Zhang²

¹National Institutes of Health, Bethesda, USA; ²Insmmed Incorporated, Bridgewater, USA; ³Orbis Data Solutions, Woburn, USA

Background: Nontuberculous mycobacterial lung disease (NTMLD) is rare but has an increased representation in individuals with bronchiectasis (BE) or chronic obstructive pulmonary disease (COPD).

Objective: This study was to evaluate the risk of NTMLD in cohorts of patients with incident BE or COPD and factors that are likely to impact the occurrence of NTMLD following the diagnosis of BE or COPD.

Methods: Individuals with ≥ 2 medical claims for BE or COPD between 2008 and 2015 were identified in a large US managed care insurance plan. Individuals were retained in the incident cohort of BE (n=15,238) or COPD (n=562,136) if they had 12 months (baseline) of medical insurance coverage and had no COPD or NTMLD diagnosis before the first BE claim or no BE or NTMLD diagnosis before the first COPD claim at baseline. NTMLD was defined with ≥ 2 medical claims ≥ 30 days apart. Number of individuals with NTMLD per 1000 person-years was estimated using Poisson regression, and time to NTMLD from first BE or COPD claim was estimated using multivariable Cox regression.

Results: Mean age was 64 vs 58 years with 63% vs 55% women in BE and COPD cohort, respectively. Charlson comorbidity score (standard deviation) was 1.52 (2.2) vs. 0.89 (1.7) for BE vs. COPD. More baseline medical claims were recorded in the BE vs. COPD cohort for asthma (18.4% vs. 11%), cancer (17.5% vs. 7.7%), cystic fibrosis (2.0% vs. 0.01%), gastroesophageal reflux disease (GERD) (21.4% vs. 12.9%), valve disease (12.2% vs. 7.2%), hyperlipidemia (48.7% vs. 38.9%), hypertension (50.7% vs. 43.2%), immunosuppressant use (36.5% vs. 24.7%), organ transplant (0.6% vs. 0.2%), pneumonia (19.9% vs. 6.2%), and rheumatoid disease (4.8 vs. 2.2%). Claims for current tobacco use were 9.4% for COPD and 3.9% for BE. NTMLD diagnosis rate was 9.13 vs. 0.24 per 1000 person-years for BE vs. COPD. Adjusted risk of NTMLD was 28 times in BE that in COPD (hazard ratio [HR]=28.04, 95% CI: 24.07-32.67; P<0.001). NTMLD risk increased nearly 50% for every additional 20 years of age in both cohorts. NTMLD was associated with female gender (HR=1.91, 1.62-2.26), aspergillosis (2.39, 1.17-4.91), cystic fibrosis (4.37, 2.54-7.52), immunosuppressant use (1.34, 1.15-1.57), immune system disorder (2.11, 1.4-3.17), moderate or severe liver disease (2.31, 1.02-5.21), and tuberculosis (5.23, 2.46-11.13) after adjustment. Congestive heart failure (CHF), dementia, diabetes, hypertension, obesity, and current tobacco use were associated with a lower rate of NTMLD diagnosis across cohorts. Unadjusted baseline claims for CHF, GERD, and valve disease in BE cohort were associated with a lower rate of NTMLD diagnosis vs. patients without CHF, GERD, or valve disease.

Conclusions: NTMLD risk in the incident BE cohort was 28 times that in the COPD cohort. Multiple factors are related to increased NTMLD risk in both BE and COPD cohorts, while a combination of BE and CHF, GERD, or valve disease was associated with a lower rate of NTMLD diagnosis. We hypothesize that CHF, GERD, and valve disease possibly exert a masking effect through shared symptoms that potentially delay or prevent diagnosis of NTMLD.

D16 [177] What is the relevance of COPD–bronchiectasis overlap for patients who fulfill both diagnoses?

Munteanu Oxana¹; Volosciuc Irina¹; Corlateanu Alexandru¹; Alexandru Sofia²; Botnaru Victor¹

¹State University of Medicine and Pharmacy “ Nicolae Testemitanu”, Chisinau, Moldova;

²Phthisiopneumology Institute "Chiril Draganiuc", Chisinau, Moldova

Aim: Identification of the proportion of patients with COPD etiology of non-cystic fibrosis bronchiectasis (non-CF) and comparative evaluation with other etiologies.

Methods: We prospectively evaluated patients admitted to our hospital between 01/12/2014 and 1/03/2016 with non-CF bronchiectasis confirmed by chest HRCT.

Results: From a total number of 177 patients with bronchiectasis (56% men, mean age 56.5 ± 13.9 years), COPD as a cause of bronchiectasis was confirmed in 31 cases (18%), 34% (61 subjects) were classified as idiopathic. Postinfectious bronchiectasis were identified more frequently - 69 cases (39%), because of a great number of post tuberculosis bronchiectasis 44 cases (25%). Compared with patients with bronchiectasis with other etiologies (146 subjects), patients with COPD/bronchiectasis (31 subjects, 94% men) were older (62.5 ± 8.9 vs 55.2 ± 14.5 , $p = 0.007$), had a worse pulmonary function (FEV $36 \pm 11.8\%$ vs 57.3 ± 26 , $p = 0.00004$; CVF 52.8 ± 14.5 vs 66.8 ± 22.7 , $p = 0.001$; FEV1/FVC 54.7 ± 14.1 vs 69.2 ± 14.3 , $p = 0.000001$) and a higher BSI (11.7 ± 3.7 vs 9.8 ± 4 , $p = 0.01$). Statistically significant differences were highlighted for mMRC dyspnea score (3.4 ± 0.6 vs 2.6 ± 0.9 , $p = 0.000006$), Sa O₂ (86.3 ± 11 vs. 92.6 ± 7.1 , $p = 0.002$), number of hospitalizations ($1.7 \pm 1.2 \pm 1$ vs 1.3 , $p = 0.04$) during the year. No statistically significant differences were found according to BMI, the number of exacerbations over a year, presence of cough and hemoptysis, presence and amount of sputum, colonization by pathogenic bacteria.

Conclusion: Due to more frequent use of CT examination in patients with COPD, the presence of “bronchiectatic” airway wall changes is increasingly documented. We have revealed that each 5th patient with bronchiectasis was due to COPD. These subjects were older, had a worse pulmonary function, a higher BSI and mMRC dyspnea score and lower Sa O₂, and needed more hospitalizations during the year. Highlighting these features may result in some changes for optimal management.

C40 [118] Late diagnosed unilateral pulmonary vascular abnormalities in advanced non CF-bronchiectasis

Munteanu Oxana¹; Volosciuc Irina¹; Rusu Doina¹; Onea Leonid²; Botnaru Victor¹

¹State University of Medicine and Pharmacy " Nicolae Testemitanu", Chisinau, Moldova; ²German Diagnostic Center, Chisinau, Moldova

Congenital abnormalities of the pulmonary vasculature occur in both pulmonary arteries and veins. Many congenital abnormalities are increasingly diagnosed in the adulthood, as they mimic other thoracic pathologies or are asymptomatic in the childhood. The extent of the anomaly varies considerably. Isolated hypoplasia of the left pulmonary artery is a rare entity and seems to be frequently associated with a maldevelopment of the lung. There is a small number of cases described in the literature associated with severe bronchiectasis.

We present a case of left pulmonary artery hypoplasia, left inferior pulmonary vein agenesis and left superior pulmonary vein hypoplasia associated with saccular bronchiectasis that was diagnosed at the age of 60 years. Frequent pulmonary infections were present from childhood, but the bronchiectasis were suspected at the age of 40 years. Multiple cystic bronchiectasis with the left lung smaller, ipsilateral shift of the mediastinum and elevation of the left hemidiaphragm were confirmed on the first HRCT performed at the age of 54 years. Hyperinflated contralateral lung with herniation across the mediastinum to the smaller hemithorax and bronchiectasis (cylindrical bronchiectasis in the right lower lobe; Reiff score 7) were noted. The enlargement of main pulmonary artery till 3.6 cm was considered as a sign of pulmonary hypertension due to bronchiectatic disease.

Contrast enhanced chest CT (fig. 1 A) performed six years later because of lung cancer suspicion showed left pulmonary artery hypoplasia (1.5 cm), enlarged main pulmonary artery (3.6 cm) and right main branchus (2.4 cm) with left inferior pulmonary vein agenesis and left superior pulmonary vein hypoplasia better seen in multiplanar 3D reconstruction (fig. 1 B). Progressive worsening in lung structure (increase in severity of bronchiectasis (fig. 1 C) with Reiff score 13 and airway wall thickening in both lungs) and function (severe obstructive defect, and hyperinflation in pulmonary function tests - FEV1 25%, RV 192%, DLCO 60%) due to chronic infection (*Klebsiella* in sputum culture) and inflammation were noted.



A

B

C

Figure 1

Conclusions: We describe a case of pulmonary artery hypoplasia which masqueraded as cystic bronchiectasis. Careful observation of the pulmonary vasculature on chest X-ray could suggest hypoplasia/agenesis of a pulmonary artery; nowadays a number of imaging techniques are available to aid the diagnosis. Physicians should bear in mind the possibility of undiagnosed congenital abnormalities of the pulmonary vasculature in adults.

C39 [174] Clinical, imaging and functional correlations in patients with non-CF bronchiectasis and *Pseudomonas aeruginosa*: the experience of a country center

Munteanu Oxana¹; Volosciuc Irina¹; Rusu Doina^{1,2}; Calaras Diana¹; Botnaru Victor¹

¹State University of Medicine and Pharmacy " Nicolae Testemitanu", Chisinau, Moldova;

²Phthisiopneumology Institute "Chiril Draganiuc", Chisinau, Moldova

Aims: To identify the clinical, imaging and functional profile of patients with non-CF bronchiectasis colonised by *Pseudomonas aeruginosa* and to find the correlation between different severity and radiology score for bronchiectasis.

Methods: We prospectively evaluated non-CF adult bronchiectasis patients confirmed by chest high resolution computed tomography during a 30-months period (November 2014 - April 2017). Etiology, clinical data, microbiological profile, lung function, radiology score (Reiff, Bhalla) and severity score (BSI, FACED) were analysed.

Results: Among the 278 patients with non-CF bronchiectasis, bronchial colonization with *P. aeruginosa* was identified in 14% (39 patients). Of these, 59% (23 patients) were females, all non-smokers. From 16 male patients, 8 were current smokers and 8 ex-smokers. Mean age was 50.6 ± 16.1 years and only 26 % were ≥ 65 years old. Mean duration of illness was 20.3 ± 15.5 years.

Past tuberculosis (36%) and COPD (21%) were the most commonly identified underlying conditions, while no cause was found in 33% of the patients. The main symptoms were cough (100%), mucopurulent sputum (100%), dyspnea (100%) and haemoptysis (46%).

Patients with *P. aeruginosa* had a more long-standing disease (mean duration of symptoms 9.4 ± 10.8 years) with the obstructive pattern as the most frequent and severe impairment of pulmonary function (FEV1% 44 ± 18 %).

Saccular bronchiectasis at least in one lobe were identified in 67 % of cases (26 patients), almost one collapsed lobe seen in 72% (28 cases) of patients colonised with *P. aeruginosa*.

Despite the fact that just in 14 cases the patients had a history of treated TB, in 80% of cases (31 patients) were found calcifications as a marker of TB sequela (calcifications of lymph nodes 41%, parenchymal calcifications 50%, pleural calcification 23% of cases).

Radiological severity of the disease was mainly related to impaired lung function, *P. aeruginosa* isolation in sputum and frequent exacerbations. The median score for all patients according to the Bhalla system was 14.2 ± 3.7 (range from 8 to 23) and for modified Reiff score 9.8 ± 4.5 (range from 2 to 18). Modified Reiff score correlated well with the Bhalla score ($r = 0.6$, $p < 0.05$). The mean derived FACED score was 4.7 ± 1 and BSI score was 14 ± 2.3 . While according to the value of the derived overall FACED score 21% of cases were classified as moderate and 79% as severe, according to the value of BSI score, all the patients were sorted as severe. FACED score correlated well with the BSI score ($r = 0.57$, $p < 0.05$).

Conclusions: An important cause of severe non-CF bronchiectasis colonised by *Pseudomonas aeruginosa* in a high burden TB country like Republic of Moldova, remains "past" tuberculosis.

Colonisation with *Pseudomonas aeruginosa* define a specific phenotype of patients with non-CF bronchiectasis who share a more severe disease, worse clinical, functional characteristics and radiological score. Modified Reiff Score correlated well with the Bhalla score. FACED score correlated well with the BSI score, but compared with the BSI, the distribution of FACED scores appeared to be more skewed towards moderate bronchiectasis.

D18 [102] Prognostic factors associated with bronchiectasis in uncontrolled moderate-to-severe asthma

Alicia Padilla¹; Casilda Oliveira²; Luis Fernández de Rota¹; Isabel Marco³; José Joaquín Cebrian¹; Miguel Ángel Martínez-García⁴

¹Agencia Sanitaria Costa del Sol. Pneumology Unit, Malaga, Spain; ²Hospital Regional Universitario de Málaga. Pneumology Department, Malaga, Spain; ³Hospital de Alta Resolución de Benalmádena. Radiology Department., Malaga, Spain; ⁴Hospital Universitario La Fe. Pneumology Department., Valencia, Spain

Background: Asthma and bronchiectasis (BC) are different conditions that can coexist in many patients, and both have a high prevalence and incidence. The presence of BC in patients with asthma can influence the clinical, diagnostic tests, control and in the treatment of these subjects. However the factors associated with this condition are unknown.

Objective: Our aim is to analyze the factors associated with the presence of bronchiectasis in patients with uncontrolled moderate-to-severe asthma (UMSA).

Methods: We prospectively included 398 consecutive UMSA patients (according to GINA guidelines) from our specific asthma outpatient clinic. All of them underwent a chest High-Resolution CT scan and an standardized protocol including sociodemographic data (age, gender), asthma clinical profile (severity, evolution of asthma, atopy, ACT –asthma control test-, expectoration), comorbidities, exacerbations, treatments, basic blood test, functional (spirometry, FeNO- fractional exhaled nitric oxide-) and radiological severity (Bhalla and modified Bhalla) and prognosis (FACED and BSI scores) of bronchiectasis. Patients with a previous diagnosis of bronchiectasis and current or former smokers of more than 10 packs per year were excluded (to avoid the possibility of concomitant COPD diagnosis).

Results: Patients with bronchiectasis were older, had more severe asthma, lower values of ACT, FEV₁ (ml), FVC (ml) and FeNO, and more chronic expectoration, purulent sputum, exacerbations and use of antibiotics, and they used more health resources. In the fully-adjusted multivariate logistic regression the presence of bronchiectasis was associated with a higher frequency of chronic expectoration (OR, 2.95; 95% CI, 1.49-5.84; p=0.002), greater severity of asthma (OR, 2.43; 95% CI, 1.29-4.57; p=0.006), at least one previous episode of pneumonia (OR, 2.42; 95% CI, 1.03-5.69; p=0.044), and lower levels of FeNO (OR, 0.98; 95% CI, 0.97-0.99; p=0.016).

A score called NOPES (FeNO, Pneumonia, Expectoration and Severity) was developed. The weight of each variable was the (rounded) value of beta coefficients (severity of asthma: moderate=0, severe=1; chronic bronchial expectoration: No=0, Yes=1; previous pneumonia: No=0, Yes=1; FeNO >20.5ppb=0, FeNO ≤20.5ppb=1). The score ranges from 0 to 4 (where 0 means “less severity” and 4, “high severity”). The AUC-ROC for the NOPES score for the prognosis of the presence of BQ was 0.7. Table 1 shows sensitivity, specificity, positive and negative predictive values, and prevalence of bronchiectasis according to the NOPES score (≥1, ≥2 and ≥3). According to the Youden index, the best model was that based on NOPES scores ³2. With a score of 3, this model showed excellent specificity (95%) and good negative (76%) predictive values.

Conclusions: In patients with UMSA, the presence of bronchiectasis was independently associated to the severity of asthma, previous pneumonia episodes, chronic expectoration and low values of FeNO. NOPES score appeared as an easy-to-use predictive tool for bronchiectasis in UMSA patients.

Table 1. NOPES score by cut-off point.

NOPES Score	≥1	≥2	≥3
Sensitivity (%)	98.7	68.9	24.3
Specificity (%)	14.1	59.2	95.1
Validity index (%)	38.4	62	74.8
Positive predictive value (%)	31.6	40.5	66.7
Negative predictive value (%)	96.3	82.6	75.8
Youden index	0.13	0.28	0.19
Prevalence of BE (%)	31.6	40.8	66.7

BE: Bronchiectasis

D17 [154] Prevalence and radiological characteristics of bronchiectasis in patients with uncontrolled asthma.

Alicia Padilla¹; Casilda Oliveira²; Ana Carmona³; Luis Fernández de Rota¹; Isabel Marco⁴; José Joaquín Cebrian¹; Miguel Ángel Martínez-García⁵

¹Agencia Sanitaria Costa del Sol. Pneumology Unit, Malaga, Spain; ²Hospital Regional Universitario de Málaga. Pneumology Department, Malaga, Spain; ³Universidad de Malaga, Malaga, Spain; ⁴Hospital de Alta Resolución de Benalmádena. Radiology Department., Malaga, Spain; ⁵Hospital Universitario La Fe. Pneumology Department., Valencia, Spain

Background: Asthma and bronchiectasis are two conditions with high prevalence and morbidity that can coexist. In the bibliography available, the studies that evaluate the prevalence of bronchiectasis in patients with asthma are heterogeneous and have many bias.

Objective: Our aim is to analyze the prevalence of bronchiectasis in patients with uncontrolled moderate-to-severe asthma (UMSA), who are being followed in a specific asthma unit and describe their radiological characteristics.

Methods: This is a prospective study of data from consecutive patients with UMSA. Patients with a previous diagnosis of bronchiectasis, smokers, and former smokers of more than 10 packs per year were excluded (to eliminate asthma-COPD overlap). Once the diagnosis of bronchiectasis was confirmed by high resolution computed tomography scan (HRCT), the patient underwent a complete examination, following specific guidelines, to investigate the aetiology of bronchiectasis, including alpha 1-antitrypsin deficiency, allergic bronchopulmonary aspergillosis, cystic fibrosis, immunodeficiency and systemic diseases. Patients with these conditions were excluded. A HRCT was performed to every patient. Cylindrical bronchiectasis only visible in a single pulmonary segment were not considered. On inclusion, patients were required to have been in a stable phase. A standardized protocol was applied for the collection of sociodemographic data (age, gender), degree of severity, comorbidities, exacerbations, ED visits, use of oral corticoids and/or antibiotics in the previous year, chronic expectoration and/or sputum purulence, functional data (spirometry, FENO-fractional exhaled nitric oxide-) and bronchiectasis severity (Bhalla and modified Bhalla) and prognosis (FACED and BSI scores).

Results: A total of 398 patients with UMSA (60% with severe asthma) were included. Patients studied had a mean age of 57±15.6 years, 70% were women, with a BMI of 29±5, time of evolution of asthma 17±16 years, asthma control test 15±4, Charlson's index 3.2±2.1, previous pneumonia 15.8%, FEV₁ post-BD 80±23% and FEV₁/FVC post-BD 69±11%, FeNO 30±30ppb, blood eosinophils 310±254, IgE 269±541 and positive sputum culture 24%. The prevalence of bronchiectasis was 28.4%. However, statistically significant differences between patients with moderate asthma against the ones with severe asthma were found (20.6% vs 34%, p=0.005). Bronchiectasis were cylindrical in 92.9% and cystic in 7.1%. 73.5% were bilateral bronchiectasis. Thickening of bronchial wall was in 100% of bronchiectasis. Bhalla was 16.97±2.76 and modified Bhalla 16.74±2.8. FACED score was 1.45±1.21 and BSI score was 4.82±2.98. Other findings were: mucous plugs (78.8%), atelectasis (61.9%), bronchiolitis signs (61.1%), expiratory flow limitation (22.1%) and radiological signs of pulmonary hypertension (1.8%).

Conclusions: Almost a third of the patients with UMSA had bronchiectasis, with predominance of cylindrical and bilateral.

C14 [176] Chronic fungal infection in patients with bronchiectasis: clinical and functional correlations

Eva Padrão¹; Margarida Redondo¹; Manuela Ribeiro²; Adelina Amorim^{1,3}

¹Pulmonology Department of São João Hospital Center, Porto, Portugal; ²Clinical Pathology Department of São João Hospital Center, Porto, Portugal; ³Faculty of Medicine, University of Porto, Porto, Portugal

Background: Patients with bronchiectasis may have different clinical evolution and a large number of variables may contribute to this fact. Among these, the role of chronic infection, namely bacterial infection, has already been established, with the triggering of a vicious cycle of airway inflammation and progressive tissue destruction. However, the role of chronic fungal infection in patients with bronchiectasis remains unclear.

Objective: Clinical and functional characterization of patients with bronchiectasis and chronic fungal infection and evaluation of its impact in the evolution of these patients.

Methods: Prospective analysis of patients with bronchiectasis, documented by high resolution computed tomography, with at least 1 year of follow up at outpatient clinic. Chronic fungal infection was defined using the same definition usually applied for bacterial infection: isolation of the same fungus in 2 sputum cultures with at least 3 months apart within a year. Clinical and functional data were collected and a p-value <0.05 was considered statistically significant.

Results: We included 186 patients with mean age of 54.7 (± 16.2) years and 60.8% (n=113) were female. Almost half of the patients (n=90, 48.4%) met criteria of chronic fungal infection: 74 cases of isolation of leveduriform fungi, 10 cases of *Aspergillus fumigatus*, 4 cases of *Aspergillus niger*, 2 cases of *Scedosporium spp.* These patients were significantly older (59.1 \pm 15.2 vs. 50.6 \pm 16.1, $p < 0.001$), with a higher mean age at diagnosis (45 \pm 19 vs. 36 \pm 18, $p = 0.003$), higher follow up time (1511 \pm 544 vs. 1259 \pm 640 days, $p = 0.001$). They also had higher bronchiectasis severity index (BSI) score (6 \pm 4 vs. 5 \pm 3, $p = 0.002$) and were more likely women (70%, $p = 0.012$). A distinct mMRC score was found among groups ($p = 0.014$), with 21.2% of patients with chronic fungal infection having mMRC score between 2 and 4 (vs. 10.4%). Regarding sputum characteristics, patients with chronic fungal infection had higher estimated sputum production volume (28 \pm 28 vs. 20 \pm 17 mL/day, $p = 0.046$), with a more frequent ($p = 0.02$) pattern (76.7% vs. 59.4% with daily sputum production), and more purulent ($p = 0.068$). Concerning pulmonary function tests, patients with chronic fungal infection had lower values of FVC (2.55 \pm 0.98 L vs. 3.04 \pm 0.97 L, $p < 0.001$) and FEV₁ (1.74 \pm 0.8 L vs. 2.01 \pm 0.84 L, $p = 0.016$). In these patients the frequency of exacerbations, both those treated in outpatient clinic ($p < 0.01$) and those requiring hospitalization ($p = 0.006$), was significantly higher. Furthermore, a positive correlation between chronic fungal and chronic bacterial infection was seen ($p = 0.012$). There were significant differences ($p = 0.036$) regarding the etiology of bronchiectasis, being the postinfectious and idiopathic more frequent in patients with chronic fungal infection. No significant differences between groups were found in smoking habits, body mass index and previous history of hemoptysis.

Conclusions: In this cohort of patients, chronic fungal infection seems to have a negative impact in disease evolution. This group of patients present with a higher BSI score, older age, higher dyspnea score, lower FEV₁ and higher exacerbation frequency. However, the association with chronic bacterial infection can contribute for this clinical severity. Since research regarding fungal infection has been neglected, further analysis should be performed to understand its real impact and predisposing factors.

C41 [200] Self-reported asthma as a co-morbidity of bronchiectasis in the EMBARC registry

Eva Polverino¹; Pierluigi Paggiaro²; Stefano Aliberti³; Francesco Blasi³; Charles Haworth⁴; Stuart Elberon⁵; Michael Loebinger⁵; Rosario Menendez⁶; Antony De Soyza⁷; Felix Ringshausen⁸; Tobias Welte⁸; Antoni Torres⁹; Robert Wilson⁵; Katerina Dimakou¹⁰; James Chalmers¹¹

¹VHIR- Hospital Valle D'Hebron, Barcelona, Spain; ²Respiratory Disease Department University of Pisa, Pisa, Italy; ³Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; ⁴Cambridge Centre for Lung Infection, Papworth Hospital, Cambridge, United Kingdom; ⁵Host Defence Unit, Royal Brompton Hospital, Imperial College, London, UK, London, United Kingdom; ⁶Respiratory Disease Dpt. Hospital La Fe, Valencia, Spain; ⁷Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK; Bronchiectasis Service, Freeman Hospital,, NewCastle, United Kingdom; ⁸Department of Respiratory Medicine, Hannover Medical School, Member of the German Centre for Lung Research,, Hannover, Germany; ⁹Servei de Pneumologia, Hospital Clínic de Barcelona, Universitat de Barcelona, IDIBAPS, CIBERES, Barcelona, Spain; ¹⁰10 5th Pulmonary Department, "Sotiria" Chest Hospital, Athens, Greece; ¹¹Scottish Centre for Respiratory Research, Ninewells Hospital and Medical School, Dundee, United Kingdom

Introduction: Self reported or physician reported asthma is common in healthcare databases in association with bronchiectasis. Small studies suggest a higher incidence of exacerbations in patients with co-existing asthma. The aim of this study was to characterise patients with bronchiectasis and asthma in the European Bronchiectasis Registry dataset.

Methods: Multicentre prospective registry across 23 European Countries.

Results: 7841 patients were included in this analysis. 58% were female, median age 68 years (IQR 58-75), 55.9% never smokers. The most frequently isolated pathogen was *Pseudomonas aeruginosa*. 52.1% had 2 or more exacerbations in the previous year and 28.4% had been hospitalized for a severe exacerbation in the previous 12 months.

2393 (30.5%) patients had a self-reported history of asthma. In 6.8% of patients, asthma was reported to be the cause of bronchiectasis. Patients with self reported asthma had no differences in age or gender (median age 67, 62% female), or other clinical characteristics to patients without asthma (median BSI score 7 vs 7, p=0.6)

Using a zero-inflated poisson regression model, self reported asthma was associated with a significant increase in the frequency of exacerbations (incident rate ratio 1.27 95% CI 1.23-1.31, p<0.0001). There was no corresponding increase in the frequency of severe exacerbations (IRR 1.03 95% CI 0.96-1.11, p=0.4). Respiratory symptoms using the QOL-B were less severe in patients with self reported asthma than in patients with asthma, but at a level below with minimum clinically important difference, mean 54.4 (sd 22.6) vs 59.0 (sd 29.8), p<0.0001.

Conclusion: Asthma is a commonly reported co-morbidity, paradoxically associated with lower symptoms and a higher frequency of exacerbations.

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[126] Pathophysiology of bronchiectasis: beyond FEV1 and airflow obstruction

Dejan Radovanovic¹; Pierachille Santus¹; Giovanni Sotgiu²; Francesca D'Arcangelo³; Edoardo Simonetta³; Francesco Blasi⁴; Peter C. Goeminne^{5,6}; James D. Chalmers⁷; Stefano Aliberti⁴

¹Department of Biomedical and Clinical Sciences (DIBIC), University of Milan, Pulmonary Unit, Ospedale L. Sacco, ASST Fatebenefratelli-Sacco, Milano, Italy; ²Clinical Epidemiology and Medical Statistics Unit, Department of Biomedical Sciences, University of Sassari., Sassari, Italy; ³School of Medicine, University of Milan Bicocca, Respiratory Unit, AO San Gerardo., Monza, Italy; ⁴Department of Pathophysiology and Transplantation, University of Milan, Cardio-thoracic unit and Adult Cystic Fibrosis Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico., Milano, Italy; ⁵Department of Respiratory Disease, AZ Nikolaas., Sint-Niklaas, Belgium; ⁶Department of Respiratory Disease, UZ Leuven., Leuven, Belgium; ⁷Scottish Centre for Respiratory Research, University of Dundee, DD1 9SY., Dundee, United Kingdom

Background: bronchiectasis has always be defined as an obstructive disease, and the forced expiratory volume in one second (FEV₁) has been employed to evaluate functional impairment and to integrate disease severity scores. However, pulmonary pathophysiology of bronchiectasis is complex and remains poorly understood.

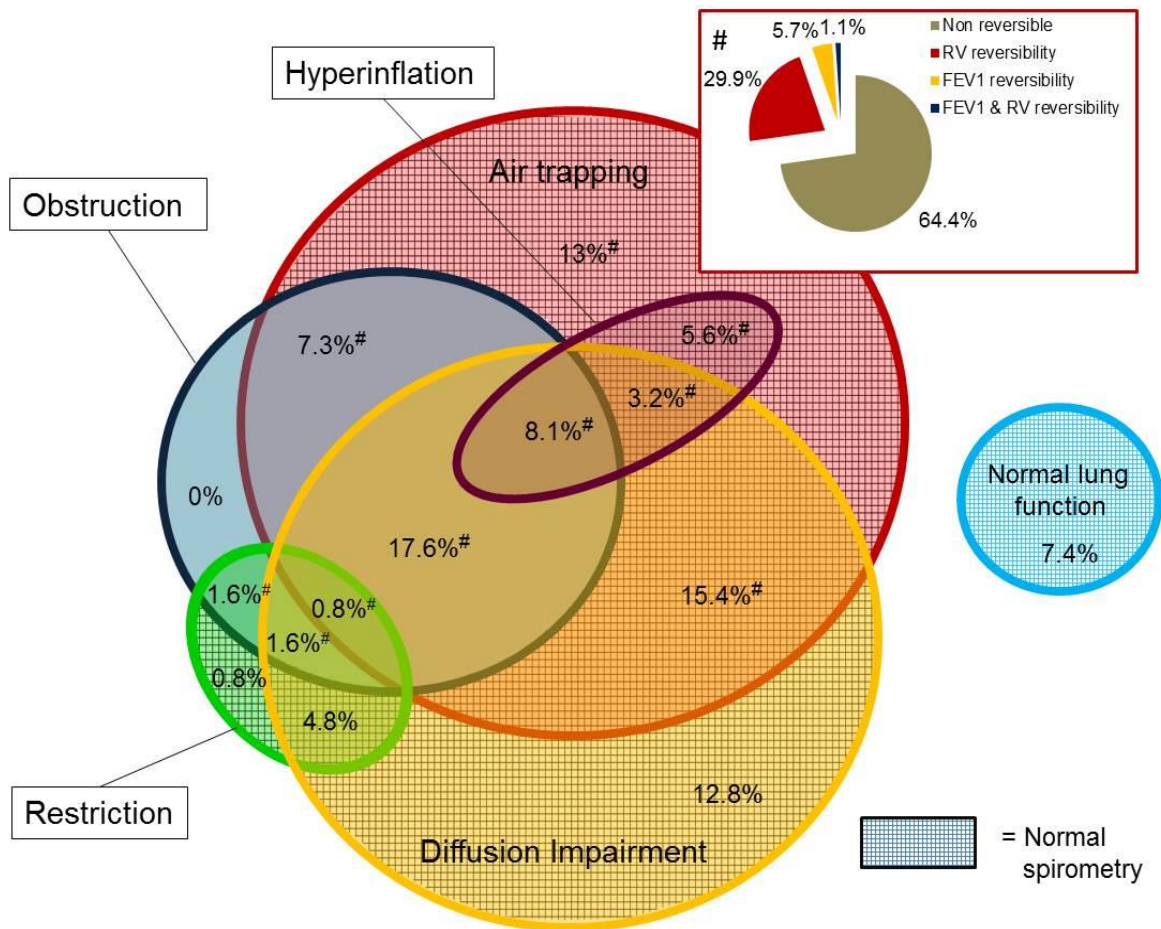
Objective: to characterize lung function and identify specific functional sub-groups in patients with non-cystic fibrosis bronchiectasis.

Methods: this was a prospective, observational study that recruited consecutive clinically stable adult outpatients with clinically significant bronchiectasis attending the bronchiectasis clinic at the San Gerardo Hospital, Monza (Italy), from January 2012 to December 2013. Patients underwent spirometry, body-plethysmography and diffusing lung capacity (DL_{CO}) and were followed-up for 3 years during which exacerbations and mortality were recorded. During the follow up, all treatments, including inhaled bronchodilator and corticosteroid therapy, were left to the clinical judgment of the attending physician that was blind to the scope of the study. Patients with airflow obstruction and/or air trapping at baseline underwent acute bronchodilation testing with salbutamol 400 µg. Lower limit of normal criteria were used to define obstruction and restriction. Air trapping and hyperinflation were defined as a residual volume (RV)>120%predicted and a total lung capacity>120%predicted, respectively. A diffusion impairment was considered a DL_{CO} <80%predicted. FEV₁ reversibility (FEV_{1rev}; ≥12% and 200 ml increase of control) and reversibility of air trapping (RV_{rev}; ≥10% reduction of control) identified acute bronchodilator responsiveness. Air trapping, airflow obstruction, acute reversibility and presence of restriction represented the four-step criteria used to identify a priori the functional sub-groups.

Results: 124 patients were enrolled, with a median (IQR) age of 70 (61-74) years; 32.3% males. At baseline, although 63% of patients had a normal spirometry, only 7.4% had an overall normal lung function. Lung function abnormalities greatly overlapped and were distributed as follows: air trapping (71%), impaired DL_{CO} (60.5%), airflow obstruction (37.0%), hyperinflation (16.9%) and restriction (9.6%). RV_{rev} (16.1% - 29.9% of tested) was more frequent than FEV_{1rev} (4% - 6.8% of tested) (Figure 1). A sensitivity analysis that excluded patients with concomitant asthma and/or COPD did not change the results. During the follow up, the overall annual frequency of exacerbation was 2 (IQR – 0-4) and 7 patients died. The main functional sub-groups identified were: I) patients with normal plethysmography (20.2%), II) patients with RV_{rev} (16.1%) and III) patients with acutely non-reversible obstruction (50.0%). Compared with non-reversible patients, patients with RV_{rev} had more severe

obstruction [mean(SD) FEV₁%pred: 82.6(25.1) vs 67.2(26.5); P=0.02], air trapping [RV%predicted, 153.4(28.3) vs 171.9(46.4); P=0.033] and higher specific airway resistances [median(IQR) sRAW%predicted, 141.5(118.9-186.9) vs 211.5(134.7-245.3); P<0.001], but did not differ in terms of DL_{CO}, exacerbations, mortality, comorbidities and chronic inhaled bronchodilator and corticosteroid therapy.

Conclusions: in bronchiectasis, the involvement of small airways appears predominant, with air trapping and reduced DL_{CO} representing the most common functional abnormalities. RV_{rev} is a more sensible marker of airway responsiveness than FEV₁ and is related to a more severe functional impairment. These results highlight the need for a comprehensive lung function assessment in clinical practice and may support the functional stratification in future trials investigating the efficacy of inhaled treatments in bronchiectasis.



C15 [153] Antibiotic resistance in non-cystic fibrosis bronchiectasis - a result of earlier diagnosis and aggressive management?

Daniel Ratnaraj¹; Naveen Pillarisetti¹

¹Starship Children's Hospital, Park Road, Grafton, Auckland, New Zealand

Background: Non-cystic fibrosis bronchiectasis is being increasingly reported in children from both developing and developed countries. It is a significant problem in New Zealand with higher incidence compared to other OECD countries. The disease is being diagnosed at a very young age with our median age of diagnosis as low as three years in recent cohorts. With earlier diagnosis these children are treated on an aggressive pathway with intravenous and oral antibiotics, intensified physiotherapy and close monitoring. While these interventions lead to clinical improvements, antibiotic resistance is a cause for concern in these children.

Objective: To review the airway microbiology and the prevalence of in-vitro antibiotic resistance in children with non-CF bronchiectasis at Starship Children's Hospital.

Methods: The medical records of children under active follow-up at the Starship Bronchiectasis Clinic who live in the Auckland metropolitan area were reviewed. HRCT imaging from the time of diagnosis was reviewed to record the extent of the disease. Pharmacy dispensing records were reviewed to determine each patient's total number of antibiotic courses in the last 12 months. The two most recent sputum, bronchoalveolar lavage or tracheal aspirate microbiology samples were reviewed.

Results: The mean age of diagnosis of n=59 children was 3.9 years and the current mean age was 8.7 years. The cohort consisted largely of children of Pasifika and Māori ethnicity. A significant number of children came from socio-economically deprived areas. 13 children were defined as having pan-lobar bronchiectasis on imaging and 24 with at least 3 lobes involved. The average number of antibiotic courses the children received in the preceding 12 months was 4.7, with a range of 0-20. Six children were identified as being on long term prophylactic antibiotic treatment. 107 airway samples were available for review on the hospital system. 27% (29/107) of airway samples grew at least one resistant organism. *Haemophilus influenzae* was the most common micro-organism detected in 35% (37/107) of samples. 41% of these isolates (15/37) displayed resistance (7 to Amoxicillin, 7 to Co-trimoxazole and 1 to Tetracyclines). *Streptococcus pneumoniae* was the second most common organism to be isolated in 8% (9/107) of samples. 56% (5/9) showed antibiotic resistance. *Moraxella catarrhalis* was isolated in 8 samples. 75% (6/8) of these isolates showed resistance to Amoxicillin. *Pseudomonas aeruginosa* was grown in four samples, with 50% displaying antibiotic resistance. 41% (24/59) of children had at least one antibiotic resistant micro-organism isolated in at least one airway sample.

Conclusion: There is significant antibiotic resistance in airway samples of children with non-CF bronchiectasis. The prevalence of antibiotic resistance in this group of children possibly reflects the degree of antibiotic use in this population and also the general population. This needs to be further evaluated in larger studies. There is an urgent need for antibiotic stewardship, more rational use of antibiotics and consideration of alternative therapies in the management of non-CF bronchiectasis.

B10 [119] PROGNOSIS - the German Bronchiectasis Registry- first results from 505 patients

Jessica Rademacher¹; Andrés de Roux²; Grit Barten³; Roland Diel⁴; Pontus Mertsch⁵; Joelle Naim³; Annegret Zurawski⁶; Tobias Welte^{1,6}; Felix Ringshausen^{1,6}

¹Hannover Medical school, Respiratory medicine, Hannover, Germany; ²Pneumologische Praxis at Schloss Charlottenburg, Berlin, Germany; ³CAPNETZ STIFTUNG, Hannover, Germany; ⁴Institut für Epidemiologie, UKSH, Kiel, Germany; ⁵Ludwig-Maximilians-University, Respiratory medicine, München, Germany; ⁶Biomedical Research in End-stage and Obstructive Lung Disease Hannover (BREATH), German Center for Lung Research (DZL), Hannover, Germany

Rational: Bronchiectasis is a chronic, progressive respiratory disease associated with irreversible widening of the bronchi. Until now there is no licensed therapy for bronchiectasis in Germany. The objective of PROGNOSIS (www.bronchiektasen-register.de) is to establish a representative registry to study the epidemiology of bronchiectasis and to promote collaborative clinical, basic and translational research in Germany.

Methods: Prospective, non-interventional and longitudinal register study with baseline and follow-up data collection every year; sector overspanning recruiting. Inclusion criteria: bronchiectasis proven by CT-scan, age ≥ 18 years, not known CF, no lung transplantation, written consent [1].

Results: During the first two years more than 800 patients were recruited in 36 centers (13 practices, 14 specialized hospitals and 9 university hospitals). The first 505 validated data sets showed: average age 62 (49-72) years (60% female; 54% never-smokers); median annual exacerbation and hospitalisation rate 1 (0-3) resp. 0 (0-1); on average moderate obstructive ventilation deficiency (FEV1 $68 \pm 27\%$ pred.; Tiffeneau $0,67 \pm 0,16$); average BMI 24 ± 5 kg/m²; 38% with chronic rhino sinusitis; duration of bronchiectasis in 49 % >10 years; most common etiology: idiopathic (34%); most common relevant pathogen if clinically stable: *Pseudomonas aeruginosa* (18%; 34% ever). The radiologic distribution shows 75% in the lower lobes, followed by 62 and 50% in the middle lobe and lingula. The upper lobes are rarely affected (46 resp. 38%). 90% of patients receive regular bronchiectasis therapy, 19% of patients inhale with antibiotics and 33% have azithromycin as long-term therapy. Within the inhaled antibiotics gentamicin was used most frequently, followed by colistin (28%) and tobramycin (27%). 12% had previous thoracic surgery. Vaccination status: PSV23 50%, PCV13 38%, seasonal influenza 79%. 44% had participated in a rehabilitation and 8% in clinical trials.

Conclusion/Perspective: The recruitment of PROGNOSIS proceeds faster than expected, underlining the clinical need of this project. Demographic data of German patients is similar to demographic data of the European bronchiectasis registry EMBARC. Pneumococcal vaccination and rehabilitation are not commonly applied. *Pseudomonas aeruginosa* is the most relevant pathogen and correlates with more exacerbations, a lower quality of life and reduced lung function. Due to the lack of evidence for the treatment of bronchiectasis, there is an urgent need for more clinical studies, to optimize the treatment. Within the registry, it is possible to build up networks to improve access to clinical trials with well-phenotyped patients with bronchiectasis.

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[1] Rademacher J, de Roux A, Ringshausen FC. PROGNOSIS - The PROspective German NON-CF Bronchiectasis Patient Registry. *Pneumologie*. 2015 Jul;69(7):391-393

D26 [132] Non-cystic fibrosis bronchiectasis: physiotherapy experience in New Zealand's tertiary children's hospital.

Laura Rensford¹; Anna Mulholland¹; Una Wainivetau¹; Naveen Pillarisetti¹

¹*Department of Respiratory Medicine, Starship Children's Hospital, Auckland, New Zealand*

Background: Non-cystic fibrosis bronchiectasis is being increasingly reported in children from both developing and developed countries. It is a significant problem in New Zealand with higher incidence reported amongst OECD countries. While physiotherapy is regarded as an important adjunct of treatment in non-cystic fibrosis bronchiectasis there is little objective evidence to support this. Despite this lack of evidence, it is important to incorporate airway clearance techniques in treatment of non-cystic fibrosis bronchiectasis and assess its effectiveness and adherence.

Objective: To review the age of diagnosis, demographics, extent of lung disease, physiotherapy techniques and adherence in children diagnosed with non-cystic fibrosis bronchiectasis at Starship Children's Hospital.

Methods: The medical records and bronchiectasis database at Starship Children's Hospital were reviewed. Demographic data, type of airway clearance used and patient adherence were recorded. Adherence was measured using patient or parent reported data.

Results: There are 250 children currently under active follow up at Starship Children's bronchiectasis clinic. These include 146 (58%) males and 104 (42%) females. The median current age was 8.5 years (range 1-17 years), and ethnicity consisted largely of Pacific Island (59%) and Maori (25%) children. A significant number of children came from socio-economically deprived areas. The most common cause of non-cystic fibrosis bronchiectasis were post infectious or idiopathic. Disease severity ranged from mild to severe, with two children using non-invasive ventilation and oxygen, of which one is on the lung transplant list.

Formal physiotherapy was taught to 240 children (96%). The most commonly used primary physiotherapy in children under five years was chest percussion (n=46; 85.2%); and for children over five years consisted a PEP device (TheraPEP, PariPEP, Acapella) (n = 130; 67%). Secondary physiotherapy techniques were taught to 59 children (23.6%) and mostly consisted of exercise (n= 22; 8.8%). Hypertonic saline was used in 16 children (6.4%). A high frequency chest wall oscillator was used in three children (1.2%).

Patient and parent self-reported adherence was documented for 219 children (91.3%). 78 children (32.55%) reported doing regular physiotherapy as prescribed, 80 (33.3%) reported occasional adherence, and 61 (25.45%) reported not doing any physiotherapy.

Conclusion: Starship Children's Hospital has a large population of children with non-cystic fibrosis bronchiectasis where physiotherapy plays an integral part of clinical management. While most of the children are taught airway clearance techniques, there is a significant amount of non-adherence, especially in a deprived and vulnerable population. Further research in the use, and efficacy of primary and secondary physiotherapy techniques in the management of non-cystic fibrosis bronchiectasis is required.

A01 [124] Burden of non-tuberculous mycobacterial pulmonary disease in Germany



Felix C. Ringshausen^{1,2}; Josephine Jacob³; Niklas Lampenius⁴; Michael Loebinger⁵; Albert Nienhaus^{6,7}; Klaus F. Rabe⁸; Roland Diel^{8,9}

¹Hannover Medical School, Hannover, Germany; ²Member of the German Center for Lung Research (DZL), Hannover, Germany; ³Institute for Applied Health Research and Elsevier Health Analytics, Berlin, Germany; ⁴Dept of Accounting and Finance, University of Hohenheim, Stuttgart, Germany; ⁵Royal Brompton Hospital and National Heart and Lung Institute, Imperial College, London, United Kingdom; ⁶Institute for Health Service Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany; ⁷Institution for Statutory Accident Insurance and Prevention in the Health and Welfare Services (BGW), Hamburg, Germany; ⁸Lung Clinic Grosshansdorf, Member of the German Center for Lung Research (DZL), Grosshansdorf, Germany; ⁹Institute for Epidemiology, University Medical Hospital Schleswig-Holstein, Kiel, Germany

Background: The incidence of non-tuberculous mycobacterial pulmonary disease (NTM-PD) is considered to be on the increase worldwide. However, estimates of the cost of treatment for patients with newly diagnosed NTM-PD are currently not available for any European country.

Objective: The objective of this study was to estimate the burden of disease in incident patients with NTM-PD.

Methods: A sample of 7,073,357 anonymized persons covered by German public statutory health insurances was used to identify patients with NTM-PD. In total, 125 patients with newly diagnosed NTM-PD in 2010 and 2011 were matched with 1,250 control patients by age, sex and Charlson Comorbidity Index, and followed for 39 months.

Results: The incidence rate for NTM-PD was 2.6 per 100,000 insured persons (95% CI 2.2–3.1). During the observational period, the mortality rate for patients with NTM-PD and the control group in the observational period was 22% and 6%, respectively ($p < 0.001$). In subjects with concomitant COPD the mortality rate was 42% and 16% in subjects with and without NTM-PD, respectively ($p < 0.001$). Mean direct expenditure per NTM-PD patient was €39,559.60 (95% CI 26,916.49–52,202.71), nearly 4-fold (3.95, 95% CI 3.73–4.19) that for a matched control (€10,006.71, 95% CI 8,907.24–11,106.17). Hospitalizations were three times higher in the NTM-PD group and accounted for 63% of the total costs. Attributable annual direct costs and indirect work-loss costs in NTM-PD patients were €9,093.20 and €1,221.05 per control patient, respectively. Regarding antibiotic use, only 74% of NTM-PD patients received antibiotic therapy of any type during the 3-year follow-up period, but only 68 out of 125 patients (54%) had begun treatment at the time of diagnosis. Overall, a variety of 29 different antibiotic two- or multidrug regimens were prescribed and nearly 12% were prescribed macrolide monotherapy.

Impact and conclusions: To our knowledge, our study represents the first investigation of healthcare costs brought about by incident NTM-PD and of respective antibiotic prescription patterns in Europe. Although NTM-PD is considered rare, the attributable mortality and financial burden in Germany are high. Efforts to heighten awareness of appropriate therapy are urgently needed.

C24 [92] Exacerbation Rate of Non-Cystic Fibrosis Bronchiectasis in Patients with Asthma-COPD Overlap Syndrome.

Alizaman Sadigov¹; Ibrahim Isayev¹; Aydin Aliyev²

¹Medical University of Baku, Department of Pulmonary Medicine, Baku, Azerbaijan; ²Medical university of Baku, Department of Radiology, Baku, Azerbaijan

Background: Coexisting COPD and bronchiectasis is associated with poor outcomes and co-morbidity is associated with more frequent exacerbations and mortality. Bronchial asthma coexisting with bronchiectasis is also associated with more frequent exacerbations compared with bronchiectasis alone. Where asthma and COPD occur together (the asthma and COPD overlap syndrome (ACOS)), there are increased rates of bronchiectasis compared with asthma or COPD alone. However, the effects of ACOS and bronchiectasis coexisting, in terms of disease progression and exacerbation rates are unknown.

Objectives: The aim of our study was to investigate the exacerbation rate of non-cystic fibrosis (non-CF) bronchiectasis in patients with asthma and COPD overlap syndrome.

Methods : All patients had investigated by using lung CT scan, sputum culture, pulmonary lung function and blood and sputum inflammatory biomarkers (C-reactive protein and interleukin-6, sputum neutrophil elastase) and arterial blood gas analysis. ACOS in patients with non-CF bronchiectasis was defined according to: persistent airflow limitation on spirometry despite adequate administration of short-acting bronchodilator in subjects 40 years of age or older; a significant history of cigarette smoking; a physician diagnosis of asthma before 40 years of age. Depending on existing ACOS all patients with non-CF bronchiectasis were divided in two groups: 1) 28 patients with non-CF bronchiectasis associated with ACOS; 2) 39 patients with non-CF bronchiectasis without ACOS.

Results: From October 2014 to November 2016 we had investigated 67 patients with non-CF bronchiectasis patients with -or without ACOS. All investigated patients had admitted to Pulmonary Medicine Department of University Hospital in Baku. Our investigation shown that in patients with non-CF bronchiectasis coexisting ACOS leads to the more frequent exacerbation compared with patients with bronchiectasis alone (4.2 ± 1.8 vs 2.0 ± 0.9 ; $P < 0.001$). In patients with co-morbid condition the FEV1 at the time of admission to the hospital was less than in patients with non-CF bronchiectasis without ACOS ($42 \pm 16.8\%$ vs $67 \pm 14.6\%$; $P < 0.001$). In patients with coexisting condition multi-lobe involvement on CT lung scan was higher compared with patients without ACOS ($24 [86\%]$ vs $22 [56\%]$; $P < 0.05$). The presence of *Pseudomonas aeruginosa* infection was higher in patients with coexisting non-CF bronchiectasis + ACOS ($P < 0.05$). The need to the non-invasive ventilation and oxygen support and ICU admission was more frequent among patients with coexisting condition compared with non-CF bronchiectasis alone ($P < 0.001$). Mortality rate was higher among patients with non-CF bronchiectasis + ACOS compared with patients without ACOS ($P < 0.05$).

Conclusion: Coexisting ACOS significantly impact to the exacerbation rate and disease progression in patients with non-CF bronchiectasis. ACOS lead to the more frequent and severe exacerbations in patients with non-CF bronchiectasis. In patients with non-CF bronchiectasis coexisting ACOS lead to the more severe clinical features of the disease and more diffuse radiological features with multi-lobe involvement. Presence of *Pseudomonas aeruginosa* infection in patients with coexisting condition lead to the more frequent admission to the ICU department and need to the ventilatory support. Coexisting ACOS is increased risk of mortality in patients with non-CF bronchiectasis.

C17 [71] Antimicrobial and antibiofilm activity of N-acetylcysteine against *Stenotrophomonas maltophilia* and *Burkholderia cepacia* complex

Francesco Sergio¹; Lucia Pallecchi²; Giulia Landini²; Tiziana Di Maggio²; Daniela Girelli³; Antonio Teri³; Lisa Cariani³; Francesco Blasi^{3,4}; Gian Maria Rossolini^{5,6,7}

¹Global Respiratory Medical Affairs, Zambon S.p.A, Milano, Italy; ²University of Siena, Siena, Italy; ³IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano, Italy; ⁴University of Milan, Milan, Italy; ⁵University of Florence, Florence, Italy; ⁶Florence Careggi University Hospital, Florence, Italy; ⁷Don Carlo Gnocchi Foundation, Florence, Italy

Background: N-acetylcysteine (NAC) is commonly administered for treatment of lower respiratory tract infections and in the management of cystic fibrosis. Besides its mucolytic properties, an increasing amount of data point to an intrinsic antimicrobial and anti-biofilm activity of NAC. Here, we evaluated the *in vitro* antimicrobial and antibiofilm activity of NAC against clinical isolates of *Stenotrophomonas maltophilia* and *Burkholderia cepacia* complex (BCC) grown in planktonic phase and in biofilm.

Material/methods: Sixteen *S. maltophilia* and 16 BCC (i.e. *B. cepacia*, *B. cenocepacia*, *B. multivorans*, *B. metallica*, *B. seminalis*, *B. stabilis*) clinical isolates were investigated. Minimal Inhibitory Concentrations (MICs) were determined by the broth microdilution method. The effect of sub-MIC concentrations of NAC on growth curves, and time-kill kinetics were further determined with eight selected strains (4 *S. maltophilia* and 4 BCC isolates). The ability of NAC in inhibiting biofilm formation was investigated using the MBEC High-Throughput Assay, and evaluated by viable cell count (VCC).

Results: MICs of NAC were 16 mg/ml for nine and seven isolates of *S. maltophilia* and BCC, respectively, and 32 mg/ml for the remaining ones. Sub-MIC NAC concentrations slowed down the growth of all the tested isolates. Time-kill assays showed a bactericidal activity (i.e. a reduction of bacterial inoculum by more than 3 logs) of NAC at 32 mg/ml against one *S. maltophilia* and one BCC isolate. NAC was found to inhibit biofilm formation in a dose-dependent fashion with all *S. maltophilia* and two BCC isolates. The Δ log CFU/peg, compared to control, ranged from 0.75 to 3.8 log CFU/peg and from 2.5 to 5.8 log CFU/peg at NAC 8 mg/ml and NAC 16 mg/ml, respectively.

Conclusions: High NAC concentrations, achievable by topical administration, were found to exert some antimicrobial activity against *S. maltophilia* and BCC clinical isolates, and showed a promising efficacy in preventing biofilm formation by those pathogens.

C16 [72] Activity of N-acetylcysteine in combination with colistin against a collection of colistin resistant *Acinetobacter baumannii* clinical isolates

Francesco Sergio¹; Lucia Pallecchi²; Tiziana Di Maggio²; Teresa Spanu³; Barbara Fiori³; Gian Maria Rossolini^{2,4,5}

¹Global Respiratory Medical Affairs, Zambon S.p.A, Milan, Italy; ²University of Florence, Florence, Italy; ³Univ. Cattolica del Sacro Cuore, Rome, Italy; ⁴Florence Careggi University Hospital, Florence, Italy; ⁵Don Carlo Gnocchi Foundation, Florence, Italy

Background: *Acinetobacter baumannii* is a relevant respiratory pathogen, representing a leading cause of nosocomial pneumonia and being increasingly identified also in patients affected by Cystic Fibrosis (CF). Colistin represents a last-line agent for the treatment of infections caused by extensively drug resistant *A. baumannii*. In this perspective, great concerns arise from the rising trend of resistance to colistin in this pathogen.

Material/Methods: Seven colistin resistant *A. baumannii* clinical isolates were investigated. Classic checkerboard assays were used to investigate potential synergism between colistin (range 0.25-256 µg/ml) and N-acetylcysteine (NAC, range 0.5-32 mg/ml). Fraction inhibitory concentration indices (FICIs) were calculated and synergism was defined as FICI values < 0.5. Synergy between colistin and NAC was also confirmed by time-kill assays performed with one isolate, using two different concentrations of colistin (2 and 8 µg/ml) and NAC (1.6 and 8 mg/ml).

Results: Synergism between colistin and NAC was observed in checkerboard assays with all tested isolates. In particular, a restoration of colistin susceptibility (i.e. MIC ≤ 2 µg/ml) was observed with 100% and 52% of tested strains in the presence of NAC 4 mg/ml and NAC 2 mg/ml, respectively. Time-kill curves confirmed the synergy observed by checkerboard assays, demonstrating a bactericidal effect of NAC/colistin combinations at sub-MIC concentrations.

Conclusions: The combination NAC plus colistin might represent a strategy to overcome colistin resistance in *A. baumannii* and prevent *in vivo* resistance selection during colistin treatment

C18 [73] Synergistic activity of colistin and N-acetylcysteine against *Stenotrophomonas maltophilia*

Francesco Sergio¹; Lucia Pallecchi²; Giulia Landini²; Tiziana Di Maggio²; Samantha Sottotetti³; Lisa Cariani³; Francesco Blasi^{3,4}; Gian Maria Rossolini^{5,6,7}

¹Corporate Respiratory Medical Affairs, Zambon S.p.A, Milan, Italy; ²University of Siena, Siena, Italy; ³IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milan, Italy; ⁴University of Milan, Milan, Italy; ⁵Florence Careggi University Hospital, Florence, Italy; ⁶Don Carlo Gnocchi Foundation, Florence, Italy; ⁷University of Florence, Florence, Italy

Background: Treatment of *Stenotrophomonas maltophilia* infections is complicated by intrinsic multidrug resistance, and an increasing trend of acquired resistance to first-line treatment options. Colistin is among the second line options, with the advantage of being also administrable by nebulization. Here we investigated the synergistic activity of colistin with N-acetylcysteine (NAC), a mucolytic agent with antioxidant and anti-inflammatory properties, commonly co-administered with antibiotics for treating lower respiratory tract infections.

Methods: Twenty *S. maltophilia* clinical isolates were tested. Synergism between colistin (range 0.25-256 µg/ml) and NAC (range 0.5-32 mg/ml) was investigated by classic checkerboard assays. Fraction inhibitory concentration indices (FICIs) were calculated, and synergism was defined as FICI values < 0.5. Time-kill assays were performed with two clinical isolates (including one strain resistant to trimethoprim-sulphamethoxazole, and one from CF). For this purpose, two different concentrations of colistin (2 and 8 µg/ml, representing concentrations achievable in serum and epithelial lining fluid - ELF, respectively) and NAC (1.6 and 8 mg/ml, likely achievable in ELF by topical administration) were tested alone and in combination.

Results: Colistin MICs ranged from 0.5 µg/ml to 128 µg/ml (MIC₅₀, 16 µg/ml; MIC₉₀, 64 µg/ml). The MIC of NAC was 16 mg/ml for nine isolates, >32 mg/ml for one isolate, and 32 mg/ml for the remaining ones. Synergism between colistin and NAC was observed in checkerboard assays with all tested isolates. Time-kill curves confirmed the synergy observed by checkerboard assays, demonstrating a bactericidal effect of colistin/NAC combinations at sub-MIC concentrations.

Conclusions: NAC concentrations achievable by topical administration showed remarkable *in vitro* synergy with colistin against *S. maltophilia* isolates. This combination might represent a valid option for treatment of difficult-to-treat *S. maltophilia* respiratory infections.

[97] Prevalence, risk factors and prognosis of Non Tuberculous mycobacteria infection and active disease among patients with bronchiectasis in Israel: a patient database search



Michal Shteinberg^{1,2,8}; Stein Nili^{3,8}; Adir Yochai^{1,8}; Shitrit David^{4,5}; Bendayan Danielle^{6,5}; Fuks Leonardo^{5,7}; Saliba Walid^{3,8}

¹Pulmonology Institute, Carmel Medical Center, Haifa, Israel; ²CF Center, Carmel Medical Center, Haifa, Israel; ³Department of Community Medicine and Epidemiology, Carmel Medical Center, Clalit Health Services, Haifa, Israel; ⁴Pulmonology Department, Meir Medical Center, and Tel Aviv University, Kfar Sava, Israel; ⁵Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; ⁶Pulmonary and Tuberculosis department, Shmuel Harofe Hospital, Beer Yaacov, Israel; ⁷Pulmonary Institute Rabin Medical Center, Petah Tikva, Israel; ⁸Technion- Israel Institute of Technology, the B. Rappaport Faculty of Medicine, Haifa, Israel

Background: The prevalence of Non Tuberculous mycobacteria (NTM) infection in Israel has not been previously reported. While bronchiectasis is known to be associated with NTM infection, estimated NTM prevalence among bronchiectasis patients is largely based on specialized centers, therefore the overall prevalence may be lower than previously reported.

Clalit Health Services (CHS) is the largest health maintenance organization (HMO) in Israel, with ~4.2 million customers (56% of Israel's population). CHS keeps a registry of its customers which includes data from primary care physicians, specialty clinics, hospitals, laboratories, and pharmacies.

Objective: To assess the prevalence of NTM growth, colonization and treated disease among patients with bronchiectasis in Israel, and to determine risk factors and prognosis for NTM growth.

Methods: The CHS database was retrospectively searched for adult patients diagnosed with bronchiectasis without cystic fibrosis before January 1, 2010. From this population we defined three categories of NTM: "Growth"- a single culture positive for any NTM; "Colonization"- At least two cultures positive for the same NTM species; "Treated"- patients in either of the above categories, who were treated with a combination of at least three anti- mycobacterial drugs. Risk factors for the three categories of NTM disease among patients with bronchiectasis, compared to patients with bronchiectasis and no NTM growth, was retrospectively determined, including demographics, comorbidity and hospitalizations, as well as general antibiotic and macrolide antibiotic use prior to NTM growth. Socioeconomic status (SES) was defined based on the SES score of the clinic neighborhood as defined by the Israeli Central Bureau of Statistics.

Results: Among 2,704,486 adults in CHS, 6369 had a diagnosis of bronchiectasis, representing a prevalence of 235:100,000. Samples for mycobacterial culture were available for 1930 patients (30%). 110 patients had growth of NTM, representing 5.7% of patients with samples, but only 1.7% of all bronchiectasis patients. 33 patients had colonization of NTM (1.7% and 0.5%, respectively), and only 13 were treated for NTM (0.65% and 0.2%, respectively). Univariate analysis defined the following factors to be associated with NTM growth: Female sex (71% vs. 55.7%, p=0.002); having never smoked (73.6% vs. 59.1%, p=0.003); and medium or high SES (78.3% vs. 57.5, p<0.0001). Age, prior hospitalizations and macrolide treatment were not associated with NTM growth. On multivariate analysis, female sex (OR 1.62 [1.01-2.58], p=0.045), medium or high SES (OR 2.47 [1.4-4.3], p=0.002-medium; OR 2.8 [1.5-5.2], p=0.001- high SES) were associated with a high risk for acquiring NTM, while

past or present smoking was negatively associated with NTM (OR 0.53 [0.33-0.87], $p=0.012$). Growth of NTM was not associated with increased mortality (HR 1.4 (0.95-2.15, $p=0.083$).

Conclusions: Prevalence of NTM growth and of NTM disease among patients with bronchiectasis is quite low compared to previously published data. The differences may result from including all patients with bronchiectasis rather than patients in referral centers, true differences in NTM prevalence in different geographic areas, or under-diagnosis of NTM lung infection outside of specialty centers. A high SES, female sex and having never smoked are risk factors for TNM growth among bronchiectasis patients.

C25 [138] Incidence of bronchiectasis related exacerbations after long term treatment with high frequency chest wall oscillation (HFCWO).

Chet Sievert¹; Caroline Beaner¹

¹*Electromed, Inc., New Prague, USA*

Background: The clinical effectiveness of HFCWO therapy for cystic fibrosis patients to enhance pulmonary mucus clearance and improve bronchial drainage has been long established and accepted. Other diseases commonly associated with compromised airway mucus clearance have also been reported to receive clinical benefits from HFCWO therapy. However, long term HFCWO treatment effectiveness studies in a bronchiectasis patient population have been limited.

Aim: Compare the exacerbation rates of bronchiectasis patients with HFCWO therapy to rates without therapy.

Methods: Exacerbations were defined as hospitalizations, emergency department visits and antibiotic prescriptions. Exacerbations, respiratory related only, were recorded by review of the patient's medical records and by phone interview for one year prior to start of HFCWO treatment and for 2½ after starting HFCWO treatment. Each patient served as their own control. The SmartVest Airway Clearance System (Electromed, New Prague, MN USA) was used by all patients. Patients offered quality of life information at phone interview. P values were calculated by paired t-test.

Results: Thirty-nine patients with a confirmed bronchiectasis diagnosis, who were compliant with the prescribed HFCWO treatment regimen, met the inclusion/exclusion criteria for the study. Exacerbations in all categories were significantly reduced; hospitalizations by 45% (P=0.007); emergency department visits by 75% (P=0.008); and antibiotic prescriptions by 40% (P=0.0005). Sixty-eight percent of study participants reported a significant improvement in their quality of life and a noticeable reduction in the number as well as the severity of their exacerbations.

Conclusion: The significant reduction in the bronchiectasis related exacerbation rates demonstrates the considerable potential for HFCWO therapy in this population. Furthermore, secondary benefits such as the potential to reduce antibiotic use and thereby not contribute to the antibiotic resistance pandemic may have even greater general population benefits. Considering the progressive nature of bronchiectasis these results warrant further investigation with a larger sample size.

D27 [62] LUNG FLUTE IS COMPARABLE TO FLUTTER DEVICE FOR ADULTS WITH NON-CYSTIC FIBROSIS BRONCHIECTASIS

Yasmin Silva¹; Tracy Greer²; Claude Farah²; Frank Li¹; Lucy Morgan²

¹Physiotherapy Department, Concord Repatriation General Hospital, Sydney, Australia; ²Respiratory Medicine, Concord Repatriation General Hospital, Sydney, Australia

Background: Airway clearance techniques are a vital part of routine care for subjects with bronchiectasis. There is no clear superior modality. The Flutter combines oscillations (6-20Hz) and positive expiratory pressure; the Lung Flute combines positive expiratory pressure and low frequency acoustic waves (18-22Hz), to augment clearance.

Objective: Lung Flute has been proposed as an alternative to Flutter. However there is no evidence supporting the use of Lung Flute in Bronchiectasis. The project aimed to compare these devices.

Method: This was a randomised crossover study of adult subjects with stable non-cystic fibrosis bronchiectasis (expectorating >25ml/day). Subjects attended two separate outpatient visits, one week apart, completed supervised sputum clearance regime and Lickert scale (8 questions regarding patient perception of the experience using each device). Total sputum expectorated during supervised intervention (T1) and after 30 minutes from end of T1 (T2) was recorded as Wet Sputum Weight (WSW). Total WSW desiccated in a microwave (10 min at 300W), allowed measurement of total Dry Sputum Weight (DSW). Data compared using paired t-test.

Results: 40 subjects, (mean±SD) age=63±16yrs were recruited. Overall there was no significant difference in WSW (5.78g ± 6.47 Flutter: 5.75g ± 0.22 Lung Flute) and DSW (0.40g ± 0.86 Flutter : 0.22g ± 0.21 Lung Flute). At T1, WSW was higher for Flutter (5.10g ± 6.26) compared to Lung Flute (3.74 ± 3.44), (p=0.04). At T2 WSW was higher for Lung Flute (2.02g ± 3.01) compared to Flutter (0.68g ± 0.75), (p=0.001). Subjects perceived Flutter as being significantly (p<0.05) easier to use and more useful for secretion clearance, with clearer instructions compared to Lung Flute.

Conclusions: Both devices were well tolerated and successfully augmented secretion clearance. Most subjects preferred the Flutter because of increased speed of secretion clearance and easier to use.

D19 [120] Smoking as the most common etiologic factor in the development of chronic respiratory diseases: difference between bronchiectasis and COPD.

Dusan Skrbic^{1,2}; Mirna Djuric^{1,2}; Djordje Povazan^{1,2}; Dusanka Obradovic^{1,2}

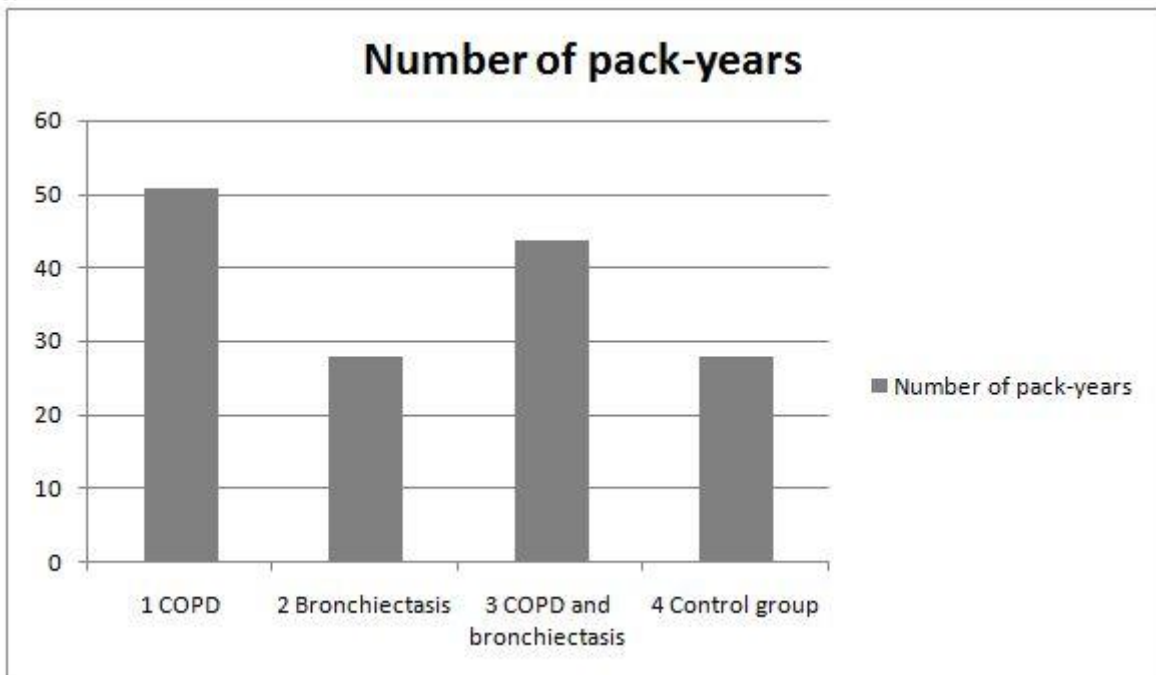
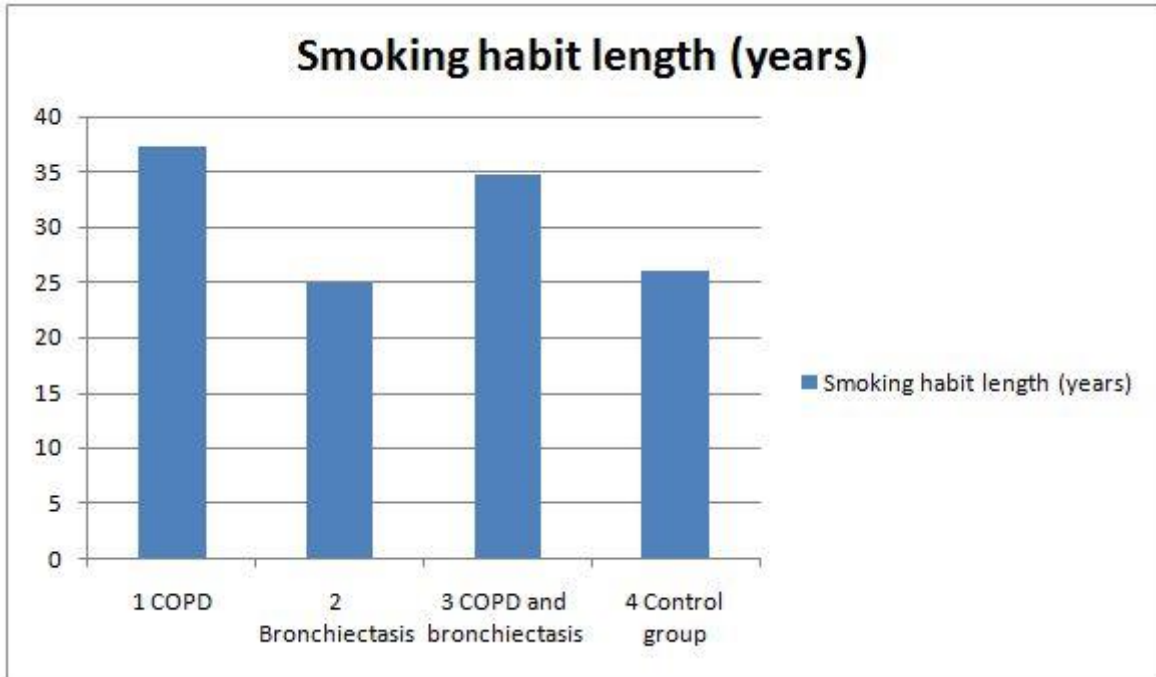
¹*Institute for Pulmonary Diseases of Vojvodina Sremska Kamenica, Sremska Kamenica, Serbia;* ²*Faculty of Medicine, University of Novi Sad, Novi Sad, Serbia*

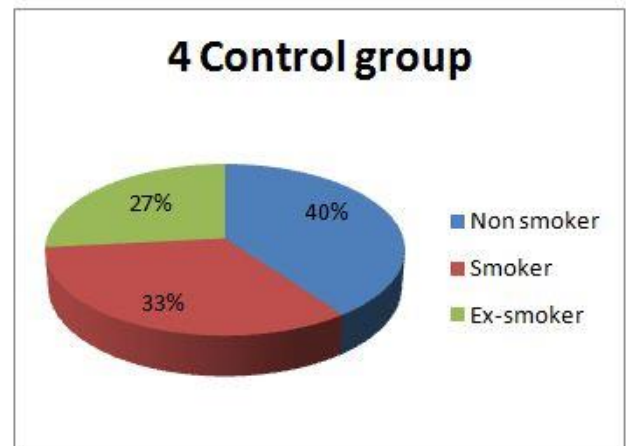
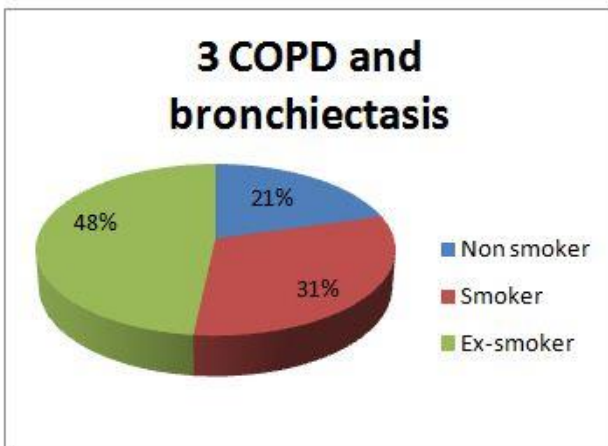
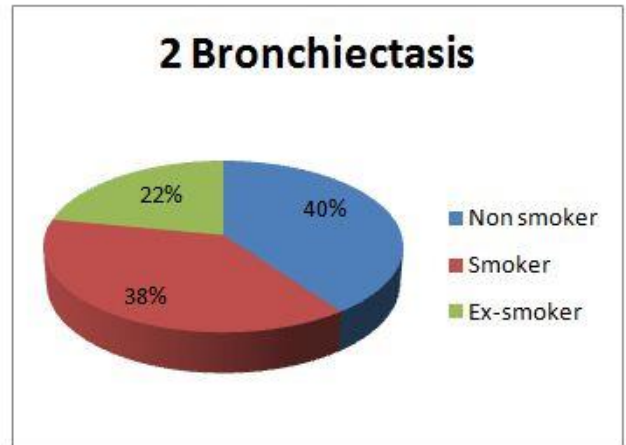
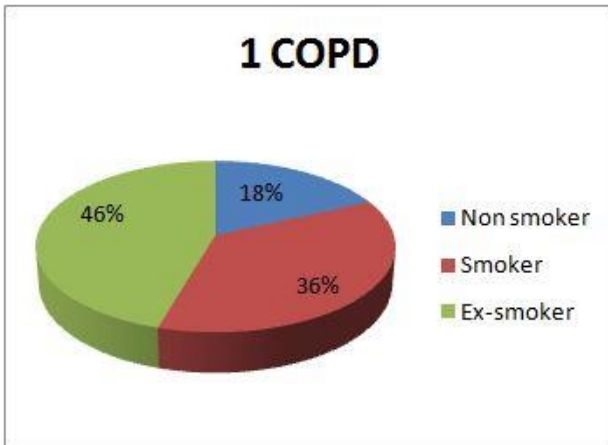
Background: Tobacco smoking is the major risk factor for chronic respiratory diseases. Prevalence of the respiratory diseases in different countries is related to rates of smoking and time of introduction of cigarette smoking.

Aim: The aim of study was to estimate the incidence of smoking on patients with COPD and non-cystic fibrosis bronchiectasis.

Methods & results: The study included 193 subjects classified into four groups: Group 1 - COPD without bronchiectasis (n=55), Group 2 - bronchiectasis without obstructive lung disease (n=50) and Group 3 - patients with concurrent COPD and bronchiectasis (n=58). The control group 4 included 30 subjects without respiratory disease. The diagnosis of bronchiectasis was confirmed by HRCT scanning and diagnosis of COPD was confirmed with spirometry. According to the gender structure 71.5% were men and 28.5% woman. The average age of patients was 61.82 ± 12.7 years. Patients in Group 1 (COPD) and Group 3 (COPD with bronchiectasis) had longer smoking time than groups 2 and 4. If smoking time is observed, the average smoking habit length among our patients smokers was 32.3 ± 11.8 years. The study showed that patients in Group 1 (COPD) had a statistically significant longer smoking habit length ranging from 50.64 ± 23.5 years, then group 2 patients (27.77 ± 15.2) and patients from control group 4 (27.94 ± 10.3). Group 3 patients (COPD with bronchiectasis) had average 43.64 ± 23.86 years of smoking habit length, statistically significantly longer than those in Group 2 (bronchiectasis) and group 4 (control). The average number of pack-years in our sample was 40.45 ± 22 . There is a statistically significant difference in the number of pack-years between the patients in groups 1 and 3 compared to the patients from groups 2 and 4. The largest number of patients in our study were either smokers or former smokers. According to the results, there were 82% of active smokers and ex-smokers (n = 139). The number of current and ex-smokers in group 1 (HOBP-81%) and group 3 (COPD and bronchiectasis 79%) was higher than in group 2 (bronchiectasis-60%) and control group 4 (59%). There are statistically significant number of ex-smokers in group 1 (HOBP-45%) and group 3 (COPD and bronchiectasis 48%) than 22% in group 2 (bronchiectasis-22%) and 4 (control group -26%).

Conclusions: The patients with longer smoking habit length and higher rates of smoking developing COPD concomitant with bronchiectasis





B17 [202] The epidemiology of hospitalized exacerbations of bronchiectasis in Italy from 2006 to 2014

Giovanni Sotgiu¹; Simone Dore¹; Stefano Aliberti²; Laura Saderi¹; Francesco Amati²; Elisa Franceschi²; Leonardo Terranova³; Francesco Blasi²

¹*Dept of Biomedical Sciences, University of Sassari, Sassari, Italy;* ²*Department of Pathophysiology and Transplantation, University of Milan, Internal Medicine Department, Respiratory Unit and Cystic Fibrosis Adult Center, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy;* ³*Paediatric Highly Intensive Care Unit, Department of Pathophysiology and Transplantation, Università degli Studi di Milano, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano, Italy*

Background: Bronchiectasis is an increasingly recognized clinical health issue worldwide. Its morbidity and mortality burden is heterogeneously known owing to missing systematic and mandatory notification systems. Exacerbations play an important role in bronchiectasis-related morbidity, especially those requiring hospitalization. Epidemiology of hospitalized exacerbations of bronchiectasis and their impact on the healthcare system in Italy is unknown.

Objective: To assess the epidemiological burden of hospitalized exacerbations of bronchiectasis among Italian adults and to compare the characteristics of hospitalized patients with exacerbation vs. pneumonia vs. neither exacerbation nor pneumonia.

Methods: A retrospective longitudinal study was carried out in 2016. The population target included hospitalized bronchiectasis patients (*i.e.*, ordinary or day hospital admissions). The temporal recruitment period ranged from 2006 to 2014. Demographic, epidemiological, and clinical variables were collected in an *ad hoc* electronic form. Italian national data were retrieved from the Diagnosis-Related Group (DRG) notification system of the Italian Ministry of Health (Ministro della Salute - Direzione Generale della Programmazione Sanitaria-Banca Dati SDO) using all the DRG codes related to bronchiectasis. Three study groups were identified: patients with exacerbation without pneumonia (Group 1), patients with pneumonia (Group 2) and patients with bronchiectasis with neither exacerbation nor pneumonia (Group 3).

Results: Among 99,778,020 hospital admissions across Italy from 2006 to 2014, 66,622 were due to exacerbation of bronchiectasis (0.067%; Group 1), 8,524 to pneumonia in bronchiectasis (0.009%; Group 2) and 43,001 to neither exacerbation nor pneumonia in a bronchiectasis patient (Group 3). The majority of the patients were Italian (>95%). The proportion of males ranged from 49.0% in Group 3 to 51.7% in Group 2. The median (IQR) age was significantly higher in Group 1 (72 [61-79] years) and lower in Group 3 (65 [44-75] years). The highest proportion of admissions were ordinary for all groups (range: 68%-90%); however, admissions in a day-hospital regimen were significantly higher in the Group 3 (32.4% VS. 12.3% and 10.0% in the groups with exacerbations and pneumonia, respectively). A 67% increase in prevalence of hospitalizations due to either exacerbation of bronchiectasis or pneumonia in bronchiectasis patients has been detected from 2006 to 2014, see Table 1. The median (IQR) duration of the hospital stay was statistically lower in patients in Group 3 (7 [3-13] days VS. 10 [6-15] days and 11 [7-16] days Groups 1 and 2, respectively). However, it was significantly higher in the group of patients diagnosed with a pneumonia. Mortality rate was higher in the Groups 1 and 2 (2.0% and 2.2%, respectively) than that recorded for patients in Group 3 (0.5%); it ranged from 1.8% to 2.2% and from 1.7% to 2.7% in patients in Group 1 and 2, respectively.

Conclusions: The admission rate for low respiratory tract infections of bronchiectasis patients in Italy seems high with a temporal increasing trend. The ordinary admission regimen is frequently prescribed,

but the clinical appropriateness cannot be proved. The long duration of the hospital stay has implied relevant direct and indirect costs. The relatively few variables collected by the DRG system hinder the investigation on the drivers of patients' admissions. However, a more detailed assessment including bronchiectasis patients managed in outpatient settings and a cost-effective analysis from a healthcare and societal perspective could better clarify the burden of the disease.

Table 1. Prevalence of exacerbations of bronchiectasis and pneumonia in hospitalized patients with bronchiectasis, 2006-2014.

Year	Exacerbations	Pneumonia	Exacerbations/Pneumonia
2006	6,319/11,964,092 (0.053%)	706/11,964,092 (0.006%)	7,025/11,964,092 (0.058%)
2007	6,715/12,342,537 (0.054%)	791/12,342,537 (0.006%)	7,506/12,342,537 (0.061%)
2008	7,146/12,112,389 (0.059%)	848/12,112,389 (0.007%)	7,994/12,112,389 (0.066%)
2009	7,681/11,674,098 (0.066%)	881/11,674,098 (0.008%)	8,562/11,674,098 (0.073%)
2010	7,561/11,294,892 (0.067%)	872/11,294,892 (0.008%)	8,433/11,294,892 (0.075%)
2011	7,663/10,757,733 (0.071%)	972/10,757,733 (0.009%)	8,635/10,757,733 (0.080%)
2012	7,734/10,259,780 (0.075%)	1,015/10,259,780 (0.009%)	8,749/10,259,780 (0.085%)
2013	7,796/9,843,992 (0.079%)	1,171/9,843,992 (0.012%)	8,967/9,843,992 (0.091%)
2014	8,007/9,528,507 (0.084%)	1,268 /9,528,507 (0.013%)	9,275/9,528,507 (0.097%)
Total	66,622/99,778,020 (0.067%)	8,524/99,778,020 (0.009%)	75,146/99,778,020 (0.075%)

[21] Identification of *Pseudomonas aeruginosa* Airway Colonization by an Electronic Nose in Bronchiectasis Patients



Guillermo Suarez-Cuartin^{1,2}; Jordi Giner^{1,2}; Jose Luis Merino³; Ana Rodrigo-Troyano^{1,2}; Anna Feliu^{1,2}; Ana Alonso^{1,2}; Ferran Sanchez-Reus^{2,4}; Vicente Plaza^{1,2}; James D Chalmers⁵; Oriol Sibila^{1,2}

¹Department of Respiratory Medicine, Hospital de la Santa Creu i Sant Pau. Universitat Autònoma de Barcelona., Barcelona, Spain; ²Institut d'Investigació Biomèdica Sant Pau (IIB Sant Pau)., Barcelona, Spain; ³Electronic Systems Group. Universitat de Les Illes Balears (GSE-UIB)., Palma de Mallorca, Spain; ⁴Department of Microbiology, Hospital de la Santa Creu i Sant Pau. Universitat Autònoma de Barcelona., Barcelona, Spain; ⁵Scottish Centre for Respiratory Research, University of Dundee., Dundee, United Kingdom

Background: Airway colonization by Potentially Pathogenic Microorganisms (PPM) in bronchiectasis is associated with worse clinical outcomes. However, its diagnosis in clinical practice is sometimes complicated. The electronic nose is a non-invasive technology capable of distinguishing volatile organic compounds (VOC) breath-prints in exhaled breath. However, there is no data available regarding the utility of this new technology for detecting PPM airway colonization in bronchiectasis patients.

Objective: The aim of this study is to explore if an electronic nose can reliably discriminate the presence of PPM airway colonization in patients with bronchiectasis.

Methods: Seventy-three clinically stable bronchiectasis patients were consecutively included in a cross-sectional study. The presence of PPM in the airways was determined using spontaneous sputum culture. At the same time, exhaled breath was collected in Tedlar bags and VOC breath-prints were detected by the commercially available electronic nose Cyranose 320[®]. Cross-validation accuracy was assessed using discriminant analysis on principal component reduction. Area Under Receiver Operating Characteristic (AUROC) curve was calculated as a test of diagnostic accuracy.

Results: Forty-one patients with bronchiectasis (56%) were colonized with PPM. *Pseudomonas aeruginosa* (n=27, 37%) was the most common PPM, followed by *Haemophilus influenzae* (n=7, 10%). VOC breath-prints from colonized and non-colonized patients were different (accuracy of 72%, AUROC 0.75, p<0.001). In addition, VOC breath-prints from *Pseudomonas aeruginosa* colonized patients were significantly different from those of patients colonized with other PPM (accuracy of 89%, AUROC 0.97, p<0.001) and non-colonized patients (accuracy 73%, AUROC 0.83, p=0.007).

Conclusions: An electronic nose can accurately identify the presence of airway bacterial colonization in clinically stable bronchiectasis patients, especially in those with *Pseudomonas aeruginosa*.

[134] The impact of macrolide therapy on the lung resistome: a novel pooled-template shotgun metagenomics combined with bespoke gene-specific quantitative PCR

Steven Taylor^{1,2}; Jocelyn Choo^{1,2}; Lex Leong^{1,2}; Fredrick Mobegi^{1,2}; Steve Wesselingh^{1,2}; Lucy Burr³; Geraint Rogers^{1,2}



¹South Australian Health and Medical Research Institute, Adelaide, Australia; ²SAHMRI Microbiome Research Laboratory, School of Medicine, Flinders University, Adelaide, Australia; ³Department of Respiratory Medicine, Mater Adult Hospital, Brisbane, Australia

Background: Identifying the emergence of antibiotic resistance within a population allows the prediction of reduced treatment efficacy and the dissemination of resistant pathogens to the wider population. Clinical trials of macrolide therapies in bronchiectasis have been limited to culture-based sensitivity testing, which neither identifies the genetic basis of resistance, nor the emergence of resistance within the wider airway microbiota. While shotgun metagenomics is a powerful tool for resistome analysis, large-scale studies are prohibitively expensive. We have developed a novel strategy that involves identification of resistance genes through metagenomic sequencing of pooled sputum DNA, followed by the application of bespoke quantitative (q) PCR assays to individual samples.

Objective: Our aim was to assess the ability of pooled-template shotgun metagenomics and bespoke qPCR assays to determine the impact of long-term macrolide therapy on the lung resistome.

Methods: Culture-independent resistome mapping was assessed using samples from the BLESS randomised controlled trial. Induced sputum from adult bronchiectasis patients were collected at baseline, and after 48 weeks of twice-daily erythromycin ethylsuccinate (400 mg, n=32) or placebo control (n=31). Sputum DNA was extracted and treatment group DNA was pooled at each time-point, prior to metagenomic shotgun sequencing using the Illumina HiSeq 2500 system. Non-human reads were aligned to the Comprehensive Antibiotic Resistance Database (CARD). qPCR assays were then designed for the specific enumeration of detected resistance genes and applied to individual DNA extracts from both treatment and control groups.

Results: A total of 90 discrete resistance genes were detected within the study cohort, including transmissible elements conferring reduced susceptibility to aminoglycosides, fluoroquinolones, beta-lactams, tetracyclines, and macrolides. Forty-one of these resistance genes were higher following 12 months of erythromycin compared to placebo. A subset of genes that showed the greatest increases in prevalence were selected for sample-specific quantification by qPCR. The plasmid-encoded erythromycin resistance methylase gene, *ErmB*, increased significantly in patients who received erythromycin ($p=0.007$), but not placebo. Carriage of *ErmB* confers substantial resistance to all macrolide drugs, is carried by a wide range of different bacteria, and is readily transmissible between commensal and pathogenic populations. In contrast, no significant increases were observed in levels of *ErmA* or *ErmC*, methyltransferase genes whose carriage is limited to staphylococci. The *Haemophilus influenzae* multidrug resistance gene, *HmrM*, was detected in all *H. influenzae*-dominated samples, and was positively correlated with *H. influenzae* abundance ($r=0.77$, $p<0.001$). *HmrM* significantly decreased in response to erythromycin therapy ($p=0.04$), reflecting its constitutive carriage in *H. influenzae*, and supporting previous reports of decreased *H. influenzae*-dominance in this group.

Conclusions: Pooled-template shotgun metagenomics provides a means to identify resistance genes carried within a patient population. In combination with gene-specific qPCR assays, this allows comprehensive and cost-effective characterisation of antibiotic treatment impact. This strategy provides a powerful tool for clinical trials of antibiotic therapies, as well as shifts in resistance within patient populations. The metagenomic sequence data on which the resistome analysis is based also provides a wealth of microbial data, including the carriage of emerging pathogens, including non-tuberculous mycobacteria.

A11 [90] Mortality in patients with Mycobacterium Avium Complex lung disease – a review of published literature

Roald van der Laan¹; Marko Obradovic¹

¹*Insmmed Inc, Utrecht, Netherlands*

Background: Nontuberculous mycobacteria (NTM) are ubiquitous environmental bacteria and the prevalence in human clinical samples is increasing worldwide. Mycobacterium avium Complex (MAC) has been reported to be the most common causative agent in NTM lung disease worldwide. Treatment outcomes in NTM lung disease are sparsely reported and as of today only one systematic literature review on quality of life, co-morbidities and mortality, and one meta-analysis on treatment success rate have been published. However, no review of long-term mortality specifically in patients with MAC lung disease has been published yet.

Aim: The objective of the analysis was to collect available data from the published literature on 5-year all-cause mortality in patients with MAC lung disease and to explore study characteristics that may have contributed to variability in all-cause mortality reports.

Results: We have identified 13 published studies reporting 5-year mortality in patients with MAC lung disease. Ten studies were retrospective and three were prospective, with sample sizes from 34 to 782 patients with MAC lung disease. 5-year mortality rates ranged between 10% and 66%, and 10 of the 13 studies reported a rate exceeding 25%. The Q-statistics ($Q=172$, degrees of freedom (df)=12) suggest substantial deviations of study-specific mortality from an aggregate mortality estimate. The I²-statistic ($I^2=93\%$) indicates that 93% of the observed variability in mortality rates was likely due to true heterogeneity in mortality rates among the studies. Lower mortality rates were reported by studies in patients with predominantly nodular disease, whereas higher rates by studies in patients with predominantly cavitary disease or in case of macrolides resistance.

Conclusions: Risk of all-cause mortality in patients with MAC lung disease varies across studies. Most of the studies document a 5-year mortality rate greater than 25%, indicating a substantial health threat to people with the disease.

D28 [158] Physiotherapy self-management education work-shop for patients with bronchiectasis

Naama Yaari BPT¹, Devorah Israeli MPH¹, Ofra Tsuk BPT^{1,3}, Vered Mualem MPT¹, Yochai Adir MD, FCCP^{2,4} and Michal Shteinberg MD, PhD^{2,3,4}

¹Physiotherapy Institute, Carmel Medical Center, Haifa, Israel; ²Pulmonology Institute and ³CF Center, Carmel Medical Center; ⁴Technion- Israel Institute of Technology, the B. Rappaport Faculty of Medicine, Haifa, Israel

Background: Bronchiectasis can be controlled with the combination of proper medical and physiotherapy daily routine. However, implementing this everyday routine is often tedious and time consuming and patient adherence may be suboptimal. Studies on the benefits of self- help groups for people with chronic diseases showed several beneficial effects: impact on disease-related stress; impact on patient behavior towards professional service and improved adherences. Personal experience and practice, feedback and reinforcement, analysis of causes of failure and vicarious experience are important strategies to enhance self-efficacy and adherence. Thus, there is a need for an adequate self-management education program that would be beneficial for patients with bronchiectasis, as a self-help group.

Objective: We aimed to assess the feasibility and efficacy of a group self-management work-shop to help patients integrate the practice into their daily routine. The work-shop included: information regarding the disease and its treatment, practice of physical exercise and airway clearance techniques.

Methods: In a pilot program, we invited a group of bronchiectasis patients for a 3 meetings work-shop. For infection control, patients were preselected by a pulmonologist according to the colonization status, excluding patients colonized by *Pseudomonas aeruginosa* and other resistant bacteria. The meetings were conducted by a professional respiratory physiotherapist. Each meeting lasted two hours and consisted of three parts: informative (including oral information about bronchiectasis and methods of airway clearance), exercise practice (aerobic, strength and stretching) and mastering of airway clearance techniques (autogenic drainage, positive expiratory pressure (PEP) with "trigym" and oscillating PEP with a blow bottle and "aerobika" devices), all geared to facilitate and train self-management at home. Written guidelines were given to each participant during the first meeting. Quality of life was assessed by the bronchiectasis quality of life questionnaire (QOL-B) before the first meeting, at the end of the last meeting and two months after completing the workshop.

Results: 10 patients were included, 5 men and 5 women. Mean age was 63 years (range, from 47 to 79). Three of the patients were physiotherapy naïve, having not practiced regular airway clearance prior to the workshop. At the end of the workshop, all patients could successfully self employ all airway clearance techniques taught. There were no significant changes found in the different domains of the QOL-B questionnaire, although non-significant improvements were seen in the Physical Function domain (55% to 63%, p=0.359), and in the Vitality domain (52% to 62%, p= 0.75). During the work-shop the patients shared with the group their own unique strategies and incites for coping with the treatment burden, they asked questions to clarify and master the airway clearance techniques taught and shared their difficulties.

Conclusions: A physiotherapy workshop is a feasible means of educating patients on airway clearance techniques, as well as gaining advantages of peer support. A proper selection of patients is needed to optimize mastering of airway clearance techniques. A longer lasting education program is expected to give a better support and well implementation into the patients' daily routine.



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74, BD D'ITALIE, MONACO
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