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8th WORLD BRONCHIECTASIS CONFERENCE

ABSTRACT BOOK

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8th WORLD BRONCHIECTASIS CONFERENCE

ABSTRACT BOOK

RISING STARS

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[37] [2.06.37] Gene Expression Profiling of Airway Epithelium in Mycobacterium avium Complex Lung Disease

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Background/Aims: Impaired mucociliary clearance is associated with nontuberculous mycobacterial lung disease (NTM-LD). Airway epithelial cells (AECs) play a key role not only in maintaining mucociliary function but also in producing antimicrobial molecules and initiating inflammatory responses. Although several studies have explored the roles of AECs in NTM infection using in vitro models, gene expression patterns in human samples remain largely unexplored. To address this knowledge gap, we examined AEC gene expression using surgical specimens from patients with *Mycobacterium avium* complex lung disease (MAC-LD).

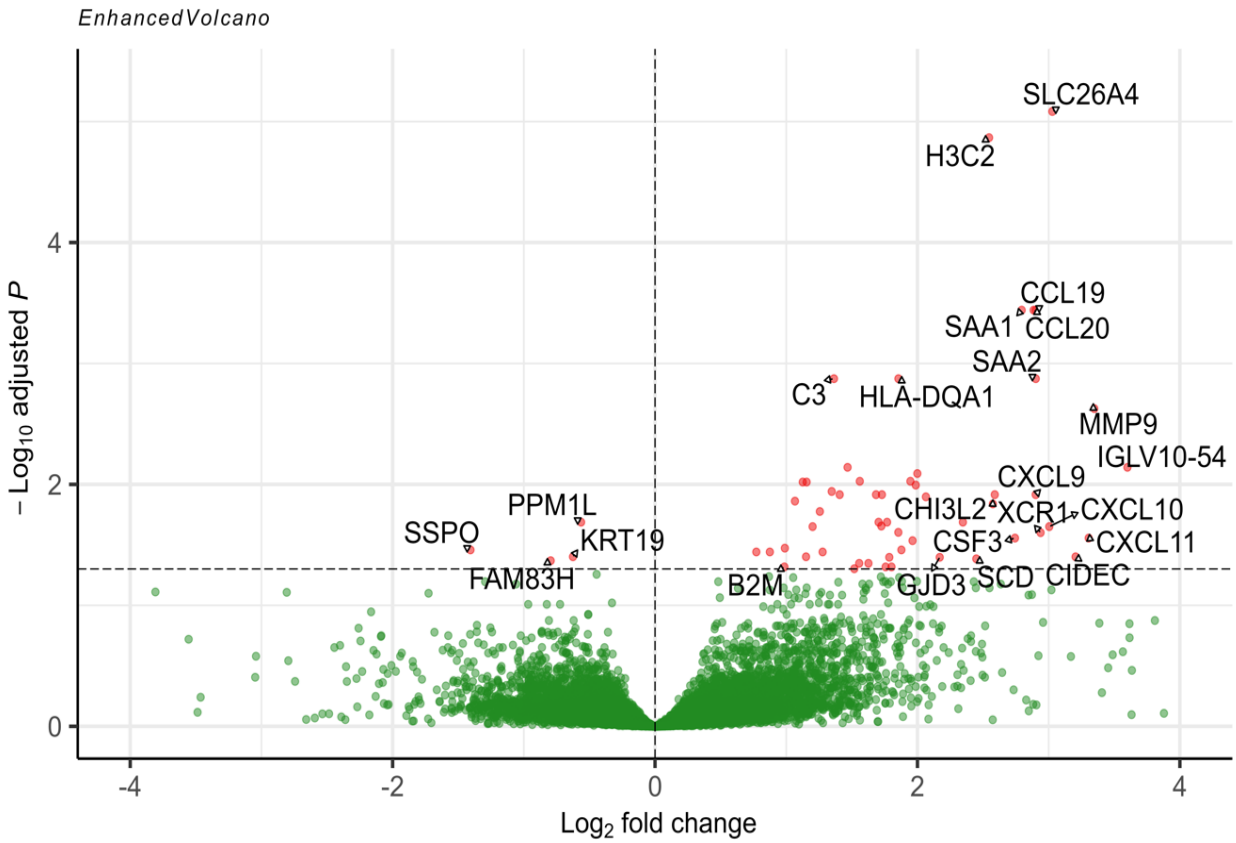
Methods: Patients with MAC-LD or non-infectious lung diseases who underwent thoracic surgery at Fukujuji Hospital between June 2014 and August 2016 were prospectively enrolled. We selected age-matched female MAC-LD patients (n=8) and non-infectious controls (n=8) for RNA sequencing of AECs. One MAC-LD patient was excluded because the pathology of the surgical specimen revealed carcinoma complications. An independent validation cohort of 19 female MAC-LD patients and 25 female non-infectious controls was also selected. AECs were isolated from the large bronchi of the resected lungs for RNA sequencing. We chose representative genes based on the results of differentially expressed gene analysis and weighted gene co-expression network analysis. Selected genes were subsequently validated by quantitative real-time reverse transcription PCR (qRT-PCR) in both the discovery and validation cohorts. Finally, we examined the associations between AEC gene expression and the clinical phenotypes of MAC-LD patients.

Results: We identified 54 upregulated and 4 downregulated genes in AECs from MAC-LD patients (Figure 1). Upregulated genes were primarily immune related and enriched in adaptive and humoral immune response, B-cell-mediated immunity, antigen presentation, complement and coagulation cascades, neutrophil migration, and the IL-17 signaling pathway. In addition to various immune related genes, *SLC26A4*, which encodes the anion exchanger pendrin, was markedly upregulated in MAC-LD (log2 fold change=3.0, FDR=0.8×10-5). The differential expression of four representative genes, *CCL20*, *MMP9*, *C3*, and *SLC26A4*, was verified by qRT–PCR, and these findings were confirmed in the validation cohort. Among the

26 MAC-LD patients, the expression level of *MMP9* was significantly greater in patients with cavitary lesions than in those without cavitary lesions. Furthermore, only the *SLC26A4* expression level exhibited a positive relationship with the bronchiectasis score (r=0.523, p<0.01), while no correlation was found for the other genes

Conclusions: In addition to various immune-related genes, the expression of *SLC26A4*, encoding the anion exchanger pendrin, was significantly upregulated in airway epithelium of MAC-LD. The correlation between gene expression and key clinical phenotypes provides valuable insights into the pathogenesis of MAC-LD. These findings suggest *SLC26A*4 as a potential disease susceptibility gene and a promising target for novel therapeutic approaches.

Conflict of interest(s) (if any – not included in the 500 words): All authors declare no conflicts of interest.



[55] [2.02.55] Economic evaluation of a physiotherapy-led community-based airway clearance service for people with chronic lung conditions: single group interrupted time series

Laura Cooper[1,2]; Kris Rogers[3]; Kylie Johnston[2]; Marie Williams[2]; Tracey-Lea Laba[3]

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Background/Aims: Chronic lung conditions affect 455 million people worldwide and have a significant clinical and economic impact on health care systems, and people's lives. Mucus hypersecretion is a common clinical symptom in bronchiectasis that can be managed with airway clearance strategies delivered by physiotherapists. We aimed to evaluate the impact of a community-based, airway clearance service (ACS) on public hospital admissions, emergency department (ED) presentations, length of stay (LOS) and associated health care costs.

Methods: A single group interrupted time series design was used to analyse public hospital health care usage in adults who attended the ACS between 2017 and 2021 (n=1510). Segmented regression modelling was employed to estimate the change in number of hospital admissions (primary outcome) with a respiratory-related diagnosis post the initial ACS session (immediate, 12 and 24 months). The number of ED presentations, LOS, and associated costs were secondary outcomes.

Results: Following the initial ACS session, ITS analysis estimated a reduction of 10.83 respiratory-related hospital admissions per 30 days (95% CI: -17.37 to -4.29, $p<0.05$) with a further decrease of 0.95 admissions over each of the following months (95% CI: -1.44 to -0.46, $p<0.001$). This was assosciated with immediate cost savings ($AUD, 2024) of $85 174 (95% CI: -142 475 to -27 873), with a further decrease of $8 694 over each of trhe following months (95% CI: -12 827 to -4 560). Significant reductions were also seen in respiratory-related ED presentations and LOS.

Conclusions: Participation in a community-based ACS reduced acute public hospital healthcare usage and provided value for money to the local health service.

Conflict of interest(s) (if any – not included in the 500 words): The author is the Manager of the Airway Clearance Service and works as an Advanced Respiratory Physiotherapist within the service.

[61] [2.12.61] Development and validation of a bronchiectasis child-specific quality of life instrument: The BC-QoL

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Background/Aims:
Quality of life (QoL), the highest prioritized outcome rated by patients and parents of children with bronchiectasis, is a patient-reported outcome measure which is increasingly considered essential when evaluating health and interventions. Yet, to date, there are no validated instrument that specifically measures QoL relating to child bronchiectasis. Research question: We aimed to develop and validate a new bronchiectasis child-specific parent-proxy QoL instrument (BC-QoL).

Methods:
A draft 44-item BC-QoL was first developed from: (a) parental responses to questions about the burden of bronchiectasis on their child, themselves, and their family; (b) clinicians' impression of parents' burden; and (c) previous child QoL instruments. This was followed by a prospective cohort study where 143 parents completed the draft BC-QoL, and other measures (cough scores, measures of child and parental QoL) over three-weeks at different phases of their child' illness (stable state, exacerbation and recovery). Responses were analysed using psychometric and clinical impact techniques to reduce the items and determine the instrument's reliability and validity. Minimally important difference (MID) was calculated

Results:
The final 23-item BC-QoL instrument with its three domains (emotional, physical, social well-being), demonstrated high split half reliability (0.95), Cronbach's alpha (0.97) and intraclass correlation scores (0.74, 95%CI 0.62, 0.82), and demonstrated evidence of validity and reliability in most tests. It had high and significant ($p < 0.01$) spearman correlations with measures of child and parental health and wellbeing, notably, 0.43, 0.41, 0.47 respectively with the matching emotional, social and physical domains of the PEDSQL4.0. BC-QoL 's MID was 0.74-1.32.

Conclusions:
This first bronchiectasis child-specific parent-proxy QoL instrument, BC-QoL is valid, and can be used to help us better understand the burden of bronchiectasis and for clinical research to evaluate the impact and effectiveness of interventions.

Conflict of interest(s) (if any – not included in the 500 words):

The authors declare no competing interests

[88] [2.09.88] Exome sequencing in a large cohort of primary ciliary dyskinesia: comprehensive evaluation of known genes and identification of new potential candidates

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Background/Aims:
Primary ciliary dyskinesia (PCD) is a genetically heterogenous disease resulting in motile cilia dysfunction. While primarily autosomal recessive, X-linked and autosomal dominance inheritance can also occur. Screening of known PCD genes in affected individuals usually involves a limited panel approach, with diagnostic rates of 40-60%. Here we aimed to identify the underlying genetic aetiology of an Australian paediatric PCD cohort.

Methods:

Exome sequence data from 102 individuals with PCD were filtered retaining novel/rare variants (minor allele frequency <0.01) predicted pathogenic/potentially pathogenic. A hierarchical approach was adopted: 1) biallelic variants in the 77 known PCD genes; 2) biallelic variants in 249 other ciliopathy-associated genes; and 3) novel gene discovery analysis.

Results:
Forty-six of 98 participants (47%) carried variants in known PCD genes (9 homozygotes, 35 compound heterozygotes, and two hemizygous males with novel X-linked variants). *DNAH5* and *DNAH11* were the most frequently implicated PCD genes (11 cases each), followed by *CCDC39* (3 cases) and *CCDC103, CCDC40, HEATR2*, and *DNAI1* (2 cases each). Screening of ciliopathy genes identified a complex *CFTR* allele in an individual subsequently diagnosed with bronchiectasis. Lastly, one individual was homozygous for a novel frameshift variant in ciliopathy gene *AK8*

Conclusions:
DNAH5 and *DNAH11* variants were the commonest aetiology for PCD in this cohort. Ciliopathy genes *AK8* and *CFTR* may contribute to PCD, though additional analyses are warranted. A hierarchical approach to analysing exome data can broaden the phenotypic spectrum for disease genes, and fuel new gene discovery.

[90] [2.10.90] Unraveling the pathogenicity of Mycobacterium abscessus in cystic fibrosis pulmonary epithelial cells and mouse models of respiratory infection.

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Background/Aims: Nontuberculous mycobacteria (NTM) are widespread environmental microorganisms that can colonize lungs, leading to chronic damage and a condition known as NTM pulmonary disease (NTM-PD). This disease particularly affects individuals with pre-existing lung conditions such as bronchiectasis, chronic obstructive pulmonary disease, and cystic fibrosis (CF). Among NTM species, *Mycobacterium abscessus* (*Mabs*) is especially concerning due to its natural resistance to antibiotics and significant genetic and phenotypic variability. *Mabs* exists in smooth (S) and rough (R) morphotypes and includes globally dominant circulating clones, though their specific roles in disease progression and lung inflammation remain unclear. The current understanding of how *Mabs* interacts with immune system responses during chronic infection is limited.

This study aims to elucidate the pathogenic mechanisms by which *Mabs* modulates host immune responses and inflammatory processes during respiratory chronic infection.

Methods: We analysed 11 *Mabs* isolates from 5 people with CF across asymptomatic and NTM-PD phases using morphotype and genome sequencing. Host responses to these isolates were studied in CF epithelial cell line (CFF-16HBEgeCFTRΔF508) via bulk RNA sequencing (bulk-RNAseq) and cytokine assays. Two clonal and longitudinal early (S) and advanced (R) *Mabs* clinical strains from the same patients with chronic infection were evaluated for their pathogenic potential in an air-liquid interface (ALI) model of CF human primary bronchial epithelial cells (CF-HBEpC) by single-cell RNA sequencing (scRNAseq), ELISA and Luminex. Moreover, the same two longitudinal isolates were tested in mouse model of chronic airway infection, utilizing flow cytometry and Visium spatial transcriptomics.

Results: Epithelial cells infected with *Mabs* strains revealed that the morphotype primarily drives the host response, as evidenced by over 2,000 differentially expressed genes identified comparing R with S infection via bulk-RNAseq and increased IL-6 and IL-8 protein release. Using CF-HBEpC in ALI culture, combined with scRNAseq, revealed that basal and secretory

cells significantly contributed to the immune response following infection with R and S strains. Specifically, R strain infections upregulated pathways related to cytokine and innate immune responses, mainly associated to type 1 and 17 immunity. We also found that late R strains elicited higher levels of pro-inflammatory cytokine (IL-6, TNF-α and G-CSF) and chemokines recruiting neutrophils and monocytes (Cxcl10 and MCP1) than early S strains.

We challenge C57bl/mice with the longitudinal S and R strains, and observed that both strains persist for 14 days with similar incidence of chronic infection and bacterial burden. In term of inflammatory response, mice chronically infected with R strains displayed greater recruitment of macrophages, Th1 and Th17 cells when compared to those infected with S strain. Spatial transcriptomics enabled the characterization of granuloma-like structures and confirmed that mice challenged with R strain exhibited the highest proinflammatory tissue profiles, characterized by sustained oxidative stress (e.g.Nos2), neutrophil and type II interferons pathways.

Conclusions: Our findings suggest that morphotype impacts the interaction between the lung epithelium and bacteria, with R strains inducing stronger type 1 and 17 proinflammatory immune response during bacterial persistence in the lung.

Acknowledgment: supported by Italian CF foundation FFC#7/2022 and FFC#23/2020

Conflict of interest(s) (if any – not included in the 500 words): I declare that there are no conflicts of interest.

[107] [2.14.107] Factors associated with hemoptysis in patients with non-cystic fibrosis bronchiectasis: cross-sectional analysis of data from the BE-China Registry

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Background/Aims:

Approximately 20% to 23% of patients with bronchiectasis experience hemoptysis. Compared to other respiratory diseases, hemoptysis in bronchiectasis is often more severe, with greater volumes and higher recurrence rates. However, limited evidence exists regarding the factors associated with hemoptysis in bronchiectasis. This study aimed to identify potential risk factors using data from the BE-China national registry.

Methods:

Data were extracted from the BE-China Registry between January 10, 2020, and May 1, 2024. Patients without recorded hemoptysis status were excluded. Baseline variables at enrollment, including demographics, clinical symptoms, etiology, comorbidities, radiological features, and microbiological results, were analyzed. Logistic regression was performed to identify factors associated with hemoptysis.

Results:

A total of 9,954 bronchiectasis patients from 95 centers were included. The prevalence of hemoptysis was 22.3%. The BSI score was higher in patients with hemoptysis (median [interquartile range] = 10 [7–13] vs 9 [5–12], $p < 0.001$). Factors significantly associated with an increased risk of hemoptysis included longer disease duration (OR = 1.017, 95% CI: 1.012–1.022, p < 0.001), greater number of exacerbations in the past year (OR = 1.107, 95% CI: 1.060–1.155, p < 0.001), isolation of *Pseudomonas aeruginosa* (OR = 1.220, 95% CI: 1.036–1.437, p = 0.017), and comorbid liver disease (OR = 2.191, 95% CI: 1.343–3.572, p = 0.002). Factors associated with a lower risk included being from an upper-middle-income region (OR = 0.850, 95% CI: 0.737–0.982, p = 0.027) and having sputum production (OR = 0.393, 95% CI: 0.326–0.473, p < 0.001). Compared to idiopathic bronchiectasis, non-infectious bronchiectasis was associated with reduced risk (OR = 0.662, 95% CI: 0.528–0.830, p < 0.001), whereas post-tuberculosis bronchiectasis showed an elevated risk (OR = 1.313, 95% CI: 1.062–1.623, p = 0.012).

Conclusions:

Accurate identification of bronchiectasis etiology is essential, and greater attention should be given to the risk of hemoptysis in patients with post-tuberculosis bronchiectasis. Close

monitoring is also warranted for patients with comorbid liver disease. Targeted eradication of *P. aeruginosa* may contribute to reducing the burden of hemoptysis in bronchiectasis.

Conflict of interest(s) (if any – not included in the 500 words):
The authors declare that they have no competing interests.

[155] [2.16.155] Targeting the Jagged-1/Notch pathway for the treatment of muco-obstructive lung diseases

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Background/Aims:

Mucus hypersecretion and/or impaired mucociliary clearance is a pathogenic feature of many chronic "muco-obstructive" lung diseases, including non-CF bronchiectasis, primary ciliary dyskinesias, asthma, chronic obstructive pulmonary disease, and cystic fibrosis (CF). This mucus is implicated in symptoms, poor QoL, airflow limitation, airway plugging, recurrent infection, severity, progression and mortality. Jagged-1, one of 5 human Notch receptor ligand members, is involved in cell fate specification. In the lung, Jagged-1, acting predominantly through Notch2, controls the balance of secretory club cells and ciliated cells. Local or systemic inhibition of the Jagged-1/Notch pathway ex vivo and in vivo redirects lineage specification towards ciliated cells and promotes loss of club cells, thus preventing their differentiation into mucus-secreting goblet cells which profoundly reduces mucus burden in the airways. As the Notch pathway is active in multiple other organs, an inhaled intervention which maximizes local-to-systemic therapeutic index is especially suited to maximize clinical benefit and minimize the risk of systemic side effects.

Methods:

Anticalin® proteins derived from human lipocalins can be engineered to bind to their targets with high potency, selectivity and a binding affinity similar to that of antibodies, but with a small size of 15 to 20 kDa. This small size, and their physical stability and robustness, are well suited to inhalation. Here we characterize the inhalable Jagged-1 targeting tool Anticalin, PRS-400, in comparison to a monoclonal anti-JAG1 antibody AMG 430 in in vitro (human) and in vivo (murine) models.

Results:

PRS-400 dose-dependent suppressed JAG1-notch signalling in a human luciferase reporter system. ***In vitro:*** In human ALI cultures PRS-400 penetrated mucus, suppressed FOXA3+ goblet cell metaplasia and epithelial remodelling induced by IL-13 and IL-17 and restored

FOXJ1+ ciliated cells. ***In vivo*****:** PRS-400 prevented and reversed goblet cell metaplasia and mucus hypersecretion, epithelial remodelling and restored FOXJ1 ciliated cells in IL-13, house dust mite “asthma” and bENAC-tg “CF” murine models.

Conclusions:

Targeting the Jagged-1/Notch-2 signalling axis by inhalation, exemplified by PRS-400, shows great potential for the treatment of muco-obstructive lung diseases.

Conflict of interest(s) (if any – not included in the 500 words):

[170] [2.11.170] CC16 as a biomarker of bronchial infection and disease severity in bronchiectasis

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Background/Aims: Protease/antiprotease balance is altered in bronchiectasis patients and impacts tissue remodelling and structural airway damage, which participate in the establishment of bronchial infections. Club cell secretory protein (CC16) is a small protein with immunosuppressive and immunomodulatory functions produced almost exclusively in the airway epithelium by Club cells. To date, it has not been described in bronchiectasis. We hypothesized that the pulmonary CC16 levels are altered in patients with bronchiectasis and that these alterations can be detected in blood. Therefore, we aimed to determine the relationship between CC16 levels, bronchial infections and disease severity in bronchiectasis, both at pulmonary and systemic levels.

Methods: A total of n=233 clinically stable non-cystic fibrosis bronchiectasis patients (mean age 67±15, 37% airway *P.aeruginosa* isolation and mean BSI was 6.8±4.4) from 2 tertiary hospitals in Barcelona and n=30 age- and sex-matched healthy controls with normal lung function were included in the study. At baseline, serum samples were collected from all of them, and n=92 spontaneous sputum samples from bronchiectasis patients. Disease severity was evaluated in patients by Bronchiectasis Severity Index score (BSI). Bronchial infection was defined by isolating potentially pathogenic bacteria at $>10^3$ cfu/ml in quantitative sputum culture. The levels of CC16, antimicrobial peptides and inflammatory cytokines were measured by ELISA and Luminex assays in serum and sputum samples. Sputum DNA extraction was performed and quantified by Qubit. Statistical analyses and graphs were conducted using RStudio and GraphPad.

Results: CC16 levels were higher in sputum than in serum ($p<0.0001$). Severe patients (BSI ≥9) had lower sputum CC16 levels than moderate and mild patients ($p=0.007$). Sputum CC16 levels were strongly correlated with lung function parameters ($p<0.001$). Patients with bronchial infection, specially caused by *P. aeruginosa*, had also decreased sputum CC16 levels ($p=0.007$). The lowest sputum CC16 levels were also found in those sputum samples with the highest bacterial load ($p=0.001$). Sputum CC16 levels were negatively correlated with the pro-inflammatory proteins LL-37, NE and IL-1β, whereas they were positively correlated with the anti-inflammatory and remodelling markers of SLPI, lysozyme, EGF and

TGF-α. A deep analysis based on sputum CC16 tertiles identified a subset of patients with the lowest CC16 levels that exhibited the more severe disease and the highest NE activity. Regarding the systemic compartment, no significant association between serum and sputum CC16 levels was found in bronchiectasis patients, and similar systemic CC16 levels were found between bronchiectasis patients and controls.

Conclusions: Low sputum CC16 levels are related to disease severity, bronchial infection, airflow limitation and airway inflammation, but this is not reflected in the systemic compartment. Further studies focused on Club cells and their role in tissue remodelling mechanisms in bronchiectasis are needed to identify new potential therapeutic targets.

Funding: *Instituto de Salud Carlos III (PI21/00419), SEPAR, SOCAP, Sara Borrell (CD23/00093) and Serra Hunter Program.*

Conflict of interest(s) (if any – not included in the 500 words):
None of authors had conflict of interests directly related to this work.

[195] [2.04.195] Racial and Ethnic Disparities in Bronchiectasis Outcomes in an Urban Safety-Net Hospital

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Background/Aims: Bronchiectasis is a chronic lung disease characterized by progressive airway damage, recurrent infections, and diminished quality of life. Although racial and ethnic disparities are well documented in other chronic respiratory illnesses, limited data exist on this topic in bronchiectasis. NYC Health + Hospitals (H+H), the largest municipal health system in the United States, includes NYC H+H/Bellevue as a key site. In 2021, the Bellevue Hospital Bronchiectasis Clinic (BHBC) was established to provide specialized care for patients with bronchiectasis and nontuberculous mycobacterial (NTM) pulmonary disease. We examined racial and ethnic differences in characteristics and outcomes among BHBC patients and explored the contribution of neighborhood-level social determinants of health.

Methods: BHBC Patients were enrolled in a bronchiectasis registry. Retrospective data was collected including demographics, clinical characteristics, bronchiectasis exacerbations, and pulmonary hospitalizations. Residential addresses were geocoded and linked to New York City Community Districts, as defined by the New York State Community Action Association. We stratified by race and ethnicity and examined neighborhood-level socioeconomic indicators based on patients' community district of residence. Analyses were performed using SAS version 9.4.

Results: From 2021 to 2025, 58 patients were enrolled (Table 1). The cohort had a mean age of 60 years and was 66% female. Racial/ethnic distribution was 33% White, 29% Hispanic, 21% Asian, and 17% Black. Black and Asian patients had the highest mean annual exacerbation rates (0.45 and 0.42), while Hispanic patients had the lowest (0.24). A similar pattern was seen for pulmonary hospitalizations, with Black (2.1) and Asian (0.67) patients having the highest rates and Hispanic patients the lowest (0.24).

Post-hoc comparisons showed Hispanic patients were more likely to have Medicaid or no insurance (94% vs. 42% among White patients, adjusted p = 0.0013) and were less likely to have a history of smoking (12% vs. 58% among White patients, p = 0.0058)(Table 2). Compared to White patients, Black patients lived in districts with higher poverty (23% vs. 16%, p = 0.008) and unemployment rates (9% vs. 6%, p = 0.002).

In negative binomial regression models adjusting for age, sex, eosinophil count, smoking status, and *Pseudomonas* presence, race and ethnicity were associated with differential risk for hospitalizations (Figure 1). Compared to Hispanic patients, Asian and Black patients had significantly higher hospitalization rates (RR 3.38, 95% CI 1.13–10.08 for Asian; RR 3.58, 95%

CI 1.17–11.00 for Black patients). A similar trend was observed for exacerbations, although associations did not reach statistical significance (RR 4.22, 95% CI 0.90–19.85 for Asian; RR 3.86, 95% CI 0.70–21.14 for Black patients).

Conclusions: This study identifies significant racial and ethnic disparities in bronchiectasis outcomes, with Black and Asian patients experiencing higher rates of hospitalizations. These differences correlated with community-level indicators of socioeconomic disadvantage, particularly poverty and unemployment. Initiatives aimed at improving access, education, and resource allocation in historically marginalized communities are urgently needed. Future research in larger, prospective bronchiectasis cohorts is critical in identifying modifiable drivers of inequity and guiding interventions to close these gaps.

Conflicts of Interest:

Robert C. Flowers: none; Alexandria E. Imperato: none; Rudra Ramanathan: none; Keshav Mangalick: none; Isabella Atandi: none; Shivani Singh: none

Doreen Addrizzo-Harris: Advisory boards for Paratek and Sanofi, Clinical Chair for the Bronchiectasis and NTM Association

Leopoldo N. Segal: COPD Foundation

Ashwin Basavaraj: none

All authors declare no relevant commercial interests related to this abstract.

[198] [2.07.198] Airway Interleukin-7 is a biomarker of exacerbation risk in patients with Pseudomonas aeruginosa infection in bronchiectasis

Rebecca Hull[1]; Emma Johnson[1]; Ashleigh Foubister[1]; Hollian Richardson[1]; Chloe Hughes[1]; Rachel Galloway[1]; Eve McIntosh[1]; Zsofia Eke[1]; Holly Lind[1]; Chandani Hennayake[1]; Daniela Alferes de Lima Headley[1]; Jennifer Pollock[1]; Morven Shuttleworth[1]; Pieter C Goeminne[2]; Michal Shteinberg[3]; Anthony De Soyza[4]; Stefano Aliberti[5]; Josje Altenburg[6]; Charles S Haworth[7]; Oriol Sibila[8]; Eva Polverino[9]; Michael Loebinger[10]; Felix C Ringshausen[11]; Natalie Lorent[12]; Katerina Dimakou[13]; Adelina Amorim[14]; Raul Mendez[15]; Anne Marie Mclaughlin[16]; Zoe Borrill[17]; Robert Lord[18]; Simon Finch[19]; Francesco Blasi[20]; Jeffrey Huang[1]; Jamie Stobo[1]; Merete Long[1]; Amelia Shoemark[1]; James D Chalmers[1]

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Background/Aims:

Chronic *Pseudomonas aeruginosa* airway infections in patients with bronchiectasis are associated with increased disease severity and exacerbation frequency. Impaired adaptive immunity has been linked to with worse outcomes. IL-7 is a key regulator of T and B cell

development, survival and function. We aimed to determine whether IL-7 sputum levels are associated with disease severity and inflammatory endotypes in bronchiectasis.

Methods:

Baseline sputum was analysed from patients with chronic *P. aeruginosa* infections in the parallel phase 3 trials of inhaled liposomal ciprofloxacin ORBIT-3 (n=116) and ORBIT-4 (n=148), and from patients with CT confirmed bronchiectasis in the pan-European EMBARC-BRIDGE observational study (n=85). IL-7 was measured using Olink® Target 48 (ORBIT-3, EMBARC-BRIDGE) or MSD V-PLEX Human IL-7 Kit (ORBIT-4). In ORBIT-4, label-free sputum proteomics and 16S rRNA sequencing (LoopSeq) were also performed. Bacterial infections were identified in EMBARC-BRIDGE with the BioFire® FilmArray® Pneumonia Plus Panel.

Results:

Patient demographics were: ORBIT-3, age 62.2±14.0 [mean±SD], 66·3% female; ORBIT-4, age 62.5±13.9, 67.6% female; EMBARC-BRIDGE age 62.5±16.5, 48.2% female.

Low levels of IL-7 were identified as a reproducible biomarker of increased exacerbation risk. In ORBIT-3, lower IL-7 levels were associated with increased exacerbation risk (HR=1.67, 95CI 1.12-2.43, p=0.012, Figure 1A). This finding was validated in ORBIT-4 using MSD targeted quantification (HR=1.42, 95CI 1.03-1.96, p=0.034, Figure 1B). In ORBIT-4, IL-7 levels were not significant associated with FEV1 (p=0.14, r^2=0.008) or QolB respiratory score (p=0.27, r^2=0.0016).

Proteomics in ORBIT-4 found that 84 proteins increased with lower IL-7 concentrations, including neutrophilic activation and chemotaxis markers (ITGAM, ITGB2, ELANE, MMP8, HDAC6). Conversely, 30 proteins increased with increased IL-7 concentrations, particularly antimicrobial peptides (LYZ, PRB3, BPIFA1, LPO), and immunoglobulin related proteins (HMGB2, IGLV3_19, IGKV1D_42) (Figure 1C).

Low IL-7 levels were associated with decreased microbiome alpha diversity (p<0.001, r^2=0.12) and changes in beta diversity (p=0.001, sum of squares=2.12, R^2=0.085). Higher IL-7 correlated with increased relative abundance of commensals (*Rothia, Streptococcus, Granulicatella* and *Gemella*) and reduced abundance of pathogens (*Pseudomonas* and *Haemophilus*) (Figure 1D).

In EMBARC-BRIDGE, IL-7 levels were lower in patients with 1 or more ≥10^6 copies/ml bacterial infections (2.61±2.47 pg/ml vs. 1.61±3.14 pg/ml, p<0.001) and in those with *P. aeruginosa* infections (2.51±3.04 pg/ml vs. 0.92±1.08 pg/ml, p=0.004, Figure 1E). IL-7 correlated weakly with FEV1 (p=0.014, r^2=0.08, Figure 1F).

Conclusions:

Reduced airway IL-7 is identified as a reproducible biomarker of increased exacerbation risk in people with *P. aeruginosa* infection in bronchiectasis. IL-7 is linked to reduced neutrophilic inflammation, increased antimicrobial proteins, enhanced microbiome diversity and higher commensal abundance. Lower IL-7 in high bacterial load infections suggests a potentially targetable immunomodulatory pathway.

Conflict of interest(s) (if any – not included in the 500 words):

Funded by the European Respiratory Society through the EMBARC3 consortium. EMBARC3 is supported by project partners Armata, AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, Grifols, Insmed, Janssen, Lifearc, Novartis, and Zambon

[212] [2.08.212] Results from the GREAT-2 phase II randomised placebo-controlled trial of the bispecific monoclonal antibody gremubamab targeting Pseudomonas aeruginosa in people with bronchiectasis

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Background/Aims: *Pseudomonas aeruginosa* is commonly detected in the airways of people with bronchiectasis and is associated with significantly increased risk of exacerbations, hospitalisation and mortality.

Gremubamab is a bivalent, bispecific monoclonal antibody targeting *P. aeruginosa* exopolysaccharide psl (key to immune evasion and biofilm formation) and T3SS component pcrV (key to bacterial virulence). In the GREAT-1 study, we showed that gremubamab could

enhance neutrophil killing and phagocytosis of *P. aeruginosa ex-vivo* and reduce virulence *in-vitro* and in a murine acute infection model.

In the GREAT-2 proof-of-concept trial in bronchiectasis patients with *P. aeruginosa* infection, we aimed to investigate the safety and efficacy of gremubamab treatment.

Methods: People with CT-confirmed bronchiectasis and *P. aeruginosa* infection from 15 centres (UK and Spain) were randomised 1:1:1 to 1500mg or 500mg gremubamab intravenous infusion, or placebo, once every four weeks for 12 weeks, with a further 12-week off-treatment follow-up.

On days 1, 7, 14, 28, 56, 84 (end-of-treatment; EoT), and 168 (12-weeks post-treatment) serum and sputum samples were collected. The primary outcome was change from baseline in quantitative sputum cultures at day 84. Key secondary outcomes were change from baseline in the St. George's Respiratory Questionnaire (SGRQ), quality-of-life bronchiectasis questionnaire (QoL-B), Bronchiectasis Impact Measure (BIM), time to first exacerbation (TFE), FEV1 and adverse events. Statistical significance was pre-specified at the 1-sided $p<0.1$ level for this proof-of-concept study. Exploratory outcomes included sputum molecular bacterial load by qPCR, microbiome 16s sequencing and sputum proteomics.

Results: 37 participants were randomised: 1500mg n=12, 500mg n=13, placebo =12. Mean(±SD) age for each group was 65.7±13.8, 60.3±16.7, and 65.9±14.4, and 66.7%, 84.6% and 66.7% of the group were female, respectively.

Bacterial load at EoT (day 84) was significantly reduced with the 500mg dose of gremubamab vs. placebo treatment (estimate[80%CI]: -1.25 log units (-2.33 to -0.16); 1-sided p=0.071; ANCOVA), meeting the trial primary endpoint, with a similar trend observed for the 1500mg dose (-0.66(-1.71 to 0.39),p=0.2). Molecular *P. aeruginosa* load (Oprl) by qPCR was also reduced with a significant effect in the 1500mg arm (1500mg: -0.52(-0.93 to -0.10), 1-sided p=0.056; 500mg: -0.33(-0.74 to 0.09),p=0.158).

Clinically meaningful improvements across multiple quality of life measures were demonstrated with gremubamab treatment; the SGRQ was significantly improved at EoT (500mg: -10.8(-4.93 to -16.7),p=0.02; 1500mg: -12.1(-6.5 to -17.7),p=0.008). Improvement in symptoms using the BIM was noted for cough (p=0.021), sputum (p=0.099), breathlessness (p=0.049), and also daily activity (p=0.016) with gremubamab 1500mg. Clinically significant benefit was observed for multiple QoL-B domains. Protocol-defined TFE was significantly prolonged at the 1500mg dose (p=0.046; restricted mean survival time methods). No effect on FEV1 was identified. Adverse events were reported in similar proportions between groups (1500mg: 91.7%, 500mg: 84.6%, placebo: 89.2%).

Conclusion: Gremubamab treatment reduced *P. aeruginosa* airway bacterial load, confirmed by multiple measurements, and improved patient-reported quality-of-life in people with

bronchiectasis. Ongoing exploratory analysis of the airway microbiome and proteome will further unravel specific beneficial mechanisms of action.

8th WORLD BRONCHIECTASIS CONFERENCE

ABSTRACT BOOK

ORAL COMMUNICATIONS

Lung Foundation Australia

The University Of Queensland AUSTRALIA

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[24] [2.05.24] Molecular Epidemiological Surveillance for Non-Tuberculous Mycobacterial Pulmonary Disease: A Single Center Prospective Cohort Study.

Kiyoharu Fukushima[1,2]; Kazuki Hashimoto[1]; Atsushi Funauchi[1]; Kazuki Hashimoto[1]; Shota Nakamura[1]; Hiroshi Kida[2]

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Background/Aims:

Nontuberculosis mycobacteria (NTM) comprise approximately 200 species, and their associated infectious diseases have seen a significant increase globally. While precise identification of NTM species is essential for effective treatment, it often necessitates a combination of multiple tests, which can be time-consuming, labor-intensive, and expensive. We have previously developed a novel sequence-based method for comprehensive identification of NTM at the subspecies level through core genome multi-locus sequence typing (cgMLST) analyzed with *mlstverse* software and to predict macrolide and amikacin resistance based on previously reported mutations in *rrl*, *rrs*, and *erm(41)*. There remain several unresolved questions about NTM-PD. The dynamics at the strain level during the course of NTM-PD remain unclear. Variable number tandem repeat (VNTR) typing is a standard technique for identifying bacterial strains; however, it is labor-intensive and time-consuming, making it unsuitable for routine clinical use. Despite these recognized difficulties, there is a lack of comprehensive longitudinal studies examining the frequency of strain change and the impact of NTM infections over time. In this study, we aimed to elucidate species-subspecies and strain dynamics in NTM infection and to develop a simple sequence-based method for strain-level determination.

Methods:

We performed a single-center prospective cohort study of 112 patients with NTM-PD to investigate mycobacterial species/subspecies and strain transitions using cgMLST and VNTR typing. Whole genome sequencing was performed on two sputum samples collected at enrolment and at the end of follow-up at intervals of more than 6 months. VNTR typing was then performed. We developed a simple long-read sequencing-based digital VNTR (dVNTR) typing method and evaluated its efficacy.

Results:

Among the 112 patients with culture-positive specimens followed, the median interval was 1.5 years (interquartile range, 1.1–1.9). CgMLST revealed species/subspecies changes in 13 patients (11.6%); VNTR typing detected strain changes in 16 patients (14.3%) without species/subspecies changes. Pathogen shifts occurred in 29 patients (shift [+] group, 25.9%), whereas 83 had no detectable pathogen shift (shift [-] group, 74.1%). Interestingly, macrolide

and amikacin susceptibility changed in both groups, but resistance remained consistently higher in shift (-) patients. In addition, the shift (-) group had more patients with cavitary lesions and drug-resistant conditions than the shift (+) group. dVNTR results were consistent with those of conventional VNTR typing.

Conclusions:

In our study, approximately one quarter of the patients showed pathogen changes over 1.5 years. Because cavitation and drug resistance were more common in the shift [-] group, dominant infection by a single strain may contribute to disease progression in NTM-PD patients. No clear distinction can be made between cases of strain variation based on clinical background, prompting the development of a novel surveillance system that integrates next-generation sequencing for both species-subspecies identification and strain-level molecular epidemiology. This innovation enables real-time monitoring of pathogen dynamics, allowing clinicians to promptly adjust treatment strategies and improve patient care through more informed decision making. We are obtaining 3-year follow-up data and will report on longer-term analysis of infection dynamics in NTM.

Conflict of interest(s) (if any – not included in the 500 words): None

[148] [2.01.148] Study design of a Phase III study (AIRTIVITY®) of the novel dipeptidyl peptidase 1 (cathepsin C) inhibitor BI 1291583 in people with bronchiectasis

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Background/Aims:

Bronchiectasis is a chronic lung disease characterised by neutrophilic inflammation, where neutrophil serine proteases (NSPs) overwhelm antiproteases, impairing the protease–antiprotease balance. Chronic inflammation and infection, impaired mucociliary clearance and progressive structural lung damage contribute to a vicious vortex that leads to pulmonary exacerbations (PExs) and disease progression. NSPs are activated by dipeptidyl peptidase 1 (DPP1, or cathepsin C). Therefore, DPP1 inhibition reduces active NSPs in circulating

neutrophils, and may thus improve the protease–antiprotease imbalance in the airways of people with bronchiectasis. This hypothesis is supported by the Phase II AIRLEAF® study, which demonstrated that the DPP1 inhibitor BI 1291583 reduced PEx risk in adults with bronchiectasis. Here, we outline the design of a Phase III study (AIRTIVITY®) assessing the efficacy, safety and tolerability of BI 1291583 in people with bronchiectasis of various aetiologies (including cystic fibrosis, asthma, chronic obstructive pulmonary disease and established [not newly diagnosed] immune deficiency).

Methods:

AIRTIVITY® is a randomised, double-blind, placebo-controlled study that will include ~1680 people with bronchiectasis of various aetiologies receiving BI 1291583 2.5mg or placebo (2:1) for 52 to 76 weeks (Figure 1). Participants must be ≥18 years old and have computed tomography-confirmed bronchiectasis, with a history of PExs requiring antibiotic treatment prior to screening (either ≥2 PExs in the past year or ≥1 PEx in the past year plus St. George's Respiratory Questionnaire Symptoms score >40). The safety of BI 1291583 will be monitored through clinical assessment, adverse event reporting and monitoring of safety laboratory parameters.

Results:

The primary objective of AIRTIVITY® is to demonstrate the superiority of BI 1291583 2.5mg compared with placebo based on the primary endpoint, the annualised rate of PExs up to Week 76. The main secondary endpoints at Week 52 are absolute lung function changes from baseline (per cent predicted forced expiratory volume in 1 second and forced vital capacity) and absolute change from baseline in Quality of Life-Bronchiectasis respiratory symptoms domain score. Up to Week 76, the main secondary endpoints are time to first PEx and annualised rate of severe PExs (defined as PExs leading to hospitalisation and/or intravenous antibiotic administration, or with a fatal outcome). Key exploratory assessments will include pharmacokinetics and biomarker assessments, as well as patient-reported outcomes.

Conclusions:

AIRTIVITY® intends to further evaluate evidence for the efficacy, safety and tolerability of BI 1291583 2.5mg in a large and broad population of people with bronchiectasis. AIRTIVITY® is due to begin in Q2 2025.

Conflict of interest(s) (if any – not included in the 500 words):

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[326] [2.15.326] Identification of a Response Regulator Controlling Antibiotic Persister Formation in Pseudomonas aeruginosa

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Background/Aims:

Pseudomonas aeruginosa is the predominant pathogen isolated from sputum samples of bronchiectasis patients and plays a pivotal role in disease progression. Although antibiotic therapy targeting *P. aeruginosa* is recommended by clinical guidelines, its efficacy remains suboptimal. Recent studies suggest that the formation of bacterial persisters contributes to chronic airway infections by evading antibiotic treatment.

Methods:

We introduced a nonsense mutation in *PA5364*, a gene encoding a response regulator associated with inorganic phosphate transport, in the *P. aeruginosa* clinical isolate FKA2 using base editing. Persister formation was assessed under tobramycin treatment (20× MIC, 40 μg/ml), with MIC determined via microdilution. Transcriptomic analysis and chromatin immunoprecipitation sequencing (ChIP-seq) were employed to identify PA5364 regulatory targets. Intracellular ATP and polyphosphate levels were quantified using flow cytometry.

Results:

The *PA5364* mutation significantly reduced persister formation in *P. aeruginosa*. Transcriptomic profiling revealed that PA5364 acts as a negative regulator of the *pstSCAB* operon, which is involved in phosphate uptake. Disruption of *PA5364* upregulated *pstSCAB* expression, enhancing bacterial metabolic activity by increasing the proportion of cells with elevated intracellular ATP and proliferative capacity.

Conclusions:

Our findings suggest that targeting the phosphate transport system, particularly via PA5364 inhibition, may serve as a novel strategy to diminish *P. aeruginosa* persister formation and improve antibiotic efficacy in chronic infections.

Conflict of interest(s) (if any – not included in the 500 words):

None.

[349] [2.13.349] Alpha-1 Antitrypsin Deficiency and Asthma: Modelling a Candidate Bronchiectasis Risk Nexus

Sarah Walker[1]; Aowen Zhuang[1]; Swati Varshney[2]; Rhiannon Werder[3,4]; Gary P Anderson[1]

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Background/Aims: Asthma, chronic obstructive pulmonary disease (COPD) and bronchiectasis are muco-obstructive diseases whose features commonly overlap, where inflammation and mucus overproduction are linked to adverse outcomes. Alpha-1 Antitrypsin Deficiency (AATD) is a known cause of COPD and genetic variations in AATD are over-represented in asthma population studies. AATD is also a potential risk factor for bronchiectasis development. Despite this, no mechanisms explaining this overlap have been proposed. As both AATD and asthma are often associated with productive wet cough, fundamental changes in the epithelium, and the high volume expansion ratio of secreted mucus, which can stretch airways, cause regional hypoxia and promote infection and local inflammation, may provide a plausible mechanistic overlap with bronchiectasis development. As such, we characterised lung function and pathophysiology in a genetic mouse model of AATD (C57BL/6J-*Serpina1*^{em3Chmu}/J: "AAT-/- mice", of both genders, which have biallelic deletion of all five Serpina1 paralogue genes) after house dust mite (HDM) sensitisation and challenge to induce asthma-like airway inflammation.

Methods: We used mass spectrometry to confirm AAT depletion in the AAT-/- model. Lung function (SciREq) was assessed by pressure-volume loop analysis and airway hyperresponsiveness (AHR) to methacholine challenge (0-16mg/ml). We tested for possible interactions between asthma and AATD using forced oscillation respiratory mechanics of the airways and lung tissue compartments. Statistical significance between groups was determined by two-way ANOVA, with Šidák multiple comparisons. Precision pressure formalin fixed lung tissues were examined histologically, utilising both haematoxylin-eosin (H&E) staining for pathology and Alcian Blue-Periodic Acid-Schiff (AB-PAS) staining for enumeration of mucin-containing goblet cells.

Results: AHR was significantly augmented in both the airways and tissues of AAT-/- + HDM mice relative to the AAT-/- + saline, wildtype (WT) + HDM and WT + saline controls (p<0.05, multiple unpaired t-tests). Notably, male mice were more responsive than female mice in all lung function parameters. Qualitative grading of lung sections revealed a marked intensification of inflammation with marked intensification of neutrophilic infiltrates and airway smooth muscle thickening. Notably, goblet (mucus) cell metaplasia and excessive secreted mucus organising into plugs (red arrows) was observed in AAT-/- + HDM mice compared to controls (Figure).

Conclusions: Together, these findings indicate that AAT-/- + HDM mice had substantially poorer lung function relative to controls, which may in part be due to excessive mucus production. As excessive mucus has recently been linked to ectatic dilation of small airways, a putative early process in bronchiectasis development, and DPP-1 neutrophil serine protease inhibitors are clinically effective, these findings may in part, provide a plausible mechanistic overlap between AATD, asthma and bronchiectasis. We propose that studying the role of neutrophilic inflammation and neutrophil elastase biology linked with elastin degradation and epithelial cell lineage muco-secretory differentiation leading to mucus hypersecretion, may provide further molecular explanation(s) of these findings.

Conflict of interest(s) (if any – not included in the 500 words):
There are no conflicts of interest.

8th WORLD BRONCHIECTASIS CONFERENCE

ABSTRACT BOOK

POSTER PRESENTATIONS

Lung Foundation Australia

The University Of Queensland AUSTRALIA

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SESSION 1: BASIC SCIENCE

[15] [0.02.15] Possible animal model of bronchiectasis? Chronic Pseudomonas aeruginosa infection provoked enlargement of small bronchus lumen in CCSP-deficient mice.

Masaki Fujita[1]

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Background/Aims:

Club cell secretory protein (CCSP) was located in small airways, however, the relationship between CCSP and bronchiectasis remains unknown. Previously we have reported that chronic inflammation caused chronic bronchitis and emphysematous changes.

Methods:

In this study we analyzed the pathogenesis of bronchial system. The pathophysiology of chronic lung inflammation induced by *Pseudomonas aeruginosa* in CCSP deficient mice was determined. A tube of 5 mm in length was soaked in a fluid containing *P. aeruginosa* (PAO01) for one week and inserted into the trachea of CCSP-deficient mice. One week later *P. aeruginosa* was administered into the trachea. Five weeks after insertion of tube, the mice were sacrificed. The lung histology and physiology were examined.

Results:
P. aeruginosa was continuously detected and neutrophils were increased in the bronchoalveolar lavage fluids from the CCSP-deficient mice in comparison to wild-type mice. A histological study demonstrated that chronic inflammation around bronchus. In new analysis, bronchial wall was widened, and bronchial lumen was enlarged compared with bronchial artery in the CCSP-deficient mice.

Conclusions:
Previous analysis, we misunderstand that we put too much emphasis on bronchial wall thickening and thought it was a stenosis. Chronic *P. aeruginosa* inflammation resulted in chronic bronchitis, emphysematous changes, and might lead to bronchiectasis in the CCSP-deficient mice.

Conflict of interest(s) (if any – not included in the 500 words): No

[75] [0.06.75] Microbiological and Pathophysiological Profile in Cases with Recurrent Exacerbation of Bronchiectasis: A Two-Center Experience

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Background/Aims:

Recurrent exacerbation in bronchiectasis accounts for increase in morbidity with poor outcomes, morality due to progression of disease and cost of care associated with intensive care unit hospitalization. This study was conducted to analyse the microbiological patterns, pathophysiological type and HRCT severity associated with recurrent exacerbations. COPD associated bronchiectasis were associated with poor outcome in COPD and targeting these cases will increase survival and cost of care in both COPD and bronchiectasis. Bronchiectasis disease subtype associated with immunodeficiency should be suspected in cases with history of recurrent respiratory infections since childhood and we have done special emphasis in this subcategory.

Methods:

A prospective observational study was conducted at Venkatesh Chest Hospital, Latur, and the Pacific Institute of Medical Sciences, Udaipur, India, from November 2022 to November 2024. The study included 145 patients aged over 18 years with confirmed bronchiectasis on high-resolution computed tomography (HRCT) and a history of ≥3 exacerbations per year. Institutional Review Board (IRB) approval was obtained (VCC:38/2022, dated 01/11/2022). All patient data were systematically recorded, including demographics, comorbidities, HRCT-guided disease severity (Modified Reiff Score), sputum microbiological cultures with drug sensitivity testing (DST), inflammatory markers (CRP), pulmonary function tests (including FEV1 decline), and immunological markers (immunoglobulin levels and CD4 counts in selected cases). The Medical Research Council (MRC) dyspnoea scale was used to assess breathlessness.

Pathophysiological subtyping of bronchiectasis was carried out as follows:

- **Tuberculosis-related subtype:** Based on a history of tuberculosis or its treatment.
- **ABPA-related subtype:** Identified through ABPA panel analysis in patients with bilateral central or proximal disease and typical clinical features and history.
- **COPD-related subtype:** Diagnosed in cases with predominant emphysema on HRCT, with or without documented COPD, and spirometry showing FEV1/FVC ratio <0.7 with reduced FEV1.

- **Immunodeficiency-related subtype:** Based on immunoglobulin and CD4 count assessments in patients with a history of recurrent infections since childhood.
- **Post-infective subtype:** Included patients with documented recurrent infections, with or without hospitalization.
- **Idiopathic subtype:** Included cases with no identifiable etiology or pathophysiological mechanism.

Statistical analysis was performed using the Chi-square test, Chi-square test for independence or Fisher's Exact Test and ANOVA test were used.

Results:

The mean age of the patients was 50.11 years (range: 20–79 years); 45.51% were males (66/145) and 54.48% were females (79/145).

The etiopathophysiological classification of bronchiectasis included, Post-TB in 37.24% (54/145), Idiopathic in 21.37% (31/145), ABPA-associated in 13.79% (20/145), Post-infective in 12.41% (18/145), Immunodeficiency disorder in 6 cases and COPD-associated in 16 cases. Microbiological analysis identified *Pseudomonas* in 65 cases (44.82%), predominantly in post-TB, ABPA-associated, and post-infective bronchiectasis, with 51 cases (78.46%) showing resistance in DST [$p<0.0001$].

Haemophilus influenzae was found in 15 cases (12.41%), predominantly in idiopathic bronchiectasis, with 20% of cases resistant in DST. *Klebsiella pneumoniae* was identified in 34 cases (23.44%), mainly in COPD-associated bronchiectasis, with 26 cases (76.47%) showing resistance in DST. *Staphylococcus aureus* was detected in 26 cases (17.93%), predominantly in bronchiectasis associated with immunodeficiency, with 16 cases (61.53%) resistant in DST [$p<0.00001$].

FEV1 predictions, based on bronchiectasis severity, and CRP titer analysis at hospital admission showed a significant association with etiopathophysiological types [$p<0.00001$]

Conclusions:

Recurrent exacerbations of bronchiectasis are associated with chronic bacterial colonization, heightened systemic inflammation, and progressive lung function decline. Post-TB bronchiectasis is the most common type, followed by idiopathic and ABPA-related bronchiectasis. Immunological assessment can be beneficial in cases associated with immunodeficiency disorders, as targeted interventions with immunoglobulin therapy may lead to positive outcomes.

COPD-related bronchiectasis is more common than previously predicted and represents a distinct 'phenotype' of mucus plug-related disease. It requires timely assessment and

treatment with mucus clearance techniques to reduce mortality and healthcare costs due to recurrent exacerbations.

Drug-resistant bacteria are predominantly associated with more frequent exacerbations, significantly impacting future disease progression, increasing healthcare costs, and raising mortality rates. Antibiotic stewardship, along with mucus clearance and routine vaccination, is crucial for achieving successful outcomes and improving longevity in these cases.

Conflict of interest(s) (if any – not included in the 500 words): None

[103] [0.10.103] Profiling DPP-1 signalling networks underlying lung immune defence

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Background/Aims: Dipeptidyl peptidase-1 (DPP1) is a cysteine exopeptidase that activates neutrophil serine proteases, such as neutrophil elastase, to drive the immune response. While neutrophilic inflammation is central to many lung diseases, the full proteolytic impact of DPP1, including its substrates and cascades, is still not well understood. With the growing clinical interest in DPP1 inhibitors, we aim to characterise the proteolytic signalling network of DPP1 to understand its immune regulatory roles. We first aim to profile the effects of DPP1 on downstream protease activity in the lung and bone marrow using activity-based probe labelling.

Methods: To understand the role of DPP1 in both inflammatory and normal physiological conditions, we gavaged mice for 10 days with either the covalent reversible DPP1 inhibitor brensocatib (30 mg/kg/day) to suppress DPP1 activity or the drug vehicle control. On day 11, lipopolysaccharide (LPS) or saline was administered intratracheally (IT), and the lungs and bone marrow cells were collected 24h and 72h after the LPS or PBS IT (n=3-4 per group). Activity-based probes were used to profile protease activities. Total protease levels were measured by immunoblotting.

Results: DPP1 activity in the bone marrow was significantly increased in brensocatib-treated mice compared to vehicle-treated controls under both inflamed ($p \leq 0.05$) and naïve ($p \leq 0.05$) conditions at 24 and 72 hours. This suggests a potential compensatory upregulation of DPP1 in response to brensocatib treatment. This compensatory mechanism is further supported by increased DPP1 expression in the bone marrow of brensocatib-treated groups ($p \leq 0.05$). Downstream elastase activity in the bone marrow was significantly reduced in the brensocatib-treated groups in both healthy and LPS-challenged animals ($p \leq 0.0001$). The residual elastase activity may be mediated by alternative neutrophil serine protease-activating proteases. Bone marrow elastase expression was also significantly reduced by brensocatib in both naïve and LPS-challenged animals at 24h ($p \leq 0.0001$) and 72h ($p \leq 0.01$). Contrary to the upregulated DPP1 activity in bone marrow, brensocatib-treated animals exhibited significantly reduced DPP1 activity in the lungs at both 24h and 72h post PBS or LPS IT ($p \leq 0.05$). Similarly, a decrease in elastase activity and expression following brensocatib treatments was observed in the inflamed lungs at both timepoints compared to the LPS-only group ($p \leq 0.05$). Together, these data support that inhibition of DPP1 leads to reduction in serine protease activation. In the bone marrow, cathepsin X, B and S activity was increased in the brensocatib + LPS treated groups compared to the LPS-only group within the 72h cohorts ($p \leq 0.05$). Similarly, in the lung, cathepsin B and legumain activity were increased in the brensocatib + LPS treated group

compared to the LPS-only group ($p \leq 0.05$). This suggests that other cysteine proteases may be altered upon DPP1 inhibition to maintain proteolytic balance.

Conclusions: We identified that 30 mg/kg/day brensocatib significantly reduced DPP1 activity, along with a corresponding reduction in elastase activity in the murine lung. This establishment of DPP1 inhibition in brensocatib-treated vs drug vehicle-treated groups will enable us to proceed with enrichment-free N-terminomics to identify changes in global protein abundance and proteolytic cleavages mediated by DPP1.

Conflict of interest(s) (if any – not included in the 500 words): NA

Acknowledgement: EKSF acknowledge support from the Uni Melb Research Grant 2025 and the Impetus Grant 2025.

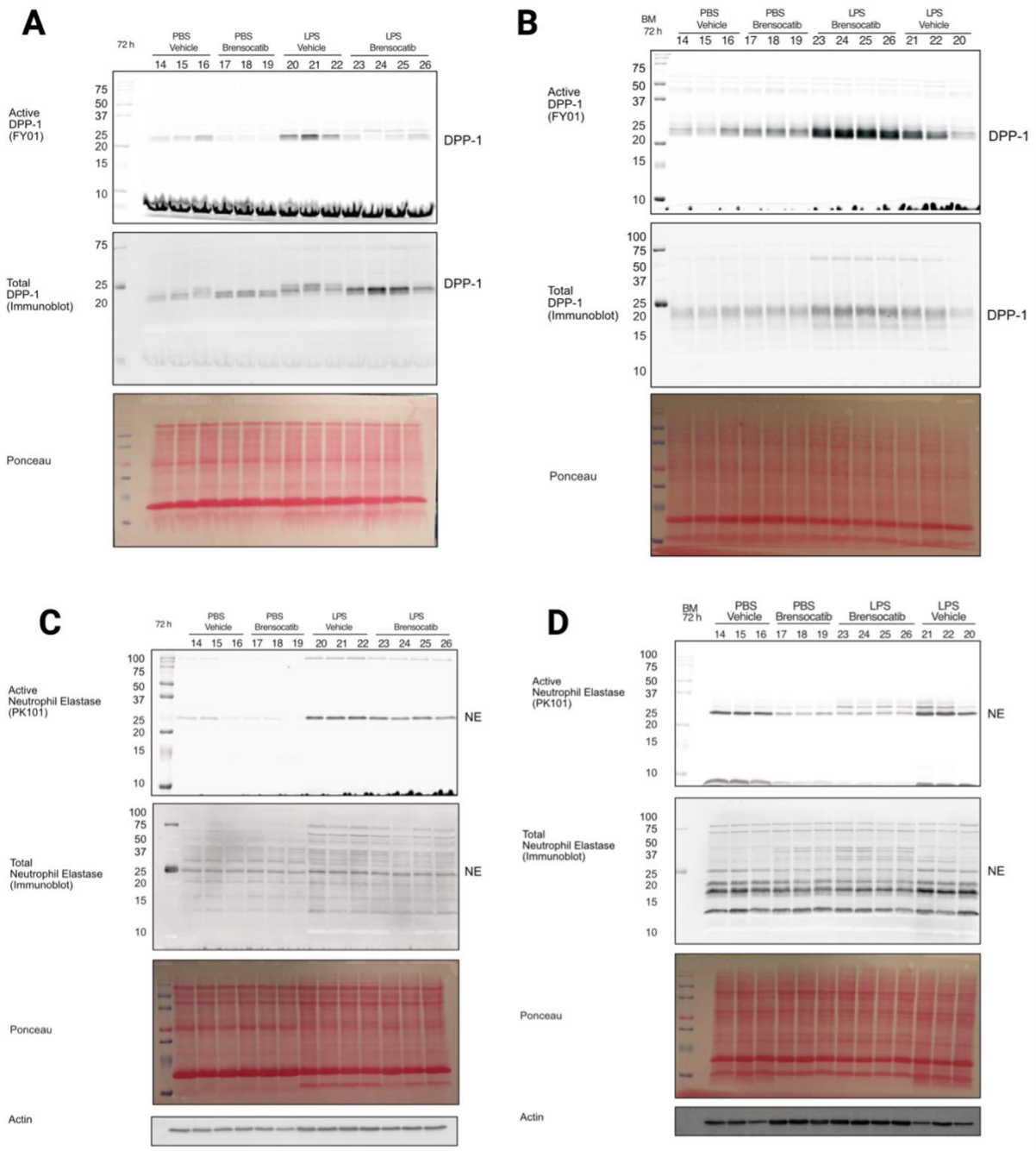

Figure 1. FY01 labelling and immunoblot of DPP1 activity and expression in the (**A)** lungs and **(B)** bone marrow cell lysates. PK101 labelling and immunoblot of NE activity and expression in the (**C)** lungs and **(D)** bone marrow cell lysates. Lungs and bone marrow cells were collected from mice that received oral gavage with either brensocatib or vehicle treatment for 11 days, collection of tissue was at 72 hours after PBS or LPS intratracheal administration, n = 3–4 per group.

[109] [0.05.109] Functional and phenotypic neutrophil characteristics in bronchiectasis in adult humans.

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Background/Aims:

Bronchiectasis (BE) is a chronic respiratory disease primarily characterised by mucociliary dysfunction, lung damage, and neutrophilic inflammation. It is now recognised that neutrophil transcriptional diversity may underlie divergent responses to environmental or inflammatory stimuli and affect neutrophil function. We hypothesised that the programming and responsiveness of peripheral blood neutrophils to stimulation would be aberrant in patients with BE compared to healthy controls.

Methods:

To unravel the functional and phenotypic differences in BE in comparison to healthy individuals, we recruited ten BE patients and eleven healthy controls who consented to blood donation. Neutrophils were purified via a dextran sedimentation step, followed by ficoll centrifugation to obtain a >95% pure population. The cells were stained with a 27-colour antibody panel at baseline and following a 4 hour stimulation with FMLP (1µM) or LPS (100 ng/ml). The cells were acquired on a Fortessa and Aurora spectral flow cytometer and analysed by Flowjo and OMIQ (using UMAP algorithm followed by FlowSOM visualization analysis) to assess functional and phenotypic differences in surface antigen expression.

Results:

To determine whether FMLP or LPS stimulation affected degranulation (function), we first assessed their effect on the level of expression of the degranulation markers, CD66b, CD11b, CD63 and CD45. There was no difference between disease states as neutrophils from both BE and the healthy controls (HC) upregulated the expression of CD66b and CD11b, implicating the release of secondary and tertiary granules respectively with no observable change in CD63 and CD45 levels indicative of primary granules and secretory vesicles respectively. Unsupervised analysis of the combined BE and HC neutrophils at baseline and following stimulation divided the neutrophils into 8 clusters, and revealed significant disease-specific differences in response to LPS or FMLP. Stimulation with either ligand led to an increase in cluster 7 but only in the BE group, whereas cluster 2 became more abundant but only in the healthy control group. Notably in cluster 7, neutrophil IL-6R expression decreased in the BE subjects but not the healthy controls suggesting the loss of this receptor. Cleavage of IL-6R to

generate soluble IL-6R promotes IL-6 trans-signaling, which is typically highly inflammatory and promotes type-17 and neutrophilic inflammation. In addition, upon stimulation, CD71 and CD74, markers associated with proliferative neutrophils and antigen presentation respectively, were upregulated more strongly in healthy controls, whereas the levels of MHC class-II expression was higher in the BE group in response to stimulation.

Conclusions:
We demonstrate that neutrophil surface antigen expression differs between BE subjects and healthy controls following activation with an innate microbial stimuli. The differences in cellular clusters between the two disease states is suggestive of neutrophil heterogeneity. Further elucidation of specific surface markers to identify and target the subpopulations of neutrophils that are deleterious, while not perturbing host defense, may provide an opportunity to ameliorate disease and reduce exacerbations.

Conflict of interest(s) (if any – not included in the 500 words):
All authors report no conflicts of interest

[116] [0.07.116] A single cell RNA sequencing pipeline to assess airway inflammation using induced sputum samples from a prospective cohort of children with bronchiectasis

Craig Schofield[1,2]; Ramsey Kathryn[1,2]; Schultz André[1,2,3]; Bourke Crystal[1,2,4]; Casella Julia[1]; Kakuda Ng Marina[1]; Garratt Luke[1,2]

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Background: The majority of bronchiectasis in adults originates in childhood, and airway inflammation is a key driver of paediatric bronchiectasis. Single cell RNA sequencing (scRNAseq) is a method of investigating the signalling pathways of cells through determining their individual RNA transcripts. Induced sputum (IS) samples provide a non-invasive method to prospectively access biologically relevant samples from the lung for scRNAseq analysis. We aimed to develop a scRNAseq pipeline for IS samples obtained from a prospective cohort of children with bronchiectasis. The key feasibility parameters assessed were IS collection rates, the viability and capture of IS cells, and the number of cells that passed quality control (QC) at data analysis.

Methods: Samples were collected from individuals with a CT diagnosis of non-cystic fibrosis bronchiectasis aged between 6-18 years. Sputum was induced by using nebulized hypertonic saline for up to 30 minutes. Cells from IS were counted using trypan blue to determine cell viability, with >20% viability required to proceed onto the pipeline. Here, cells underwent fluorescent activated cell sorting (FACS) to capture up to 20,000 live leukocytes, determined by two viability stains and positive CD45 expression. scRNAseq was performed using the HoneyComb HIVE V1 kit, and samples were preserved at -20°C for up to 6 months for batched library preparation, as per the manufacturer's instructions. Libraries were prepared in house and sequenced at the Australian Genome Research Facility. QC data analysis was performed using the R packages dropletUtils, scDblFinder and Seurat.

Results: An IS sample was successfully collected in 24/30 (80%) individuals (average age 12.5 years ± 3.3 SD). From the 24 IS samples, 18 (75%) met the >20% cell viability criteria to proceed to scRNAseq, with an average cell viability of 54.6% ± 20.3 SD. The subsequent FACS analysis observed viable leukocyte frequency of 29.45% ± 23.39 SD, and an average of 16,720 ± 4,417 SD live leukocytes were captured for scRNAseq. To date, 12 of the 18 samples have undergone library preparation and sequencing, obtaining 55,500 unique barcodes. Applying QC methods of empty well and doublet exclusion yielded 21,771 barcodes (39.6% of total). Following QC steps of excluding barcodes with a low transcript count (<50 transcripts) and high mitochondrial genes (>25% of total transcripts) resulted in 10,757 barcodes (19.6% of total) for analysis. Cell annotation identified 3,762 were neutrophils, based on the expression of the

neutrophil marker genes S100A8, S100A9 (both calprotectin dimers), FCGR3B (CD16) and CSFR3 (G-CSF receptor).

Conclusion: Collection of IS from a prospective cohort of paediatric bronchiectasis is feasible and in the majority of cases, provides sufficient yield of live leukocytes to perform scRNAseq and pass downstream QC analyses. The next steps are to sequence the remaining samples for scRNAseq, perform gene set enrichment analysis to discover the important biological pathways in paediatric bronchiectasis, and perform pseudotime analysis to determine cell maturity and activation. Applying scRNAseq to paediatric bronchiectasis will enhance our understanding of airway inflammation and disease mechanisms.

Conflict of interest(s) (if any – not included in the 500 words): No conflicts of interest.

[135] [0.09.135] Strong correlations between location of Bronchiectasis and scintigraphic sites of lobar pulmonary micro-aspiration of gastoesophageal refluxate

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Background/Aims: Bronchiectasis is a chronic respiratory disease with a growing trend of increasing incidence and prevalence worldwide. There is a wealth of literature exploring the connection between pulmonary micro-aspiration (PMA) of gastro-oesophageal refluxate (reflux) and bronchiectasis/ chronic lung disease. We have developed and validated a new scintigraphic technique utilising single-photon emission computed tomography fused with x-ray computed tomography (SPECT/ CT) to evaluate the disease both at the level of the oesophagus and in the upper and lower airways. We hypothesised that there would be a significant co-location of refluxate at the lobar level and lobar disease on CT.

Methods: All patients referred for the PMA study with high resolution CT evidence for bronchiectasis were entered into a prospective database over 4 years. Multiple variables were entered including BMI, reflux symptom index (RSI), cough severity index (CSI), diagnosis date etc. Early dynamic and late SPECT/ CT studies were obtained after oral administration ~100MBq of 99mTc Fyton in water. Oxygen saturation was continually monitored during supine acquisition. Scans were reported by a senior Nuclear Medicine physician and Radiologist.

Results: A cohort of 114 patients (68%F, 32%M) with mean age 69 yrs (Range 46-93), mean BMI 25.5, mean RSI 18.5 and mean CSI 14.0 were studied. One patient had no evidence of PMA but lobar disease on CT. All patients had laryngopharyngeal reflux and 35% had hiatus hernias. CT identified 391(L=196, R=195) involved lobes and scintigraphy 406. Tight correlations (CT/Scint) were found in the lower lobes (213/211), lingula (55/58) and right middle lobe (58/61) but not the upper lobes (65/78). Spearman correlation coeffs were significant ($p<0.001$) for all lobes and varied from 0.677 (RLL) to 0.808 (RML), 0.842 (Ling) and 0.335 (LUL). Oxygen saturation fell during supine acquisition by a mean of 4%.

Conclusions: SPECT/ CT shows a strong correlation for lobar co-location of refluxate and CT evidence of bronchiectasis. This was less so in the upper lobes. It does suggest a significant role for PMA of refluxate in the aetiology of the disease. Over 50% of patients had been

labelled as either asthma or recurrent infection. Most patients had significant RSI scores but less than 50% complained of heartburn.

Conflict of interest(s) (if any – not included in the 500 words): Nil to declare

[169] [0.03.169] Targeted Multiplex PCR for Characterising Infection Dynamics in Bronchiectasis

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Background/Aims:

Molecular diagnostics enable rapid detection of bacteria, viruses and antimicrobial resistance (AMR) genes. In bronchiectasis, bacterial infections are associated with increased inflammation and exacerbation risk. We aimed to use BioFire® sputum PCR to enhance characterisation of infections and associated inflammation in stable patients with bronchiectasis.

Methods:

We analysed 210 stable patients with CT confirmed bronchiectasis from the pan-European EMBARC-BRIDGE study using the BioFire® FilmArray® Pneumonia Plus Panel on baseline sputum samples. Antimicrobial peptides SLPI (n=98), OLFM4 (n=147), DEFA3 (n=123), PR3 (n=138), AZU1 (n=147) and neutrophil elastase (NE) (n=117) were measured by ELISA, and 45 cytokines by Olink® Target 48 (n=85).

Results:

The mean age was 61.7±15.8(SD); 48.6% were male. 74.3% had at least one bacterial infection with *H. influenzae* (HI) (37.6%) and *P. aeruginosa* (PA) (27.1%) most frequently identified.

PA infections were associated with lower FEV1(82.9±26.6[mean±SD] vs. PA 63.6±24.4, p<0.001), increased hospitalisations (p<0.001), reduced survival in the 1-4 year follow up period (HR 3.57, 95CI 1.28-9.95, p=0.015) with a trend towards more frequent exacerbations (RR 0.67, 95CI 0.45- 1.03, p=0.067). PA infection risk was increased with asthma (RR=0.14, 95CI= 0.030-0.54, p=0.007) and ICS use (RR=6.0, 95CI=1.8-23.1, p=0.005). PA prevalence varied by region: Spain (36.6%), UK (19.7%) and other regions (44%), p=0.003, with no such variation for HI infections (p=0.42). BioFire® showed higher PA sensitivity compared to culture, detecting 11/32 PA infections in patients without recorded infection in the past 2 years.

HI infections were linked to male sex, (RR= 3.3, 95CI= 1.49-7.57, p=0.004), higher QolB role scores (61.9±26.4 vs.71.4±22.1, p=0.024) and QolB social scores (57.4±26.5 vs. 69.3±23.7, p=0.004), but not QolB respiratory scores (p=0.15). HI was associated with reduced hospitalisations (p=0.004), independent of PA infections. HI infection was not predicted by comorbid COPD (p=0.4) or asthma (p=0.4), ICS use (p=0.4) or long-term antibiotic therapies (p=0.1).

High load infections (≥10^6 copies/ml) were found in the presence of *H. influenzae* (41%), *P. aeruginosa* (34%), *M. catarrhalis* (7.5%) and *S. pneumoniae* (7.5%) infections and associated with a lower FEV1 (84.4±27.1 vs. 71.7±26.3, p=0.002).

PA infections were associated with elevated sputum AZU1, OLFM, MMP1 and CSF1(all p<0.001). HI infections were associated with increased IL1β and TNF (both p<0.001). 11 peptides, including IL1B, OLFM4, AZU1, TNF, CSF and PR3 (all p<0.001) were elevated in high-load infections. In high load infections NE showed a significant increase (p=0.013) and SLPI was significantly decreased (p.adj<0.001).

Viral infections occurred in 16.6% of stable patients, with Rhinovirus in 8.6% of patients. AMR genes (CTX-M or mecA/C MREJ) were found in 3.3% of patients and were associated with decreased QolB health score (p=0.043, no AMR genes, 48.2±23.1, AMR gene 29.2±14.7) and a trend towards lower FEV1 (p=0.053, no AMR genes, 78.4±27.3, AMR gene 58.0±21.0).

Conclusions:

Molecular detection of bacteria, viruses and AMR genes correlates with disease severity in bronchiectasis. PA detection via Biofire® was more sensitive than culture and linked to poorer outcomes. Bacterial infections were associated with increased inflammation.

Conflict of interest(s) (if any – not included in the 500 words): Funded by the European Respiratory Society through the EMBARC3 consortium. EMBARC3 is supported by project partners Armata, AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, Grifols, Insmed, Janssen, Lifearc, Novartis, and Zambon

[215] [0.01.215] Anti-inflammatory and clinical effects of oral resveratrol supplementation in bronchiectasis

Benjamin Diggins[1,2]; Alain Vandal[3]; Mandy Zheng[4]; Adam Ghafouri[3]; William Good[2,5]; Lata Jayaram[6,7]; Hsien-Chen Cheng[2]; Conroy Wong[2,5]

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Background / Aims

The pathogenesis of bronchiectasis is centred around the "vicious vortex" theory of airway inflammation, infection, endothelial and mucociliary dysfunction and resultant airway damage. Resveratrol is a naturally occurring antioxidant with anti-inflammatory and antimicrobial properties, found in foodstuffs such as red wine, grapes and berries. In laboratory studies, resveratrol reduces levels of neutrophil elastase (NE) and other cytokines such as interleukin (IL)-8 that drive inflammation in bronchiectasis and are linked to increased disease severity.

The primary aim of this study was to assess whether oral resveratrol supplementation has anti-inflammatory effects in adults with bronchiectasis, as well as determining tolerability and safety, and the optimal dose of resveratrol in this context.

Methods

We undertook a single-centre, open-label, pre-post, single-arm study of oral resveratrol supplementation in adults with bronchiectasis, at Middlemore Hospital in Auckland, New Zealand. The study incorporated a sub-study that compared two doses of resveratrol (1g daily and 2g daily), for 12 weeks. The primary endpoint was change in sputum NE levels. Secondary endpoints included sputum cytokine levels, health-related quality of life scores (including the Bronchiectasis Health Questionnaire (BHQ)), as well as tolerability and safety data.

Results

32 patients were enrolled in the study. 23/32 (71.9%) were male and the mean age was 67 years. 8/32 patients (25.0%) were of Māori ethnicity, 3/32 Pasifika (9.4%), 6/32 Asian (18.8%) and 16/32 (50.0%) were NZ European. 53.1% of patients had never smoked (17/32).

16 patients were randomised to receive 1g daily, and 16 to receive 2g daily. There was no overall significant change in sputum NE levels over the 12 weeks of treatment (mean change of 312 ng/ml from baseline to week 12, p=0.644); there was also no difference between the 1g and 2g groups. Interleukin (IL)-8 levels overall were not affected, but in the 2g daily group, IL-8 levels fell significantly from 1629 pg/ml at baseline to 564 pg/ml at 12 weeks (SD 422-754 pg/ml, p<0.001).

For BHQ, no overall difference was seen but, when adjusting for the baseline score, mean score was 10.7 points lower at study completion for the 2g daily group (69.7 vs 59.0 points (95% confidence interval (CI) 0.98-20.47, p=0.034). Lower scores in the BHQ indicate increased symptom burden.

Adverse effects (AEs) were significantly more common in the 2g daily group than the 1g group (ratio 3.06:1 per participant), (95% CI 1.26-7.40, p=0.013). There were two serious AEs in the higher dose group, which were felt to be unrelated to treatment by the investigators.

Conclusions

This study suggests a signal for an effect of high dose resveratrol on reducing markers of neutrophilic airway inflammation. However, the higher dose of resveratrol was associated with an increased frequency of adverse effects and a lower BHQ score compared to the lower dose group, although there was no overall effect noted on quality-of-life scores compared to baseline.

Conflict of interest(s) (if any – not included in the 500 words):

None to declare

[219] [0.08.219] First Nationwide Screening of Cystic Fibrosis Among Chinese Bronchiectasis Patients: Distinct Clinical and Genetic Profiles with Therapeutic Implications.

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Background/Aims:

Cystic fibrosis (CF) is a rare genetic disorder in China, with bronchiectasis being the primary clinical manifestation. However, population-based data on CF prevalence are scarce. This study aims to screen bronchiectasis patients for CF, and to characterize the clinical, radiological, and genetic features of CF in China.

Methods:

A total of 1,116 bronchiectasis patients were recruited from four national centers across China. CF diagnosis was based on sweat chloride concentrations and whole exome sequencing (WES) to identify CFTR mutations. Patients were categorized into CF, CF-related diseases (CF-RD), or idiopathic bronchiectasis based on clinical and genetic profiles. In vitro studies assessed the functional recovery of chloride channels in Class II CFTR mutations using the Tezacaftor-Elexacaftor-Ivacaftor combination therapy.

Results:

Among the 1,116 patients, 37 (3.4%) were diagnosed with CF based on sweat chloride concentrations ≥60 mmol/L, and 4 (0.4%) had sweat chloride levels between 30-60 mmol/L with biallelic CFTR mutations confirmed by WES. Additionally, 23 patients (2.1%) were diagnosed with CF-related diseases (CF-RD), characterized by a single pathogenic CFTR mutation. CF patients had a younger age at diagnosis, earlier symptom onset, and higher rates of malnutrition and acute exacerbations compared to idiopathic bronchiectasis patients. Radiologically, CF patients exhibited upper lobe cystic bronchiectasis with non-tuberculous mycobacteria (NTM) as the predominant pathogen. Genetic analysis revealed 31 CFTR mutations, including 22 undefined variants in CFTR2 database. The most common mutations were G970D and I556V, both Class II mutations. Mutations also included Class I (premature termination), Class III (defective regulation), and Class V (alternative splicing), leading to defective chloride channel function. In vitro studies demonstrated that Tezacaftor-Elexacaftor-Ivacaftor therapy restored chloride ion channel function in almost all Class II mutations.

Conclusions:

This study represents the first large-scale CF screening in bronchiectasis patients in China, uncovering novel CFTR mutations and revealing distinctive clinical features of CF in this population. The identification and classification of CFTR mutations in this cohort significantly deepen the understanding of CF in China. Furthermore, Tezacaftor-Elexacaftor-Ivacaftor therapy shows promise in restoring CFTR function in Class II mutation carriers. These findings highlight the need for expanded CF screening and genetic testing in China, where CF remains underdiagnosed, and suggest that targeted therapies could improve patient outcomes. Further research is needed to explore the broader application of CFTR modulators in this region.

Conflict of interest(s) (if any – not included in the 500 words):

No conflict of interest need to be declared.

[330] [0.04.330] Exploring Immune Dysfunction in Bronchiectasis: A Focus on Natural Killer Cells using Single-Cell Transcriptomes

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Background/Aims:
Bronchiectasis describes chronic airway inflammation involving various immune cells; however, little information is available regarding cell-type-specific pathogenic changes that influence disease development of bronchiectasis.

We aimed to investigate immune dysregulation in bronchiectasis through single-cell RNA sequencing (scRNA-seq) of peripheral blood mononuclear cells (PBMCs).

Methods:
PBMCs from eight bronchiectasis patients and eight healthy controls were isolated and subjected to scRNA-seq using the 10X Genomics platform. Frequencies of immune cell subsets were compared between groups, and functional implications were inferred based on transcriptional signatures.

Results:
The overall innate immune cell composition was similar between bronchiectasis patients and healthy controls, but significant subset-level alterations were observed. Bronchiectasis patients exhibited increased CD4+ and CD8+ effector memory T cells, suggesting chronic inflammatory activated status of T cells. Notably, *FCER1G*+ NK cells were significantly reduced in bronchiectasis patients, accompanied by decreased expression of chemokines such as CCL3, CCL4, XCL1, and XCL2. In bronchiectasis patients, pro-inflammatory CD14+ monocyte tended to be decreased, showing reduced CXCR4 expression.

Conclusions:
The overall innate immune cell composition was similar between bronchiectasis patients and healthy controls, but significant subset-level alterations were observed. Bronchiectasis patients exhibited increased CD4+ and CD8+ effector memory T cells, suggesting chronic inflammatory activated status of T cells. Notably, *FCER1G*+ NK cells were significantly reduced in bronchiectasis patients, accompanied by decreased expression of chemokines such as CCL3,

CCL4, XCL1, and XCL2. In bronchiectasis patients, pro-inflammatory CD14+ monocyte tended to be decreased, showing reduced CXCR4 expression.

Conflict of interest(s) (if any – not included in the 500 words):
None.

SESSION 2: COMORBIDITIES & DIFFICULT CASES

[76] [0.16.76] Routine pathology testing prior to bronchoscopy: Limited clinical impact with significant economic and environmental costs

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Background/Aims:

Routine preprocedural pathology testing is no longer recommended for minor and intermediate-risk elective surgeries. The British Thoracic Society guidelines for diagnostic bronchoscopy advise that coagulation studies, platelet count, and haemoglobin testing should be performed only in patients with risk factors for abnormal coagulation, such as chronic liver or kidney disease or haematological malignancies. However, preoperative pathology testing is frequently conducted without clear clinical indications prior to bronchoscopic procedures, resulting in unnecessary financial and environmental costs. Our study aimed to evaluate the prevalence of routine preprocedural blood testing prior to bronchoscopic procedures, its impact on clinical management, and its association with complications. Additionally, we assessed the financial and environmental costs to provide a broader perspective on their overall value.

Methods:

A retrospective review of electronic medical records was conducted for all outpatient bronchoscopic procedures at the Royal Melbourne Hospital, a tertiary referral centre, between January 1 and December 31, 2021. Preprocedural pathology testing was defined as any laboratory test ordered at the time of bronchoscopy referral or repeated within six weeks prior to the procedure. We evaluated its impact on clinical management and association with significant complications. Financial costs were estimated using Medical Benefits Schedule (MBS) prices, and environmental impact was assessed via carbon dioxide equivalent (CO_2e) emissions.

Results:

A total of 436 outpatient bronchoscopic procedures were performed, with all patients undergoing preprocedural pathology testing. Abnormal results were identified in 8.3% of cases, but only 4.0% led to clinical intervention, all in patients with established risk factors for coagulation abnormalities. No interventions were required for patients without these risk factors despite abnormal results, and no procedures were delayed or cancelled. There was no clear correlation between abnormal blood test results and procedural complications. Overall,

routine testing incurred a total cost of AUD 22,851.30 and generated an estimated carbon footprint of 103.2 kg CO_2e at our department.

Conclusions:

Routine preprocedural pathology testing for bronchoscopic procedures offers limited clinical value, with most results not influencing management of procedural safety. Clinically significant abnormalities requiring intervention were observed only in patients with established risk factors for coagulation abnormalities, supporting a targeted, risk-based approach. Given the significant financial and environmental costs, transitioning to selective, evidence-based testing is essential to optimise resource use, enhance patient care, and improve healthcare sustainability.

Conflict of interest(s) (if any – not included in the 500 words):

N/A

[83] [0.19.83] The treatable traits approach is highly acceptable and a positive experience for patients in a regional Australian bronchiectasis outpatient clinic

Kirsty Watson[1,2]; Annemarie Lee[3]; Marita Dale[1]; Tiffany Dwyer[1,4]; Zoe McKeough[1]

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Background/Aims: Treatable traits are identifiable, measurable, clinically relevant and treatable features of disease, and traits specific to bronchiectasis have been identified. The treatable traits clinical care approach, when implemented in chronic respiratory diseases, has demonstrated improvements in quality of life, hospitalisation, and 1-year all-cause mortality, but the acceptability of the approach and patient experience has not been determined. The study aim was to determine if implementation of the treatable traits approach in a bronchiectasis outpatient clinic in regional Australia would be acceptable to patients and promote a positive patient experience.

Methods: A qualitative study using a relativist, constructionist thematic analytic approach.

New patients with confirmed bronchiectasis who attended an outpatient clinic, implementing a treatable traits approach to care with a physiotherapist and nursing team in Rockhampton, Australia between 2021-2023 were invited to participate. Semi-structured interviews were conducted after the three-month clinic review appointment. The interview guide was designed to evaluate the components of the Theoretical Framework of Acceptability and the patient experience of attending the clinic. Interviews were audio recorded and transcribed verbatim. Codes and themes were developed by two researchers, and reviewed by a third and fourth, through an iterative process of code exploration and clustering, and the redefinition of themes upon repeated re engagement with the transcripts.

Results:

There were 10 participants recruited [mean (SD) age 70 (12) years; 70% female; Bronchiectasis Severity Index (%) mild (20), moderate (50), severe (30)]. Participants described clinic acceptability and experience according to five key themes: (1) motivation to engage and change- participation in the clinic motivated participants to exercise and improve quality of life; (2) multi-interventional clinical care was highly valued- participants emphasised the role of airway clearance therapy, exercise interventions, physical activity advice, bronchiectasis action plans, disease specific education, technique practise, referrals to other health professionals and a comprehensive tailored plan in delivering a valuable clinic experience; (3) psychosocial and physical health benefits-participants described that when they improved their lung health, they improved overall quality of life, through improved mood, reducing the

burden of symptoms such as cough and having greater social interaction; (4) the long-term understanding and acceptance of self-management- with the strategies developed in the clinic, participants could take positive steps forward to self-manage their bronchiectasis. The clinic also provided a safety net, through the knowledge that participants could receive care for bronchiectasis management into the future if required; (5) persistent challenges of living with bronchiectasis- participants described there are major impacts on their life from bronchiectasis, some of which don't change through the strategies of the clinic. These include both physical and psychosocial limitations.

Conclusions:

Attending the bronchiectasis outpatient clinic utilising a treatable traits approach was a highly acceptable and valued experience for adults with bronchiectasis in a regional Australian setting, but persistent challenges to life with a chronic disease do remain.

Conflict of interest(s) (if any – not included in the 500 words): There are no conflicts of interest to declare.

[86] [0.12.86] Role of nebulised amikacin as an 'adjunct' to standard care in recurrent exacerbation Bronchiectasis during acute care hospitalization and follow-up period of 52 weeks: A two-tertiary care center study

Shital Patil[1,2]; Gondhali Gajanan[2]; Acharya Abhijit[2]; Bhadake Manoj[2]; Patil Swati[1]; Patil Rajesh[1]; Patil Deepak[2]

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Background/Aims: Recurrent exacerbations in bronchiectasis contribute to increased morbidity, poor outcomes, higher mortality due to disease progression, and elevated healthcare costs associated with ICU hospitalization. Role of nebulised tobramycin for eradication of microbiological factors leading to recurrent exacerbation of bronchiectasis is largely studied globally, but is has limitation in countries like India due to cost factor. This study aimed to analyse the role of nebulized amikacin in reducing hospitalization duration during acute care and its impact on the frequency and severity of future exacerbations, including recovery time, exacerbation-free days, time to exacerbation over a 52-week follow-up period including tolerability and adverse events.

Methods: Prospective, observational, 52 weeks follow-up study, approved by IRB and ethics committee (VCC:02/2023, dated 03/01/2023), conducted in Venkatesh chest hospital, Latur and MIMSR Medical college, Latur, India, during January 2023 to December 2024, screened 178 hospitalised cases age >18 years, diagnosed with bronchiectasis confirmed in HRCT imaging's and having history of ≥3 exacerbations in last year; after a written, informed and valid consent from all included cases as the protocol of study. All cases data were recorded as demographics, comorbid illnesses, sputum culture with DST, hematological, inflammatory markers and spirometry. The Medical Research Council (MRC) dyspnoea scale was used to evaluate breathlessness. Finally, 144 cases were included with two specified inclusions as, those having HRCT severity of Modified Reiff Score>10 and sputum microbiological culture was positive for gram negative species such as pseudomonas, Acinetobacter, klebsiella, E. coli; and staphylococcus aureus with DST patterns showing drug resistance to commonly used antibiotics for treatment of bronchiectasis during exacerbation. Two groups of 72 patients were randomly assigned using a randomization protocol, with one group receiving standard care plus nebulized amikacin and the other receiving standard care only. Standard care constitutes antibiotics according to DST, bronchodilators, mucolytics during hospitalization and bronchodilators plus mucous clearance techniques with mucolytics at home after discharge. Nebulised amikacin was given 250 mg injection solution via get nebulizer three times daily till discharge during hospitalization. After discharge, both the groups offered similar medications in standard care except amikacin nebulization. In home nebulization group of amikacin, dose was protocolised as 250 mg two times daily for 4 weeks and then one time daily for 48 weeks. Primary objectives were to analyse the benefit of nebulised amikacin in reducing hospitalization interval and decreasing the frequency, severity as classified according

to FACED/BSI score (mild, moderate and severe) & duration of exacerbation in both the groups during follow up period of 52 weeks. Secondary objectives were exacerbation free days and time to first exacerbation in both the groups. Additionally, nebulised Amikacin related renal function abnormalities as diagnosed with rise in baseline creatinine level resulting into stoppage of medication is tertiary end point of the study. Renal functions were followed in amikacin group every 4 weeks interval. Statistical analysis by t-test, chi-test and ANOVA.

Results:

Age and gender distribution in amikacin nebulization plus standard care group (n=72) & standard care group (n=72) were 50.88 years (23-70 years) & 49.68 years (21-72 years) respectively; males 45.83%(33/72) & females 54.16%(39/72), and males 48.61%(35/72) & females 51.38%(37/72) respectively. Duration of hospitalization in acute exacerbation in indoor setting during enrolment in amikacin nebulization plus standard care group (n=72) was 7.48±1.02 days and 12.5±1.09 days in standard care group (n=72) [p<0.0001].Sputum microbiological workup with culture and DST, pseudomonas species in 45.13%(65/144) cases & resistance in 64.61%(42/65) cases, Acinetobacter species in 18.75% (27/144) cases & resistance in 74.07%(20/27) cases, Klebsiella species in 18.05%(26/144) & resistance in 73.07%(19/26) cases, Staphylococcus species in 14.58%(21/144) cases & resistance in 57.14%(12/21) cases & E. coli in 3.47% (5/144) cases & resistance in 40% (2/5) cases. During follow-up, Exacerbation frequencies with severity (FACED/BSI Core) as mild (n=43), moderate (n=45) and severe (n=34) were 31, 22 & 8 episodes respectively in amikacin nebulization plus standard care group and 12, 23 & 26 episodes respectively in standard care group [p<0.00012]. Exacerbation duration of mild category in both the groups were 4.54±1.05 days versus 7.5±0.52 days [p<0.0001], moderate category in both the groups were 7.04 ±1.29 days versus 10.91±1.47 days [p<0.0001] & severe category in both the groups were 8.17±1.38 days versus 12.38±1.09 days [p<0.0001].Mean time to exacerbation in mild category in both the groups were 97.38±12.87 days versus 68.25±10.36 days [p<0.0001], moderate category in both the groups were 97.81±9.31 days versus 73.65±13.86 days [p<0.0001] & severe category in both the groups were 95.5±10.87 days versus 77.72±12.07 days [p<0.0008]. Difference in mean time to exacerbation in both groups were 29.13% in mild, 24.16% in moderate and 17.78% in severe category. Exacerbation free days in mild category in both the groups were 96.4±11.24 days versus 78.33±10.79 days [p<0.0001], moderate category in both the groups were 108.59 ±9.34 days versus 81.26±10.66 days [p<0.0001] & severe category in both the groups were 81.26 ±10.66 days versus 76.03 ±10.29 days [p<0.0001]. Difference in Exacerbation free days in both groups were 17.71% in mild, 27.33% in moderate and 46.22% in severe category. No any systemic or real function related adverse events documented in present study

Conclusions: Nebulized amikacin serves as an 'effective adjunct' to the standard treatment protocol for recurrent bronchiectasis in the acute care setting, significantly reducing both hospitalization duration and time to recovery. Additionally, its role in decreasing the frequency and severity of future exacerbations, prolonging the time to the first exacerbation, and increasing exacerbation-free days underscores its consistent and pivotal importance in

managing these cases. Identifying high-risk microbiological and pathophysiological markers can aid in tailoring individualized treatment strategies to prevent further exacerbations and disease progression. Nebulized amikacin is a well-tolerated inhaled antibiotic therapy, with no adverse effects observed over this 52-week follow-up study. Notably, it is cost-effective, with treatment costs lower than those associated with exacerbations and other inhaled antibiotics such as tobramycin. Therefore, we recommend the use of nebulized amikacin for the prevention of future exacerbations in patients with recurrent episodes, particularly as a result of the eradication of microbiological factors.

Conflict of interest(s) (if any – not included in the 500 words): None to disclose

[132] [0.11.132] Unmasking disease in ulcerative colitis-associated bronchiectasis after treatment with vedolizumab

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Background/Aims:

Bronchiectasis and suppurative bronchitis are relatively uncommon extraintestinal manifestations of ulcerative colitis (UC) and are often underdiagnosed. Vedolizumab, a gut-selective $\alpha_4\beta_7$ integrin antagonist, has emerged as a mainstay of UC therapy in recent years. However, its gut-selective mechanism may not address systemic inflammation and can potentially lead to the unmasking of extraintestinal manifestations.

Methods:

We present two cases of people with UC who developed significant airway symptoms after transitioning from less selective immunotherapies to vedolizumab.

Results:

Case 1: A 34-year-old woman with a diagnosis of UC was referred with a chronic, productive cough of over 12 months duration. Her bowel disease was in remission after treatment with infliximab and tofacitinib. She had plans to conceive so her UC treatment was switched to vedolizumab, and at this point she developed the productive cough. Despite numerous courses of oral antibiotics her cough did not improve. There evidence of mild obstruction on lung function and CT thorax was normal. Bronchoscopy demonstrated widespread airway mucosal inflammation, but washings were negative on culture. Inhaled corticosteroids were commenced UC-associated large airways disease with chronic purulent bronchitis and trial of low dose azithromycin was considered pending mycobacterial culture. However, she then experienced a UC flare during pregnancy which was treated with a prolonged course of oral steroids which also resolved her sputum production which demonstrated the airway inflammatory symptoms were due to uncontrolled UC-associated inflammation.

Case 2: A 51-year-old man with longstanding UC, previous colectomy, and pouch formation, developed ileoanal pouchitis and was treated with vedolizumab. Development of with recurrent cough and sputum production coincided with starting vedolizumab. A CT thorax demonstrated bronchial wall thickening and bronchiectasis. Sputum cultures grew *Serratia marcescens* but despite numerous antibiotic courses, inhaled corticosteroids and bronchodilators, low dose azithromycin and carbocisteine, he continued to wheeze and produce mucopurulent sputum. He had rapid reduction in sputum production after a short course of steroids however symptoms recurred on cessation of oral steroids. He was

maintained on low dose prednisone while he was transitioned to Ustekinumab for his UC. At repeat review both respiratory and intestinal symptoms were under control with the new therapy.

Two people with UC experienced a marked increase in sputum production, cough, and breathlessness following vedolizumab initiation. Resolution of symptoms occurred with commencement of oral corticosteroids in both cases.

Conclusions:

These cases highlight the potential for vedolizumab to unmask bronchiectasis symptoms in people with UC, possibly due to its gut-selective immune mechanism. Pulmonologists and gastroenterologists should be aware of this issue and should have a high index of suspicion for bronchiectasis in people with worsening airway symptoms on vedolizumab, particularly when repeat antibiotic courses are ineffective. Adjustments to UC therapy, aimed at broader systemic immunomodulation, may be necessary to address both intestinal and pulmonary disease effectively. Currently, there is an unmet need for disease-modifying UC medications for people with UC-respiratory involvement and more treatment recommendations need to be explored.

Conflict of interest(s) (if any – not included in the 500 words):
No conflicts of interest to disclose.

[137] [0.13.137] Bronchiectasis and Recurrent Infections in Thymoma Patients Attributable to Anti-Cytokine Autoantibodies

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Background/Aims: Bronchiectasis is the sequelae of recurrent, long-standing lung pulmonary infection or immunodeficiency. The increased risks of infections associated with thymic neoplasms is progressively being recognized and this conventionally has been described in context of Good's syndrome with hypogammaglobulinemia. However, non-tuberculous *Mycobacterium (NTM)* and recurrent infections in bronchiectatic thymoma patients are being encountered whereby immunoglobulin levels may not be low. We seek to investigate alternative etiologies to account for these susceptibilities.

Methods: In two patients with thymoma and *M. abscessus* pulmonary infections, immunoglobulin levels and lymphocyte subset immunophenotyping were performed. Detection of neutralizing auto-antibodies against cytokines were detected using a sandwich ELISA platform. Confirmation of specific immune signaling pathway disruption was through serum switch experiment using sera of patients and healthy controls in presence of control peripheral blood mononuclear cells. Immune signal outputs were probed using Western Blot or flow cytometry.

Results: The two patients had normal immunoglobulin G, A, M levels and normal CD19+ cell numbers which were not characteristic of Good's syndrome. But they encountered recurrent bacterial infections by mostly intra-cellular pathogens consisting of *Mycobacterium abscessus*, *Klebsiella pneumoniae* as well as pulmonary aspergillosis in one of them on background of reticulonodular pattern of bronchiectasis. Notably both patients were detected to harbour autoantibodies specifically against interleukin (IL)-12 and/or interferon alpha (IFNα). We further showed that both anti-IL12- and anti-IFNα-containing sera of the patients were neutralizing. Sera from these thymoma patients interfered with ability of peripheral blood mononuclear cells ability to respond to IL12 and IFNα stimulation resulting in compromised STAT1- and STAT4-phosphorylation respectively; these pathways being critical mediators of host immune response against intra-cellular microbes.

Conclusions: As an alternative etiology to Good's syndrome, the presence of neutralizing anti-cytokine autoantibodies against interferon alpha and interleukin-12 may account for susceptibility to NTM and recurrent bacteria infections in thymoma patients.

Conflict of interest(s) (if any – not included in the 500 words):
Nil

[179] [0.15.179] How do comorbidities affect outcomes in the New Zealand bronchiectasis population?

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Background:

Understanding associations between comorbidities and worse outcomes in bronchiectasis enables targeted management. The aim of this study was to investigate the association between selected comorbidities and respiratory outcomes in the New Zealand (NZ) bronchiectasis population, in particular metabolic syndrome related comorbidities including cardiovascular disease (CVD), diabetes mellitus (DM), high body mass index (BMI) and obstructive sleep apnoea (OSA). The effect of ethnicity and non-tuberculous mycobacteria (NTM) on outcomes independent of comorbidities was also investigated.

Methods:

Data were extracted from the NZ bronchiectasis database population (n=332). Outcome measures included: health status (QOL-B, BHQ scores); breathlessness (mMRC score); lung function (FEV1 %predicted); exacerbation rate; hospitalisation rate; and presence of *Pseudomonas aeruginosa (PsA)*. Comorbidities investigated relating to metabolic disease included abnormal BMI, DM, CVD, angiotensin inhibitor prescription, statin prescription, and OSA. Other comorbidities included cirrhosis, renal failure, neoplastic disease, gastro-oesophageal reflux disease, rhinosinusitis, rheumatoid arthritis, connective tissue disease, inflammatory bowel disease, and anxiety and depression. Univariate and multivariate analyses used R4.4.2 software. Multivariate comparison also adjusted for age, gender, ethnicity, NZ born status, NZ deprivation decile, (NzDep), duration of bronchiectasis, and smoking status. False discovery rate was used to adjust p values for multiple comparisons.

Results:

Median age was 69; 56.8% female; ethnicity 52.7% European, 17.3% Māori, 12.4% Pacific. Prevalence of comorbidities included CVD 26.8%, DM 16.0%, statin prescription 34.1%, angiotensin inhibitor prescription 28.6%. Median BMI was 27.3.

In univariate analysis, CVD was associated with worse QOL-B physical functioning score (51 versus 63, p=0.005); worse mMRC dyspnoea score (1.7 versus 1.1, p=0.005); increased annual respiratory exacerbations (3.9 versus 2.6, p=0.005); and increased hospitalisations (0.9 versus 0.3, p=0.005). DM was associated with higher risk of *PsA* isolation (OR 4.18, p=0.05). No

association was found between statin or angiotensin inhibitor prescription and outcomes. No association of OSA diagnosis and outcomes was found in the 21/181 (11.6% of patients with data available). In multivariate analysis, BMI 35-40 was associated with higher %predicted FEV1 versus BMI 18.5-25 (p=0.05). No other comorbidities had significant associations with outcomes.

Compared with European ethnicity, Māori and Pacific ethnicity was associated with increased annual hospitalisations (Māori 3.1/ year, p=0.03; Pacific 2.6/ year, p=0.04; non- Māori non-Pacific ethnicity 0.4/ year) and was independently associated in multivariate analyses (Māori 6.2 times, p=0.033; Pacific 7.2 times, p=0.039).

NTM were present in 22/328 patients with samples available. These patients were on average older (72.5 versus 69.0, p=0.041), predominantly European (77.3% versus 50.5%, p=0.018), and higher socioeconomic background (NzDep 4 versus 6, p=0.018). Their annual respiratory hospitalisation rate was 1.18 versus 0.45/ year (p=0.024); 7.78 times the risk when NTM status was added to the multivariate analysis (p<0.005).

Conclusions:

This study found associations between CVD and adverse respiratory outcomes including health status, breathlessness and exacerbations. High BMI was associated with better lung function. DM was associated with *PsA* isolation. Māori and Pacific peoples had more hospitalisations even after correcting for comorbidities. NTM isolation was associated with increased hospitalisations. This information is relevant for bronchiectasis healthcare providers in terms of investigations and management, and encouraging treatment adherence.

[187] [0.14.187] Are we missing sinus disease in bronchiectasis? A sub-study of the Bactek-O trial.

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Background/Aims: Heterogeneity of bronchiectasis impacts both patient management and clinical research. There is an increasing focus on different clinical phenotypes in bronchiectasis, including frequent exacerbators, *Pseudomonas* colonisation and the presence of co-existent asthma. Recent research has also highlighted the importance of co-existent sinus disease on clinical outcomes. We aimed to describe the participants in the Bactek-O study with co-existent sinus disease and determine any relationship between co-existent sinus disease and other clinical characteristics, including markers of bronchiectasis severity.

Methods: This was a pre-defined sub-study of a single centre, double-blinded, randomised controlled trial investigating the role of Bactek-O, a sublingual bacterial vaccine in patients with bronchiectasis. All measurements from baseline assessment were analysed including participant demographics, sputum inflammatory markers including neutrophil elastase, quality of life scores, pulmonary exacerbations, Bronchiectasis Severity Index and Bronchiectasis Aetiology and Comorbidity Index. Sinus disease was based on the presence of nasal and para-nasal sinus mucosal inflammation as per international guidelines. All participants underwent a baseline CT sinus shortly after randomisation to the Bactek-O clinical trial unless they had previous sinus imaging within the past 12 months. Analyses were undertaken with *R version 4.x*.

Results: The Bactek-O baseline cohort had high rates of co-existent sinus disease with 30 of the 46 (65.2%) identified as having co-existent sinus disease. Binary analysis found significantly lower rates of co-existent COPD in those with confirmed sinus disease (p=0.027). Logistic regression analysis was then performed investigating the presence of co-existent sinus disease. The presence of sinus disease was significantly associated with non-smokers (p=0.047) and a higher eosinophil percentage of total white cell count on blood testing (p=0.004). There was no association with the chronic rhinosinusitis specific quality of life score SNOT-22 (p=0.477). Co-existent sinus disease had significantly higher numbers of pulmonary exacerbations in the previous year (p=0.043). Despite this they appeared to have improved quality of life scores with higher BHQ and LCQ scores.

Conclusion: Sinus disease is a common and important comorbidity in bronchiectasis. This study highlights its association with eosinophilic inflammation, the impact on quality of life and pulmonary exacerbations. The role of SNOT-22 as a chronic rhinosinusitis specific quality

of life score, needs to be considered in patients with bronchiectasis and raises the possibility that this important comorbidity is likely under-diagnosed.

Grant Support: HRC Clinical Research Training Fellowship #18/113. Counties Manukau Health Research Grant, Counties Manukau DHB #810.

Conflict of interest(s): None.
Ethics approval: HDEC approval (18/CEN/127).

[192] [0.18.192] Clinical Benefit Analysis of Erdosteine plus azithromycin in comparsion to standard care in preventing exacerbation in recovered cases of acute exacerbation of Bronchiectasis: A long-term Comparative Efficacy Study

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[1]*Venkatesh Chest Hospital and critical care center, Latur, Latur, India;* [2]*Pacific Institue of Medical Sciences, Udaipur, India;* [3]*MIMSR Medical college, Latur, India*

Background/Aims: The long-term use of azithromycin and or mucolytics has shown benefits in reducing the frequency of exacerbations and the number of related hospitalizations in cases with Recurrent exacerbations in bronchiectasis. However, real-world data on the combination therapy is lacking in the published literature. This study aimed to analyze the role of the long-term use of oral formulations of azithromycin plus erdosteine in reducing exacerbation frequency, hospitalization duration due to exacerbations including recovery time, increasing exacerbation-free days, and prolonging the time to subsequent exacerbations over a 36-week follow-up period. The study also assessed tolerability and adverse events associated with the therapy

Methods: Prospective, observational, 36 weeks follow-up study, approved by IRB and ethics committee (VCC:10/2024, dated 01/03/2024), conducted in Venkatesh chest hospital, Latur and MIMSR Medical college, Latur & Pacific Institute of medical sciences, Udaipur, India during March 2024 to February 2025, included 158 cases of bronchiectasis recently hospitalized and treated for acute exacerbation at one of the three participating centers, confirmed in HRCT imaging's (Modified Reiff Score) and having history of ≥3 exacerbations in last year, following the provision of valid written informed consent. All cases data were recorded as demographics, symptomatology, comorbid illnesses, sputum culture with DST, hematological, inflammatory markers and spirometry. The Medical Research Council (MRC) dyspnoea scale was used to evaluate breathlessness Two groups of 79 patients were randomly assigned using a randomization protocol, with one group receiving oral formulations of azithromycin plus erdosteine and the other receiving standard care only. Sputum rheology indices were monitored during follow-up period: sputum viscosity & clearance (thick, thin and sticky), sputum volume (<50 ml, 50-100 ml and >100ml), sputum colour (mucoid-clear white, mucopurulent-yellow/green, purulent-dark green) and odour (foul smelling versus nonfoul smelling) as a protocol. Azithromycin and Erdosteine dose schedule: Azithromycin was administered as 500 mg tablets three times per week for the first month, followed by 250 mg three times per week for the subsequent eight months. Erdosteine was given at a dose of 300 mg twice daily for nine months. Standard care constitutes bronchodilators plus mucous clearance techniques (pulmonary physiotherapy) without mucolytics and any antibiotic drug. All cases were followed monthly for clinical assessment and were advised to seek emergency room visits on a priority basis if any signs of clinical deterioration were noticed by the patient or their attendants. The primary

objectives were to analyze the benefits of combination therapy with Erdosteine and Azithromycin in decreasing the frequency and severity of exacerbations—classified according to the FACED/BSI score (mild, moderate, and severe)—as well as the duration of exacerbations in both groups during the 36-week follow-up period. The secondary objectives included evaluating the number of exacerbation-free days and the time to first exacerbation in both groups. Additionally, tertiary endpoints involved assessing systemic adverse events related to the long-term use of Erdosteine and Azithromycin that resulted in discontinuation of medication. Statistical analysis by t-test, chi-test and ANOVA.

Results: Age and gender distribution in Erdosteine plus azithromycin group & standard care group were 52.05 years (23-71 years) & 51.19 years (21-72 years) respectively; males 47.76%(32/67) & females 52.23%(35/67), and males 53.73%(36/67) & females 46.26%(31/67) respectively. Sputum microbiological workup with culture and DST showed pseudomonas species in 30.37%(48/158) cases & resistance in 66.66%(36/48) cases, Acinetobacter species in 11.39%(18/158) cases & resistance in 72.22%(13/18) cases, Klebsiella species in 12.65%(20/158) & resistance in 65.00%(13/20) cases, Streptococcus pneumoniae species in 17.08%(27/158) & resistance in 29.62%(8/27), Haemophilus species in 10.12% (16/158) & resistance in 18.75%(3/16), staphylococcus species in 15.18%(24/158) cases & resistance in 55%(12/24) cases & E. coli in 3.16%(5/158) cases & resistance in 20%(1/5) cases. During follow-up, exacerbation frequencies with severity (FACED/BSI Core) as mild (n=46), moderate (n=45) and severe (n=43) were 29, 16 & 12 episodes respectively in Erdosteine plus azithromycin group and 17, 19 & 31 episodes respectively in standard care group [p<0.0018]. Exacerbation duration of mild category in both the groups were 4.20±0.88 days (n=29) versus 7.29±0.82 days (n=17)[p<0.0001], moderate category in both the groups were 6.76±1.15 days (n=26) versus 11.15±1.42 days (n=19)[p<0.0001] & Severe category in both the groups were 8.83 ±1.06 days (n=12) versus 12.58±1.45 days (n=31)[p<0.0001]. Mean time to exacerbation in mild category in both the groups were 95.82±11.89 days (n=29) versus 65.42±12.39 days (n=17)[p<0.0001], moderate category in both the groups were 103.57±12.10 days(n=26) versus 71.00±12.86 days (n=19)[p<0.0001] & severe category in both the groups were 129.25±24.29 days (n=12) versus 72.29±12.59 days (n=31)[p<0.0001]. Difference in mean time to exacerbation in both groups were 30.40% in mild, 32.57% in moderate and 56.96% in severe category. Exacerbation free days in mild category in both the groups were 95.62±9.23 days (n=29) versus 73.76±11.19 days (n=17)[p<0.0001], moderate category in both the groups were 107.65±8.88 days (n=26) versus 82.84±9.33 days (n=19)[p<0.0001] & severe category in both the groups were 173±21.01 days (n=12) versus 77.96±11.80 days (n=31)[p<0.0001]. Difference in exacerbation free days in both groups were 22.86% in mild, 24.81% in moderate and 95.04% in severe category. Indices of sputum rheological properties in both the groups, sputum viscosity and clearance in 62/79(78.48%) cases versus 22/79(27.84%) cases, Reduced sputum volume in 67/79(84.81%) cases versus 11/79(13.92%) cases, improved sputum colour in 69/79(87.34%) cases versus 14/79(17.72%) cases showed significant improvement [p<0.00001]. No any major systemic or auditory functions related adverse events

documented in present study

Conclusions: Long-term combination therapy with azithromycin and the mucolytic erdosteine has shown significant clinical and microbiological benefits in bronchiectasis patients with recurrent exacerbations. The combination works synergistically to reduce exacerbation frequency, shorten recovery time, and prolong exacerbation-free intervals. Improvements in sputum rheological properties such as viscosity, clearance, volume, and color are maintained longer with this regimen, regardless of microbial cause. Erdosteine's added antibacterial and antioxidant effects enhance the overall efficacy of the combination. The therapy is well tolerated, with minimal gastrointestinal or auditory side effects, and offers a cost-effective option for managing a high-morbidity condition. However, individualized assessment is recommended due to the potential risk of macrolide resistance with prolonged use.

Conflict of interest(s) (if any – not included in the 500 words): None to disclose

[358] [0.17.358] Impact of the February 6,2023 Earthquake-Induced Environmental Pollution on Exacerbation Rates in Patients with Bronchiectasis

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Background/Aims:

On February 6, 2023, a series of devastating earthquakes struck southeastern Türkiye and Syria resulting in significant structural damage and loss of life. The disaster generated substantial environmental pollution, including dust,smoke, particulates, toxic gases and asbestos exposure can lead to various respiratory health pathologies like exacerbation of pre-existing respiratory diseases. This study aimed to be the first to investigate the relationship between earthquake-induced environmental pollution and exacerbation rates in patients with bronchiectasis residing in Adıyaman, one of the six provinces in Türkiye most severely impacted by the February 6 earthquake.

Methods:

In this cross-sectional study, we included 37 patients diagnosed with non-cystic fibrosis bronchiectasis (NCFB) who presented to our pulmonary diseases outpatient clinic between January 1, 2025, and April 30, 2025. Patients' demographic characteristics, comorbidity indices such as the BACI (Bronchiectasis Aetiology Comorbidity Index) and Charlson Comorbidity Index, as well as modified Reiff scores, were recorded. Retrospective data on outpatient pulmonary clinic visits, emergency department visits, and hospitalizations were collected from hospital records and the National Health Information Database (e-Nabız).

Results:

The mean age of the patients included in the study was 62 ± 14 years, with 60% being female. 46% of the participants were still residing in prefabricated housing units at the time of the study. 62% of patients had involvement of the lower lobes, and 62% had cystic-type bronchiectasis. A history of prior tuberculosis was present in 22% of the patients.The modified Reiff scores were between 0 and 4 in 65% of the cohort. Regarding comorbidity, 46% of the participants had a BACI score ranging between 1 and 5. An increase in respiratory symptoms following the earthquake was reported by 43% of the patients. Among those living in prefabricated housing, 56% experienced an increase in exacerbations and hospital admissions; however, this increase was not statistically significant ($p = 0.27$). Similarly, although a higher frequency of exacerbations was observed in patients with cystic-type bronchiectasis, this association also did not reach statistical significance ($p = 0.65$).

Conclusions:

Based on our findings, The environmental pollution following the February 6 earthquakes significantly the increase in hospital admissions cannot be overlooked. While a numerical rise in exacerbations and healthcare utilization was evident, statistical significance was not achieved, which may be attributed to the small sample size. These findings highlight the need for targeted respiratory health monitoring and air quality management during natural disasters, particularly for vulnerable populations.

Conflict of interest(s) (if any – not included in the 500 words):

The author declares no conflicts of interest

SESSION 3: DIVERSITY

[25] [0.28.25] Blood eosinophil counts, airway infections and inhaled antibiotic treatment in bronchiectasis

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Background/Aims: The eosinophilic endotype has been recognized in bronchiectasis, but the interplay between airway infection, blood eosinophil counts (BECs), clinical characteristics and the efficacy of inhaled antibiotics treatment remains unclear. To investigate the association between airway infection and BECs, explore how inhaled antibiotic treatment influences BECs, and determine whether BECs levels affect the therapeutic efficacy of inhaled antibiotic.

Methods: We conducted a cohort study to explore the association between BECs, clinical characteristics and airway infections across different disease states. We did a post-hoc analysis to determine the changes in BECs upon inhaled tobramycin and evaluated the therapeutic outcomes stratified by BECs levels.

Results: We included 312 patients, among whom *P. aeruginosa* infection correlated with higher BECs. BECs decreased at exacerbation onset, but were higher among patients with *P. aeruginosa* infection than those without at stable state and exacerbation onset. A lower relative abundance of genus *Pseudomonas* was associated with lower BECs at stable state and exacerbation. Patients with coexisting elevated BECs and *P. aeruginosa* infection demonstrated markedly greater disease severity. Viral detection did not significantly affect BECs. In a randomized trial involving 367 patients with *P. aeruginosa* infection, BECs significantly increased during inhaled tobramycin treatment compared with baseline. Furthermore, inhaled tobramycin therapy improved symptoms, as measured by the *Quality-of-Life Bronchiectasis Respiratory Symptom Scale*, regardless of baseline BECs levels.

Conclusions: Higher BECs are associated with *P. aeruginosa* infection in bronchiectasis, correlating with more severe disease. Inhaled antibiotics may increase BECs and ameliorate symptoms, irrespective of baseline BECs levels.

Conflict of interest(s) (if any – not included in the 500 words): All authors declared no potential conflict of interest related to this abstract.

[29] [0.23.29] Bronchiectasis Pocket Guide

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Background/Aims:
Bronchiectasis is a chronic respiratory condition, with the clinical hallmarks of chronic cough and sputum production due to irreversible dilatation of bronchial airways causing recurrent respiratory tract infections and leading to overall higher morbidity and mortality. Knowledge of appropriate investigations and management of bronchiectasis is critical to prevent recurrent exacerbations and hospital admissions. There are well established guidelines that are developed for clinicians in this regard. However, due to competing priorities in clinical practice, access and time to follow these large clinical practice guidelines may not be always feasible. More specifically for health care workers such as nurses, remote & rural health practitioners, Indigenous/Aboriginal health workers and allied health personnel. This is particularly pronounced in the context of the Northern Territory where there are high rates of Bronchiectasis, particularly in those living in rural and remote areas. Hence, there is a clear need to establish a simplified tool that is more applicable and adaptable. Therefore, we developed such a tool the **"Bronchiectasis Pocket Guide" (BPG)** for use in day-to-day clinical practice.

Methods:
The proposed **BPG** tool was developed by the Respiratory division based at the Royal Darwin Hospital, in the Northern Territory, Australia. Previously published bronchiectasis diagnosis & management guidelines were reviewed, including other relevant reports to develop the **BPG.** Consultation and collaboration with input from medical students, respiratory trainees, respiratory clinical nurse consultants, allied health practitioners, primary care physicians and respiratory physicians was undertaken.

Results:
The final version of the **BPG** is illustrated in **figure 1** below. The contents represented in the **BPG** tool is designed for quick reference guide to improve awareness on pathophysiology, aetiology, diagnosis, appropriate investigations, including treatment & monitoring of bronchiectasis.

BRONCHIECTASIS POCKET GUIDE

Dr Dayna Duncan & Prof Subash Heraganahally

Definition

Irreversible dilation of the airways leading to impaired mucous clearance and recurrent infections. Diagnosed on chest CT with clinical features. Location of the bronchiectasis may give a clue to the aetiology:

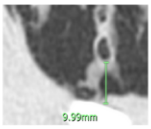
Focal

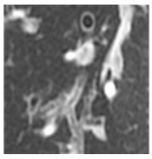
May be due to obstruction, consider bronchoscopy.
Extrinsic: tumour, lymph node
Intrinsic: Aspirated foreign body, tumours, congenital narrowing

Diffuse

Diffuse: infection, immunodeficiency states, genetic diseases (e.g. CF), autoimmune (Sjogren's, IBD), recurrent aspiration, idiopathic
Upper lung fields: CF, post-radiation
Mid-lung fields: non-TB mycobacterium (NTM)(e.g. MAC)
Lower lung fields: Chronic aspiration, end stage fibrotic lung disease
Central airways: Allergic broncho-pulmonary aspergillosis

Imaging





CT Signs

- Bronchus within 1cm of the pleural surface
- Lack of tapering (tram tracks)
- Increased bronchoarterial ratio (>1.5)(signet Ring)
- Bronchial wall thickening
- Mucoid impaction
- Air-trapping and mosaic perfusion
- Bronchial arterial enlargement/ hypertrophy

Bronchiectasis may be cylindrical/ tubular, cystic or varicose. Varicose or cystic bronchiectasis typically has poorer outcomes.

Investigations

Minimum Investigations	Relevance
HRCT	Diagnosis
FBC, WCC	Eosinophilia
Vitamin D	Nutritional deficiency
IgA, IgE, IgM, IgG+subset	Immunoglobulin deficiency
Sputum Mycobacteriology	TB, NTM
Sputum MCS	Bacterial colonisation
Additional Investigations	**Interpretation**
Alpha 1 antitrypsin	Emphysema
Aspergillus IgE/IgG	ABPA
Aspiration risk assessment	Aspiration
Bronchoscopy	Obstruction
Cystic fibrosis testing	Cystic fibrosis
Connective tissue disease screen	Autoimmune lung disease
HIV	Immune deficiency
HTLV1	Immune deficiency
Primary ciliary dyskinesia	Impaired sputum clearance

Spirometry
Goals
1. Identify co-existing COPD to be treated (confers poorer mortality)
2. Determine severity and monitor progression

Restrictive pattern is typical of bronchiectasis (low FVC)

Bronchodilators

- LAMA: Bronchodilation with the additional benefit of reducing secretions
- LABA: Improves outcomes in co-existing COPD
- ICS: May be beneficial if there is severe COPD or bronchodilator reversibility, but may increase risk of infective exacerbations
- Combination therapy (LAMA/ LABA/ ICS): beware of risk of excessive muscarinic antagonism, atrovent should not be co-administered

Management- Acute

Exacerbations are defined as a deterioration of symptoms accompanied by increased dyspnoea or change in sputum production lasting three days or more.
Management of an exacerbation is as follows;

- Sample and culture sputum every exacerbation

Antibiotics

- Extended course- **14 days total** (IV + PO)
- Targeted to previous bacteriology

Sputum Clearance (Chest Physio)

- Adequate hydration
- Flutter valves- bottle PEP or acapella

Sputum Microbiology

Exacerbations are largely caused by typical flora for pneumonia (e.g. H.Influenzae). If a patient is colonised with pseudomonas or MAC, this confers a higher mortality. Antibiotics should be based on empiric guidelines on Therapeutic Guidelines with consideration of previous bacteriology.

Management- Long Term

Goals: identify aetiology, prevent progression, reduce exacerbations, improve function and quality of life
Sputum Clearance

- Daily sputum clearance even when well

Smoking Cessation

- Consider pharmacotherapy (NRT or varenicline)

Nutrition

- Low BMI has increased risk of mortality
- Address barriers e.g. dentition, food scarcity

Alcohol cessation
Physical Activity

- Improves sputum clearance

Vaccination

- Influenza, COVID, Pneumococcal, RSV

Annual specialist review
Annual sputum surveillance
Consider long term antibiotics

access to bronchiectasis toolbox

Abbreviation List

CF (cystic fibrosis), IBD (inflammatory bowel disease), MAC (mycobacterium avium complex), HRCT (high resolution computed tomography), FBC (full blood count), WCC (white cell count), TB (tuberculosis), MCS (microscopy, culture and sensitivity), ABPA (acute bronchopulmonary aspergillosis), HIV (human immunodeficiency virus), HTLV1 (human t-lymphocyte virus), LAMA, (long acting muscarinic antagonist) LABA (long acting beta agonist), ICS (inhaled corticosteroid), NRT (nicotine replacement therapy)

References

Chang, A. B., Bell, S. C., Byrnes, C. A., Dawkins, P., Holland, A. E., Kennedy, E., ... & Grimwood, K. (2023). **Thoracic Society of Australia and New Zealand (TSANZ)** position statement on chronic suppurative lung disease and bronchiectasis in children, adolescents and adults in Australia and New Zealand. Respirology, 28(4), 339-349.

Conclusions:

The proposed **BPG** tool could support primary care clinicians, particularly in remote areas, to provide the best standard of guideline-directed care to patients and reduce inequity in healthcare due to rurality.

Conflict of interest(s) (if any – not included in the 500 words):

[38] [0.25.38] The Indigenous Bronchiectasis Assessment Scale - IBAS

Timothy Howarth[1,2]

[1]*Darwin Respiratory and Sleep Health, Darwin, Australia;* [2]*University of Eastern Finland, Kuopio, Finland*

Background/Aims:

Bronchiectasis is more prevalent, presents earlier, displays a greater array of comorbidities and has a higher mortality rate among Indigenous populations. Current severity assessment scales do not account for the younger age of Indigenous patients, the greater prevalence of comorbidities and the resulting lower lung function - typically classing Indigenous patients as "Mild" due to the significance placed on age in these tools. As such, there are currently no tools suitable for or specific to Indigenous patients with bronchiectasis. Therefore, this study aimed to develop such a tool - the “Indigenous bronchiectasis assessment scale” (IBAS).

Methods:

454 adult Indigenous Australian patients, residing in the Northern Territory of Australia, with chest CT confirmed bronchiectasis were included. Age, sex, residence location (urban or remote), body mass index, radiological findings, sputum microbiology data, lung function parameters and respiratory hospitalisation history were utilised to predict 5-year all-cause mortality and 5-year hospitalisations. In univariate Cox regression models parameters with a p-value<0.20 were considered for inclusion in the IBAS. Among those parameters which were included, their score within the IBAS was determined as the mean β effect on mortality and hospitalisations rounded to the nearest 0.5. Parameters which rounded to 0 or below were excluded.

Results:

Age (30-50, 50-70 & 70+ years) (1, 2 & 3 points respectively), urban residence (2 points), FVC (% predicted) (30-50% & <30%) (1 & 2 points respectively), right lower lobe involvement (1 point), history of *haemophilus* spp., *pseudomonas* spp., *yeast* spp. or *moraxella* spp. (1 point each), 2-year respiratory hospitalisation history (2 & 3+ admissions) (2 & 3 points respectively), and comorbid chronic obstructive pulmonary disease, asthma and arterial hypertension (1 point each) were included in the IBAS.

The maximum score was 18, with thresholds at 0-4 (mild), 5-7 (moderate) and ≥8 (severe). The area under the curve for 5-year mortality from the continuous IBAS score was 0.777 (95% CI 0.701, 0.854) and for the 3-category model was 0.761 (95% CI 0.688, 0.835). There was significant delineation in mortality between mild and moderate (moderate HR 3.45 (95% CI 1.57, 7.58)) and between moderate and severe categories (severe HR 2.43 (95% CI 1.45, 4.07)).

Conclusions:

The proposed IBAS tool incorporates factors which are more relevant among Indigenous patients with bornchiectasis, including younger age thresholds, more comorbidity inclusions, and more sputum culture findings. The IBAS appears to perform better than exsting tools in assessing bronchiectasis severity in Indigenous patients. Further prospective studies are warranted to assess the validity and utility of the IBAS in wider Indigenous populations.

Conflict of interest(s) (if any – not included in the 500 words):

[78] [0.21.78] Morbidity and mortality burden from bronchiectasis in the United Kingdom: An observational cohort study

Eleni Bacopanos[1,3]; Doug Forrester[1,2,3]; Girdler Ella[2]; Quint Jennifer[4]; Navaratnam Vidya[1,3,4]

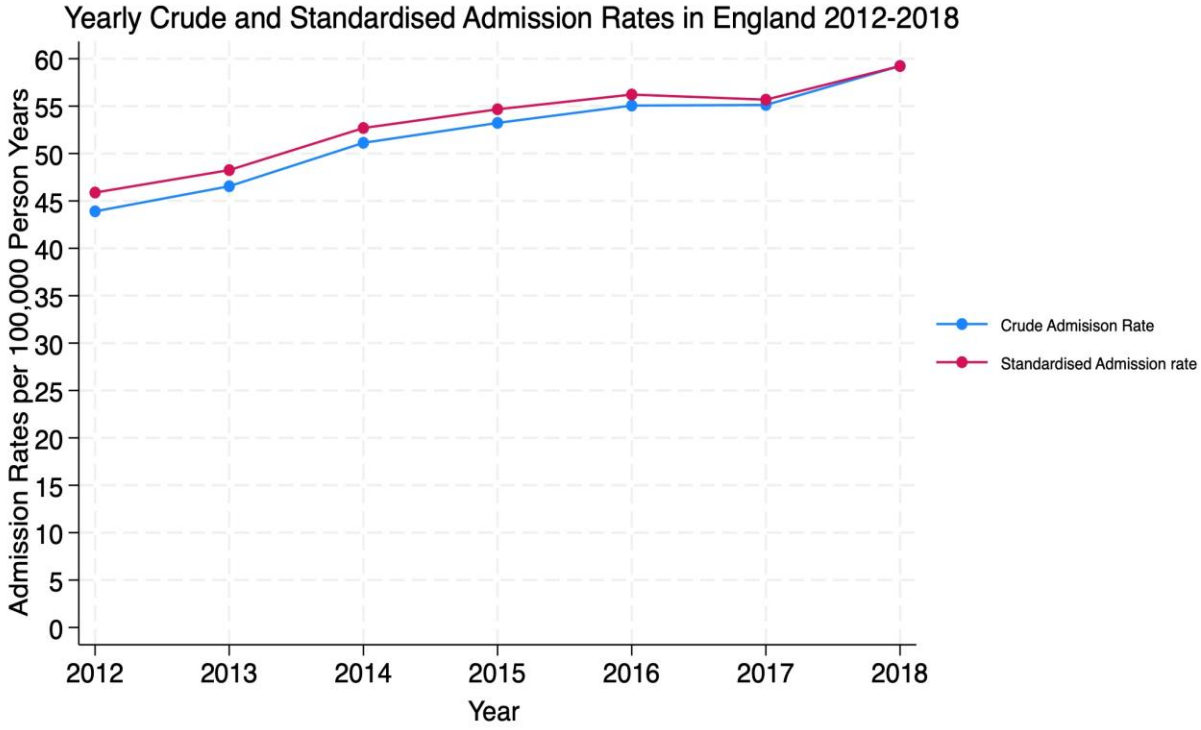
[1]*Institute for Respiratory Health, University of Western Australia, Perth, Australia;* [2]*Curtin University Medical School, Perth, Australia;* [3]*Department of Respiratory Medicine, Sir Charles Gairdner Hospital, Perth, Australia;* [4]*School of Public Health, Imperial College London, London, United Kingdom*

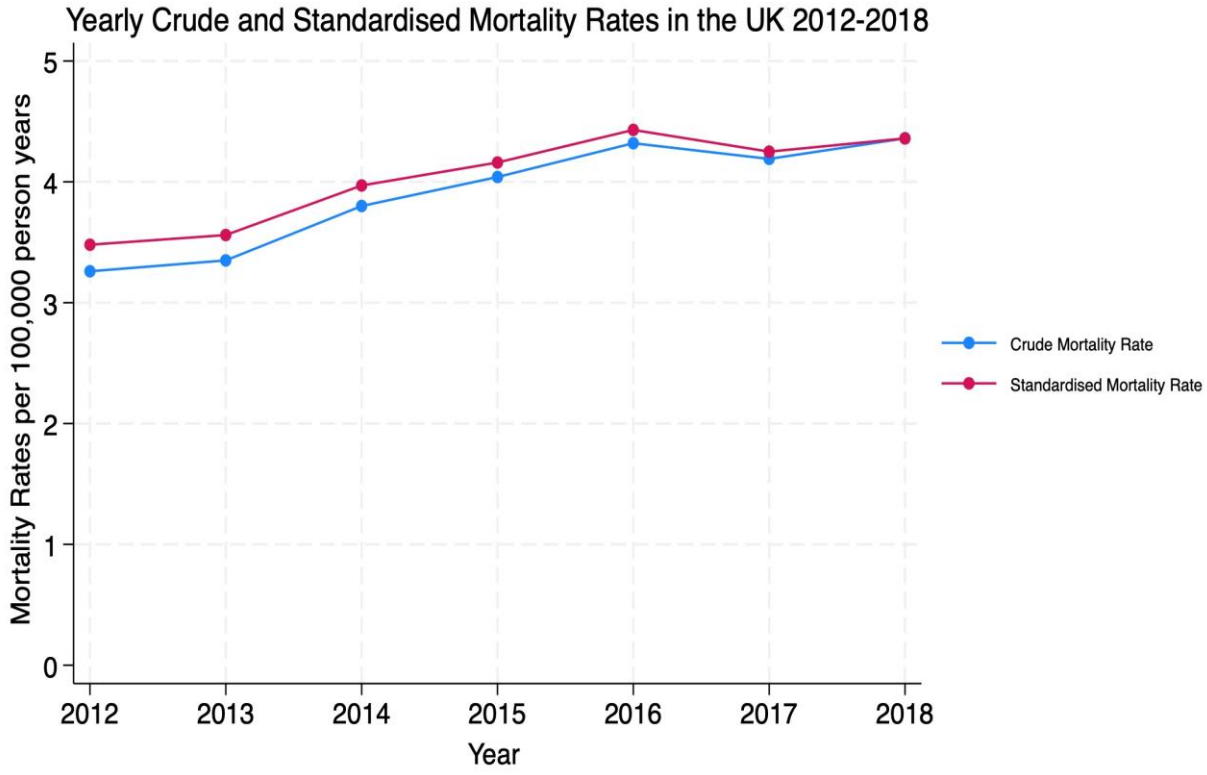
Background/Aims: The incidence and prevalence of non-cystic fibrosis (CF) bronchiectasis is increasing globally. However, there are limited data on the burden of bronchiectasis in terms of hospital admissions and mortality. Up to date estimates are essential for allocation of healthcare resources, and planning of service pathways. The aim of our study was to provide up to date trends in the number of hospital admissions in England and mortality rates from bronchiectasis in the United Kingdom from 2012 to 2018.

Methods: We extracted data from Hospital Episode Statistics (HES) to obtain annual number of hospital admissions (Finished Consultant Episodes) between 2012 and 2018 for all National Health Service (NHS) hospital trusts in England. We used the ICD-10 codes J47.0 and Q33.4, to identify individuals whose primary reason for admission to hospital was bronchiectasis. The same ICD-10 codes were used to obtain the annual number of registered deaths where bronchiectasis was the underlying cause of death in the United Kingdom from the European Statistics Institution (EUROSTAT) database. Annual crude admission and mortality rates stratified by age group, sex and year were calculated. We used direct standardization to estimate annual age-standardized admission and mortality rates, standardised to the 2018 English and UK population respectively. Segmented regression modelling was used to generate average annual percentage change (AAPC) in admissions and mortality. We used Poisson regression modelling to examine admission and mortality trends by age group and sex.

Results: The total number of hospital admissions from bronchiectasis in England was 150,139 between 2012 and 2018 whilst the total number of deaths from bronchiectasis across the UK was 13,556 over the same period. Age-standardized admission rates increased from 45.9 (95% Confidence Interval [CI] 45.2 to 46.6) per 100,000 person years in 2012 to 59.2 (95% CI 58.5 to 60.0) per 100,000 person-years in 2018 (Figure 1). This equates to a 4.3% yearly increase in admissions throughout the study period (AAPC 4.31%, 95% CI 3.53 to 5.14). Age and sex standardized mortality rates increased from 3.26 (95% CI 3.10 to 3.42) per 100,000 person years in 2012 to 4.18 (95% CI 4.18 to 4.54) per 100,000 person years in 2018 (Figure 2). Annual mortality rates increased by an average of 3.8% (AAPC 3.80, 95% CI 2.91 to 4.80) over the six years. We found that both admission and mortality rates increased with age. Admissions were highest in the 75-79 age category (RR 19.11, 95% CI 18.76-19.47) compared to those under 55

years of age. Mortality was 20 times higher in people over 80 years age (RR 20.64 95% CI 18.70-22.77) compared those in the 60-64y age category.





Conclusion: Our findings suggest that both secondary care and mortality burden from bronchiectasis in the UK is increasing at a similar rate and therefore remains a larger than appreciated burden on healthcare services. Our estimates suggest that deaths from bronchiectasis now account for 11% of deaths from all chronic respiratory diseases in the UK. Further investment is required for both provision of care and research to improve treatment options for this group of patients.

Conflict of interest(s) (if any – not included in the 500 words):

[93] [0.22.93] A clinical approach to the diagnosis and management of Bronchiectasis in adult Aboriginal patients in the Top End Northern Territory Australia

Dayna Duncan[1,2]; Timothy Howarth[3,4]; Subash Heraganahally[1,2,3,4]

[1]*Department of Respiratory and Sleep Medicine, Royal Darwin Hospital, Darwin, Northern Territory, Australia;* [2]*Flinders University, College of Medicine and Public Health, Darwin, Northern Territory, Australia;* [3]*Darwin Respiratory and Sleep Health, Darwin Private Hospital, Darwin, Northern Territory, Australia;* [4]*School of Medicine, Charles Darwin University, Darwin, Northern Territory, Australia*

Background/Aims: Bronchiectasis is a condition which disproportionately affects Aboriginal Australians and those in rural and remote areas are over-represented in the Northern Territory (NT) of Australia. Recent evidence has demonstrated that bronchiectasis in the NT is more prevalent, more severe, and affects people younger than other international cohorts, including higher morbidity and mortality. The vast landscape of the NT also means that patients rely on remote health care works, including primary care physicians, nurses, and Aboriginal Health Practitioners to ensure that they receive the best standard of care in the absence of readily available specialist medical care. However, a clinical approach guideline to bronchiectasis diagnosis and management specific for this unique population in NT Australia is lacking.

Methods: Literature was reviewed of national and international guidelines alongside locally available data on the differences in epidemiology, aetiology, microbiology, and trajectory of bronchiectasis, with a particular focus on remote and rural Aboriginal patients. A clinical approach was constructed by consensus of local clinicians, with consultation of primary care practitioners to ensure that they were easily readable and practical given locally available resources.

Results: EPIDEMIOLOGY: The prevalence of bronchiectasis among the adult Aboriginal Australians is estimated to be around 9.8% Australia wide, and the prevalence is higher in the Top End region of the NT (23%) and could be up to 14.9/1000 and even higher in rural and remote areas, where 80% of the Australian Aboriginal people reside in the NT. Most patients are in the age group of 40 to 60 years with slightly higher female predominance with a median age of death at 59 years, as compared to >70 years with international data; **CLINICAL FEATURES:** Cough, sputum production, shortness of breath (short wind) are the cardinal symptom. On physical examination, aside from course crackles, finger clubbing and lower body mass index could be observed. Concurrent presence of COPD and other medical co-morbidities are frequent. **INVESTIGATIONS:** A presumptive diagnosis may be made based on clinical features and chest X-ray (CXR) findings if access to chest CT is limited, however confirmatory HRCT could be facilitated when feasible. Restrictive impairment is predominant on spirometry (lower forced vital capacity (FVC)). H. Influenzae, P. aeruginosa and non-

aspergillus fungus are common on sputum microbiology. Other relevant investigations need to be considered to determine aetiology [Connective tissue disease screen, HTLV I/II]. **MANAGEMENT:** Patient education, sputum clearance, smoking cessation (tobacco, cannabis and bucket bong), nutrition assessment, exercise and physical activity and vaccination are vital. In relation to pharmacotherapy - long-acting muscarinic antagonists (LAMA) and long-acting bronchodilator (LABA) are associated with a decreased risk of mortality. However, inhaled Corticosteroids (ICS) should be used with caution. Exacerbations should be managed as per local guidelines.

Conclusions: This proposed clinical approach aimed at primary care practitioners, particularly when working with Aboriginal peoples in remote and regional centres could be of aid in the diagnosis, workup, and management of bronchiectasis in the adult Aboriginal patients.

Conflict of interest(s) (if any – not included in the 500 words): Nil

[181] [0.27.181] Bronchiectasis mortality trends across Europe between 2011 – 2018.

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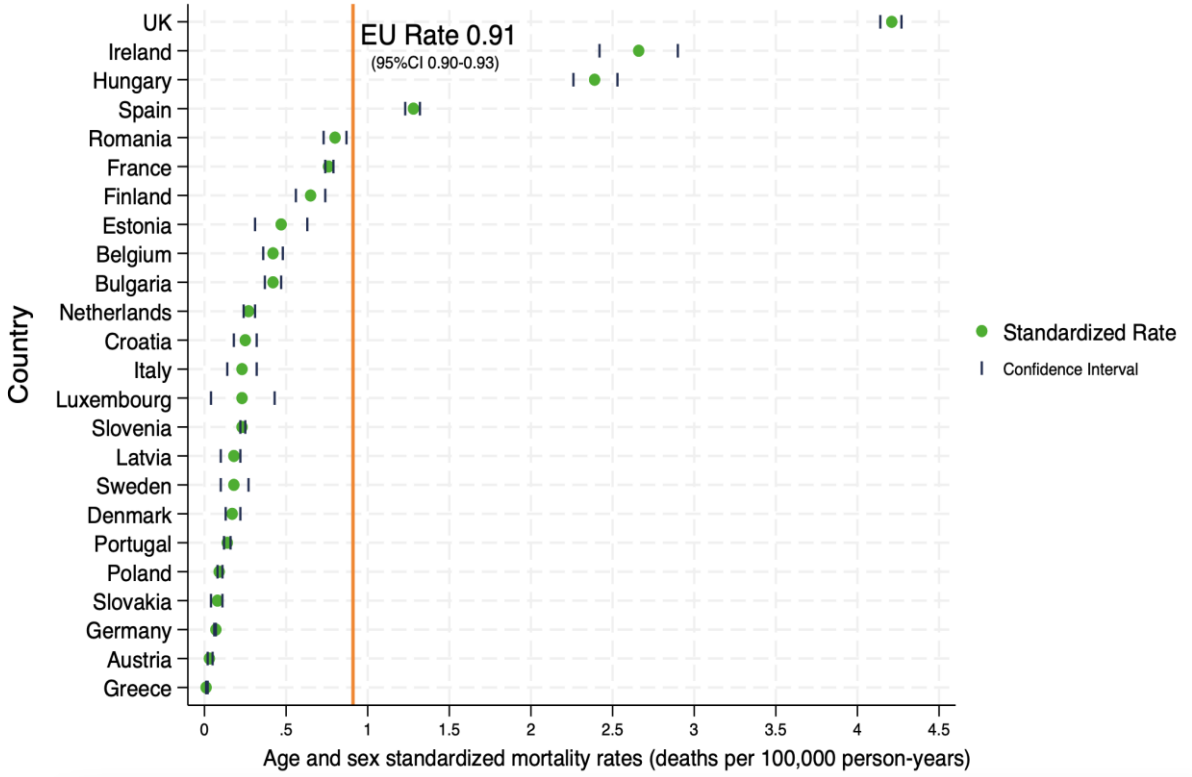
Background/Aims: Bronchiectasis incidence and prevalence rates appear to be increasing world-wide. However, there have been no studies examining trends in Bronchiectasis mortality across Europe. Our aim was to provide up to date estimates of mortality rates for Bronchiectasis across 24 European Countries between 2011 – 2018.

Methods: Using data from the European Statistics Institution (EUROSTAT), we obtained the annual number of registered deaths due to Bronchiectasis from 24 European country between2011 to 2018. We used the ICD-10 codes J47.0 and Q33.4 to identify individuals whose underlying cause of death was bronchiectasis, stratified by age and sex. Crude and age and sex standardized mortality rates stratified by year and country were estimated, standardized to the European 2018 population. Average Annual Percentage Change (AAPC) was calculated using segmented regression to examine annual trends across the study period.

Results: The total number of bronchiectasis deaths across Europe during the study period was 26,872. Deaths increased from 2775 in 2011 to 3658 in 2018. Age and sex standardized mortality rates during the study period and was heterogeneous across the different countries (Figure 1). The United Kingdom had the highest standardized mortality rate of 4.2 (95% Confidence Interval [CI] 4.14 – 4.27) per 100,000 person-years for the overall study period. In contrast, Greece had the lowest standardized mortality rate of 0.01 (95% CI 0.01-0.02) per 100,000 person-years. The average annual increase in mortality across all 24 countries combined was 1.3% (AAPC 1.32, 95% CI -0.36 to 3.34).



Conclusions: Overall, the mortality burden from bronchiectasis across Europe remained stable between 2011 and 2018, but with significant inter-country variation, some of which is consistent with data from the European Bronchiectasis Registry (EMBARC). This heterogeneity may be due to differences in access to health care, diagnostic practices, altered microbiology and varying infection rates across Europe. These data highlight the substantial impact of bronchiectasis, in terms of mortality in Europe. Particularly importance of standardized diagnosis and care pathways are vital.

Conflict of interest(s) (if any – not included in the 500 words):

[193] [0.24.193] Sociodemographic Factors Associated with Health Outcomes in a Sample of the U.S. Bronchiectasis and Nontuberculous Mycobacteria Research Registry

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Background/Aims:

Sociodemographic factors have been demonstrated to impact health outcomes in lung diseases. In the United States (US), bronchiectasis has been described and investigated in predominantly White middle-aged or elderly women, although the actual population affected is much broader. Regional variability in sociodemographic factors has not been evaluated in persons living with bronchiectasis (pwBE). In asthma and COPD, exacerbation and hospitalization rates correlate to sociodemographic factors, but no such correlation has been evaluated in bronchiectasis. We sought to evaluate sociodemographic factors that may impact health outcomes in pwBE utilizing lung function, exacerbations and healthcare utilization as surrogate measures.

Methods:

The US Bronchiectasis and Nontuberculous Mycobacteria (NTM) Research Registry (BRR) is a centralized clinical database and three geographically distinct sites within the BRR were included. Standardized data fields collected for social determinants of health (SDH) included English proficiency, educational attainment, marital and employment status, occupational or environmental exposures, housing or food insecurity, substance use, and healthcare utilization, including missed appointments and scheduled follow-up visits. SDH data were summarized descriptively and compared across sites using F-tests and chi-square tests for continuous and categorical variables, respectively. We performed a multivariable generalized linear model to assess the mean difference in FEV1(L) by educational attainment, after adjusting for age, sex, race, exacerbation history, NTM diagnosis, and site.

Results:

Three sites were included: Site A in the Southeast (n=141), Site B in the West (n=112), and Site C (n=87) in the Southwest. Overall, 82.8% of patients were classified as non-Hispanic White but significant differences in race and ethnicity were seen between sites ($p<0.001$). English as the primary language was lowest in Site B (92.0%) and highest in Site C (100%). There were

significant differences in educational attainment across sites with one half of patients having completed college, and one third graduate or professional school ($p<0.001$). A higher percentage of patients at Site C completed high school or less (C: 36.8% vs. A: 13.6% vs. B: 18.8%). In terms of environmental exposures, a significantly higher number of patients from Site C reported hazardous occupational or environmental exposures (C: 37.9% vs. A: 20.7% vs. B: 9.8%, $p<0.001$). Patients at Site C were also significantly less likely to have a follow-up appointment scheduled (C: 52.9% vs. A: 12.8% vs. B: 17.9%, $p<0.001$). After adjusting for age, sex, race, exacerbation history, NTM diagnosis, and site, there is a significant difference in mean FEV1(L) and educational attainment (p-value=0.03). Patients whose highest level of completed education was high school or less have a 0.24(L) mean decrease in FEV1(L) (95% CI: 0.03 to 0.44 (L) decrease) compared to patients who completed graduate or professional school.

Conclusions:

In this multicenter analysis from three demographically unique BRR sites, we observed significant differences in SDH. One site demonstrated a significant correlation of lower level of education and occupational or environmental exposures, which may be correlated to outcomes in lung function. Regional and SDH differences must be further investigated to aid in predictive measures, disease course and meaningful health interventions.

Conflict of interest(s) (if any – not included in the 500 words):
The authors would like to acknowledge the Bronchiectasis and NTM Association, who manages the Bronchiectasis and NTM Research Registry, a 501(c)(3) nonprofit organization. The Registry is funded by the Richard H. Scarborough Bronchiectasis Research Fund, the Anna-Maria and Stephen Kellen Foundation, a Research Grant from Insmed Incorporated, and the Bronchiectasis and NTM Industry Advisory Committee. It should also be noted that this work would not have been possible without the comprehensive chart reviews and recording of data by the dedicated research coordinators and PIs at each of the participating Registry sites.

[337] [0.20.337] Chronic Bronchiectasis Complicated by Common Variable Immunodeficiency (CVID): A Case Study of Multidisciplinary Management"

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Background: Chronic pulmonary conditions such as bronchiectasis can be complicated by immune deficiencies like Common Variable Immunodeficiency (CVID), which necessitate comprehensive clinical management. This case study describes the diagnosis and treatment of a 28-year-old female with bronchiectasis complicated by CVID.

Case Presentation: A 28-year-old female with a longstanding history of bronchiectasis since childhood and recurrent respiratory infections presented for evaluation. Previous medical advice included a lobectomy, which was not pursued. The patient exhibited symptoms such as diminished air entry in the left lower zone and coarse diffuse crepitations across the chest. Her exacerbations were frequent, occurring every 1-2 months.

Investigations: Diagnostic investigations included CT chest, pulmonary function tests (PFTs), and extensive immunological assessments, revealing bilateral lower lobe predominant varicose bronchiectasis, reduced lung function, and significantly low levels of immunoglobulins. Genetic testing was suggested to explore underlying causes, specifically assessing for CVID.

Diagnosis: The patient was diagnosed with bronchiectasis secondary to CVID, based on her clinical presentation, immunodeficiency, and imaging findings.

Management: Management included subcutaneous immunoglobulin therapy, which significantly reduced infection frequency, alongside chronic azithromycin therapy. Pulmonary rehabilitation and ongoing evaluation by pulmonology and immunology were recommended.

Conclusion: This case highlights the importance of considering immune deficiency in patients with chronic bronchiectasis and the effectiveness of multidisciplinary management. Genetic testing plays a crucial role in confirming the diagnosis of CVID, thereby guiding appropriate therapy to reduce complications and improve quality of life.

[339] [0.26.339] Comprehensive Diagnostic and Management Approach in a Case of Bilateral Bronchiectasis with Hemoptysis in a Heavy Smoker

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Background: Bilateral bronchiectasis presents significant diagnostic and therapeutic challenges, especially in patients with heavy smoking histories and concurrent symptoms like hemoptysis. This case report discusses the interdisciplinary approach taken for a 47-year-old male smoker, emphasizing the importance of thorough investigations and targeted management strategies.

Case Presentation: A 47-year-old male with a history of heavy smoking (2-3 packs/day) presented with bilateral bronchiectasis and episodes of hemoptysis. The patient, a professional driver, also complained of severe gastroesophageal reflux disease (GERD). Initial investigations included chest X-rays, comprehensive blood tests, sputum cultures, and immunoglobulin levels, all yielding normal or negative results, pointing to non-infectious etiologies.

Diagnostic Focus: The diagnostic strategy employed high-resolution computed tomography (HRCT), which showed ground-glass opacities (GGO), cystic changes, and multiple small nodules in the left lung, suggestive of a complex interplay of airway disease and potential remote granulomatous disease. Follow-up HRCT indicated stable disease without progression of noted abnormalities.

Management: Management included pharmacological treatment with Nexium 40 mg for GERD and Tiotropium for bronchial symptoms. Recommendations for lifestyle modifications, particularly smoking cessation, airways clearance techniques, and vaccinations, were emphasized to reduce symptom exacerbation and prevent future complications.

Outcomes: The patient's condition remained stable with the implemented treatment regimen. Follow-up plans included a repeat CT chest and echocardiogram to monitor the disease's progression and cardiac function, which remained within normal limits during the initial assessment.

Conclusion: This case underscores the necessity for a holistic approach in the management of bronchiectasis, particularly in patients with significant smoking histories. Regular monitoring, combined with comprehensive diagnostic evaluations and tailored therapeutic interventions, is crucial for managing such complex cases effectively.

SESSION 4: EPIDEMIOLOGY & REGISTRIES

[59] [0.33.59] Tailored AI Model for the Prediction of Severe Acute Exacerbation in an Asian

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Background/Aims: Classical scoring models such as the Bronchiectasis Severity Index (BSI) and FACED have shown good performance in predicting acute exacerbation (AE) in bronchiectasis. However, these models were developed based on cohorts of European ancestry, and population-specific models for predicting severe AE in Asian populations have yet to be established. This study aimed to develop an artificial intelligence (AI) model to accurately predict severe AE in Asian populations using a local database.

Methods: This study included 492 patients with 1-year follow-up data registered in the Korean Multicenter Bronchiectasis Audit and Research Collaboration registry. To develop AI models to predict severe AE, we compared the performance of three models—extreme gradient boosting (XGBoost), logistic regression (LR), and multilayer perceptron (MLP)—with classical scoring models, including the BSI and (FACED).

Results: Of the 492 participants, 83 (8.9%) experienced severe AE. Among the three AI models, the MLP model demonstrated better performance in predicting severe AE than did the other two models. Additionally, it outperformed the classical scoring models in terms of sensitivity, specificity, F1-score, and area under the receiver operating characteristic curve (AUROC). The Shapley additive explanation (SHAP) analysis revealed key predictors of severe AE, including BSI, sputum color and volume, and a history of tuberculosis and pneumonia.

Conclusions: Although classical scoring models demonstrated good performance in predicting severe AEs, a population-specific AI model incorporating local data outperformed them in predicting severe AEs in an Asian population with bronchiectasis.

Conflict of interest(s) (if any – not included in the 500 words): None

[85] [0.30.85] Reproductive Lifespan and Post-menopausal Bronchiectasis in U.S. Postmenopausal Women: An investigation of the Women's Health Initiative Cohort

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Background/Aims:
Non-cystic fibrosis bronchiectasis disproportionately affects older women. The role of reproductive hormones in pathogenesis of bronchiectasis is not well characterized. This study examined data from the large prospective cohort of postmenopausal women enrolled in the Women's Health Initiative (WH) study to test the hypotheses that (1) shorter reproductive lifespan and (2) earlier menopause are associated with higher risk of bronchiectasis development.

Methods:
To ensure that encounters in which bronchiectasis is diagnosed are captured, we only included participants with fee-for-service Medicare A (inpatient) + B (outpatient) coverage. Participants who had any gap in coverage longer than one year were excluded. The exposures of interest included ages at menarche and menopause, and time from menarche to menopause (reproductive lifespan). The outcome of interest was the first incidence of bronchiectasis after Medicare enrollment, based on the presence of initial appearance of the corresponding International Classification of Diagnoses (ICD) 9 and 10 codes in the Medicare Claims Data linked to the participants' WHI records. Incidence rates per 1,000 person-years were calculated and a series of Cox proportional hazards models controlling for age at Medicare enrollment, race, ethnicity, BMI, smoking behavior, oophorectomy, hormone therapy (HT) use, oral contraceptive use, and comorbid conditions were created. As HT use was theorized to modify the effect of reproductive age on bronchiectasis risk, we conducted these analyses overall and stratified by HT use.

Results:
A cohort of 96,996 women was included in this study. Cumulative incidence of bronchiectasis was 3.0%. Shorter reproductive lifespan was associated with higher bronchiectasis risk (p_{trend}=0.02). Women with the longest reproductive lifespan (≥40 years) were at 12% lower risk of bronchiectasis than those with the shortest reproductive lifespan (<30 years; aHR=0.88 [95% CI: 0.81, 0.96]). HT use modified this relationship (p<0.01): shorter reproductive lifespan was related to bronchiectasis risk in women who did not use HT (p_{trend}=0.01), and not in women who used HT (p_{trend}=0.25). Without HT use, women with longest reproductive lifespans (≥40 years) were at 22% lower risk of bronchiectasis than those with the shortest reproductive lifespans (<30 years; 0.78 [95% CI: 0.68, 0.89]). Similar

findings were observed for the age of menopause: women with later ages of menopause (45-49, 50-54 and ≥55 years) were at lower risk than women with the earliest age of menopause (<40 years; aHRs=0.81 [95% CI: 0.68, 0.96], 0.74 [95% CI: 0.62, 0.87], and 0.76 [95% CI: 0.63, 0.91], respectively)

Conclusions:
Both a longer reproductive lifespan and later age of menopause are associated with reduced risk of non-cystic-fibrosis bronchiectasis in post-menopausal women – but only in those without history of HT use.

Conflict of interest(s) (if any – not included in the 500 words):

No conflicts of interest to report

[98] [0.36.98] Adults with paediatric-onset bronchiectasis (POBE) have greater disease severity compared to those with adult-onset bronchiectasis (AOBE): A multicenter EMBARC registry study

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Background/Aims:

Bronchiectasis, a heterogeneous disease, can manifest during childhood or adulthood. Adults with pediatric-onset bronchiectasis (POBE) may represent a distinct phenotype. However, this remains poorly characterized. This study aimed to compare the severity of POBE to adult-onset bronchiectasis (AOBE) in adults.

Methods:

Data from four EMBARC centers were analyzed. POBE was defined as symptom onset before 18 years of age, while AOBE was defined as symptom onset at or after 18 years. Symptom duration was defined as the difference between the current age and the age at symptom onset. Multivariable analyses evaluated lung function, *Pseudomonas* infection, exacerbations, and hospitalizations with disease onset, symptom duration, and aetiologies as variables.

Results:

Among 1,422 patients, 249 (17.5%) had POBE (mean onset age: 6.5 years), and 1,173 had AOBE (mean onset age: 55.4 years). POBE patients were younger (mean age 50.3 vs. 66 years), had longer disease duration (43.3 vs. 10.8 years), worse lung function (FEV1%: 70.8 vs. 84.2), greater radiological extent (Reiff index: 6.0 vs. 4.4), higher bacterial infection rates (72.3% vs. 54.6%), and more exacerbations (median: 2 vs. 1); $p<0.001$ across all comparisons, results were similar when only idiopathic and post-infectious aetioogies were included. Longer symptom duration was independently associated with *Pseudomonas* infection, hospitalizations, exacerbations, and reduced FEV1%. Congenital etiologies- primary ciliary dyskinesia and primary immune deficiency further contributed to disease severity. 142 adults were younger than 40 years. Compared to older adults, they were more likely to have POBE

(63.4% vs. 12.4%, p<0.001) and experience exacerbations (82.9% vs. 71.3%, p = 0.012) with no differences in lung function, airway infection rates, radiological severity, and quality of life.

Conclusions:

Adults with POBE exhibit greater disease severity compared to those with AOBE, likely due to prolonged symptom duration and congenital etiologies. Conventional bronchiectasis severity scores may underestimate severity in young people with POBE. Optimized care, including a structured transition to adult care, may help mitigate disease progression in POBE patients.

Conflict of interest(s) (if any – not included in the 500 words):

[124] [0.37.124] The frequent exacerbator phenotype in bronchiectasis revisited: Data from the European Bronchiectasis Registry (EMBARC)

Oriol Sibila[1]; Lidia Perea[2]; Pierre Regis Burgel[3]; Eva Polverino[4]; Michal Shteinberg[5]; Jennifer Pollock[6]; Jamie Stobo[6]; Holly Lind[6]; Charles Haworth[7]; Katerina Dimakou[8]; Apostolos Bossios[9]; Raja Dhar[10]; Michael Loebinger[11]; Rosario Menendez[12]; Antoni Torres[1]; Francesco Blasi[13,14]; Montserrat Vendrell[15]; Pieter Goeminne[16]; Felix Ringshausen[17]; Anthony De Soyza[18]; Stefano Aliberti[19,20]; James D Chalmers[6]

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Background/Aims: Frequent exacerbations are a risk factor for disease progression in bronchiectasis (BE). Prior exacerbations are used to guide treatment in guidelines. We explored the relationship between prior and future exacerbations across regions and aetiologies in BE patients. We aimed to test if the ability of prior exacerbations to predict future exacerbation varies by region or aetiology.

Methods: Data analysis of the European Bronchiectasis Registry (EMBARC) from adults with BE from 31 countries (European countries and Asia). Baseline exacerbation history was tested the association with future exacerbations using negative binomial regression with time in study as an offset.

Results: From 19324 patients, each prior exacerbation increased the risk of future exacerbations by 17% (RR 1.17 95%CI 1.16-1.18, p<0.0001), even after adjustment for multiple confounders (1.14 95%CI 1.13-1.15, p<0.0001). No significant interaction between aetiology and prior exacerbations existed. Of the common aetiologies, idiopathic (1.16 95%CI 1.15-1.18), postinfective (1.16 95%CI 1.14-1.19), PCD (1.18 95%CI 1.12-1.24), COPD (1.13 95%CI 1.11-1.16) had a consistent relationship with future exacerbations. There was no significant difference in the relationship between prior and future exacerbations across regions – North and Western Europe (1.17 95%CI 1.16-1.19), Southern Europe (1.18 95%CI 1.14-1.21), Central and Eastern Europe (1.18 95%CI 1.13-1.23) and Asia (1.28 95%CI 1.122-1.34). Patients with ≥2 and ≥3 prior exacerbations were at markedly increased risk independent of region and aetiology.

Conclusions: The frequent exacerbator phenotype is highly consistent across BE populations globally.

Conflict of interest(s):

PRB reports grants or contracts from GSK and Vertex, to the institution; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Astra-Zeneca, Chiesi, GSK, Insmed, MSD, Pfizer, Vertex, Viatris and Zambon. CH reports consulting fees from 30 Technology, Chiesi, Infex, Insmed, LifeArc, Pneumagen, Vertex, Zambon; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Chiesi, Insmed, Vertex, Zambon; and Payment for expert testimony from Zambon. EP reports grants or contracts from Grifols; consulting fees from Insmed, Pari, Electromed, Pari, Grifols and Chiesi; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Insmed, Pari, Electromed, Pari, Grifols, Chiesi and GSK; support for attending meetings and/or travel from Insmed; participation on a Data Safety Monitoring Board or Advisory Board from Insmed. MS reports grants or contracts from GSK, Trudell pharma and Tel Aviv league for lung diseases; consulting fees from AstraZeneca, Boehringer Ingelheim, Dexcel, Kamada, Synchrony Medical, Trumed, Vertex and Zambon; payment or honoraria for lectures, presentations, speakers

bureaus, manuscript writing, or educational events from AstraZeneca, Boehringer Ingelheim, GSK, Sanofi, Insmed and Kamada; support for attending meetings or travel from Boehringer Ingelheim, AstraZeneca, Rafa, GSK Israel and Kamada; participation on a Data Safety Monitoring Board or Advisory Board for Bonus Biotherapeutics, Boehringer Ingelheim, and AstraZeneca; leadership or fiduciary role in other board, society, committee, or advocacy group with AJRCCM Associate Editor, Israeli Pulmonology Society, Israeli Society for Tuberculosis and Mycobacterial Diseases; and receipt of equipment, materials, drugs, medical writing, gifts, or other services from Trudell Medical International. KD reports payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Novartis, Boehringer Ingelheim, GSK, NORMA Hellas, Chiesi, ASTRA-ZENECA, Zambon; and support for attending meetings or travel from Novartis, Boehringer Ingelheim, GSK, NORMA Hellas, Chiesi, ASTRA-ZENECA, Menarini; Participation on a Data Safety Monitoring Board or Advisory Board from Novartis, GSK, Chiesi. AB reports Grants or contracts from AstraZeneca outside the submitted work; honoraria and lecture fees from Chiesi, GSK and AstraZeneca ,paid to my institution, outside the submitted work; Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid from Head of Assembly 5 (Airway diseases, asthma, COPD, and chronic cough), European Respiratory Society; co-chair of the Nordic severe asthma network; member of the steering committee of SHARP, ERS severe asthma Clinical Research Collaboration; member of the steering committee of the Swedish National Airway Register. FB reports Grants or contracts from Astrazeneca, GSK and Insmed; consulting fees from Menarini, OM Pharma and Boehringer; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Astrazeneca, Chiesi, GSK, Grifols, Insmed, Menarini, OM Pharma, Pfizer, Sanofi, Vertex, Viatris and Zambon. FR reports grants or contracts from German Center for Lung Research (DZL), Mukoviszidose Institute, Novartis, Insmed Germany, Grifols, Bayer, and InfectoPharm, to the institution; consulting fees from Parion, Boehringer, Insmed and Chiesi; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from IDE Werbeagentur GmbH, Insmed, Grifols, Universitätsklinikum Frankfurt am Main, University Hospital Hamburg, AstraZeneca and Sanofi; participation on a Data Safety Monitoring Board or Advisory Board for Insmed, Boehringer Ingelheim, Parion Sciences and Chiesi; leadership or fiduciary role in other board, society, committee, or advocacy groups as a former coordinator of the ERN-LUNG Bronchiectasis Core Network, co-chair of the German Bronchiectasis Registry PROGNOSIS; and fees for clinical trial participation paid to the institution from AstraZeneca, Boehringer Ingelheim, Insmed, Novartis, Parion, Recode, Ruhr University-Bochum, University of Dundee, Vertex. MV reports Consulting fees from Chiesi; Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events from Insmed and Teva; Support for attending meetings and/or travel from Pari, Chiesi and Zambon; Participation on a Data Safety Monitoring Board or Advisory Board from Insmed. PG reports payment or honoraria for a lecture on bronchiectasis from Insmed; Support for attending meetings and/or travel from Astrazeneca and Chiesi; Participation on a Data Safety Monitoring Board or Advisory Board from Boehringer, AstraZeneca and Merck. ML reports consulting fees from Armata, 30T, Astra Zeneca, Parion,

Insmed, Chiesi, Zambon, Electromed, Recode, Boehringer Ingelheim, Ethris, Mannkind, AN2 Therapeutics; payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from Insmed. JC reports grants or contracts from Grifols; consulting fees from Antabio, AstraZeneca, Boehringer Ingelheim, Chiesi, Glaxosmithkline, Grifols, Insmed, Janssen, Novartis, Pfizer, and Zambon; and leadership or fiduciary roles as Chair of European Respiratory Society (ERS) Bronchiectasis Guideline Task Force, Chief Editor of European Respiratory Journal, and Chair of EMBARC Clinical Research Collaboration. All other authors have no potential conflict of interest.

[130] [0.32.130] U.S. BRONCHIECTASIS AND NTM CARE CENTER NETWORK: Improving the Diagnosis and Treatment of Bronchiectasis and Nontuberculous Mycobacterial Lung Disease

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Background/Aims: Bronchiectasis and nontuberculous mycobacterial lung disease (BE-NTMLD) are chronic diseases that include symptoms of cough, mucus production, dyspnea, fatigue, hemoptysis, weight loss, and recurrent lung infections. Patients experience reduced quality of life and increased anxiety and depression. Over time, BE-NTMLD can lead to impaired lung function and long-term disability and have been associated with increased mortality. Despite the increasing prevalence, diagnoses are commonly delayed.

Effective disease management is multifaceted and requires substantial resources. The economic impact can be significant, especially among those who experience frequent exacerbations.

Considering the burden of the diseases, combined with economic impact and increasing prevalence, the Bronchiectasis and NTM Association established the Bronchiectasis and NTM Care Center Network (CCN), to reduce time to diagnosis, support high-quality care, enrich clinical research activities, improve outcomes, and increase access to underserved/diverse communities.

Methods:

Bronchiectasis and NTM CCN Structure

Designated centers meet core requirements established by the Association. The CCN Steering Committee includes experts in BE-NTMLD patient care and clinical research, and includes patient representation. Centers receive one of two designations, Care Center (CC) or Clinical Associate Center (CAC), depending on institutional resources. Requirements include a comprehensive set of deliverables:

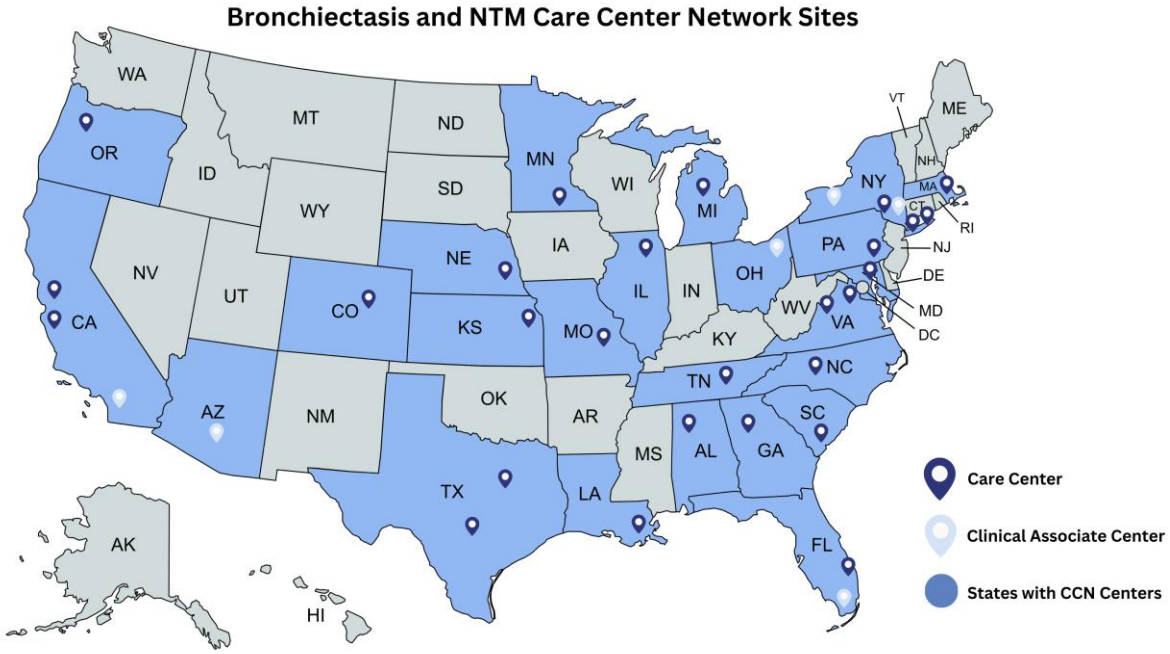
- personnel training, education, and expertise;
- institutional resources for diagnosis and patient care;
- patient education, advocacy, and engagement;
- participation in patient-centered research and clinical trials.

Results:

Timeline and Goals

Currently, the CCN has 33 designated sites. (see Fig 1). The overall goal is 150 centers.

Figure 1: Map of CCN Sites in the U.S 2024



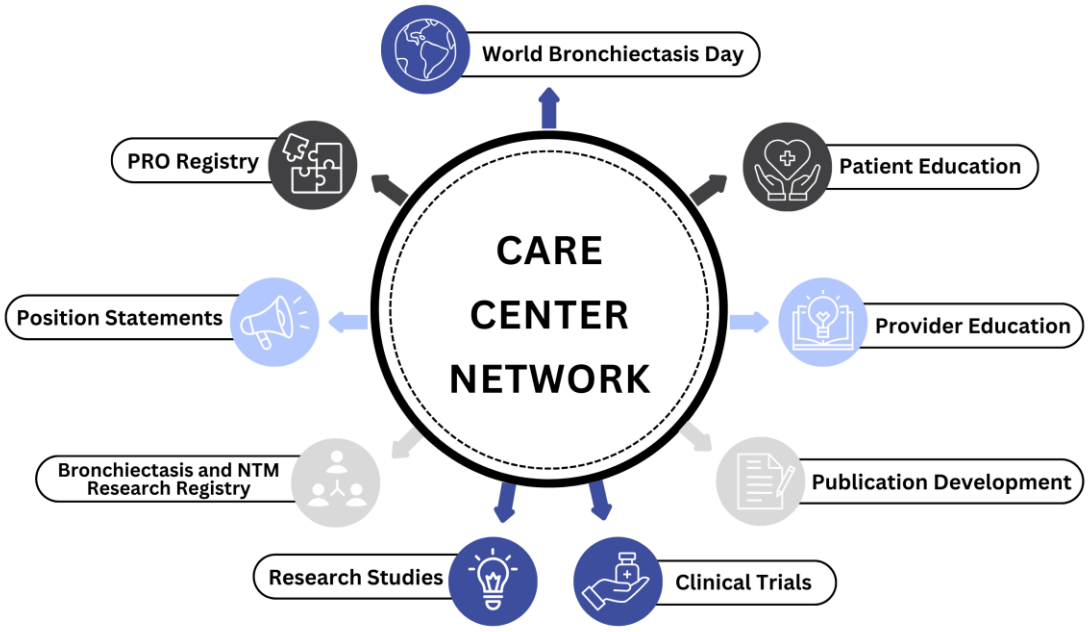
Education and Research

The CCN objectives include identifying educational gaps among providers, patients, and caregivers through surveys and direct feedback. Development of educational resources will be coordinated by collaborating with stakeholders following Association policies and procedures. Collaborations with medical professional organizations will provide an avenue to develop increased resources for the sites.

Working groups have been established to produce position statements targeting key areas for improving care delivery. Clinical and patient-reported data collection with insight from the CCN steering committee will inform and enrich CCN objectives to address unmet clinical needs and promote research.

CC and CAC differ in the size of the program, available resources, and research component. CC have robust research programs, often including participation in the U.S. Bronchiectasis and NTM Research Registry (BRR). CAC without a clinical research program will enhance access to clinical care and either develop a clinical research program or a referral pathway to CC with established clinical trials programs. (see Fig 2)

Figure 2: CCN Objectives



The Association will also create an additional research platform establishing a BE-NTMLD patient-reported registry (PRO). This registry will allow individuals to self-enroll, regardless of whether their provider participates in the BRR or CCN. More robust patient representation through this PRO will accommodate a broader cross-section of geographic, socioeconomic status, and underserved/diverse communities increasing access to patient education and clinical research activities.

Conclusions: Establishing a network of expert care centers aspires to reduce the time to diagnosis, support the delivery of high-quality care, enrich clinical research activities, and improve access and outcomes in people with BE-NTMLD.

Conflict of interest(s) (if any – not included in the 500 words):

Dr. Doreen Addrizzo-Harris: Chair of the Bronchiectasis and NTM Care Center Network Steering Committee, Member of the Bronchiectasis and NTM Association Leadership Council

Dr. Timothy Aksamit: Medical Director of Bronchiectasis and NTM Association, Member of the Bronchiectasis and NTM Care Center Network Steering Committee, Member of the Bronchiectasis and NTM Association Leadership Council

Dr. Charles Daley:: Chief Research Officer of the Bronchiectasis and NTM Association, Member of the Bronchiectasis and NTM Association Leadership Council

No other relevant COI

[136] [0.29.136] Sunshine Coast Hospital and Health Service Bronchiectasis Registry: First local insights into an increasing healthcare burden

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Background/Aims:

Bronchiectasis, a chronic lung disease defined by abnormal bronchial dilatation with symptoms of chronic cough, sputum production and recurrent pulmonary exacerbations, is becoming increasingly recognised both worldwide and in Australia, with the Australian Bronchiectasis Registry (ABR) formed in 2015. In 2022, a specialist bronchiectasis service was developed within the Sunshine Coast Hospital and Health Service (SCHHS) Respiratory Department, a regional, tertiary Hospital in Queensland Australia, with the aim of developing a focused and improved service for this cohort, and of contributing to the national ABR. This study provides the first local report this specific regional adult bronchiectasis cohort within the SCHHS.

Methods:

A retrospective cohort study was performed capturing adults with diagnosed non-cystic fibrosis bronchiectasis managed within the SCHHS Respiratory Department's specialist bronchiectasis service from 1st January 2022-current. We captured and analysed baseline demographic and clinical characteristics, in addition to long-term management strategies in line with the ABR data parameters.

Results:

Baseline data were available for 91 adults (61 female), median age 68 years (interquartile range 14 years). The underlying aetiology frequencies in our cohort were 39 patients (42%) with idiopathic bronchiectasis, 15 (16%) post infectious, 14 (15%) connective-tissue disease related, and 3 (3%) immunodeficiency. 6 patients were cystic fibrosis (CF) heterozygotes (7%). 1 (1%) had primary ciliary dyskinesia. 26 patients (29%) had chronic Pseudomonas aeruginosa infection, 5 (5%) had chronic Haemophilus influenzae, 8 (9%) had grown Staphylococcus aureus, and 27 (30%) had chronic non-tuberculous mycobacteria. A high proportion had moderate or severe disease based on the Bronchiectasis Severity Index (BSI) (41 patients, 45%) and FACED (50 patients, 55%) composite scores. 49 patients (54%) had normal spirometry; 34 (37%) had airflow obstruction (FEV1/FVC < LLN). 21 patients (23%) experienced frequent exacerbations (defined as >2 in the preceding year), and 30 (33%) had elevated eosinophils (defined as > 0.3 x10^9/L). 25 patients (27%) were on long-term macrolides, 4 (4%) on asthma biologics, and 9 (10%) on long-term inhaled antibiotics.

Conclusions:

This is the first reported data on our local and regional Queensland bronchiectasis cohort managed within the SCHHS. This data will add to the current national Australasia Bronchiectasis Registry and aid in fostering further research and service development of this disease locally and nationally.

Conflict of interest(s): Nil

[138] [0.34.138] Medicare and Pharmaceutical Benefit Scheme utilisation in Australians with Bronchiectasis: A report of linked data from the Australian Bronchiectasis Registry.

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Background/Aims: Bronchiectasis is a chronic lung condition associated with substantial healthcare utilisation and economic impact which has received limited research in the Australian context. This study aimed to describe for the first time, patterns of pharmaceutical and out-of-hospital healthcare utilisation and expenditure among children and adults with bronchiectasis using Australian Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) claims, which form the basis of the Australian universal healthcare system.

Methods: Participants included patients enrolled in the Australian Bronchiectasis Registry who consented to linked MBS and PBS healthcare utilisation and costs data. The time-horizon for each participant's data was one year before and after registry enrolment. Monetary values were inflated to 2024 AUD. To describe utilisation and costs across age strata, estimates were calculated separately for: adults, school-aged children, and preschoolers. Associations between clinical and demographic factors and expenditure were explored using multivariable regression analyses.

Results: A total of 627 participants (398 adults, 96 school-aged, 133 preschoolers) had minimum registry data linked to MBS and PBS records. The median (IQR) ages in years were 69 (62-76), 9 (8-13) and 3 (2-5) for adults, school-aged and preschoolers, respectively. Adults had higher annual respiratory related costs (median AU$4,181; IQR $2,363-6,972) than school aged (median AU$1,412; IQR $826-2,404), or preschool (AU$977; $712-1,577)

children. Registration site, aetiology and prior PBS claims for certain medications were features consistently associated with total costs.

Conclusions: In this first exploration of costs across age group strata for people living with bronchiectasis in Australia (inclusive of non-hospital medical services and pharmaceuticals), we identified substantial healthcare utilisation, particularly in adults. The scope of MBS and PBS claims is a limitation of this study, meaning estimates are conservative and complementary in nature to prior reports of hospital resource use among people with bronchiectasis.

Conflict of interest(s) (if any – not included in the 500 words):
The authors declare no competing interests

[174] [0.31.174] Treatment patterns by exacerbation history in adults with bronchiectasis: data from the U.S. Bronchiectasis and NTM Research Registry

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Background/Aims: Bronchiectasis (BE) treatment guidelines focus on symptom control, reducing exacerbation frequency, and prevention of disease progression. There is a lack of evidence on effectiveness of pharmacotherapy for BE. This study aimed to describe treatment patterns based on exacerbation history in adults within the U.S. Bronchiectasis and Nontuberculous Mycobacteria (NTM) Research Registry (BRR).

Methods: Adults with BE alone, excluding those with coexisting chronic obstructive pulmonary disorder or asthma diagnoses, were included. Baseline data from two years prior to consent were analyzed cross-sectionally. Patients were grouped by annualized exacerbation rate at baseline, defined as 0/year, >0-1/year, >1-2/year, and >2/year. We calculated the proportion who had taken treatments at any time during the baseline period grouped by each of four categories: mucociliary clearance (e.g. bronchial hygiene therapy, mucous active therapy), airway inflammation (e.g. bronchodilators, inhaled corticosteroids [ICS], oral corticosteroids [OCS]), antibiotic maintenance therapy (inhaled, oral, or non-NTM regimen macrolides), and antibiotics for exacerbations (oral, inhaled, intravenous) by annualized exacerbation rate. Denominators included those with complete data available within each treatment category. All comparisons were descriptive.

Results: Of 6182 in the BRR, the study population included 3861 patients with BE alone (62%). The median age was 69.0 years, and the majority were female (82%). Overall, 19% had no mucociliary clearance treatment, 27% had no airway inflammation treatment, and 70% had no maintenance antibiotic therapy (Table). Among those with any exacerbation history, 30-33% had no antibiotic treatment for exacerbations. History of mucociliary clearance use increased with exacerbation frequency, from 63% to 79% for bronchial hygiene and 57% to

78% for mucoactive agents. Bronchodilators, ICS, and OCS increased slightly with exacerbation history. In contrast, maintenance antibiotics were similar across comparison groups. Antibiotic treatment for exacerbations was consistent with the exacerbation history.

Conclusions: Treatment patterns were generally consistent with clinical guidelines, with the majority taking mucociliary clearance and/or airway inflammation treatment. However, a large number of patients with exacerbations did not have evidence of treatment with maintenance antibiotic therapy, or had taken ICS despite the absence of asthma. Future studies of prescribing practices are needed to identify factors influencing management of BE.

Table. Pharmacotherapy by annualized exacerbation history during the 2-year baseline period in the U.S. Bronchiectasis and NTM Research Registry, among those with bronchiectasis alone (excluding those with chronic obstructive pulmonary disease or asthma)

		Baseline Exacerbation Frequency			
	Overall	**0**	**>0 - 1 / year**	**>1 - 2 / year**	**>2 /**
Impaired mucociliary clearance					
N	2122	1110	709	172	68
Bronchial hygiene therapy, n (%)	1440 (67.9)	704 (63.4)	516 (72.8)	126 (73.3)	54 (
Oxygen supplementation, n (%)	85 (4.0)	33 (3.0)	37 (5.2)	5 (2.9)	7 (10
Pulmonary rehabilitation/ maintenance rehabilitation, n (%)	115 (5.4)	53 (4.8)	36 (5.1)	10 (5.8)	9 (13
Mucous active agents, n (%)	1299 (61.2)	636 (57.3)	451 (63.6)	119 (69.2)	53 (
None, n (%)	410 (19.3)	261 (22.3)	109 (15.4)	20 (11.6)	4 (5.
Airway inflammation					
N	986	169	584	146	64
Bronchodilators, n (%)	666 (67.5)	117 (69.2)	366 (62.7)	116 (79.5)	49 (
Oral steroids, n (%)	191 (19.4)	28 (16.6)	105 (18.0)	35 (24.0)	18 (
Inhaled steroids, n (%)	252 (25.6)	48 (28.4)	126 (21.6)	45 (30.8)	23 (
Macrolides, n (%)	139 (14.1)	49 (29.0)	59 (10.1)	12 (8.2)	15 (
None, n (%)	262 (26.6)	37 (21.9)	186 (31.8)	25 (17.1)	11 (
Bacterial infection - maintenance therapy					
N	2441	730	1057	285	150
Oral antibiotics, n (%)	585 (24.0)	230 (31.5)	202 (19.1)	56 (19.6)	38 (
Inhaled antibiotics, n (%)	246 (10.1)	60 (8.2)	91 (8.6)	44 (15.4)	28 (
Macrolides, n (%)	476 (19.5)	178 (24.4)	169 (16.0)	47 (16.5)	35 (
None, n (%)	1716 (70.3)	465 (63.7)	806 (76.3)	198 (69.5)	96 (

Exacerbations					
N	2406	719	1051	284	149
Any antibiotics, n (%)	1373 (57.1)	228 (31.7)	737 (70.1)	196 (69.0)	100
Oral antibiotics, n (%)	752 (31.3)	35 (4.9)	512 (48.7)	133 (46.8)	57 (
Inhaled antibiotics, n (%)	52 (2.2)	3 (0.4)	21 (2.0)	12 (4.2)	10 (
Intravenous antibiotics, n (%)	111 (4.6)	5 (0.7)	60 (5.7)	24 (8.5)	19 (
None, n (%)	1033 (42.9)	491 (68.3)	314 (29.9)	88 (31.0)	49 (

Conflict of interest(s) (if any – not included in the 500 words):

The authors would like to acknowledge the Bronchiectasis and NTM Association, who manages the Bronchiectasis and NTM Research Registry, a 501(c)(3) nonprofit organization. The Registry is funded by the Richard H. Scarborough Bronchiectasis Research Fund, the Anna-Maria and Stephen Kellen Foundation, a Research Grant from Insmed Incorporated, and the Bronchiectasis and NTM Industry Advisory Committee. It should also be noted that this work would not have been possible without the comprehensive chart reviews and recording of data by the dedicated research coordinators and PIs at each of the participating Registry sites.

EL, FR, CC, GA, RH are employed by AstraZeneca

GS: grant funding by Vertex, BiomX, AstraZeneca, Insmed, Electromed, Splisense, NIH, COPD Foundation, and CFF.

[196] [0.38.196] The Impact of Proton Pump Inhibitor (PPI) Use on Exacerbation Rates in Patients with Bronchiectasis: An Analysis of the US Bronchiectasis and NTM Research Registry

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Background/Aims: Proton pump inhibitors (PPIs) are commonly prescribed to patients with bronchiectasis, particularly for managing gastroesophageal reflux disease (GERD), which is prevalent in this population. However, PPIs may alter the microbiome and immune response, potentially influencing exacerbation rates in patients with bronchiectasis. We hypothesized PPI use is associated with an increased rate of exacerbations compared to those not on PPI. To address this, we evaluated the characteristics of those on PPI and modeled the relationship with exacerbation rates over time among patients enrolled in the US Bronchiectasis and Non-Tuberculous Mycobacteria Research Registry (BRR).

Methods: Adult non-cystic fibrosis bronchiectasis patients with known data for gastric acid suppression therapy and exacerbation history at baseline were evaluated through a cross-sectional analysis of their baseline characteristics. Patients were defined by PPI therapy use at baseline (yes vs. no). Demographics and clinical characteristics, including co-existing conditions, lung function (ppFEV1), exacerbation history, sputum culture and concomitant therapies were described (aim 1). Differences between groups were evaluated using the Wilcoxon-Mann-Whitney test for continuous variables and chi-square test for categorical variables. To determine the relationship between PPI use and future exacerbations, we identified patients from aim 1 with at least two follow-up years of exacerbation and lung function data over a 5-year period (aim 2). We fit a Poisson regression model for the relationship between baseline PPI therapy and number of exacerbations during follow-up after adjusting for smoking history, GERD diagnosis, baseline H2 blocker therapy, baseline exacerbation history, baseline chronic *Pseudomonas aeruginosa* colonization, and change in FEV1 %predicted between baseline and follow-up.

Results: 3236 patients were included, with 815 (25.2%) on PPI therapy and 2421 (74.8%) not. Amongst those on PPI, they were older (median age 71 vs. 70, p=0.019) and more likely to be current or former smokers (41.8% vs. 36.9%, p=0.013), albeit with similar rates as compared to those not on PPI. Apart from GERD, there were no significant differences across co-existing conditions nor across microbiology culture positivity. Those on PPI had a higher annualized rate of exacerbations (0.7 vs. 0.5, p<0.001), were more likely to be hospitalized in the 2 years prior to enrollment (23.0% vs. 16.2%, p<0.001) and had greater severity of disease as compared to those not on PPI (modified-bronchiectasis severity index score of 7 vs. 6,

p=0.004). Over a two-year follow up period, the rate of exacerbations is expected to increase by a factor of 1.5 (95% CI: 1.14-1.98) among patients using PPI therapy after adjusting for smoking history, GERD diagnosis, H2 blocker therapy, exacerbation history, chronic *P. aeruginosa* and change in FEV1 %predicted (p-value=0.004) as compared to those not on PPI.

Conclusions: In this cohort, PPI therapy was associated with higher hospitalization frequency and overall disease severity compared to those not on PPIs. Moreover, when adjusted for presence of GERD, PPI users had a significantly increased rate of exacerbations. This suggests PPI exposure may independently associate with longitudinal clinical outcomes in bronchiectasis and requires further investigation.

Conflict of interest(s) (if any – not included in the 500 words):

Dr. Thornton reports the following conflicts: grant funding by Insmed, CHEST Foundation, Trudell Medical, Cystic Fibrosis Canada, Cystic Fibrosis Foundation, Weston Foundation and the Canadidan Institutes of Health Research
Dr. Solomon reports the following conflicts: grant funding by Vertex, BiomX, AstraZeneca, Insmed, Electromed, Splisense, NIH, COPD Foundation, and CFF.

[345] [0.35.345] Respiratory vaccination practices and infection experiences of Australian adults living with bronchiectasis

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Background/Aims:
Australian adults living with bronchiectasis are recommended to receive COVID-19, influenza, and pneumococcal vaccines, with RSV vaccination recommended from age 60. The vaccines are free for them, except RSV. The RSV vaccine came onto the Australian market in 2024 and is under consideration for public funding for Australians aged 75+ and Aboriginal and Torres Strait Islander people aged 60–74. Vaccination coverage data for Australians living with lung disease, including bronchiectasis, is limited. As part of Lung Foundation Australia's advocacy work, we conducted a survey on adult vaccination with our lung disease client cohort and the general public. This analysis focuses on respondents with bronchiectasis to better understand their vaccination status.

Methods:
Data were collected in mid-2024 (n=3,352) via an online platform. Respondents consented to Lung Foundation Australia using their responses for our advocacy work. The survey explored vaccination practices, beliefs, motivations, barriers, and preferences, as well as experience with respiratory infection and support for vaccination policies. Data were analysed using descriptive statistics.

Results:

There were 263 respondents living with bronchiectasis, with 43% also living with asthma, 19% with COPD, and 13% with a rare or interstitial lung disease. The majority (81%) of respondents are female, with 70% aged 65+, 19% aged 50–64 and 11% aged 18–49. Most (57%) live in a metropolitan area and six percent identify as Aboriginal and/or Torres Strait Islander.

Respondents reported high rates of annual influenza vaccination (85%) and receipt of a COVID-19 vaccine in the last 12 months (82%). Most had received pneumococcal vaccination (60%), or intend to receive it (21%), with 12% stating that it was not currently recommended for them. The remaining 7% are undecided, unwilling, or unable to afford it. Over a third (35%) reported having had pneumococcal disease with 60% reporting they were not vaccinated against it at the time. Forty-two percent who had the disease required hospitalisation and for 31% the disease has majorly impacted their health. Regarding RSV vaccination, 55.5% intend to receive it, though a third would only do so if it were free. Thirty-one percent are undecided, 7% do not intend to receive it and 6% stated they had received it.

Conclusions:
Respondents are likely more health engaged than the general population living with

bronchiectasis given recruitment largely from a client cohort. Despite this, the findings on pneumococcal and RSV vaccination indicate room for improvement in coverage rates, intention to vaccinate and vaccine accessibility. Lung Foundation Australia is advocating for free RSV vaccination (~300 AUD on private script) for older Australians, particularly those living with lung disease. To improve data on vaccination coverage for Australians living with lung disease, we advocate for greater linkage of the Australian Immunisation Register with other data sources, including disease registries. High respiratory vaccination coverage is vital for Australians living with bronchiectasis to protect against exacerbations, severe illness and death.

Conflict of interest(s) (if any – not included in the 500 words):

Lung Foundation Australia's Adult Vaccination Survey was supported by untied funds from GSK Australia, Moderna Australia, and Sanofi Australia.

SESSION 5: INFECTIONS

[48] [0.46.48] Blood eosinophil counts, airway infections and inhaled antibiotic treatment in bronchiectasis

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Background/Aims: The eosinophilic endotype has been recognized in bronchiectasis, but the interplay between airway infection, blood eosinophil counts (BECs), clinical characteristics and the efficacy of inhaled antibiotics treatment remains unclear. To investigate the association between airway infection and BECs, explore how inhaled antibiotic treatment influences BECs, and determine whether BECs levels affect the therapeutic efficacy of inhaled antibiotic.

Methods: We conducted a cohort study to explore the association between BECs, clinical characteristics and airway infections across different disease states. We did a post-hoc analysis to determine the changes in BECs upon inhaled tobramycin and evaluated the therapeutic outcomes stratified by BECs levels.

Results: We included 312 patients, among whom *P. aeruginosa* infection correlated with higher BECs. BECs decreased at exacerbation onset, but were higher among patients with *P. aeruginosa* infection than those without at stable state and exacerbation onset. A lower relative abundance of genus *Pseudomonas* was associated with lower BECs at stable state and exacerbation. Patients with coexisting elevated BECs and *P. aeruginosa* infection demonstrated markedly greater disease severity. Viral detection did not significantly affect BECs. In a randomized trial involving 367 patients with *P. aeruginosa* infection, BECs significantly increased during inhaled tobramycin treatment compared with baseline. Furthermore, inhaled tobramycin therapy improved symptoms, as measured by the *Quality-of-Life Bronchiectasis Respiratory Symptom Scale*, regardless of baseline BECs levels.

Conclusions: Higher BECs are associated with *P. aeruginosa* infection in bronchiectasis, correlating with more severe disease. Inhaled antibiotics may increase BECs and ameliorate symptoms, irrespective of baseline BECs levels.

Conflict of interest(s) (if any – not included in the 500 words):
No

[60] [0.45.60] Microbiological profile of sputum cultures in patients with severe bronchiectasis: a cross-sectional study

WITHDRAWN

[91] [0.44.91] A paradoxical role of antibodies driving complement-mediated inflammation in Pseudomonas aeruginosa pulmonary infections

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Background/Aims: *Pseudomonas aeruginosa* is a multi-drug resistant, opportunistic pathogen which causes chronic pulmonary infections in the compromised lungs of people with cystic fibrosis (pwCF), non-CF bronchiectasis (NCFB), lung transplant recipients and other lung diseases. In such disorders, impaired pathogen clearance and *P. aeruginosa* (PA) virulence contribute to severe inflammation resulting in irreversible lung damage and disease progression. Our laboratory has found up to 40.7% of patients with PA lung infections to have high titres of O-antigen specific IgG2 and/or IgA which instead of protecting against infection, inhibited complement-mediated serum killing of infecting strains. These 'cloaking antibodies' (cAb) were associated with worse lung function in NCFB and higher mortality in lung transplant recipients. The clinical importance of cAb is further highlighted through their successful removal and replacement in three published case studies via the salvage therapy of plasmapheresis resulting in PA eradication. However, how cAb contribute to disease remains unclear. We aimed to explore whether cAb to PA drive inflammation through the overactivation of the complement and increased release of proinflammatory anaphylatoxins such as C5a. This study was investigated in pwCF, however these findings are likely relevant to other disease settings such as NCFB and lung transplant recipients where cAb are prevalent.

Methods: Health data, serum, sputum and infecting PA were collected from an Australian (AUS) cohort of 43 pwCF (128 PA strains) and 25 pwCF (25 PA strains) from a United States of America (USA) cohort. Serum and sputum were screened for the anaphylatoxin C5a or lipopolysaccharide (LPS)-specific antibodies via ELISA, and the ability of antibodies to kill infecting isolates via complement determined by serum bactericidal assays. Multiple aspects of complement activation were explored by examining deposition of C1q, C3c and terminal C5b-8/C5b-9 in the presence of antibodies from patient serum by flow cytometry.

Results: We found 30.3% of patients from the AUS cohort had high titres of LPS-specific IgG2 and/or IgA cAb in their serum or sputum that could inhibit complement killing of their cognate bacterial isolate. Interestingly, we found increased LPS-specific IgA and not IgG2 cAb correlated to worse lung function in the serum of both AUS and USA cohorts. However, both LPS-specific IgA and IgG2 levels in the serum correlated to increased complement deposition

of C1q, C3 and C5-8/C5-9 proteins on PA. C5a was detected in patient sputum and negatively correlated to body mass index.

Conclusions: These findings suggest antibodies specific to PA LPS have the potential to drive increased complement activation with limited killing capabilities allowing for the accumulation of inflammatory anaphylatoxins. We highlight the potential of IgA that is prevalent at the site of infection to induce this frustrated complement response warranting further purification studies. This research will open avenues for novel therapeutics for PA infection across multiple disease settings such as plasmapheresis previously utilised by our laboratory, and complement inhibitors to decrease inflammation and restore immune killing of infecting microbes regardless of their multi-drug resistance.

Conflict of interest(s): None

[99] [0.42.99] Sputum antibacterial sensitivity and resistance patterns among adult Aboriginal Australians with Bronchiectasis in the Top End Northern Territory Australia

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Background/Aims:

Previous research has demonstrated that the bronchiectasis disease burden is substantial amongst adult Aboriginal Australians in the Top End, Northern Territory of Australia giving rise to high exacerbation rates and hospital admissions. However, data pertaining to sputum microbiology and antibacterial sensitivity or resistance patterns in this population are sparce. Therefore, this study explored sputum microbiology data against antimicrobial sensitivity and resistant patterns amongst adult Aboriginal patients diagnosed with bronchiectasis.

Methods: Adult Aboriginal patients with a confirmed diagnosis of bronchiectasis via chest CT scan between 2011 and 2020 were included, if results of sputum antibacterial sensitivity and resistance patterns were available during a hospital admission due to exacerbation of airway disease.

Results: 459 patients were identified to have bronchiectasis between 2011 to 2020, of whom 174 (37.9%) patients had antibacterial sensitivity / resistance recorded during an acute hospital admission. These patients recorded 480 admissions with sensitivity / resistance testing for which the sputum cultures revealed: 410 (85.4%) recorded *Haemophilus spp.*, 339 (70.6%) *Pseudomonas spp.*, 309 (64.4%) *Streptococcus spp.*, 248 (51.7%) *Moraxella spp.*, 86 (17.9%) *Staphylococcus spp.*, 44 (9.2%) *Klebsiella spp.* and 34 (7.1%) *Burkholderia spp.*. Four admissions (0.8%) did not record any antibacterial sensitivity, 148 (30.8%) recorded sensitivity to a single antibacterial agent and the remaining 328 (68.3%) recorded sensitivity to multiple antibacterial agents. Regarding antibacterial resistance; 51 (10.6%) recorded mono-antibacterial resistance and 63 (13.1%) recorded multi-antibacterial resistance. *Klebsiella spp*. recorded the highest frequency of antibacterial resistance at 36.4%, within which resistances were identified for: Ampicillin 91.7%; Penicillin 59%; Clindamycin and Erythromycin 30%; Amoxycillin/Clavulanic acid 27%; and Flucloxacillin and Cephalothin each 25%. Among those hospital admissions which cultured *Haemophilus spp.* and *Pseudomonas spp*., antibacterial resistance was identified in 22.4 & 20.4%, with the most common resistances identified against Ceftazidime (8.6%) for *Haemophilus spp.* and Ampicillin (5.3%) for *Pseudomonas spp.*. For *Streptococcus spp.* (21% antibacterial resistance) the most common resistance was against

Erythromycin (19.6%) and Trimethoprim (18.6%). For *Staphylococcus spp.* (22.1% antibacterial resistance) it was Penicillin (59%) and for *Moraxella spp.* (20.2% antibacterial resistance) it was equally Ampicillin, Erythromycin, Penicillin and Trimethoprim at 4.7% each.

Conclusions: The results of the study may be of use in choosing appropriate antibacterial therapy during bronchiectasis exacerbations among adult Aboriginal patients in this region. Future prospective studies may be warranted to understand the long-term prognostic implications among patients demonstrating multiple antibacterial resistance.

Grant Support: Nil to declare.

Conflict of interest(s) (if any – not included in the 500 words): Nil

[100] [0.41.100] Respiratory viral pathogens during exacerbation of airway disease among adult Aboriginal Australians with bronchiectasis in the Top End Northern Territory Australia

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Background/Aims:

Previous research has demonstrated that the bronchiectasis disease burden is substantial amongst adult Aboriginal Australians in the Top End, Northern Territory of Australia giving rise to recurrent exacerbations and frequent hospital admissions. However, literature detailing the respiratory viral pathogens during bronchiectasis exacerbations is sparsely reported in adult Aboriginal patients. Therefore, this study explored sputum viral pathogens data [polymerase chain reaction (PCR)] amongst adult Aboriginal patients diagnosed with bronchiectasis during a hospital admission secondary to exacerbation of airway disease.

Methods:

Adult Aboriginal patients with a confirmed diagnosis of bronchiectasis via chest CT scan between 2011 and 2020 were included, if results of sputum viral PCR, recorded during an acute hospitalisation were available.

Results:

Of the 459 patients identified to have bronchiectasis between 2011 to 2020, 245 (53.4%) had at least one viral PCR recorded. Viral sputum PCRs were recorded in 828 (29.7%) of 2,790 acute hospitalisations and were negative in the vast majority (n=748, (90.3%)). Of the remaining 80 positive viral PCRs, 61 (76.3%) recorded Influenza A, 11 (13.8%) recorded Influenza B, four (5%) recorded Respiratory syncytial virus (RSV), three (3.8%) recorded Human Rhinovirus/enterovirus and a single viral PCR (1.3%) recorded Influenza A, Influenza B and RSV together. Hospitalisations which recorded a viral PCR were longer than those which did not, regardless of whether the viral PCR was positive or negative (beta 1 (95% CI 0.71, 1.29)). However, there was no significant association with length of stay and a positive finding of Influenza A (p=0.313), Influenza B (p=0.130), RSV (p=0.744) or Human Rhinovirus (p=0.169). There were also no significant differences in lung function parameters (forced expiratory volume in 1 second (FEV1) or Forced vital capacity (FVC)), nor in frequency of chronic obstructive pulmonary disease (COPD), asthma, hypertension or diabetes between a positive or negative PCR, or any of Influenza A, Influenza B, RSV or Human Rhinovirus/enterovirus.

Conclusions:

This study demonstrates that nearly 10% of adult Aboriginal patients with bronchiectasis test positive for viral PCR during acute hospital admissions related to exacerbations of airway disease. However, the isolation of viral pathogens does not appear to significantly impact hospitalisation outcomes or correlate with associated medical comorbidities. It is important to note that only a minority of hospitalisations in this cohort were tested for viral PCR. Given these findings, future prospective studies are needed to better understand the risk factors driving exacerbations of bronchiectasis in this patient population.

Conflict of interest(s) (if any – not included in the 500 words): Nil

[171] [0.40.171] The Impact of Nebulised Fucose/Galactose on Pseudomonas aeruginosa Airway Infection

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Introduction and Aim

Pseudomonas aeruginosa (PsA) infections are a major cause of morbidity in people with bronchiectasis, accelerating lung function decline and increasing mortality. PsA lectins bind to carbohydrate residues, fucose and galactose, on the airway epithelial glycocalyx. This enables bacterial attachment, which in turn leads to respiratory cilia inactivation, impairing mucociliary clearance and promoting persistent infection and biofilm formation. PsA biofilms form through bacterial secretion of an extracellular matrix composed mainly of alginate, which provides a scaffold enabling bacterial macro-colony formation under a protective mucoid sheath. This transforms PsA into a chronic state that is challenging to eradicate with antibiotics. Therefore, blocking the initial stages of PsA attachment, as well as preventing biofilm formation is critical. Previous *in vitro* studies using conventional submerged cultures suggested that adding fucose and galactose (FG) may compete with PsA lectins for binding sites, thereby inhibiting bacterial attachment. Our aim was to evaluate the impact of nebulized FG on PsA adhesion to the airway glycocalyx and cilia, using air-liquid interface (ALI) cultures to better mimic *in vivo* conditions, and to assess the subsequent effects on cilia function, epithelial integrity, and biofilm formation.

Methods

Nasal airway epithelial cells from 10 healthy volunteers were cultured using ALI conditions. Half of the cultured cells were treated with nebulized FG, while the other half served as untreated controls. All cells were then challenged with PsA. Outcomes were assessed over 24 hours, comparing treated and untreated cells, including cilia beat frequency (CBF) measurements, colony forming unit (CFU) counts representing attached bacteria, cytokine levels, and Scanning Electron Microscopy (SEM) images to demonstrate epithelial integrity and biofilm formation.

Results

Cells treated with nebulized FG showed significantly better preservation of epithelial architecture, improved ciliary function, reduced bacterial adhesion, and lower inflammatory responses compared to untreated controls. At baseline, CBF was similar between treated and untreated cells (8.6Hz and 8.3Hz, respectively), but remained higher in FG-treated cells at 16 hours (6.9±0.9Hz vs 5.8±0.8Hz, $p<0.001$) and 24 hours (6.0±1.1Hz vs 4.4±1.3Hz, $p=0.002$), corresponding to a 30% and 47% decline from baseline, respectively. PsA attachment was reduced by 50% in FG-treated cells, with mean±SD CFU counts of 2585±2204 versus 5176±3744 ($p=0.005$). IL-8 levels at 24 hours were significantly lower in the FG group (659pg/ml vs 2223pg/ml), consistent with reduced inflammation. SEM images

of FG-treated samples showed well-preserved epithelial architecture and cilia, with scattered bacteria and minimal alginate production, whereas untreated cells displayed bacterial aggregates, alginate mesh formation, disrupted cilia, and epithelial damage.

Conclusion

Our results suggest that nebulized fucose and galactose treatment of respiratory epithelial cells prior to *Pseudomonas aeruginosa* exposure reduces bacterial adhesion, preserves ciliary function, maintains airway epithelial integrity, and decreases alginate deposition required for biofilm formation. These findings offer a novel non-antibiotic approach for managing PsA infections in bronchiectasis.

Declaration of Interest Statement: All authors declare no conflicts of interest.

[200] [0.47.200] Population diversity and antimicrobial resistance profiling of Pseudomonas aeruginosa isolated from Australians with bronchiectasis

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Background: *Pseudomonas aeruginosa* is a serious concern for global public health, primarily due to its virulence, multidrug resistance (MDR), and association with poor clinical outcomes. *P. aeruginosa* infections in people with bronchiectasis (BE) result in poorer lung function, advanced lung lobe involvement, worse quality of life, and a higher likelihood of exacerbation requiring hospitalisation. Compared to international cohorts, little is known about population diversity, antimicrobial resistance (AMR), persistence, and transmission dynamics of *P. aeruginosa* infections in Australians with BE.

Methods: Eighty-four *P. aeruginosa* isolates were obtained from 35 Australians with BE. All isolates were subjected to antimicrobial susceptibility testing (AST) against 11 antipseudomonal drugs using disc diffusion, and broth micro-dilution for colistin, to determine minimum inhibitory concentrations. Isolates are in the process of being whole-genome sequenced (WGS) and characterised using comparative genomics, along with *in silico* identification of AMR-conferring variants using our *P. aeruginosa* ARDaP-compatible AMR database.

Results: We identified high AMR rates in Australian BE-derived *P. aeruginosa*, with 55% (46/84) resistant to at least one antibiotic, 17% (14/84) classified as MDR (i.e. AMR towards three or more antibiotic classes), and 3% (3/84) extremely drug resistant. Ciprofloxacin resistance was most common (33% of strains), followed by ceftazidime (25%), aztreonam (25%), cefepime (17.9%), meropenem (16.7%), piperacillin/tazobactam (14.3%), imipenem (13.1%), ceftolozane/tazobactam (12.2%), and amikacin (6%) resistance. Unlike in cystic fibrosis, where we saw decreased susceptibility towards tobramycin in 79% of *P. aeruginosa* isolates, we observed no AMR towards tobramycin in our BE cohort. Similarly, no AMR was so observed towards the last-line antibiotic, colistin, despite several participants in our cohort receiving long term nebulised colistin.

Preliminary WGS of longitudinal BE sputa has identified persistent *P. aeruginosa* infection in ~60% of participants, and multi-lineage infections in a third of these participants. Potential transmission events were identified between patients on two occasions. Using multi-locus sequence typing, 16 sequence types (ST) were identified, three novel, indicating likely under-sampling of *P. aeruginosa* from Australian BE cohorts. The highest AMR levels were seen for ST1097 and ST915, both rarely reported, followed by the more common ST274. *In silico* AMR

phenotype prediction from WGS data demonstrated excellent correlation, demonstrating that most BE-derived isolates develop AMR in known ways. Currently, no high-risk mobile genetic elements, such as the *bla*$_{VIM}$ carbapenemase, have been identified in our Australian BE isolates.

Conclusions: Our findings shed much-needed light on the diversity, transmission dynamics, prevalence, and genetic basis of AMR in *P. aeruginosa* from Australians with BE. Our work found no evidence of AMR towards tobramycin or colistin, supporting the use of these antibiotics in treatment-refractory cases. *In silico* analysis showed that AMR determinants can be readily identified in Australian BE isolate genomes, with excellent correlation with AMR phenotypes. This discovery opens up new personalised treatment avenues (qPCR, genomics, metagenomics) for rapid molecular-based AMR diagnosis. Finally, our findings highlight the importance of infection control to prevent patient-to-patient spread of AMR and MDR clones, and the need for accurate AST or genomic of *P. aeruginosa* to effectively eradicate infections, prevent persistence, and reduce patient morbidity and mortality.

Conflict of interest(s) (if any – not included in the 500 words):

None

Grant Support: Wishlist Foundation SERTF Grant – $290,000.

[205] [0.43.205] Non-Cystic Fibrosis Bronchiectasis: Clinical Experience from Gold Coast University Hospital

WITHDRAWN

[210] [0.49.210] Pushing the boundaries of virtual wards? Medication regimes traditionally considered high risk for home administration delivered safely via a virtual ward, and the potentially under-considered trauma of long inpatient stays

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Background/Aims:

Virtual Wards (VW) provide an alternative to hospital admission for many patients with good evidence to show a reduction in Length of Stay (LOS) with similar or improved clinical outcomes (Leong MQ et al. 2021). We aim to provide evidence that respiratory patients requiring prolonged intravenous therapy for complex infection can be safely managed on a VW with significantly improved patient experience.

Methods:

Here we present a case series of 4 patients requiring complex intravenous therapy; 2 managed as a hospital inpatient (IP) and 2 managed via a Respiratory VW. These patients were selected due to similar pathologies and similar medical management, delivered in different healthcare settings. Case notes were reviewed to assess clinical course and potential complications arising from management in either setting. Patient's undertook structured interviews about their care and challenges and benefits experienced during their treatment.

Results:

Patients A and B were treated for poly-resistant non-tuberculous mycobacterial pulmonary infections; A under the VW and B as an inpatient. Patient A received IV amikacin for 130 days on the VW; patient B had a 57 day IP LOS receiving IV amikacin, then switched to tigecycline and ceftazamide with avibactam due to development of ototoxicity. Patient A did have a slight creatinine rise over the course of their treatment, regularly monitored on the VW with subsequent return to normal range.

Patients C and D were treated for cavitating fungal pneumonia on a background of severe emphysematous lung disease; C as an inpatient and D as both inpatient and then under the VW. Patient C had a 42 day IP LOS and was managed with IV caspofungin, and Patient D a 56 day LOS (over 3 admissions) also managed with caspofungin alongside IV antimicrobials.

Patient interviews regarding their experience in both healthcare settings highlighted recurrent themes of "isolation" and "psychological trauma" associated with prolonged hospital admission despite clinical improvement. Conversely, patients on the VW spoke of "fewer limitations on independence" and "stability" despite prolonged treatment courses.

Conclusions:

Selecting patients to manage on VWs comes with inherent risk and benefit considerations. Amikacin in particular has significant toxicities requiring close monitoring, historically requiring inpatient admission to manage due to complexity. As demonstrated here, VW patients were able to receive appropriate monitoring for toxicity despite their outpatient setting with no adverse events.

Whilst the covid-19 pandemic has starkly emphasised the risks associated with nosocomial infections, these patients highlighted risks of significant psychological trauma from admission that may traditionally have been underestimated by healthcare professionals.

Notwithstanding, the 130 day duration of Patient A's IV treatment would have approximated £76,250 in hospital bed days alone.

Overall, VW's continue to demonstrate that many treatments previously only delivered as IP can be safely continued at home, and the risks of managing complex respiratory infections - and even potentially toxic medication regimes, should be balanced not just against cost of IP care and risk of noscomial infection, but also harder to measure outcomes such as patient experience and psychological impact of prolonged hospital stays.

Conflict of interest(s) (if any – not included in the 500 words):

None

[218] [0.50.218] Pulmonary nocardiosis with a nodular-bronchiectatic pattern: A potential cause and aggravator of bronchiectasis

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Background/Aims:
Pulmonary nocardiosis is a rare and underrecognized infection, sometimes mimicking nontuberculous mycobacterial pulmonary disease (NTM-PD). We aimed to characterize chest CT patterns and treatment outcomes in pulmonary nocardiosis, with a particular focus on the nodular-bronchiectatic (NB) pattern, a radiological pattern resembling bronchiectasis and potentially relevant to its diagnosis and management.

Methods:
We retrospectively reviewed 12 patients diagnosed with pulmonary nocardiosis over a 10-year period across three Japanese hospitals. Clinical data, immune status, radiological findings, microbiological results, and treatment outcomes were analyzed. CT findings were categorized into three radiological patterns: cavitary (C), consolidation/infiltrative (CI), and nodular-bronchiectatic (NB). Statistical analysis was performed using Fisher's exact test.

Results:
The NB pattern was the most frequently observed radiological feature (58%) and was exclusively found in immunocompetent patients. In contrast, C and CI patterns were predominantly observed in immunocompromised individuals. Treatment outcomes were significantly more favorable in patients with the NB pattern ($p = 0.0476$). Notably, in some cases, bronchiectasis appeared to newly develop or worsen in association with Nocardia infection and improved following treatment.

Conclusions:
Pulmonary nocardiosis with a nodular-bronchiectatic pattern, especially in immunocompetent patients, closely resembles NTM-PD and is associated with favorable outcomes. Importantly, *Nocardia* infection is not limited to patients with preexisting bronchiectasis; it may also contribute to its onset or progression. This potential dual role underscores the need to consider *Nocardia* infection in the differential diagnosis of bronchiectasis with nodular features on CT, particularly in immunocompetent individuals.

Conflict of interest(s):
The authors declare no conflict of interest.

[324] [0.39.324] Isolation of Multidrug Resistant Bacteria from hospitalized Bronchiectasis patients in Developing Countries

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Background/Aims:

Antimicrobial Resistance has become a major threat to health system globally**.** Bronchiectasis (Chronic) has become a major respiratory disease in developing countries. The chronic infection of dilated mucus filled airways promote bacterial production followed by bronchial inflammation and permanent lung injury. Accurate pathogen identification and antimicrobial susceptibility is critical for appropriate treatment. In Low Middle Income setups bronchiectasis is often treated with broad spectrum antibiotics and patients are thus at risk of acquiring multidrug resistant (MDR) bacteria. The aim was to identify risk factors associated with isolation of MDR pathogens in bronchiectasis.

Methods: Retrospective observational study of bronchiectasis exacerbations in hospitalized patients. Data was compared between two groups according to isolation of MDR bacteria.

Results: The sample from 60 hospitalized patients with a mean age of 72.6. MDR bacteria were isolated in 34,6% of the patients being MDR *Pseudomonas aeruginosa (PA)* the most prevalent (n=22). The most common empiric antibiotherapy was Levofloxacin. Patients with MDR pathogen isolation were older, had longer hospitalization history and were more resistance to empiric treatment, p<0,05. *PA* cultures were found associated with increased risk of MDR infection, p<0,05. Hospitalization or a higher number of exacerbations in last year history, systemic corticosteroid treatment or antibiotherapy in the previous 3 months were associated with MDR pathogen isolation, p<0,05. No correlation was found between comorbidities evaluated, lower FEV1 values, ICS therapy, inhaled antibiotics, oxigenotherapy or NIV and isolation of MDR pathogens. Death had comparable frequency in both groups.

Conclusion: Various factors, such as long hospitalization, *PA* colonization, recent antibiotherapy and systemic corticosteroids, may contribute for MDR bacterial infection in hospitalized patients in LMICs with acute exacerbations of bronchiectasis. Awareness is required to consider empiric broad spectrum antibiotics in certain high risk patients.

Conflict of interest(s) (if any – not included in the 500 words):

NA

[354] [0.48.354] Systematic review of clinical practice guidelines to identify vaccination recommendations for adults living with chronic lung disease

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Background/Aims:

Adults with chronic lung diseases, including bronchiectasis, are at elevated risk from vaccine-preventable diseases. Individuals with bronchiectasis face particular vulnerability, as underlying immunodeficiency can be a cause of bronchiectasis and result in atypical vaccine responses, necessitating tailored immunisation strategies. Despite this, the extent to which international clinical practice guidelines address immunisation recommendations remains unclear. This systematic review aimed to synthesise vaccination recommendations within national and international clinical practice guidelines for chronic lung diseases, including bronchiectasis and alpha-1 antitrypsin deficiency.

Methods:

As part of a pre-registered systematic review protocol (CRD42022383991) we searched guideline repositories of major respiratory societies: American Thoracic Society (ATS), British Thoracic Society (BTS), American College of Chest Physicians (CHEST), European Respiratory Society (ERS), Thoracic Society of Australia and New Zealand (TSANZ). Guidelines were eligible if: a systematic literature search and review were performed; systematically developed statements were presented to guide health care decisions; endorsed by national or international respiratory societies; and published from 2017 onwards. Two reviewers independently screened titles and abstracts of all identified guidelines. Full-texts of any records not excluded by title or abstract were screened for eligibility by two reviewers independently. Data extraction focused on location, publication year, guideline development process and vaccination content, including vaccine types, specific recommendations, and documented evidence gaps. The AGREE-II instrument was used to assess the methodological quality.

Results:

From 415 documents initially identified, 391 were excluded on title or abstract. Of 24 full-texts screened, 13 were excluded (specific treatments only n=5, no systematically developed

statements n=8). Eleven clinical practice guidelines met the inclusion criteria, representing the United Kingdom (n=2), Europe (n=4), the United States (n=4), and Australia/New Zealand (n=1). Disease coverage included asthma (n=2), bronchiectasis (n=2), COPD (n=2), and interstitial lung diseases (n=5). AGREE II assessments revealed variable methodological quality across the guidelines: median scaled domain scores, scope and purpose: 100%; stakeholder involvement: 86%; rigour of development: 83%; clarity of development: 94%; applicability: 60%; editorial independence: 96%.

Four guidelines (36%) mentioned vaccination-related content (Table 1), although only two provided substantive recommendations. The BTS 'guideline for bronchiectasis in adults' (2019) provided grade D recommendations for annual influenza and pneumococcal vaccination in adults with bronchiectasis, with additional consideration for vaccinating household contacts and selecting vaccines based on potential immunodeficiency and serology. TSANZ 'COPD-X plan' (2024) provided detailed protocols with Level I evidence.

Conclusions:

This systematic review reveals that vaccination guidance is severely limited within international clinical practice guidelines for chronic lung disease management. For bronchiectasis, only one of the two identified guidelines provided specific vaccination recommendations, acknowledging that there is limited direct evidence from randomised controlled trials of vaccinations in bronchiectasis. Our findings highlight the need for respiratory societies to incorporate systematic evidence-based vaccination recommendations into clinical practice guidelines and for larger-scale vaccine trials in high-risk populations such as those with chronic lung diseases.

Conflict of interest(s):

J.T. has no conflicts to declare

Y.H.K. is the board director and previous Chair for Clinical Care and Resources Sub-Committee of Thoracic Society of Australia and New Zealand, a guideline methodologist and Clinical Problems Assembly Program Committee of the American Thoracic Society, and associate editor for the *European Respiratory Journal of the European Respiratory Society*. Y.H.K. reports fellowship support from NHMRC Investigator Grant, during the conduct of the study, grants from MRFF, Austin Medical Research Foundation, Lung Foundation Australia/ Thoracic Society of Australia and New Zealand, RACP, and in-kind trial support from Air Liquide Healthcare.

A.W.J. is a member of the Clinical Care and Resources Sub-Committee of the Thoracic Society of Australia and New Zealand and the European Respiratory Society Guideline Methodology Network. AWJ reports grants from the MRFF, Lung Foundation Australia, and the Thoracic Society of Australia and New Zealand during the conduct of the study.

SESSION 6: NTM1

[49] [0.60.49] Supportive Care Gaps in Bronchiectasis Patients with NTM-PD: A Retrospective Study

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Background/Aims:

Non-tuberculous mycobacterial pulmonary disease (NTM-PD) is a growing concern, contributing to progressive lung function decline and reduced quality of life. Bronchiectasis, a major risk factor for NTM-PD, requires multidisciplinary management including supportive care measures such as airway clearance therapy and vaccinations. However, the impact of NTM-PD status on the delivery of these essential care components remains poorly understood. This study evaluates gaps in supportive care among bronchiectasis patients with NTM-PD compared to those without, assessing its impact on healthcare utilization and preventative care.

Methods:

A retrospective review of deidentified electronic medical records was conducted for bronchiectasis patients diagnosed between 2018 and 2023 at Singapore General Hospital. Patients were categorized into two groups: bronchiectasis patients with NTM-PD (defined as having at least two positive sputum cultures for NTM within one year) and the bronchiectasis control group (patients without NTM positivity). Demographics, comorbidities, healthcare utilization, and referrals for supportive care, including physiotherapy, were compared, along with influenza and pneumococcal vaccination uptake.

Results:

Among 164 bronchiectasis patients with NTM-PD, the most commonly detected species were M. abscessus (42.1%), M. fortuitum (11.6%), Mycobacterium avium complex (MAC) (9.5%), and M. kansasii (6.1%), with the remaining 29.9% classified as other species. The median age was 68 years (IQR: 19), 51% were female, and the average BMI was 21.4 (SD: 5.85). Healthcare utilization differed between groups: bronchiectasis patients with NTM-PD had more frequent clinic visits than those without (1.97 vs. 1.61 visits per year, $p = 0.49$), and hospital length of stays were significantly longer (13.9 vs. 7.6 days per year, $p = 0.0098$). Despite increased medical interactions, supportive care remained underutilized in bronchiectasis patients with NTM-PD. Fewer were referred for chest physiotherapy for airway clearance compared to those without NTM-PD (12% vs. 27%, $p = 0.0006$), suggesting that supportive care was deprioritized

in this population. Vaccination rates were low in both groups, with no significant differences. In 2023, influenza vaccination uptake was 25.8% in bronchiectasis patients with NTM-PD compared to 29.4% in those without NTM-PD (p = 0.79). Pneumococcal vaccination uptake between 2018 and 2023 was similarly low, with 20.7% of bronchiectasis patients with NTM-PD receiving either Prevenar 13 or Pneumovax® 23, compared to 15.9% of those without NTM-PD (p = 0.40).

Conclusions:

While bronchiectasis patients with NTM-PD have more frequent medical encounters, their access to supportive care remains inadequate. The clinical focus on diagnosing NTM and determining antimicrobial treatment needs may inadvertently overshadow supportive care, particularly physiotherapy and vaccinations. This represents a missed opportunity to provide comprehensive, patient-centered management that addresses both the infection and overall lung health. Implementing structured multidisciplinary care pathways at the time of NTM diagnosis could help bridge these gaps, ensuring that antimicrobial decisions are complemented by essential supportive therapies. Further research is needed to assess the long-term impact of NTM-PD on patient outcomes and to develop integrated care strategies that optimize both antimicrobial treatment and supportive care.

Conflict of interest(s) (if any – not included in the 500 words):

The authors have no conflict of interest to declare.

[64] [0.52.64] The rising incidence of nontuberculous mycobacterial infections in First Nations People in Queensland, Australia 2001–2024.

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Background/Aims: Nontuberculous mycobacteria (NTM) are ubiquitous environmental organisms and are a neglected and emerging public health threat. The incidence of NTM infections is rising worldwide, however there is little data on the epidemiology of NTM in First Nations People. Geospatial and human host factors are known to affect disease risk. This study aims to assess the incidence and geospatial epidemiology in First Nations People in Queensland.

Methods: NTM infection data was obtained from the Queensland Health Notifiable Conditions Database from 2001 to 2024 and subset based on Indigenous status. Incidence was defined as one notification per species per year. Estimated resident population data per Statistical Area 2 was obtained from the Australian Bureau of Statistics and stratified to Queensland Hospital and Health services (HHS). HHS boundaries were obtained from the Queensland Spatial Catalogue. Poisson regression models were used to assess incidence rate ratios (IRR) for HHSs per year.

Results: In Queensland from 2001-2024, there were 820 NTM notifications in First Nations People. The median age was 53 years (IQR 36-64 years), with 54.63% of notifications reported in males. There were more males than females in all age ranges, with significantly more males than females in the 30-44 age range (Chi-square test = 13.85, $P = 0.00019$). NTM incidence increased significantly from 0.084 per 100,000 in 2001 to 1.361 per 100,000 in 2024 (IRR 16.203, CI 5.339-80.315, $P < 0.0001$). The greatest increases in incidence rates were observed in the Cairns and Hinterland (IRR 0.47, CI 0.33-0.64, $P < 0.001$), Torres and Cape (IRR 0.45, CI 0.32-0.61, $P < 0.001$) and Townsville (IRR 0.33, CI 0.24-0.46, $P < 0.001$) HHSs. We identified 31 different species or groupings, with *Mycobacterium intracellulare* (n=212/820; 25.85%), *M. abscessus* (n=91/820; 11.10%), *M. fortuitum* (n=56/820; 6.83%), and *M. avium* (n=35/820; 4.27%) as the top 4 species, comprising 48.05% of all notifications. Additionally, we were able to classify 95% of the NTM notifications as either pulmonary (605/820, 73.78%) or extrapulmonary (175/820, 21.34%) infections. The incidence rate for both infection types significantly increased, with the IRR of extrapulmonary infections almost double that of pulmonary infections (pulmonary IRR 7.2, CI 2.9-23.04, $P < 0.0001$; extrapulmonary IRR 13.085, CI 2.09-542.33, $P = 0.0004$).

Conclusions: The incidence of NTM infections in First Nations People has significantly increased in Queensland between 2001 and 2024. The midlife male dominance differs from previous NTM epidemiology research in Queensland showing a median age of 66-years in the adult population, with a female predominance in pulmonary infections. While the proportions of pulmonary to extrapulmonary infections matched previous research, there is a paucity of information on the increasing incidence of extrapulmonary NTM infections. Notably, the greatest increase in incidence rates was in Far North Queensland and tropical coastal regions, like previous research on the geospatial NTM epidemiology of the overall Queensland population. Characterising the variables influencing this increase in NTM incidence and the preponderance of extrapulmonary infections in First Nations People in Queensland warrants urgent attention.

Conflict of interest(s) (if any – not included in the 500 words): None

[69] [0.57.69] Epidemiology and clinical significance of NTM isolates at a tertiary centre in Victoria, Australia.

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Background/Aims:

The incidence of nontuberculous mycobacteria (NTM) related diseases is increasing globally. As NTM are not notifiable in Victoria, there has been little data available since a published national survey more than 25 years ago. We investigated NTM isolates at a Victorian hospital to consider epidemiology and clinical significance.

Methods:

A single-centre retrospective analysis was conducted on all positive NTM cultures from adult patients managed at the Royal Melbourne Hospital (RMH), available from the RMH microbiology laboratory from 31st November 2017 to 1st December 2023. Speciation was undertaken by molecular testing with 16S-ITS region sequencing. Data were extracted from electronic medical records. Clinical significance was determined on the basis of contemporaneous clinician recommendation to initiate treatment. NTM pulmonary and extrapulmonary disease was defined as those who met the diagnostic criteria described in the 2007 American Thoracic Society / Infectious Diseases Society of America (ATS/IDSA) guidelines.

Results:

206 positive isolates were included from 174 patients. No cystic fibrosis patients were included, as these patients were not treated in our centre during the study period. 95 (45.1%) were isolated from sputum samples, 83 (40.3%) from bronchoscopy aspirates, 17 (8.3%) from tissue 4 (1.9%) from blood cultures and 9 (4.4%) from multiple or other sites.

61 (29.6%) positive isolates from 44 patients were considered clinically significant, 39 (18.9%) isolates were from 27 patients with NTM pulmonary disease and 22 (10.7%) isolates were from 17 patients with disseminated or extrapulmonary disease. 56 (27.2%) of isolates were from 40 patients who met ATS/IDSA criteria for NTM pulmonary or extrapulmonary disease.

The most common species isolated was *M. avium complex* (MAC) accounting for 115 (55.8%) of isolates, of which 37 (32.2%) were considered clinically significant; MAC was also the most common species to cause clinically significant disease. *M. abscessus complex* was the second most common species to be clinically significant. 11/19 (57.9%) of all *M. abscessus complex* isolated and 8/15 (53.5%) of those isolated from pulmonary samples were clinically significant.

Conclusions:

To our knowledge, this is the first study to characterise the epidemiology of NTM isolates from adult patients in Victoria in over two decades. Although NTM are primarily isolated from sputum or bronchoscopy aspirates, they changed clinical management in less than a quarter of cases. The most common clinically significant species was MAC, followed by *M. abscessus complex*. Further research is needed to develop a clinical prediction tool to risk stratify positive isolates which would aid early diagnosis and treatment of NTM infections.

Conflict of interest(s) (if any – not included in the 500 words): No conflicts of interest to declare.

[115] [0.55.115] Rapid and Comprehensive Identification of Nontuberculous Mycobacteria from Sputum: NALC-Seq

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Background/Aims: Mycobacteria, encompassing over 200 species including *Mycobacterium tuberculosis* and non-tuberculous mycobacteria (NTM), present significant global health challenges due to their pathogenicity and drug resistance. Traditional diagnostic methods, such as mass spectrometry, are limited by subspecies coverage and long culture times. To overcome these limitations, we developed NALC-Seq, a culture-independent method that enables direct subspecies-level identification of mycobacteria by performing targeted DNA enrichment via capture sequencing. This study aimed to evaluate the diagnostic accuracy of NALC-Seq directly from sputum specimens.

Methods: We conducted a single-center, prospective diagnostic accuracy study at Osaka Toneyama Medical Center between 2023 and 2024. A total of 125 sputum samples were collected from 115 patients with suspected or confirmed pulmonary NTM disease and 10 patients with non-NTM disease. Samples were pretreated with semi-alkaline protease (SAP) and N-acetyl-L-cysteine-sodium hydroxide (NALC-NaOH), then analyzed by two workflows: (1) a standard culture-based method with species identification via core genome multilocus sequence typing (cgMLST) using whole genome sequencing, and (2) NALC-Seq, a culture-independent method utilizing target capture sequencing with custom-designed RNA probes, followed by cgMLST. The performance of NALC-Seq was evaluated using the culture method as the reference standard.

Results: Of the 115 pulmonary NTM disease specimens, 93 were culture-positive and 57 were smear-positive. Culture identified *M. avium* subsp. *hominissuis* (48 cases, 51.6%), *M. intracellulare* subsp. *intracellulare* (22, 23.7%), *M. intracellulare* subsp. *chimaera* (5, 5.4%), *M. abscessus* subsp. *abscessus* (7, 7.5%), *M. abscessus* subsp. *massiliense* (5, 5.4%), and one case each of *M. tuberculosis*, *M. kansasii*, *M. paragordonae*, *M. mucogenicum*, and *M. simiae*. All 10 non-NTM control specimens were negative by both smear and culture, and NALC-Seq yielded no false-positive results in this group.

Among NTM specimens, NALC-Seq performance was stratified by smear and culture results. In smear-negative, culture-negative specimens (n = 22), NALC-Seq was negative in 21 cases (95.5%) and detected *M. intracellulare* in one case. This case was previously diagnosed with

NTM pulmonary disease caused by *M. intracellulare*, suggesting a culture false-negative result. In smear-negative, culture-positive specimens (n = 36), NALC-Seq correctly identified the subspecies in 6 cases (16.7%), misidentified in 2 cases (5.6%), and yielded negative results in 28 cases (77.8%). In smear-positive, culture-positive specimens (n = 57), NALC-Seq demonstrated higher sensitivity, correctly identifying the subspecies in 45 cases (77.2%) and misidentifying it in 5 cases (9.3%). Concordance rates progressively increased with smear grade: 61.5% in ±, 76.2% in 1+, 94.7% in 2+, and 100% in 3+.

Importantly, NALC-Seq enabled species identification within hours from sequencing initiation, significantly reducing turnaround time compared to culture-based methods.

Conclusions:NALC-Seq achieved high accuracy for direct subspecies-level identification, with 77.2% accuracy in smear-positive sputum samples.
NALC-Seq enables rapid identification of 212 species of non-tuberculous mycobacteria and *M. tuberculosis* complex, representing a promising diagnostic tool for mycobacterial infection.

Conflict of interest(s) (if any – not included in the 500 words): None declared.

[118] [0.54.118] Strain-Level Concordance Between Gastric Aspirate and Sputum Samples in Pulmonary Non-Tuberculous Mycobacterial Disease: A Retrospective Analysis

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Background/Aims:

The utility of gastric aspirate testing for diagnosing non-tuberculous mycobacterial (NTM) disease has garnered increasing attention. Unlike Mycobacterium tuberculosis, NTM are ubiquitous environmental organisms, and the diagnostic value of gastric aspirate testing for pulmonary NTM disease has long been debated. Recently, several studies have demonstrated species-level concordance between sputum and gastric aspirate samples in pulmonary NTM disease. Based on these findings, the Japanese Society for Tuberculosis and Nontuberculous Mycobacteriosis proposed provisional diagnostic criteria in 2024: at least one positive sputum culture and one positive gastric aspirate culture. However, it remains unclear whether the NTM isolates from these specimens are identical at the strain level. To assess the strain-level concordance of NTM detected in gastric aspirate and sputum samples.

Methods:
We retrospectively analyzed cases at Osaka Toneyama Medical Center from January 2022 to January 2025, where both sputum and gastric aspirate cultures were obtained within one month and yielded positive results. Species identification was performed by core genome multi-locus sequence typing (cgMLST), and strain typing was conducted by digital variable-number tandem repeat (VNTR) analysis via whole genome sequencing. The results were validated using transcription–reverse transcription concerted (TRC) reaction, and PCR-based VNTR analysis.

Results:
A total of 54 cases were analyzed, including 11 with pulmonary tuberculosis (TB) and 43 with pulmonary NTM disease. Among the NTM cases, the species distribution was as follows: Mycobacterium. avium (n=22), M. intracellulare (n=17), M. abscessus (n=2), M. kansasii (n=1), and M. paragordonae (n=2). For TB cases, M. tuberculosis was detected in both gastric aspirate and sputum samples in all 11 cases (100%), with identical VNTR types between paired specimens. For NTM cases, 42 (97.7%) showed the same species in both specimens, and among these, 36 (85.7%) had matching VNTR types. Patients with concordant species and strains had significantly lower BMI than those with discordant strains (median [IQR]:

19.6 [18.0–22.3] vs. 22.1 [20.9–23.2] kg/m2; p = 0.045). No significant differences were observed in gender or the presence of cavitary lesions.

Conclusions:
While the strain-level concordance rate (83.3%) was high, it was not complete. The discordance seems to reflect the known high frequency of polyclonal infections in pulmonary NTM disease, but the possibility of environmental contamination cannot be ruled out, necessitating further studies. Nevertheless, the high concordance between sputum and gastric aspirate strains supports the validity of the 2024 provisional diagnostic criteria, which are comparable to international standards requiring two positive sputum cultures for diagnosis.

Conflict of interest(s) (if any – not included in the 500 words):

The authors declare that they have no competing interests.

[177] [0.59.177] In vitro efficacy of sulbactam-durlobactam combined with β-lactam antibiotics in Australian Mycobacterium abscessus isolates

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Background/Aims: *Mycobacterium abscessus* has extensive innate and acquired antibiotic resistance resulting in limited antibiotic treatment options and poor clinical outcomes. Currently the only β-lactam antibiotics with efficacy against *M. abscessus* are imipenem and cefoxitin. Durlobactam is a β-lactamase inhibitor that may overcome intrinsic resistance mechanisms and enable the use of alternative oral β-lactam antibiotics. The aim of this project was to determine if sulbactam-durlobactam increases the susceptibility of *M. abscessus* to alternative β-lactam antibiotics.

Methods: Antibiotic susceptibility testing was performed for durlobactam, meropenem, cefuroxime and amoxicillin alone, and sulbactam-durlobactam alone and in combination with meropenem, cefuroxime and amoxicillin according to Clinical Laboratory Standards Institute (CLSI) standards.

Results: Sulbactam-durlobactam significantly lowered the MICs of *M. abscessus* to meropenem, cefuroxime, and cefuroxime-amoxicillin to MICs comparable to those of imipenem and imipenem-relebactam. The culture medium used had a significant impact on MIC, with Middlebrook 7H9 having significantly lower MICs for all combinations containing durlobactam compared with CLSI standard CAMHB media.

Conclusions: Sulbactam-durlobactam significantly increased susceptibility to oral and intravenous β-lactam antibiotics in the form of cefuroxime, amoxicillin and meropenem against clinical isolates of *M. abscessus*. Further research is required to determine if the *in vitro* data correlates with clinical efficacy with the optimal culture methods for determining MIC in *M. abscessus* remaining uncertain.

Conflict of interest(s) (if any – not included in the 500 words):

[180] [0.61.180] Characteristics and Prognosis in Patients with Bronchiectasis Receiving Long-Term Oxygen Therapy

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Background/Aims: British Thoracic Society guidelines recommend that the same long-term oxygen therapy (LTOT) eligibility criteria as for chronic obstructive pulmonary disease (COPD) be used for bronchiectasis, the evidence supporting LTOT in bronchiectasis is limited, and no studies have evaluated the prognosis of these patients. The aim of the present study was to investigate the characteristics and prognosis of bronchiectasis patients receiving LTOT.

Methods: This retrospective cohort study included patients with bronchiectasis who started LTOT at Fukujuji hospital between April 2011 and September 2022. Patients with COPD who started LTOT during the same period, as well as patients with interstitial lung disease (ILD) who started LTOT after June 2020 while receiving anti-fibrotic therapy, were also included. Baseline clinical data at the initiation of LTOT and the prognosis were collected from medical records. We compared baseline characteristics and survival time among patients with bronchiectasis, COPD, and ILD. Furthermore, among patients with bronchiectasis, we compared these parameters between those with non-tuberculous mycobacteria (NTM) culture-positive and negative results.

Results: A total of 93 consecutive patients with bronchiectasis were newly initiated on LTOT. The median age was 73 [67–81] years, with 70 (77.2%) being female, and 35 (38.0%) testing positive for NTM culture. Compared to patients with COPD and ILD, those with bronchiectasis were significantly more likely to be female, and had a lower BMI and %FVC. Additionally, $\%FEV_1$ in bronchiectasis patients was lower than those with ILD. Bronchiectasis patients with NTM culture positive had a lower median age, a higher modified Reiff score, a higher rate of cavitary lesions, a lower infection rate with *Pseudomonas aeruginosa*, a higher infection rate of *Aspergillus* and a higher PaO_2 compared to those who were NTM culture negative. Among 66 patients with bronchiectasis who were followed for outcomes after the initiation of LTOT, the median survival time was 664 [372–1078] days. The 1-year and 2-year mortality rates were 23.8% and 55.2%, respectively. The median survival time of COPD patients was 1008 [590–1722] days, and for those with ILD patients, it was 669 [208–989] days. Patients with bronchiectasis had significantly shorter survival compared to those with COPD, while no significant difference was observed compared to ILD (Figure1). For patients with NTM culture positive, the median survival time was 405 [156–646] days, while for those with NTM culture negative, it was 946 [573–1380] days. Patients with NTM culture positive had significantly shorter survival days compared to those with negative.

Conclusions: The survival time of bronchiectasis patients was extremely short. Notably, the prognosis of patients with bronchiectasis requiring LTOT was similar to that of patients with ILD. Early management before disease progression is important. Since the poor prognosis of bronchiectasis patients receiving LTOT with NTM culture positive, appropriately timed initiation of antimicrobial treatment for NTM is also essential.

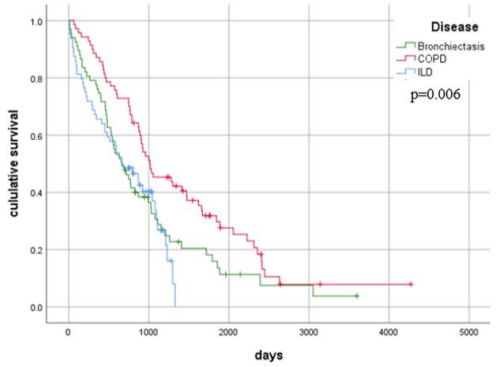

Figure1 Kaplan-Meier analysis of overall survival by disease.
The difference between the survival curves was significant (p=0.006, log-rank test).

[183] [0.53.183] Nontuberculous Mycobacterial Pleuritis in Congestive Heart Failure and Hypothyroid Patient

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Introduction. Nontuberculous mycobacterial (NTM) pleuritis is an uncommon manifestation of NTM infection. It has been reported in immunocompromised hosts as one of the clinical features of disseminated NTM disease. With the increasing of NTM lung disease worldwide, the number of reports describing NTM pleuritis in immunocompetent patients has increased recently.

Case report. A 70-year-old female was referred from a hospital in Yogyakarta due to shortness of breath, cough, weakness. Patient has a history of hypertension and hypothyroidism. Despite previous treatment, patient's symptoms were still persistent. Chest X ray showed cardiomegaly and right pleural effusion. Patient underwent thoracentesis (amount of drained fluid was 750 cc). Pleural fluid analysis showed exudate with mononuclear dominant. Pleural fluid PCR was positive for NTM. Patient was also diagnosed with congestive heart failure. Patient received Rifampicin, Isoniazid, Ethambutol, and Azitromycin. For NTM infection. Patient also received Rivaroxaban, Furosemide, Bisoprolol, Candesartan, and Levothyroxine. Patient has been on these medication for 4 months and all of her symptoms are significantly improved.

Discussion. Although the pathogenesis of NTM pleuritis is uncertain, the rupture of the subpleural focus in the lung into the pleural space could be considered as a trigger in the pathogenesis of the disease. However, the pleura is an uncommon site for an extra-pulmonary NTM infection. Despite the increased incidence of NTM infections and the established guidelines for managing NTM pulmonary disease, consensus for management of NTM pleural infection is still lacking.

[190] [0.58.190] Pulmonary NTM epidemiology in Japan-Analysis of Medical Claim from National Database 2012-2019

Eriko Morino[1,2]; Ishimaru Miho[1]; Terada Junko[1]; Takahashi Emily[1,3]; Masaaki Hojo[1]; Satoshi Mitarai[4]; Hasegawa Naoki[2]; Morimoto Kozo[5]

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Background/Aims:

Non-tuberculous mycobacterial (NTM) disease is rising worldwide, and epidemiological information is important. This study aims to evaluate the epidemiology of pulmonary NTM (pNTM) disease in Japan.

Methods:

We collected medical claim data of patients with the International Classification of Diseases, 10th revision (ICD-10) code associated with NTM disease between Sep 2009 and March 2020 from the National Database. We defined prevalent cases where a claim met the case definition in the relevant year and incident cases where a claim met the case definition in the relevant year, provided no claims met the definition in the previous two years. For sensitivity analysis, we prepared three types of case definitions: (1) at least one disease code (ICD-10 code A310 and A319), (2) at least one disease code combined with mycobacterial culture test, and (3) at least one disease code combined with treatment regimen (treatment case). Treatment was defined as using two or more standard drugs, including a macrolide plus either rifamycin or ethambutol, in the relevant year. In assessing the incidence rate, cases that met definition (3) and had a prescription of treatment when the first ICD code was assigned were defined as "immediate treatment cases." We calculated the annual incidence rates and prevalence rates overall and by sex, the number of patients overall, by sex and age group using these definitions, and discussed the changes over time from 2012 to 2019.

Results:

The incidence (per 100,000 people) of pNTM defined by definition (1) increased consistently from 40.1 in 2012 to 48.4 in 2019. The incidence of "treated pNTM," defined by definition (3), was 9.1 in 2012, peaked at 10.3 in 2017, and decreased slightly to 10.2 in 2019. The incidence of immediate treatment was 6.3 in 2012, 6.6 in 2013, and gradually decreased to 6.0 in 2019. A similar trend was observed in incidence by definition (2). The prevalence rates defined by all definitions increased consistently, from 121.9 to 210.2 by definition (1) and 22.8 to 34.7 by definition (3). The prevalence by definition (3) in females increased from 31.8

to 51.4, a 1.64-fold increase, and those in males increased from 13.3 to 17.1, a 1.28-fold increase from 2012 to 2019. The proportion of females and females aged over 70 among the treatment cases increased gradually from 70.7% to 76.0% and 36.8 % to 46.7 %, respectively, over the 8-year period.

Conclusions:

The estimated incidence and prevalence of pNTM disease in 2019 were at least 10.2 and 34.7 per 100,000, respectively. The incidence of pNTM patients under treatment has been flat in recent years; the increase in incidence may be mainly due to untreated mild cases. The high prevalence compared to the incidence speculates that pNTM patients who were uncurable even after treatment contribute to the increase in the prevalence. The number of prevalent treated patients increased mainly in women in their 70s and 80s.

COI: None

[191] [0.62.191] Role of Rifampin in the treatment of Pulmonary Mycobacterium avian Complex disease: a systematic review and analyses of target attainment

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Background/Aims:

A combination of macrolides, ethambutol, with or without a rifamycin, form the backbone of guideline-based therapy (GBT) for pulmonary *Mycobacterium avium* complex (P-MAC) diseases. However, the role of rifampin, the preferred rifamycin, remains unclear. We performed a systematic review of existing clinical and hollow fiber infection model (HFIM) data to determine role of rifampin in P-MAC therapy.

Methods:

We compared all-cause death rates and prevalence of acquired macrolide resistance from clinical pharmacokinetics (PK) and pharmacodynamics (PD) studies performed in comparative studies of rifamycin-containing versus rifamycin-free regimens. Rifampin exposures and PK/PD indices associated with bacterial kill, bacteriostasis, and resistance suppression endpoints in HFIM studies were used in Monte Carlo Simulations (MCS) to calculate PK/PD-derived rifampin susceptibility breakpoints, optimized doses, and probability of target attainment for P-MAC.

Results:

We identified 2018 participants from 12 clinical studies (2 randomized trials, 1 prospective cohort, and 9 retrospective cohorts); macrolide dosing varied significantly between GBT based regimens with some regimens containing aminoglycosides and fluoroquinolones. Of these, 1227 (65%) received rifamycin-containing therapy GBT, 433 (24%) received rifamycin-free GBT, and 194 (11%) received non-GBT regimens. The weighted average all-cause death proportions were 19%, 22%, and 34%, respectively. Mortality and macrolide resistance were significantly higher with non-GBT regimens, $p<0.001$. For macrolide resistance, the proportions were 2%, 2%, and 13%, respectively. However, there was no significant difference between rifampin-containing and rifampin-free GBT.

In the 5 HFIM studies, none use clarithromycin, azithromycin was the only macrolide used. Both rifampin-containing (azithromycin plus ethambutol plus rifampin) and rifampin-sparing (azithromycin plus ethambutol) regimens containing human equivalent of daily GBT failed to

contain bacterial growth below day 0 (stasis) for >3 days at tested doses for isolates with MIC values of 0.5 mg/L or higher (**Fig A**). Simulations showed that in humans, a rifampin 8-12mg/kg dose achieved intracellular bacteriostatic exposures in only 58% of patients and failed to achieve exposures required for any bacterial killing, even with the lowest MIC of 0.25 mg/L (**Fig B-C**). Rifampin 35 mg/kg, though, achieved bacteriostasis in HFIM (and activity in our MCS) suggesting rifampin at this dose could still have a significant role for P-MAC.

Conclusions:
In summary, at current doses, the contribution of rifampin to P-MAC regimens is limited. Simulations suggest a potential clinical benefit with higher doses, a hypothesis that should be studied prospectively.

Conflict of interest(s) (if any – not included in the 500 words):

[207] [0.56.207] Treatment outcomes and safety of clofazimine in nontuberculous mycobacterial pulmonary disease

Shaun Kang[1,2,3,4]; Adrian Watt[5]; Malcolm Wilson[2,4,5]; Geoffrey Eather[1,2,4]; Timothy Baird[6]; Ieuan Evans[3,4]; Andrew Burke[3,4]; Rachel Thomson[2,3,4,7]

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Background/Aims: Nontuberculous mycobacterial (NTM) infections are difficult to treat and are associated with significant morbidity and mortality. Reported success rates with guideline-based therapy vary depending on NTM species and up to 70% experience treatment related side effects. There is limited data on the safety and efficacy of clofazimine, a commonly used second line drug in the treatment of NTM pulmonary infections.

Methods: All patients with NTM pulmonary disease treated with clofazimine between June 2017 and June 2022 across five major metropolitan hospitals were analysed to determine the success rates of clofazimine containing regimens and associated adverse events, in the treatment of NTM pulmonary disease. Success was defined as microbiological or clinical cure according to the 2018 NTM-NET consensus statement.

Results: A total of 157 patients were included in the analysis. Clofazimine was used as first line therapy in 93 patients (59%), substitution therapy in 29 patients (19%) and rescue therapy in 35 patients (22%). Of the 147 patients who had a treatment outcome recorded, 88 patients (60%) had successful treatment outcomes (61% [65/106] with *Mycobacterium avium complex*; 56% [19/34] of patients with *M. abscessus* infection). Success was more likely when clofazimine was used as part of a first line treatment regimen (62%) or as a substitute treatment (68%) than as salvage therapy (47%). Adverse events were reported in 50% (79/157) of patients, mostly dermatological (41/157, 26%) and gastrointestinal (36/157, 23%). 42 patients (26%) with an adverse drug reaction were able to continue their clofazimine treatment without a dose reduction or treatment interruption, while only 21 patients (13%) had to permanently discontinue the drug due to an adverse drug reaction.

Conclusions: The inclusion of clofazimine in treatment regimens for NTM pulmonary disease resulted in comparable outcomes and a favourable safety profile when compared with guideline-based therapy. Although half of patients experienced side effects on treatment, only a minor proportion of these patients had to discontinue clofazimine due to side effects.

Conflict of interest(s) (if any – not included in the 500 words): Nil

[327] [0.51.327] The impact of the introduction of the Cepheid Xpert MTB/XDR on mycobacterium tuberculosis clinical management in Western Australia

Hind Al-Abbasi[1]

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Background/Aims:

The increase in drug- resistant tuberculosis (TB) threatens global progress towards the World Health Organisation's (WHO) End TB goals. Isoniazid-resistant, rifampicin-susceptible tuberculosis (Hr-TB) is the most common form of drug resistance, accounting for an estimated 8% of new cases. In its 2018 treatment guidelines for Hr-TB, the WHO recommends adding fluoroquinolones to first-line therapy in all patients with Hr-TB to improve clinical outcomes and minimise progression to multidrug resistance. Therefore, rapid detection of Hr-TB is crucial to initiate the recommended treatment without delay. The Xpert MDR/XDR is a rapid, automated and less complex test. It can detect genotypic resistance to first- and second-line TB treatments.

Methods: Retrospective review of cases with Hr-TB between January 2018 and December 2023, collected from the Western Australia Tuberculosis Control Programme (WATCP) digital medical record. Data included demographics, site of TB disease, time to susceptibility results (DST), and time to initiation of appropriate treatment. Xpert MTB/XDR was launched at PathWest Laboratory Medicine in Western Australia in April 2023.

Results: Forty-nine cases of Hr-TB were included. The median age was 42 years, 55% were male and 53 % were diagnosed with pulmonary tuberculosis. Forty-three cases (88%) were diagnosed before the introduction of Cepheid MTB/XDR. The median time to DST availability was 36 days (IQR 25) before the availability of Cepheid MTB/XDR compared to only one day after (p= 0.031). The median time to initiation of correct therapy was 46 days (IQR 21) before MTB/XDR availability compared to 8 days after (IQR 30.7) (p = 0.031).

Conclusion: The introduction of Cepheid MTB/XDR provided significantly faster resistance information, with a much shorter delay to starting the correct treatment.

Conflict of interest(s) (if any – not included in the 500 words): No conflict of interest.

SESSION 7: MICROBIOTA

[58] [1.04.58] Sputum microbiology in severe bronchiectasis: A cross-sectional study

WITHDRAWN

[65] [1.03.65] Bacterial Profiles in Inhaler Devices after 30 Days of Use by Patients with Non-Cystic Fibrosis Bronchiectasis

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Background/Aims:

Previous studies have raised possible contamination issues associated with the use of inhaler devices. Pressurized metered-dose (pMDI) inhalers and Respimat® devices (Boehringer Ingelheim®) are widely used by patients with bronchiectasis. Considering the different structures of both devices, we hypothesize that pMDI, compared to Respimat®, can be more prone to contamination related to their use.

Methods:

We prospectively evaluated 17 patients followed at the Bronchiectasis Outpatient Clinics of the Ulsan University Hospital (Republic of Korea) from June 2018 to March 2019. After enrollment, all patients received new inhalers according to their current treatment and were instructed to provide them after 30 days in exchange for a new one. After collection, all inhalers were exposed to ultraviolet light for at least one hour to prevent contamination during canister removal. Then, all canisters were opened within a biosafety cabinet, and their liquid content was collected and centrifuged. After discarding the supernatant, the pellets were resuspended in PBS and re-centrifuged for DNA extraction. Subsequently, library DNA preparation was performed using the Illumina MiSeq® platform targeting the V4 region of the 16S rRNA gene. Raw sequencing data were processed using the QIIME2® pipeline. The Divisive Amplicon Denoising Algorithm was applied for denoising, chimera removal and clustering of sequencing reads into amplicon sequence variants. The baseline control group comprised of twenty inhalers (pMDI, n=11; Respimat®, n=9), which had never been previously used.

Results:

Of those 17 participants, ten completed our study protocol (seven were excluded due to loss of follow-up). As two participants were on both inhaler devices, both pMDI and Respimat® groups consisted of six subjects, thus twelve inhalers (pMDI, n=6; Respimat®, n=6) were collected for microbiome analyses after 30 days. Overall, our study participants had a mean age of 63.5 years, showed a relatively preserved lung function (mean FEV_1 of 85% of predicted), and the vast majority were females (n=9/10, 90%). Both pMDI and Respimat® groups did not differ from each other regarding the frequency of *P. aeruginosa* colonization and FACED scores. Over 30 days, compared to baseline samples, bacterial loads (number of 16S rRNA gene copies) increased significantly in both groups (pMDI: p=0.0002; Respimat®: p=0.0004). α-diversity analyses did not reveal any significant differences in microbial richness or the Shannon Index among inhaler groups. On the other hand, β-diversity analyses showed a significant shift in microbial communities (baseline vs. Day-30th) in the pMDI group (p=0.016), as opposed to non-significant shifts in the Respimat® group (p=0.349).

Conclusions:

Among bronchiectasis patients, both pMDI and Respimat® devices showed significant bacterial contamination of their contents over a relatively short period of 30 days of use. Given the significant shifts in microbial profiles observed only in pMDI, these inhalers might be more prone to contamination over usage compared to Respimat® devices. Whether this is clinically relevant and whether these findings may be extended to other respiratory diseases need to be clarified.

Conflict of interest(s) (if any – not included in the 500 words):

None.

[123] [1.05.123] Pseudomonas aeruginosa-Driven Airway Dysbiosis and Machine Learning Prediction of Acute Exacerbations in Non-Cystic Fibrosis Bronchiectasis

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Background/Aims:

While *Pseudomonas aeruginosa* (PA) colonization is linked to poor outcomes in bronchiectasis, emerging evidence suggests that microbial community collapse—marked by diversity loss and depletion of commensal taxa—may better reflect disease progression than pathogen load alone. This study investigates whether airway microbiota dysbiosis driven by PA colonization induces ecological fragility and evaluates the predictive utility of integrating microbial diversity indices with systemic inflammation markers to forecast 1-year acute exacerbation risk using interpretable machine learning.

Methods:

Thirty NCFB patients in clinically stable status (no acute exacerbations or antibiotic use within the preceding 4 weeks) were recruited from Shanghai Pulmonary Hospital, with 7 excluded based on predefined criteria. The remaining 23 eligible patients underwent bronchoalveolar lavage fluid (BALF) collection and 16S rRNA gene sequencing. Patients were stratified into PA-colonized (P1, n=8*) and non-colonized* (P2, n=15) groups. Microbial diversity (alpha/beta diversity), community structure differences. An XGBoost model was developed to predict 1-year acute exacerbation risk by integrating microbial taxa relative abundances, alpha diversity indices, inflammatory markers and clinical parameters. To avoid multicollinearity, BSI was excluded from the model. Model performance was evaluated using AUC, precision, recall, and F1-score, with SHapley Additive exPlanations (SHAP) analysis employed to interpret feature contributions. Sensitivity analysis assessed the impact of key features (e.g. *Pseudomonas* abundance, CRP levels) on model performance, and bootstrapping (1,000 iterations) was used to estimate metric stability. Calibration plots compared predicted probabilities with observed exacerbation frequencies.

Results:

PA-colonized patients (P1) exhibited significantly worse clinical severity than non-colonized patients (P2), with higher Bronchiectasis Severity Index scores (8.38 vs. 4.33, $P<0.01$), poorer quality-of-life (SGRQ: 35.75 vs. 22.79; CAT: 24.00 vs. 16.26, $P<0.01$), and elevated dyspnea (mMRC: 1.62 vs. 0.95, $P<0.05$). P1 also had more acute exacerbations annually (retrospective:

3.00 vs. 1.20; prospective: 3.75 vs. 0.80, *P*<0.05–0.001). Notably, P1 exhibited significantly reduced alpha diversity compared to P2 (Shannon index: 1.96 vs. 3.47; Simpson index: 0.46 vs. 0.77, $p<0.05$). Weighted UniFrac PCoA revealed distinct clustering between groups ($R^2=0.162$, $p<0.05$). Dominance of *Pseudomonas* in P1 correlated with reduced relative abundances of *Veillonella*, *Prevotella*, and *Streptococcus* (FDR-adjusted $p>0.05$). The XGBoost model, integrating microbial taxa relative abundances, alpha diversity indices, and inflammatory markers demonstrated robust performance in predicting 1-year acute exacerbation risk (AUC = 0.85). SHAP analysis identified the microbial diversity, rather than *Pseudomona* abundance was the most influential predictor of exacerbation risk.

Conclusions:

PA colonization disrupts airway microbial diversity and outcompetes commensal species in bronchiectasis, yet our XGBoost model reveals that ecological resilience—not pathogen load—best predicts exacerbation risk when integrated with inflammatory markers. This paradigm shift from pathogen-centric to ecosystem-driven risk assessment provides an actionable framework for personalized management and antibiotic stewardship in chronic airway diseases.

Conflict of interest(s) (if any – not included in the 500 words):
All authors declare no conflict of interests in this paper.

[151] [1.02.151] Gut Microbiome Signatures Discriminate Nontuberculous Mycobacterial Pulmonary Disease Patients Requiring Treatment From Those With Stable Disease

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Background/Aims:

Nontuberculous mycobacterial pulmonary disease (NTM-PD) has emerged as an important health concern globally. The intestinal microbiome has been established to play an important role in lung immunity due to the existence of the Gut-Lung Axis (GLA). While perturbations (dysbiosis) of the intestinal microbiota has been explored in other respiratory diseases, its involvement with NTM-PD is unknown. The aim of this study was to determine if gut (faecal) microbiome signatures of NTM-PD patients were related to progression or severity of NTM-PD.

Methods:

Faecal samples were obtained from NTM-PD patients recruited through Gallipoli Medical Research at Greenslopes Private Hospital. NTM-PD was diagnosed according to ATS/IDSA criteria. Patients not requiring immediate treatment were deemed to have stable/milder disease (SD), and those with progressive disease (PD) provided a sample prior to initiation of antibiotic therapy. Faecal DNA was extracted using the Maxwell ® RSC Faecal Microbiome DNA Kit and microbiome signatures were produced by shotgun metagenomic sequencing on the Illumina Novaseq 6000 platform.

Results:

There were 16 SD patients, 85.7% female with mean (±SD) age 72.34±10.05 years, and 35 PD patients, 93.8% female, age 70.54±8.86 years. There were no significant clinical differences between the two groups with respect to BMI or BACES severity score. Analysis of within sample (alpha) diversity measures revealed no significant difference between the SD and PD groups (Shannon, Simpson, Chao1 or Observed indices, all $p>0.05$). However, some gross differences and similarities were observed in the relative abundance of different taxa between the groups. Stool samples from both groups possessed a larger relative proportion of the Gram-negative Bacteroidota than Gram-positive Bacillota. However, the relative size of the Bacillota membership was further reduced in the PD group, with a coincident expansion of the members of the Verrucomicrobiota phylum. Analysis of the differential abundance of bacterial species also revealed differences in abundance between the groups.

Conclusions:

This preliminary analysis suggests that the gut microbiome of all the NTM-PD subjects has a relatively larger proportion of bacteria assigned to the Gram-negative anaerobe group Bacteroidota, but the Bacilotta:Bacteroidota ratio is reduced in the PD group. Furthermore, subjects in the PD group, who were deemed to require antibiotics, share a signature whereby select Gram-positive bacteria assigned to Verrucomicrobiota are increased, relative to persons with stable disease. Further analyses and studies are warranted into the functional and clinical significance of these differences and the potential use of species 'biomarkers' of disease stability or progression to treatment.

Conflict of interest(s) (if any – not included in the 500 words): NIL

[156] [1.01.156] Using Meta-Omics to Advance Precision-Based Bronchiectasis Management

Tim Baird[1,2,3,4]; Kellie Strickland[2,3]; Emily Dunn[2,3]; Miriana Littlejohn[2,3]; Jacob Christiansen[1]; Joshua Brock[1]; Louise McIntosh[1]; Julia Bashford[1,2]; Derek Sarovich[1,2]; Erin Price[2,3]

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Background/Aims:

Bronchiectasis (BE) is a progressive lung disease characterised by abnormal airway dilation, chronic infection and frequent exacerbations. Despite increasing prevalence worldwide, there remains incomplete knowledge about the spectrum of microbial drivers associated with BE pathogenesis. Furthermore, there is a need for improved diagnostics to inform personalised treatment strategies, particularly for combatting infectious exacerbations. To address these knowledge gaps, our study will comprehensively characterise bacterial, fungal, and viral populations in adult Australians with BE. In Aim 1, we will profile the stable BE lung microbiome to uncover microbiome signatures associated with the major BE phenotypes. In Aim 2, we will assess longitudinal changes in the BE lung microbiome at stability and during exacerbations. In Aim 3, we will profile *Pseudomonas aeruginosa* genetic diversity and antimicrobial resistance (AMR) in BE subjects. This abstract will report on the preliminary Aim 2 and 3 findings in subjects recruited up until 31st April 2025.

Methods:

Prospective expectorated sputa from 60 subjects with high-resolution computed tomography-confirmed BE managed at the Sunshine Coast University Hospital (SCUH) will be collected. Additionally, a subset of 20 BE subjects will have 'longitudinal' sputa collected across 3 timepoints: at stability (B0); at exacerbation commencement prior to treatment (P; Day 0), and towards the end of treatment (T; Day 7-14). *P. aeruginosa* isolates will be subjected to antimicrobial susceptibility testing AST, whole-genome sequencing, and bioinformatic AMR variant prediction using our ARDaP software. Microbial-enriched shotgun metagenomics and metatranscriptomics will be carried out on all specimens, with analysis linked to subject clinical data in line with the Australian Bronchiectasis Registry.

Results:

To date, sputa from 25 of the planned 60 BE subjects have been collected, from which 44 *P. aeruginosa* strains have been isolated and AST-profiled. 18 subjects have had additional longitudinal samples collected during exacerbations across the 3 above-mentioned timepoints. Human host-depleted DNA extractions are nearing completion for these samples

in preparation for Illumina metagenomic sequencing. Metagenomic results for this cohort will be presented as preliminary study findings.

Conclusions:

Our preliminary metagenomic data will provide species- and strain-level insights into BE microbiome composition and diversity, including high-resolution characterisation of fungi, DNA viruses, and fastidious organisms, and will identify both co-pathogen infections and previously unrecognised exacerbation-associated pathogens. Additionally, we expect to identify microbial signatures (e.g. interspecies networks, increased bacterial/fungal load, decreased richness) associated with BE phenotypes. Finally, we anticipate higher rates of AMR and multidrug-resistant *P. aeruginosa* in cases where antimicrobial treatment fails to eradicate this formidable pathogen.

Conflict of interest(s): Nil

Grant Support: Wishlist Foundation SERTF Grant – $290,000 AUD.

[206] [1.07.206] The Impact of Microbiome on the Pathophysiology following Early-life Respiratory Syncytial Virus Infection

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Background and aim: Early-life respiratory syncytial virus (RSV) infection is leading cause of respiratory illness and hospitalization in infants and infects almost all infants during the first 2 years of life. Previous studies have suggested that the respiratory and gastrointestinal microbial composition might be associated with its disease severity. However, little is known about how the lung and gastrointestinal microbiome following early-life RSV infection impact the development of RSV-immunopathology and pathophysiology. The aim of this study is to elucidate the role of the lung and gastrointestinal microbiome following early-life RSV infection using an animal model.

Methods: Neonate mice (Balb/c) were infected intranasally with RSV A2/L19-F at 7 days of age. Lung and cecal samples were harvested at 8 days and 4 weeks post-RSV infection (8 dpi and 4 wpi) for microbiome analysis. The V4 region of the 16S ribosomal RNA gene was amplified, and sequencing was performed using an Illumina MiSeq platform. Expressions of mucus-associated genes were measured by quantitative (qPCR). Lung histology was also evaluated, and pulmonary function test (PFT) was performed at 4 wpi to evaluate the RSV-pathophysiology.

Results: Neonatally RSV-infected mice had more mucus production compared to non-infected mice at 4 wpi. PFT parameters including inspiratory capacity, vital capacity, and lung compliance measurements at 4 wpi were significantly deteriorated in RSV-infected mice compared to uninfected mice. The overall microbial composition in the lungs at 4 wpi showed significant differences between RSV-infected mice and uninfected mice. The overall microbial composition in the cecum at both time points following early-life RSV infection were significantly different between RSV-infected mice and uninfected mice. Moreover, predicted metagenomes of gastrointestinal microbiome using PICRUSt2 analysis demonstrated that lipid biosynthesis, nucleotide biosynthesis, and carbohydrate biosynthesis pathways were downregulated in RSV-infected mice at both time points following early-life RSV infection.

Conclusions: Altered microbiome in lung and/or gut following early-life RSV infection is associated with lung function changes that may have long term disease effects later in life.

Conflict of interest(s) (if any – not included in the 500 words):

SESSION 8: NTM2

[17] [1.09.17] A case of Disseminated Mycobacterium Kansasii Infection with Interferon-ɣ Auto-antibodies

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Background/Aims:

We describe a case of disseminated non-tuberculous mycobacterial (NTM) infection with Mycobacterium Kansasii in an adult male with Interferon-ɣ autoantibodies (IFN-ɣ AutoAb).

Methods:

Patient is a 49-year-old Chinese male with no significant past medical history or long-term medication. He presented with symptoms of back and chest pain, nocturnal fevers and chills, loss of appetite and weight over a month's duration. Physical examination revealed low-grade fever and focal tenderness over the right posterior chest wall. No lymph nodes were externally palpable.

Initial tests revealed raised C-reactive protein (CRP) 211.7 mg/L, Total White Cell Count 21.4 x 109/L, and Erythrocyte Sedimentation Rate (ESR) 117mm/hr.

A Computed Tomography (CT) scan of the thorax revealed lymph nodes in the supraclavicular, mediastinal, and axillary regions, and an expansile destructive/necrotic lesion in the right posterior 5th rib with soft tissue component 4.8 x 2.5cm extending into the right T4-5 neuroforamen. There was also a pathological fracture of the right posterior 10th rib and lytic changes in the right posterior 8th rib and right scapula.

Magnetic resonance imaging (MRI) spine revealed extensive marrow signal changes in the spine, sacrum, iliac bones and ribs, and similar right 5th /8th rib and T4-5 bony changes seen on CT. Overall findings were suspicious for bone metastases.

A CT-guided biopsy of the right 5th rib and the right hemi-sacrum was performed. Histology showed multinucleated histiocytic giant cells with Touton-type and osteoclast-type giant cells. Ziehl-Neelsen stain showed scattered acid-fast bacilli (AFB), suggesting a mycobacterial infection. Fungal and bacterial cultures were negative. AFB smear and Xpert MTB/RIF were negative and AFB cultures were pending.

A bone marrow biopsy was also performed, which did not show any lymphomatous involvement. Myeloma screen was negative.

Results:

He was started on Rifampicin, Isoniazid, Ethambutol and Pyrazinamide for treatment of presumptive disseminated tuberculosis in view of histology findings.

Right 5th rib and hemi-sacrum AFB cultures returned a month later as Mycobacterium Kansasii, sensitive to Rifampicin.

Pyrazinamide and Isoniazid were stopped. Moxifloxacin and Azithromycin were added to his regimen.

Work-up for immunodeficiency was performed: Human immunodeficiency virus screen negative, IgG/A/M/E/D levels were normal. Test for anti-IFN-ɣ autoantibody was positive: titre of 1:100,000 plasma dilution for 50% inhibition of IFN-ɣ.

A multi-disciplinary discussion proposed the administration of 2 doses of intravenous Rituximab 1g 2 weeks apart. IFN-ɣ AutoAb titres 8 months after showed decrease in IFN-ɣ AutoAb levels, from 1:100,000 to 1:45,086 plasma dilution to achieve 50% inhibition. This effect was sustained a year later, with a titre of 1:4701.

The patient was continued on Rifampicin, Ethambutol, Moxifloxacin and Azithromycin for 1.5 years.

Serial CRP and ESR showed drastic improvements. Repeat MRI showed resolution of right 5th rib expansile soft tissue mass and healing of rib fractures. CT thorax showed resolution of previously enlarged lymph nodes. There was resolution of rib pain with fever lysis, and weight increase from 48.5kg pre-treatment to 53.9kg at end of treatment.

Conclusions: The exact prevalence of IFN-ɣ AutoAb is unknown: case series point to a Asian and Southeast Asian preponderance. The diagnosis should be considered in the context of disseminated mycobacterial infections with no apparent immunocompromising conditions.

Conflict of interest(s) (if any – not included in the 500 words): Nil

[47] [1.08.47] Management of Refractory Pulmonary Mycobacterium abscessus Infection in a Patient with Bronchiectasis: A Case Experience

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Background

Mycobacterium abscessus (Mabs) is one of the most challenging non-tuberculous mycobacterial (NTM) pathogens to treat, due to its intrinsic multidrug resistance and frequent treatment failures. The current ATS/IDSA guidelines recommend an initial intensive phase with at least three antimicrobial agents, including intravenous (IV) and oral therapies, followed by a maintenance phase with at least three oral and/or inhaled agents for a minimum of 12 months after sputum culture conversion. However, treatment is often limited by intolerable toxicity, and sustained culture clearance is difficult to achieve. This case underscores the complexities of managing refractory Mabs pulmonary disease, highlighting the need to balance antimicrobial intensity with tolerability, while considering a transition from eradication to symptom management and quality-of-life optimization.

Case

A 71-year-old female with underlying bronchiectasis was referred for evaluation of a chronic cough. High-resolution computed tomography revealed bilateral apical scarring, cystic bronchiectasis (predominantly in the middle lobes and lingula), tree-in-bud nodularity, and right upper lobe cavitation. Sputum acid-fast bacilli (AFB) culture confirmed Mabs with no *Mycobacterium tuberculosis* detected. Further cultures from bronchoscopy and bronchoalveolar lavage in January 2023 identified two distinct Mabs subspecies—*Mycobacterium abscessus ssp massiliense* and *Mycobacterium abscessus ssp abscessus*. During this period, the patient's condition progressively worsened, with radiological deterioration (**Figure 1**), resulting in multiple emergency visits and hospital admissions.

Treatment with IV amikacin, IV cefoxitin, oral clarithromycin, and oral clofazimine was initiated on 21 June 2023, but was frequently interrupted by adverse events, including transaminitis, urticarial rash (requiring allergist review and cefoxitin challenge), and PICC complications. As a result, only 3.5 months of treatment were completed over 6 months. Alternative agents (IV meropenem, oral trimethoprim-sulfamethoxazole) were also poorly tolerated. During this period, the patient also had two hospitalizations for infective exacerbations of bronchiectasis with haemoptysis.

In February 2024, following NTM specialist input, the regimen was revised to IV amikacin, IV tigecycline, oral linezolid, and oral clofazimine. After 8 weeks, the patient opted to discontinue

IV therapy due to treatment fatigue, transitioning to oral clofazimine, oral linezolid, and nebulized amikacin from April 2024 to present.

Despite the formidable challenges of dual-strain Mabs infection and treatment-limiting complications, the patient demonstrated clinical improvement, evidenced by resolution of haemoptysis, cessation of hospital admission since December 2023, and stabilization of reported breathlessness and radiological changes. Transient sputum clearance was achieved on three occasions (**Table 1**), though sustained eradication of Mabs was not achieved.

Conclusion

This case underscores the challenges in managing pulmonary Mabs infection, where the combined burden of disease severity, treatment-related toxicities and adverse effects profoundly impact patient quality of life. Despite adherence to guideline-based regimens, sustained culture clearance—the traditional marker of treatment success—may remain unattainable in complex cases, necessitating a pragmatic shift in goals of care from microbiological cure to symptom control, functional stability, and prevention of further decline. There is an urgent need for studies to guide optimal treatment regimens beyond first-line agents for refractory or partially responsive disease, and long-term strategies when culture clearance cannot be achieved.

Conflict of interest(s): Nil

[51] [1.15.51] Clinical Significance of Discordant ESR and CRP Levels in Nontuberculous Mycobacterial Pulmonary Disease

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Background/Aims: Nontuberculous mycobacterial pulmonary disease (NTM-PD) presents heterogeneous clinical manifestations, complicating accurate prognostication. Although the erythrocyte sedimentation rate (ESR) has recently been considered an informative prognostic marker, its clinical utility remains uncertain, especially when results are discordant with the widely used inflammatory marker C-reactive protein (CRP). This study aimed to investigate the clinical implications of discordance between ESR and CRP in NTM-PD, focusing on clinical characteristics, disease progression, treatment response, and survival outcomes.

Methods: Analysis was conducted using two NTM-PD cohorts from South Korea: a retrospective registry from Seoul National University Bundang Hospital (May 2003 to April 2018) and a prospective cohort from Seoul National University Hospital (July 2011 to June 2023). Patients diagnosed according to the ATS/IDSA 2007 criteria were screened. ESR values measured within one year of diagnosis and CRP values within one week of the ESR measurement were collected. Patients were categorized into two discordant groups: "high ESR" (elevated ESR with normal CRP) and "high CRP" (elevated CRP with normal ESR). Clinical deterioration (defined as initiation of treatment), microbiological responses, and all-cause mortality were analyzed. Multivariate Cox proportional hazards regression analyses were conducted, adjusting for demographic variables, comorbidities, and microbiological characteristics.

Results: Among 994 eligible NTM-PD patients screened, 344 (34.6%) exhibited discordance between ESR and CRP: 312 (90.7%) in the high ESR group and 32 (9.3%) in the high CRP group. The high ESR group was predominantly female (73.1% vs. 37.5%, p<0.001), had significantly higher prevalence of bronchiectasis (79.5% vs. 37.5%, p<0.001), but lower frequencies of diabetes mellitus (7.7% vs. 25.0%, p=0.001) and malignancy (9.9% vs. 34.4%, p<0.001) compared with the high CRP group. Dyspnea was more frequent in the high ESR group (37.8% vs. 12.5%, p=0.003). The median follow-up durations for the high ESR and high CRP groups were 5.73 and 6.41 years, respectively. Rates of clinical deterioration were similar (48.1% vs.

46.9%, p=0.897), and the time to deterioration also revealed no significant difference (median 21.3 vs. 28.6 months, p=0.897). Post-treatment culture conversion rates were comparable between the two groups (63.5% vs. 73.3%, p=0.577). Multivariate analysis indicated that ESR/CRP discordance was not independently associated with post-treatment culture conversion (adjusted HR=0.658 for high ESR group, 95% CI 0.344–1.257, p=0.205). Although univariate analysis indicated better survival in the high ESR group (crude HR=0.528, 95% CI 0.309–0.901, p=0.019), multivariate analysis revealed ESR/CRP discordance was not an independent predictor of mortality (HR=0.794, 95% CI 0.411–1.534, p=0.492). Independent predictors of mortality included older age (HR=1.114, 95% CI 1.078–1.151, p<0.001) and male sex (HR=2.890, 95% CI 1.575–5.291, p=0.001).

Conclusions: The discordance rate between ESR and CRP in NTM-PD patients is not rare, affecting approximately one-third of patients. The discrepancy is mostly due to elevated ESR with normal CRP, reflecting higher sensitivity of ESR compared to CRP. The discrepancy characterizes distinct clinical phenotypes but does not independently predict clinical deterioration, post-treatment culture conversion, or all-cause mortality. Therefore, the combined use of ESR and CRP can be beneficial, considering the higher sensitivity of ESR and their similar prognostic value.

Conflict of interest(s) (if any – not included in the 500 words): This work was funded by the Seoul National University Bundang Hospital Research Fund (22-2024-0013). The authors do not have any conflicts of interest to declare.

[104] [1.12.104] A pharmacokinetic-pharmacodynamic modeling approach to optimize ethambutol dosage based on in vitro time-kill assay against Mycobacterium avium

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Background/Aims:

Macrolides are key drugs used to treat *Mycobacterium avium* (*M. avium*) pulmonary disease. Preventing the emergence of macrolide resistance is crucial, and ethambutol (EB) is important in its prevention. Therefore, side effects of EB should be managed by optimizing the dose and continuing taking EB. However, the relationship between EB exposure and its preventive effects on macrolide resistance remains unknown. This study aimed to characterize this relationship using *in vitro* time-kill assay (TKA) of *M. avium*. Furthermore, we built a pharmacokinetic/pharmacodynamic (PK/PD) model to predict the emergence of macrolide resistance based on the EB dosage.

Methods:

TKA was performed against the logarithmic growth phase of *M. avium* ATCC 700898 strain in Middlebrook 7H9 broth supplemented with 10% Oleic Albumin Dextrose Catalase (OADC) and 0.05% Tween-20. *M. avium* was inoculated into the medium and cultured by azithromycin (AZM) alone or combined with EB at various concentrations (from 0.25 to 16x minimum inhibitory concentrations [MIC] for AZM and 0.06 to 2x MIC for EB). All experiments were performed at 37℃ and 135 rpm for 28 days with four replicates. The bacterial burden was quantified using Middlebrook 7H10 agar supplemented with 10% OADC, whereas macrolide-resistant bacteria were quantified on the same agar containing 32 mg/L clarithromycin. For the PK/PD modeling approach, previously reported pharmacokinetic parameters and the transition rate to epithelial lining fluid (ELF) and alveolar macrophages (AM) were used for the intrapulmonary drug concentration profiles. The relationship between drug concentrations in ELF/AM and the risk of emergence of macrolide resistance was modeled based on the values observed in this study.

Results:

The MIC of AZM and EB was 8 mg/L. The presence of the A2058C mutation in the rrl region was confirmed in colonies grown on agar medium containing 32 mg/L clarithromycin. During the culture period, macrolide-resistant bacteria were observed most frequently at a concentration of 4x the MIC of AZM and rarely at concentrations below the MIC. The emergence of macrolide resistance was observed 7–10 days after the initiation of culture, which increased gradually. As EB was co-incubated with 4x MIC of AZM, EB completely suppressed the emergence of macrolide resistance at concentrations > 0.25x MIC (figure).

The PKPD model analysis revealed that a single dose of AZM at 250 mg/day poses a high risk of macrolide resistance, especially in AM. Current guidelines recommend an EB dose of 15 mg/kg/day, which is sufficient to suppress macrolide resistance even in AM. Furthermore, we plan to use the Monte Carlo method to simulate the risk of macrolide resistance at various EB doses.

Conclusions:

EB inhibited macrolide resistance at sub-MIC levels. Furthermore, a PK/PD model was constructed to determine individual EB doses.

Conflict of interest(s):

All authors declare no conflicts of interest.

[120] [1.16.120] Adverse Drug Reactions During the Treatment of Nontuberculous Mycobacterial Pulmonary Disease: a Systematic Review and Meta-analysis

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Background: Nontuberculous mycobacterial pulmonary disease (NTM-PD) treatment involves the long-term administration of multiple drugs, often resulting in adverse drug reactions (ADRs). The incidence and severity of ADRs during treatment are not fully understood. To assess the burden of ADRs during NTM-PD treatment, we performed a systematic review and meta-analysis of prospective studies reporting ADRs during NTM-PD treatment up to August 23, 2023.

Methods: We evaluated the incidence rates of ADRs, medication discontinuation, and ADR-related deaths. Secondary outcomes included the clinical manifestation of ADRs and incidence rates according to the causative species.

Results: In total, 7,425 studies were identified through database searches, 30 of which were included in the analysis, including 22 non-randomized prospective studies (1,617 patients) and eight randomized controlled studies (1,332 patients). The overall ADR incidence rate was 59% (95% confidence interval [CI], 37%–78%), with ADR-related drug discontinuation and death rates of 14% (95% CI, 8%–20%) and 2% (95% CI, 1%–3%), respectively.
The clinical manifestation rates of ADRs ranged from 2% to 65%, with gastrointestinal symptoms being the most common. For the treatment of NTM-PD caused by *Mycobacterium avium* complex, the incidence rate of ADRs was 57% (95% CI, 31%–79%). The outcomes were similar between randomized and non-randomized studies.

Conclusion: ADRs during NTM-PD treatment are notably frequent, leading to drug discontinuation and possible mortality. Clinicians should be vigilant of ADRs during NTM-PD management, and further research is required to alleviate the burden of ADRs and improve treatment outcomes.

Conflict of interest(s) (if any – not included in the 500 words): None

[154] [1.14.154] Adverse events leading to Treatment Withdrawal and Interruption in Mycobacteroides abscessus pulmonary disease

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Background/Aims: Treatment for *Mycobacteroides abscessus* pulmonary disease (MABC-PD) is characterised by prolonged use of multiple antibiotics that are expensive, exhibit substantial toxicity and often poor effectiveness. Treatment guidelines are based upon consensus-derived expert opinion, rather than being evidence-based. The Finding the Optimal Regime or *Mycobacteroides abscessus* Treatment (FOR*Ma*T) adaptive platform trial attempts to address these limitations. The intervention program consists of an intensive phase with intravenous, inhaled and oral antibiotics and a consolidation phase using oral and inhaled antibiotics, based on current standard of care (13 drugs). We describe treatment-emergent adverse events (TEAEs) leading to treatment withdrawals and interruption.

Methods: TEAEs are reported by trial investigators, and data capture for TEAEs includes relationship to study medications (assigned by trial site investigators using a reference safety information) and any action taken with the implicated drugs. TEAEs are coded and graded by the FOR*Ma*T pharmacovigilance team according to the Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. The CTCAE is a subset of the Medical Dictionary for Regulatory Activities (MedDRA). All TEAEs defined as 'possibly', 'probably' or 'definitely' related to study medications that involved treatment interruption or withdrawal were analysed along with the details of which study medications were implicated in each event.

Results: Overall, from 44 participants, 26 (59%) participants had 104 TEAEs reported with interruption and/or withdrawal of one or more study medication(s). Of the 104 implicated TEAEs, 83 (80%) were adverse events and 21 (20%) were serious adverse events. Seven (16%) participants recorded adverse events that led to interruption of a least one study

medication, seven (16%) recorded adverse events leading to withdrawal of at least one or more study medications, while 12 (27%) had adverse events where study drugs were both interrupted and withdrawn. Table 1 lists CTCAE Classification of TEAEs that resulted in treatment interruption and/or withdrawal. Nausea (n=9), increased serum alanine transaminase (n=7), increased serum aspartate aminotransferase (n=7) and hearing impairment (n=6) were the most reported TEAEs.

Imipenem-cilastatin was reported as withdrawn in 15 TEAEs from nine participants, with nausea being the most reported adverse event associated with withdrawal (n=4). Intravenous amikacin was reported as withdrawn in 11 TEAEs from eight participants, with hearing impairment being the most reported TEAE associated with withdrawal (n=6). Tigecycline was reported as withdrawn in 12 TEAEs in six participants, with increased serum alanine transaminase levels implicated in two cases. These data also show that often a combination of TEAEs may lead to treatment discontinuation. Table 2 shows the MedDRA classification of TEAEs possibly, probably or definitely related to the study drug(s) leading to their withdrawal.

Table 1: CTCAE Classification of TEAEs that resulted in treatment interruption and/or withdrawal

Total number of TEAEs	***n=104***
Nausea	9 (8.7%)
Alanine aminotransferase increased	7 (6.7%)
Aspartate aminotransferase increased	7 (6.7%)
Hearing impaired	6 (5.8%)
Diarrhea	5 (4.8%)
Hoarseness	5 (4.8%)
Gamma-glutamyl transferase increased)	5 (4.8%)
Alkaline phosphatase increased	3 (2.9%)
Thrush	3 (2.9%)
Vomiting	3 (2.9%)
Abdominal pain	2 (1.9%)
Blood lactate dehydrogenase increased	2 (1.9%)
Creatinine increased	2 (1.9%)
Electrocardiogram QT corrected interval prolonged	2 (1.9%)
Proteinuria	2 (1.9%)
Sore throat	2 (1.9%)
Bronchospasm	1 (1.0%)
Chest pain - cardiac	1 (1.0%)
Palpitations	1 (1.0%)
Pancreatitis	1 (1.0%)
Pneumonitis	1 (1.0%)
Other miscellaneous CTCAE terms	34 (32.7%)

Table 2: MedDRA classification of TEAEs possibly, probably or definitely related to study drug that resulted in imipenem-cilastatin, tigecycline and intravenous amikacin withdrawal

Total TEAEs	n=38
Imipenem-cilastatin (40 of 44 participants received imipenem-cilastatin)	**n=15 (in 9 participants)**
Nausea	**4**
Alanine aminotransferase increased	1
Albumin low	1
Blood lactate dehydrogenase increased	1
Diarrhoea	1
Drug interaction^	1
Paraesthesia	1
Total protein low	1
Vomiting	1
Gamma-glutamyl transferase increased	1
Allergic drug rash	1
Brain fog	1
Tigecycline (42 of 44 participants received tigecycline)	**n=12 (in 6 participants)**
Alanine aminotransferase increased	**2**
Acute pancreatitis	1
Albumin low	1
Aspartate aminotransferase increased	1
Blood lactate dehydrogenase increased	1
Drug interaction^	1
Nausea	1
Total protein low	1
Gamma-glutamyl transferase increased	1
Allergic drug rash	1
Brain fog	1
Amikacin Intravenous (29 of 44 participants received IV amikacin)	**n=11 (in 8 participants)**
Hearing impaired	**6**
Creatinine increased	1
Drug interaction^	1
Proteinuria	1
Vestibular disorder	1
Brain fog	1

^Drug interaction reported as definitely related to concomitant medication lithium and possibly related to study drugs imipenem-cilastatin, tigecycline and IV amikacin.

Conclusions: Almost two-thirds of participants had treatment interruption or withdrawal of treatment for MABC-PD, highlighting the toxicity of current standard of care therapies. This substantial rate of discontinuation underscores the urgent need for safer, more effective therapeutic options to improve adherence and resulting patient outcomes.

Conflict of interest(s) (if any – not included in the 500 words):

No conflicts of interest reported.

[160] [1.10.160] Tigecycline Rechallenge for Pulmonary Mycobacterium abscessus Infection Following Hemorrhagic Pancreatitis: A Case Report

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Background/Aims: Non-tuberculous mycobacterial (NTM) infections have shown a marked global increase in prevalence over recent decades, with *Mycobacterium abscessus* emerging as a particularly concerning pathogen. This rapidly growing environmental mycobacterium, ubiquitous in soil and water systems, demonstrates broad pathogenic potential—causing pulmonary infections, skin/soft tissue infections, and rarely central nervous system disease. Its intrinsic multidrug resistance to conventional antibiotics complicates therapeutic strategies, necessitating use of alternative agents like tigecycline, a parenteral glycylcycline. Acute pancreatitis, though uncommon, represents a clinically significant adverse event that frequently necessitates permanent discontinuation of tigecycline therapy.

Methods: We describe the clinical course and therapeutic management of a 23-year-old female with cystic fibrosis-related bronchiectasis and *M. abscessus* pulmonary infection with prior haemorrhagic pancreatitis attributed to this agent who subsequently underwent tigecycline rechallenge.

Results/Conclusions: The patient successfully resumed tigecycline therapy, demonstrating the feasibility of cautious rechallenge in carefully selected cases.

Conflict of interest/Disclosure: No financial or commercial conflicts of interest to declare for any of the listed authors.

Competing interest disclosures: No competing interests to declare for any of the listed authors.

[201] [1.11.201] Does lignocaine effect growth of nontuberculous mycobacteria?

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Background/Aims:
Bronchoscopy is used to investigate nontuberculous mycobacterial (NTM) pulmonary disease, particularly in patients who cannot produce sputum for culture. Lignocaine is frequently used as a local anaesthetic during bronchoscopy. It has been previously found to inhibit the growth of Mycobacterium tuberculosis and other bacteria, and may reduce the diagnostic yield of bronchoalveolar lavage cultures. This project aimed to investigate whether lignocaine used during bronchoscopy inhibits growth of nontuberculous mycobacteria in vitro.

Methods:
Lignocaine concentrations in routine bronchoalveolar lavage samples were measured to determine the range achieved in clinical samples. Lignocaine susceptibility for M. peregrinum ATCC, M. abscessus ATCC and M. intracellulare ATCC by broth microdilution was performed as per CLSI guidelines. Minimum Inhibitory Concentrations (MICs) determined were compared to the range of lignocaine levels measured in bronchoalveolar lavage samples.

Results:
There was significant variability in the lignocaine concentrations measured in routine bronchoalveolar lavage samples. Lignocaine MICs determined for M. peregrinum ATCC, M. abscessus ATCC and M. intracellulare ATCC were greater than the highest lignocaine concentration seen in the bronchoalveolar lavage samples.

Conclusions:
Lignocaine MICs for reference strains of NTM were greater than the concentrations measured in routine bronchoalveolar lavage samples suggesting topical lignocaine is unlikely to affect BAL yield for NTM. Further investigation of the effect of lignocaine on growth of clinical NTM isolates to verify these findings is warranted.

Conflict of interest(s) (if any – not included in the 500 words):

[346] [1.13.346] Concurrent Malignant Pleural Mesothelioma with Pulmonary-Pleural Effusion Due to Non-Tuberculous Mycobacteria (NTM); a Rare Case Report

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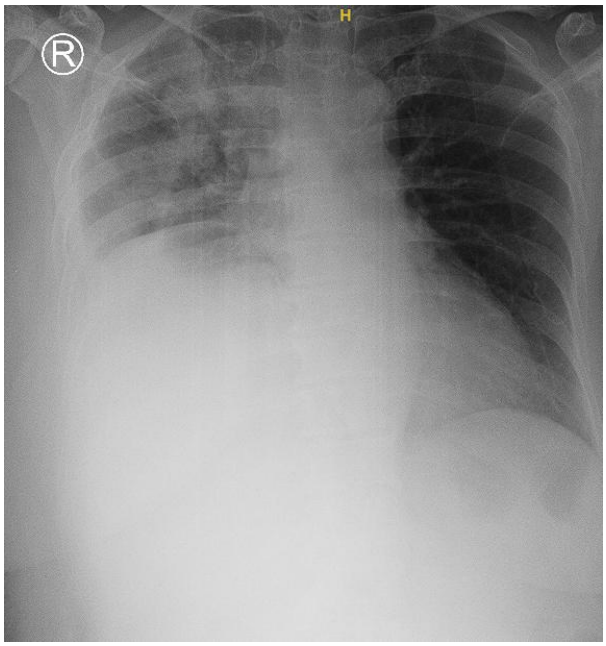
Background/Aims:
Non-tuberculous mycobacteria (NTM) are emerging pathogens that cause chronic lung infections, particularly in individuals with pre-existing lung disease or compromised immune systems. Their clinical and radiologic features often resemble tuberculosis (TB), making diagnosis challenging in TB-endemic areas like Indonesia. Malignant pleural mesothelioma (MPM) is a rare, aggressive cancer that can present with similar symptoms. The co-occurrence of MPM and NTM infection is extremely rare and may result in misdiagnosis and inappropriate treatment.

Objective:
To report a rare case of concurrent malignant pleural mesothelioma and pulmonary-pleural effusion due to NTM infection, and to highlight the importance of distinguishing infection from malignancy in TB-endemic settings.

Case Report:

A 65-year-old female farmer with a known history of pleural mesothelioma presented with persistent cough, weight loss, low-grade fever, and fatigue for three months. She denied TB contact and was not receiving immunosuppressive therapy. Physical examination revealed bilateral crackles in the upper lung fields and diminished breath sounds over the left lower lung area. Laboratory studies showed normocytic, normochromic anemia. Chest CT revealed nodular opacities in the left lung and moderate pleural effusion, raising concern for either cancer progression or superimposed infection.

Initial sputum tests for *Mycobacterium tuberculosis* using AFB smear and GeneXpert MTB/RIF were negative. Cytology of pleural fluid showed reactive mesothelial cells with granulomatous inflammatory reaction. Due to persistent symptoms, bronchoscopy with bronchoalveolar lavage (BAL) was performed. AFB staining remained negative, but mycobacterial culture from BAL fluid grew a non-tuberculous mycobacterium species. Subsequent tissue biopsy obtained via Video-Assisted Thoracoscopic Surgery (VATS) confirmed malignant pleural mesothelioma. Based on clinical, microbiologic, and histopathologic findings, the final diagnosis was concurrent MPM and pulmonary-pleural effusion due to NTM infection.



Discussion:

This case highlights the diagnostic challenge of distinguishing chronic infection from malignancy in TB-endemic regions. In such settings, NTM is often overlooked or misdiagnosed as TB, particularly in patients with known cancer. Overlapping symptoms, including cough, fever, and pleural effusion, may obscure a dual pathology. Negative TB-specific tests, such as *GeneXpert,* should prompt further evaluation, including cultures for NTM. In this case, BAL culture played a pivotal role in identifying NTM infection.

Recognizing co-infection is essential, as treatment for NTM differs significantly from TB and cancer-directed therapies. Misdiagnosis can delay appropriate management and worsen outcomes.

Conclusions:

NTM infection should be considered in patients with persistent respiratory symptoms, even those with underlying pleural malignancy. A comprehensive diagnostic approach, including clinical evaluation, imaging, cytology, histopathology, and microbiological studies, is vital to avoid misdiagnosis. Improved clinician awareness and expanded diagnostic capacity are critical in TB-endemic regions to ensure timely and appropriate treatment.

Conflict of interest(s) (if any – not included in the 500 words):
The author(s) declared no potential conflicts of interest for the research, authorship, and/or publication of this article.

SESSION 9: PAEDIATRIC

[112] [1.18.112] Lung clearance index is more sensitive than spirometry to detect lung function impairment in children and adolescents with bronchiectasis

Crystal Bourke[1,2]; Julia Casella[1]; Marina Kakuda Ng[1]; Craig Schofield[1,3]; Kitty Obando[1]; Tabitha Cleary[1]; Alana Harper[1]; Yuliya Karpievitch[1,4]; Luke Garratt[1,3]; Anne Chang[5]; Peter Richmond[3]; Andre Schultz[1,3,6]; Kathryn Ramsey[1,3]

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Background/Aims: Spirometry is the conventional lung function test used to monitor children and adolescents with bronchiectasis, however spirometry is difficult to perform for young children and is not sensitive to early, small airway disease. The lung clearance index (LCI), measured using the multiple breath washout test (MBW), is a tidal breathing lung function test which is easier to perform and is more sensitive to assess ventilation inhomogeneity of the small airways. LCI is a sensitive marker of lung disease in children with cystic fibrosis but has not been extensively studied in children with bronchiectasis. We aimed to determine if LCI detects lung function impairment in children with bronchiectasis, and assess relationships between LCI, aetiology, and spirometry.

Methods: We prospectively performed MBW and spirometry on children and adolescents with bronchiectasis (n=41; 113 visits; 10.16 ± 3.86 years; 54% male) and healthy controls (n=50; 87 visits; 8.77 ± 4.17 years; 44% male) as part of the BRIGHT longitudinal cohort study. Nitrogen MBW data were collected using the Eco Medics Exhalyzer® D device and analysed using Spiroware 3.3.1. Lung function data were collected according to international guidelines and presented as global lung function initiative z-scores. Data are presented as mean ± standard deviation.

Results: LCI was significantly elevated (worse) in children with bronchiectasis (2.26 ± 2.35 z-scores) compared with healthy controls (0.25 ± 0.67 z-scores; t-test: $p<0.001$). The bronchiectasis aetiology groups with the highest LCI values were bronchiolitis obliterans, chronic aspiration, and immunodeficiencies. At stable baseline visits, 47% (15/32) of children with bronchiectasis had an abnormal LCI (>1.64 z-scores) compared to 25% (7/28) with abnormal spirometry (<-1.64 z-scores). LCI z-scores positively correlated with age in children with bronchiectasis (Pearson coefficient: 0.29, $p=0.02$) but not in healthy controls (0.05,

p=0.64). LCI z-scores correlated with FEV_1 z-scores in children with bronchiectasis (Pearson coefficient: -0.55, p<0.0001). More than a third of children with bronchiectasis had an abnormal LCI but normal FEV_1 values (11/28: 39%).

Conclusions: LCI is more sensitive than FEV_1 to detect lung function impairment in children and adolescents with bronchiectasis. These findings support further research to assess the utility of LCI for clinical monitoring and as an outcome measure for clinical trials in children with bronchiectasis. Our next steps will be to examine relationships between LCI and markers of disease severity (hospitalisations, extent of lung disease on CT, inflammatory markers from sputum samples) and assess how LCI changes over time.

Conflict of interest(s) (if any – not included in the 500 words): Nil

[134] [1.26.134] Are we completing the recommended first-line investigations for children with bronchiectasis at Starship Hospital?

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Background

Bronchiectasis is a significant health problem for New Zealand children, especially for children of Māori and Pacific ethnicity. The Starship Bronchiectasis Clinic is a large multidisciplinary clinic that reviews children from the Auckland region and other centers with complex medical issues. Most cases are thought to be post-infectious, but investigations are conducted to exclude other causes.

Aim

To review which recommended chronic cough investigations are routinely completed in the Starship Bronchiectasis Clinic.

Methods

Retrospective analysis of children currently attending the Bronchiectasis Clinic was conducted 9th April 2025. Data included demographics, CT scan information, chronic cough investigation results, recent lung function results, and available sputum results.

Results

163 children currently seen in the Bronchiectasis Clinic. Median age is 9.1 years (range 2.5–16.8 years) and median age of CT diagnosis is 3.7 years (range 0.3–14.4 years). The children's ethnicities are: 36 (22%) Māori, 57 (35%) Pacific, 45 (28%) NZ European, and 25 (15%) other. Their disease is extensive with 108(66%) having bilateral disease, 23(14%) have all lobes affected and 14(9%) with bronchiolitis obliterans.
The most common aetiology is post-infectious with 52(35%) having recurrent lower respiratory infections and 18(12%) a severe respiratory infection. Aspiration is also common with 44(30%) of children having this as contributing cause. There are 5(3%) children with PCD, 10(7%) with a primary immunodeficiency and 11(7%) with bronchiectasis post oncology treatment.
A sweat test was performed for 97 (60%) children and 19 (12%) had cystic fibrosis gene testing. Immunoglobulin levels were checked for 147 (90%), vaccine responses for 115 (70%), and pneumococcal serology post-Pneumovax23 for 16 (10%). Flexible bronchoscopy was performed for 116 (71%) children.

Haemophilus influenzae (26%), Moraxella catarrhalis (8%) and Streptococcus pneumonia (8%) were the most common organisms identified in sputum samples. Nine children had pseudomonas cultured at least once.
Lung function was performed for 96 (59%) children. The reason for not testing due to young age or developmental delay. Of those tested, 39 had a low FEV1 (Z-score <1.64SD). The median FEV1 percent predicted was 85% (range 35%–129%), and the median Z-score was -1.21 (range -5.17–2.2).

Conclusion

The Starship Bronchiectasis Clinic has children with extensive disease usually caused by recurrent or severe early life infections but also includes complex primary immunodeficiency and oncology patients. Most children are diagnosed young and meet the recommended first-line investigations as recommended by the TSANZ bronchiectasis guidelines.
Our review highlighted the benefit of auditing investigations and identified areas for improvement. Establishing a national pediatric bronchiectasis database would allow ongoing review, identify long-term trends and implement improvement in completing investigations. It will mean we can compare with national paediatric bronchiectasis clinics and collaborate with international registries.

Conflict of interests Nil known conflict of interests

[139] [1.20.139] BRONCHIECTASIS EXACERBATIONS IN CHILDREN: CAN HOSPITAL STAYS BE SHORTER?

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Background/Aims:

Effective intravenous antibiotic (IVAB) treatment of bronchiectasis exacerbations is critical to preventing disease progression. However, a long course of inpatient IVAB is onerous on the child and their family. On average, children miss 12d school and caregivers miss 3.5d work per child-year due to bronchiectasis hospitalisations. Children and families describe hospital as an 'inhospitable place' and long hospitalisations have a significant impact on physical, social and emotional aspects of everyday life for the child, family and community. Patients, caregivers, and healthcare workers identify shorter hospital stays as a research priority. This study asks if shorter hospitalisations are as effective as the current standard-of-care.

Methods:

A retrospective audit of children aged ≤16y, with radiographically proven bronchiectasis, and hospitalised at Kidz First or Starship hospitals for IVAB treatment. We included all admissions during the study period (2018-2022). We collected demographic and clinical data from medical records. The primary outcome was time to next exacerbation, with a significance level of $P<0.05$.

Results:

There were 143 admissions (43% female) for bronchiectasis exacerbations over the study period. We compared children admitted for <10d (n=64, 45%) versus ≥10d (n=79, 55%) IVAB treatment (Figure 1). There was no significant difference in the primary outcome of time to next exacerbation between those receiving IVAB for <10d and ≥10d (Figure 2). There was also no significant difference between the groups in the secondary outcomes of time to next hospital admission ($P=0.553$) or time to next oral antibiotics ($P=0.113$). The most common reason for early discharge was clinical improvement (67%). Most children receiving <10d IVAB (95%) needed oral antibiotics on discharge compared to the ≥10d IVAB group (39%, $P<0.001$). Children received professional chest physiotherapy while in hospital and their usual caregiver-facilitated physiotherapy following discharge home. Most children were asymptomatic at discharge, however 16% of <10d and 4% of ≥10d still had cough symptoms ($P=0.014$).

Conclusions:

Our findings suggest that a shorter course of IVAB for bronchiectasis exacerbations could be as effective as the current 12-14-day course. A shorter hospital stay means the child getting home sooner, with clear social, cultural, educational and financial benefits. We are developing a New Zealand multisite non-inferiority, single-blind randomised controlled trial to compare the efficacy of (i) a 7-day course of IVAB plus 7-days oral antibiotics, with (ii) 14 days IVAB for management of bronchiectasis exacerbations in children. Both arms will receive professional chest physiotherapy while in hospital and usual caregiver-provided physiotherapy following discharge.

Conflict of interest(s) (if any – not included in the 500 words):
The authors have no conflicts of interest.

[147] [1.19.147] Incidence and potential underlying aetiologies of paediatric bronchiectasis in the US: 2018–2022

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Background/Aims: Paediatric bronchiectasis is often neglected, despite increasing recognition and the promise of better outcomes through early diagnosis and treatment in children and adolescents. The aim of this study was to provide a more current assessment of the incidence and potential underlying aetiologies (causality could not be inferred from the data) of paediatric bronchiectasis in the US.

Methods: Using anonymised healthcare claims data from a US database, Optum® Clinformatics® Data Mart, the incidence and underlying aetiologies of bronchiectasis were estimated for children and adolescents. International Classification of Diseases codes 9 and 10 were used for all disease definitions. Those included had ≥1 day of registration during the index period (1 January 2018–31 December 2022), with the index date defined as the earliest date in the index period when people had ≥365 days of claims history. People were aged <18 years, and had no existing bronchiectasis diagnosis prior to the index date. Those with missing/ambiguous age and sex information were excluded. The study population for estimating the distribution of underlying bronchiectasis aetiologies comprised all incident bronchiectasis cases identified between 2018–2022 who were aged <18 years on their incident bronchiectasis diagnosis date. A bronchiectasis case was defined as ≥2 outpatient claims on separate days with a diagnosis code of bronchiectasis, or ≥1 hospitalisation record with a principal/secondary diagnosis of bronchiectasis. People with and without cystic fibrosis (CF) were included. The incidence of bronchiectasis between 2018–2022 was estimated and stratified by age. The frequency and type of underlying aetiologies, determined using comorbidities previously linked to bronchiectasis, were summarised among all incident cases and defined as 'potential' (data are administrative claims collected for billing purposes and not intended for disease diagnosis and management). Underlying aetiologies were stratified by age and grouped by pre- and post-bronchiectasis diagnosis. An underlying aetiology was recorded as 'post-diagnosis' if not present/ascertained in the pre-diagnosis period.

Results: In total, 267 incident paediatric bronchiectasis cases were identified, with a mean±standard deviation (SD) age of 10±5.4 years, and 47.2% were female. The incidence of

bronchiectasis was 2.9 per 100,000 person-years (95% confidence interval 2.6–3.3) (Table 1). The mean±SD number of underlying aetiologies was 3.0±1.6 per person, with 98.9% of people having ≥1. Approximately 83.9% of people had ≥2 aetiologies and 16.5% had ≥5. The most common underlying aetiologies included respiratory infection (85.0%), asthma (50.2%), gastro-oesophageal reflux disease (36.0%), CF (32.2%), and chronic bronchitis and other obstructive diseases (23.2%) (Figure 1). Of note, the incidence of primary ciliary dyskinesia Kartagener syndrome was 5.2%.

Conclusions:

This study provides an up-to-date estimation of the incidence and potential underlying aetiologies of paediatric bronchiectasis in the US. These data indicate that the incidence of paediatric bronchiectasis was 2.9 per 100,000 person-years, with events identified in young as well as older children. On average, children and adolescents with bronchiectasis had three potential concurrent underlying aetiologies.

Conflict of interest(s) (if any – not included in the 500 words):
DISCLOSURE STATEMENT

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CONFLICT OF INTEREST

PAF reports support for the present publication from Boehringer Ingelheim; grants or contracts from Boehringer Ingelheim, Insmed and Synchrony; consultancy fees from Insmed; and serves on advisory boards and is a site principal investigator for Boehringer Ingelheim and Insmed. **KI** reports receiving consulting fees for this project through CERobs Consulting, who were contracted by Boehringer Ingelheim. **WKM**, **LZ** and **ATE** are employees of Boehringer Ingelheim. **CMM** reports receiving grants or contracts from the Cystic Fibrosis Foundation; consulting fees from Boehringer Ingelheim; and payment or honoraria from The France Foundation.

[159] [1.24.159] Gene expression profiling of peripheral blood identifies systemic T-cell and neutrophilic immune response in paediatric bronchiectasis

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Background/ Aims: In children with bronchiectasis, there is currently no data on biomarkers and little data on its pathobiology. Gene expression (GE) signatures are proven biomarkers for disease progression and can identify underlying pathobiological pathways in chronic respiratory diseases. We aimed to assess the transcriptomic profile of bronchoalveolar lavage fluid and peripheral blood in children with bronchiectasis, compared to controls.

Methods: Bronchoalveolar lavage (BAL) and peripheral blood were collected from 10 children with bronchiectasis and 10 controls (children without chronic wet cough), who did not have a clinical upper respiratory infection. Investigations were done at the time of diagnosis with bronchiectasis in the former group. RNA was extracted from samples, RNA-sequencing libraries prepared and sequenced using the Illumina NovaSeq 6000. Fastq files were generated using bcl2fastq2, trimmed, quality assessed, and mapped to the human reference genome. LIMMA was used to normalize and identify differentially expressed genes and pathways were assessed using Ingenuity Pathway Analysis.

Results: Children with bronchiectasis (70% male) had a median age of 1.9 years (IQR 1.3, 2.6), while controls (80% male) was 4.2 years (IQR1.3, 7.9, p=0.17). The main bronchiectasis aetiologies were post-infective (30%) and idiopathic (60%). Serum C-reactive protein was significantly elevated in the bronchiectasis children compared to controls (3 [IQR 2, 6.5] vs. 2 [IQR 2, 2], p=0.02). BAL neutrophil % was significantly (p=0.01) higher in the bronchiectasis group (48% [IQR 15.75, 78.25] vs. 7% [IQR 1.75, 14.5]). The bronchiectasis group had higher (60%) viral detection (respiratory syncytial virus, adenovirus, parainfluenza and/or human metapneumovirus) compared to controls (10%, p=0.02) and culture of pathogenic bacteria (>=cfu^4/mL *Haemophilus influenzae*, *Moraxella catarrhalis* and/or *Streptococcus pneumoniae*, bronchiectasis with 70% vs. controls 20%, p=0.03).

There were 433 upregulated and 205 significantly downregulated genes in BAL from children with bronchiectasis (adj p<0.05, log fold change (FC) >1, <-1). The top significantly upregulated genes included MUC3A (FC 4.09, adj-p=0.04), CSF3 (FC 4.03, adj-p=0.04) and 17 immunoglobulins genes (all FC >4 and adj p<0.05). Pathway analysis revealed the top biological themes were activation of interferon (IFN) signalling, inflammatory response and transcription factors responsible for amplifying the immune response. The most significantly

activated upstream regulators included antiviral genes IFNα2, tumour-necrosis factor (TNF) and IFNg.

In those with matched bloods (n=6 bronchiectasis, n=6 controls), blood GE identified 164 genes upregulated and 510 genes significantly downregulated (adj $p<0.05$, FC >1, and <-1) in children with bronchiectasis. The top significantly upregulated genes included T-cell receptor genes TRBJ2-4, TRBJ2-3 and TRAV8-5 (all FC >2.6 and adjusted $p<0.05$), which all play a crucial role in adaptive immunity. The top biological themes included leukocyte homeostasis and immune regulation, T-cell activation and neutrophil degranulation.

Conclusions: The BAL GE in children with bronchiectasis at the time of diagnosis reflects a generic immune-inflammatory response. In contrast, blood GE markers included T-cell receptor and neutrophilic-associated genes. Both BAL and blood hold specific and different biological information and provide data on biological processes. These warrant further investigation and validation in independent paediatric bronchiectasis cohorts.

Conflict of interest(s) (if any – not included in the 500 words): Nil

[175] [1.22.175] Are we prescribing the correct antibiotics for positive respiratory cultures from our children with bronchiectasis?

Victoria Irons[1]; Katherine Rose[1]; Miriam Manga[2]; Alana Ainsworth[1,2]; Catherine A Byrnes[1,2,3]; Anna Mulholland[1]

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Background/Aims:

The Starship 'chronic wet cough guideline' suggests using amoxicillin or amoxicillin + clavulanic acid (augmentin) for first line management of chronic wet cough. It advises the use of co-trimoxazole with prior use of high dose amoxicillin. Health pathways (the general practice guideline) suggests high dose amoxicillin for two weeks for chronic wet cough. The European Society Statement on protracted bacterial bronchitis (Chang AB et al, 2017) reports the most commonly used antibiotic is augmentin. The aim of this review was to review the sensitivities of the positive respiratory cultures in children with bronchiectasis, to determine we are using the correct antibiotics for infective exacerbations.

Methods:

Using the Starship and Kidz First Hospitals bronchiectasis REDCap database we reviewed the positive bronchoalveolar lavage (BAL) and sputum samples and determined the sensitivities against the most common organisms cultured from either sample type between October 2023- October 2024. In cases where a single child had multiple positive sputum samples, the most common sensitivities were recorded. No tracheal aspirates were included.

Results:

We had data on results from respiratory cultures on 309 children aged 6 months to 18 years. The most common result was mixed oropharyngeal flora in 99 (32%), then *Haemophilus influenzae* in 51 (16.5%), then *Moraxella catarrhalis* 17 (5.5%) followed by other bacteria (*Streptococcus pneumoniae, Staphylococcal aureus, Pseudomonas aeruginosa*) collectively at 35 (11.2%).

The sensitivity profiles showed with *Haemophilus influenzae* infection of the 51 samples 12 (23.5%) were resistant to amoxicillin, 5 (9.8%) were resistant to augmentin and 16 (32%) were resistant to co-trimoxazole. The sensitivity profiles showed with *Moraxella catarrhalis* 4 (23.5%) were resistant to amoxicillin but the remaining 14 samples were not tested, and all samples were sensitive to both augmentin and co-trimoxazole. Overall the BAL samples showed more sensitivities than sputum samples, likely due to being done earlier in the disease process and often at first diagnosis.

Conclusions:

There was less resistance of *Haemophilus Influenzae* to amoxicillin than expected, and on occasion, especially to lessen the gastrointestinal adverse events of the other drugs it may be a first option at times. However it is ineffective against the other common infecting organism of *Moraxella catarrhalis*.

Conflict of interest(s): No conflicts of interest to declare

[176] [1.17.176] Prospective ten year follow-up of an early intervention versus control study for children with severe bronchiolitis or pneumonia.

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Background/Aims:
The Healthy Lungs Study (2010-2014) conducted at Kidz First Hospital, included 400 children < 2 years admitted to hospital with severe lower respiratory tract infection (LRTI). They were randomised into an intervention group with two years of planned community assessments or the control group receiving standard care. These children are now over the age of 10 years and were invited to participate in a follow-up study with the aim to determine the prevalence of asthma and bronchiectasis among this high risk cohort.

Methods: A prospective study of participants from the original healthy lung study. Follow-up review included a clinical assessment and spirometry. A non-contrast inspiratory CT chest was performed for all participants who consented. Two radiologists scored the CT scans using the modified Bhalla score.

Results: A total of 205 children were reviewed in the follow-up study of which 105 (51%) were from the original intervention group. Median age 11.9 years (range 10.3 – 14.1). Almost all children were Pacific (60%) or Maori (29%) ethnicity and from areas of high socioeconomic deprivation. When seen in clinic 66 children had a wet cough (33%), 9 (4%) had crackles and 12 (6%) were wheezy. BMI was above 99.6th centile for 65 (32%) of children and 48 (24%) had a positive OSA questionnaire. Acceptable spirometry was performed for 168 children of which 30 (18%) had abnormal lung function. There were 55 (27%) children who had a diagnosis of asthma. A chest CT scan was completed for 152 children and the mean modified bhalla score was 25 (from a total of 27). At least mild bronchiectasis was scored on the CT scan for 47 (30%) children with 18 of these children having symptoms consistent with bronchiectasis. When comparing the initial intervention and control groups there was no significant difference seen in lung function, CT scores or the prevalence of asthma or bronchiectasis.

Conclusions: Young children hospitalised with early severe respiratory infections should be considered at high risk of developing asthma and bronchiectasis.

Conflict of interest(s) (if any – not included in the 500 words):

[197] [1.23.197] Koira4Rukahukahu: Lungs4Life: The development of a preventive program for chronic respiratory disease.

Miriam Manga[1]; Wainivetau Unaisi[2]; Ainsworth Alana[1,2]; Munro Karen[3]; Trenholme Adrian[1]; Byrnes Catherine A[1,2,4]

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Background/Aims:

The incidence of bronchiectasis is 7.7 per 100,000 children < 15 years with an increase in hospitalizations to 184 per year. The prevalence of asthma is 14.9% in New Zealand children <15 years of age with approximately 3,050 admissions per year. Both these chronic lung diseases are associated with early age hospital admissions for bronchiolitis and/or pneumonia. To try and prevent progression from early acute to later chronic lung disease the Lungs4Life program – a community follow-up program - was developed. The aim of this study was to review outcomes of those in the program for 2 years.

Methods:

This clinical program was launched in July 2021 in the Northern Region (Kidz First, Starship, Waitakere & Whangarei Hospitals). Children hospitalized for 3 respiratory admissions aged <2 years were enrolled. Follow-up visits occurred at 30 days, 3 months, 12 months & 24 months with extra visits as needed.

Results:

By April 2024 there are 477 children enrolled; 38.2% female; 47.1% Māori, 38.7% Pacific, 39.8% European, 10.2% Other with 66% in the most deprived quintile. At the time of enrolment 68% had immunizations up-to-date, 35.4% were smoke exposed, and 95% had focal changes on chest x-ray on their last admission. After 12 months in the program (n=255) 66% had required additional visits (the majority for respiratory issues), 3.7 additional courses of antibiotics and 1.3 hospital admissions. At time of being seen 33.3% had ongoing respiratory symptoms, 11.3% had abnormal ear examinations, 31.5% had skin conditions, and 19.1% had developmental issues. Referrals had been made to physiotherapy in 6.8%, speech language therapy in 20.3%, housing improvements in 36.5%, smoking cessation for 8.1%, general paediatrics 9.5%, and specialty services for 4.1%. At 24 months in the program (n=159) 10.9% had required additional visits in the previous 12 months, 32.4% still had respiratory issues, 13.2% with abnormal ear examinations, 20.2% with skin conditions, 25.9% with developmental issues. There were 2.9 courses of antibiotics and 0.6 admissions. At this time

69.9% had been prescribed asthma medications; 98% bronchodilators and 47.3% an additional preventer medication. By this time 90.7% now had immunizations up-to-date.

Conclusions:

These children with early and recurrent hospitalization for respiratory disease have significant ongoing respiratory morbidity. We still need to determine if early follow-up with access to investigations and treatment will improve the longer term outcomes in early childhood.

Conflict of interest(s) (if any – not included in the 500 words): Nil

[224] [1.21.224] Bringing physiotherapy to First Nations children with chronic lung conditions in remote NT communities.

Grace Hendriks[1]; Jordan Trunfio[1]

[1]*Community Allied Health Team - East Arnhem Region, Casuarina, Australia*

Project Statement

Our aim is to develop a model of care to raise awareness and effectively manage Chronic Suppurative Lung Diseases in First Nations children in regional and remote NT, thereby improving the lung health and overall well-being of these children. The Community Allied Health Team will raise community awareness through culturally secure health promotion activities and tools, as well as supporting staff in remote health clinics through ongoing advocacy and education to reflect best practice guidelines.

Background

Bronchiectasis is a chronic lung disease with a high prevalence among First Nations children in the Northern Territory—affecting approximately 1 in 68 children and is associated with significant early mortality (Singleton et al. 2014). Children living in regional and remote NT communities face unique challenges, as access to consistent healthcare services is often limited. Currently, there are no established physiotherapy pathways from the point of diagnosis to ensure ongoing support and management for these children. Barriers to Physiotherapy access include the following

· Low community awareness of chronic wet cough

· Limited understanding of referral pathways

· Lack of dedicated allied health services for paediatric respiratory care

· A predominantly medical model of care with minimal allied health involvement

· High staff turnover in remote areas

· Broader impacts of social determinants of health

Project Aims

· Develop an evidence-based physiotherapy model of care for Chronic Suppurative Lung Disease (CSLD) and bronchiectasis in remote First Nations communities.

· Increase awareness of chronic lung disease and the significance of chronic wet cough through culturally appropriate health promotion, supporting earlier detection and intervention.

Project Activities

· Perform initial and six-monthly respiratory assessments for children with bronchiectasis and as needed for CSLD.

· Prescribe and teach airway clearance therapy and recommend exercise.

· Educate families with culturally secure information on disease and management.

· Provide local staff with tools, resources, and training on respiratory care.

· Deliver PD to non-medical staff and connect doctors with expert resources.

· Advocate for appropriate referrals, including to respiratory paediatricians.

· Run health promotion activities in community settings like Families as First Teachers (FAFT) and childcare.

Evaluation (Dec 2025)

· Audit of physiotherapy service data to assess service reach and utilisation

· Analysis of referral sources, including identification of referring and non-referring clinicians/services.

· Client-reported experience and perceived impact on health and quality of life (QOL).

· Comparison of physiotherapy referral numbers to the Community Allied Health Team (CAHT) pre- and post-implementation.

· Qualitative data from key stakeholders involved in health promotion activities

[340] [1.25.340] Physical Activity Levels in Children with Bronchiectasis Living in Counties Manukau, New Zealand.

Laura Rensford[1]; Richard Ellis[2]; Tom Stewart[3]; Irene Zeng[2]; Sarah Mooney[2,4]

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Background/Aims: Bronchiectasis guidelines encourage children to participate in regular physical activity (Chang et al., 2023), but there is limited understanding of current physical activity levels. This study investigated how physically active children with bronchiectasis living in Counties Manukau, are compared to their healthy peers, and how often they achieved daily recommendations of 60 minutes of moderate to vigorous physical activity (MVPA). Secondary aims explored associations between MVPA and demographic or disease severity markers, and the mode of activity and time of day children with bronchiectasis engage in physical activity.

Methods: A quantitative, cross sectional, observational study was undertaken. Thirty-one children aged 7 to 12 years participated in two groups: Bronchiectasis Group n=18; Control Group n=13. Time spent in MVPA was measured over seven consecutive days using wrist-based ActiGraph wGT3X+ accelerometers. Mode of activity and time of day that participants engaged in physical activity was measured using the Physical Activity Questionnaire for Children (PAQ-C).

Results: The Bronchiectasis Group completed 26.0 (95% CI = 2.3, 49.7) fewer minutes of MVPA per day than the Control Group, with both groups demonstrating significantly higher MVPA minutes on weekdays, 20.7 minutes (95% CI = 11.5, 30.0), compared to weekend days. On average, 62.3% of the Bronchiectasis Group and 86.4% of the Control Group achieved the World Health Organisation's MVPA recommendations. Weak to moderate associations were found between MVPA minutes and body mass index and socioeconomic hardship. Both groups were most active at school, engaging more in informal school yard games.

Conclusions: Children with bronchiectasis are less active than their peers and would benefit from routine physical activity assessments to proactivity identify and manage inactivity and its potential comorbidities.

Conflict of interest(s) (if any – not included in the 500 words):
Nil

SESSION 10: PCD

[125] [1.31.125] Creating evidence for the use of HypErtonic saLine in People with Primary Ciliary Dyskinesia – the multicenter, randomized, double-blind, crossover proof-of-concept clinical trial HELP-PCD

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Background:

Primary Ciliary Dyskinesia (PCD) is a rare, hereditary disorder causing defective mucociliary clearance and chronic respiratory disease. Despite its significant disease burden, there is a lack of evidence-based therapies. Hypertonic saline (HS) inhalation has shown promise in cystic fibrosis and is used empirically in PCD, but robust data from clinical trials are lacking.

Methods:

HELP-PCD is a multicenter, randomized, double-blind, crossover proof-of-concept trial evaluating the efficacy of nebulized 6% HS versus 0.9% normal saline (NS) in people with PCD (pwPCD) aged ≥12 years. Participants undergo two 8-week treatment phases with HS and NS, separated by washout periods. The primary endpoint is change in lung clearance index (LCI). Secondary endpoints include changes in FEV_1, quality of life (QOL-PCD, EQ-5D-5L), and exercise capacity (6-minute walk test). Exploratory endpoints assess pulmonary exacerbation rates as well as lung morphology and function via non-contrast, phase-resolved functional lung (PREFUL) Magnetic Resonance Imaging (MRI). Safety, treatment adherence, and biomaterial collection are also included.

Expected Results:

It is hypothesized that HS inhalation will significantly improve LCI, lung function, QOL, and exercise tolerance compared to NS, and reduce pulmonary exacerbations. MRI is expected to detect treatment-induced improvements in ventilated lung volume.

Conclusions:

This trial aims to generate high-quality evidence for the clinical use of HS in pwPCD. If successful, it could inform treatment guidelines, improve access to reimbursed therapy, and enable earlier interventions to slow disease progression. The inclusion of innovative imaging and biomarker sub-studies will further support translational research in this underrepresented population.

[141] [1.30.141] Optimising Primary Ciliary Dyskinesia Screening in Adult Bronchiectasis. The value of nasal Nitric Oxide and PICADAR scoring.

Caitlin Meechan[1]; Lucy Burr[1]; Grace Madden[1]; Rebecca Keating[1]; Alcira Carballo[1]

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Background/Aims:

Primary Ciliary Dyskinesia (PCD) is a rare inherited disorder resulting in abnormal cilia motility. This culminates in impaired mucociliary clearance, commonly manifesting as recurrent ear, sinus and lower respiratory tract infections. PCD is genetically and phenotypically heterogenous, resulting in difficulty identifying patients, especially in adulthood. This has led to widespread underdiagnosis. Crucially, early diagnosis is fundamental to reducing morbidity and mortality, making the topic of effective diagnosis an important one. Diagnosis currently requires electron and high-speed microscopy to assess ciliary beat pattern and frequency. This requires extensive skill and resources, emphasising the need for effective screening.

Nasal Nitric Oxide (nNO) is significantly lower in PCD than healthy controls. Although use of nNO is increasingly common, there is a lack of consensus on its usage protocol. One instance is the lack of universal cut off values which should trigger diagnostic testing. Moreover, nNO remains a relatively new practice in non-specialist centres. Alongside nNO, PrImary CiliARy DyskinesiA Rule (PICADAR) scoring has emerged. Comprising of seven predictive variables, it is the first validated screening questionnaire for PCD, however, it has not yet been adopted into formal guidance in adult practice.

This study aimed to determine whether there is a relationship between nNO and PICADAR in adult subjects with broncheictasis, to assess whether a nNO value can predict and/or exclude PCD and to describe the trend of PICADAR for patients with low nNO.

Methods:

This was a retrospective, single centre, observational study. The population were patients with a diagnosis of bronchiectasis reviewed at Mater Hospital bronchiectasis clinic in Brisbane, Australia, with one or more nNO reading (n=127). Patients without nNO testing were excluded (n=31). Data was collected manually from electronic records.

Results:

Of the 127 patients, 6 had known PCD. We found a significant negative association between PICADAR Score and nNO $\rho = -0.301$ ($n=127$, $p = 0.0006$). We found nNO levels <300ppb did not miss any known PCD patients (sensitivity 1.0). However, nearly 20% of patients had a nNO <300ppb without a known diagnosis of PCD (specificity 0.8). Ultimately, we found that a nNO >300ppb excluded known PCD (NPV 1.0). Additionally, having a nNO <300ppb increased the likelihood of PCD by 5.5 (LR 5.5).

Of the 22 patients with a nNO <300ppb and no known PCD, their PICADAR trended towards higher values suggestive of possible undiagnosed PCD in this population (p=0.08, MWU). Collectively, we found patients with a nNO <300ppb had a significantly higher PICADAR than the residual population (p = 0.007, MWU).

Conclusions:

In conclusion, we found significant correlation between high PICADAR and low nNO in a mixed aetiological cohort of adult bronchiectasis patients. Furthermore, our data supported the use of nNO as a tool of exclusion for PCD at higher values (>300ppb). PICADAR is a low cost, screening questionnaire that can be easily implemented into physician practice. When used in conjunction with nNO, this could aid identification of patients requiring specialist testing for PCD.

Conflict of interest(s) (if any – not included in the 500 words):

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

[142] [1.28.142] Use of rhDNase in Primary Ciliary Dyskinesia Bronchiectasis

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[1]*Rabin Medical Center, Petach TIkva, Israel*

Background/Aims: Recombinant human deoxyribonuclease I (rhDNase) cleaves DNA in mucus, allowing for increased mucociliary clearance of purulent sputum. RhDNase in cystic fibrosis (CF) patients improves pulmonary function and decreases exacerbations. Conversely, rhDNAse use in non-CF bronchiectasis patients has not yielded similarly effective results in a prior clinical trial. (1) We explored the effectiveness of rhDNAse in patients with bronchiectasis due to primary ciliary dyskinesia (PCD).

(1) O'Donnell et al, Treatment of idiopathic bronchiectasis with aerosolized recombinant human DNase I, Chest 1998; 113:1329-34.

Methods: We provided rhDNase to PCD patients suffering from viscous mucus and moderate to severe bronchiectasis. Patients were instructed to use the medication up to once daily, primarily when their sputum became viscous. We monitored the patients over six months of usage, tracking pulmonary function tests, pulmonary exacerbations and quality of life.

Results: We tracked eight PCD patients with moderate-severe bronchiectasis, with an average forced expiratory volume in the first second (FEV1) of 46%. (Table 1) Use of rhDNase varied between full to half dose daily, to every other day, to intermittent use. As compared to prior to rhDNase, patients reported increased overall quality of life and reduced sputum viscosity. Average number of pulmonary exacerbations (PEx) were reduced from 3.1 to 2.3 in the comparable periods. Pulmonary function tests, as measured by forced vital capacity and FEV1, remained relatively stable compared to prior to commencing rhDNase (in contrast to the prior clinical trial).

Conclusions: Use of rhDNase in PCD patients lead to improved quality of life and decreased exacerbations, without impacting lung function, in contrast to earlier trial results in non-CF bronchiectasis with heterogeneous etiologies. Further clinical data is required to identify the population of PCD patients who can benefit from rhDNase, as well as the appropriate timing and dosing.

Conflict of interest(s) (if any – not included in the 500 words): None

[185] [1.27.185] Seeing the Unseen: Regional Lung Function Assessment in PCD and non-PCD Bronchiectasis using a Novel XV Scanner

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Background/Aims:

Early and accurate detection of lung disease in patients with bronchiectasis enables timely interventions that may slow disease progression. X-ray Velocimetry (XV) analysis is a novel technique to quantify regional lung ventilation using information captured by X-ray fluoroscopy. The utility of this technology to sensitively measure regional lung ventilation has been established in animal[1 2] and human trials.[3 4] The XV scanner is a new, non-invasive, quick and purpose-built device to capture images for XV analysis. This study aims to assess the feasibility of the XV scanner for assessment of lung function in patients with bronchiectasis due to Primary Ciliary Dyskinesia (PCD) and other causes.

Methods:

Participants ≥ 18 years old with PCD and non-PCD bronchiectasis are being recruited from four sites across Sydney, Australia. Participants attend a single site, Research Imaging NSW, for their study visit. Each participant performs multiple breath nitrogen washout (MBNW) via tidal breathing and spirometry according to American Thoracic Society and European Respiratory Society standards. An XV scan is then performed, with cinefluorographic images across four synchronised angles captured during one breath cycle while the participant is seated in the XV scanner. The acquired images are combined with recent CT chest images of the participant, and XV analysis is performed to generate XV metrics and regional ventilation maps.

Results:

Ten participants with bronchiectasis (6 PCD and 4 non-PCD bronchiectasis) have been recruited to this study. Demographics and baseline characteristics are shown in Table 1.

Metric	PCD (n=6)	Non-PCD bronchiectasis (n=4)	Total group (n=10)
Age, years	31 (24-50)	55 (37-60)	43 (24-57)
FEV_1 % predicted	45 (39-55)	49 (35-69)	45 (39-56)
FEV_1 z-score	-4.1 (-3.7 - -4.9)	-3.8 (-2.1 - -4.8)	-4.1 (-3.1 – -4.9)
FVC % predicted	72 (59-91)	76 (67-93)	73 (62-91)
FVC z-score	-2.1 (-0.7 - -3.5)	-1.7 (-0.5 - -2.6)	-2.0 (-0.7 - -3.2)
FEV_1/FVC %	53 (52-60)	57 (43-60)	55 (52-60)
FEV_1/FVC z-score	-3.5 (-3.1 - -3.6)	-3.1 (-2.6 - -4.1)	-3.3 (-2.9 - -3.6)
$LCI_{2.5}$	14 (12-16), n=5	19.5, n=1	15 (13-16)
TV, mL	483 (354-521)	520 (410-723)	483 (397-617)
VDP %	14 (13-17)	12 (10-18)	14 (10-17)
Total VH %	49 (44-52)	44.7 (40-55)	48 (43-52)
LVR %	18 (16-32)	30 (5-55)	18 (8-44)

Table 1 Summary of patient demographics and baseline characteristics. Data presented as median (IQR). LCI, lung clearance index; TV, tidal volume; total VH, total ventilation heterogeneity; VDP, ventilation defect percentage; LVR, low ventilation region.

All participants were able to complete acceptable and reproducible spirometry and the XV scan. One participant was unable to complete acceptable and reproducible MBNW. Three participants did not attempt MBNW due to infection control precautions at the study site.

Ventilation defect percentage (VDP) significantly correlated with FEV_1 z-score (R^2 = 0.47, p=0.029) but not FEV_1/FVC z-score or $LCI_{2.5}$. There was no correlation between ventilation heterogeneity (VH) or low ventilation regions (LVR) and FEV_1 z-score, FEV_1/FVC z-score or $LCI_{2.5}$ (Figure 1).

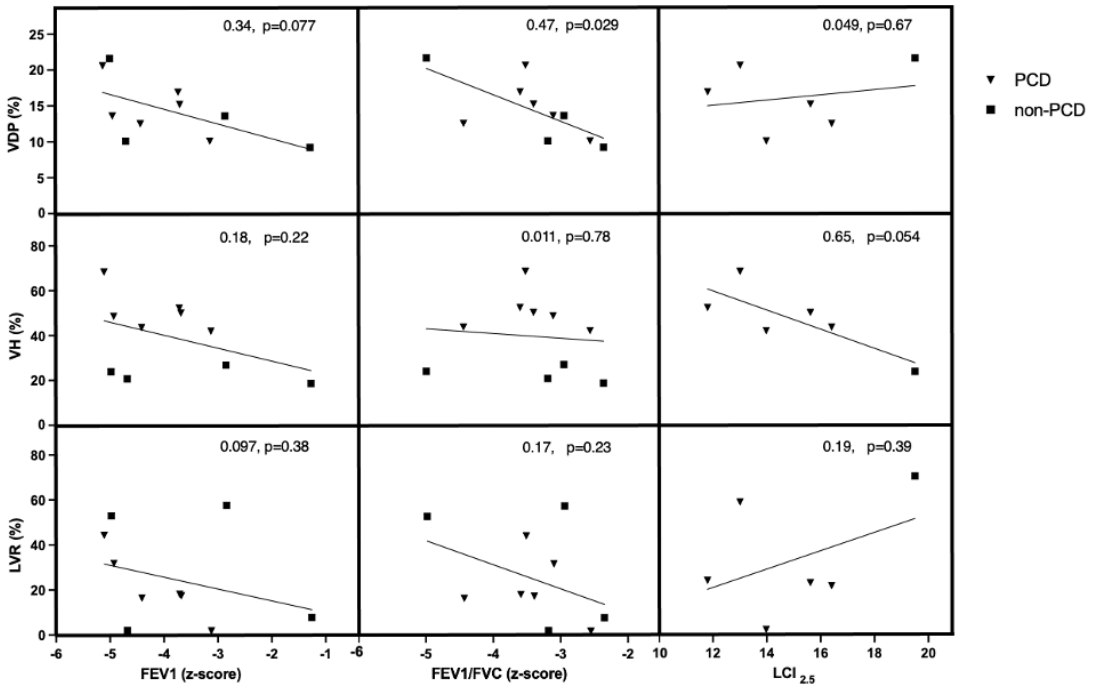

Figure 1 Scatterplots and linear regression (lines) of XV-derived ventilation metrics (VDP, VH and LVR) compared with spirometry (FEV_1 and FEV_1/FVC z-score) and MBNW ($LCI_{2.5}$) derived metrics. R-squared values derived from Pearson's correlation coefficient and *p*-values are reported for each plot. VDP, ventilation defect percentage; VH, ventilation heterogeneity; LVR, low ventilation region.

XV derived maps reveal the location of areas of lower than average ventilation in each participant (Figure 2).

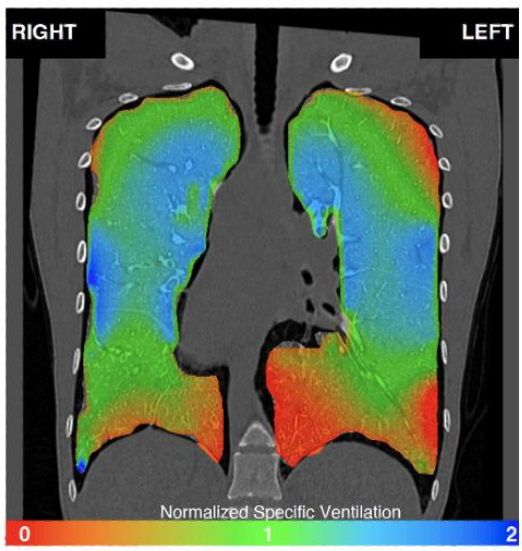

Figure 2 XV maps showing regional lung ventilation. Normalized specific ventilation reflects the specific ventilation throughout each participant's lungs normalized to their mean. Green represents areas of average ventilation, blue represents areas of higher than average ventilation, and red represents areas of lower than average ventilation. A) XV ventilation map of Case 1 with PCD, showing areas of lower than average ventilation in the left lower lobe, left upper lobe and right lower lobe. B) XV ventilation map of Case 2 with non-PCD bronchiectasis, showing areas of lower than average ventilation in the right lower lobe.

Conclusions: This study demonstrates the feasibility of using the XV scanner to assess regional lung ventilation in adults with bronchiectasis. XV analysis of the images captured using the XV scanner provides detailed regional ventilation maps that highlight areas of ventilation heterogeneity not captured by global lung function tests. These early findings support the potential utility of the XV scanner as a sensitive, non-invasive tool for evaluating regional lung ventilation in bronchiectasis. Recruitment for this study is ongoing to further investigate these findings in a larger cohort.

Conflict of interest(s) (if any – not included in the 500 words): Nil to declare

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[353] [1.29.353] From the Paddock to the Hospital Room: Raising a Child with Primary Ciliary Dyskinesia in Rural Australia

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Background/Aims:
Primary Ciliary Dyskinesia (PCD) is a rare, genetically inherited disorder that disrupts mucociliary clearance and often leads to bronchiectasis. Effective management requires lifelong, multidisciplinary care, typically delivered through tertiary health services. In rural Australia, access to such care is limited, resulting in significant logistical, financial, and psychosocial burdens for families. This case study explores the lived experience of a South Australian family raising a son with PCD on a regional farm, highlighting systemic barriers and the resilience required to navigate long-term care in a rural context. It also underscores the need for tailored healthcare models, rare disease advocacy, and improved awareness and education about PCD.

Methods:

This qualitative case study draws on over a decade of lived experience, using data from personal diaries, healthcare journey mapping, medical records, and informal logs kept by the child's family. It explores the intersection of health systems, rurality, rare disease, and family life, offering insights into patient and carer experiences beyond metropolitan settings.

Results:

Over a decade, the family has travelled more than 30,000 km for specialist care, averaging 250 km per month. This excludes travel by the child's second parent, who juggled life on the farm, siblings, and hospital visits. The cumulative toll included parking, accommodation, meals, disrupted routines, lost income, and emotional fatigue.

After eight years, the child became eligible for the Hospital in the Home (HITH) program. However, due to distance, "home" remained too remote. The family accessed accommodation close to the hospital. Ronald McDonald House was supportive but often at capacity. HITH reduced infection risk and offered respite from the hospital environment, but for rural families, it often felt like another relocation rather than true in-home care.

With limited local PCD knowledge, the family built informal care networks; weekly hydrotherapy, school-based physiotherapy, and peer support through PCD Australia. Private tutoring and Ronald McDonald House education support helped address school disruption.

Advocacy became essential. The child's mother became a consumer representative, chaired the Carer and Consumer Advisory Committee, and contributed to multiple working groups. She aimed to ensure rural voices were heard and raise PCD's profile. Guest speaking began

with fundraising and evolved into broader state and national health advocacy, including as a Starlight Foundation ambassador.

Despite progress, gaps remain. Australia has no national PCD registry, limited clinical trial access, and underdeveloped rare disease pathways; though improving since the 2020 launch of the *National Strategic Action Plan for Rare Diseases*, led by Rare Voices Australia.

Conclusions:

This case highlights the compounded challenges of geography, rarity, and system complexity in managing PCD for a family in rural South Australia. Future priorities as identified by the family include:
- Establishing a national PCD registry.
- Expanding Australian-led research and clinical trial access for PCD.
- Providing targeted psychosocial and logistical support for rural families
- Implementing scalable models of care closer to home
- Developing a national rural health strategy that embeds lived experience
- Continuing to ensure co-design and personal and family centred care is embedded in all aspects of care.

Conflict of interest(s) (if any – not included in the 500 words):
Disclosure:
This abstract is submitted from a lived experience perspective by a rural mother and consumer advocate, not a clinical researcher.

SESSION 11: PHYSIOTHERAPY & ALLIED HEALTHCARE

[28] [1.35.28] Healthcare access for children with bronchiectasis across an expansive geographical area: Analysis of inclusive paediatric physiotherapy service across metropolitan, regional and remote Queensland.

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Background/Aims:

Current international guidelines aim to improve the clinical outcomes and reduce treatment burden in children and adolescents with bronchiectasis (without cystic fibrosis) through optimising research and clinical practice including improving resource allocation, education and advocacy (1). Recent evidence demonstrates reversibility of bronchiectasis in 40% children and improvement in a further 40% with optimal management(2). The guidelines recommend access to age-appropriate respiratory physiotherapy assessment within six months of diagnosis and minimum six-monthly reviews (1).Queensland's expansive geography including remote and challenging to access communities, is a key consideration for service provision with potential for health inequity based on residential location and cultural identification, in management and research.

The Queensland Children's Hospital respiratory physiotherapy service partners in care with regional and remote centres within Queensland to provide reviews across inpatient admissions, outpatient clinics, telehealth appointments and outreach services. Outreach services to regional and remote locations provide direct patient care as well as education and capacity building and support for local clinicians via multidisciplinary service.

We aimed to audit physiotherapy provision to Queensland children and adolescents diagnosed with bronchiectasis who had completed repeat chest computerised tomography scans between 2013-2021. Timeliness of initial assessment and frequency of follow up, including admissions was assessed, to ascertain if standards of care were being meet. Additionally, assessment for disparity based on severity, age, cultural identification and location was completed.**Methods:**
Retrospective quantitative analysis of paediatric respiratory physiotherapy service delivery across all Queensland Hospital and Health Services (HHSs).

Results:

We reviewed records of 76 patients. Physiotherapy service provision occurred:

- 92% within 6 months of diagnosis
- during 98% of inpatient admissions for IVABs including regional hospitals
- 32% locally by outpatient reviews in local hospital or during respiratory outreach clinics
- 44% received biannual reviews

Of the 56% who did not receive biannual reviews

- 16% identified as First Nations
- 88% had mild lung disease
- 75% where aged 0 – 6 and resided across 13 of Queensland HHS

Conclusions:

Over 90% children were reviewed within the recommended time-period post diagnosis and during admissions including within local HHS, but over half of the patients did not receive recommended biannual reviews. With the changing paradigm of paediatric bronchiectasis, it is vital to continue to support physiotherapists statewide to provide care closure to home, ensuring health equity, positive health trajectory and improved clinical outcomes.

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Conflict of interest(s) (if any – not included in the 500 words):

Nil

[66] [1.38.66] Effectiveness of a stepwise model of airway clearance techniques in bronchiectasis: a prospective cohort study

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Background/Aims:
Airway clearance techniques (ACTs) are considered first line therapy in bronchiectasis. To date, research has explored the efficacy of single interventions whilst guidelines suggest a flexible, incrementally titrated approach. This study aimed to explore the effectiveness of the British Thoracic Society stepwise airway clearance model on of life, lung function and rate of pulmonary exacerbations.

Methods:
Adults with physician-diagnosed bronchiectasis attending private practice physiotherapy for initiation of ACTs were prospectively enrolled in a cohort study. Participants were commenced with a baseline ACT, which was reviewed at 1, 3 and 12 months with treatment escalated as clinically indicated. The stepwise ACT model included: Level 1, The Active Cycle of Breathing Technique (ACBT); Level 2, Positive Expiratory Pressure/Oscillating Positive Expiratory Pressure (PEP/OPEP); Level 3, PEP/OPEP + nebulised isotonic saline; Level 4, PEP/OPEP + nebulised hypertonic saline (HTS). The primary outcome was the change in Quality-of-Life Bronchiectasis (QoL-B) respiratory symptom domain over 12 months. Secondary outcomes included change in FEV_1% predicted, FVC% predicted, and 12-month pre/post treatment pulmonary exacerbations (PEx). Changes in continuous outcomes were assessed using paired t-tests and repeated measures analysis of variance. Change in PEx was assessed using Wilcoxon Sign Ranked test.

Results:
Forty-five participants were recruited and 40 (89%) completed the study. 31 (69%) participants were female, mean age 68 years (SD14.5). Disease severity on the Bronchiectasis Severity Index was 31% mild, 40% moderate, and 29% severe.

39% of follow up reviews required therapeutic intervention including ACT escalation (20%), encouragement to improve compliance (10%), and technique correction (9%).

Table 1. Participant initial and final ACT prescription.

ACT Level	Initial ACT (n=45)	Final ACT (n=40)
Level 1 (ACBT)	7 (16%)	2 (4%)
Level 2 (PEP/OPEP)	31 (69%)	18 (40%)
Level 3 (PEP/OPEP + 0.9%)	6 (13%)	16 (36%)
Level 4 (PEP/OPEP + HTS)	1 (2%)	4 (9%)

After baseline initiation of ACTs there was a significant improvement in the QoL-B respiratory symptoms at 1 month (MD 8.1, 95%CI: 2.9-13.3) which was sustained at 12 months (MD: 13.6, 95%CI 6.9-20.2). From baseline to 12 months there was a significant improvement in FVC% predicted (MD 5.5%, 95% CI: 2.5-8.4) but not FEV_1%predicted (MD 2.1% 95% CI -0.6-4.7). There was a significant reduction in the number of PEx from the 12 months pre-enrolment to 12 months post-enrolment (median 2.5 (IQR 2,4) and 1 (IQR 0,2) respectively, $p<0.001$).

Conclusions:
The implementation of a stepwise model of ACTs with interval review and titration, significantly improved QoL and FVC% predicted and reduced the number of PEx in people with bronchiectasis over 12-months.

Conflict of interest(s) (if any – not included in the 500 words):

This research was conducted in a primary care setting in a private billing practice. The primary author is the director and lead clinician of this practice.

All therapy devices including PEP devices and nebulisers were kindly donated by Air Liquide. Air Liquide had no other involvement in the study and were not involved in the study development, implementation or interpretation of results in any way.

[82] [1.37.82] Active cycle of breathing technique, oscillating-PEP therapy or walking with huffing during a bronchiectasis exacerbation

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Background/Aims:

While airway clearance techniques are recommended for adults with bronchiectasis, it is unclear which techniques should be prescribed when individuals are experiencing an acute exacerbation. The aim of this study was to compare the effects of the active cycle of breathing technique, oscillating positive expiratory pressure therapy and walking with huffing on sputum expectoration and health-related-quality-of-life for adults hospitalised with exacerbations of bronchiectasis.

Methods:

A multi-site randomised controlled trial was completed. Fifty-five adults were randomised within 48-hours of hospital admission. The primary outcome measure was sputum collected during airway clearance sessions, one-hour post session and the following 23 hours, with total 24-hour sputum and percentage of 24-hour sputum produced during session and one-hour post session calculated. The secondary outcome measure was health-related-quality-of-life (Bronchiectasis Health Questionnaire, Quality-of-Life Bronchiectasis questionnaire and Leicester Cough Questionnaire). All measures were collected day two of hospital admission and discharge day.

Results:

62% had severe bronchiectasis. There was no significant difference between groups in the primary outcome measure at either time point. Only active cycle of breathing technique group experienced a clinically significant reduction in 24-hour total sputum at discharge. Active cycle of breathing technique and walking with huffing significantly improved scores in all quality-of-life measures. Walking with huffing group demonstrated significant improvement compared to oscillating positive expiratory pressure in Leicester Cough Questionnaire total score. No other significant differences between groups in secondary outcome measures were observed.

Conclusions:

There was no significant difference in sputum expectoration between three common airway clearance techniques during hospital admission. Walking with huffing and active cycle of breathing technique significantly improved quality-of-life during hospital admission. Findings

support walking with huffing as a stand-alone airway clearance technique in adults hospitalised during an exacerbation of bronchiectasis.

Conflict of interest(s) (if any – not included in the 500 words):
Nil

[89] [1.40.89] Exploring the barriers and enablers of airway clearance therapy and exercise amongst adults with bronchiectasis: a patient perspective

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Background/Aims: Airway clearance therapy (ACT) and physical exercise are recommended to prevent pulmonary exacerbations and improve secretion clearance and exercise tolerance in adults with bronchiectasis. Adherence with routine ACT is frequently poor, and engagement in regular exercise is relatively unknown. This study explored the barriers and enablers of performing ACT, physical exercise and attending pulmonary rehabilitation (PR) from the perspective of adults with bronchiectasis.

Methods: Adults with a confirmed diagnosis of bronchiectasis undertook a semi-structured interview. Interviews were recorded, transcribed verbatim and coded. Inductive content analysis was used to explore the barriers and enablers and establish key themes.

Results: Thirty adults were included; 18 (60%) were female, median age 74 (interquartile range 67-80) years. Positive experiences with ACT to manage respiratory symptoms facilitated engagement. Barriers to ACT were the negative emotional connotations, including stigma, monotony and the time-consuming nature of therapy. Enablers of exercise engagement were physical, psychological and respiratory health benefits, and that exercise was a time efficient form of ACT. Lack of ability or self-belief was a barrier to engaging with physical exercise. Flexibility in PR model delivery and confidence in the supervised exercise and education programme provided by healthcare providers were enablers of PR, while lack of awareness of potential benefits, and geographical restrictions were barriers to PR participation.

Conclusions: Engagement with ACT, physical exercise or PR relies on participants' recognition of the benefits in daily life. Identification and appreciation of these barriers and enablers may facilitate uptake and engagement.

Conflict of interest(s): Nil to disclose

[113] [1.33.113] High frequency chest wall oscillation (HFCWO) data in the Bronchiectasis and Nontuberculous Mycobacteria (NTM) Research Registry (BRR)

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Background/Aims:

Airway Clearance is a mainstay of guideline-based bronchiectasis management. High frequency chest wall oscillation (HFCWO) has been associated with improved bronchiectasis (BE) management.

Methods:

This retrospective analysis of the Bronchiectasis and Nontuberculous Mycobacteria Research Registry (BRR) analyzed BE patient data for bronchial hygiene measures at baseline for differences in demographics and clinical characteristics between patients with and without HFCWO devices (Aim 1). Patients with no HFCWO device at baseline were further stratified as those having a productive cough or >2 exacerbations/year (i.e., meeting CMS criteria for HFCWO use) versus not (Aim 2). Productive cough was defined as a usually productive cough among those experiencing regular bouts of coughing in the 2 years prior to enrollment. Patients meeting Aim 2 inclusion with at least 1 year of follow-up over a 3-year period were explored for incident HFCWO therapy (Aim 3). Differences between groups for all aims were compared using Wilcoxon-Mann-Whitney and independent two-sample t-tests for continuous variables and chi-square tests for categorical variables.

Results:

This study compared patients (N=5673, median age: 69 years) who were using HFCWO (N=518) versus not (N=5155) at baseline and found an increased incidence of asthma (31.7 vs. 25.3%, p=0.002), gastroesophageal reflux disease (GERD) (48.5 vs. 41.9%, p=0.004), primary ciliary dyskinesia (PCD) (5.8 vs. 2.1%, p<0.001), allergic bronchopulmonary aspergillosis (ABPA) (3.3 vs. 1.7%, p=0.013) and nontuberculous mycobacteria (NTM) (20.1 vs. 15.7, p=0.011). The cohort using HFCWO also had more severe disease indicated by symptoms of dyspnea (72.1 vs. 38.5%, p<0.001), fatigue (61.5 vs. 46.8%, p<0.001), cough (90.9 vs. 76.6%, p<0.001), and hemoptysis (27.1 vs 19.8%, p<0.001). As expected, median modified

bronchiectasis severity index (mBSI) score was higher in patients on HFCWO vs. not (8 vs. 7, p<0.001). Furthermore, patients receiving baseline HFCWO were more likely to receive antibiotics, inhaled bronchodilators, hypertonic saline, inhaled corticosteroids, and oral corticosteroids; all signs of higher burdened disease (data not shown).

More than half (58%, 2,703/4679) of the patients without HFCWO therapy at baseline met the CMS guideline criteria for HFCWO therapy, and these patients were similar to those receiving HFCWO at baseline (**Figure**).

Only 13% (220/1709) of these patients with available data received incident HFCWO therapy during the follow-up period, and 68% of them (149/220) met CMS criteria. These patients were more likely to have decreased lung function (73.3 vs. 80.3 FEV1 %predicted, p=0.002) and experience at least 1 exacerbation during a 1-year period (47.8% vs. 28.1%, p<0.001) compared to patients not on HFCWO therapy.

Conclusions:

In this cross-sectional BRR analysis, patients with BE already prescribed HFCWO at baseline had severe disease. More than half of the BE patients without an HFCWO prescription at baseline met CMS criteria for an HFCWO prescription and had similar baseline characteristics to patients already on HFCWO. Preliminary analysis of longitudinal outcomes indicates there may be a need for education on HFCWO prescribing indications and guidelines.

Conflict of interest(s) (if any – not included in the 500 words):

The authors would like to acknowledge the Bronchiectasis and NTM Association, who manages the Bronchiectasis and NTM Research Registry, a 501(c)(3) nonprofit organization. The Registry is funded by the Richard H. Scarborough Bronchiectasis Research Fund, the Anna-Maria and Stephen Kellen Foundation, a Research Grant from Insmed Incorporated, and the Bronchiectasis and NTM Industry Advisory Committee. This work would not have been possible without the comprehensive chart reviews and recording of data by the dedicated research coordinators and PIs at each of the participating Registry sites. This research was funded by a joint research effort conducted by Electromed (makers of SmartVest) and the Bronchiectasis and Nontuberculous Mycobacteria Research Registry (CF and AEB are employees, respectively). RC declares no relevant conflict of interest, CJR reports: advisory board service for Insmed. France Foundation, clinical trials for Insmed, Vertex, Verona, Mannkind and grants from CFF, GMS reports: grants from Vertex, BiomX, AstraZeneca, Insmed, Electromed, Splisense, NIH, COPD Foundation, and CFF. Frestedt Incorporated was funded to assist in writing this abstract.

[114] [1.34.114] Feasibility of Electrical Impedance Tomography in assessing short-term effects of airway clearance techniques in adults with bronchiectasis, an observational study

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Background/Aims:

Background: There is a lack of robust evidence regarding the effectiveness of airway clearance techniques (ACTs) due to the absence of reliable and sensitive outcome measures. Electrical Impedance Tomography (EIT) has been reported to provide measures of lung ventilation distribution and reliable and valid short-term outcomes for ACTs in patients with cystic fibrosis. However, the feasibility of EIT in assessing ACTs has not been established in patients with bronchiectasis.

Aims: To assess changes in lung ventilation during airway clearance techniques (ACTs) in adults with bronchiectasis using electrical impedance tomography (EIT) and inform the feasibility of EIT to provide outcomes of ACTs in bronchiectasis and of using EIT in a busy clinic setting.

Methods:

Design: Prospective, observational study.

Setting: Single-centre adult bronchiectasis clinic.

Participants: 16 adult participants with bronchiectasis were recruited.

Intervention: An EIT belt was applied around the chest wall for continuous recording using the Drager Pulmovista. Participants then performed their routine ACTs. Participants provided feedback on their experiences performing ACTs during EIT measurements. Clinicians provided insights on their experiences managing patients during concurrent data collection sessions.

Results:
No difference pre-post ACTs for global EELI ($p=0.47$), regional EELI ($p>0.18$), global TV ($p=0.13$), local TV ($p>0.07$) (Wilcoxon signed ranks tests). There were, however, significant individual changes. There was variation in the quality & type of ACTs used.

EIT measurements did not affect the self-perceived effectiveness of ACTs, nor did EIT data collection affect the clinician's ability to manage patients. EIT is useful as a feedback tool in ACTs

Limitations:

- Small sample size.
- Convenience sampling – population representation.
- Significant variance in ACTs, discretion in interpreting the overall EIT outcome in this study.
- Fixed belt position.

Conclusions:
It is unclear whether EIT is sensitive to detecting changes in lung ventilation in adults with stable bronchiectasis. However, EIT is feasible for assessing the outcomes of ACTs in clinic settings. Continued data collection is planned to address the limitation of a small sample size. Further investigation is required to determine the short-term effects of supervised ACTs in patients with bronchiectasis.

Conflict of interest(s) (if any – not included in the 500 words): N/A

[325] [1.36.325] Pulmonary Rehabilitation in Chronic Bronchiectasis: A Case Report on Sustained Improvements Through Individualized Therapy

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Background/Aims:

Bronchiectasis is a progressive respiratory disease marked by chronic cough and excessive sputum production, leading to recurrent infections and reduced quality of life. Unlike other chronic respiratory diseases (i.e., COPD, ILD) it often affects a younger population (40–60 years), highlighting the need for age-appropriate, mucus-focused interventions. Physiotherapy is essential, using airway clearance techniques and targeted exercise to relieve symptoms, improve function, and enhance quality of life. These strategies are also vital for optimizing physical readiness in patients being considered for lung transplantation. Current guidelines support regular exercise and recommend including bronchiectasis patients in structured pulmonary rehabilitation programs. This study aims to evaluate the effects of self-management techniques that integrate secretion clearance strategies (i.e., active cycle breathing techniques, Aerobika use and postural drainage) with exercise training, including both aerobic and resistance components. The primary outcomes include symptom control, exercise capacity, and quality of life. Additionally, the intervention seeks to facilitate the timely initiation of pulmonary rehabilitation and optimize physical conditioning and functional status, particularly in patients being considered for lung transplantation.

Methods:

A 44-year-old male with bronchiectasis secondary to Williams-Campbell Syndrome and chronic pansinusitis was managed at the Physiotherapy Division, Universiti Malaya Medical Centre (UMMC). Serial HRCT scans revealed progressive emphysema, bronchiectasis, and bilateral lower lobe fibrosis. Pulmonary function tests in 2021 showed severe obstruction: FEV_1/FVC 53%, FEV_1 0.87 L (30% predicted), and FVC 1.62 L (43% predicted). He had a 10-pack-year smoking history and had been on long-term oxygen therapy (2–3 L/min via nasal prong) since 2018. Although referred to pulmonary rehabilitation in 2015, he only re-engaged after a hospitalization in July 2024. Improved adherence followed treatment for depression, physiotherapy counselling, and motivation after being listed for lung transplantation in December 2023. He subsequently completed a 12-week rehabilitation program involving one supervised and four home-based sessions per week (40–60 minutes each), combining aerobic and resistance training. Each session included a 4-minute warm-up, 20–30 minutes of walking or cycling at 40%–80% heart rate reserve (Karvonen formula), and resistance training using isokinetic machines, quadriceps benches, and sandbags with progressive load increments.

Results:

The patient exhibited notable improvements in SF-CRQ scores and walking distance following 12 sessions of pulmonary rehabilitation. Continued progress was evident after 24 sessions, with a reduction in mMRC grade, further enhancement in walking distance, and sustained improvements in quality of life and transition dyspnoea index scores, as illustrated in Figure 1. The patient started with 12 sessions of low-intensity exercise, showing steady progress, and progressed to moderate intensity during an extended program, maintaining functional improvements throughout. These progressive outcomes reflect symptom reduction, enhanced exercise tolerance, and improved overall functional capacity as a result of a prolonged, individualized pulmonary rehabilitation program.

Conclusions:

This case demonstrates that individualized and extended PR can significantly enhance symptom control, exercise capacity, and QOL in a patient with complex chronic respiratory conditions. Continued engagement in PR is critical in optimizing long-term outcomes, particularly for patients awaiting advanced interventions such as lung transplantation.

Conflict of interest(s) (if any – not included in the 500 words):

The authors declare no conflicts of interest related to this study.

[338] [1.32.338] Effectiveness of Airway Clearance Techniques in Bronchiectasis Management

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Background/Aims:

Bronchiectasis is a lung disease that has seen an increasing prevalence over recent years. Due to its significant burden on society, it is critical to develop effective treatment strategies. Among these, airway clearance techniques (ACTs) are some of the most commonly used methods for managing bronchiectasis. This study aims to evaluate the effectiveness of various ACTs in managing bronchiectasis, including during acute exacerbations and in non-cystic fibrosis bronchiectasis.

Methods:

An extensive search was conducted on online databases such as Google Scholar and PubMed. Articles published in English within the last five years were included in the study. A total of five articles were selected for review. These articles discussed various forms of ACTs, including huffing, exercise, the active cycle of breathing technique (ACBT), instrumental strategies, chest physiotherapy (with or without saline nebulization), positive expiratory pressure (PEP), and the ELTGOL technique (L'Expiration Lente Totale Glotte Ouverte en Décubitus Latéral).

Results:

The results of the reviewed studies demonstrated that different forms of ACTs are significantly effective in managing bronchiectasis, including in cases with acute exacerbations and non-cystic fibrosis bronchiectasis. Among the various techniques, bubble-positive expiratory pressure was identified as the most effective form of ACT for managing the condition.

Conclusions:

ACTs are proven to be effective in the management of bronchiectasis, significantly reducing complications associated with the disease. Among these techniques, bubble-positive expiratory pressure stands out as the most effective. The findings highlight the importance of incorporating ACTs as part of comprehensive treatment plans for patients with bronchiectasis.

[347] [1.39.347] Web-based resources for healthcare professionals and individuals with bronchiectasis: A scoping review

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Background/Aims:

While individuals with bronchiectasis gain information through discussions with their healthcare team, comprehensive multidisciplinary health services are frequently concentrated in metropolitan areas, with fewer resources available in regional or remote locations. There is a growing trend of using the Internet as an additional source of health information, especially when access to health services is limited. Several online resources have been developed to provide information on physiotherapy practices in bronchiectasis, including airway clearance and exercise. However, the degree of variability in the quality and credibility of health websites for bronchiectasis and enablers and barriers to implementing information from these sources is unknown. This review aimed to: (1) Identify websites that provide information on the physiotherapy management of bronchiectasis for adults or children and summarise what is currently available on these websites; (2) evaluate the quality of websites to help guide consumers in choosing a reputable source; and (3) undertake a scoping review to determine the barriers and enablers to the implementation of the web-based information into practice.

Methods:

The review was conducted in three stages. Stage 1: The World Wide Web was examined using search engines Google, Yahoo, and Bing. The first 20 pages of web pages generated from each search were screened. Stage 2: Two researchers evaluated the websites identified in Stage 1 using the Health Information Website Evaluation Tool (HIWET) and provided an overall grade (poor, moderate or good). Stage 3: Six electronic databases (MEDLINE, CINAHL, Cochrane Library, Scopus, Web of Science and PEDro) were searched for studies reporting on barriers and enablers to the implementation of knowledge provided on a website in clinical practice, with screening conducted by two reviewers.

Results:

Nine websites met the inclusion criteria for Stage 1. A comprehensive summary of information was compiled with websites consistently including details of: intended consumers, explanation of the condition, management of exacerbations, information on airway clearance,

exercise and accompanying videos. Stage 2: Six websites scored an overall quality grade of good, two websites a moderate grade, with only one scoring a poor grade. Stage 3: Three studies met the inclusion criteria. Enablers to implementation were: (i) comprehensive content and resources; (ii) a clear process for educating patients; (iii) resources that enhance engagement; (iv) promotion of socialisation in lung health; (v) resources are both carer and patient orientated; and (vi) ease of use. Barriers to implementation were: (i) access to the website; (ii) device and technology limitations, (iii) knowledge of the website; and (iv) time availability in a clinic.

Conclusions:
Several current websites for adults and children with bronchiectasis provide comprehensive information on the physiotherapy management for this condition, and website evaluation may assist in guiding consumers in choosing a reputable source for their information. The mix of enablers and barriers to implementing knowledge into practice will direct and influence clinical use.

Conflict of interest(s) (if any – not included in the 500 words):

SESSION 12: TREATMENTS AND NEW DRUGS

[16] [1.49.16] From Exacerbations to Relief: Harnessing Biologics in the Dual Challenge of Severe Asthma and Bronchiectasis

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Background/Aims:

Bronchiectasis is an uncommon yet significant comorbidity in severe asthma, often linked to worse clinical outcomes and greater disease burden. Biologic therapies have demonstrated efficacy in reducing exacerbations and enhancing asthma control, and reports have shown their potential in managing Allergic Bronchopulmonary Aspergillosis. This study aimed to explore the clinical characteristics, treatment outcomes, and effectiveness of biologic therapies in patients with bronchiectasis and co-existing severe eosinophilic or allergic asthma displaying a T2-high phenotype.

Methods:

This retrospective observational study reviewed the case files and electronic medical records of two patients with severe asthma and concomitant bronchiectasis who were treated with biologics for at least one year at Hospital Raja Perempuan Zainab II, Kota Bharu, Kelantan, Malaysia, between February 2020 and December 2024. Clinical data, including symptoms, radiological findings, and functional characteristics were analyzed.

Results:

Two patients were included in this case series. Both were on a combination of a long-acting muscarinic antagonist, long-acting beta-agonist, inhaled corticosteroid, and Azithromycin as an immunomodulator prior to biologic therapy.

Patient 1, a 52-year-old retired teacher with severe eosinophilic asthma (eosinophil counts of 450–500 cells/µL) and bilateral cystic bronchiectasis due to recurrent childhood infections, was dependent on oral corticosteroids and long-term oxygen therapy, in addition to triple inhaler therapy. She had frequent exacerbations (2–3 hospitalizations per year) and was unable to walk more than 50 meters due to dyspnea. After initiating benralizumab, she showed significant improvement, including the discontinuation of OCS and LTOT within one month. Exacerbation frequency dropped to zero, and while no lung function improvement

was seen, her symptom control and quality of life improved substantially. She regained the ability to cook and travel by car, previously limited by dyspnea. The treatment was well tolerated with no adverse effects during 18 months of follow-up.

Patient 2, a 68-year-old retired nurse with severe allergic asthma (eosinophil count of 300 cells/µL, elevated IgE of 1411 kU/L) and right-sided bronchiectasis, had frequent uncontrolled symptoms, impaired physical activity, and required rescue nebulization 3–4 times per week. After starting omalizumab, she showed significant improvement over one year, with better asthma control, reduced exacerbations, and no longer needing reliever medications. Her sleep quality also improved, and she felt well enough to have her omalizumab dose reduced from every two weeks to monthly. Unfortunately, she passed away at home just over a year after starting omalizumab, with the cause of death unrelated to the biologic treatment or asthma. The therapy was well tolerated with no adverse effects reported.

Conclusions:

This case series highlights the potential effectiveness of biologics in managing severe allergic or eosinophilic asthma with concomitant bronchiectasis. Notable improvements were observed in exacerbation frequency and the improvement in quality of life, with treatment generally being well tolerated. While these results from a small cohort are promising, larger studies are necessary to better understand the long-term impact of biologics in patients with this dual diagnosis.

Conflict of interest(s) (if any – not included in the 500 words):
None.

[80] [1.46.80] Efficacy of Brensocatib in Patients with Eosinophilic Inflammation in Bronchiectasis: An Analysis of the ASPEN Trial

James Chalmers[1]; Patrick Flume[2]; Anthony De Soyza[3]; Pierre-Regis Burgel[4]; Charles Daley[5]; Sebastian Fucile[6]; Vivian Shih[6]; Ariel Teper[6]; Hannah Shorb[6]; Kevin Mange[6]; Carlos Fernandez[6]

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Background/Aims: Non-cystic fibrosis bronchiectasis (hereafter bronchiectasis) is a chronic and progressive respiratory disease. Neutrophilic inflammation plays a key role in the pathophysiology of bronchiectasis. Neutrophil serine proteases (NSPs), especially neutrophil elastase, have been associated with disease progression and poorer clinical outcomes. Brensocatib, an oral, selective, competitive, and reversible inhibitor of dipeptidyl peptidase 1, prevents activation of NSPs. In the phase 3, randomized, double-blind ASPEN trial (NCT04594369), treatment with once-daily brensocatib 10- and 25-mg significantly reduced the annualized rate of adjudicated pulmonary exacerbations over 52 weeks vs placebo; the 25-mg dose also significantly reduced lung function decline and nominally improved patient-reported symptoms. Eosinophilia is also present in ~20% of patients with bronchiectasis; a subtype of the condition, which has been called eosinophilic inflammation in bronchiectasis. The significance and impact on treatment outcomes are unclear. Here, we report ASPEN subgroup analysis findings in patients with and without eosinophilic inflammation in bronchiectasis.

Methods: ASPEN enrolled patients with bronchiectasis and a history of pulmonary exacerbations in the 12 months prior to screening (adults [18-85 years], ≥2; adolescents [12-<18 years], ≥1). Patients were randomized to receive once-daily brensocatib (10- or 25-mg) or matching placebo for 52 weeks (adults, 1:1:1; adolescents, 2:2:1). Subgroup analyses were explored in patients with high (≥300/µl) or low (<300/µl) blood eosinophil counts at screening. Endpoints were annualized exacerbation rate, time to first exacerbation, proportion of patients remaining exacerbation-free, rate of severe exacerbation, change in post-bronchodilator forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) at 52 weeks, change in Quality of Life-Bronchiectasis Respiratory Symptoms Domain score (QOL-B RSS) at 52 weeks, and safety.

Results: Demographics and baseline characteristics were balanced between subgroups, with

the exception of lower lung function and higher inhaled corticosteroid use in the high eosinophil subgroup (see Table). Consistent with overall ASPEN results, brensocatib 10- and 25-mg reduced the annualized rate of exacerbations, prolonged the time to first exacerbation, and increased the odds of remaining exacerbation-free in both subgroups (see Table). Brensocatib 25-mg reduced both FEV_1 and FVC decline, and improved QOL-B RSS at week 52 vs placebo regardless of baseline blood eosinophil count (see Table). Adverse events were similar across treatment groups, and consistent with the overall ASPEN results.

Conclusions: Consistent with the overall study population, both brensocatib doses reduced the annualized rate of exacerbations, and brensocatib 25-mg also reduced lung function decline and nominally improved patient-reported outcomes regardless of high or low blood eosinophil counts at baseline.

Conflict of interest(s) (if any – not included in the 500 words):

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Pierre-Régis Burgel: grants from Vertex and GSK, outside the submitted work. Dr Burgel also reports Clinical trials: advisory activity for AstraZeneca, Chiesi, GSK, Insmed Incorporated, MSD, Viatris, Vertex, Zambon; substantial financial contributions to the budget of his institution: Association Vaincre la Mucoviscidose, Filière MUCO-CFTR, GSK, Société Française de la Mucoviscidose, and Vertex.

Charles Daley: grant support, advisory board fees, and consulting fees from Insmed Incorporated. Dr. Daley also reports grant support from AN2 Therapeutics, Bugworks, Juvabis, and Paratek Pharmaceuticals; advisory board work with AN2 Therapeutics, AstraZeneca, Cepheid, Galapagos, Hyfe, MannKind, Matinas Biopharma, NobHill, Spero Therapeutics, and Zambon; consulting with Genentech and Pfizer; data monitoring committee work with the Bill & Melinda Gates Foundation, and Otsuka Pharmaceutical.

Sebastian Fucile, Ariel Teper, Hannah Shorb, Kevin Mange, and Carlos Fernandez are employees and shareholders of Insmed Incorporated.

Vivian H. Shih was an employee of Insmed Incorporated for the duration of the study.

[81] [1.42.81] Lung Function in Patients With Non-Cystic Fibrosis Bronchiectasis By Prespecified Subgroups in the Phase 3, Randomized, Double-Blind, Placebo-Controlled Aspen Trial

Timothy Aksamit[1]; James Chalmers[2]; Pierre-Regis Burgel[3]; Charles Daley[4]; Anthony De Soyza[5]; Charles Haworth[6]; David Mauger[7]; Michael Loebinger[8]; Naoki Hasegawa[9]; Kozo Morimoto[10]; Felix Ringshausen[11]; Kevin Mange[12]; Ariel Teper[12]; Carlos Fernandez[12]; Chunpeng Fan[12]; Xiangmin Zhang[12]; Mark Metersky[13]

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Background/Aims: Non-cystic fibrosis bronchiectasis (hereafter bronchiectasis) is a chronic, progressive, inflammatory respiratory disease with diverse causes and variable clinical features. Brensocatib, an oral, selective, competitive, and reversible inhibitor of dipeptidyl peptidase 1 (DPP1), prevents activation of neutrophil serine proteases, key mediators of neutrophilic inflammation. In the global, phase 3, randomized, double-blind ASPEN trial (NCT04594369), treatment with once-daily brensocatib 10- and 25-mg significantly reduced the annualized rate of adjudicated pulmonary exacerbations over 52 weeks (primary endpoint) vs placebo by 21% (*P*=0.0019) and 19% (*P*=0.0046), respectively. Post-bronchodilator forced expiratory volume in 1 second (FEV_1) at week 52 (secondary endpoint) declined from baseline by 62 mL in placebo-treated patients vs declines of 50 mL (*P*=0.3841) and 24 mL (*P*=0.0054) in brensocatib 10- and 25-mg groups, respectively. Here we report change in post-bronchodilator FEV_1 at week 52 for prespecified subgroups of patients in the ASPEN trial.

Methods: ASPEN enrolled patients with bronchiectasis and a history of pulmonary exacerbations in the 12 months prior to screening (adults [18-85 years], ≥2; adolescents [12-<18 years], ≥1). Patients were randomized to receive once-daily brensocatib (10- or 25-mg) or matching placebo for 52 weeks (adults, 1:1:1; adolescents, 2:2:1). Adults were stratified by

screening sputum *Pseudomonas aeruginosa* culture status, number of exacerbations in the 12 months before screening, and geographic region. Prespecified subgroup analyses of primary and secondary endpoints included baseline characteristics of age, sex, race, ethnicity, number of exacerbations in the prior 12 months (2, ≥3), chronic antibiotic use, maintenance use of macrolides, *P. aeruginosa* colonization status, Bronchiectasis Severity Index, bronchiectasis-computed tomography score (<median, ≥median), FEV_1 % predicted (<50%, ≥50%), region, eosinophil count (<300 cells/µL, ≥300 cells/µL), smoking status, use of inhaled steroids, history of asthma, history of chronic obstructive pulmonary disease, and hospitalization in prior 24 months. Results on stratification factor subgroups are reported.

Results: Consistent with overall ASPEN results, least squares mean difference for brensocatib 25-mg demonstrated a reduced decline in post-bronchodilator FEV_1 at week 52 vs placebo for all prespecified subgroups, including ***P. aeruginosa* status,** (*positive* 40 mL [95% CI, 2-78], *negative* 37 mL [2-73]), **number of exacerbations in the prior 12 months** (*2* 38 mL [7-70], *≥3* 35 mL [-16-87]), and **geographic region** (*North America* 77 mL [-5-159], *Europe* 35 mL [-8-78], *Japan* 97 mL [32-162], *rest of world* 20 mL [-20-60]); positive values indicate less decline vs placebo. Similarly, results for patients treated with brensocatib 10-mg among subgroups were aligned with the overall trial population. The incidence of adverse events (AEs) was similar across treatment groups. The most common AEs in the brensocatib groups were COVID-19, nasopharyngitis, cough, and headache. Data for all prespecified subgroups will be presented.

Conclusions: Consistent with the results of the overall ASPEN trial population, brensocatib 25-mg reduced FEV_1 decline vs placebo for all subgroups analyzed. These results demonstrate that brensocatib has a positive impact on post-bronchodilator FEV_1 across all subgroups evaluated, an important observation in a heterogeneous disease like bronchiectasis. Previously presented at CHEST 2024.

Conflict of interest(s) (if any – not included in the 500 words):

This study was funded by Insmed Incorporated. Medical writing support was provided by David Cope, PhD, of Envision Pharma Group and funded by Insmed Incorporated.

James D. Chalmers, Pierre-Régis Burgel, Charles L. Daley, Anthony De Soyza, Charles S. Haworth, David Mauger, and Mark L. Metersky served as members of the ASPEN trial steering committee.

Timothy R. Aksamit, James D. Chalmers, Pierre-Régis Burgel, Charles L. Daley, Anthony De Soyza, Charles S. Haworth, Michael R. Loebinger, and Mark L. Metersky were investigators in the ASPEN trial.

Due to lack pf space, conflicts of interest for individual authors are included in the accompanying document.

[108] [1.48.108] Barriers to Guideline-Directed Therapy for Stable Non- Cystic Fibrosis Bronchiectasis in Australia and New Zealand: A Narrative Review

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[1]*Department of Respiratory and Sleep Disorders Medicine, The Royal Melbourne Hospital, Melbourne, Australia;* [2]*Department of Medicine, University of Melbourne, Melbourne, Australia*

Background/Aims: Bronchiectasis is a chronic lung condition frequently associated with recurrent infections, progressive respiratory decline and a significant impact on quality of life. The burden of disease in Australia and New Zealand is significant, with high healthcare costs and a particularly high incidence of disease and hospitalization rates among Māori, Pasifika, and Aboriginal and Torres Strait Islander populations. Although major society guidelines recommend a number of evidence-based pharmacological and non-pharmacological therapies to improve patient outcomes, access to and uptake of these therapies remain limited.

Methods: We conducted a narrative review regarding access to guideline-directed therapies for patients with bronchiectasis not related to cystic fibrosis in Australia and New Zealand. A literature search was performed. Additionally, we reviewed major society guidelines and government healthcare sources, including subsidy schedules (PBS and PHARMAC). The review focused on treatments for patients with stable bronchiectasis.

Results: Access to recommended pharmacological therapies is limited. Macrolides are not TGA approved nor subsidised by the PBS in Australia. They are only available via the special authority under PHARMAC in New Zealand for an unapproved indication. Similarly, inhaled antibiotics are not available on the government subsidy schedule in either country. Whilst some patients may be able to access these medications through their local healthcare networks, access is variable and the costs to patients may be significant. Systemic barriers to participation in pulmonary rehabilitation include limited service availability, workforce shortages and geographic inequity. At an individual level, uptake may be limited by low referral rates from treating clinicians, and a reluctance to participate in pulmonary rehabilitation amongst those patients referred. A limited understanding of the benefits and details of pulmonary rehabilitation was identified as a significant factor in both cohorts. Effective airway clearance techniques (ACT) often require the use of adjunctive equipment that is not consistently subsidised, while studies investigating access to specialist physiotherapy for ACT are lacking. A table outlining the costs of guideline recommended therapies will be included in the presentation at the conference.

Conclusions:

Bronchiectasis remains associated with significant morbidity and healthcare costs. The uptake of guideline recommended therapy in Australia and New Zealand remains

considerably limited. Medication access is hampered by a lack of public subsidy and regulatory approval for key therapies, while non-pharmacological interventions are constrained by workforce limitations, service design, and inequitable access. Patients enrolled in registries may overrepresent those already accessing specialised care, suggesting that the uptake of guideline-recommended therapies may be lower amongst other populations. A call for coordinated action to improve access to guideline-directed care is required. Education of both health care providers and patients regarding the benefits of guideline-recommended therapies may improve uptake of these treatments and patient outcomes. Strategies to improve access to care include education campaigns and further trials, including economic analyses, to support regulatory approval and subsidy of existing and novel therapies.

Conflict of interest(s) (if any – not included in the 500 words):

N/A

[133] [1.45.133] Reducing the treatment burden for people with bronchiectasis: a protocol for deprescribing inhaled corticosteroids

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Background/Aims:

Inhaled corticosteroids (ICS) are frequently prescribed for people with bronchiectasis, often without evidence of their benefit. ICS use is associated with an increased risk of pneumonia and other adverse effects, and contributes to the already significant treatment burden for people with bronchiectasis. Recent EMBARC registry analysis shows around a third of people with bronchiectasis were prescribed ICS without a clear indication. Routine ICS deprescribing is rarely undertaken and there are no evidence-based guidelines on how to approach this. This project aims to implement a structured ICS deprescribing protocol within a specialist bronchiectasis clinic to reduce patient treatment burden while maintaining symptom control.

Methods:

We designed a single-centre quality improvement protocol in a specialist bronchiectasis clinic with approximately 800 patients. Adults with confirmed bronchiectasis and established ICS use will be identified. Exclusion criteria include history of clinically-confirmed asthma, COPD, allergic bronchopulmonary aspergillosis, elevated blood eosinophils (>0.3x10^9) or inflammatory bowel disease-associated bronchiectasis.

Briefly, the deprescribing protocol follows a stepwise approach:

1. Baseline assessment: review for historical asthma diagnosis, documented bronchodilator response, blood eosinophilia or IgE level, exacerbation frequency and inhaler technique for DPI switch where possible.

2. Structured ICS reduction: For patients identified reduction of ICS will follow as per Table 1.

Table 1. Inhaled Corticosteroid (ICS) Stepdown Protocol

High dose ICS/LABA or ICS/LABA/LAMA	Step down to medium dose ICS/LABA or ICS/LABA/LAMA for 4-8 weeks
Medium dose ICS/LABA or ICS/LABA/LAMA	Step down to medium dose ICS/LABA or ICS/LABA/LAMA for 4-8 weeks

Low dose ICS/LABA	Switch to PRN bud/formoterol or bdp/formoterol for 4-8 weeks

Interim phonecall with patient (approximately 4-8 weeks) to check compliance and ensure stability. Patients reporting worsening symptoms will be invited for spirometry, reversibility, full blood count (FBC) and fractional exhaled nitric oxide (FeNO).

3. Follow up assessment at 6 months for outcome measures and repeat markers of type 2 inflammation.

Outcomes measures

We will evaluate the proportion of patients undergoing successful ICS deprescribing without worsening symptoms, increased frequency of exacerbations or deteriorating spirometry. Our secondary evaluation will include reduction in treatment burden (number of daily inhalers and medications), plus a calculation of theoretical reduction in carbon footprint. In addition, we will examine transition to carbon-friendly inhalers as part of our attempt to address concerns of therapy burden on the patient but also the environment.

Results:

We expect that a significant proportion of patients will successfully discontinue ICS without deterioration in clinical status, reducing their overall medication burden. This project will also provide real-world evidence on the feasibility and safety of ICS deprescribing in a bronchiectasis population.

Conclusions:

This protocol offers a structured approach to ICS deprescribing in people with bronchiectasis, aligning with current guideline recommendations for other chronic respiratory conditions. By reducing unnecessary medication use, we aim to reduce the risk of ICS-related adverse effects and reduce the burden of treatment for people with bronchiectasis.

Conflict of interest(s) (if any – not included in the 500 words):
No conflicts of interest to disclose.

[150] [1.51.150] A Phase II study (CLAIRAFLY®) to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of the dipeptidyl peptidase 1 (cathepsin C) inhibitor BI 1291583 in adults with cystic fibrosis bronchiectasis

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Background/Aims:

Cystic fibrosis (CF) lung disease (CF bronchiectasis [CFBE]) is characterised by chronic neutrophilic inflammation resulting from dysregulated neutrophil serine protease (NSP) activity. NSPs are activated by dipeptidyl peptidase 1 (DPP1, or cathepsin C). In the Phase II AIRLEAF® study, the DPP1 inhibitor BI 1291583 reduced pulmonary exacerbation (PEx) risk in adults with non–CFBE. We present results from a Phase II study (CLAIRAFLY®; NCT05865886) investigating the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of BI 1291583 in adults with CFBE, comparing these results to those from AIRLEAF® to evaluate if people with CFBE can be included as another aetiology of BE in a Phase III (AIRTIVITY®).

Methods:

This double-blind study randomised 22 adults (2:1) to receive once-daily BI 1291583 (5 mg) or placebo for 12 weeks. Participants had a CF diagnosis, computed tomography-confirmed BE and a history of PExs requiring antibiotic treatment prior to screening (either ≥2 PExs in the

past year or ≥1 PEx in the past year plus St. George's Respiratory Questionnaire Symptoms score >40). Randomisation was stratified by CF transmembrane conductance regulator modulator therapy (CFTRmt) use. The primary endpoint was the occurrence of treatment-emergent adverse events (TEAEs) up to Week 16. Potential mode-of-action (MoA)-related adverse events (AEs) were also assessed. Secondary endpoints examined PK and PD (sputum neutrophil elastase [NE] activity).

Results:

Demographic and baseline characteristics were generally similar between people in the BI 1291583 (n=15) and placebo (n=7) groups. Comparing TEAEs in the BI 1291583 versus placebo group, the rates of all AEs, (93.3% [n=14] versus 85.7% [n=6]), serious AEs (SAEs) (33.3% [n=5] versus 14.3% [n=1]) and drug-related AEs (13.3% [n=2] versus 0% [n=0]) were similar. All SAEs required hospitalisation/prolonged hospitalisation (33.3% [n=5] of BI 1291583-treated people versus 14.3% [n=1] of placebo-treated people). Potential MoA-related AEs occurred only in the BI 1291583 group, with preferred terms skin exfoliation (13.3% [n=2]; considered mild and self-resolving whilst continuing treatment with BI 1291583) and gingival recession (6.7% [n=1]) at 1 tooth. The safety profile of, and PK (exposure) of BI 1291583 in CLAIRAFLY® was comparable to AIRLEAF®. PD (percentage NE inhibition) was similar across both studies: at Week 8 of CLAIRAFLY®, NE inhibition in the BI 1291583-treated individuals was 89%, which is similar to that observed in people with non–CFBE in AIRLEAF®.

Conclusions:

The safety, tolerability, PK and PD of BI 1291583 were similar in both CLAIRAFLY® and AIRLEAF®. These findings support the inclusion of both people with CFBE and non–CFBE in the Phase III AIRTIVITY® study.

Conflict of interest(s) (if any – not included in the 500 words):

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[173] [1.47.173] Results from a Phase II study (AIRLEAF®) of the dipeptidyl peptidase 1 (cathepsin C) inhibitor BI 1291583 in adults with bronchiectasis

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Background/Aims:

Uncontrolled neutrophil serine protease (NSP) activity contributes to the vicious vortex of airway neutrophilic inflammation, infection, mucociliary dysfunction, and structural lung damage in bronchiectasis, resulting in morbidity and pulmonary exacerbations (PExs). Dipeptidyl peptidase 1 (DPP1; or cathepsin C) inhibition can reduce levels of active NSPs, thus dampening the impact of this vortex. We present the results of a Phase II dose-finding study that assessed efficacy and safety of the DPP1 inhibitor BI 1291583 in adults with bronchiectasis (AIRLEAF®).

Methods:

In this double-blind study, 322 participants with computed tomography-confirmed bronchiectasis were randomised to one of three once-daily doses of BI 1291583 (1mg, 2.5mg or 5mg) or placebo (≥24–48 weeks of treatment). Participants had a history of PExs requiring

antibiotic treatment prior to screening (either ≥2 PExs in the past year or ≥1 PEx in the past year plus a St. George's Respiratory Questionnaire Symptoms score >40). A multiple comparison procedure and modelling approach was used to assess the primary objective, to demonstrate a non-flat dose–response curve based on the primary endpoint: time to first PEx up to Week 48. The secondary objective was to demonstrate the superiority of BI 1291583 5mg versus placebo on time to first PEx up to Week 48, as well as on the key secondary endpoint: the rate of PExs up to Week 48. Further objectives included assessing the effect of BI 1291583 on severe PExs, and lung function- and quality of life (QoL)-related parameters. Adverse events (AEs) were monitored throughout the study.

Results:

A statistically significant dose-dependent benefit of BI 1291583 over placebo on time to first PEx up to Week 48 (E_{max}; adjusted p=0.0448) was observed, meeting the primary objective. BI 1291583 2.5mg and 5mg numerically reduced the risk of a PEx by ~30% over the treatment period (2.5mg: adjusted HR, 0.66 [95% CI, 0.40–1.08]; 5mg: adjusted HR, 0.71 [95% CI, 0.48–1.05]). Furthermore, compared with placebo, the reduction in the annual rate of PExs was numerically higher with the 2.5mg dose (32%) than with the 5mg dose (11%). BI 1291583 2.5mg reduced the risk of experiencing a severe PEx within 48 weeks compared with placebo (HR, 0.12 [95% CI, 0.02–0.95]). At Week 24, the greatest numerical increases from baseline in lung function were seen with BI 1291583 2.5mg. Patient-reported outcomes of QoL showed a trend in favour of the BI 1291583 2.5mg and 5mg doses. BI 1291583 1mg was identified as a subtherapeutic dose. Overall, all three doses of BI 1291583 had a similar safety profile to placebo.

Conclusions:

Results from AIRLEAF® show that the DPP1 inhibitor BI 1291583 at a dose of 2.5mg and 5mg reduced the risk of experiencing a PEx in adults with bronchiectasis, while demonstrating a similar safety profile to placebo. These results support the continued clinical development of BI 1291583, with the 2.5mg dose to be assessed in the Phase III AIRTIVITY® study that is planned to begin in Q2 2025.

Conflict of interest(s) (if any – not included in the 500 words):

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[184] [1.50.184] Bacterial load, respiratory symptoms and inhaled antibiotic treatment in adults with bronchiectasis

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Background/Aims: Inhaled aztreonam improves symptoms, particularly cough and sputum production, in patients with bronchiectasis and Gram-negative bacterial colonization, with baseline bacterial load predicting treatment response in Western populations. However, evidence for inhaled tobramycin, a widely used alternative, remained limited, particularly in non-Western settings. To investigate the impact of baseline bacterial load on respiratory symptom response to inhaled tobramycin, and identify specific symptom improvements in adults with bronchiectasis and *P. aeruginosa* infection, using the Quality-of-Life Bronchiectasis Respiratory Symptoms Scale (QoL-B-RSS).

Methods: We performed a post hoc analysis of a randomized, placebo-controlled trial involving 357 adults with bronchiectasis and *P. aeruginosa* infection in China. Patients received inhaled tobramycin or placebo in two 28-day on/off cycles, with follow-up to day 85. Respiratory symptoms were assessed using the QoL-B-RSS (minimum clinically important difference [MCID], 8 points). Treatment response was stratified by baseline bacterial load (low: $<10^5$ cfu/g; moderate: 10^5-10^6 cfu/g; high: $\geq 10^7$ cfu/g), measured by quantitative sputum culture.

Results: At baseline, 68.3% of patients had high and 29.1% had moderate bacterial load. Compared with placebo, significant QoL-B-RSS improvements were observed with tobramycin in the high (mean difference of 8.28, 95%CI 5.45-11.10; $p<0.0001$) and moderate (mean difference of 6.51, 95% CI 2.68-10.34; $p=0.0011$) bacterial load groups on day 29, with benefits sustained to day 85. A greater proportion of tobramycin-treated patients exceeded the MCID versus placebo in both high (48.3% vs 13.2%; $p<0.001$) and moderate (45.5% vs 9.4%; $p<0.001$) groups at day 29. Inhaled tobramycin significantly improved specific QoL-B-RSS items, including cough, sputum production, sputum color, congestion, breathlessness on daily activity and chest pain at both day 29 and day 85 (all $p<0.05$).

Conclusions: Inhaled tobramycin significantly alleviates respiratory symptoms in patients with bronchiectasis and *P. aeruginosa* infection, particularly in those with high baseline bacterial load. Improvements in cough, sputum, congestion, breathlessness and chest pain support its role as an effective symptom-targeted therapy for this population.

Conflict of interest(s) (if any – not included in the 500 words): All authors have no conflict of interest to declare.

Figure 1. Changes in QoL-B-RSS from baseline during the treatment in patients with bronchiectasis and *P. aeruginosa*, in high and moderate bacterial load groups, respectively.

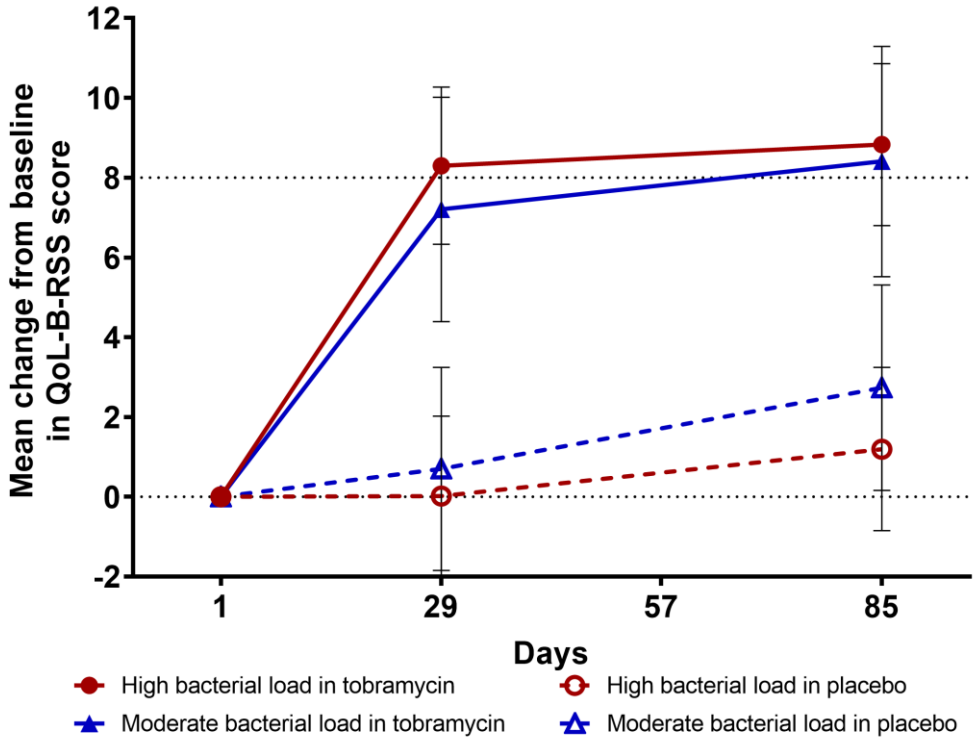
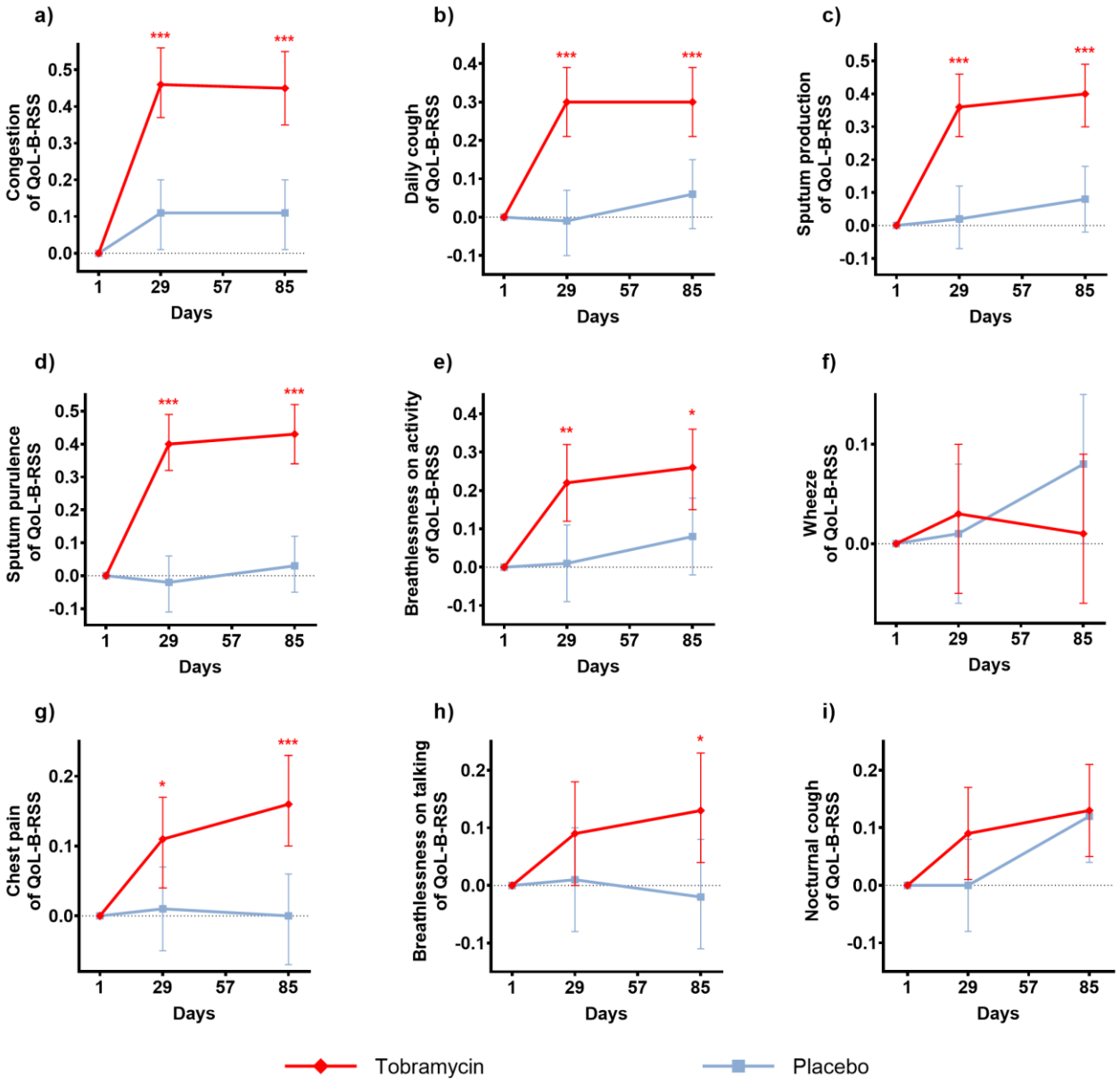


Figure 2. Mean changes from baseline in individual symptoms of QoL-B-RSS comparing inhaled tobramycin versus placebo in patients with high and moderate bacterial loads.



***: p<0.001; **: p<0.01; *: p<0.05.

[186] [1.52.186] Impact of Elexacaftor/Tezacaftor/Ivacaftor (Trikafta) on bone density in patients with Cystic Fibrosis: a retrospective study.

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CFTR modulators have revolutionised the treatment of cystic fibrosis lung disease for individuals with F508del mutation within the CFTR gene. We know that CFTR modulators improve lung function, weight and quality of life, however there is a paucity of data regarding its effect on bone density. Given bone loss in CF is multifactorial but includes poor nutrition, chronic inflammation and decreased mobility, one would hypothesise that treatment with CFTR modulators would slow bone loss or improve it in an otherwise young adult population.

To answer this we conducted a retrospective chart review analysing bone density measurements before and after the use of the highly effective CFTR modulator, Elexacaftor/Tezacaftor/Ivacaftor (Trikafta).

32 patients treated with Trikafta had bone density measurements available before and after treatment. The mean age was 36.1 years old, with 43% of male. The median time between dual energy X-ray absorptiometry (DEXA) scan was 4.15 years (IQR 3.48-5.08). 28% of individuals had low bone density in at least 1 of the 3 tested regions (spine/hip/femur) prior to treatment with Trikafta. Surprisingly more individuals (34% vs 28%) had low done density following treatment with Trikafta. Interestingly, when analysed using a paired group analysis, there was no significant difference in individual scores across each of the regions tested (p values >0.05) after initiation of Trikafta. Bone loss continued despite the introduction of Trikafta with a 26% loss of bone density measured in the femoral neck between serial DEXA scans over the average of 4.15 years. This amounts to approximately 6% loss per year, much higher than the age expected decline of less than 1% per year.

In contrast, there was global improvement in lung function across these 32 patients, with median FEV1 (% predicted) values increasing by 7%. From a nutritional perspective, there was a 4kg weight gain across the 4.15 years.

This study is limited by its retrospective nature and potentially confounded by the timing of the post Trikafta DEXA scan. Nonetheless, this data suggests that Trikafta does not slow bone loss in individuals living with cystic fibrosis despite significant improvements in lung function and weight over time. This highlights the importance of ongoing optimisation of bone health and screening for osteoporosis within this patient cohort.

[188] [1.41.188] Efficacy, Safety, Cost and Antimicrobial Resistance Potential of Long-term Inhaled Colistimethate Sodium in Bronchiectasis: A Real-World Regional Australian Single-Centre Experience

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Background/Aims: Bronchiectasis (BE) is a progressive lung disease characterised by abnormal airway dilation, chronic infection and frequent exacerbations. Chronic *Pseudomonas aeruginosa* infection is associated with increased exacerbation frequency and greater mortality. Long-term inhaled antibiotic use in this cohort is suggested in international guidelines, however randomised clinical trial data demonstrating benefit has been inconsistent. Recently, the PROMIS-I Trial demonstrated inhaled colistimethate sodium (IC) delivered via the I-Neb to reduce exacerbation frequency and improve health-related quality of life. Our real-world study reports on our local, regional Australian experience of IC use in pwBE with a focus on efficacy, safety, antimicrobial resistance and healthcare-related cost.

Methods: We conducted a retrospective cohort study between 1st Jan 2019 and 31st Dec 2023 of pwBE with frequent exacerbations and chronic *P. aeruginosa* infection treated with IC for > 6 months at the Sunshine Coast University Hospital (SCUH), a regional tertiary centre in Queensland, Australia. We captured baseline demographic and clinical characteristics and compared annual exacerbation and admission rates for the 12-months prior-to and post-IC use. Additionally, we captured pre/post spirometry and patient-reported adverse events, and underwent post IC antimicrobial resistance testing where feasible. Finally, we compared the direct healthcare-related costs per patient based on the total annual drug-supply cost vs. the total costs for BE exacerbation-related admissions.

Results: Fourteen patients (mean age 69; 90% female) treated with IC for > 6 months were captured over the 5-year period. Five (36%) had idiopathic bronchiectasis, 3 (21%) post-infectious; 3 (21%) allergic bronchopulmonary aspergillosis / Asthma; 2 CFTR-heterozygosity; and 1 (0.7%) neonatal lung disease and connective-tissue disease respectively. Mean baseline Bronchiectasis Severity Index (BSI) was 16 (range 12-20), and mean pre-IC FEV1 was 52% (range 18%-98%). Seven patients were co-colonised with other potential pathogens including *Staphylococcus aureus*, *Aspergillus sp.*, *Achromobacter sp.,* and non-tuberculous mycobacteria. Ten (71%) were on ICS/LABA/±LAMA inhalers, and 9 (64%) were on long-term oral macrolides. All patients utilised a non-I-Neb Jet Nebuliser (JN - Salter NebuTech HDN ©). Mean annual exacerbation rate pre-IC use was 4.21 (range 3-6) compared to 1.21 (range 0-6)

on IC ($p < 0.05$). Mean annual admission rate pre-IC use was 2.64 (range 1-4) compared to 1.07 (range 0-9) on IC ($p < 0.05$). Four patients (28%) reported adverse events including chest tightness (2), cough (1), and haemoptysis (1); three (21%) discontinued IC use within the 12-month treatment period. No post-IC antimicrobial resistance was detected according to broth microdilution susceptibility testing. Estimated healthcare-related cost saved per individual patient on IC was $10,007 per annum.

Conclusions: Our real-world experience of IC use in pwBE bronchiectasis suffering frequent exacerbations and chronic *P. aeruginosa* infection demonstrates clinically notable efficacy, generally good tolerance amongst a frail patient cohort, no antimicrobial resistance development, and a reduction in treatment-associated healthcare cost.

Conflict of interest(s): Nil

[202] [1.53.202] Initial assessment of the "Chronic Airways Assessment Test" (CAAT™) as a drug development tool in bronchiectasis

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Background/Aims: The CAAT™ is an adaptation of the COPD Assessment Test (CAT™) introductory statement to support its application in other conditions. The aim of this study was to assess the potential of this simple 8 question questionnaire as a drug development tool in bronchiectasis.

Methods: The CLIMB study was a Phase 2, randomized, double-blind, placebo-controlled 28 day intervention study of nebulized ARINA-1 in individuals with non-cystic fibrosis bronchiectasis and excess mucus and cough defined by a total CAAT score >10 and a score on question 2 "phlegm in my chest" of >2. Quality of life was assessed at baseline and day 28 of treatment using the CAAT, SGRQ-C and QoLB-Respiratory symptoms (QOL-B RSS). Statistical analysis including Spearman correlation coefficients were calculated using GraphPad Prism 10. The impact of treatment was assessed using least-squares means [95% CI]; significance ($p<0.05$) was assessed by mixed-effects adjusted t-test.

Results: 40 patients were randomized (70% were female). Mean BSI score was 6.8 versus 5.7 in ARINA-1 (n=29) versus placebo (n=11) groups, respectively. At baseline, ARINA-1 versus placebo groups had similar median CAAT scores (20 Vs. 20), mean SGRQ-C (43.4 vs 42.4) and median QoL-B-RSS scores (61.2 in both groups). At baseline, there was a statistically significant correlation between the CAAT and the SGRQ ($r=0.71$; two-tailed t-test $p<0.0001$), SGRQ symptom domain ($r= 0.5682$; $p<0.0001$), and QoL-B RSS (Spearman $r=-0.6194$; $p<0.0001$, **Figure Panel A**). At Day 28, a trend in improvement was observed for CAAT and SGRQ, but not for QoL-B. Individual changes at day 28 in CAAT and SGRQ-total score were modestly correlated (n=23, **Figure Panel B**). Sputum neutrophil elastase and mucus rheology at day 28 were not correlated with PRO scores (data not shown).

Conclusions: The baseline data demonstrated a strong correlation of the CAAT with longer PROs commonly used in bronchiectasis trials, as previously demonstrated for the CAT in the TRIBE cohort (Finch et al. *Chest* 2020). The intervention data highlights a role for the CAAT as a simple and feasible drug development tool to select and enrich trials for symptomatic participants and as a clinical trial outcome measure to determine a therapy's impact on

patient symptoms. To fully define its utility, there are several ongoing CAAT validation efforts in global observational studies in bronchiectasis.

COI:

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CLD reports consulting fees from AN2 Therapeutics, AstraZeneca, Galapagos, Genentech, Hyfe, Insmed, MannKind, Matinas BioPharma Holdings, Inc., NobHill, Paratek Pharmaceuticals, Pfizer, Spero Therapeutics and contracted research with AN2 Therapeutics, Bugworks, Cystic Fibrosis Foundation, COPD Foundation, Insmed, Juvabis, MannKind, Paratek Pharmaceuticals, Renovion, and Verona.

RTS discloses consulting fees from AstraZeneca, Boehringer Ingleheim, Renovion, Roche, GSK, COPD Foundation, GAAPP, ENA Respiratory, Immunomet, Teva, and Itay and Beyond. She is a retiree and shareholder of GSK and holds share options in ENA.

[208] [1.43.208] Targeting the Jagged-1/Notch pathway for the treatment of muco-obstructive lung diseases

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Background/Aims:

Mucus hypersecretion and/or impaired mucociliary clearance is a pathogenic feature of many chronic "muco-obstructive" lung diseases, including non-CF bronchiectasis, primary ciliary dyskinesias, asthma, chronic obstructive pulmonary disease, and cystic fibrosis (CF). This mucus is implicated in symptoms, poor QoL, airflow limitation, airway plugging, recurrent infection, severity, progression and mortality. Jagged-1, one of 5 human Notch receptor ligand members, is involved in cell fate specification. In the lung, Jagged-1, acting predominantly through Notch2, controls the balance of secretory club cells and ciliated cells. Local or systemic inhibition of the Jagged-1/Notch pathway ex vivo and in vivo redirects lineage specification towards ciliated cells and promotes loss of club cells, thus preventing their differentiation into mucus-secreting goblet cells which profoundly reduces mucus burden in the airways. As the Notch pathway is active in multiple other organs, an inhaled intervention which maximizes local-to-systemic therapeutic index is especially suited to maximize clinical benefit and minimize the risk of systemic side effects.

Methods:

Anticalin® proteins derived from human lipocalins can be engineered to bind to their targets with high potency, selectivity and a binding affinity similar to that of antibodies, but with a small size of 15 to 20 kDa. This small size, and their physical stability and robustness, are well suited to inhalation. Here we characterize the inhalable Jagged-1 targeting tool Anticalin, PRS-400, in comparison to a monoclonal anti-JAG1 antibody AMG 430 in *in vitro* (human) and *in vivo* (murine) models

Results:

In vitro: PRS-400 dose-dependent suppressed JAG1-notch signalling in a human luciferase reporter system.In human ALI cultures PRS-400 penetrated mucus, suppressed FOXA3+ goblet cell metaplasia and epithelial remodelling induced by IL-13 and IL-17 and restored FOXJ1+ ciliated cells.
In vivo**:** PRS-400 prevented and reversed goblet cell metaplasia and mucus hypersecretion, epithelial remodelling and restored FOXJ1+ ciliated cells in IL-13, house dust mite "asthma" and bENAC-tg "CF" murine models.

Conclusions:
Targeting the Jagged-1/Notch-2 signalling axis by inhalation, exemplified by PRS-400, shows great potential for the treatment of muco-obstructive lung diseases.

Conflict of interest(s) (if any – not included in the 500 words):

[209] [1.44.209] CERTAIN Study: Ceftolozane/tazobactam continuous infusion for outpatient treatment of exacerbations of Cystic Fibrosis and Bronchiectasis

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Background/Aims:

Infective exacerbations of CF and non-CF bronchiectasis can frequently be managed safely on Outpatient Parenteral Antimicrobial Therapy (OPAT) programs, which entail significant financial and logistical benefits compared with treatment in hospital. Feasibility of OPAT programs is greatly improved by antibiotics being infused over a 24-hour period rather than via bolus several times per day. Many antibiotics that are effective in treating *pseudomonas aeruginosa* and *burkholderia cepacia* complex infections do not meet the acceptable threshold of stability at room temperature, defined by the European and US Pharmacopoeias as >90% stability at 24 hours, and are therefore not feasible options for once-daily OPAT administration. Ceftolozane/tazobactam has recently been demonstrated to meet these standards thus is highly likely to be feasible option for treatment of these infections on OPAT programs. This study will determine whether continuous infusion ceftolozane/tazobactam administered in an OPAT setting is a well-tolerated and practical alternative to other antibiotics for the treatment of acute infective exacerbations in people with cystic fibrosis (CF) and non-CF bronchiectasis. In addition, the study will describe the relative bacterial load over the course of ceftolozane/tazobactam treatment by use of quantitative PCR (qPCR) on sputa; and in vitro antimicrobial susceptibility of respiratory pathogens by antimicrobial susceptibility testing, whole-genome sequencing (WGS), culturomic sequencing, and bioinformatic analysis.

Methods:

This is a phase IV feasibility trial aiming to recruit 30 patients diagnosed with either CF or non-CF bronchiectasis, known to be colonized with either *pseudomonas aeruginosa* or *burkholderia cepacia* complex who have a current exacerbation deemed suitable for treatment on OPAT by their treating physician. Participants are administered intravenous ceftolozane/tazobactam via a volumetric infuser in their home setting, supported by their respective hospitals' OPAT service. Clinical response and adverse event monitoring are performed at mid- and end-treatment reviews, via means of patient-reported symptoms, blood tests and standardised questionnaires. Therapeutic drug monitoring will be performed throughout treatment. Participants are followed up via phone and chart review for 3 months following administration of ceftolozane/tazobactam. Sputa specimens are collected before, during and after the course of ceftolozane/tazobactam and tested as described above.

Results:

To date, 22 patients have been recruited and received the planned treatment course across the three study sites. Thus far treatment has been demonstrated to be safe, well-tolerated and effective. The reported adverse event profile has been consistent with the adverse event profile described in previous studies of ceftolozane/tazobactam, and no SAEs related to the medication have been reported. Full clinical data and the preliminary results of the tested respiratory samples will be presented as study findings.

Conclusions:

Thus far, ceftolozane/tazobactam has been demonstrated to be a safe, well-tolerated and effective alternative to other antimicrobial agents used to treat infectious exacerbations of CF and bronchiectasis associated with these difficult pathogens.

Conflict of interest(s) (if any – not included in the 500 words):

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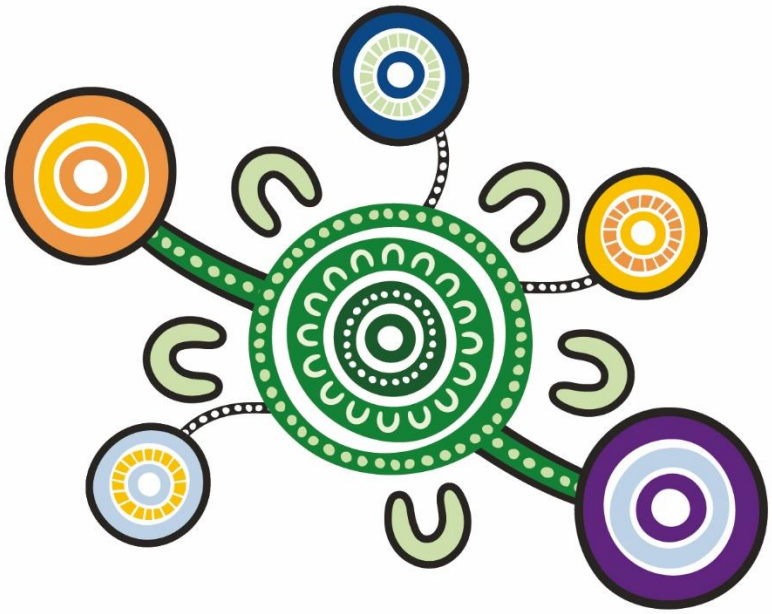

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