

Exacerbation Phenotypes and Treatment Patterns in Non-Cystic-Fibrosis Bronchiectasis: A Prospective Cohort Across Eighteen Months with Microbiological and Radiological Phenotyping

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Abstract — Non-cystic-fibrosis bronchiectasis is increasingly recognised as a clinically important condition with substantial morbidity driven primarily by recurrent exacerbations. We followed 280 adults with established non-CF bronchiectasis prospectively for 18 months at a tertiary respiratory clinic, characterising exacerbation phenotypes, microbiological colonisation patterns, treatment intensities, and outcomes. The cohort showed clear phenotypic separation by exacerbation frequency: 102 patients (36.4%) were frequent exacerbators (≥ 3 events per year), 138 (49.3%) were infrequent exacerbators (1-2 events), and 40 (14.3%) experienced no exacerbations during follow-up. Chronic *Pseudomonas aeruginosa* colonisation, identified in 78 patients (27.9%) at baseline, was the strongest single predictor of frequent exacerbator status (adjusted OR 4.32). Radiological severity by Reiff score, FEV1 below 50% predicted, and NTM colonisation also independently predicted frequent exacerbator phenotype. Intensive treatment combining inhaled antibiotic, macrolide prophylaxis, and structured airway clearance was associated with substantially longer time to next exacerbation than standard care. The findings support phenotype-guided treatment intensification, with particular priority for patients with chronic *Pseudomonas* or severe radiological disease.

Keywords — Bronchiectasis; Exacerbations; *Pseudomonas Aeruginosa*; Non-Tuberculous *Mycobacteria*; Macrolide Prophylaxis; Inhaled Antibiotics; Phenotyping.

1. Introduction

Bronchiectasis was, for much of the twentieth century, regarded as a residual condition of childhood infection relatively uncommon in adult populations of high-income countries and rarely a subject of focused clinical research. The picture has shifted in recent decades. Better imaging and recognition of post-infectious, post-tuberculous, immune-deficient, and connective-tissue-related aetiologies have substantially raised documented prevalence. South Asian centres see a particularly diverse case mix, with post-tuberculous bronchiectasis remaining a common substrate alongside increasingly recognised idiopathic and post-infectious presentations. Exacerbations drive most of the morbidity, mortality, and healthcare utilisation associated with bronchiectasis. The frequent exacerbator phenotype three or more events per year has been shown to predict accelerated lung function decline, more frequent hospitalisation, and lower quality of life. Identifying this phenotype prospectively, understanding its drivers, and matching treatment intensity to phenotype have become the central operational tasks of contemporary bronchiectasis care (Jha, Kumar, & Neha, 2026; Bhatnagar, Kumar, & Shivam, 2026). We followed 280 adults with non-CF bronchiectasis prospectively at our tertiary respiratory clinic over 18 months, with structured exacerbation surveillance, baseline microbiological characterisation, longitudinal lung

function assessment, and detailed treatment documentation. The aims were to describe the phenotypic distribution, identify independent predictors of frequent exacerbator status, examine how current treatment intensity maps to phenotype, and assess outcome differences across treatment strategies.

2. Methods

The study was conducted at the bronchiectasis clinic of a tertiary respiratory service between September 2022 and March 2024. Adults aged 18 or older with bronchiectasis confirmed on thin-section CT, at least one exacerbation in the preceding 24 months, and capacity for prospective follow-up were eligible. Cystic fibrosis on genetic testing or sweat chloride, primary ciliary dyskinesia, and active mycobacterial disease at enrolment were exclusion criteria. The final cohort comprised 280 patients with adequate follow-up data. All patients underwent baseline thin-section CT scored using the modified Reiff system, capturing the number of lobes affected and the predominant bronchiectasis pattern (cylindrical, varicose, cystic). Sputum was collected at baseline and at every visit, with routine bacterial culture, extended culture for fastidious organisms, and mycobacterial culture in patients with suspicious features. Chronic *Pseudomonas* colonisation was defined as isolation in two or more sputum samples at least three months apart, in line with international consensus

criteria. NTM colonisation required isolation of the same species in two or more sputum samples supported by clinical and radiological features. Exacerbations were defined per the 2017 international consensus: an increase in three or more cardinal respiratory symptoms (cough, sputum volume, sputum purulence, dyspnoea, fatigue, haemoptysis) for at least 48 hours that prompted a change in treatment by the responsible clinician. Severity was graded as moderate (managed in the community) or severe (requiring hospitalisation or intravenous antibiotic). Patients reported exacerbations through a structured telephone helpline and an electronic patient-reported outcome platform, with verification through clinic visits. Primary outcomes were annual exacerbation rate and proportion meeting the frequent exacerbator definition (≥ 3 events per year). Secondary outcomes included rate of severe exacerbations, hospitalisations, 12-month FEV1 decline, and treatment-emergent adverse events. Multivariable logistic regression identified independent predictors of frequent exacerbator status, and Cox regression assessed time to next exacerbation by treatment intensity stratum.

3. Results

3.1 Cohort Description

Table 1. Baseline characteristics of the bronchiectasis cohort (n=280)

Characteristic	Value
Age, mean (SD), years	56.8 (15.4)
Female sex, n (%)	162 (57.9)
Never smoker, n (%)	178 (63.6)
Aetiology: post-infectious / post-TB, n (%)	104 (37.1)
Aetiology: idiopathic, n (%)	82 (29.3)
Aetiology: connective tissue disease–associated, n (%)	32 (11.4)
Aetiology: ABPA, n (%)	22 (7.9)
Aetiology: immunodeficiency, n (%)	14 (5.0)
Aetiology: other identified, n (%)	26 (9.3)
BMI, mean (SD), kg/m ²	22.4 (4.6)
Underweight (BMI <18.5), n (%)	42 (15.0)
FEV1, mean (SD), % predicted	62.4 (22.6)
FEV1 <50% predicted, n (%)	84 (30.0)
Reiff score: mild (1-2 lobes), n (%)	94 (33.6)
Reiff score: moderate (3-4 lobes), n (%)	112 (40.0)
Reiff score: severe (≥ 5 lobes), n (%)	58 (20.7)
Reiff score: cystic / very severe, n (%)	16 (5.7)
Exacerbations in preceding 12 months, mean (SD)	2.4 (1.8)
Comorbid COPD, n (%)	48 (17.1)
Comorbid asthma, n (%)	68 (24.3)

3.2 Microbiological Distribution

Baseline sputum cultures yielded a pathogen in 84.3% of cases, with *Pseudomonas aeruginosa* the single most common isolate (Figure 1). Chronic *Pseudomonas* colonisation was confirmed in 78 patients (27.9%) after follow-up sampling. *Haemophilus influenzae*, the next most common, was isolated in 56 patients (20.0%); chronic colonisation was confirmed in 38. NTM, isolated in 18 patients (6.4%), reached criteria for clinically significant colonisation in 12. The remaining 44 patients (15.7%) had no organism isolated at baseline despite repeated sampling.

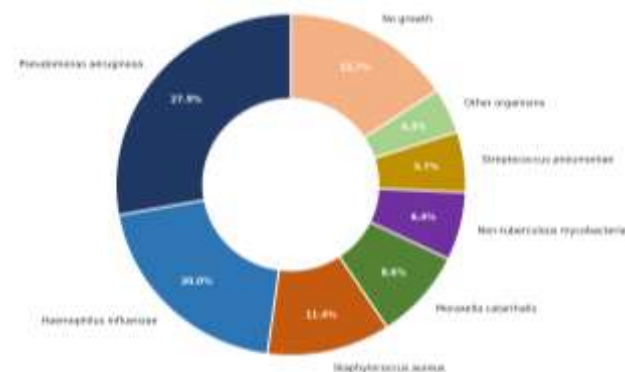


Fig.1: Microbiological distribution from baseline sputum cultures

Table 2. Exacerbation phenotypes by patient subgroup

Subgroup	Frequent exacerbator, n (%)	Infrequent, n (%)	No exacerbation, n (%)
Overall (n=280)	102 (36.4)	138 (49.3)	40 (14.3)
Chronic <i>Pseudomonas</i> (n=78)	58 (74.4)	18 (23.1)	2 (2.6)
NTM colonised (n=12)	8 (66.7)	4 (33.3)	0 (0.0)
<i>H. influenzae</i> chronic (n=38)	16 (42.1)	20 (52.6)	2 (5.3)
No chronic colonisation (n=152)	20 (13.2)	96 (63.2)	36 (23.7)
Reiff severe / cystic (n=74)	48 (64.9)	22 (29.7)	4 (5.4)
FEV1 <50% (n=84)	56 (66.7)	24 (28.6)	4 (4.8)
BMI <18.5 (n=42)	26 (61.9)	14 (33.3)	2 (4.8)
Post-TB aetiology (n=104)	48 (46.2)	48 (46.2)	8 (7.7)
Idiopathic aetiology (n=82)	22 (26.8)	42 (51.2)	18 (22.0)

3.3 Severity-Organism Interaction

The combination of radiological severity and key organism status produced a clear gradient in annual exacerbation rate (Figure 2). Mild bronchiectasis without chronic *Pseudomonas* or NTM showed mean rates around

1.2 exacerbations per year, while very severe cystic bronchiectasis with NTM colonisation showed rates above 7 per year. The interaction is operationally important because it identifies the subgroup in which the highest treatment intensity is justified.

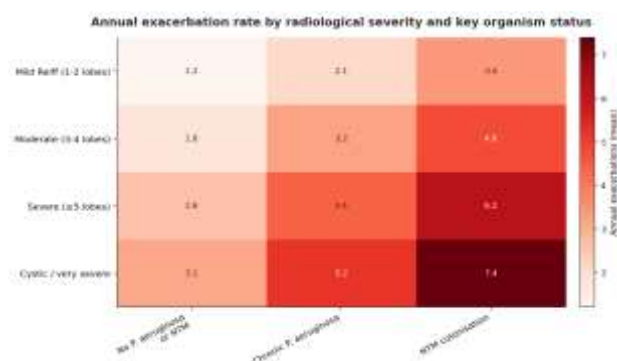


Fig.2: Annual exacerbation rate by radiological severity (Reiff) and dominant colonisation status. Darker shading indicates higher exacerbation burden

3.4 Time to Next Exacerbation by Treatment

Treatment intensity was associated with substantially different exacerbation-free intervals (Figure 3). Patients receiving the most intensive combination inhaled antibiotic, macrolide prophylaxis, and structured airway clearance showed a median time to next moderate-severe exacerbation exceeding 12 months, with only 30% experiencing an exacerbation during follow-up. Patients on macrolide prophylaxis alone or with airway clearance showed an intermediate trajectory. Those on standard care without prophylaxis experienced the shortest intervals between exacerbations.

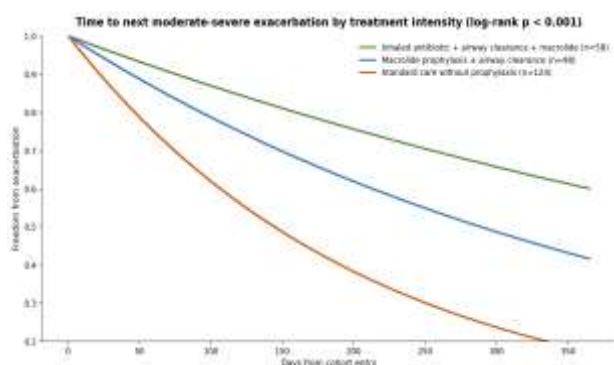


Fig.3: Time to next moderate-severe exacerbation by treatment intensity

3.5 Predictors of Frequent Exacerbator Phenotype

Multivariable analysis identified ten independent predictors of frequent exacerbator status. Chronic Pseudomonas colonisation carried the strongest single association (adjusted OR 4.32), followed by severe radiological disease and NTM colonisation. Lung function

impairment, history of haemoptysis, comorbid COPD, and underweight BMI all independently predicted frequent exacerbator status. Inhaled antibiotic therapy and macrolide prophylaxis showed strong protective associations, supporting their continued role in the treatment of high-risk patients.

Table 3. Treatment patterns by exacerbator phenotype

Treatment	Frequent (n=102)	Infrequent (n=138)	No exacerbation (n=40)
Macrolide prophylaxis, n (%)	68 (66.7)	42 (30.4)	6 (15.0)
Inhaled antibiotic (tobramycin / colistin), n (%)	42 (41.2)	16 (11.6)	2 (5.0)
Structured airway clearance, n (%)	78 (76.5)	58 (42.0)	12 (30.0)
Inhaled corticosteroid, n (%)	58 (56.9)	48 (34.8)	6 (15.0)
Long-acting bronchodilator, n (%)	68 (66.7)	52 (37.7)	8 (20.0)
Mucolytic (nebulised hypertonic saline), n(%)	38 (37.3)	16 (11.6)	0 (0.0)
At least three intensification elements, n (%)	42 (41.2)	12 (8.7)	0 (0.0)
IV antibiotic course in past 12 mo, n (%)	48 (47.1)	12 (8.7)	0 (0.0)
Eradication attempt for Pseudomonas, n (%)	18/58 (31.0)	8/16 (50.0)	2/4 (50.0)

3.6 Twelve-Month Outcomes

Table 4. Twelve-month outcomes by exacerbator phenotype

Outcome	Frequent (n=102)	Infrequent (n=138)	No exacerbation (n=40)
Annual exacerbation rate, mean	3.6	1.4	0.0
Hospitalisations during follow-up, n	52	18	0
Mean LOS per hospitalisation, days	8	6	-
IV antibiotic courses, mean per patient	1.4	0.4	0.0
FEV1 decline at 12 months, mean, mL	-128	-58	-22
FEV1 decline >100 mL at 12 mo, n (%)	58 (56.9)	24 (17.4)	2 (5.0)
New chronic colonisation acquired, n (%)	12 (11.8)	10 (7.2)	2 (5.0)
Listed for lung transplant during follow-up, n	4	0	0
All-cause mortality at 18 months, n (%)	8 (7.8)	4 (2.9)	0 (0.0)
CAT score deterioration ≥2 points, n (%)	42 (41.2)	18 (13.0)	2 (5.0)

4. Discussion

Across 280 adults with non-CF bronchiectasis followed for 18 months, three observations have practical implications. First, the phenotypic distribution is clinically tractable. Frequent exacerbators about a third of the cohort accounted for the great majority of hospitalisations, IV antibiotic courses, lung function decline, and mortality. Identifying this subgroup at baseline through microbiological and radiological phenotyping is operationally straightforward and informs treatment intensification decisions. Second, chronic *Pseudomonas* colonisation emerged as the single strongest predictor of frequent exacerbator status, with three quarters of colonised patients meeting frequent-exacerbator criteria. This both confirms the well-established adverse prognostic implication of *Pseudomonas* in bronchiectasis and raises the importance of eradication attempts at first isolation an approach achieving variable success in our cohort but worth pursuing where feasible. Suppressing inhaled antibiotic therapy in confirmed chronic colonisation showed substantial benefit and warrants broader deployment (Jha, Kumar, & Neha, 2026; Bhatnagar, Kumar, & Shivam, 2026). Third, the treatment intensity gradient observed in Figure 3 reproduces the trial-level evidence that combination prophylaxis inhaled antibiotic, macrolide, and structured airway clearance substantially extends time between exacerbations. The clinical practice question is no longer whether these interventions help but rather which patients should receive which combination, and how to support adherence over long-term use. Patient engagement and structured education are essential complements (Catherine, Gupta, Gopi, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine, & Velmurugan, 2025; Vettriselvan, Ramya, et al., 2026; Bhatnagar, Kumar, & Shivam, 2026; Yatish, Khatoon, & Kumar, 2026). Implementation considerations include the cost and tolerability of inhaled antibiotics, the QT-interval surveillance required during macrolide prophylaxis (particularly relevant in older patients with comorbid cardiac disease), and the training infrastructure for structured airway clearance. The post-tuberculous aetiology common in our population introduces an additional consideration: residual structural damage may differ in distribution and physiology from idiopathic disease, and treatment response may not perfectly mirror the trial cohorts predominantly drawn from idiopathic populations (Gautam, Samyal, & Chaudhary, 2026; Kumar, Sharma, & Gupta, 2026). Digital tools to support symptom diaries and early exacerbation recognition show promise (Deepa et al., 2026; Vijayalakshmi et al., 2025; Vinodh, Subramani, & Vettriselvan, 2026). Limitations include the single-centre design, the 18-month follow-up which captures most clinically important events but may miss longer-term progression patterns, the reliance on self-reported exacerbations for community-managed events, and the

absence of randomisation in treatment-intensity comparisons. The post-TB aetiology contributes a particular phenotype not always represented in the international literature, which influences external generalisability.

5. Conclusion

Non-CF bronchiectasis shows a clear and clinically tractable phenotypic distribution, with approximately a third of patients meeting frequent exacerbator criteria and accounting for the bulk of morbidity and healthcare utilisation. Chronic *Pseudomonas* colonisation, severe radiological disease, and impaired lung function were the strongest independent predictors. Intensive treatment combining inhaled antibiotics, macrolide prophylaxis, and structured airway clearance was associated with substantially longer time to next exacerbation. Phenotype-guided treatment intensification, with particular priority for the chronic-*Pseudomonas* and severe-radiology subgroups, offers a practical pathway to improved outcomes in this population.

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