



# Prevalence and types of treatable traits in bronchiectasis: a multicentre, cross-sectional study

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## To the Editor:

Bronchiectasis is a heterogeneous chronic respiratory disease characterised by permanent bronchial dilation, daily productive cough and frequent exacerbations [1]. In recent years, the understanding of bronchiectasis has evolved beyond the paradigm of recurrent infections and structural lung damage. Systemic inflammation and coexisting comorbidities are now recognised as integral components of disease pathophysiology [2–4]. Moreover, patients increasingly emphasise the need for personalised and flexible management strategies, pointing out the limitations of a one-size-fits-all approach [5]. Bronchiectasis has multiple potential causes, and a systematic aetiological evaluation to identify coexisting conditions is recommended, as distinct aetiologies may require specific treatments [6]. This perspective has led to the concept of treatable traits (TTs), originally introduced in COPD and asthma, and now extended to bronchiectasis [7, 8]. TTs refer to clinically relevant, identifiable, and modifiable disease phenotypes, comorbidities, or underlying biological mechanisms (endotypes). While current guidelines provide management strategies involving antibiotics, pulmonary rehabilitation, and airway clearance, they do not adequately address comorbidities, lifestyle, or psychological health [9, 10]. Limited data regarding the prevalence and distribution of TTs in bronchiectasis are available. Thus, the current study aimed to identify and characterise TTs in adults with bronchiectasis.

This was a secondary analysis of three prospective, observational studies conducted at the Bronchiectasis Programmes of the IRCCS San Gerardo dei Tintori, Monza, Italy (2012–2016), IRCCS Fondazione Cà Granda Ospedale Maggiore Policlinico, Milan (2016–2020), and IRCCS Humanitas Research Hospital, Milan (2021–2025), following a common study protocol. All studies received ethical approval from the respective institutional review boards, and informed consent was obtained from all patients.

Consecutive adults ( $\geq 18$  years) with clinically and radiologically confirmed bronchiectasis were included, defined as bronchial dilation in  $\geq 1$  lobe along with compatible symptoms. Patients with cystic fibrosis or traction bronchiectasis secondary to interstitial lung diseases were excluded.

Clinical, laboratory, microbiological and radiological data were collected according to local standard operating procedures and the 2010/2019 British Thoracic Society and 2017 European Respiratory Society guidelines [9, 10]. A total of 28 TTs were assessed across four domains at the time patients were referred to the bronchiectasis programmes: pulmonary traits, extrapulmonary comorbidities, aetiological diseases and lifestyle risk factors [8]. The primary endpoint of this study was to determine the prevalence of TTs in adults with bronchiectasis. The secondary endpoint was to compare the distribution of these TTs across centres, acknowledging that each centre represents a different time frame in the evolution of bronchiectasis care, reflecting modifications in clinical practice through the years. All analyses were performed using STATA v18.

A total of 1614 patients were included in this study: 574 from Humanitas (median (interquartile range (IQR)) age: 63 (54–70) years, 75% female), 700 from Policlinico (median (IQR) age: 62 (48–71) years, 77% female), and 340 from San Gerardo (median (IQR) age: 69 (58–75) years, 61.2% female). The median (IQR) bronchiectasis severity index (BSI) was 5.0 (3.0–8.0) at Humanitas, 5.5 (3.0–9.0) at Policlinico, and 6.0 (4.0–9.0) at San Gerardo, with 18.4%, 26.2%, and 29.4% classified as severe (BSI  $\geq 9$ ), respectively.



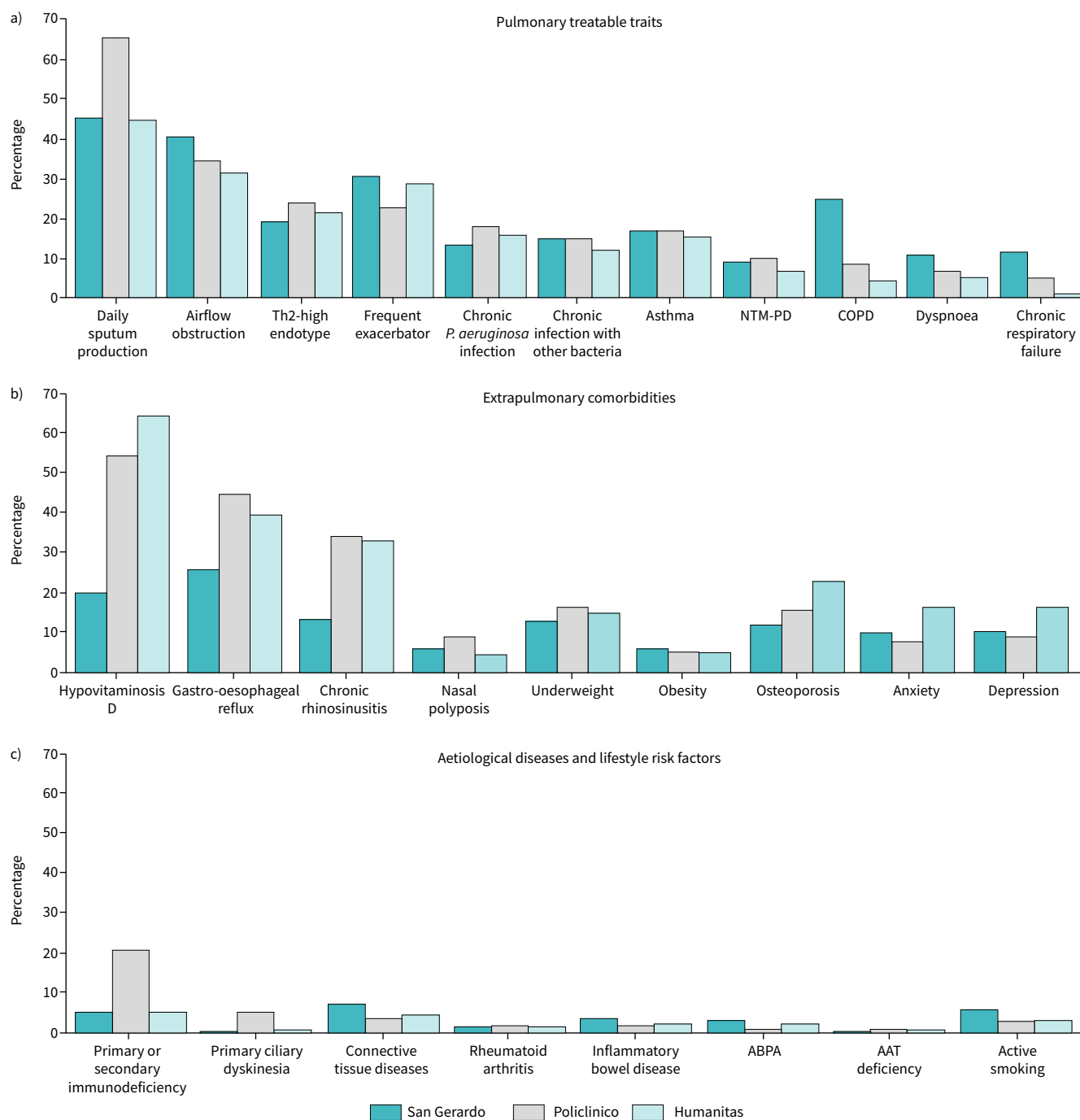
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**Treatable traits in bronchiectasis are diverse and reflect patient heterogeneity. Identifying these traits can guide personalised care, improve outcomes and optimise resource allocation in real-world clinical practice.** <https://bit.ly/3TqDgun>

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Median (IQR) body mass index was 21.0 (19.0–23.5) at Humanitas, 21.4 (19.1–24.1) at Policlinico, and 22.6 (18.8–25.8) at San Gerardo. The distribution of the 28 TT across the three centres is shown in figure 1. Chronic bacterial infection was observed in 25.3% at Humanitas, 34.9% at Policlinico, and 28.2% at San



**FIGURE 1** Distribution of treatable traits according to clinical domain in three Italian bronchiectasis cohorts. **a)** Pulmonary treatable traits: daily sputum production, airflow obstruction, T2-high endotype (defined as blood eosinophils  $\geq 300$  cells· $\mu\text{L}^{-1}$  or exhaled nitric oxide fraction  $\geq 25$  ppb), frequent exacerbator phenotype ( $\geq 3$  exacerbations per year), chronic *Pseudomonas aeruginosa* infection, chronic infection with other bacteria, asthma, non-tuberculous mycobacterial pulmonary disease (NTM-PD), COPD, dyspnoea (modified Medical Research Council score 3–4), and chronic respiratory failure (requiring home long-term oxygen therapy or noninvasive ventilation). **b)** Extrapulmonary comorbidities: hypovitaminosis D, gastro-oesophageal reflux, chronic rhinosinusitis, nasal polyposis, underweight, obesity, osteoporosis, anxiety, and depression. **c)** Aetiological diseases and lifestyle risk factors: primary or secondary immunodeficiency, primary ciliary dyskinesia, connective tissue diseases, rheumatoid arthritis, inflammatory bowel disease, allergic bronchopulmonary aspergillosis (ABPA), alpha-1 antitrypsin (AAT) deficiency, and active smoking.

Gerardo. Airway clearance techniques were used by 50.5%, 65.7%, and 36.8%, respectively. Median (IQR) forced expiratory volume in 1 s % predicted was 86 (71–98) at Humanitas, 86 (69–101) at Policlinico, and 83 (61–102) at San Gerardo.

Pulmonary traits were among the most frequently identified TTs, including daily sputum production (65.7% at Policlinico, 43.9% at Humanitas, 45.3% at San Gerardo), T2-high endotype (24.0%, 21.1%, 19.1%), frequent exacerbator phenotype (22.9%, 28.4%, 30.6%), and chronic *Pseudomonas aeruginosa* infection (18.0%, 15.6%, 13.2%). Airflow obstruction and COPD were more common at San Gerardo (40.6% and 24.7%) compared to Policlinico (34.7% and 8.1%) and Humanitas (17.6% and 3.9%), possibly reflecting differences in phenotyping and patient selection. Dyspnoea and chronic respiratory failure were also more prevalent at San Gerardo (10.9% and 11.8%) than at Policlinico (6.9% and 4.7%) and Humanitas (5.0% and 0.9%).

Extrapulmonary comorbidities were also common, with hypovitaminosis D being the most frequent extrapulmonary trait, ranging from 44.7% at San Gerardo to 63.2% at Humanitas. Gastro-oesophageal reflux (44.4%, 38.2%, 25.6%), chronic rhinosinusitis (33.7%, 32.5%, 13.2%), osteoporosis (15.3%, 22.1%, 11.5%), anxiety (7.4%, 15.8%, 9.7%) and depression (8.4%, 15.4%, 10.3%) were also prevalent across centres, with variation possibly reflecting the growing awareness of extrapulmonary traits among pulmonologists over time. The prevalence of primary or secondary immunodeficiency varied widely, ranging from 21.0% at Policlinico to 5.1% at Humanitas and 5.3% at San Gerardo, while primary ciliary dyskinesia, though rare, was also more common at Policlinico (5.1%).

To our knowledge, this is the first real-world study to characterise a wide range of TTs in a bronchiectasis cohort. Our findings confirm that many patients exhibit multiple coexisting TTs across different domains. These traits can significantly impact quality of life and disease progression, further supporting the need for comprehensive, multidisciplinary care models. These prevalence insights may help clinicians prioritise interventions, allocate resources more effectively, and design individualised treatment strategies. The study spans more than 10 years across three different centres offering a longitudinal perspective on how clinical awareness and diagnostic practices have shaped patient populations over time. Daily sputum production remains a significant burden in bronchiectasis, but the imbalance between pulmonologists and respiratory physiotherapists in Italy may hinder the effective implementation of airway clearance techniques. Similarly, despite the high prevalence of airflow obstruction, routine bronchodilator use remains controversial, with limited evidence supporting their benefit [11]. Hypovitaminosis D, the most common extrapulmonary trait, has been linked to disease severity, radiological progression, and exacerbation frequency; however, routine supplementation is not currently supported by strong evidence [12, 13].

Importantly, the distribution of TTs varied significantly across centres, reflecting changes in clinical practice, growing disease awareness, and increasing recognition of the importance of managing non-respiratory comorbidities over time. The progressively declining prevalence of COPD and chronic respiratory failure in bronchiectasis clinics may indicate a paradigm shift in respiratory medicine. As bronchiectasis becomes recognised as a distinct clinical entity with unique pathophysiological and radiological features [1], fewer COPD patients with coexisting bronchiectasis may be managed in dedicated bronchiectasis clinics. Finally, the higher prevalence of primary ciliary dyskinesia and immunodeficiencies observed at Policlinico reflects its role as a referral centre for rare respiratory diseases and its ongoing research on immunodeficiencies during the study period. Despite the strengths of the multicentre approach and the moderate sample size, several limitations should be acknowledged. First, the cross-sectional design of the study precludes assessment of the impact of TT-targeted interventions on disease progression. Second, the data were derived from three specialised centres in Northern Italy, which may limit the generalisability of these findings to other healthcare systems, geographic regions, or patient populations. Third, some relevant TTs – such as anaemia, sarcopenia, physiotherapy adherence, sleep disorders, and exposure to air pollution – were not consistently captured across centres. Future prospective, multicentre studies with standardised data collection and longitudinal follow-up are needed to validate these findings and to assess the impact of TT-based management on clinical outcomes.

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