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Review

Tuberculosis-Associated Persistent Airflow Limitation: Terminology, Epidemiology, Pathogenesis and Clinical Features

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Abstract

Previous pulmonary tuberculosis (TB) is associated with airflow obstruction, including in never-smokers. This narrative review synthesises terminology, epidemiological evidence, pathogenetic mechanisms and clinical features of tuberculosis-associated persistent airflow limitation, drawing on PubMed/MEDLINE publications from 2000–2026. Tuberculosis-associated obstructive pulmonary disease (TOPD) describes an obstructive phenotype of post-tuberculosis lung disease (PTLD) in which residual damage likely contributes substantially to persistent post-bronchodilator airflow limitation after treatment. Chronic obstructive pulmonary disease (COPD) may develop in lungs already affected by tuberculosis. Conversely, active TB may complicate established COPD. Airflow obstruction reflects bronchial distortion and stenosis, bronchiectasis, post-cavitary changes, regional hyperinflation and small airway disease. Inflammatory and immune alterations may contribute, but their role in progression and the clinical value of biomarkers remain uncertain. Persistent symptoms, heterogeneous functional impairments and imaging abnormalities characterise the clinical presentation; symptom severity may not correspond to spirometric impairment. Evidence on exacerbations and hospitalisation derives partly from COPD cohorts with a history of TB. Differences in study populations, tuberculosis ascertainment and outcome definitions limit comparability. An author-developed framework describes coexisting structural and functional PTLD components and distinguishes coexisting COPD. Consistent criteria and longitudinal assessment are needed to clarify prognosis and support individualised long-term care.

Keywords: tuberculosis; persistent airflow limitation; TOPD; post-tuberculosis lung disease; PTLD; airflow obstruction; epidemiology; pathogenesis; clinical features

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1. Introduction

Respiratory tuberculosis and chronic obstructive pulmonary disease (COPD) remain major causes of impaired quality of life, loss of work capacity and premature death [1–3]. In clinical practice, these diseases require different approaches: tuberculosis (TB) is considered an infectious disease, whereas COPD is a chronic non-communicable disease primarily associated with smoking and other inhalational exposures [4]. Persistent airflow limitation after tuberculosis should nevertheless be distinguished from a diagnosis of COPD. Systematic reviews and meta-analyses associate previous pulmonary tuberculosis with an increased likelihood of persistent airflow limitation and chronic respiratory diseases, including COPD [5–7].

The term post-tuberculosis lung disease (PTLD) is increasingly used to describe the long-term consequences of tuberculosis. This concept encompasses residual radiological

changes and a broad spectrum of clinical, functional and structural abnormalities: chronic dyspnoea, cough, reduced exercise tolerance, obstructive, restrictive and mixed ventilatory impairments, bronchiectasis, fibrotic scarring, cysts, pleural thickening and chronic respiratory failure. Imaging studies and clinical reviews show that post-tuberculosis changes may affect the airways, parenchyma, pleura and pulmonary vasculature [3,8–10].

Tuberculosis-associated persistent airflow limitation is an obstructive manifestation within the broader category of PTLD. The English-language literature uses the terms tuberculosis-associated COPD, TB–COPD and tuberculosis-associated obstructive pulmonary disease (TOPD). These terms are applied inconsistently: some studies refer to patients with COPD and active or previous tuberculosis, others to persistent airflow limitation detected after TB, and others to a broader obstructive pattern of post-tuberculosis lung damage. Recent reviews describe heterogeneous combinations of structural lung damage, airway remodelling, chronic inflammation, bronchiectasis, fibrotic changes and conventional COPD risk factors, particularly smoking [4,11–13]. In this review, persistent airflow limitation associated with previous tuberculosis is the main focus; COPD is retained when referring to a coexisting diagnosis or to the definitions used in the cited studies.

Active tuberculosis and its residual changes can cause irreversible parenchymal damage, distortion of the bronchial tree, peribronchial fibrosis, bronchiectasis, localised emphysema, loss of lung tissue elasticity and chronic airway inflammation. Prolonged pulmonary tuberculosis may compound existing lung impairment in COPD [4,11]. Pre-existing COPD is associated with greater susceptibility to active tuberculosis. Proposed contributing factors include impaired mucociliary clearance, altered local immune responses, structural lung damage, smoking, older patient age, comorbidity and, in some patients, the use of inhaled corticosteroids (ICS) [14–17].

The clinical significance of post-tuberculosis airflow limitation depends on spirometric measures, the severity and persistence of symptoms, limitations in physical activity, and the occurrence of respiratory exacerbations, hospitalisation and adverse outcomes. In broader PTLD populations, some patients continue to report multiple respiratory symptoms long after tuberculosis treatment. Assessment reveals reduced forced expiratory volume in one second (FEV_1), an abnormal FEV_1/forced vital capacity (FVC) ratio, mixed ventilatory impairment and reduced exercise tolerance [18,19]. Post-tuberculosis lung function impairment is associated with poorer quality of life, and spirometric screening after treatment completion is being investigated as an approach to the early detection of PTLD [20,21].

The inflammatory and immunological component of tuberculosis-associated persistent airflow limitation warrants consideration in its own right. Recent studies suggest possible contributions from systemic inflammation, neutrophilic responses, immune dysregulation, autoantibodies, oxidative stress and fibrosis to post-tuberculosis lung damage and chronic airflow limitation [13,17,22–24]. The role of persistent inflammation in the progression of post-tuberculosis airflow limitation and the clinical value of biomarkers have not yet been established.

The practical importance of this problem is reinforced by the need to assess persistent respiratory impairment after completion of anti-tuberculosis therapy and provide appropriate respiratory specialist follow-up. International clinical standards emphasise the assessment of symptoms, lung function, radiological changes, physical activity, quality of life and rehabilitation needs in people with post-tuberculosis lung damage [10]. Pulmonary rehabilitation is considered a promising component of PTLD management: pharmacotherapy does not reverse the structural sequelae of tuberculosis, and restoring physical activity, educating patients and controlling dyspnoea have clinical value in their own right [25–27]. The organisation of post-cure care remains unresolved; however, com-

pletion of anti-tuberculosis treatment does not, by itself, ensure subsequent respiratory specialist follow-up [3].

Despite the increasing number of publications, studies of tuberculosis and chronic airflow limitation remain methodologically heterogeneous. Tuberculosis history is ascertained in different ways, using records of previous TB, codes for active tuberculosis or its sequelae, chest radiography and computed tomography (CT) findings, patient self-report or registry data. The outcomes assessed also differ: some studies apply COPD definitions incorporating spirometry or examine an isolated reduction in FEV_1/FVC, whereas others use a clinical diagnosis, COPD-related hospitalisation, mortality, quality of life, physical activity or chronic respiratory failure. Patients with conventional smoking-related COPD, post-tuberculosis bronchiectasis, fibrotic–restrictive changes, post-tuberculosis cavities, mixed ventilatory impairment and chronic bacterial colonisation are often combined in a single analytical group. This hinders comparisons across studies and highlights the need to clarify the terminology, pathogenesis, and clinical and epidemiological characteristics of tuberculosis-associated persistent airflow limitation [9,10,12,28].

Scope and Literature Selection

This narrative review synthesises current understanding of tuberculosis-associated persistent airflow limitation as an obstructive manifestation of PTLD. Its aims are to distinguish this impairment from COPD and the broader spectrum of PTLD; to assess the epidemiological evidence linking tuberculosis with airflow obstruction; to describe the mechanisms of structural remodelling and chronic inflammation; and to characterise the clinical features of affected patients.

The review focuses on adults who have completed treatment for pulmonary tuberculosis. It also considers lung injury during active tuberculosis, the course of tuberculosis in patients with established COPD, and implications for diagnosis, treatment and follow-up.

This narrative review was based on a topic-focused selection of PubMed/MEDLINE publications from 2000–2026, with an emphasis on studies published in 2015–2026. The initial selection was compiled on 15 May 2026. The present version also includes publications added during subsequent manuscript revision. The search terms were post-tuberculosis lung disease, PTLD, tuberculosis-associated COPD, TOPD and post-TB obstructive disease, combined with COPD, airflow obstruction, spirometry, FEV_1, bronchiectasis, pulmonary rehabilitation, matrix metalloproteinase, inhaled corticosteroids, pulmonary hypertension, microbiome and impulse oscillometry; reference lists and relevant guidelines were also examined. We considered observational and randomised studies, systematic reviews, meta-analyses, clinical standards and consensus documents addressing adults with tuberculosis, PTLD, obstructive impairment or COPD. Indirect evidence was interpreted with appropriate caveats; case reports, letters and protocols were used for illustration. We took account of the Scale for the Assessment of Narrative Review Articles (SANRA), which is not a standard for systematic searching [29].

2. Core Concepts: PTLD, Persistent Airflow Limitation and COPD

Tuberculosis-associated persistent airflow limitation, post-tuberculosis lung disease and COPD are related but not interchangeable concepts. Conflating them results in the grouping together of patients with pre-existing COPD, airflow obstruction following tuberculosis and non-obstructive post-tuberculosis changes [9,30].

PTLD is the broadest concept. Clinical standards define it as chronic respiratory disease that may be wholly or partly attributable to previous pulmonary tuberculosis, with or without symptoms [10]. PTLD encompasses both obstructive and non-obstructive post-tuberculosis impairments [9,31]. The 2026 research case definition requires previous

pulmonary or pleural tuberculosis, absence of current tuberculosis, and abnormalities attributable at least partly to tuberculosis in at least two of three domains: respiratory symptoms, lung function and chest imaging [32]. In cohorts meeting this definition, persistent post-bronchodilator obstruction identifies an obstructive subgroup. An isolated low ratio satisfies only the lung function domain. The broader clinical definition covers the full spectrum of tuberculosis sequelae that require follow-up, rehabilitation and disability prevention [3,10,33,34].

In this review, TB–COPD denotes the clinical and epidemiological coexistence of active or previous tuberculosis and a diagnosis of COPD [4,12]. The term is useful for assessing the frequency of coexisting diagnoses, hospitalisation, mortality and care needs, but does not establish causality. Airflow obstruction may precede tuberculosis, arise predominantly as a consequence of it, or develop through a combination of post-tuberculosis changes, smoking, emphysema and age-related comorbidity [35,36]. Airflow obstruction first detected after tuberculosis does not, by itself, establish COPD, and tuberculosis-associated persistent airflow limitation is not treated here as a subtype of TB–COPD.

Here, TOPD describes an obstructive phenotype within PTLD without presupposing a COPD diagnosis. The 2023 taxonomy of the Global Initiative for Chronic Obstructive Lung Disease (GOLD), retained in 2026, distinguishes smoking-related COPD (COPD-C) from infection-related COPD (COPD-I), which includes tuberculosis-associated COPD [2,37]. Gai et al. also use TOPD for tuberculosis-associated COPD as a proposed subtype [38]. The two usages overlap when patients with obstructive PTLD meet the clinical and spirometric criteria for COPD.

In this review, tuberculosis-associated persistent airflow limitation describes an obstructive manifestation of PTLD: persistent post-bronchodilator airflow limitation after completion of treatment for pulmonary tuberculosis, to which post-tuberculosis airway or parenchymal damage is likely to make a substantial contribution. For brevity, "post-tuberculosis airflow limitation" refers to this working definition. This terminology emphasises the association between airflow obstruction and tuberculous damage: small airway injury, peribronchial fibrosis, bronchial distortion and stenosis, bronchiectasis, post-cavitary changes, regional hyperinflation and loss of elastic recoil [11,36]. It does not imply a diagnosis of COPD. A histologically characterised case of post-tuberculosis airflow obstruction in a young non-smoker illustrates morphological differences from smoking-related COPD and isolated bronchiectasis. This single case is illustrative and does not allow conclusions about the prevalence of this morphological pattern [39].

The working definition has clear limitations. Ventilatory impairments may change during and after tuberculosis treatment, so persistent airflow obstruction needs to be reconfirmed after therapy is completed [10,40]. Active tuberculosis in a patient with pre-existing COPD is described here as TB–COPD; this coexistence alone does not establish tuberculosis-associated persistent airflow limitation. Isolated post-tuberculosis restriction without airflow obstruction, in turn, belongs to PTLD but falls outside the obstructive impairment considered here. "Airflow obstruction" denotes a reduced FEV_1/FVC ratio on spirometry; a low FVC does not, by itself, confirm restriction [41]. The working definition above requires post-bronchodilator confirmation, while findings from cited studies retain their original definitions. For research phenotyping after completion of pulmonary tuberculosis treatment, symptoms and serial post-bronchodilator spirometry can be interpreted alongside earlier lung function, available CT findings, asthma or COPD predating tuberculosis, and tobacco, biomass or occupational exposures [7,10,36,42]. New obstruction after previously normal spirometry, together with damage in the affected lung, supports a contribution from tuberculosis. A predominant structural finding can be recorded alongside overlapping

changes. When earlier measurements are unavailable or several causes coexist, their relative contributions often remain uncertain.

Morphological changes underlying post-tuberculosis airflow limitation may differ from those in conventional smoking-related COPD [39,43]. In a comparative study, patients with a history of treated pulmonary tuberculosis had lower diffusing capacity and inspiratory capacity, and more pronounced air trapping and fibrosis, despite a comparable extent of emphysema [36]. These findings suggest differences in the mechanisms of airflow obstruction. In smokers, post-tuberculosis damage may coexist with injury caused by tobacco smoke; the respective contributions should be considered separately rather than attributing all impairment to COPD [12].

The working definitions and boundaries of PTLD, persistent airflow limitation and coexisting COPD are shown in Figure 1.

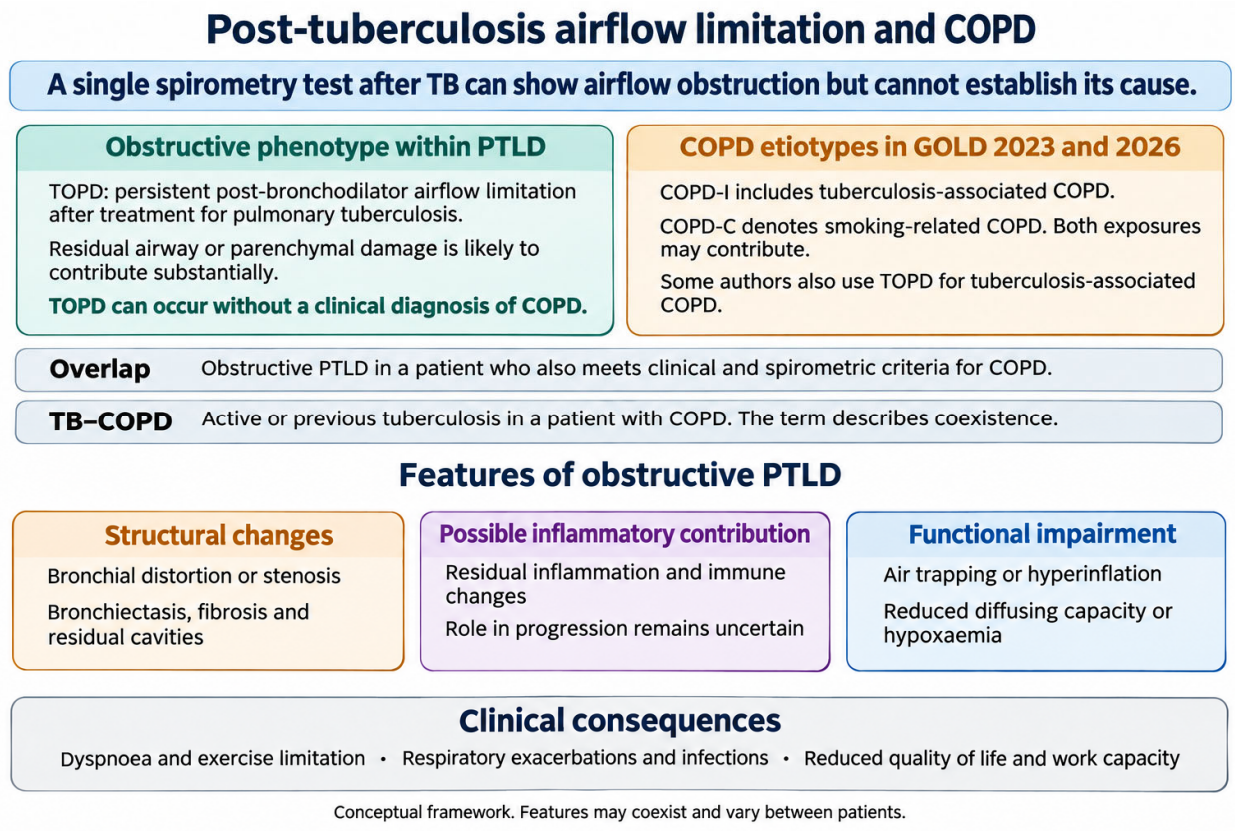

Figure 1. Post-tuberculosis airflow limitation and its relationship to chronic obstructive pulmonary disease (COPD). A single post-bronchodilator spirometry test after pulmonary tuberculosis (TB) can document airflow obstruction at that visit. The result alone cannot establish its cause or persistence over time. In this review, tuberculosis-associated obstructive pulmonary disease (TOPD) describes a phenotype of post-tuberculosis lung disease (PTLD) in which residual airway or parenchymal damage is likely to contribute substantially to persistent airflow limitation. TOPD can occur without a clinical diagnosis of COPD. The two descriptions overlap when a patient with obstructive PTLD also meets the clinical and spirometric criteria for COPD. The GOLD 2023 and 2026 reports include tuberculosis-associated COPD within the infection-related etiotype (COPD-I) [2,37]. Some authors also use TOPD for this proposed COPD subtype [38]. The lower panels summarise features that may coexist in obstructive PTLD. The contribution of residual inflammation to progression remains uncertain. This author-developed framework is conceptual and awaits clinical validation.

3. Epidemiological Evidence on Tuberculosis-Associated Persistent Airflow Limitation

The principal epidemiological evidence concerns the association of previous tuberculosis with subsequent or concurrently detected airflow obstruction [5–7,42]. Studies of baseline COPD or impaired lung function followed by active tuberculosis are discussed separately as context [14,44]. The applicability of these findings to tuberculosis-associated persistent airflow limitation depends on study design and outcome definitions (Table 1); COPD diagnoses and COPD-related outcomes are retained as defined in the original studies.

3.1. Tuberculosis as a Risk Factor for Chronic Airflow Obstruction

The association between previous pulmonary tuberculosis and chronic airflow limitation has been consistently demonstrated across studies. In the population-based Latin American Project for the Investigation of Obstructive Lung Disease (PLATINO) study (5571 participants aged ≥40 years from five Latin American cities), post-bronchodilator airflow obstruction was detected in 30.7% of participants with a history of tuberculosis and 13.9% of those without; tuberculosis history was based on participants' reports of a previous physician diagnosis. Thus, the study allows a comparison of the prevalence of airflow obstruction, but not an estimate of its incidence after tuberculosis [45]. In the same project, airflow obstruction was also associated with a history of tuberculosis among never-smokers [46]. In the international Burden of Obstructive Lung Disease (BOLD) study (14,050 adults aged ≥40 years from 19 centres), tuberculosis history was associated with airflow obstruction after adjustment for age, sex, body mass index and smoking: adjusted odds ratio (aOR) 2.51 (95% confidence interval [CI] 1.83–3.42); the corresponding estimate for low FVC was 2.13 (1.42–3.19) [42]. In this study, low FVC described a spirometric finding and did not indicate confirmed restriction, which requires measurement of total lung capacity (TLC) [41].

Systematic reviews and meta-analyses confirm this association. In the meta-analysis by Fan et al. (23 studies), the pooled odds ratio for COPD in people with a history of tuberculosis was 2.59 (95% CI 2.12–3.15), and 2.41 (1.74–3.32) among never-smokers [7]. Findings in non-smokers make an explanation solely based on smoking less likely. However, they do not exclude confounding by age, exposure to biomass combustion products and occupational dust, social circumstances, or access to healthcare [4,42]. When an outcome is common, an odds ratio cannot be treated as a risk ratio without qualification. Earlier systematic reviews found an association between previous tuberculosis and a broad range of chronic respiratory diseases, including COPD and bronchiectasis [5,6].

Cohort studies establish the temporal sequence of events and complement cross-sectional evidence, but use different outcome definitions. In a Korean registry (31,033 patients after tuberculosis and 31,033 matched controls), the incidence of newly recorded COPD was 36.7 versus 18.8 per 1000 person-years (adjusted hazard ratio [aHR] 1.63; 95% CI 1.54–1.73), and the rate of COPD-related hospitalisation was 10.7 versus 4.3 per 1000 person-years (aHR 2.03; 1.81–2.27); diagnoses were based on administrative data without uniform requirements for spirometric confirmation [47]. In the multicentre retrospective cohort of Joo et al., post-tuberculosis COPD, as defined by the authors, was identified in 71 of 352 patients, corresponding to 20.56 cases per 1000 person-years; factors associated with COPD development were older age at tuberculosis diagnosis, baseline $FEV_1 < 80\%$ predicted (aOR 3.98; 95% CI 1.92–8.24), ever smoking (3.23; 1.14–9.17) and multilobar involvement (2.04; 1.08–3.85) [48]. This estimate describes incidence in a selected clinical cohort and cannot be directly compared with the prevalence of airflow obstruction in population surveys. In a small prospective cohort reported by Sheng et al. ($n = 53$), post-bronchodilator airflow obstruction was detected in 7 patients during treatment after sputum smear conversion and

in 9 five years after treatment completion [49]. A population-based cohort of immigrants in British Columbia demonstrated an increased risk of airway disease after respiratory tuberculosis, including in a setting with a low incidence of tuberculosis [50].

Other studies indicate an association between functional impairment, imaging findings and the extent of lung involvement. In a Korean population survey, airflow obstruction was detected in 26.3% of people with radiological signs of previous tuberculosis, compared with 8.6% of those without [51]. Among people with spontaneously healed, asymptomatic tuberculous lesions identified from imaging and interferon-gamma release assay (IGRA) results, airflow obstruction was more frequent than among those with a normal chest radiograph (13.4% versus 7.4%); however, this population differs from cohorts of patients who completed treatment for microbiologically confirmed tuberculosis [52]. In a small retrospective study (41 patients), more extensive disease was accompanied by a greater annual decline in FEV_1 and FVC. This finding is consistent with an association between the extent of lung involvement and the severity of functional impairment, but does not establish that greater disease extent determines the degree of lung function decline [53].

Lung function follows different trajectories after tuberculosis treatment. In a Malawian cohort, 60.7% of patients reported respiratory symptoms at treatment completion; spirometric abnormalities were detected in 34.2%, and moderate-to-severe bronchiectasis in at least one lobe was present in 170 of 385 participants who underwent CT (44.2%) [54]. Of the 405 participants, 301 attended the three-year follow-up. At that visit, 59 of 301 (19.6%) reported respiratory symptoms and 76 of 272 (27.9%) had abnormal spirometry. Mean FEV_1 and FVC improved, predominantly during the first year, whereas FEV_1 declined by more than 100 mL in 29.7% of participants with comparable measurements [18]. Thus, improvement in group averages does not exclude deterioration in individual patients. Nevertheless, PTLD should not be regarded as inevitably progressive. In a meta-analysis of residual impairment after successful treatment (61 studies, 41,014 participants), the authors classified impairment using pre-bronchodilator spirometry. Across the 42 studies reporting impairment by type, any spirometric abnormality was detected in 59.1%, an obstructive pattern in 17.8%, a restrictive pattern in 21.3% and a mixed pattern in 12.7% [19]. Given the high heterogeneity of the studies and differences in participant age and diagnostic criteria, these proportions cannot be interpreted as the frequency of tuberculosis-associated persistent airflow limitation. Furthermore, "restrictive" impairments were not confirmed by TLC measurement. A separate meta-analysis comparing lung function after tuberculosis with that of healthy controls confirms reductions in FEV_1 and FVC [55].

The available evidence supports a multifactorial model of post-tuberculosis airflow limitation: the severity of initial disease and residual structural changes act alongside smoking, age and comorbidities [48,56]. The relative contribution of each factor has not yet been established; evidence on comorbidity and PTLD is heterogeneous, and the certainty of pooled estimates remains very low [57].

Table 1. Key quantitative findings on the association between tuberculosis and airflow obstruction.

Study	Design and Outcome	Main Finding	Key Limitation
PLATINO [45]	Population-based cross-sectional study; post-bronchodilator airflow obstruction (FEV_1/FVC <0.70); 5571 participants aged ≥40 years	30.7% with a history of TB versus 13.9% without	Self-reported TB; comparison of prevalence, not incidence
BOLD [42]	Cross-sectional study, 14,050 participants, 19 centres; post-bronchodilator FEV_1/FVC below the LLN	aOR for airflow obstruction 2.51 (95% CI 1.83–3.42); for low FVC 2.13 (1.42–3.19)	Cross-sectional design; residual confounding; low FVC does not confirm restriction

Table 1. *Cont.*

Study	Design and Outcome	Main Finding	Key Limitation
Fan et al. [7]	Systematic review and meta-analysis of 23 studies; COPD definitions and spirometric protocols varied	Pooled OR 2.59 (2.12–3.15); in never-smokers 2.41 (1.74–3.32)	Different definitions of TB and COPD; an OR is not equivalent to a relative risk
Kim et al. [47]	Korean registry; 31,033 patients after TB and 31,033 controls; newly recorded COPD	36.7 versus 18.8 per 1000 person-years; aHR 1.63 (1.54–1.73); hospitalisation aHR 2.03 (1.81–2.27)	COPD diagnosis based on administrative data without spirometric confirmation
Joo et al. [48]	Retrospective multicentre cohort, 352 patients; FEV_1/FVC <0.70 on pre- or post-bronchodilator spirometry	71 cases; 20.56 per 1000 person-years; factors: baseline FEV_1 <80%, smoking, multilobar involvement	Selected clinical cohort; the estimate does not reflect the population prevalence of post-tuberculosis airflow limitation
Sheng et al. [49]	Prospective cohort, 5 years, $n = 53$; post-bronchodilator FEV_1/FVC <0.70	Obstruction in 7/53 during treatment after sputum smear conversion and 9/53 five years after treatment completion	Very small sample; limited generalisability of five-year lung function changes and estimates of individual progression risk
Taylor et al. [19]	Meta-analysis of residual impairment after treatment; 61 studies, 41,014 participants	Any spirometric abnormality 59.1%; obstruction 17.8%; restrictive pattern 21.3%; mixed pattern 12.7%	I^2 >90%; impairment classified using pre-bronchodilator spirometry; restriction not confirmed by TLC
Nightingale et al. [18]	Prospective cohort, Malawi, 3 years; post-bronchodilator spirometry; 301 of 405 enrolled participants attended follow-up	Symptoms in 59/301 (19.6%); abnormal spirometry in 76/272 (27.9%); FEV_1 decline >100 mL in 73/246 (29.7%)	Incomplete follow-up; group averages may obscure deterioration in individual patients
Inghammar et al. [14]	Registry cohort, 115,867 patients with COPD recorded during hospitalisation; outcome: active TB	aHR 3.0 (95% CI 2.4–4.0)	Reverse direction of association; hospitalised patients with COPD, not the entire COPD population
Kim et al. [44]	Population-based cohort, 16,457 participants; baseline pre-bronchodilator spirometry; outcome: newly diagnosed TB	Obstructive impairment aHR 2.03 (1.12–3.68); spirometric restrictive pattern 2.19 (1.12–4.29)	Small number of events (72 TB cases); wide confidence intervals

OR, odds ratio; aOR, adjusted odds ratio; aHR, adjusted hazard ratio; CI, confidence interval; LLN, lower limit of normal; TLC, total lung capacity. Estimates relate to different outcomes and populations; their magnitudes should not be compared directly. TB, tuberculosis; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; PLATINO, Latin American Project for the Investigation of Obstructive Lung Disease; BOLD, Burden of Obstructive Lung Disease. I^2 quantifies between-study heterogeneity.

3.2. Contextual Evidence: COPD as a Risk Factor for Tuberculosis

As contextual evidence, epidemiological studies show an increased risk of tuberculosis in patients with COPD. In a Swedish registry cohort of 115,867 patients hospitalised with COPD, the adjusted hazard ratio for developing active tuberculosis was 3.0 (95% CI 2.4–4.0) compared with matched controls. This finding applies to patients whose COPD was recorded during hospitalisation and does not estimate risk across all patients with mild airflow obstruction. Among those who developed active tuberculosis, patients in the COPD cohort had higher odds of death from any cause within one year of tuberculosis diagnosis

than population controls who also developed tuberculosis (age- and sex-adjusted OR 2.2, 95% CI 1.2–4.1) [14]. Impaired lung function at baseline is also a marker of increased risk: in a national population-based cohort (16,457 participants, 72 tuberculosis cases; median follow-up 5.5 years), obstructive impairment was associated with subsequent tuberculosis with an aHR of 2.03 (95% CI 1.12–3.68), and a spirometric restrictive pattern with an aHR of 2.19 (1.12–4.29) [44]. The incidence estimates concern susceptibility to tuberculosis in patients with pre-existing COPD or lung function impairment; they do not establish that persistent airflow limitation after tuberculosis is COPD. However, these studies do not distinguish reactivation of latent infection from newly acquired infection.

Possible mechanisms include impaired mucociliary clearance, structural lung remodelling, chronic inflammation and weakened local antimicrobial defence [4,11]. Frequent exacerbations, age, smoking, undernutrition and comorbidity may also contribute [4,17]. The contribution of each factor has not been quantified: observed associations and biologically plausible mechanisms do not yet establish a single causal cycle.

The use of inhaled corticosteroids (ICS) warrants separate consideration. Observational studies and a meta-analysis associate ICS use with a higher frequency of active tuberculosis in patients with obstructive lung diseases, while registry studies identify differences between fixed-dose combinations [15,16,58]. These findings do not imply that ICS are contraindicated in all patients with COPD and a history of tuberculosis, but they do require an individual assessment of infection risk [2,16].

3.3. Shared Risk Factors

The frequent coexistence of tuberculosis and COPD is partly explained by shared risk factors: smoking, low socioeconomic status, occupational and household inhalational exposures, and undernutrition [4]. Interpretation of studies also requires consideration of age, sex, diabetes mellitus, human immunodeficiency virus (HIV) infection, alcohol misuse, access to care and timely disease detection [17,56]. These factors do not have the same importance for active tuberculosis, COPD and post-tuberculosis impairment. In a 2026 meta-analysis of comorbidity and PTLD, the association with diabetes was uncertain, while people living with HIV had lower odds of spirometric impairment; the certainty of these estimates was very low. None of the included studies assessed the combined effects of multiple chronic diseases on PTLD risk [57].

Smoking is one of the most important shared risk factors. It increases the likelihood of COPD, impairs mucociliary clearance and sustains chronic airway inflammation [2,4]. Smoking is associated with tuberculosis infection and active tuberculosis [59,60], while tobacco use is associated with disease recurrence and mortality during treatment [61]. Studies of tuberculosis-associated persistent airflow limitation need to account for smoking both as a conventional COPD risk factor and as a factor that may modify the association between tuberculosis and airflow limitation. In the observational cohort of Joo et al., smoking was associated with subsequent COPD detection; this is not equivalent to evidence of accelerated FEV_1 decline after tuberculosis [48].

Age and comorbidities also influence the coexistence of tuberculosis and COPD. In COPD, ageing, cardiovascular disease, diabetes mellitus, polypharmacy and reduced physiological reserve complicate patient management [2]. Older age is also associated with pulmonary sequelae of tuberculosis, although this association does not establish the cause of functional impairment in an individual patient [56]. In the cohort of Joo et al., older age at tuberculosis diagnosis and lower baseline FEV_1 were associated with subsequent airflow obstruction [48], indicating the relevance of patients' health before and during tuberculosis to the observed epidemiological association.

Social vulnerability and limited access to care may hinder timely diagnosis and long-term follow-up for both diseases [4]. Delayed tuberculosis diagnosis is considered a factor in post-tuberculosis damage [9,17]. After treatment, loss of income, limitations in work capacity and other social consequences may impede access to care, so an assessment of patients' needs should also address these circumstances [3].

4. Mechanisms of Tuberculosis-Associated Persistent Airflow Limitation

Recent reviews describe potential contributors to post-tuberculosis airflow limitation, including a combination of structural lung damage (cavitation, fibrosis, bronchial remodelling and emphysematous changes), chronic inflammation, immune dysregulation, putative vascular abnormalities and the systemic consequences of inflammation [11,13,62].

Three levels of evidence need to be distinguished. The first concerns mechanisms of injury during active tuberculosis, studied in cellular and experimental models and in samples from patients with active disease. The second comprises observations in patients after cure, including cross-sectional studies and a limited number of prospective cohorts [63,64]. The third comprises hypotheses about mechanisms of progression of post-tuberculosis airflow limitation, for which longitudinal data remain scarce [17,65]. The available evidence does not justify linking these levels into a causal chain of "active inflammation → persistent inflammation → progression of airflow obstruction": after treatment, lung function may recover, stabilise or deteriorate [18,49].

Smoking-related COPD is associated with prolonged exposure to tobacco smoke and other inhaled particles and gases [2]. In tuberculosis-associated persistent airflow limitation, prior infectious and inflammatory lung injury is an important contributor. After microbiological cure, this damage forms the morphological basis of PTLD. Airflow obstruction may reflect small airway inflammation and mechanical distortion of bronchopulmonary structures [11,36,39].

4.1. Structural Lung Remodelling After Tuberculosis

After tuberculosis, some patients have persistent fibrotic scarring, bronchial distortion and stenosis, bronchiectasis, residual cavities, areas of tissue destruction, pleural adhesions, regional hyperinflation, reduced elastic recoil and altered airway geometry. A systematic review of the imaging manifestations of PTLD (37 studies) confirms the diversity of lesions affecting the parenchyma, bronchi, pleura and vasculature [8]; reviews of non-infectious post-tuberculosis disorders describe their functional consequences [28,31].

Post-tuberculosis remodelling produces airflow obstruction through several pathways. First, fibrosis and traction-related distortion narrow the bronchial lumen and alter bronchial geometry, including that of the small airways [39,43]. Second, bronchiectasis and bronchial distortion promote secretion retention, recurrent infections and persistent inflammation [66]. Third, residual cavities, localised parenchymal destruction and pleural adhesions may alter elastic recoil and the uniformity of ventilation, promoting air trapping and regional hyperinflation; conversely, predominant fibrosis and lung volume loss are accompanied by reduced TLC [31,36,63]. Airflow limitation may also develop in patients without conventional COPD risk factors [39,46].

Observational studies show an association between the severity of initial disease and the degree of subsequent impairment: extensive involvement, cavitation, recurrent episodes of tuberculosis, residual CT abnormalities and bronchiectasis are associated with persistently impaired lung function [48,53,54,64]. After treatment, a substantial proportion of patients continue to experience respiratory symptoms, reduced spirometric measures, limited physical activity and poorer quality of life [20,54,55].

Post-tuberculosis remodelling affects the entire respiratory system: fibrosis and pleural changes reduce lung compliance, bronchiectasis sustains chronic inflammation and infective exacerbations, residual cavities may provide a site for fungal colonisation and the development of chronic pulmonary aspergillosis, and localised destruction disrupts ventilation–perfusion matching [31,62,67]. Bronchiectasis is not synonymous with persistent airflow limitation, as it can occur with or without airflow obstruction, and a residual cavity is not equivalent to emphysema. These components should be described separately because they require different clinical decisions.

4.2. Chronic Inflammation and Immune Dysregulation

Structural changes do not fully explain the severity of symptoms and functional impairment in some patients [63]. Reviews of PTLD mechanisms suggest a possible role for persistent inflammation, immune dysregulation and impaired lung tissue repair, but emphasise the lack of longitudinal studies linking immune alterations to lung function trajectories [17,22,65,68]. In an exploratory cross-sectional study of 48 adults within the first 6 months after successful treatment, the extent of positron emission tomography/CT (PET/CT) abnormalities and functional impairment was associated with immune measures in blood and bronchoalveolar lavage fluid [63]. In a prospective cohort of 205 adults in Kenya, a subgroup of whom underwent transcriptomic analysis, an obstructive spirometric pattern 6 months after treatment was associated with enhanced interferon transcriptional responses at treatment completion [64]. These findings support the hypothesis that residual inflammation has a role, but do not establish that it causes progressive post-tuberculosis airflow limitation.

In active tuberculosis, inflammation involves the activation of macrophages, neutrophils, T lymphocytes, epithelial cells and stromal cells. At different stages of disease, tissue injury involves tumour necrosis factor-α (TNF-α), interleukin (IL)-1β, IL-6, IL-8, IL-17, transforming growth factor-β (TGF-β), chemokines, matrix metalloproteinases (MMPs), reactive oxygen species and mediators of fibrosis. These mechanisms are necessary for controlling mycobacterial infection, but excessive activation or dysregulation contributes to extracellular matrix destruction, lung tissue breakdown, fibrosis and airway remodelling [11,69].

Neutrophils contribute to antimicrobial defence, but their excessive activation in tuberculosis is associated with tissue injury, caseous necrosis, reactive oxygen species production, extracellular trap formation and increased protease activity [70–72]. In a mouse model, the neutrophilic response was linked to lung tissue necrosis and an adverse inflammatory course [73]; neutrophilic inflammation is also relevant to conventional COPD [11]. Macrophages, the principal target cells of *Mycobacterium tuberculosis*, control infection during chronic inflammation while also sustaining the production of cytokines, profibrotic factors and matrix-degrading enzymes [17,68]. In vitro, apoptotic neutrophils enhanced the inflammasome-mediated, IL-1β-dependent response of infected human macrophages, while improving intracellular control of mycobacteria [74]; in a mouse model, inflammatory macrophages were associated with tissue injury and fibrosis that persisted for weeks during antibacterial therapy [75].

Another mechanism is protease–antiprotease imbalance. In active tuberculosis, increased MMP activity contributes to extracellular matrix degradation, cavitation and remodelling; its regulation depends on the cytokine environment and cellular interactions [76,77]. Neutrophil-derived MMP-8 has been studied in cellular models and biopsy samples from patients with active tuberculosis [78], membrane type 1 matrix metalloproteinase (MT1-MMP; MMP-14) in monocytes, granulomas and sputum [79], and epithelial MMP-9 in a cellular model in which its secretion increased in response to medium conditioned by infected mono-

cytes [80]. Studies in rabbits and patient samples implicate the cysteine protease cathepsin K in cavitation and collagen turnover [81]. IL-17 has divergent effects on proteases: in epithelial cells, IL-17 increased MMP-3 but reduced MMP-9 [82]. These studies elucidate mechanisms of infection-related injury, but do not establish a role for any specific protease in the progression of post-tuberculosis airflow limitation after microbiological cure.

Systemic inflammation has been investigated in studies using the TOPD label. The systemic inflammation response index (SIRI), calculated from blood neutrophil, monocyte and lymphocyte counts, was examined in a single-centre cross-sectional sample of 737 patients, 83 of whom were classified as having TOPD by the study authors; the area under the receiver operating characteristic (ROC) curve was 0.702 before and 0.668 after propensity score matching [24]. The index showed moderate discrimination between existing groups: the study does not establish a validated diagnostic threshold for clinical use or demonstrate that SIRI predicts the development or progression of post-tuberculosis airflow limitation. Differences in autoantibody profiles and lymphocyte subsets were described in a small exploratory study (44 patients classified as having TOPD) [23]. These findings generate immunological hypotheses but do not confirm an autoimmune basis for persistent airflow limitation or justify immunomodulatory treatment. In a multicentre cross-sectional study, patients with tuberculosis-associated COPD differed from those with smoking-related COPD in systemic inflammatory marker levels and predictors of exacerbations [83]. These data are insufficient to support a clinical score, but suggest possible immunobiological differences between the studied groups. The original study labels are retained here; their applicability to tuberculosis-associated persistent airflow limitation depends on the respective inclusion criteria. In a prospective study of 169 patients, baseline inflammatory measures were associated with the severity of post-treatment CT abnormalities [84], while in a study of 71 participants after therapy, serum interferon-γ-inducible protein 10 (IP-10) and TNF-α correlated with residual lung metabolic activity on PET/CT [85]. These findings concern structural abnormalities and metabolic activity and cannot be extrapolated to the prediction of progressive airflow obstruction.

Oxidative stress also links inflammation to tissue injury. Reactive oxygen species contribute to antimicrobial responses while also aggravating epithelial injury, neutrophil activation and matrix destruction. Mechanisms by which mycobacteria evade killing by reactive oxygen species, as well as the generation of low-density granulocytes during infection, have been described [86,87]. In a randomised trial of N-acetylcysteine in 140 adults with active tuberculosis, glutathione levels increased and TNF-α decreased, but mycobacterial clearance from sputum was also slower [88]. These divergent findings were obtained during active disease and do not justify antioxidant therapy for established post-tuberculosis airflow limitation.

The airway and gut microbiomes have been studied in active tuberculosis and during the first months of treatment. Dysbiosis and evidence of increased movement of microorganisms between airway compartments have been described, together with changes in gut microbiota associated with anti-tuberculosis therapy, nutrition and previous antibiotic use [89,90]. Hazra et al. found lower bacterial alpha diversity in sputum from patients who had completed tuberculosis treatment than in healthy controls [91]. Whether such changes precede recurrent respiratory infection or sustained airway inflammation in patients with confirmed post-tuberculosis airflow limitation remains unclear.

4.3. Bronchial Remodelling

Bronchial wall thickening, peribronchial fibrosis, small airway distortion, traction bronchiectasis, stenosis, impaired bronchial drainage, mucus hypersecretion and susceptibility to recurrent infections may persist after tuberculosis [9,31,66]. These changes can

give rise to chronic airflow obstruction even when emphysematous changes are only moderate [36].

Post-tuberculosis bronchiectasis may result from fibrotic traction, destruction of the bronchial wall within inflamed areas, chronic infection and impaired drainage. Unlike conventional COPD, in which airflow obstruction is more often associated with small airway disease and emphysema, post-tuberculosis airflow limitation may also involve distortion of large and medium-sized bronchi [9,11]. This can lead to chronic secretion retention, bacterial colonisation, recurrent infective exacerbations and sustained neutrophilic inflammation [66,92]. Recurrent infections aggravate bronchial wall injury, while chronic inflammation sustains remodelling, completing the vicious cycle described in bronchiectasis [43,66]. Clinically, this pattern may resemble COPD with frequent exacerbations, although post-tuberculosis bronchial distortion and focal or regional damage may play a substantial role [36,39].

Reviews of post-tuberculosis disorders describe tracheobronchial stenosis, broncholithiasis, bronchial anthracofibrosis and other forms of airway involvement that increase airflow resistance and cause symptoms not explained by the spirometric abnormalities characteristic of COPD [28,31].

4.4. Emphysema and Post-Tuberculosis Lung Destruction

Conventional smoking-related COPD is associated with centriacinar emphysema, chronic small airway inflammation and progressive loss of alveolar septa [2,11]. Post-tuberculosis destruction, by contrast, is focal, cavity-forming and associated with scarring and distortion; it involves necrosis, cavitation, fibrosis, traction-related bronchial changes and local disruption of normal parenchymal architecture [31,68]. The role of bronchial obstruction in the pathogenesis of post-primary tuberculosis and cavitation has been discussed separately [93].

Cavitation in tuberculosis is both a marker of active disease severity and a potential basis for subsequent chronic changes [31,68]. Tissue destruction around a cavity is accompanied by altered collagen turnover, protease activity and inflammation; the role of proteases has been demonstrated in models of active tuberculosis and in patient samples [76,81]. Residual cavities, scar contraction, bronchial distortion and impaired ventilation may persist after treatment. Cavity closure alone does not indicate restoration of normal structure and function in the affected region [8,31].

In smokers with a history of tuberculosis, emphysematous changes may coexist with localised hyperinflation, scar-related distortion, residual cavities and bronchiectasis [12,36]. This combination may be accompanied by dyspnoea, reduced exercise tolerance and infectious complications [31,83]. However, it is not yet possible to conclude that the risk of these manifestations exceeds that in COPD alone or residual post-tuberculosis changes alone, because direct comparative data are limited [43,66].

A reduced FEV_1/FVC ratio after tuberculosis may reflect small airway disease as well as structural changes and regional ventilation abnormalities [36,39,49]. To understand the mechanisms of airflow obstruction, this measure should be interpreted in the context of tuberculosis history, CT findings and the clinical features [10,43].

4.5. Vascular and Cardiovascular Components

The vascular component is less well studied than structural damage and bronchial remodelling. PTLD may involve the pulmonary vasculature; proposed mechanisms include chronic hypoxaemia, ventilation–perfusion mismatch, fibrotic destruction of the capillary bed, pulmonary vascular remodelling, endothelial dysfunction and the consequences of systemic inflammation [62,94]. Pulmonary hypertension after tuberculosis is thought to

develop through a combination of chronic parenchymal damage, hypoxic vasoconstriction, vascular remodelling and concomitant COPD [62]; its frequency depends on patient selection and the method of detection. A meta-analysis estimated the prevalence of pulmonary hypertension after tuberculosis at 6.3% among community-dwelling participants who were not seeking healthcare, 42.4% among symptomatic or hospitalised patients, and 67.0% among those with chronic respiratory failure [95]. In a single-centre cross-sectional study of 100 patients completing treatment, one met the study's echocardiographic criterion for pulmonary hypertension and three others had possible pulmonary hypertension [96]. Pulmonary artery enlargement on CT and an echocardiographic probability of pulmonary hypertension are not equivalent to haemodynamic confirmation [62].

Systemic inflammation, hypoxaemia, endothelial dysfunction, smoking and metabolic abnormalities are considered possible links between tuberculosis and cardiovascular risk [62,97,98]. Basham et al. found a higher pooled risk of major adverse cardiovascular events, including cardiovascular death, after a diagnosis of active tuberculosis [97]. The cohort study by Kim found that excess mortality persisted long after tuberculosis. The review by Wang summarises these long-term consequences [97–99]. In COPD, cardiovascular diseases have a substantial effect on mortality and quality of life [2,100]. Whether these risks are additive or amplified specifically in patients with tuberculosis-associated persistent airflow limitation remains insufficiently examined in comparative studies. Future studies should assess hypoxaemia, signs of pulmonary hypertension, endothelial dysfunction, cardiovascular disease and long-term mortality alongside FEV_1 and imaging abnormalities.

5. Clinical Features of Tuberculosis-Associated Persistent Airflow Limitation

The clinical presentation of tuberculosis-associated persistent airflow limitation reflects both chronic airflow obstruction and accompanying post-tuberculosis lung damage; it cannot be reduced to a spirometric criterion or residual abnormalities on a chest radiograph. Associated features include chronic respiratory symptoms, functional limitations, structural CT abnormalities, susceptibility to infections, a risk of exacerbations and hospitalisation, and reduced quality of life [20,31,43]. In addition to airflow obstruction, patients may have a mixed ventilatory defect or prominent bronchiectatic or fibrotic–destructive changes [12,63]. Evidence from broader PTLD populations is considered below to describe these accompanying features; patients without persistent airflow limitation fall outside the principal focus of this review.

5.1. Symptoms

The most typical clinical manifestations and consequences include dyspnoea, chronic cough, sputum production, reduced exercise tolerance, frequent respiratory infections, fatigue, weight loss and poorer quality of life. Episodes of haemoptysis may occur in the presence of post-tuberculosis bronchiectasis or residual cavities [31,101]. Symptom severity may not correspond to the degree of FEV_1 reduction: dyspnoea and activity limitation may depend on airflow obstruction as well as fibrosis, hyperinflation, impaired gas exchange, bronchiectasis, muscle dysfunction and the systemic consequences of chronic inflammation [101–103].

Evidence from populations not restricted to patients with persistent airflow limitation shows that respiratory symptoms often persist after treatment. In a small study of patients who had been cured ($n = 45$), the mean distance covered in the 6-min walk test (6MWT) was 294.5 m, well below reference values, and lung function abnormalities were detected in 48% [104]. In the Malawian cohort, 60.7% of patients reported symptoms at treatment completion and 30.7% at one year [54]. Symptoms may persist for years after microbiological cure [18].

Dyspnoea has multiple causes, including post-tuberculosis changes and concomitant cardiovascular disease. In a selected group of adults with PTLD undergoing assessment for possible surgery, spirometric measures and diffusing capacity of the lung for carbon monoxide (DL_{CO}) correlated only weakly with peak oxygen uptake, whereas the FEV_1/FVC ratio was not associated with it [102]. Spirometry is therefore supplemented with the modified Medical Research Council (mMRC) dyspnoea scale and COPD Assessment Test (CAT), assessment of physical activity, pulse oximetry and, where possible, exercise testing [10].

A bronchiectatic component is typically associated with chronic productive cough, recurrent infections, bacterial colonisation and episodes of haemoptysis [31,66]. In a study of the clinical, radiological and functional characteristics of post-tuberculosis bronchiectasis, cough was a leading symptom, and spirometry identified obstructive, restrictive and mixed patterns [92]. Cough after tuberculosis should not automatically be attributed solely to COPD: it may indicate bronchiectasis, a residual cavity, chronic infection or complications of PTLD [9,10].

Weight loss and fatigue may reflect the consequences of previous tuberculosis, chronic inflammation, nutritional deficiency, sarcopenia, reduced physical activity, comorbidities, anxiety and depression [65,101]. Unintentional weight loss requires investigation of its cause, including active infection, rather than nutritional support alone [9,10].

5.2. Lung Function Impairment

Functional impairments in post-tuberculosis lung disease are highly heterogeneous. Patients may have obstructive ventilatory impairment, a spirometric pattern suggesting restriction, a mixed pattern, reduced diffusing capacity, hyperinflation, impaired gas exchange, exercise-induced desaturation and a reduced 6MWT distance. Severity ranges from minimal abnormalities to severe chronic respiratory failure [19,55,94,101].

Persistent post-bronchodilator airflow limitation is the defining functional abnormality considered in this review. Population-based and clinical studies have demonstrated an association between previous tuberculosis, airflow obstruction and reduced FEV_1/FVC, including in never-smokers [42,45,46]. Clinical series covering the broader spectrum of post-tuberculosis impairment have described different spirometric patterns: among 47 treated patients selected for chronic exertional dyspnoea, an obstructive defect was detected in 55.3%, a restrictive pattern in 29.7% and a mixed pattern in 14.8% [105]. In three PTLD cohorts from Brazil, Italy and Mexico, the predominant patterns were obstructive, mixed and normal, respectively [106]. In a prospective study during treatment, changes in FEV_1 were associated with the radiological assessment of disease extent [107]. Classifying patients simply as having or not having COPD does not capture this diversity.

Spirometry alone cannot confirm restriction. A reduced FVC with a preserved FEV_1/FVC ratio only raises suspicion of restriction, or may reflect inadequate effort and a non-specific pattern; in the presence of airflow obstruction, low FVC may result from air trapping. Restriction is confirmed by a TLC below the lower limit of normal; a mixed impairment requires confirmation of both airflow obstruction and reduced TLC [41]. Thus, the proportions of "restrictive" and "mixed" abnormalities in post-tuberculosis spirometry studies should be interpreted as the proportions of corresponding patterns, rather than confirmed defects.

Reduced DL_{CO} may reflect emphysematous changes, fibrosis, loss of the capillary bed, vascular abnormalities and ventilation–perfusion mismatch [36,41,62]. In some patients, dyspnoea severity and reduced exercise tolerance are related more closely to impaired gas exchange, lower peak oxygen uptake and exercise-induced desaturation than to FEV_1. In a cross-sectional study of 60 adults with PTLD, measures from cardiopulmonary exercise

testing, spirometry, oscillometry and chest radiography showed different correlations with quality of life [103].

Exercise tests identify functional limitations that are not always apparent on spirometry. The 6MWT distance and peak oxygen uptake help assess actual activity limitation; in a prospective cohort of patients with various chronic lung diseases, the 6MWT distance independently predicted mortality [108]. The 6MWT and incremental shuttle walk test (ISWT) are distinct methods with their own reference values; their results should not be combined into a single outcome [109]. In rehabilitation studies of patients with chronic post-tuberculosis lung disease, walking distance and quality-of-life measures were the main outcomes, and improvements were observed in these measures [25,26,110].

In a pilot study comprising three groups of 10 participants each—people with tuberculosis sequelae, people who had recovered from tuberculosis without sequelae, and healthy individuals—impulse oscillometry (IOS) identified increased peripheral resistance and abnormal reactance in some patients with post-tuberculosis changes [111]. In a quasi-experimental study of home-based rehabilitation, oscillometric measures and performance on the Glittre activities-of-daily-living test improved, although spirometric measures did not increase [112]. These observations do not establish that oscillometry identifies clinically relevant post-tuberculosis small airway dysfunction before spirometric airflow obstruction is detected or predicts progression to persistent airflow obstruction; this requires evaluation in longitudinal studies.

5.3. Imaging Findings

CT findings in PTLD include fibrotic scarring, bronchiectasis, residual cavities, emphysema, atelectasis, pleural thickening, hilar distortion, localised hyperinflation, traction-related bronchial distortion and signs of impaired ventilation. The diversity of these structural sequelae and their persistence after treatment are confirmed by a systematic review of PTLD imaging manifestations [8]. These findings may accompany post-tuberculosis airflow limitation but do not establish its presence without functional assessment.

CT allows more accurate assessment of bronchiectasis, localised emphysema, residual cavities, traction-related changes and mosaic ventilation than chest radiography [8,10]; bronchiectasis can already be detected during active tuberculosis [113]. However, CT describes morphological abnormalities without establishing the cause of airflow obstruction or distinguishing the contributions of smoking and tuberculosis in an individual patient. International standards recommend CT after tuberculosis when the additional information may alter a clinical decision, rather than routinely in all patients [10].

Post-tuberculosis bronchiectasis is a key CT finding linking previous tuberculosis with chronic symptoms and exacerbations. It may be tractional, cylindrical, varicose or mixed, often occurs in areas of previous disease, and coexists with fibrosis, bronchial distortion and volume loss [66]. Its presence changes the interpretation of symptoms: sputum production, frequent infections and haemoptysis may be attributable to the bronchiectatic component of PTLD [31,66]. Residual cavities have independent relevance: in a brief report from the follow-up of a prospective cohort, cavities were associated with less improvement in the bodily pain score at 6 months, with no significant differences in changes in other quality-of-life domains [114]. Cavities also require an assessment of the risk of haemoptysis, fungal colonisation and chronic pulmonary aspergillosis [31,67].

In smokers, emphysema may be consistent with conventional COPD, whereas in individuals with previous tuberculosis, localised hyperinflation may reflect post-infectious parenchymal destruction and architectural disruption [12,36]. CT reports should describe the presence and distribution of emphysema and its relationship to areas of fibrosis, cavitation and bronchiectasis. Promising approaches include standardised CT scores for post-

tuberculosis damage and quantitative assessment of bronchiectasis, fibrosis, emphysema and air trapping, with comparison against FEV_1, DL_{CO}, exercise test results and quality of life [8,63]. Comparisons of imaging abnormalities, lung function, oxygen uptake during exercise and quality of life show that individual spirometric measures do not fully capture the severity of limitations in PTLD [103].

5.4. Exacerbations and Hospitalisation

Evidence on respiratory exacerbations and hospitalisation includes COPD cohorts with a history of tuberculosis and registry studies of COPD-related outcomes among tuberculosis survivors [35,47]. Chronic airflow obstruction, bronchiectasis, impaired bronchial drainage, bacterial colonisation, residual cavities, reduced pulmonary functional reserve, hypoxaemia, systemic inflammation and concomitant cardiovascular disease may contribute to the severity of these events; these factors require individual assessment [31,43,62]. Direct evidence comparing event frequency and severity between patients with tuberculosis-associated persistent airflow limitation and those with post-tuberculosis changes without airflow obstruction is insufficient.

Among 598 patients hospitalised with a COPD exacerbation, 93 (15%) had a history of tuberculosis; they were younger on average, were hospitalised more often, had lower lung function and higher arterial carbon dioxide tension ($PaCO_2$). Their COPD was diagnosed at a younger age. The mean age at death was also lower in those with previous tuberculosis, although three-year survival did not differ significantly [35]. In the Korean registry, COPD-related hospitalisation was approximately twice as frequent among tuberculosis survivors as among controls (aHR 2.03; 95% CI 1.81–2.27) [47]. These findings indicate greater healthcare needs in patients with both a history of tuberculosis and COPD, although only a few studies have directly compared event frequency with that in smoking-related COPD.

Respiratory exacerbations in patients with post-tuberculosis airflow limitation may have different causes. In patients with coexisting COPD, these may include COPD exacerbations associated with viral or bacterial infections and air pollution [2]. Decompensation of comorbid conditions may also mimic or aggravate an exacerbation [2]. In patients with post-tuberculosis bronchiectasis and residual cavities, deterioration may be related to bacterial infection in bronchiectatic airways, haemoptysis, aspergillosis, non-tuberculous mycobacteria (NTM) or recurrent tuberculosis; the differential diagnosis therefore needs to be broader than for a conventional COPD exacerbation [9,31,67]. In a multicentre cross-sectional study, systemic inflammatory profiles and predictors of exacerbations differed between patients with tuberculosis-associated COPD and those with smoking-related COPD [83].

Hospitalisation for COPD exacerbations in the general COPD population is associated with high subsequent mortality, readmission and a poorer prognosis [115–118]; applying these findings to tuberculosis-associated persistent airflow limitation represents extrapolation. In patients with post-tuberculosis airflow limitation, reduced pulmonary functional reserve, hypercapnia, hypoxaemia, bronchiectasis and comorbidity may make additional contributions [35,43]. Hospitalisation for respiratory deterioration in a patient with airflow obstruction and a history of tuberculosis should be regarded as a high-risk marker requiring referral to a respiratory specialist and assessment of rehabilitation needs [10]. The consequences of tuberculosis persist beyond the active episode: morbidity, healthcare use and mortality remain elevated, and post-tuberculosis changes increase the lifetime burden of disease [1,99,119].

6. Methodological Challenges in Research on Tuberculosis-Associated Persistent Airflow Limitation

Combining patients with different disease sequences and mechanisms of airflow obstruction limits the comparability of studies on tuberculosis-associated persistent airflow limitation. The observed association may therefore reflect several partially overlapping forms of lung damage rather than a single mechanism [43,55].

In PLATINO and BOLD, tuberculosis history was associated with airflow obstruction and impaired lung function. However, this information was based on patient reports, and neither CT morphology nor the severity of previous disease was assessed [42,45]. Standardised post-bronchodilator spirometry in adults over 40 years and clinical history are sufficient for population-level assessment, but not for comprehensive clinical characterisation or distinguishing the contributions of tuberculosis, smoking, structural changes, age, comorbidity, social vulnerability and the organisation of care [3,43].

6.1. Differences in the Ascertainment of Tuberculosis History

Studies ascertain tuberculosis through patient reports, a clinical diagnosis of active disease, codes A15–A19 and B90, registries, hospital records, fluorography, chest radiography or CT. The terms "history of TB", "active TB", "previous TB", "post-TB lung disease", "tuberculosis sequelae" and "post-TB chronic lung disorders" are not equivalent. Reliance on patient reports may underestimate or overestimate previous disease, especially when the diagnosis was remote or uncertain; these limitations are considered when interpreting studies based on clinical history [42,45]. Codes A15–A19 denote active tuberculosis at different anatomical sites, not residual lung damage; studies of pulmonary sequelae need to identify respiratory disease sites specifically. Code B90 denotes tuberculosis sequelae [120]. However, a code does not confirm a specific structural or functional abnormality, and its recording depends on documentation practices; it therefore does not, by itself, establish PTLD or persistent airflow limitation [10,121]. CT better characterises morphology, but requires standardised reporting and is not always available in population samples [8,10].

Establishing the temporal sequence requires lung function data before tuberculosis, during treatment and afterwards [49]. Concurrent recording of airflow obstruction and tuberculosis history supports an association with chronic airflow limitation but limits causal interpretation. Assessment of newly diagnosed COPD after tuberculosis requires the exclusion of pre-existing COPD [47,50].

Registry studies should describe the source of diagnostic codes, the observation period and follow-up start date, the patient selection algorithm, handling of duplicate records, exclusion criteria, outcome ascertainment and data completeness. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement and its REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) extension are appropriate reporting frameworks [122–124]. These standards promote complete reporting, but do not establish the validity of clinical classifications or replace an analysis plan, consideration of bias and sound study design.

6.2. Differences in Outcome Definitions

A second problem is inconsistency in outcome definitions. Some studies use a COPD diagnosis based on criteria incorporating spirometry as the outcome; others use reduced FEV_1/FVC, low FEV_1, a clinical diagnosis of COPD, COPD-related hospitalisation, death, reduced quality of life, decreased physical activity, chronic respiratory failure or the presence of PTLD. These outcomes are not interchangeable: they describe lung function, the clinical course, the organisation of care, prognosis and the impact of disease on patients' lives [10,47,55].

A reduced post-bronchodilator FEV_1/FVC ratio identifies airflow obstruction, which is not specific for COPD and requires interpretation in the clinical context [2]. Spirometric assessment is useful for epidemiological studies but does not encompass all manifestations of PTLD. A patient who has recovered from tuberculosis may have severe symptoms, bronchiectasis, reduced DL_{CO}, exercise-induced desaturation, residual cavities and poor quality of life despite only a moderate reduction in FEV_1 [10,103]. A reduced FEV_1/FVC ratio may reflect bronchial distortion, traction bronchiectasis and regional emphysema associated with post-tuberculosis damage; it should not automatically be attributed to COPD [43]. Interpretation of a low FVC requires lung volume data; if these are unavailable, it should be stated explicitly that restriction has not been confirmed [41].

A clinical COPD diagnosis in medical records or a registry depends on access to spirometry, diagnostic practice, coding and healthcare use. Functional impairment may be present without a COPD code, while a code may be present without documented post-bronchodilator spirometry, creating a risk of outcome misclassification [121,125]. Hospitalisation and death are harder outcomes, but they also depend on access to care, social support, comorbidity and healthcare organisation. Studies need to specify whether outcomes are all-cause, respiratory, or related to COPD or tuberculosis. Patient-important outcomes—quality of life, dyspnoea, CAT, mMRC, activity, 6MWT and work capacity—are often absent from registries: diagnoses, healthcare contacts and deaths are recorded more reliably than functional limitations. The completeness of recording should therefore be checked separately for each outcome [10,121].

6.3. Conflation of Structural and Functional Components

Combining patients with smoking-related COPD, post-tuberculosis structural changes, active inflammation, recurrent tuberculosis and different ventilatory defects increases sample size, but complicates the pathogenetic interpretation of findings [43,55].

Despite an identical reduction in FEV_1/FVC, smoking-related emphysema and post-tuberculosis bronchial distortion may differ in their mechanisms, complications and treatment approaches. Including patients with restriction but no airflow obstruction in a group intended to represent post-tuberculosis airflow limitation distorts assessment of obstructive impairment [41,43].

When COPD coexists with obstructive PTLD, COPD guidance informs the choice of inhaled therapy [2]. Bronchiectasis or residual cavities broaden the differential diagnosis of worsening symptoms to include bacterial infection, NTM disease and chronic pulmonary aspergillosis [31,66,67]. Published PTLD standards use symptom burden and functional limitations to identify rehabilitation and follow-up needs [10].

To improve comparability across studies, the authors propose recording the structural and functional components of PTLD and any coexisting COPD in patients with airflow obstruction (Table 2) as coexisting features that influence management, rather than mutually exclusive classes. This working framework is based on the diversity of morphology and heterogeneity of post-tuberculosis functional impairments described in the literature [8,43,55]. A minimum description of a study group includes age, smoking and other inhalational exposures, the outcome of tuberculosis treatment and the time since treatment completion, recurrent episodes, the criterion for airflow obstruction, FEV_1, FVC and clinically relevant structural abnormalities [10,124].

Table 2. Structural and functional components of PTLD and coexisting COPD in the assessment of patients with airflow obstruction.

Pattern or Component	Morphology	Functional Profile	Risks	Management Priorities
Smoking-related COPD with a history of TB (a coexisting or alternative diagnosis)	Centriacinar emphysema and small airway disease; post-tuberculosis structural damage may coexist	Obstructive	Exacerbations, cardiovascular outcomes	LABA/LAMA; smoking cessation; standard COPD treatment
Post-tuberculosis airflow limitation with predominant bronchial distortion	Peribronchial fibrosis, bronchial distortion and stenosis; localised hyperinflation	Reduced post-bronchodilator FEV_1/FVC; FEV_1 quantifies impairment, and a raised RV/TLC suggests air trapping	Persistent dyspnoea, low pulmonary reserve	Spirometry, lung volumes, CT, rehabilitation; careful consideration of ICS
Bronchiectatic component	Traction and post-infectious bronchiectasis, impaired drainage	Obstructive or mixed; bronchiectasis may also occur without airflow obstruction	Sputum production, recurrent infections, haemoptysis; number of infective exacerbations per year	Airway clearance, sputum cultures, antibiotic selection, vaccination
Cavitary–destructive component	Residual cavities, localised parenchymal destruction	Variable; DL_{CO} may be reduced	Haemoptysis, chronic pulmonary aspergillosis and NTM disease; recurrent TB enters the differential diagnosis when symptoms worsen	CT, Aspergillus IgG, microbiological investigations; vigilance for aspergillosis and NTM
Fibrotic component	Fibrosis, pleural adhesions, volume loss	Reduced TLC, sometimes with reduced DL_{CO}; isolated restriction without airflow obstruction belongs to non-obstructive PTLD	Exercise-induced desaturation, pulmonary hypertension	Body plethysmography, DL_{CO}, echocardiography, rehabilitation
Combined pattern	A combination of emphysema, fibrosis, bronchiectasis and cavities	Obstructive and mixed impairments may occur	The risk of exacerbations and adverse outcomes depends on the combination of components	Individualised multidisciplinary approach

Components may coexist in an individual patient. Smoking-related COPD is included as a coexisting or alternative diagnosis, not as a component of PTLD solely on the basis of a history of TB. This framework is intended to describe lung damage and stratify patients; it is not a validated classification. Coexisting COPD informs inhaler selection [2]. Bronchiectasis or residual cavities broaden the differential diagnosis when symptoms worsen [126–128]. Published PTLD standards relate rehabilitation and follow-up to symptoms and functional impairment [10]. Investigations and treatment are selected according to clinical indications; identifying the corresponding component alone is insufficient. LABA, long-acting β_2-agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroids; NTM, non-tuberculous mycobacteria. TB, tuberculosis; COPD, chronic obstructive pulmonary disease; PTLD, post-tuberculosis lung disease; CT, computed tomography; DL_{CO}, diffusing capacity of the lung for carbon monoxide; TLC, total lung capacity; RV, residual volume; IgG, immunoglobulin G.

6.4. Inadequate Consideration of Smoking and Social Vulnerability

A fourth problem is incomplete consideration of smoking, age, sex, social status, access to healthcare and comorbidity. These factors simultaneously influence the likelihood of tuberculosis, the risk of chronic airflow obstruction, disease severity, healthcare use and the probability of receiving a diagnosis [2,59,60,129].

A binary smoker/non-smoker classification may underestimate the contribution of smoking: duration, intensity, pack-years, current or former smoking, passive smoking and

occupational inhalational exposures should all be considered [2,59]. The importance of adjustment for smoking was demonstrated in PLATINO and BOLD [42,46]. COPD is more often detected at older ages, and in some populations male sex is associated with higher smoking prevalence, greater tuberculosis risk and occupational exposures [2,60]. Failure to account for these factors may lead to part of their effect being incorrectly attributed solely to tuberculosis or COPD.

Social vulnerability warrants particular attention. Low socioeconomic status, unemployment, poor housing, undernutrition, alcohol dependence, limited access to healthcare and delayed presentation may simultaneously affect tuberculosis risk, the course of chronic lung disease and the timeliness of diagnosis [2,129,130]. The social determinants of tuberculosis are well described, but fully accounting for them in studies of tuberculosis-associated persistent airflow limitation is difficult, including in studies based on registries and proxy measures [50,121,129]. Comorbid conditions—diabetes mellitus, HIV infection, cardiovascular disease, chronic kidney failure, undernutrition, alcohol use disorder and cancer—may influence the risks of tuberculosis and hospitalisation, mortality and functional status; their importance varies by condition and population [2,17,98]. Registry studies should therefore prespecify covariates and use multivariable models, stratification, sensitivity analyses and, where possible, matching [50,121].

Frequent healthcare contacts may increase the likelihood that tuberculosis and COPD are recorded, spirometry is performed and patients are hospitalised. Information bias may arise when the association between the diseases partly reflects the frequency of contact with the healthcare system [121]. Healthcare use, follow-up duration, the number of records, access to spirometry and regional care organisation therefore need to be considered [121,124].

Future studies should combine registry data, spirometry, CT and patient-important outcomes; selection algorithms should be reported in accordance with STROBE and RECORD [3,122,124].

7. Future Research Directions

The main unresolved questions are which patients develop persistent airflow obstruction after tuberculosis, what determines its progression and which interventions alter long-term prognosis [3,17]. Table 3 summarises the evidence and the questions that remain open.

The first priority is registry-based and cohort research using consistent criteria to define the study population. Tuberculosis survivors have an increased risk of chronic airway disease, greater healthcare use and more frequent adverse outcomes [47,50,131]. Studies need to distinguish active from previous tuberculosis, a code for sequelae, CT signs of PTLD, confirmed airflow obstruction, bronchiectasis and mixed impairments; validate patient identification algorithms; account for the temporal sequence of the diseases; distinguish pre-existing COPD from newly detected post-tuberculosis airflow limitation; and adjust for surveillance intensity [121,124]. The authors propose combining codes A15–A16 and B90 [120], CT findings, spirometric and clinical characterisation, inflammatory and cardiovascular markers, and information on hospitalisation, mortality, work capacity and quality of life within a registry.

The second priority is risk modelling for post-tuberculosis airflow limitation incorporating age, sex, smoking, initial disease extent, cavities, recurrences, sputum bacteriological positivity, treatment duration and characteristics, CT findings, baseline spirometry and DL_{CO}, inflammatory markers, nutritional status and comorbidity. Published models predict active tuberculosis treatment outcomes, with external validation, and CT-defined lung destruction at treatment completion, with internal validation only [132,133]. Ye et al. developed a model for incident COPD after pulmonary tuberculosis that included the systemic immune-inflammation index and the $CD4^+/CD8^+$ ratio. The model underwent internal

validation [134]. Its performance in independent cohorts and its ability to predict persistent airflow limitation attributable to tuberculosis remain unknown. The Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) statement extended to artificial intelligence (TRIPOD + AI) is an appropriate framework for reporting their development and evaluation; adherence to this standard ensures transparent reporting but does not, by itself, establish clinical utility [135]. Assigning scores and thresholds, including age thresholds, before models are developed from individual-level data and externally validated would be premature: post-tuberculosis airflow obstruction has also been described in young patients [49].

The third priority is biomarker research and immunological phenotyping. A review of the immunological mechanisms of PTLD and cross-sectional studies of autoantibody profiles and SIRI suggest possible immunobiological heterogeneity in post-tuberculosis lung impairment [23,24,68]. Longitudinal studies are needed in which C-reactive protein (CRP), inflammatory indices, cytokines, autoantibodies and the microbiome are assessed in relation to CT findings, spirometry, DL_{CO}, 6MWT, quality of life, exacerbations and long-term outcomes [17].

Research should also evaluate interventions, investigate the cardiovascular component and examine how care is organised after treatment completion.

Table 3. Evidence and research questions on persistent airflow limitation after tuberculosis.

Evidence to Date	Question for Future Studies
Bronchiectasis, bronchial distortion and fibrosis may coexist on CT [8,36].	Do independent readers agree on the predominant and overlapping CT findings in patients meeting the PTLD research definition who have persistent post-bronchodilator obstruction?
Experimental and patient studies implicate matrix metalloproteinases in tissue injury during active tuberculosis [76–80]. Residual metabolic activity and inflammatory signals have been documented at or after treatment completion [63,64,85].	Do post-treatment inflammatory markers predict FEV_1 decline or exacerbations after accounting for baseline lung damage, coexisting COPD and inhaled exposures?
Serial spirometry shows variable trajectories [18,49]. A model for incident COPD after tuberculosis has undergone internal validation [134].	How well do structural findings and risk models predict outcomes in independent cohorts with repeated spirometry and a common definition of obstruction?
Rehabilitation studies report exercise outcomes in broader post-tuberculosis populations [25,26].	Do patients with confirmed persistent obstruction differ in their response to treatment or rehabilitation according to the pattern of structural damage?

8. Conclusions

Tuberculosis-associated persistent airflow limitation is an obstructive manifestation within the heterogeneous spectrum of PTLD. Its assessment requires consideration of structural remodelling, chronic inflammation, functional impairment and systemic comorbidity. Distinguishing this functional abnormality from COPD and from non-obstructive PTLD is necessary for comparing studies and selecting a clinical approach [3,12]. Previous tuberculosis is associated with airflow obstruction. A Korean cohort found more COPD-related hospitalisations after tuberculosis than in matched controls [47]. In a Swedish cohort, patients previously hospitalised with COPD had higher all-cause mortality in the first year after a tuberculosis diagnosis than controls who also developed tuberculosis [14]. These associations do not establish causality in an individual patient or make post-tuberculosis airflow limitation synonymous with COPD [7,44,47,55]. An identical reduction in FEV_1/FVC may reflect different mechanisms [36,39,43]. Structural damage is accompanied by inflam-

matory and immune alterations; recent studies confirm persistent inflammatory activity in some patients after treatment, but its contribution to the progression of airflow limitation and the clinical value of biomarkers require further longitudinal assessment [63,64,85].

The clinical assessment of patients with post-tuberculosis airflow limitation cannot be reduced to a spirometric criterion: dyspnoea severity and activity limitation also depend on fibrosis, hyperinflation, impaired gas exchange, bronchiectasis and comorbidities, while exacerbations may have infectious causes atypical of conventional COPD [31,102,103]. Comparability across studies is limited by differences in the ascertainment of tuberculosis history and outcome definitions, conflation of structural and functional components, and incomplete consideration of smoking and social vulnerability. The proposed framework for describing PTLD components and distinguishing coexisting COPD in patients with airflow obstruction was developed by the authors and requires validation. Prognostic assessment requires consistent criteria for tuberculosis-associated persistent airflow limitation, registries with verified tuberculosis history and spirometry, externally validated risk models, and longitudinal biomarker studies [3,17]. The practical implications are the need to assess respiratory health at tuberculosis treatment completion and to use the structural and functional findings to inform diagnosis and individualised long-term management.

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Abbreviations

The following abbreviations are used in this manuscript:

6MWT	6-min walk test
aHR	adjusted hazard ratio
aOR	adjusted odds ratio
BOLD	Burden of Obstructive Lung Disease
CAT	COPD Assessment Test
$CD4^+/CD8^+$	ratio of cluster of differentiation 4-positive to cluster of differentiation 8-positive T lymphocytes
CI	confidence interval
COPD	chronic obstructive pulmonary disease
COPD-C	COPD related to cigarette smoking
COPD-I	COPD due to infections
CRP	C-reactive protein
CT	computed tomography
DL_{CO}	diffusing capacity of the lung for carbon monoxide
FEV_1	forced expiratory volume in one second
FVC	forced vital capacity
GOLD	Global Initiative for Chronic Obstructive Lung Disease

HIV	human immunodeficiency virus
I^2	proportion of variability in study estimates attributable to between-study heterogeneity
ICS	inhaled corticosteroids
IGRA	interferon-gamma release assay
IgG	immunoglobulin G
IL	interleukin
IOS	impulse oscillometry
IP-10	interferon-γ-inducible protein 10
ISWT	incremental shuttle walk test
LABA	long-acting β_2-agonist
LAMA	long-acting muscarinic antagonist
LLN	lower limit of normal
MMP	matrix metalloproteinase
mMRC	modified Medical Research Council dyspnoea scale
MT1-MMP	membrane type 1 matrix metalloproteinase
NTM	non-tuberculous mycobacteria
OR	odds ratio
$PaCO_2$	arterial carbon dioxide tension
PET/CT	positron emission tomography/computed tomography
PLATINO	Latin American Project for the Investigation of Obstructive Lung Disease
PTLD	post-tuberculosis lung disease
RECORD	REporting of studies Conducted using Observational Routinely-collected health Data
ROC	receiver operating characteristic
RV	residual volume
SANRA	Scale for the Assessment of Narrative Review Articles
SIRI	systemic inflammation response index
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
TB	tuberculosis
TB–COPD	coexistence of active or previous tuberculosis and a diagnosis of chronic obstructive pulmonary disease
TGF-β	transforming growth factor-β
TLC	total lung capacity
TNF-α	tumour necrosis factor-α
TOPD	tuberculosis-associated obstructive pulmonary disease (term used in cited literature)
TRIPOD + AI	Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis + artificial intelligence

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