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Review

Tuberculosis and chronic respiratory disease: a systematic review

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ABSTRACT

Background: Chronic respiratory disease causes substantial global morbidity and mortality. The contribution of pulmonary tuberculosis to the aetiology of chronic respiratory disease is rarely considered, but may be important in tuberculosis-endemic areas.
Methods: We performed a systematic literature review to assess the association between a history of tuberculosis and the presence of chronic obstructive pulmonary disease (COPD) or chronic suppurative lung disease (bronchiectasis). Study quality was evaluated using the National Heart Lung and Blood Institute quality assessment tool. Meta-analysis was performed using the DerSimonian and Laird random effects model.
Results: We identified 9 eligible studies for COPD and 2 for bronchiectasis. Overall, there was a significant association between a history of tuberculosis and the presence of COPD in adults aged over 40 years (pooled odds ratio 3.05 (95% confidence interval 2.42, 3.85). Among individual COPD studies the strongest associations were found in countries with a high incidence of tuberculosis, as well as among never smokers and younger people.
Conclusion: In tuberculosis endemic areas, tuberculosis is strongly associated with the presence of chronic respiratory disease in adults. Efforts to improve long-term lung health should be part of tuberculosis care.

1. Introduction

Economic development has been associated with a pronounced epidemiological transition, resulting in a decreased burden of infectious diseases, but a greatly increased burden of non-communicable diseases (NCDs)[1]. While the epidemiologic transition is in progress, as it is in many low- and middle-income countries, people face the double burden of infectious diseases and non-communicable diseases [2]. Bidirectional associations exist between "old' infectious diseases and "new" non-communicable ones [3]. Tuberculosis (TB) is an important case in point.

Since *M. tuberculosis* is spread by aerosol droplets, the lungs are most commonly affected by the disease [4,5]. It is well known that environmental exposures, such as silica dust or cigarette smoke, increase the risk of developing TB [6–8]. Diabetes, a non-communicable disease of growing importance, has also been shown to increase the risk of progression to active TB [9,10]. Conversely, it is now becoming clearer that TB itself may lead to chronic respiratory disease, particularly bronchiectasis and COPD [11,12]. The population attributable risk for COPD due to cigarette smoking varies from more than 70% in some high income countries to less than 40% in low and middle income countries [13]. The other factors that cause COPD in low and middle income countries have not been established, but TB may well play an important role [14].

Many low and middle-income countries are undergoing changes that actually increase TB risk, such as rapid urbanization with high population densities and increased rates of cigarette

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smoking [15]. In China alone it is estimated that 320 million people are current smokers, including 57% of all adult males, and if these rates do not decrease then the number of smoking-related deaths in that country will double to an estimated 2 million per year by 2020 [16,17]. The poor and socially destitute are particularly at risk, due to an increased risk of acquiring *Mycobacterium tuberculosis* infection in crowded living conditions and a greater vulnerability to progress to active disease because of co-morbid conditions [5,18]. TB occurred in an estimated 9 million people in 2013 [4]. This represents a large population at-risk of adverse lung health outcomes, especially if exposed to additional pulmonary insults.

Chronic respiratory disease is a group of disorders that primarily affect the lungs and airways. It is associated with significant morbidity and mortality[19]. The World Health Organization (WHO) estimates that 4.6 million people die prematurely each year as a result of chronic respiratory disease, accounting for more than 5% of global deaths; almost 90% of these occur in low and middle-income countries [20]. The 2010 global burden of disease report ranked COPD as the 9th leading cause of disability worldwide and this is predicted to rise to 5th by 2020 [21]. In adults COPD is the most common chronic respiratory disease and bronchiectasis is another debilitating airway disease that shares some clinical features but is often under recognised [22,23]. It is characterized by persistent airway dilation and a chronic productive cough [24], leading to repeated respiratory infections, deterioration in lung function and reduced quality of life [25,26].

This systematic review examines the available evidence on the association between TB and chronic respiratory disease, with a focus on COPD and bronchiectasis. The primary review questions were,"In the general population is a previous episode of TB associated with COPD or chronic suppurative lung disease (bronchiectasis)?"

2. Methods

We performed a systematic review of the literature in accordance with PRISMA guidelines [27]. The electronic databases of Medline (Web of Science) and the Cochrane library were screened for articles that contained the terms [28] "tuberculosis" or "respiratory tract disease". The search then focused specifically on "obstructive" lung disease or "bronchiectasis" (Figure 1). Studies relating to reactive airway disease (asthma) and the parenchymal lung diseases, including pneumoconiosis (silicosis, coal miner's pneumoconiosis, and asbestosis) and other causes of pulmonary fibrosis, were not considered. Articles were limited to human studies published between January 1975 and September 2014. No language restrictions were applied. All articles identified by the initial search were reviewed by title and abstract for relevance (by ALB). Duplicates, non-human studies and off-topic articles were excluded. Narrative reviews, case reports and case series were also excluded.

Studies that recruited participants from the general population, including population-based cohort, cross-sectional or nested case-control studies were included. Full-text of the included studies was assessed using a standard data collection form, documenting study setting, study design and participant selection, TB definition, COPD/bronchiectasis definition, key findings including hazard or odds ratio, key limitations and follow up period. Two authors (ALB & CDM) applied the National Heart Lung and Blood Institute (NHLBI) quality assessment tool for observational cohort and cross-sectional studies to assess the internal validity and risk of bias for each study [29]. They independently evaluated the components of the scale as "Yes", "No" "Not Applicable" or "Not Recorded". This was used to guide the overall rating for the quality of each study as "Good", "Fair" or "Poor". In case of disagreement a consensus opinion was reached.

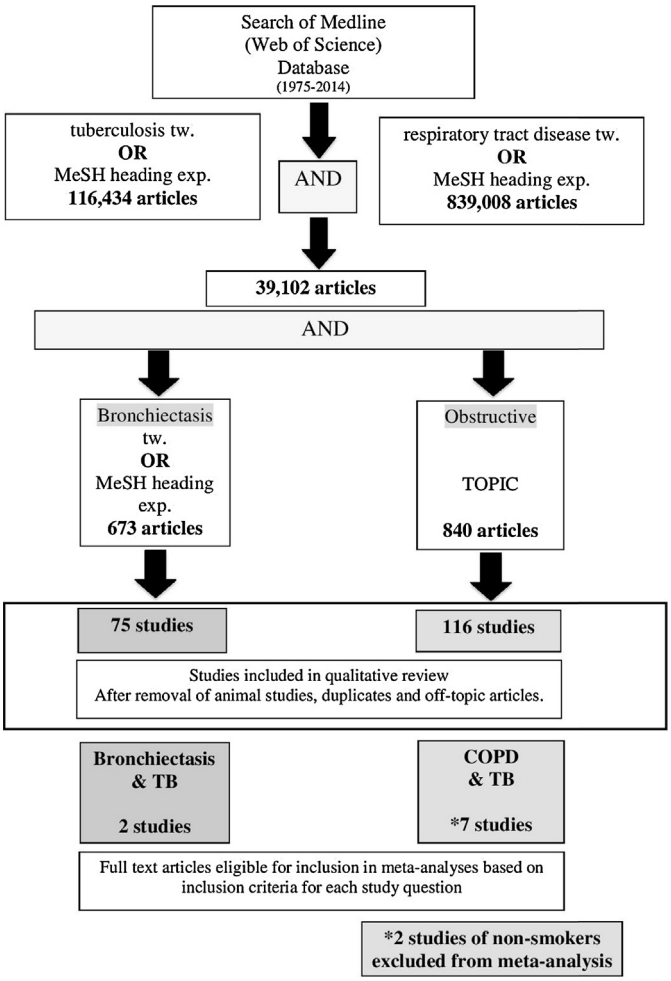

Figure 1. Flow diagram demonstrating search strategy used.
COPD excluded studies included **45** studies assessing lung function loss in TB patients (case series), **28** studies on biomass fuel or smoking, **8** studies the risk of TB infection with corticosteroid treatment for COPD, **11** studies on silicosis or pneumoconiosis and **4** studies that looked at the increased risk of lung cancer following pulmonary tuberculosis infection.
Bronchiectasis excluded studies included **22** on haemoptysis, **10** on non-tuberculosis mycobacteria, **6** narrative reviews and **25** that described bronchiectasis in select TB sub-populations.
tw.: Text words used in addition to MeSH;
TB: tuberculosis, mycobacterium tuberculosis, TB, mycobacterial infection, TBC
COPD: chronic respiratory disease, chronic lung disease, chronic obstructive lung disease, COPD, chronic airway limitation, CAL, lung disorder, asthma, obstructive lung function, lung function, spirometry, pulmonary function testing.
Bronchiectasis bronchiectasis, chronic suppurative lung disease
MeSH exp.: Medical Subject Heading expanded to include all sub-headings; Tuberculosis, Respiratory Tract Diseases, Bronchiectasis, Pulmonary Disease, Chronic Obstructive.

2.1. Meta-analysis

Odds ratios and hazard ratios for TB and chronic respiratory disease, and their associated standard errors, were log-transformed and then a random effects meta-analysis was performed in accordance with the method of DerSimonian and Laird [30]. This was implemented in SAS 9.3 (SAS Institute, Cary NC) using the *marandom* macro of Senn et al., [31]. A forest plot was created using the same authors' *maforest* SAS macro. The combined odds ratio was estimated as the exponent of the resulting meta-analytic estimate. Heterogeneity was assessed by Cochrane's Q and the I^2 statistic [32].