Overview

The seedbeds of Tuberculosis: is it time to target congregate settings and workplaces?

ALFREDO MONTECUCCO[1,2], GUGLIELMO DINI[1,2], ALBORZ RAHMANI[1,2], LAURA STICCHI[1,2], PAOLO DURANDO[1,2]
[1] Department of Health Sciences (DISSAL), University of Genoa, Italy; [2] IRCCS Polyclinic San Martino Hospital, Genoa, Italy

Keywords

Tuberculosis • TB • Latent tuberculosis infection • LTBI • Occupational medicine • Public health • Congregate settings and workplaces • Elimination

Summary

Countries where the incidence of Tuberculosis (TB) is low display a low transmission rate in the general population, and this rate has progressively declined in recent decades; however, TB epidemiology has shown a shift of the disease burden from the general population to specific populations at higher risk, such as vulnerable individuals and hard-to-reach groups. In low-incidence countries, preventive and therapeutic strategies must therefore be geared towards targeted interventions in these populations, with the priority being to promptly identify and treat latent tuberculosis infection (LTBI) rather than manage infectious cases. One of the most complex challenges in this area is to identify population subgroups with increased incidence/prevalence of LTBI/TB.

The aim of this study was to provide a concise overview of the main studies and available evidence concerning the epidemiology of TB and LTBI in non-healthcare congregate settings, with specific emphasis on studies conducted in occupational settings and workplaces.

Recognizing settings at increased risk might contribute to eliminating TB in low-incidence countries, a challenge which requires tailored responses.

Occupational and preventive medicine has a major role to play in directing ad hoc policies and programs of LTBI surveillance. If TB is to be eradicated, it is essential to contain the seedbeds of infection: indeed, as long as a large reservoir of infected subjects exists, new active TB cases may arise at any time.

Background

Tuberculosis (TB) remains the leading cause of death due to an infectious disease among adults worldwide. Currently, tuberculosis causes more than 10 million cases globally, resulting in approximately 1.5 million deaths each year [1]. The global distribution of the disease is widely heterogeneous. The lowest rates are mostly registered in high-income countries, including most Western European countries, Canada, the United States of America, Australia and New Zealand.

The epidemiology of TB in low-incidence countries (< 10 cases per 100,000 inhabitants per year) is characterized by a low transmission rate in the population at large, and this has progressively declined over recent decades.

Europe's TB burden is among the lowest in the world, and overall notifications in most countries have been decreasing over the last five years [2].

Many efforts have been made in recent years to eradicate TB, particularly through the detection and active management of TB cases. This strategy alone, however, is not enough to eliminate TB. In order to successfully break the chain of infection and disease, an integrated strategy [3, 4] that includes LTBI management is required.

In addition, it is estimated that approximately 1.7 billion people globally (a fourth of the world's population) are infected with *Mycobacterium tuberculosis* (MT) [5].

In this regard, as most new TB cases are the result of reactivation of LTBI rather than a recent primary infection, the enhancement of LTBI screening and treatment strategies is well recognized as a key driver of TB elimination, especially in areas of low TB prevalence.

The incidence of active cases is concentrated among vulnerable groups, hard-to-reach populations and cross-border migrants. One of the most complex challenges in this area is to identify population subgroups with a high incidence/prevalence of TB. Today, prioritized strategies in low-incidence countries must therefore be geared towards targeted interventions in these populations, with the aim of identifying and treating infections promptly rather than managing cases of TB disease.

It is well known that the transmission of MT is more likely in confined environments where population density is high, such as healthcare facilities, shelters for the homeless, long-term care facilities, and community settings such as schools and workplaces. The concentration of active TB cases in congregate settings engenders a greater risk of transmission of MT among those who frequent these settings. The presence of vulnerable populations in high congregate settings might constitute one of the worst scenarios, especially in non-healthcare settings. As defined by the CDC, a congregate setting is an environment where a number of people reside, meet or gather in close proximity for either a limited or extended period of time [6]. The aim of the present study was to provide an overview of the literature on the epidemiol-

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ogy of TB and LTBI in non-healthcare congregate settings, with specific emphasis on studies conducted in occupational settings or studies comparing the prevalence/incidence rates of LTBI/TB in such settings with those recorded in the general population.

Methods

An analysis of the literature by means of a method that simplifies the components of a systematic search [7] formed the basis of the rapid overview of evidence presented in this study. Medline and Embase electronic databases were searched for articles published between January 2000 and December 2019 that reported epidemiological data on TB/LTBI in congregate settings. The search was restricted to countries and territories with a low incidence of TB, as per the latest WHO data [1], and to systematic reviews and meta-analyses of observational studies. The language was restricted to English and Italian. Our search contained the following terms: tuberculosis, LTBI, prison, congregate and occupational setting (tuberculosis OR TB OR latent tuberculosis infection OR LTBI) AND ((congregate OR highly populated) OR (prisons OR correctional OR shelters)) OR (workplace OR occupational). Approval from the Ethics Committee was not required.

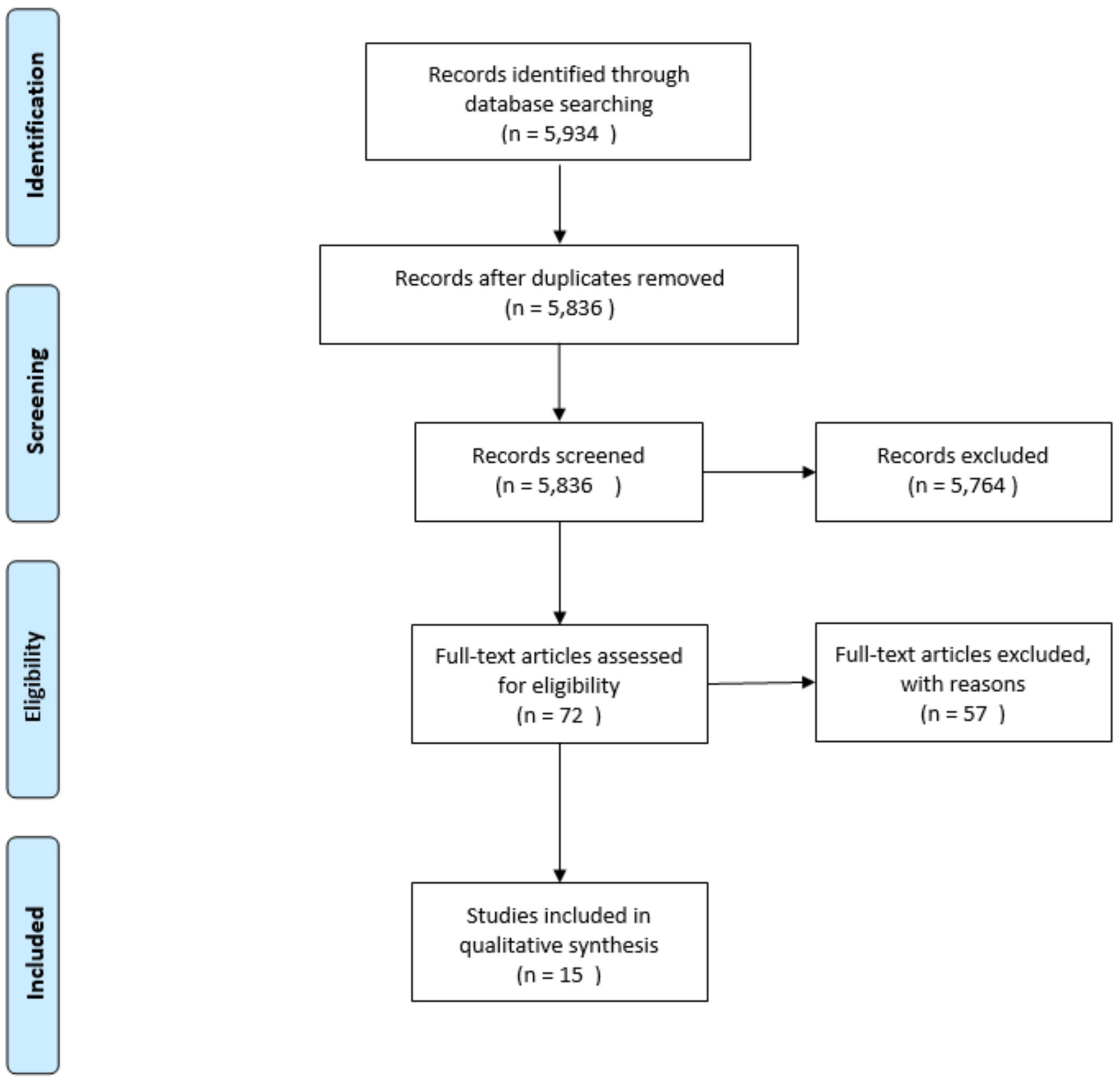
Results

A total of 5,934 citations were screened. Subsequently, 15 articles [8-22] fulfilled the eligibility criteria and were included (Fig. 1).

Summary of studies included

A briefly summary of the studies included is reported in Table I.

Fig. 1. PRISMA 2009 flow chart of the literature search.



Tab. I. Characteristics of studies included

	Setting	Study population	LTBI epidemiology	TB epidemiology	Determinants	Strategies to pursue
Baussano et al. [8]	Correctional facilities	N=31,336 inmates	Incidence 26.4 (IQR: 13.0-61.8)	Incidence 23.0 (IQR: 11.7-36.1)	Inadequate nutrition, HIV prevalence, overcrowding	Education on early identification of TB and early case management, screening of inmates on arrival, isolation of TB cases are potentially effective measures
Kawatsu et al. [9]	Correctional facilities	NA	Average prevalence 40.3%	NA	Duration of incarceration, history of previous incarcerations were identified as risk factors for high LTBI prevalence	NA
Moreira et al. [10]	Correctional facilities	NA	NA	Prevalence <1%	Transmission within the prison	Education on early identification of TB, early case management and appropriate treatment, screening of inmates on arrival, isolation of cases with positive smears
Lambert et al. [11]	Correctional facilities	n = 5878 correctional employees and inmates	NA	From 8 to 29 every 100,000	Local jails, recent arrival from non-low-incidence country	Systematic screening and treatment of LTBI and TB among correctional employees and inmates remain essential to TB prevention and control
Binswanger et al. [12]	Correctional facilities	n=81,610 correctional officers	5.5% (range 3.8-8.3%) of correctional facilities monitored reported at least one episode of cuti-conversion among employees	NA	NA	NA
Grenzel et al. [13]	Correctional facilities	n=110.393 correctional facility workers	16% ([95% IC 10-22%], I2=93,3%, p<0,001)	Incidence of active TB ranged from 0.61 to 450/10,000	LTBI-associated risk factors included duration of employment, older age, country of birth, current tobacco smoking, reported contact with prisoners, and BCG vaccination.	Systematic surveillance and infection control measures are necessary to protect these highly vulnerable workers. Need for infection control measures in such high-risk settings
Kunst et al. [14]	Reception centres for asylum seekers - Europe	Migrants and asylum seekers	Prevalence of TST positivity ranged between 27.8% and 44.9%, IGRA positivity ranged between 17.4% and 29%.	Incidence ranged between 26 and 671 TB cases every 100,000	Country of birth, the reason for migration (e.g., asylum seekers), date of entry into the host country, factors favouring progression from LTBI to active TB	Recommend harmonising case definitions, reporting standards and policies for TB/LTBI screening.
Lönnroth et al. [15]	Reception centres for asylum seekers - Europe	Migrants and asylum seekers	LTBI prevalence, with a pooled positivity of 45% on TST and 24% on IGRA.	NA	Overcrowded settings, in both the country of origin and of destination, together with factors such as malnutrition, exposure to infectious cases and increased incidence of HIV.	Integrated strategies of early diagnosis and treatment, together with active inclusion in the social and cultural fabric

continues

follows

Tab. I. Characteristics of studies included

	Setting	Study population	LTBI epidemiology	TB epidemiology	Determinants	Strategies to pursue
Bozorgmehr et al. [16]	Reception centres for asylum seekers - Germany	N=89,294 asylum seekers	NA	3,47 (95% CI: 1.78-5.73; I2 = 94.9%; p <0.0001) every 1,000	Country of origin, post-migration factors such as duration of stay in host country	Establish factors during migration and initial accommodation which may lead to higher transmission rates or re-activation of LTBI
Scotto et al. [17]	Reception centres for asylum seekers - Italy	NA	Prevalence of positivity to the TST varied between 30 and50%, of these, IGRA test positivity ranged from 26.5% to 29.6%	Immigrants accounted for 66% of new TB cases occurring in Italy	Country of birth, poor living conditions, poor nutrition	Emphasis on social protection and poverty-alleviation programmes
Bamrah et al. [18]	Homeless sheltlers - USA	N=270,948 TB cases among homeless	NA	Incidence ranged from 36 to 47 every 100,000	Difficulties regarding access to medical care, duration of contagiousness, delayed diagnosis	Identification and treatment of homeless persons with LTBI
Nava-Aguilera et al. [19]	Homeless sheltlers	NA	NA	NA	Belonging to an ethnic minority, being a native of the country, residing in an urban area, drug use, excessive alcohol consumption, previous incarceration, HIV, young age, male gender	Improvement of prevention and control strategies
Isler et al. [20]	Homeless sheltlers - Canada	N = 841	Prevalence of 12.9%. The incidence of cuti-conversion ranged from 2.3 to 3.5 per 100 people per year.	NA	Neither demographics nor workplace character-istics were associated with the incidence of con-version	Improvement of TST screening and medical surveillance of shelter workers in a low-incidence setting
Grenfell et al. [21]	Drug rehabilitation communities – Europe & North America	NA	Prevalence ranged from 17% to 52% in Europe; from 12% to 39 in US	Prevalence ranged from 0,5% to 66% with broad heterogeneity among studies	Male gender, long periods of injected substance abuse, HIV-negative status and TCD4+ lymphocyte values within normal range	Improve surveillance of TB and co-infections among people who inject drugs
Deiss et al. [22]	Drug rehabilitation communities	NA	Prevalence ranged from 10% to 59%.	NA	Age and duration of drug abuse, homelessness, alcohol abuse and history of detention	Prompt identification of LTBI, successful treatment of LTBI and TB disease

NA, not applicable

Correctional facilities

Baussano and colleagues [8] conducted a systematic review to investigate the incidence and risk of LTBI and TB in prisons in various countries in comparison with the general population. The review included 23 original studies from the 1990s to 2010. Five studies from the US and one from Brazil assessed the incidence of LTBI in penitentiaries; n = 19 investigated the incidence of TB (n = 13 in low-incidence settings); n = 2 studies investigated both the impact of infection and the disease. The estimated average annual incidence rate ratio (IRR) for LTBI was 26.4 (interquartile range [IQR]: 13.0-61.8); the IRR for TB was 23.0 (IQR: 11.7-36.1). The estimated median fraction (PAF%) of TB in the general population attributable to exposure in prison settings was 8.5% (IQR: 1.9% -17.9%) and 6.3% (IQR: 2.7% -17.2%) in low-/middle-income countries.

Kawatsu and colleagues [9] carried out a systematic review to investigate the incidence of LTBI among prison inmates. They reported an LTBI incidence of 40.3% in countries with a low incidence of TB and 73.0% in countries with a medium/high incidence. The incidence of LTBI ranged from 5.9 to 6.3 per 100 inmates in countries with a low incidence of TB, while it was 61.8 per 100 inmates in countries with a high incidence.

Moreira and colleagues [10] conducted a systematic meta-analysis review that investigated the prevalence of TB among prison inmates between 1997 and 2016. Their study included n = 29 original articles regarding 2163 cases of TB among inmates. The combined prevalence of TB among inmates was 2%. The prevalence among detainees from countries with a TB incidence between 0 and 24 cases per 100,000 inhabitants was less than 1%. In countries with a TB prevalence of 25-99/100,000, the prevalence of TB among prisoners was reported to be 3%; in countries with an incidence ≥ 300/100,000 inhabitant, the prevalence was reported to be 8%.

A study conducted in the USA by Lambert et al. [11] found 299 cases of active TB among prison employees in 35 US states; 49% of the diagnoses were made at the onset of clinical symptoms, 31% of the diagnoses were incidental, 11% were made through occupational health surveillance, and 9% were made through contact investigations of contagious cases.

The study by Binswanger et al. [12] was conducted in the USA on a population of 81,610 prison employees. Of the correctional facilities included in the study, 5.5% reported at least one episode of cuti-conversion to TST among employees.

The systematic meta-analysis review by Grenzel et al. [13] reported a prevalence of LTBI among prison workers in low-incidence countries of 16% ([95% CI 10-22%], I2 = 93.3%, $p < 0.001$). The incidence of active TB in low-burden countries ranged from 0.61 to 450 every 10,000.

Reception centres for asylum seekers

Kunst and colleagues [14] conducted a systematic review of 46 studies to investigate the prevalence of LTBI and TB among migrants in the European context. The median yield of reported cases at the reception centres was 431 cases per 100,000 assessed. N = 20 studies that investigated screening for LTBI were included. Positivity (≥ 10 mm of intradermal hardening) to TST (interquartile range) ranged between 27.8% and 44.9%, while Interferon Gamma Release Assay test (IGRA) positivity was found to be between 17.4% and 29%.

Lönnroth and colleagues [15] conducted a systematic review to investigate the prevalence of TB among migrants in low-incidence countries. The authors reported that the absolute number of TB notifications in subjects born abroad increased in 14 of the 30 low-incidence countries in the period 2009-2015. They found that asylum seekers and refugees were at increased risk of TB, owing to the difficulties faced during migration, overcrowded conditions in both the countries of origin and destination, and factors such as malnutrition, exposure to infectious cases and a higher incidence of HIV in these individuals.

Bozorgmehr and colleagues [16] investigated the screening data on asylum seekers in Germany from 1995 to 2015 through a systematic meta-analysis. They reported that the prevalence of TB among asylum seekers was between 0.72 (95% CI: 0.45-1.10) and 6.41 (95% CI: 4.19-9.37) per 1,000 subjects. The aggregate estimated prevalence of active TB cases in the studies included was 3.47 (95% CI: 1.78-5.73; I2 = 94.9%; $p < 0.0001$) per 1,000 asylum seekers.

In 2017, Scotto and colleagues [17] conducted a study on the incidence of TB among migrants in Italy in the period between 2000 and 2016. They reported that, in 2014, 66% of new cases of TB were recorded in the migrant population.

Homeless shelters

Bamrah and colleagues [18] conducted a study to analyse cases of active TB reported in the United States between 1994 and 2010. Overall, 270,948 active TB cases were reported in this time window, 16,527 (16.4%) of which occurred among homeless people.

A systematic review by Nava-Aguilera and colleagues [19] revealed that recent transmission of TB was concentrated in some vulnerable population groups, including: ethnic minorities (OR 3.03, 95% CI: 2.21-4.16); urban residents (OR 1.52, 95% CI: 1.35-1.72); drug abusers (OR 3.01, 95% CI: 2.14-4.22); alcohol abusers (OR 2.27, 95% CI 1.69-3.06); homeless persons (OR 2.87, 95% CI: 2.04-4.02); former prison inmates (OR 2.21, 95% CI: 1.71-2.86); HIV-infected subjects (OR 1.66, 95% CI: 1.36-2.05); and the young (OR 2.09, 95% CI: 1.69-2.59).

Isler and colleagues [20] investigated the results of an LTBI screening program for employees of homeless shelters in the Montreal metropolitan area between 1998 and 2005. Both subjects who were cuti-positive (10 mm cut-off) at the start of the study and cuti-converted subjects (10 mm cut-off) were included. The prevalence of subjects with TST positivity at the start of the study was 12.9%. The incidence of cuti-conversion ranged from 2.3/100 person-years to 3.5/100 person-years. The incidence of cuti-conversion was not significantly associated with demographic or occupational items such as the type of employment.

Drug rehabilitation communities

A review by Grenfell and colleagues [21] investigated the prevalence of LTBI and TB in intravenous drug users. In studies conducted in Europe, the prevalence of LTBI ranged from 17% to 52%, with a higher incidence in prison settings. In North America, intravenous drug users had an LTBI prevalence between 12% and 39%. The prevalence of active TB ranged from 0.5% to 66%; this wide heterogeneity among studies was due to differences in the methods of detection and definition of active TB.

Deiss and colleagues [22] also conducted a review investigating the prevalence of LTBI and TB in intravenous drug users. They reported that this vulnerable population was at increased risk of both LTBI and TB, with an observed prevalence of LTBI between 10% and 59%. Prolonged intravenous drug abuse and age proved to be associated with a higher prevalence of LTBI.

Brief final remarks

The studies mentioned, which were performed in countries with a low incidence of TB, provide a brief summary of the epidemiology of LTBI and TB in congregate settings and workplaces.

Adequate knowledge of up-to-date epidemiological data is a crucial first step in the risk assessment of occupational settings and a useful means of identifying reservoirs of TB infection at the community level, thereby contributing to the mapping of risk factors and the identification of groups at risk.

Furthermore, such environments (e.g. prisons), are frequently characterized by poor hygiene conditions, poor ventilation and a high prevalence of subjects at higher risk of active TB (e.g., drug abusers, alcoholics, immigrants from high-incidence areas for TB, individuals with HIV/AIDS, individuals with reduced access to care services). A lack of Infection and Prevention Controls (IPC) (e.g., administrative and environmental controls) in these settings may help to explain the increased risk of transmission of MT.

The heterogeneity of work environments makes it more difficult to assess the risk of LTBI, which is influenced by age and demographic structure, cultural factors, population density and migration patterns. Environmental factors, such as overcrowding and poor ventilation, have a direct impact on air exchange from person to person, which increases the likelihood of transmission.

Recognizing risk factors and settings at increased risk might contribute to eliminating tuberculosis in low-incidence countries, a challenge which requires tailored responses. As LTBI is most often a prerequisite for the development of TB in immunocompetent individuals, it appears essential to identify, as early as possible, those who have been infected after proven or suspected exposure to a case of contagious TB (pulmonary or laryngeal), in order to properly assess the risk of developing active TB and to implement preventive measures. Containment of the seedbeds of TB is essential in order to reach the goal of eliminating the disease: indeed, as long as a large reservoir of infected subjects remains, new active TB cases may arise at any time. Given the estimated prevalence of LTBI and the current shortage of tests and treatments, a further major effort is required. This effort should include: a surveillance system, scaling up targeted testing for LTBI in populations at risk, expanding short-term treatment regimens, involving both affected communities and medical service providers, and increasing the healthcare personnel involved in implementation and supervision. Such efforts would greatly benefit from the development of new tools, such as tests that more accurately assess the risk of reactivation as well as shorter LTBI treatment [23, 24].

In order to direct these efforts and make targeted choices, an essential first step is to identify subjects with the highest risk of exposure, who should be targeted for LTBI testing; occupational medicine could play a key role in this activity. Strategies for risk assessment are based on: (I) the workplace environment (e.g. local epidemiological and environmental features); (II) specific care activities performed; (III) risk factors for the increased likelihood of progression from LTBI to active disease. These key principles stress the role of occupational and preventive medicine in directing tailored policies for LTBI surveillance. Moreover, Occupational Health Surveillance programs, in close collaboration with the Departments of Prevention of the Local Health Authorities, could aim to reduce losses at steps of LTBI cascade of care, thereby enhancing the public health impact of proper diagnosis and treatment and contributing to achieving major results in terms of Public health.

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Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

AM conceived and designed the study and the search strategy. PD reviewed and approved the search strategy. AM and GD searched the literature, selected the studies and analyzed the data. PD and LS controlled the review process. AM and GD drafted the initial manuscript. PD, LS, and AR reviewed and edited the manuscript. All authors read and approved the final manuscript.

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Correspondence: Alfredo Montecucco, Department of Health Sciences (DISSAL), University of Genoa and IRCCS Polyclinic of San Martino Hospital, Genoa, Italy - E-mail: alfredo.montecucco@edu.unige.it

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