International Journal of Infectious Diseases xxx (xxxx) xxx



Contents lists available at ScienceDirect

# International Journal of Infectious Diseases



journal homepage: www.elsevier.com/locate/ijid

# Review

# Screening for latent tuberculosis in migrants—status quo and future challenges

Eskild Petersen<sup>1,2,3</sup>, Seif Al-Abri<sup>4,\*</sup>, Amina Al-Jardani<sup>5</sup>, Ziad A. Memish<sup>6,7</sup>, Eleni Aklillu<sup>8</sup>, Francine Ntoumi<sup>9,10</sup>, Peter Mwaba<sup>11,12</sup>, Christian Wejse<sup>13</sup>, Alimuddin Zumla<sup>14,15</sup>, Fatma Al-Yaquobi<sup>4</sup>

- <sup>1</sup> PandemiX Center of Excellence, Roskilde University, Roskilde, Denmark
- <sup>2</sup> European Society for Clinical Microbiology and Infectious Diseases Task Force for Emerging Infections, Basel, Switzerland
- <sup>3</sup> International Society for Infectious Diseases, Boston, MA, USA
- <sup>4</sup> Directorate General for Disease Surveillance and Control, Ministry of Health, Muscat, Oman
- <sup>5</sup> Central Public Health Laboratory, Ministry of Health, Muscat, Oman
- 6 Research and Innovation Center, King Saud Medical City, Ministry of Health & College of Medicine, Al Faisal University, Riyadh, Saudi Arabia
- <sup>7</sup> Hubert Department of Global Health, Rollins School of Public Health, Emory University, Atlanta, GA, USA
- <sup>8</sup> Department of Global Public Health, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden
- <sup>9</sup> Fondation Congolaise pour la Recherche Médicale, Brazzaville, People's Republic of Congo
- <sup>10</sup> Institute for Tropical Medicine, University of Tübingen, Tübingen, Germany
- <sup>11</sup> UNZA-UCLMS Research and Training Program, UTH, Lusaka, Zambia
- <sup>12</sup> Lusaka Apex Medical University, Faculty of Medicine, Lusaka, Zambia
- <sup>13</sup> Department of Public Health, Faculty of Health Science, Aarhus University, Aarhus, Denmark
- <sup>14</sup> Department of Infection, Centre for Clinical Microbiology, Division of Infection and Immunity, University College London, London, United Kingdom
- <sup>15</sup> NIHR Biomedical Research Centre, UCL Hospitals NHS Foundation Trust, London, United Kingdom

#### ARTICLE INFO

#### Article history: Received 14 February 2024 Revised 5 March 2024 Accepted 5 March 2024 Available online xxx

Keywords: Tuberculosis Latent TB Migrants Prevention Screening Treatment

#### ABSTRACT

*Objectives:* To review the evidence that migrants from tuberculosis (TB) high-incidence countries migrating to TB low-incidence countries significantly contribute to active TB cases in the counties of destination, primarily through reactivation of latent TB.

Methods: This is a narrative review. The different screening programs in the countries of destination are reviewed either based on screening and preventive treatment of latent TB pre or more commonly – post arrival

Results: Screening can be performed using interferon-gamma release assays (IGRA) or tuberculin skin tests (TST). Preventive treatment of latent TB is using either monotherapy with isoniazid, or in combination with rifampicin or rifapentine. We discuss the ethical issues of preventive treatment in asymptomatic individuals and how these are addressed in different screening programs.

Conclusion: Screening migrants from TB high endemic countries to TB low endemic countries is beneficial. There is a lack of standardization and agreement on screening protocols, follow up and treatment.

© 2024 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.

This is an open access article under the CC BY-NC-ND license

(http://creativecommons.org/licenses/by-nc-nd/4.0/)

#### Introduction

It has been previously estimated that the global prevalence of latent TB infection (LTBI) is 24% of the world's population [1,2]. The World Health Organization (WHO) estimated in 2023 that 1.8 billion people are infected with *Mycobacterium tubercu* 

E-mail address: salabri@gmail.com (S. Al-Abri).

losis, but without clinical symptoms of active tuberculosis, which is the definition of latent TB infection [3,4]. This represents a 4.5% increase from 2020. With the COVID-19 pandemic now over, TB is once again the leading cause of death from a single infectious agent, with 1.4 million deaths among HIV-negative people and 187,000 deaths among HIV-positive people estimated in 2021 [3].

Progress toward sustainable development goals and WHO Global End-TB strategy targets [3] has slowed down, and potentially reversed during the COVID-19 pandemic [5].

#### https://doi.org/10.1016/j.ijid.2024.107002

1201-9712/© 2024 Published by Elsevier Ltd on behalf of International Society for Infectious Diseases. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/)

Please cite this article as: E. Petersen, S. Al-Abri, A. Al-Jardani et al., Screening for latent tuberculosis in migrants—status quo and future challenges, International Journal of Infectious Diseases, https://doi.org/10.1016/ji.ijid.2024.107002

 $<sup>^{\</sup>ast}$  Corresponding author: Seif Al-Abri, Directorate General for Disease Surveillance and Control, Ministry of Health, Muscat, Oman.

International Journal of Infectious Diseases xxx (xxxx) xxx

Global migration continues to increase. In 2020, it was estimated that some 281 million people were living outside their country of birth, up from 173 million in 2010 [6]. About 117.2 million people will be forcibly displaced or stateless in 2023 [7].

People with LTBI are at risk of developing active TB symptomatic disease due to a number of risk factors including poor living conditions, overcrowding, malnutrition, and stress, which are common in refugee settlements [8]. Migration has a high impact on TB [9], especially since the majority of the migrants originate from low-middle-income countries with a high TB burden. This poses continuing challenges for global TB control and hinders progress toward achieving the WHO Stop TB strategy goals [10] of reducing the global TB incidence to one case per million population by 2035 [3].

Tuberculosis transmission in high-income countries with a low incidence of the disease is driven disproportionately by cases in specific groups at high risk, particularly migrants from high-incidence countries [3]. Asylum seekers and refugees, defined as persons who have fled from their country of origin for fear of persecution and have applied for protection [11], are a particularly high-risk group for developing TB [12].

Systematic testing and treatment of migrants from high incidence regions might therefore have a large impact on tuberculosis control and elimination [9,10,13,14]. The cost-effectiveness of LTBI screening of migrants in low TB burden countries has been demonstrated by numerous studies [15,16–18].

Aim

This study aims to describe the magnitude of TB among refugees and migrant populations and compare screening programs for LTBI. The comparison focuses on the screened population and factors improving the understanding to inform public health policy. We describe the challenges and opportunities to improve TB-related health of migrants in low-burden countries throughout the life-cycle of migrants to such countries.

#### Methods

We searched for articles on TB epidemiology, determinants, risk factors, and access to care among migrants to low-incidence countries in PubMed and websites of the WHO, ECDC, US-CDC (through to January 2024), and we consulted with other TB experts. Low TB incidence countries were defined as 10 TB cases or less per 100,000 persons per year. We used the definitions from the International Organization for Migration (IOM) to define the different migrant types and migration processes. An international migrant is "any person who is moving or has moved across an international border away from his/her habitual place of residence, regardless of 1) the person's legal status; 2) whether the movement is voluntary or involuntary; 3) what the causes for the movement are; or 4) what the length of the stay is" [6]. In this review, we will use the term migrant in line with this definition. We use the term regular migrant for any migrant who is part of "orderly migration," "in keeping with the laws and regulations governing exit of the country of origin and travel, transit and entry into the destination or host country" [6].

Refugees are defined as people who are outside their country and cannot return due to fear of persecution because of their race, religion, nationality, political opinion, or membership in a particular social group [7]. Whereas migrants are defined as people and/or family members moving to another country or region to better their material or social conditions and improve the prospects for themselves or their family [7].

Tuberculosis epidemiology in migrants arriving in low-incidence countries

The TB epidemic in low-incidence countries differs from highburden countries and is usually concentrated in high-risk groups with higher transmission or higher reactivation risks due to underlying illness or medication, socioeconomic circumstances, or higher TB risk in their country of origin.

Every year, approximately a half million immigrants and up to 70,000 refugees migrate to the United States of America from overseas and curtail importation of TB all migrants are required to undergo overseas TB screening. In 2018, two-thirds of new TB cases in the USA were among non-US-born persons [19]. This included 102 multidrug-resistant TB cases, and 1 Extensively drug resistant TB case reported to the US National TB Surveillance System [20]. The proportion of foreign-born TB patients out of all notified TB cases in the European Union in 2015 was 50% in 20 of the 30 low-incidence countries, and 5% in 3 [21,22]. Migration thus plays an important part in TB epidemiology in most low-incidence countries.

The absolute number of TB notifications in foreign-born individuals increased in 14 of the 30 European low-incidence countries between 2009 and 2015, it was unchanged in 2, and it declined in 14 [23]. The proportion of foreign-born TB cases out of all notified TB cases increased in 20 of 30 countries, was unchanged in 2, and decreased in 8. An increase in the absolute number of foreign-born TB notifications is mainly explained by increased immigration from high TB-endemic countries [3,23].

For all low-incidence countries combined, TB notifications in the foreign-born individuals remained stable between 2009 and 2015, whereas these decreased in the nonforeign-born and the total population [23]. The number and proportion of TB cases that are foreign-born is strongly correlated with the proportion of the foreign-born in the population [3,17]. One study found that the incidence and prevalence of TB ranged from 19 to 754 cases per 100,000 population and 18.7 to 535 cases per 100,000 population, respectively, among the included studies, and that the most reported countries of origin in TB cases among refugees and migrants were from Asia and Africa [24,25]. This implies the need to implement and improve TB prevention and control in refugees and migrant populations globally. Within migrant populations, several readily identifiable risk factors are well established [17], but the bulk of TB cases still occurs in persons without identifiable risk factors [26]. TB cases in low-burden countries now largely reflect spill-over from the intense levels of transmission in high-burden settings [27].

## Latent tuberculosis infection

People with LTBI have a persistent immune response to *M. tuberculosis*, remain asymptomatic, and noninfectious [27]. Without appropriate treatment, approximately 5-15% of LTBI cases progress to developing active TB over the patient's lifetime [28,29]. This process is known as reactivation. Reactivation rates depend on a variety of risk factors including comorbidities and the time since infection [30,31].

Those who have recently contracted the infection are more likely to reactivate and develop TB [32,33]. The risk of developing TB is highest in the first 2-5 years after arrival in migrants with LTBI [9,16,32,34–36], providing a rationale for TB preventive treatment of LTBI shortly after arrival.

One study of untreated refugees and migrants from TB high-incidence countries entering to the UK with a positive tuberculin skin test (TST) found that 16.3% progressed to active TB within 15 years of arrival [37]. Importantly, earlier diagnosis of active tuberculosis through the LTBI testing program is likely to reduce tu-

International Journal of Infectious Diseases xxx (xxxx) xxx

berculosis transmission [4,29,38]. These studies provide strong evidence that pre-entry TB screening and LTBI testing and treatment programs are contributing to this reduction, consistent with preliminary data [29,39]. Prevalence of LTBI in the population of interest varied widely between studies from below 1% in children in Japan [40] to over 40% in migrants from high-incidence countries [41]. Secondary or onward transmission of TB from patients with LTBI who develop TB was is well documented [37,42–44].

#### LTBI screening

In 2020, the WHO Consolidated Guideline on Tuberculosis [45] recommend testing for LTBI using either an interferon-gamma release assay (IGRA) or a TST [45,46]. Migrants from high TB burden countries are especially included in the group where LTBI screening should be considered [27]. LTBI disproportionately affects people living in low resource settings and the socially vulnerable [9,24,28,42]. The individual risk has been shown to vary greatly depending on country of origin, travel route, age, sex, health, social status, and reason for migration [9,24,28,42].

Review-level evidence examining LTBI progression rates in migrant populations is scarce. A systematic review by Campbell et al. [47] included three studies on progression rates in migrants from high- to low-incidence countries. MacIntyre et al. [48] reported 5 incident cases in a cohort of 437 TST-positive, treatment naive, Australia-bound refugees (1.1%) over 5 years. Truong et al. [49] found 9 cases in a cohort of 191 US-bound Tibetans (4.7%) followed over a mean of 19 months, and Harstad et al. reported 8 cases among 236 IGRA-positive, treatment naive asylum seekers in Norway (3.4%) followed for 23-32 months [50,51]. A cohort study reported a reactivation rate of up to 15.6% over 15 years in a TST-positive, treatment-naive South Asian population in England [52].

Robust evidence on reactivation rates, based on large, well-designed cohort studies, is required. However, it is fair to conclude that the positive predictive value (PPV) for all commercially available tests for LTBI is relatively low (about 1-15%) in any at-risk population, including migrants, demonstrating the need to target programs to optimize effectiveness and cost-effectiveness [53].

# Diagnostic tools for LTBI

The three currently commercially available tests for LTBI are the TST and two whole blood IGRAs, QuantiFERON (Qiagen, Hilden, Germany) and T-SPOT.TB (Oxford Immunotec, Abingdon, UK). The TST is applied through an intradermal injection of 0.1 mL purified protein derivative tuberculin, and the size of the potential induration is read after 48-72 hours. Both IGRA tests are based on detecting the release of the cytokine interferon-gamma (IFN- $\gamma$ ), which is produced in response to *M. tuberculosis* complex-specific antigens.

The sensitivity of these three tests is comparable (76-90%), but the specificity of IGRA tests is higher than for TST (93-95% vs. 57%) due to the absence of cross-reactivity with environmental mycobacteria and the Bacille Calmette–Guérin vaccine [54,55].

The advantages and disadvantages of IGRAs and the TST have been widely debated [32,56–59]. Compared to the TST, IGRAs do not rely on the subjective reading of a skin induration, only require a single patient visit, have better sensitivity and specificity, and are not impacted by previous Bacille Calmette–Guérin vaccination. On the other hand, IGRAs are more expensive than the TST and require special laboratory infrastructure and supplies.

The PPV of the QuantiFERON-TB Gold In-Tube (a whole blood IGRA) identifying LTB was 3.3%, while the reported PPV of T-SPOT TB was 4.2% and that of TST (a 15 mm cutoff was used to define positivity) was 3.5% [60]. Between the two IGRAs, the T-SPOT TB appears to be the more sensitive test, but the QuantiFERON Gold

assay is broadly equivalent, and is simpler to perform, and can be automated [61].

While there is abundant literature on sensitivity and specificity, the more important measure is the progression rate-the likelihood that a person with a positive test will go on to develop active TB. The number needed to treat to prevent one TB case from the public health system perspective is important. Several systematic reviews have estimated progression rates: Rangaka et al. [62] found progression rates of between 0.4 and 4.8/100 person-years in IGRA-positive individuals. Diel et al. [63] estimated a pooled progression rate of respectively 2.7% (95% confidence interval [CI] 2.3-3.2) and 1.5% (95% CI 1.2-1.7) for IGRAs and the TST. In another meta-analysis, Diel et al. [64] found progression rates of between 8 and 15% and 2-3% over 19-24 months, respectively, for IGRAs and the TST. However, all of these reviews were based on a mixture of studies in different groups, different contacts with active cases and variation in the inclusion criteria, methods and quality assessments of the meta-analysis. They also reported on a mixture of settings, such as high- and low-incidence countries, which may partly explain the differing results. IGRAs were consistently modeled as having higher sensitivity and specificity than TST, with OFT was having slightly lower sensitivity but slightly higher specificity than T-SPOT [40,65,66].

#### Screening migrants for LTBI

Risk of progression from LTBI to TB can be reduced with preventive treatment [33,66,67]. Systematic testing and treatment of migrants from high-incidence regions might therefore have a large impact on tuberculosis control and elimination [34,44,68].

On the basis of the epidemiology of imported LTBI [3], the risk of progression to active tuberculosis in migrants with a positive IGRA, health-economic analyses, and feasibility studies in primary care and potential screening pathways in England, a primary care-based program was launched in the United Kingdom in 2015 based on systematic LTBI testing (by IGRA) and treatment for migrants from high-incidence countries residing in areas with the highest TB burden [34,69].

To our knowledge, this is a first, nonobligatory, national public health experiment that individuals can choose to enter if they wish. If successful, this program would represent an important step toward tuberculosis elimination.

Considerations for LTBI testing include the accuracy of the test, the risk-benefit ratio of LTBI treatment and the impact of the test result upon clinical decision-making [55]. Concerns about poor effectiveness of therapy are often related to reports of low rates of LTBI treatment completion, ranging from 7% to 83% [70]. Uptake of LTBI testing and LTBI treatment completion rates can be improved with adequate patient support, and some studies have reported that patient-centered interventions (such as pharmacistled LTBI clinics, screening offered in community colleges, and free monthly drug dispensation directly through the TB clinic) improve uptake of LTBI testing (up to 75%) and LTBI treatment completion rates, among those who accepted treatment (up to 94%) [71–76]. The United Kingdom is the only country to have launched a nationwide LTBI testing and treatment program for new entrants in primary care [77]. A large, European study pooled routinely collected individual TB screening episode data from 2,107,016 migrants and identified 1658 TB cases [78]. The study also found considerable variations in yield across programs, types of migrants, and country of origin [78].

# LTBI treatment

The risk of developing active tuberculosis was 31 times higher for IGRA-positive individuals than IGRA-negative individuals and

International Journal of Infectious Diseases xxx (xxxx) xxx

LTBI treatment with a 3-month isoniazid and rifampicin regimen reduced this risk by 86% [34].

A systematic review on infectious disease screening among migrants to Europe suggests that 54% of migrants with a positive LTBI test complete treatment [28]. Another systematic review and meta-analysis analyzing the LTBI care cascade among multiple population groups estimated that only 54.6% of migrants initiate treatment, and 14.3% of all migrants' complete treatment [28].

A study with outcome data on 25,629 migrants (of whom 15,516 completed treatment) was used to calculate the proportion of individuals completing treatment subsequent to initiation [27,35]. The pooled estimate for the true proportion of LTBI treatment completion among migrants initiating treatment was 74% (95% CI 66-81; 15,516 of 25,629). Twenty-five studies included outcome data on 6652 migrants (of whom 3289 had initiated and completed treatment) were used to calculate the overall proportion of migrants positive for LTBI who completed treatment. The pooled estimate for the true proportion of migrants completing treatment after screening positive for LTBI was 52% (95% CI 40-64; 3289 of 6652). Overall, these studies suggest that there is drop-out along the treatment pathway.

A systematic review by Alsdurf et al. [78] identified significant losses to follow-up on every step of the care cascade—from screening uptake to treatment completion. An analysis of 70 independent cohorts, of which 12 consisted of migrants, found a testing uptake of 71.9% (95% CI 71.8-72.0) and a treatment completion rate of 18.8% (95% CI 16.3-19.7). However, it is worth noting that this review included a highly diverse range of studies in low-, middle, and high-income countries, addressing different target populations, types of programs, and even tests used. Another study showed effectiveness of a 3-month rifampicin and isoniazid treatment regimen for LTBI, consistent with a 2017 meta-analysis of studies done in people with HIV, and children and adults with silicosis [79].

A systematic review (23 studies) found that shorter treatment regimens and directly observed therapy correlated with treatment completion [80]. Impeded access and/or lack of entitlement to care due to system- and immigration status-related factors (e.g., the lack of health insurance and high out-of-pocket expenditure) are a major impediment to the early detection of TB disease among migrants, enabling TB transmission in the community to go unnoticed [81]. High treatment completion rates for LTBI therapy can be achieved with appropriate social and healthcare support [82]. A European study including 2,107,016 migrants identified that 1658 TB cases detected through screening, with substantial yield variation [83].

Analyzing by treatment regimen, migrants treated with 4 months of rifampicin were significantly more likely to complete treatment (89% [95% CI 67-97]; P = 0.020) than migrants prescribed 9 months of isoniazid and no other treatment regimen showed significant differences [84].

Clinical and system-related factors associated with noncompletion included side-effects, being prescribed a 3-month isoniazid plus rifampicin regimen compared with 6 months of isoniazid, receiving 4 months of rifampicin compared with 9 months of isoniazid, 6 months of isoniazid versus 9 months of isoniazid receiving LTBI treatment [27,84,85]. The WHO guidelines for treatment of LTB have been updated on February 13, 2024 to include individuals exposed to multidrug- or rifampicin-resistant TB and the latest evidence and best available practices on TB preventive treatment (TPT) regimens for individuals of all ages in contact with TB patients and dosing schedules [86].

# Cost-effectiveness of screening for LTBI

Several studies [16–18,40,87–91] explored for cost-effectiveness of testing for LTBI for migrants. In all but the two UK studies

[45,92,93], IGRA compared to TST was found to be a dominant strategy (costing less and generating more Quality-adjusted life years). The two UK studies found that TST could be the most cost-effective option, either alone or in combination with an IGRA [46,94,95]. A systematic review on the effectiveness and cost-effectiveness of screening migrants for LTBI in the EU suggested that the effectiveness of LTBI programs is limited by poorly predictive tests, long treatment durations, and a weak care cascade (i.e., many individuals are lost to follow-up at each step) [38].

To date, the effectiveness (in particular the cost-effectiveness) of such programs remains unclear, since many high-risk migrants do not attend routine follow-up visits. It seems reasonable to consider LTBI treatment as an alternative or as an addition to chest radiograph follow-up, as the benefit of LTBI treatment for high-risk groups is well documented [91,92].

The "eligible-population-yield" of the different screening programs varied by more than factor 100 and ranged between 53.1 (31.9-82.8) in a Dutch study [96] and 5927 per 100,000 (4248-8013) in a US study [10]. Of the 15 estimates with narrow 95% CIs for yields (i.e., 95% CIs with uncertainty ranges less than 1000 cases per 100,000), 12 were below 1500 cases per 100,000 eligible migrants [97].

One modeling study found that cost-effectiveness was optimal when a single IGRA test was offered to all migrants aged less than 35 years of age from countries with an estimated TB incidence of 150 per 100,000 population or more, with the estimated ability to identify 92% of infected migrants [51]. Premigration screening of Chinese and Indian students going to the USA would be cost-effective (and prevent 157 cases of TB annually) from the destination country perspective if the students paid for the screening themselves [98].

Ethics, legal status, access to care, and social factors

Complex ethical considerations around mandatory screening is a concern [27,45,97–99]. Risk factors that specifically affect migrant LTBI treatment outcomes include legal status [100], patients' mistrust, and uncertainty around legal entitlements regarding eligibility and access to medical care for migrants among patients and staff and language and cultural barriers [101,102].

Among migrant subpopulations, there was a generally positive effect of social interventions such as education, adherence coaching, peer counseling, or cultural interventions, particularly if combined with the use of shorter regimens [103].

Access to care is further impeded by immigrants' poor understanding of how the healthcare system functioned, low health literacy, misperception of TB risk due to inaccurate knowledge, as well as linguistic and cultural barriers [100–102]. Furthermore, careseeking behavior is impeded by stigma, discrimination, and fear (or risk) of being denounced to immigration authorities and being repatriated [104]. Demographic and patient-related factors associated with noncompletion include unemployment, education level, and lack of family support [37,105].

#### Challenges

Several challenges including financial and logistical barriers may face the public health authorities in adopting programs for LTBI and screening. A major step is to have a high coverage at all levels of care from entry, ensuring testing and screening till end of treatment of the LTBI. A multistakeholder approach with high degree of engagement and coordination will be needed to ensure that the uptake and adherence of the regulation are met. The other challenge is the knowledge gaps as it is still not clear or not shown by any studies on the actual impact of such programs are having on decreasing the actual incidence of TBI. Further studies are

JID: LJID

•

needed at global levels and in low-incidence countries to assure their effectiveness.

# Research and knowledge gaps

Future studies should perform qualitative and cross-nationally comparative studies on relevant aspects of the design and implementation of screening programs for LTBI.

High heterogeneity in the reported yields, the effectiveness and cost-effective of active TB screening in migrants, and a lack of reporting demographics of the screened populations as well as programs characteristics, such as measures taken to prevent loss to follow-up, organization of administration and screening cascade, and consequences of not complying with mandatory screening measures limit the ability to provide precise guidance on which type of migrants to target, the best timing to screen, or the optimal threshold of TB incidence in countries of origin.

More research is needed to assess facilitators to improve outcomes for LTBI in migrants, this could be achieved through increased involvement of migrant communities across the entire research process, from inception to dissemination, qualitative studies of migrants' perceptions of available services to assess the impact of national policy and guidance documents on refugees' and migrants' rights, access to care, and treatment adherence.

Reporting a standard set of clinical but also meta-level data to enable program evaluation within and between countries is essential to organize effective and cost-effective public health programs. Analyzing patterns of TB infection prevalence and transmission and defining high-risk thresholds for TB among migrant populations, we need to conduct cost-effectiveness studies to plan efficient targeted screening approaches.

Surveillance data often do not distinguish between types of migrants and typically only focus on the epidemiology of diseases in foreign-born compared with non-foreign-born ("native") residents or noncitizens compared with citizens. Migration status is also often not adequately documented in health records and national registries. This hampers disease surveillance, as there are differential risks between migrant groups.

More transparent and accessible reporting of national policies and guidelines on the prevention, diagnosis, treatment, and care of TB infection in migrants is required for all countries with the provision of the evidence base upon which these policy decisions are based.

Genomic evidence has previously helped to document increased TB risk along migration routes, and the migration route may in part explain the high TB detection rate in Italy. More in-depth studies are required to describe the TB risk along the route of migration and the impact of TB in migrants on the native population of the hosting countries.

The existing tests for TB diagnosis and treatment have a low PPV for the identification of subjects progressing to TB disease. Therefore, there is a great need to develop a new generation of tests that predict with higher accuracy those that will progress to disease and focus the diagnostic effort on this target population.

#### **Conclusions**

Health systems must be migrant-sensitive and should use community-based approaches, tailored health promotion and treatment support, and ensure availability and accessibility of professional interpreters and cultural mediators to overcome cultural and language barriers (Table 1).

Furthermore, cross-cultural training of healthcare workers can facilitate a well-established patient–provider relationship, and prevent stigmatization and discrimination [106].

To guide countries in implementing and optimizing TB screening and TPT among migrants, evidence-based guidelines, including best practices for the implementation of TB screening and TPT among migrants at high risk for TB, are urgently needed.

TPT uptake and completion could be improved if policies are revised, TB services are provided free of charge irrespective of migrant (undocumented vs. documented) and health insurance status, shorter TPT regimes are made available to all low TB incidence countries, and multisectoral approaches are used to facilitate referral of relocating migrants.

Evidence is still lacking on the most cost-effective or efficient approaches for TB detection and the continuum of care across national borders. The most cost-effective approach is likely to involve a combination of interventions: targeted prearrival screening for active TB followed by postarrival screening for LTBI in refugees and migrants from settings with an intermediate-high TB burden. However, evidence is limited on the cost-effectiveness of different screening approaches.

There is a lack of standardization of TB screening policies, with significant variability in the screening programs leading to highly variable outcomes. Programmatic screening for both TB and LTBI

**Table 1**Summary of main conclusions

Section	Key conclusions
Tuberculosis epidemiology in migrants arriving in low-incidence countries	TB cases in low-burden countries now largely reflect spill-over from the intense levels of transmission in high-burden settings
Latent tuberculosis infection (LTBI)	Without appropriate treatment, approximately 5-15% of LTBI cases progress to developing active TB disease over the patient's lifetime
LTBI screening	The positive predictive value (PPV) for all commercially available tests for LTBI is relatively low (about 1-15%) in any at-risk population, including migrants, demonstrating the need to target programs to optimize effectiveness and cost-effectiveness
Diagnostic tools for LTBI	The three currently commercially available tests for LTBI are the tuberculin skin test (TST) and two whole blood interferon-gamma release assays (IGRAs), QuantiFERON and T-SPOT.TB
Screening migrants for LTBI	Risk of progression from LTBI to active tuberculosis can be reduced with preventive treatment. Systematic testing and treatment of migrants from high-incidence regions might therefore have a large impact on tuberculosis control and elimination.
LTBI treatment	There are several options: 3-month isoniazid plus rifampicin regimen, 6 or 9 months of isoniazid, 1 or 3 months of rifapentine plus isoniazid
Cost-effectiveness of screening for LTBI	Modeling suggest that a cost-effectiveness model could be a single IGRA test offered to all migrants less than 35 years of age from countries with a TB incidence of 150 per 100,000 population or more.
Ethics, legal status, access to care and social factors	Complex ethical consideration around mandatory screening is a concern. This includes legal status, patients' mistrust, and uncertainty around legal entitlements regarding access to medical care, language, and cultural barriers.
Challenges and research and knowledge gaps	It is still not clear what the actual impact of screening and treatment programs are having on decreasing the actual incidence of TB.

International Journal of Infectious Diseases xxx (xxxx) xxx

can be effective and cost-effective if highly targeted and well implemented.

It is essential to ensure equitable access to high-quality patient-centered health care for all migrants while ensuring conducive social policies, protecting human rights, and minimizing stigma and discrimination.

There is an urgent need for high-quality operational research to use such data to evaluate the effectiveness and cost-effectiveness of the existing programs in a more standardized way and inform the future direction of screening and treatment approaches. More accurate tools, especially tests that predict LTBI reactivation and thus help rationalize LTBI screening and treatment, are also needed. Furthermore, improving the knowledge base of healthcare workers on LTBI, and providing accurate simple guidelines on use of appropriate diagnostic tests, the benefit of treatment to the patient and wider community benefit will enhance screening programs and treatment uptake.

Unless global efforts are accelerated, TB among migrants will remain a challenge in low-incidence countries for a long time to come.

## **Declarations of competing interest**

This article is part of a supplement entitled Commemorating World Tuberculosis Day, March 24th, 2024: "Yes! We Can End TB" published with support from an unrestricted educational grant from QIAGEN Sciences Inc.

#### Acknowledgments

Eskild Petersen acknowledge support from the Danish National Research Foundation (grant No. DNRF170). Sir Alimuddin Zumla is co-principal investigator of The Pan-African Network on Emerging and Re-Emerging Infections (PANDORA-ID-NET) funded by the European and Developing Countries Clinical Trials Partnership, Horizon 2020 Framework Programme. Sir Alimuddin Zumla is in receipt of an UK-NIHR Senior Investigator award and is a Mahathir Science Award and EU-EDCTP Pascoal Mocumbi Prize Laureate.

#### **Transparency Declaration**

This article is part of a supplement entitled Commemorating World Tuberculosis Day, March 24th, 2024: "Yes! We Can End TB" published with support from an unrestricted educational grant from QIAGEN Sciences Inc.

#### References

- [1] Cohen A, Mathiasen VD, Schön T, Wejse C. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. *Eur Respir J* 2019;**54**:1900655. doi:10.1183/13993003.00655-2019.
- [2] Vasiliu A, Martinez L, Gupta RK, Hamada Y, Ness T, Kay A, et al. Tuberculosis prevention: current strategies and future directions. *Clin Microbiol Infect* 2023;S1198-743X(23):00533-5. doi:10.1016/j.cmi.2023.10.023.
- [3] World Health Organization. Global tuberculosis report 2023. https://reliefweb.int/report/world/global-tuberculosis-report-2023. [accessed 4 February 2024].
- [4] Migliori GB, Wu SJ, Matteelli A, Zenner D, Goletti D, Ahmedov S, et al. Clinical standards for the diagnosis, treatment and prevention of TB infection. Int J Tuberc Lung Dis 2022;26(3):190–205. doi:10.5588/ijtld.21.0753.
- [5] Migliori GB, Thong PM, Alffenaar J-W, Denholm J, Tadolini M, Al-Yaquobi F, et al. Gauging the impact of the COVID-19 pandemic on tuberculosis services: a global study. Eur Respir J 2021;58(5):2101786. doi:10.1183/13993003. 01786-2021.
- [6] International Organization for Migration, IOM. World migration report 2022. https://reliefweb.int/report/world/world-migration-report-2022. [accessed 4 February 2024].
- [7] United Nations Refugee Agency, UNHCR. Global report 2022. https://reporting. unhcr.org/global-report-2022. [accessed 4 February 2024].
- [8] Varughese M, Heffernan C, Li MY, Long R. Time to diagnosis and treatment of pulmonary tuberculosis in indigenous peoples: a systematic review. BMC Infect Dis 2023;23:131. doi:10.1186/s12879-023-08098-y.

- [9] Spruijt I, Erkens C, Greenaway C, Mulder C, Raviglione M, Villa S, et al. Reducing the burden of TB among migrants to low TB incidence countries. *Int J Tuberc Lung Dis* 2023;27:182–8. doi:10.5588/ijtld.22.0662.
- [10] Wahedi K, Zenner D, Flores S, Bozorgmehr K. Mandatory, voluntary, repetitive, or one-off post-migration follow-up for tuberculosis prevention and control: a systematic review. PLoS Med 2023;20:e1004030. doi:10.1371/journal.pmed. 1004030.
- [11] United Nations Refugee Agency, UNHCR. Who we protect: refugees. https:// www.unhcr.org/about-unhcr/who-we-protect/refugees. [accessed 5 February 2024]
- [12] Litvinjenko S, Magwood O, Wu S, Wei X. Burden of tuberculosis among vulnerable populations worldwide: an overview of systematic reviews. *Lancet Infect Dis* 2023;23:1395–407. doi:10.1016/S1473-3099(23)00372-9.
- [13] Baggaley RF, Nazareth J, Divall P, Pan D, Martin CA, Volik M, et al. National policies for delivering tuberculosis, HIV and hepatitis B and C virus infection services for refugees and migrants among Member States of the WHO European Region. J Travel Med 2023;30:taac136. doi:10.1093/jtm/taac136
- [14] Rodriguez-Morales AJ, Abbara A, Ntoumi F, Kapata N, Mwaba P, Yeboah-Manu D, et al. World tuberculosis day 2023—reflections on the spread of drug-resistant tuberculosis by travellers and reducing risk in forcibly displaced populations. *Travel Med Infect Dis* 2023;53:102568. doi:10.1016/j.tmaid.2023.102568.
- [15] Beeler Asay GR, Woodruff R, Sanderson DM, Fisher CF, Marks SM, Green VD, et al. Cost-effectiveness of expanded latent TB infection testing and treatment: Lynn City, Massachusetts, USA. Int J Tuberc Lung Dis 2024;28:21-8. doi:10.5588/jitld.22.0654.
- [16] Coleman M, Nguyen TA, Luu BK, Hill J, Ragonnet R, Trauer JM, et al. Finding and treating both tuberculosis disease and latent infection during populationwide active case finding for tuberculosis elimination. Front Med (Lausanne) 2023;10:1275140. doi:10.3389/fmed.2023.1275140.
- [17] Marx FM, Hauer B, Menzies NA, Haas W, Perumal N. Targeting screening and treatment for latent tuberculosis infection towards asylum seekers from highincidence countries—a model-based cost-effectiveness analysis. BMC Public Health 2021;21:2172. doi:10.1186/s12889-021-12142-4.
- [18] Barker E, Moss J, Holmes H, Bowe C, Suryaprakash V, Alagna R, et al. A cost-effectiveness evaluation of latent tuberculosis infection screening of a migrant population in Malaysia. Sci Rep 2023;13:2390. doi:10.1038/ s41598-023-29648-z.
- [19] Schwartz NG, Price SF, Pratt RH, Langer AJ. Tuberculosis—United States, 2019. MMWR Morb Mortal Wkly Rep 2020;69:286–9.
- [20] Centers for Disease Control and Prevention. Reported tuberculosis in the United States, 2018 https://www.cdc.gov/tb/statistics/reports/2018/national\_ data.htm. [accessed 10 February 2024].
- [21] European Center for Disease Control, ECDC. Tuberculosis surveillance and monitoring in Europe, 2023. https://www.ecdc.europa.eu/sites/default/ files/documents/tuberculosis-surveillance-monitoring-2023.pdf. [accessed 5 February 2024].
- [22] Doležalová K, Kika V, Wallenfels J. Increasing incidence of TB in a low burden TB country due to migration from Ukraine. Int J Tuberc Lung Dis 2024;28:39–40. doi:10.5588/ijtld.23.0292.
- [23] Lönnroth K, Mor Z, Erkens C, Bruchfeld J, Nathavitharana RR, van der Werf MJ, et al. Tuberculosis in migrants in low-incidence countries: epidemiology and intervention entry points. Int J Tuberc Lung Dis 2017;21:624–37. doi:10.5588/ iiiid.20045.
- [24] Meaza A, Tola HH, Eshetu K, Mindaye T, Medhin G, Gumi B. Tuberculosis among refugees and migrant populations: systematic review. PLoS One 2022;17:e0268696. doi:10.1371/journal.pone.0268696.
- [25] Kontsevaya I, Cabibbe AM, Cirillo DM, DiNardo AR, Frahm N, Gillespie SH, et al. Update on the diagnosis of tuberculosis. Clin Microbiol Infect 2023;51198-743X(23):00340-3. doi:10.1016/j.cmi.2023.07.014.
- [26] Pinto PFPS, Camila Teixeira CSS, Ichihara MY, Rasella D, Nery JS, Sena SOL, et al. Incidence and risk factors of tuberculosis among 420 854 household contacts of patients with tuberculosis in the 100 Million Brazilian Cohort (2004-18): a cohort study. Lancet Infect Dis 2024;24:46-56. doi:10.1016/S1473-3099(23)00371-7.
- [27] Bigio J, Viscardi A, Gore G, Matteelli A, Sulis G. A scoping review on the risk of tuberculosis in specific population groups: can we expand the World Health Organization recommendations? Eur Respir Rev 2023;32:220127. doi:10.1183/ 16000617.0127-2022.
- [28] World Health Organization. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management <a href="https://www.who.int/publications/i/item/9789241550239">https://www.who.int/publications/i/item/9789241550239</a>; 2018 [accessed 4 February 2024].
- [29] Rustage K, Lobe J, Hayward SE, Kristensen KL, Margineanu I, Stienstra Y, et al. Initiation and completion of treatment for latent tuberculosis infection in migrants globally: a systematic review and meta-analysis. *Lancet Infect Dis* 2021;21:1701-12. doi:10.1016/S1473-3099(21)00052-9.
- [30] Flynn JL, Chan J. Tuberculosis: latency and reactivation. Infect Immun 2001;69:4195–201. doi:10.1128/IAI.69.7.4195-4201.2001.
- [31] Goletti D, Pisapia R, Fusco FM, Aiello A, Van Crevel R. Epidemiology, pathogenesis, clinical presentation and management of TB in patients with HIV and diabetes. Int J Tuberc Lung Dis 2023;27:284–90. doi:10.5588/ijtld.22.
- [32] Dale KD, Karmakar M, Snow KJ, Menzies D, Trauer JM, Denholm JT. Quantifying the rates of late reactivation tuberculosis: a systematic review. *Lancet Infect Dis* 2021;21:e303–17. doi:10.1016/S1473-3099(20)30728-3.

- [33] Migliori GB, Ong CWM, Petrone L, D'Ambrosio L, Centis R, Goletti D. The definition of tuberculosis infection based on the spectrum of tuberculosis disease. Breathe (Sheff) 2021;17:210079. doi:10.1183/20734735.0079-2021.
- [34] Ekramnia M, Li Y, Haddad MB, Marks SM, Kammerer JS, Swartwood NA, et al. Estimated rates of progression to tuberculosis disease for persons infected with Mycobacterium tuberculosis in the United States. Epidemiology 2024;35:164–73. doi:10.1097/EDE.000000000001707.
- [35] Berrocal-Almanza LC, Harris RJ, Collin SM, Muzyamba MC, Conroy OD, Mirza A, et al. Effectiveness of nationwide programmatic testing and treatment for latent tuberculosis infection in migrants in England: a retrospective, population-based cohort study. Lancet Public Health 2022;7:e305–15. doi:10.1016/S2468-2667(22)00031-7.
- [36] Gupta RK, Lule SA, Krutikov M, Gosce L, Green N, Southern J, et al. Screening for tuberculosis among high-risk groups attending London emergency departments: a prospective observational study. Eur Respir J 2021;57:2003831. doi:10.1183/13993003.03831-2020.
- [37] Pareek M, Greenaway C, Noori T, Munoz J, Zenner D. The impact of migration on tuberculosis epidemiology and control in high-income countries: a review. BMC Med 2016;14:48. doi:10.1186/s12916-016-0595-5.
- [38] Greenaway C, Sandoe A, Vissandjee B, Kitai I, Gruner D, Wobeser W, et al. Tuberculosis: evidence review for newly arriving immigrants and refugees. CMAJ 2011;183(12):E939-51. doi:10.1503/cmaj.090302.
- [39] Greenaway C, Pareek M, Abou Chakra CN, Walji M, Makarenko I, Alabdulkarim B, et al. The effectiveness and cost-effectiveness of screening for latent tuberculosis among migrants in the EU/EEA: a systematic review. Euro Surveill 2018;23:17-00543. doi:10.2807/1560-7917.ES.2018.23.14.17-00543.
- [40] Tagmouti S, Slater M, Benedetti A, Kik SV, Banaei N, Cattamanchi A, et al. Reproducibility of interferon gamma (IFN-γ·) release assays. A systematic review. Ann Am Thorac Soc 2014;11:1267–76. doi:10.1513/AnnalsATS. 201405-1880C.
- [41] Mahon J, Beale S, Holmes H, Arber M, Nikolayevskyy V, Alagna R, et al. A systematic review of cost-utility analyses of screening methods in latent tuberculosis infection in high-risk populations. BMC Pulm Med 2022;22:375. doi:10.1186/s12890-022-02149-x.
- [42] Shea KM, Kammerer JS, Winston CA, Navin TR, Horsburgh CR Jr. Estimated rate of reactivation of latent tuberculosis infection in the United States, overall and by population subgroup. Am J Epidemiol 2014;179:216–25. doi:10. 1093/aie/kwt246.
- [43] Chan IHY, Kaushik N, Dobler CC. Post-migration follow-up of migrants identified to be at increased risk of developing tuberculosis at premigration screening: a systematic review and meta-analysis. *Lancet Infect Dis* 2017;**17**:770–9. doi:10.1016/S1473-3099(17)30194-9.
- [44] Aldridge RW, Zenner D, White PJ, Williamson EJ, Muzyamba MC, Dhavan P, et al. Tuberculosis in migrants moving from high-incidence to low-incidence countries: a population-based cohort study of 519,955 migrants screened before entry to England, Wales, and Northern Ireland. *Lancet* 2016;388:2510–18. doi:10.1016/S0140-6736(16)31008-X.
- [45] World Health Organization. Use of alternative interferon-gamma release assays for the diagnosis of TB infection - WHO Policy Statement. www.who.int/news/item/28-01-2022-use-of-alternative-interferongamma-release-assays-for-the-diagnosis-of-tb-infection; 2022 [accessed 5 February 2024].
- [46] United States Preventive Services Task ForceScreening for latent tuberculosis infection in adults: US Preventive Services Task Force Recommendation Statement. JAMA 2023;329:1487–94. doi:10.1001/jama.2023.4899.
- [47] Campbell JR, Johnston JC, Cook VJ, Sadatsafavi M, Elwood RK, Marra F. Cost-effectiveness of latent tuberculosis infection screening before immigration to low-incidence countries. *Emerg Infect Dis* 2019;25:661–71. doi:10.3201/eid2504.171630.
- [48] MacIntyre CR, Ansari MZ, Carnie J, Hart WG. No evidence for multiple-drug prophylaxis for tuberculosis compared with isoniazid alone in Southeast Asian refugees and migrants: completion and compliance are major determinants of effectiveness. Prev Med 2000;30:425–32. doi:10.1006/pmed.2000.
- [49] Truong DH, Hedemark LL, Mickman JK, Mosher LB, Dietrich SE, Lowry PW. Tuberculosis among Tibetan immigrants from India and Nepal in Minnesota, 1992-1995. JAMA 1997;277:735-8.
- [50] Winje BA, White R, Syre H, Skutlaberg DH, Oftung F, Mengshoel AT, et al. Stratification by interferon-γ release assay level predicts risk of incident TB. Thorax 2018 thoraxjnl-2017-211147. doi:10.1136/thoraxjnl-2017-211147.
- [51] Harstad I, Winje BA, Heldal E, Oftung F, Jacobsen GW. Predictive values of QuantiFERON-TB Gold testing in screening for tuberculosis disease in asylum seekers. Int J Tuberc Lung Dis 2010;14:1209-11.
- [52] Zenner D, Hafezi H, Potter J, Capone S, Matteelli A. Effectiveness and cost-effectiveness of screening migrants for active tuberculosis and latent tuberculous infection. *Int J Tuberc Lung Dis* 2017;21:965–76. doi:10.5588/ijtld.16.0935
- [53] Adams S, Ehrlich R, Baatjies R, Dendukuri N, Wang Z, Dheda K. Predictors of discordant latent tuberculosis infection test results amongst South African health care workers. BMC Infect Dis 2019;19:131. doi:10.1186/s12879-019-3745-5.
- [54] Doan TN, Eisen DP, Rose MT, Slack A, Stearnes G, McBryde ES. Interferongamma release assay for the diagnosis of latent tuberculosis infection: a latent-class analysis. PLoS One 2017;12:e0188631. doi:10.1371/journal.pone.

- [55] Nolt D, Starke JR. Tuberculosis infection in children and adolescents: testing and treatment. *Pediatrics* 2021;148:e2021054663. doi:10.1542/peds. 2021-054663.
- [56] Volkman T, Muruganandah V, Graham H, Tosif S, Stokes S, Ranganathan S. QuantiFERON Gold-In-Tube for the diagnosis of mycobacterial tuberculosis infection in children under 5 years of age: a systematic review and meta-analysis. PLoS One 2024;19:e0295913. doi:10.1371/journal.pone. 0295913.
- [57] Alonzi T, Repele F, Goletti D. Research tests for the diagnosis of tuberculosis infection. Expert Rev Mol Diagn 2023;23:783–95. doi:10.1080/14737159.2023. 2240230.
- [58] Brumwell A, Tso J, Pingali V, Millones AK, Jimenez J, Calderon RI, et al. A costing framework to compare tuberculosis infection tests. BMJ Glob Health 2023;8:e012297. doi:10.1136/bmjgh-2023-012297.
- [59] Pan SW, Catanzaro DG, Seifert M, Syed RR, Hillery N, Ho ML, et al. Predicting stringent QuantiFERON-TB Gold Plus conversions in contacts of tuberculosis patients. J Microbiol Immunol Infect 2023;56:1073–83. doi:10.1016/j.jmii.2023. 07014
- [60] Goletti D, Delogu G, Matteelli A, Migliori GB. The role of IGRA in the diagnosis of tuberculosis infection, differentiating from active tuberculosis, and decision making for initiating treatment or preventive therapy of tuberculosis infection. Intl J Infect Dis 2022;124(Suppl 1):S12-19. doi:10.1016/j.ijid.2022.02.047.
- [61] Bae W, Park KU, Song EY, Kim SJ, Lee YJ, Park JS, et al. Comparison of the sensitivity of QuantiFERON-TB Gold In-Tube and T-SPOT.TB according to patient age. PLoS One 2016;11:e0156917. doi:10.1371/journal.pone.0156917.
- [62] Rangaka MX, Hamada Y, Duong T, Bern H, Calvert J, Francis M, et al. Evaluating the effect of short-course rifapentine-based regimens with or without enhanced behaviour-targeted treatment support on adherence and completion of treatment for latent tuberculosis infection among adults in the UK (RID-TB: Treat): protocol for an open-label, multicentre, randomised controlled trial. BMJ Open 2022;12:e057717. doi:10.1136/bmjopen-2021-057717.
- [63] Diel R, Loddenkemper R, Nienhaus A. Predictive value of interferon-γ release assays and tuberculin skin testing for progression from latent TB infection to disease state: a meta-analysis. Chest 2012;142:63–75. doi:10.1378/chest. 11-3157.
- [64] Diel R, Goletti D, Ferrara G, Bothamley G, Cirillo D, Kampmann B, et al. Interferon-γ release assays for the diagnosis of latent Mycobacterium tuberculosis infection: a systematic review and meta-analysis. Eur Respir J 2011;37:88–99. doi:10.1183/09031936.00115110.
- [65] Hamada Y, Gupta RK, Quartagno M, Izzard A, Acuna-Villaorduna C, Altet N, et al. Predictive performance of interferon-gamma release assays and the tuberculin skin test for incident tuberculosis: an individual participant data meta-analysis. EClinicalMedicine 2023;56:101815. doi:10.1016/j.eclinm.2022.
- [66] Yang Y, Wang H-J, Hu W-L, Bai G-N, Hua C-Z. Diagnostic value of interferongamma release assays for tuberculosis in the immunocompromised population. *Diagnostics (Basel)* 2022;12:453. doi:10.3390/diagnostics12020453.
- [67] Cho SY, Nham E, Chung DR, Kim J, Jeong J, Ko JH, et al. Effect of a latent tuberculosis infection programme for healthcare workers in a country with an intermediate tuberculosis burden. J Hosp Infect 2023;S0195-6701(23):00382– 1. doi:10.1016/j.jhin.2023.11.009.
- [68] Hussain H, Jaswal M, Farooq S, Safdar N, Madhani F, Noorani S, et al. Scaleup of rifapentine and isoniazid for tuberculosis prevention among household contacts in 2 urban centers: an effectiveness assessment. Clin Infect Dis 2023;77:638-44. doi:10.1093/cid/ciad245.
- [69] Loutet MG, Burman M, Jayasekera N, Trathen D, Dart S, Kunst H, et al. National roll-out of latent tuberculosis testing and treatment for new migrants in England: a retrospective evaluation in a high-incidence area. Eur Respir J 2018;51:1701226. doi:10.1183/13993003.01226-2017.
- [70] Sandgren A, Vonk Noordegraaf-Schouten M, van Kessel F, Stuurman A, Oordt-Speets A, van der Werf MJ. Initiation and completion rates for latent tuber-culosis infection treatment: a systematic review. BMC Infect Dis 2016;16:204. doi:10.1186/s12879-016-1550-y.
- [71] Lim VW, Wee HL, Lee P, Lin Y, Tan YR. Cross-sectional study of prevalence and risk factors, and a cost-effectiveness evaluation of screening and preventive treatment strategies for latent tuberculosis among migrants in Singapore. BMJ Open 2021;11:e050629.
- [72] Walle AD, Hunde MK, Demsash AW. Healthcare professionals' intention to adopt mobile phone-based SMS and its predictors for adherence support and care of TB patients in a resource-limited setting: a structural equation modelling analysis. BMJ Open 2023;13:e070813. doi:10.1136/ bmiopen-2022-070813.
- [73] Manoharan A, Siti Nur Farhana H, Manimaran K, Khoo EM, Koh WM. Facilitators and barriers for tuberculosis preventive treatment among patients with latent tuberculosis infection: a qualitative study. BMC Infect Dis 2023;23:624. doi:10.1186/s12879-023-08612-2.
- [74] Swift MD, Molella RG, Vaughn AlS, Breeher LE, Newcomb RD, Abdellatif S, et al. Determinants of latent tuberculosis treatment acceptance and completion in healthcare personnel. Clin Infect Dis 2020;71:284–90. doi:10.1093/cid/ciz817.
- [75] Scott NA, Sadowski C, Vernon A, Arevalo B, Beer K, Borisov A, et al. Using a medication event monitoring system to evaluate self-report and pill count for determining treatment completion with self-administered, once-weekly isoniazid and rifapentine. Contemp Clin Trials 2023;129:107173. doi:10.1016/j. cct.2023.107173.

JID: IJID [m5G;March 22, 2024;0:32

E. Petersen, S. Al-Abri, A. Al-Jardani et al.

- [76] Chung SJ, Lee H, Koo GW, Min JH, Yeo Y, Park DW, et al. Adherence to nine-month isoniazid for latent tuberculosis infection in healthcare workers: a prospective study in a tertiary hospital. *Sci Rep* 2020;10:6462. doi:10.1038/s41598-020-63156-8.
- [77] UK Govt Guidance. Latent tuberculosis testing and treatment programme for migrants https://www.gov.uk/government/publications/latent-tuberculosis-testing-and-treatment-programme-for-migrants; 2021 [accessed 10 February 2024].
- [78] Alsdurf H, Oxlade O, Adjobimey M, Ahmad Khan F, Bastos M, Bedingfield N, et al. Resource implications of the latent tuberculosis cascade of care: a time and motion study in five countries. BMC Health Serv Res 2020;20:341. doi:10.1186/s12913-020-05220-7.
- [79] Assefa DG, Bedru A, Zeleke ED, Negash SE, Debela DT, Molla W, et al. Efficacy and safety of different regimens in the treatment of patients with latent tuberculosis infection: a systematic review and network meta-analysis of randomized controlled trials. Arch Public Health 2023;81:82. doi:10.1186/s13690-023-01098-z.
- [80] Stuurman AL, Vonk Noordegraaf-Schouten M, van Kessel F, Oordt-Speets AM, Sandgren A, van der Werf MJ. Interventions for improving adherence to treatment for latent tuberculosis infection: a systematic review. BMC Infect Dis 2016;16:257. doi:10.1186/s12879-016-1549-4.
- [81] European Center for Disease Control, ECDC. Migrants in an irregular situation: access to healthcare in 10 European Union Member States. https://fra.europa.eu/sites/default/files/fra\_uploads/1771-FRA-2011-fundamental-rights-for-irregular-migrants-healthcare\_EN.pdf; 2011 [accessed 5 February 2024].
- [82] Lines G, Hunter P, Bleything S. Improving treatment completion rates for latent tuberculosis infection: a review of two treatment regimens at a community health center. J Health Care Poor Underserved 2015;26:1428-39. doi:10. 1353/hpu.2015.0126.
- [83] Menezes D, Zenner D, Aldridge R, Anderson SR, de Vries G, Erkens C, et al. Country differences and determinants of yield in programmatic migrant TB screening in four European countries. Int J Tuberc Lung Dis 2022;26:942–8. doi:10.5588/ijtld.22.0186.
- [84] Menzies D, Adjobimey M, Ruslami R, Trajman A, Sow O, Kim H, et al. Four months of rifampin or nine months of isoniazid for latent tuberculosis in adults. N Engl J Med 2018;379:440-53. doi:10.1056/NEJMoa1714283.
- [85] Pease C, Hutton B, Yazdi F, Wolfe D, Hamel C, Quach P, et al. Efficacy and completion rates of rifapentine and isoniazid (3HP) compared to other treatment regimens for latent tuberculosis infection: a systematic review with network meta-analyses. BMC Infect Dis 2017;17:265. doi:10.1186/ s12879-017-2377-x.
- [86] Tuberculosis preventive treatment: rapid communication. https://www.who. int/publications/i/item/9789240089723 [accessed 14 February 2024].
- [87] Al Abri S, Kowada A, Yaqoubi F, Al Khalili S, Ndunda N, Petersen E. Cost-effectiveness of IGRA/QFT-Plus for TB screening of migrants in Oman. In: Int J Infect Dis.; 2020. p. S72-7. 92S. doi:10.1016/j.ijid.2020.03.010.
- [88] Auguste PE, Mistry H, McCarthy ND, Sutcliffe PA, Clarke AE. Cost-effectiveness of testing for latent tuberculosis infection in people with HIV. AIDS 2022;36:1–9. doi:10.1097/QAD.000000000003060.
- [89] Yoopetch P, Chitpim N, Jittikoon J, Udomsinprasert W, Thavorncharoensap M, Youngkong S, et al. Economic evaluation of screening strategy for latent tuberculosis infection (LTBI) in contacts of tuberculosis patients: systematic review and quality assessment. Int J Environ Res Public Health 2022;19:13529. doi:10.3390/ijerph192013529.
- [90] Navarro CE, Betancur JE. Cost-effectiveness analysis comparing QuantiFERON-TB Gold plus test and tuberculin skin test for the diagnosis of latent tuberculosis infection in immunocompetent subjects in Colombia. Value Health Reg Issues 2024;41:54–62. doi:10.1016/j.vhri.2023.11.010.
- [91] Gray AT, Surey J, Esmail H, Story A, Harris M. "It's too hard"—the management of latent TB in under-served populations in the UK: a qualitative study. BMC Health Serv Res 2022;22:1464. doi:10.1186/s12913-022-08855-w.

[92] Abubakar I, Drobniewski F, Southern J, Sitch AJ, Jackson C, Lipman M, et al. Prognostic value of interferon-γ release assays and tuberculin skin test in predicting the development of active tuberculosis (UK PREDICT TB): a prospective cohort study. *Lancet Infect Dis* 2018;18(10):1077–87. doi:10.1016/ S1473-3099(18)30355-4.

International Journal of Infectious Diseases xxx (xxxx) xxx

- [93] Abubakar I, Lalvani A, Southern J, Sitch A, Jackson C, Onyimadu O, et al. Two interferon gamma release assays for predicting active tuberculosis: the UK PREDICT TB prognostic test study. *Health Technol Assess* 2018;22:1–96. doi:10. 3310/hta22560.
- [94] Dale KD, Abayawardana MJ, McBryde ES, Trauer JM, Carvalho N. Modeling the cost-effectiveness of latent tuberculosis screening and treatment strategies in recent migrants to a low-incidence setting. Am J Epidemiol 2022;191:255–70. doi:10.1093/aie/kwab150.
- [95] Kowada A. Cost effectiveness of interferon-gamma release assay for tuberculosis screening using three months of rifapentine and isoniazid among long-term expatriates from low to high incidence countries. *Travel Med Infect Dis* 2016;14:489–98. doi:10.1016/j.tmaid.2016.05.010.
- [96] Borgdorff MW, van den Hof S, Kremer K, Verhagen L, Kalisvaart N, Erkens C, et al. Progress towards tuberculosis elimination: secular trend, immigration and transmission. Eur Respir J 2010;36:339-47. doi:10.1183/09031936. 00155409.
- [97] Dobler CC, Fox GJ, Douglas P, Viney KA, Ahmad Khan F, Temesgen Z, et al. Screening for tuberculosis in migrants and visitors from high-incidence settings: present and future perspectives. Eur Respir J 2018;52:1800591. doi:10. 1183/13993003.00591-2018.
- [98] Wingate LT, Coleman MS, Posey DL, Zhou W, Olson CK, Maskery B, et al. Cost-effectiveness of screening and treating foreign-born students for tuberculosis before entering the United States. PLoS One 2015; 10:e0124116. doi:10.1371/journal.pone.0124116.
- [99] Burger IM, Kass NE. Screening in the dark: ethical considerations of providing screening tests to individuals when evidence is insufficient to support screening populations. Am J Bioeth 2009;9:3–14. doi:10.1080/15265160902790583.
- [100] European Commission. Identifying serious and complex ethics issues in EU-funded research. https://ec.europa.eu/info/funding-tenders/opportunities/docs/2021-2027/horizon/guidance/guidelines-on-serious-and-complex-cases\_he\_en.pdf; 2021 [accessed 7 February 2024].
- [101] International Organization for Migration, IOM. Migration & tuberculosis: a pressing issue. Health and development impacts of TB on migrants and communities. https://www.iom.int/sites/g/files/tmzbdl486/files/migrated\_files/What-We-Do/docs/Migration-Tuberculosis-A-Pressing-Issue.pdf; 2012 [accessed 7 February 2024].
- [102] Khatri RB, Assefa Y. Access to health services among culturally and linguistically diverse populations in the Australian universal health care system: issues and challenges. BMC Public Health 2022;22:880. doi:10.1186/s12889-022-13256-z.
- [103] Alipanah N, Jarlsberg L, Miller C, Linh NN, Falzon D, Jaramillo E. Adherence interventions and outcomes of tuberculosis treatment: a systematic review and meta-analysis of trials and observational studies. *PLoS Med* 2018;15:e1002595. doi:10.1371/journal.pmed.1002595.
- [104] Mohammadifirouzeh M, Oh KM, Basnyat I, Gimm G. Factors associated with professional mental help-seeking among U.S. immigrants: a systematic review. J Immigr Minor Health 2023;25:1118–36. doi:10.1007/ s10903-023-01475-4.
- [105] Lestari T, Graham S, van den Boogard C, Triasih R, Poespoprodjo JR, Ubra RR, et al. Bridging the knowledge-practice gap in tuberculosis contact management in a high-burden setting: a mixed-methods protocol for a multicenter health system strengthening study. *Implement Sci* 2019;14:31. doi:10.1186/s13012-019-0870-x.
- [106] Abubakar I, Aldridge RW, Devakumar D, Orcutt M, Burns R, Barreto ML, et al. The UCL-Lancet Commission on Migration and Health: the health of a world on the move. Lancet 2018;392:2606-54. doi:10.1016/S0140-6736(18)32114-7.