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Early View

Review

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Tuberculosis in adult migrants in Europe: a TBnet consensus statement

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Take home message: Migrant populations entering Europe have poorer tuberculosis outcomes than native populations. As cases of tuberculosis are rising in Europe, we need robust strategies to strengthen screening, rapid diagnosis, and treatment in these hard-to-reach populations.

ABSTRACT

Introduction: Global migration has increased in recent decades due to war, conflict, persecutions, and natural disasters, but also secondary to increased opportunities related to work or study. Migrants' risk of tuberculosis (TB) differs by reasons for migration, socioeconomic status, mode of travel and TB risk in transit, TB incidence and healthcare provision in country of origin. Despite advances in TB care for migrants and new treatment strategies, decisions for the management of migrants at risk of TB often rely on expert opinions, rather than clinical evidence.

Methods: A systematic literature search was conducted, studies were mapped to different recommendation groups and included studies were synthesized by meta-analysis where appropriate. Current evidence on diagnosis of active TB in migrants entering the European Union /European Economic Area (EU/EEA) &UK including the clinical presentation and diagnostic delay, treatment outcomes of drug susceptible TB, prevalence and treatment outcomes of multidrug/rifampicin-resistant (MDR/RR)-TB and TB/HIV co-infection was summarised. A consensus process was used based on the evidence.

Results: We document a higher vulnerability of migrants for TB, including an increased risk of extrapulmonary TB, MDR/RR-TB, TB/HIV co-infection and worse TB treatment outcomes compared to host populations. Consensus recommendations include screening of migrants for TB/ latent TB infection (LTBI) according to country data; a minimal package for TB care in

drug susceptible and MDR/RR-TB; implementation of migrant-sensitive strategies; free healthcare and preventive treatment for migrants with HIV co-infection.

Conclusion: Dedicated care for TB prevention and treatment in migrant populations within the EU/EEA &UK is essential.

INTRODUCTION

Migration is a significant global phenomenon, currently around 281 million persons (3.6% of the global population) live outside their country of origin and are defined as international migrants [1]. Reasons, circumstances, and routes of international migration vary considerably. Causes of migration include conflict and war, persecution, natural disasters, work opportunities and study [1]. Tuberculosis (TB) is an infectious disease that commonly affects the lungs. TB is the leading cause of death from a single bacterial infectious agent worldwide [2]. Migrants may have a higher risk of TB than native born individuals [3], related to factors such as TB prevalence in their country of origin, migration route, living conditions in the host country, time of residence in the host country and frequency of visiting their country of origin [3-6]. Studies have shown significant differences in the yield of TB screening in migrant workers compared with refugees and/ or asylum seekers, with highest TB prevalence among these more vulnerable migrants [6]. At the end of 2022, 108.4 million people worldwide were forcibly displaced as a result of persecution, conflict, violence or human rights violations. In 2022, over 1 in every 74 people globally have been forced to flee their homes [7]. In 2023, it was estimated that over half of all refugees under the United Nations High Commissioner for Refugees (UNHCR) mandate and other people in need of international protection come from just three countries, Syria- 6.7 million, Afghanistan- 6.1 million, and Ukraine- 5.9 million refugees [8].

In the year 2020 there were more than 9000 foreign-born individuals developing TB in the EU/EEA [9]. The number of Ukranians who were notified with TB in the EU/EEA increased from 164 (27 with multidrug/rifampicin-resistant; MDR/RR-TB) to 780 (194 with MDR/RR-TB)

between 2020 and 2022, indicating substantial changes in the TB epidemiology in EU/EEA in recent times [10].

TB programs for migrants have been a key priority of host countries in the European Union (EU)/European Economic Area (EEA) & UK. [11] Migrant-sensitive strategies, for example availability of interpreters and language-appropriate written materials, healthcare provider training in culture-sensitive issues, health education of migrants and social support are thought to be essential for migrant care [12]. Migrants should have equal and unhindered access to prevention, diagnostics, and TB treatment integrated with other health services compared to the native population.

We conducted a systematic review to investigate if migrants have different outcomes with regards to TB diagnosis, TB treatment, MDR/RR-TB and TB/HIV co-infection compared to non-migrants including use of migrant-sensitive strategies vs no strategies in migrant care. In a modified Delphi process, we developed consensus guidance for early diagnosis and effective treatment of drug susceptible TB, MDR/RR-TB, and TB/HIV co-infection in migrants in the EU/EEA & UK.

METHODS

Definition of a migrant

The definition of a migrant followed the recommendation of the European Centres of Disease Control and Prevention (ECDC): "Any individual who lives in a country temporarily or permanently away from his or her usual place of residence for at least a year" [11]. We defined migrant types according to a modified classification of migrant status of the International Organisation of Migration (IOM) (**Supplement, Table S1**).

Systematic review

Expert groups subject

Expert panel groups were convened on four topics for migrants entering the EU/EEA &UK. These are: 1) TB diagnosis; 2) TB treatment; 3) MDR/RR-TB and 4) TB/HIV co-infection.

Evidence mapping

The PRISMA systematic review methodology [13] and the RIGHT statement for reporting recommendations were followed [14]. PICOs were designed by the methods groups (BL, CL, HK) and after revisions consented by all expert chapter groups. The different chapters of the systematic review include as a population migrants and non-migrants managed at clinical TB centers in the EU/EAA &UK **(Supplement table S2).** The diagnosis of active TB chapter includes the spectrum of clinical presentation and delay in diagnosis in migrants vs non-migrants. Diagnostic delay is divided into patient delay and health system delay. [15] The TB treatment chapter includes the evaluation of the treatment of drug susceptible TB in migrants vs non-migrants and management issues including use of migrant-sensitive vs no migrant-sensitive strategies. The MDR/ RR TB chapter includes the evaluation of the

prevalence of MDR/ RR TB compared to drug susceptible TB in migrants vs non- migrants and MDR/ RR treatment outcomes in migrants vs non-migrants. In addition, management issues including use of migrant-sensitive vs no migrant-sensitive strategies in MDR/ RR TB are evaluated. The TB/ HIV co-infection chapter includes the evaluation of the diagnosis and management of TB/HIV coinfection in migrants vs non-migrants, the prevalence of TB/ HIV co-infection in migrants vs non-migrants and TB treatment outcomes in migrants vs non-migrants.

The systematic review was registered with PROSPERO [CRD42018074338]. OVID Medline, EBSCO CINAHL and Web of Science databases were searched using the subject keywords and Medical Subject Heading (MeSH) terms for 'TB' and 'migrant' **(Supplement Search strategy).**

The search was restricted to English language and included all articles from inception until April 2024 **(Supplement Figure S1).** We included observational cohort studies including non-controlled cohort studies and interventional studies. References of review papers and relevant articles were also searched. In addition, reference lists of the included studies were searched for eligible articles.

After screening publications from a literature search and subsequent selection by title, abstract or full text respectively, each publication was screened by two of four reviewers (AB, OH, BL, HK). For dissident opinions regarding article inclusion among two reviewers,

consensus was sought from the other two reviewers. Evidence bundles were distributed to the expert groups for each chapter with the request to check for possible missing relevant studies.

Data extraction in chapter groups

Data on study characteristics and addressing the PICOs were extracted for each topic by expert groups subsequently. Where evidence from the literature was limited, expert consensus on best evidence was used and agreed upon by the group. Additional references were included provided by expert groups or external experts. When data from the published articles were not clear enough, we contacted the authors for clarification.

Data synthesis and analysis

Studies were synthesized by meta-analysis when appropriate; otherwise, narrative synthesis was used. Where available, we pooled risk estimates of odds ratios (ORs) and relative risks (RRs) through meta-analysis using the R software with the *metafor* package [16]. We included pooled estimates irrespective of study design. The point estimate was calculated using random effects models to account for potential variations in effect sizes across studies. The standard error and 95% confidence intervals (CI) of risk estimates were calculated from data reported in each paper. Heterogeneity was assessed visually and using both I^2 and τ^2 measures.

Quality assessment

Quality of the studies was assessed by using the Newcastle Ottawa Scale [17]. We considered studies to have a low risk of bias if they scored four stars for selection, two for

comparability, and three for ascertainment of outcomes. Studies with two or three stars for selection, one for comparability, and two for outcome ascertainment were regarded as having a medium risk of bias, and any study scoring one star for selection or outcome ascertainment, or zero for any of the three categories was considered to have a high risk of bias. Two reviewers independently conducted the quality assessment using the Newcastle-Ottawa Scale (MA, HK) and any discrepancies were resolved with the involvement of a third reviewer.

Consensus statements

The consensus recommendations were based on the evidence found and conducted through a modified Delphi process according to previously used methodology [18-20]. We followed five steps for drafting final consensus statements:

Step 1:

Preliminary proposals for five key recommendations were drafted by the coordinating authors. Chapter leaders were asked to provide alternative statements following consultation with the co-authors of their chapter.

Step 2:

Alternative statements were collected by the coordinating authors.

Step 3:

Chapter leaders were asked to select one preferred statement among the alternative statements following consultation with the co-authors of their chapter.

Step 4:

For each recommendation, the statement that received most votes was selected for inclusion in the manuscript.

Step 5:

All co-authors were asked to indicate their agreement, disagreement or whether they preferred to abstain from a decision on a recommendation. Results of the decisions are indicated at the end of each consensus statement.

RESULTS

Evidence mapping

A total of 7420 records were identified and screened by four reviewers (AB, BL, HK, OH). We identified 492 studies that were relevant to individual chapter groups. These were put together as evidence bundles and shared with authors **(Supplement figure S1).** Of 492 studies, 113 studies were included in the narrative review and from those, 49 studies were included in the meta-analysis **(Supplement tables S3, S5, S7-S9).**

Diagnosis of active TB in migrants including the spectrum of clinical presentation and diagnostic delay

Eleven studies addressing the clinical presentation of TB in migrants compared to non-migrants were included [21-31]. Pulmonary TB (PTB) was the predominant presentation at diagnosis in all but two of the studies [26, 27]. Overall, migrants were more likely to be diagnosed with extrapulmonary TB (EPTB) than non-migrants (OR 2.14, 95%CI 1.53-3.02) **(Figure 1)**. There was significant heterogeneity between studies. The largest study based on data from The European Surveillance System ECDC (TESSy) found an OR of 3.0 (95% CI 2.96--3.01) for EPTB in migrants compared to non-migrants (study period 1995-2017; n =1,270,896)[29]. A lower proportion of EPTB was seen in Eastern Europe (17.4%; 98,656 of 566,170) and Southern Europe (29.6%, 62,481 of 210,828) compared with Western (35.7%; 89,498 of 250,517) and Northern Europe (41.8%; 101,792 of 243,381). Migrants from South-East Asia and Sub-Saharan Africa were at highest risk of EPTB, with 62.0% (55,401 of 89,353) and 54.5% (38,327 of 70,378) of cases, respectively [29]. To determine if our findings are not solely explained by the large ECDC study, we conducted a sensitivity analysis excluding this study from the meta-analysis which demonstrated no significant impact on the results **(Supplement Figure S2).**

A separate analysis using surveillance data collected by the ECDC system TESSy over a shorter period (2003-2014) examined the risk for specific organ presentations according to the region of origin of migrants. ORs varied considerably between and within regions of origin, revealing the highest ORs for lymphatic, osteoarticular and peritoneal/digestive EPTB in patients from the Indian subcontinent (OR range of 6.4-8.8) [32]. The majority of studies did not provide

data on migrant status i.e., refugee vs migrant worker. A study from Denmark reported a similar risk of EPTB among migrant subcategories. EPTB in all migrants was present in 852/1841 (46.3%); the rates of EPTB in migrant subcategories ranged from 40.2 to 49.5%. The study showed a significantly higher risk of EPTB in migrants compared to the other studies included in the meta-analysis (OR 7.5 [95%CI 5.35- 10.49]) [26].

Seven studies on diagnostic delay were identified [15, 27, 33-37]. Patient delay has been defined as the time delay from symptom onset to first consultation; and health system delay from time of first consultation to diagnosis and/or treatment initiation [15].Three studies evaluated patient and health system delay in migrants vs non-migrants **(Supplement table S4).** All three studies showed that patient delay was higher in migrants vs non-migrants, whereas health system delay was shorter in migrants compared to non-migrants [15, 35, 37]. Risk factors for patient delay among migrants included perceived stigma, distance to the health care provider and healthcare cost. Out of the three studies, two included patients with PTB and EPTB, and one study from Denmark only included cases with EPTB [35]. A study from the UK demonstrated an increase in proportion of patients with any delay above the median time from symptom onset to treatment following the introduction of a migrant cost recovery program requesting migrants to pay for their care. The difference reached statistical significance in migrants, but the same trends towards a prolonged delay were observed in UK-born patients [27]. An Italian single center study showed a diagnostic delay in migrants from high TB incidence countries almost twice as high as natives (n=48, median 153 days [IQR 7–556] vs 88 days [IQR 12-28]) [36]. A Spanish study including only migrants reported on patient and health service delays and found that delays varied according to country of origin

and education level. Delays were significantly increased in EPTB compared to PTB [34]. A UK study investigated patient and health system delays in PTB patients and found that the shorter the time since entry to the UK, the longer the health system delay [33].

Treatment of active TB in migrants and management issues

Fourteen studies [21, 23, 24, 31, 35, 38-46] were identified reporting on treatment outcomes in migrants vs non-migrants and were included in the meta-analysis **(Figure 2)**. These studies included 60,802 migrants with TB and 221,002 non-migrants with TB. Three studies [21, 43, 44] were from Spain, two from the UK [42, 45], Italy [23, 24] and France [39, 41], one from the Netherlands [38], Denmark [35], Switzerland [40], Portugal [31] and one study included several European countries [46]. Studies used different definitions of unfavourable TB treatment outcomes including those for treatment default, treatment failure and loss to follow-up. Unfavourable treatment outcomes were higher in migrants compared to non-migrants with a pooled OR of 1.76 (95% CI 1.01-3.03) **(Figure 2)**. One study from France evaluating TB mortality among migrants compared to non-migrants showed a higher mortality in the native population compared to migrants (HR 8.0, 95% CI 3.0–21.5) [47].

Included studies did not report on subcategories of migrants and therefore the analysis could not be stratified by migrant status. We could not identify any studies comparing use of migrant-sensitive strategies vs no strategies with regards to treatment adherence and completion.

Multidrug/rifampicin resistant tuberculosis and migration

We found 25 studies, reporting on MDR/RR-TB prevalence in migrants in the EU/EAA & UK [23, 24, 48-70]. Six of the included studies were from Italy [23, 24, 51, 53, 54, 66], three from the Netherlands [60, 65, 67] and France [49, 50, 55], two from Spain [56, 69], from Portugal [52, 64] and Greece [61, 63], one from Belgium [70], Czech Republic [48], Germany [58], Finland [71], Norway [62], Sweden [57] and Switzerland [59]. The rates of MDR/RR-TB varied according to geographical area and study period **(Supplement table S6 and S7)**. For example, studies from Spain and Portugal showed lower rates of MDR/RR-TB among migrants compared to studies from the Netherlands. Seven of the 25 studies [23, 51, 53, 55, 58, 62, 65] compared rates of MDR/RR-TB and drug-susceptible disease in migrants vs non-migrants, showing that MDR/RR-TB was more common in migrants compared to non-migrants with a pooled OR of 3.16 (95% CI 1.69-5.92) **(Figure 3)**.

In a Portuguese study, treatment outcomes in MDR/RR-TB were more likely to be unfavourable in migrants vs non-migrants (OR 1.78, 95% CI 1.04 –3.05) [52]. Similarly, a UK study showed better treatment outcomes in non-migrants vs migrants with an adjusted OR of 0.45 (95% CI 0.10-1.92) [72]. A study from Italy suggested that migrants with MDR/RR-TB were more likely to default from treatment compared to non-migrants, 12/39 (30.7%) vs 9/88 (10.2%) respectively [51]. A Czech study among patients with MDR/RR-TB showed that 15/17 (88.2%) of migrants compared to 21/33 (63.6%) of non-migrants achieved cure as a treatment outcome [48]. Another study from Portugal did not show a significant difference in mortality in migrants with MDR/RR-TB compared to non-migrants [64].

TB/HIV co-infection and migration

Twenty studies reported on TB/HIV co-infection prevalence and treatment outcomes in migrants compared to non-migrants. Seventeen studies [23, 24, 31, 73-86] were included in the meta-analysis on TB/HIV co-infection prevalence and three studies [81, 85, 87] reported on treatment outcomes of TB/HIV co-infection, one of them not being included in the meta-analysis [87]. Out of the 17 studies, ten [23, 24, 31, 73, 74, 77-79, 83, 84] reported on TB/HIV co-infections rates in populations with TB, and the remaining seven studies [75, 76, 80-82, 85, 86] in people living with HIV (PLHIV).

Among the ten studies conducted in TB populations, four were from Italy [23, 24, 74, 78], three from Spain [73, 77, 79], two from France [83, 84] and one from Portugal [31]. Studies showed significant heterogeneity and TB/HIV co-infection prevalence in migrants vs non-migrants varied according to country where the study was conducted. However, the overall risk of TB/HIV co-infection was lower in migrants than non-migrants with a pooled OR of 0.89 (95% CI 0.52-1.55) **(Figure 4A)**. Subgroup analysis excluding the three studies from Spain [73, 77, 79] showed higher rates of co-infection in migrants vs non-migrants with a pooled OR of 1.45 (1.18-1.77). The three Spanish studies showed lower rates of co-infection in migrants compared to non-migrants with a pooled OR of 0.29 (95% CI 0.24-0.36). Two of these studies [73, 79] reported significant higher rates of intravenous drug abuse among non-migrants compared to migrants (17% vs 1% and 27.9% vs 5.3% respectively).

Three studies which could not be included in the meta-analysis showed higher rates of TB/HIV co-infection in migrants than non-migrants. In a large cohort study from France (n=14,610), migrants had a higher rate of co-infection, compared with non-migrants, 11.0% vs 6.5 % (p=0.001) [84]. Over 10% of TB patients in a UK study were reported to have TB/HIV co-infection [88]. Patients with co-infection were more likely to be migrants compared to patients who were not co-infected or who were not tested for HIV (OR 2.6, 95% CI 2.6 to 4.4, p<0.0001 on univariate analysis). Analysis of risk factors from another UK study showed that the likelihood of TB/HIV coinfection was almost eight times higher among migrants compared to non-migrants (OR 7.9, 95% CI 4.5–14.4, p < 0.00001) [89].

The seven studies [75, 76, 80-82, 85, 86] that estimated TB rates in PLHIV also showed significant heterogeneity but overall odds of having co-infection were higher in migrants compared to non-migrants with a pooled OR of 3.67 (95%CI 1.81-7.43). Out of the seven studies, two studies were from Spain [80, 81], from Germany [75, 86] and one from Denmark [85], France [76], and Italy [82]. Rates of TB/HIV co-infection in migrants vs non-migrants varied across countries. An Italian study showed that the proportion of migrants among co-infected cases increased from 10.8% in 1993 to 64.6% in 2010 (chi-squared test for trend: p < 0.001) [82].

Subgroup analysis excluding the two Spanish studies [80, 81] showed a higher OR of TB/HIV co-infection in migrants vs non-migrants [OR 5.99 (4.21 -8.52)] **(Figure 4B).** Similar to the TB population cohort, one study from Spain showed a higher prevalence of TB among PLHIV in non-migrants compared to migrants, however intravenous drug abuse in this study was

significantly more prevalent in non-migrants compared to migrants (83.5% vs 26%, p>0.001). Nevertheless, differences in the number of active TB episodes per patient, the type of TB, CD4+ T-lymphocyte count, and viral load were not significantly different between migrants and non-migrants [81]. The other study from Spain did not report on drug abuse and showed higher rates of AIDS and TB among migrants vs non-migrants, 37.1 % and 30.8 % respectively (P = 0.02) [80].

TB treatment outcomes in TB/HIV co-infection were assessed in three studies reporting on TB in HIV populations [81, 85, 87]. Non-migrants vs migrants had an increased risk of death in a Danish study with an adjusted mortality risk of 2.3 (95% CI 1.3-4.3) [85]. Similarly, in a study from Spain better survival was associated with being a migrant (median 8.7 vs 5.4 years, P< 0.001); the overall mortality rate was 41.7% (535/1284), 17.2% for migrants (17/99) and 45.2% for non-migrants (518/1145) (P<0.001) [81]. In contrast, a study from Italy (84/ 246 were migrants) showed that migrant status was associated with a threefold increase in the risk of unfavourable treatment outcomes (OR 3.4, 95% CI 1.4–8.3, P = 0.008) [87].

Quality assessment

Eighteen out of 49 studies were assessed to be at low risk of bias, 27 studies at medium risk of bias and four studies at high risk of bias **(Supplement figure S3).**

Consensus recommendations

Based on the evidence reviewed (Table 1), eight consensus questions were developed, and the recommendations of the expert groups were concluded as below:

1. Should all migrants from countries of origin with a TB prevalence of >100 per 100,000 in the country of origin as estimated by WHO be screened for active TB and latent infection with *Mycobacterium (M.) tuberculosis* when entering the EU/EEA & UK?

All migrants from countries with a TB prevalence of >100 per 100,000 in the country of origin as estimated by the WHO should be screened for active TB and latent infection with *M. tuberculosis* when entering the EU/EEA & UK. However, screening policies should additionally be informed by local data.

Agreed n = 16 (80%), disagreed n = 3 (15%), abstained n = 1 (5%)

2. If screening for active TB or latent infection with *M. tuberculosis* was not performed when a migrant with a risk for TB entered the EU/EEA &UK, how long after entering the EU/EEA & UK should screening still be performed?

All migrants at risk for active TB or latent infection with *M. tuberculosis* regardless of whether they were screened in their country of origin or when entering the EU/EAA &UK should be screened for TB or latent infection within the first 2 years after entering the EU/EEA &UK.

Agreed n = 15 (75%), disagreed n = 4 (20%), abstained n = 1 (5%)

3. What is the minimal package that should be offered to ensure treatment adherence and completion in migrants to the EU/EEA &UK?

The minimal package for TB care for migrants with TB in any country of the EU/EEA &UK should include access to an interpreter if required, information material available in different languages and healthcare staff trained in migrant- and culture-sensitive issues. Screening for blood-borne viruses, updating vaccination schedule for vaccine preventable diseases, advice on access to health and mental health services and antenatal care, should be included in a general package for migrants including access to free primary care.

Agreed n = 19 (95%), disagreed n = 0 (0%), abstained n = 1 (5%)

4. What should be the management of migrant TB patients in the EU/EEA &UK who do not have healthcare coverage in the arriving country?

Migrants with active TB in the EU/EEA &UK who do not have the benefit of a health insurance should receive TB treatment free of charge in the host country in order to reduce the risk for non-completion of treatment, loss to follow-up and *M. tuberculosis* transmission. Migrants should have access to free healthcare inclusive of diagnostics and treatments of diseases of public health concern such as but not exclusive to TB and HIV. Migrants should not be deported until treatment has been successfully completed.

Agreed n = 14 (70%), disagreed n = 3 (15%), abstained n = 3 (15%)

5. What is the minimum package that should be offered to migrants with multidrug/rifampicin-resistant TB (MDR/RR-TB) in the EU/EEA &UK?

Migrants who are diagnosed with MDR/RR-TB in the EU/EEA &UK should receive the same comprehensive care as native patients free of charge even if healthcare coverage is not universal as per their local migratory status. Transfer back to the country of origin prior to completion of treatment is generally discouraged due to the dire consequences of treatment failure on individual prognosis and further development of drug resistance. This applies in particular to patients who migrate with known MDR/RR-TB and/or prior unsuccessful courses of treatment, which may be reflected in challenging second-line drug resistance patterns. Re-culture of biological samples and reassessment of drug-resistance patterns should always be performed even if available from the country of origin. We further recommend local follow-up for relapse-free cure for 12 months in all cases. This should be rigorously supported for medical reasons towards migratory authorities in the case of migrants who are otherwise ineligible for asylum or residence.

Agreed n = 16 (80%), disagreed n = 2 (10%), abstained n = 2 (10%)

6. Should all migrants with HIV entering the EU/EAA &UK be given preventive therapy for latent TB infection (LTBI) regardless of LTBI status?

All migrants with HIV, in whom active TB was ruled out, should have preventive therapy with a short regimen (Daily Rifapentine and Isoniazid if available) regardless of anti-retroviral treatment status and Interferon-gamma (IGRA)/ Tuberculin skin test (TST) result, as the risk of a false negative IGRA/TST outweighs risk of adverse effects from TB preventive treatment.

Agreed n = 15 (75%), disagreed n = 2 (10%), abstained n = 3 (15%)

7. Should screening for extrapulmonary TB be considered in migrants?

Prevalence of extrapulmonary TB and frequency of organ manifestations appear to vary between migrants from different regions of origin. There is insufficient evidence to warrant systematic screening. Clinicians should maintain a high index of suspicion regarding extrapulmonary manifestations, especially in migrants from South-East Asia and Sub-Saharan Africa.

Agreed n = 20 (100%), disagreed n = 0 (0%), abstained n = 0 (0%)

8. What measures should be undertaken to minimize diagnostic delay in migrants with active TB?

Access to primary care should be made available to migrants in a clear and understandable way, so that they can be reviewed, receive vaccines and boosters, health screening and access to care if required. Diagnostic delay can only be minimized by multimodal approaches. Active case finding and screening, educational campaigns to reduce stigma, low barriers to care and provider training are key elements of a minimization strategy. Costs for care for TB and HIV should be waivered.

Agreed n = 19 (95%), disagreed n = 0 (0%), abstained n = 1 (5%)

Discussion

Our systematic review highlights that migrants generally access care later and have worse TB outcomes than non-migrants. Overall, migrants were more likely to be diagnosed with EPTB than pulmonary TB compared to non-migrants, but evidence was insufficient to conclude on the risk of EPTB in migrant subgroups. Phylogenetic subgroups of *M. tuberculosis* are known to be associated with different clinical manifestations. For example, Indo-Oceanic and East-African Indian lineages have been previously associated with EPTB which may explain the higher percentage of EPTB in migrants vs non-migrants [90]. Diagnostic delays described in our review, occurred at different timepoints and were related to patient related factors (access to healthcare) and health system related factors (barriers to care, stigma, delay in diagnosis and treatment) [15]. Patient delay was higher in migrants than non-migrants, whereas health system delay was shorter in migrants compared with non-migrants however studies were limited. In addition, the studies reporting on patient and health system delay included insufficient data and a meta-analysis could not be performed.

Unfavourable TB treatment outcomes were more frequent in migrants compared to non-migrants but TB outcomes could not be stratified by migrant status. However, there was significant heterogeneity among studies and treatment outcome definitions varied. Some studies only reported on treatment default as an unfavourable treatment outcome in migrants vs non-migrants and did not include other unfavourable treatment outcomes by migrant status such as death, failure, loss to follow-up and unevaluated, as recommended by WHO guidelines [91].

There were no studies evaluating migrant-sensitive strategies although they have been shown to be essential for adherence and successful treatment outcomes (cure and treatment completion) in migrants [92]. Knowledge, attitudes, perceptions, and social vulnerability of migrant patients may impact treatment outcomes [93]. Expectations of treatment can be impacted by understanding of healthcare interactions within the community and country of origin. For example, some migrant groups may use traditional medicines from their country of origin as an adjuvant of, or instead of standard treatment [94, 95]. Migrant patients may also lack trust in the healthcare system or professionals due to previous negative experiences, impacting engagement with treatment [96-98]. Lack of financial resources, including inability to afford transportation, can negatively impact engagement with TB services and treatment [99]. Housing issues may adversely impact health amongst migrants. Social vulnerabilities can also compound distrust in healthcare services,[97, 100] and influence treatment adherence. Stigma can be a barrier to TB diagnosis and treatment uptake[98], with the duality of being both migrant, and having TB exacerbating this situation [94, 99]. Clinical teams, through outreach and key-workers, may develop links to local support and welfare systems and establish funds for patient transport, housing and community support [101]. Health system related factors include the knowledge, attitude and skills of healthcare providers, and the patient provider relationship [99]. Healthcare providers may not understand the issues that migrants are facing and often have not received training in culturally sensitive strategies [102, 103]. Approaching patient-provider relationships in a positive and culturally sensitive way is key to facilitating treatment engagement and improving outcomes [96, 104].

Our review highlighted that MDR/RR-TB is more common in migrants than non-migrants, treatment outcomes are overall worse and treatment default is higher in migrants, but we did not identify any observational or interventional studies reporting on migrant-sensitive clinical care strategies in migrants affected by MDR/RR-TB. We did not perform a meta-analysis on all 25 studies reporting on MDR/ RR TB but only included seven, as the other 18 studies did not have data on drug susceptible TB.

A previous systematic review found that countries in Europe with a low incidence of TB are declaring increasing numbers of migrants from high incidence countries, which are overrepresented among MDR/RR-TB cases [105]. Data derived from the ECDC (TESSy) for the year 2015 showed that the notification rate of MDR/RR-TB was 0.01 per 100,000 in the native population and was 64 times higher (i.e. 0.89 per 100,000) in individuals who have a nationality or place of birth different from the reporting country [106].

Our review showed unfavourable MDR/RR-TB treatment outcomes were more common in migrants. A previous systematic review in migrants with MDR/RR-TB assessing treatment adherence and using treatment outcome as a substitute for adherence concluded that treatment outcomes of MDR/RR-TB in migrants in Europe are not well recorded [107]. Management of MDR/RR-TB, compared to drug-susceptible TB, is challenging due to the longer duration of therapy required to achieve cure, even though this may change with the advent of short all-oral regimens, and overall higher rates of adverse events of treatment. This is particularly relevant for migrant populations where adherence is challenged by high mobility (including across national borders), additional social and behavioural risk factors and

uncertain access to healthcare [105]. A 'minimum package' has been proposed to ensure that cross-border TB care is provided, including continuity of care and contact investigation, a legal framework to protect migrants' rights and efficient data transfer across health facilities in different countries [108]. The implementation of these measures is recommended by the ECDC/European Respiratory Society (ERS) /European Union Standards of TB care [109]. Trans-national collaboration and the use of advanced tools for molecular epidemiology such as next generation sequencing have been shown to allow prompt investigation of multi-country MDR/RR-TB clusters related to migration [110]. In addition, a few studies performed in referral centres in high-resource and low-incidence countries in Europe have demonstrated that high rates of favourable treatment outcomes and satisfactory treatment adherence are possible to obtain in migrants through personalised MDR/RR-TB treatment, social support and culturally informed health care [67, 111-113].

Our review showed that TB/HIV co-infection rates and TB outcomes in migrants vs non-migrants varied according to country and although there was a trend for higher TB rates in migrants, there was no significant risk of worse TB treatment outcomes in migrants with TB/HIV co-infection compared to non-migrants but studies were limited. A previous systematic review also highlighted the heterogeneity of treatment outcomes in patients with TB/HIV co-infection in migrants vs non-migrants [114].

We used the Delphi process for our consensus statement as the Delphi method gives controlled feedback, it is anonymous, and a group of experts achieve consensus in a way that fits the research question with a high level of accuracy. There is a risk of expert

members dropping out when using a Delphi process but in our consensus approach this did not happen.

The strength of this review is that it represents the most updated collection of data on TB in adult migrants in the EU/ EAA & UK **(Table 1)**. The heterogeneity noted in our meta-analysis is typical of systematic reviews and highlights the opportunity to standardize future research examining the utility of strategies aiming to address TB in migrants.

Conclusion

Our systematic review highlights significant disparities in TB outcomes between migrants and non-migrants. Migrants typically seek care later, present with more extrapulmonary forms of TB, and experience worse outcomes compared to non-migrants. Rates of MDR/RR-TB and of TB/HIV co-infection in migrants were higher compared to non-migrants although this varied across countries. Consensus recommendations include screening of migrants for TB/LTBI according to country data, a minimal package for TB care in drug susceptible and MDR/ RR-TB, implementation of migrant-sensitive strategies, and LTBI preventive treatment for migrants with HIV co-infection. It is essential to develop and implement migrant-sensitive care strategies, enhance healthcare provider cultural competence, and establish robust support systems in order to improve TB outcomes in migrant populations.

Table 1: Tuberculosis outcomes of migrants vs non migrants

TB outcomes	Number of studies	Migrants number with events Number in group	Non-migrants number with events Number in group	Odds ratio (95% CI)	I^2 (%)
Diagnosis					
Extrapulmonary TB	11	156, 490 349, 000	210,129 965,589	2.14 (1.53-3.02)	99.1
Treatment					
Unfavourable treatment outcome	14	11,131 60,802	44,105 221,002	1.76 (1.01-3.05)	99.1
Drug resistance					
Multidrug/ Rifampicin resistant TB	7	1,693 31,809	457 18,542	3.16 (1.69-5.92)	95.0
TB/HIV-co-infection					
TB/HIV co-infection in TB populations	10	1720 17,599	3,577 24,328	0.89 (0.52-1.55)	97.6
TB/HIV co-infection in HIV populations	7	3,164 25,119	6,450 125,553	3.67 (1.81-7.43)	99.3

I^2 values > 50% show significant heterogeneity among the studies

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Figure 1: Diagnosis of active tuberculosis (TB) -Extrapulmonary vs pulmonary TB in migrants vs non-migrants

Figure 2: Unfavourable tuberculosis treatment outcomes in migrants vs non-migrants

Figure 3: Multidrug/rifampicin-resistant tuberculosis rates in migrants

Figure 4: Tuberculosis/HIV co-infection in TB populations (A) and in people living with HIV (B)

Supplement appendix

Search strategy

Table S1 Classification of migrants

Figure S1 Prisma flow diagram

Figure S2 Sensitivity analysis: Diagnosis of active tuberculosis (extrapulmonary vs pulmonary tuberculosis) studies

Figure S3 Quality assessment using the Newcastle-Ottawa Scale for risk of bias of studies included in the systematic review

Table S2 PICOs for each expert chapter group

Table S3 Diagnosis of active tuberculosis (extrapulmonary vs pulmonary tuberculosis) studies

Table S4 Patient and health system delay studies

Table S5 Tuberculosis treatment studies

Table S6 Multidrug/rifampicin-resistant tuberculosis studies

Table S7 Multidrug/rifampicin-resistant vs drug-susceptible tuberculosis studies

Table S8 Tuberculosis /HIV co-infection in tuberculosis populations studies

Table S9 Tuberculosis / HIV coinfection in patients living with HIV studies

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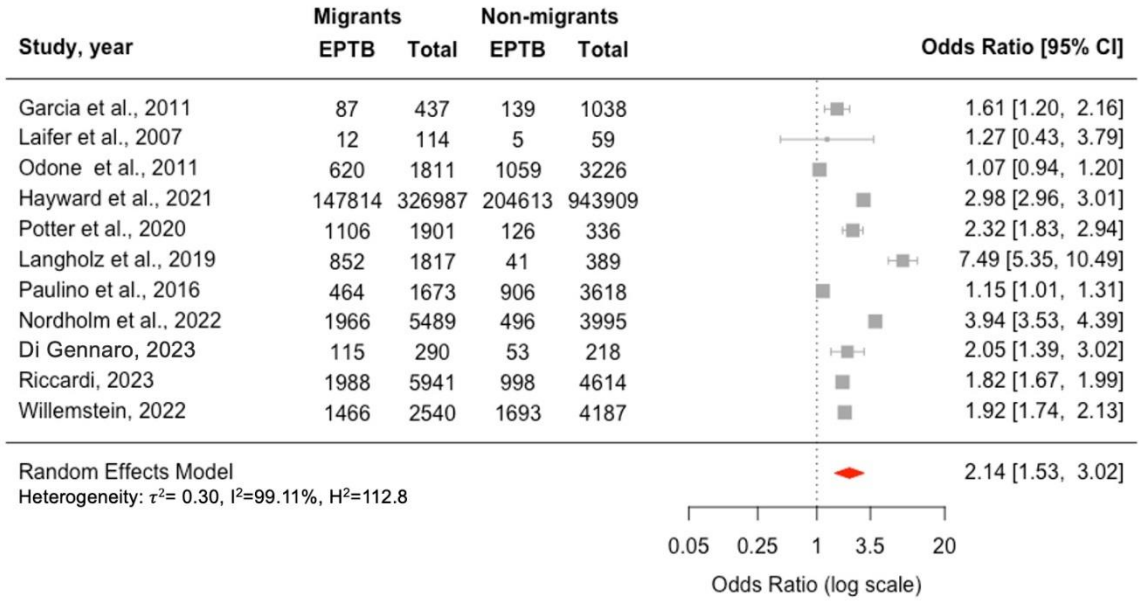
Figure 1: Diagnosis of active tuberculosis (TB) -Extrapulmonary vs pulmonary TB in migrants vs non-migrants



EPTB: Extrapulmonary Tuberculosis

Figure 2: Unfavourable tuberculosis treatment outcome in migrants vs non-migrants

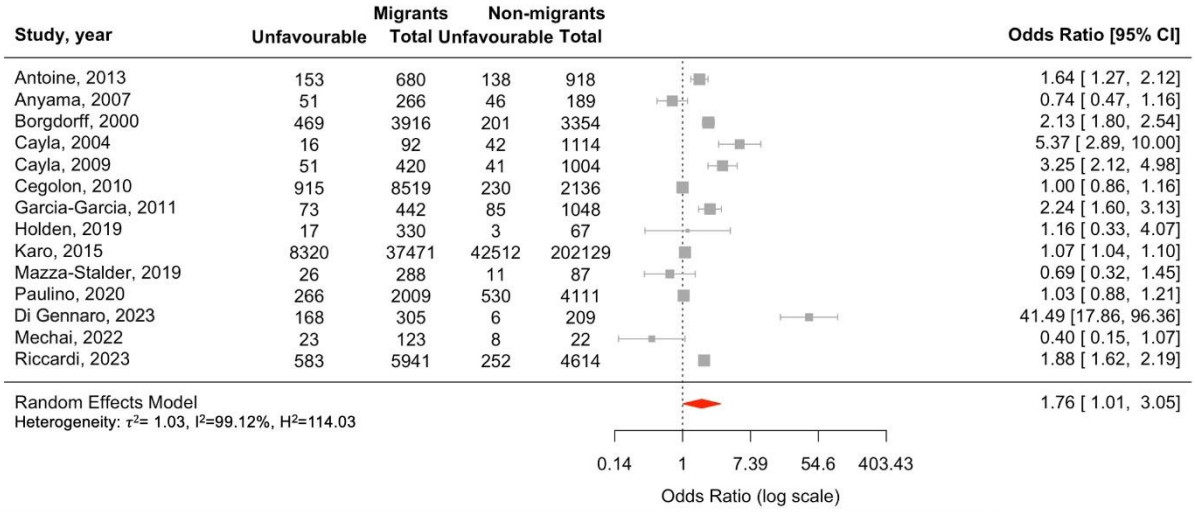
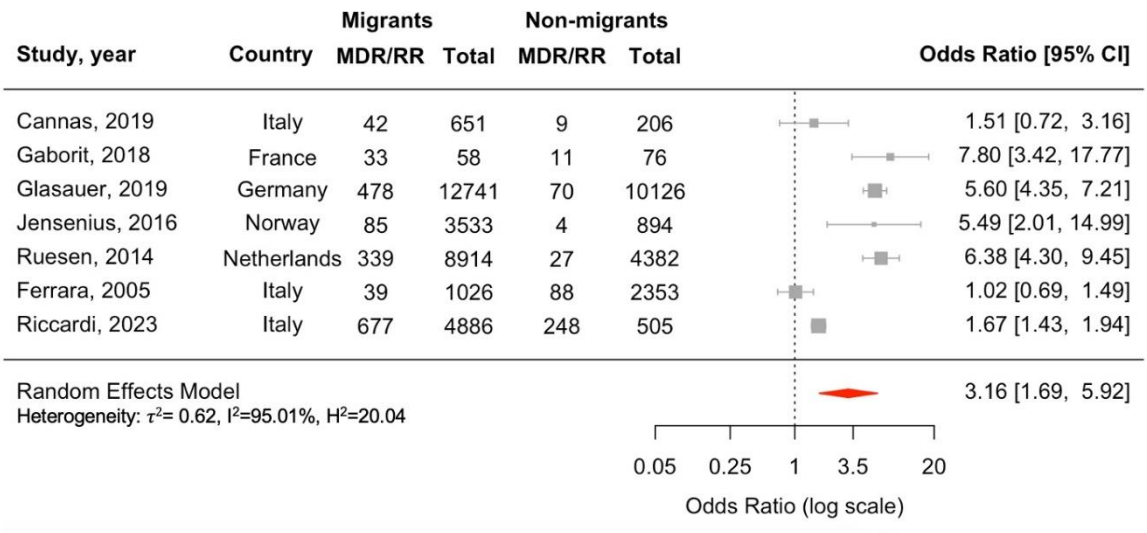
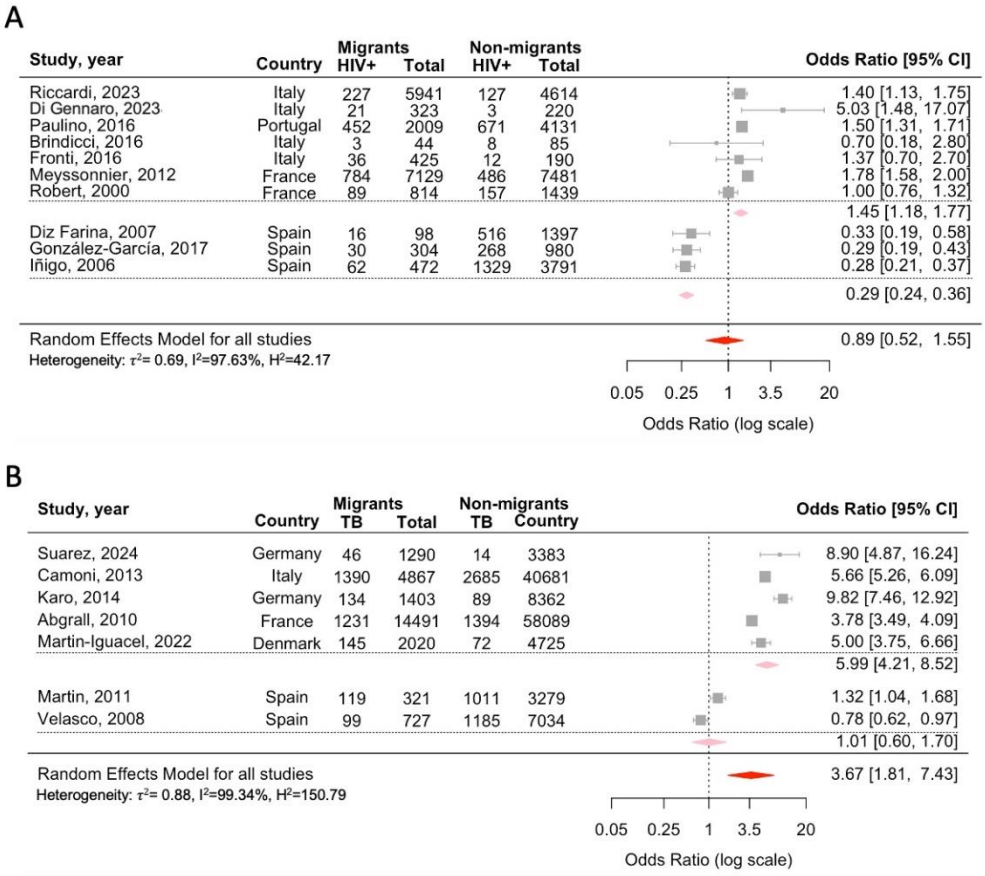


Figure 3: Multidrug/rifampicin-resistant tuberculosis rates in migrants



MDR-TB/RR-TB: Multidrug resistant/ Rifampicin resistant tuberculosis

Figure 4: Tuberculosis/HIV co-infection in tuberculosis populations (A) and in people living with HIV (B)



Supplementary material

Tuberculosis in adult migrants in Europe: a TBnet consensus statement

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1. Search strategy
2. Table S1 Classification of migrants
3. Figure S1 Prisma flow diagram
4. Figure S2 Sensitivity analysis: Diagnosis of active tuberculosis (extrapulmonary vs pulmonary tuberculosis) studies
5. Figure S3 Newcastle Ottawa scale
6. Table S2 PICOs for each expert chapter group
7. Table S3 Diagnosis of active tuberculosis (extrapulmonary vs pulmonary tuberculosis) studies
8. Table S4 Patient and health system delay studies
9. Table S5 Tuberculosis treatment studies
10. Table S6 Multidrug/rifampicin-resistant tuberculosis studies
11. Table S7 Multidrug/rifampicin-resistant vs drug-susceptible tuberculosis studies
12. Table S8 Tuberculosis /HIV co-infection in tuberculosis populations studies
13. Table S9 Tuberculosis / HIV coinfection in patients living with HIV studies
14. References

Search Strategy

The search strategy included: a specific term for respiratory infections (Infec-SP) a term for refugees, asylees and migrants (Population). Terms were combined using the following schedule:

[(Infec-SP) AND* (Population)

We did not use any search terms specifying included countries or interventions to keep the search strategy as broad as possible.

Web of Science

(tuberculo*) OR (TB) OR (LTBI) OR (latent* NEAR/2 tubercul*) OR (silicotubercul*)

AND

((Refuge*) OR (migrant*) OR (asylum*) OR (immigrant*) OR

(displaced NEAR/2 person*))

OVID

(((tuberculo*.mp.) OR (TB.mp.) OR (LTBI.mp.) OR (latent*.mp. ADJ2 tubercul*.mp.) OR

(silicotubercul*.mp.))

(AND

(((Refuge*.mp.) OR (migrant*.mp.) OR (asylum*.mp.) OR (immigrant*.mp.) OR (displaced.mp. ADJ2 person*.mp.))OR("Refugees"/))

CINAHL

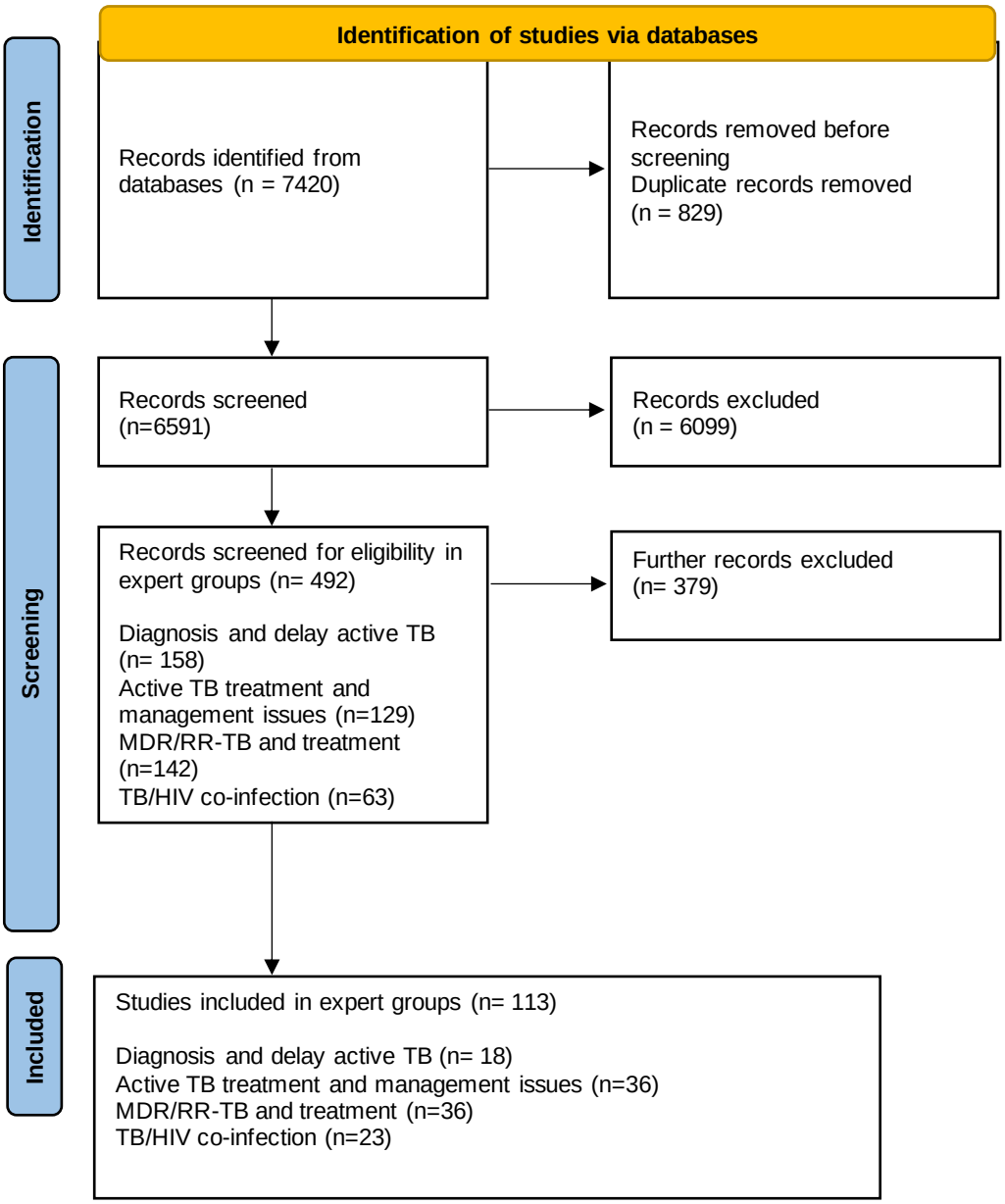
(((tuberculo*) OR (TB) OR (LTBI) OR (latent* N2 tubercul*) OR (silicotubercul*) AND ((Refuge*) OR (migrant*) OR (asylum*) OR (immigrant*) OR (displaced N2 person*))

Supplement Table S1 Classification of migrants

Migrant status	Definition
Asylum seeker	An individual who is seeking international protection. In countries with individualized procedures, an asylum seeker is someone whose claim has not yet been finally decided on by the country in which he or she has submitted it. Not every asylum seeker will ultimately be recognized as a refugee, but every recognized refugee is initially an asylum seeker.
Documented migrant	A migrant authorized to enter and to stay pursuant to the law of that State or to international agreements to which that State is a party and who is in possession of documents necessary to prove his or her regular status in the country.
Internal migrant	Any person who is moving or has moved within a State for the purpose of establishing a new temporary or permanent residence or because of displacement.
International migrant	Any person who is outside a State of which he or she is a citizen or national, or, in the case of a stateless person, his or her State of birth or habitual residence. The term includes migrants who intend to move permanently or temporarily, and those who move in a regular or documented manner as well as migrants in irregular situations.
Migrant worker	A person who is to be engaged, is engaged or has been engaged in a remunerated activity in a State of which he or she is not a national.
Migrant	An umbrella term, not defined under international law, reflecting the common lay understanding of a person who moves away from his or her place of usual residence, whether within a country or across an international border, temporarily or permanently, and for a variety of reasons. The term includes a number of well-defined legal categories of people, such as migrant workers; persons whose particular types of movements are legally defined, such as smuggled migrants; as well as those whose status or means of movement are not specifically defined under international law, such as international students.
Refugee	A person who, owing to a well-founded fear of persecution for reasons of race, religion, nationality, membership of a particular social group or political opinion, is outside the country of his nationality and is unable or, owing to such fear, is unwilling to avail himself of the protection of that country; or who, not having a nationality and being outside the country of his former habitual residence as a result of such events, is unable or, owing to such fear, is unwilling to return to it .
Undocumented migrant	A non-national who enters or stays in a country without the appropriate documentation.

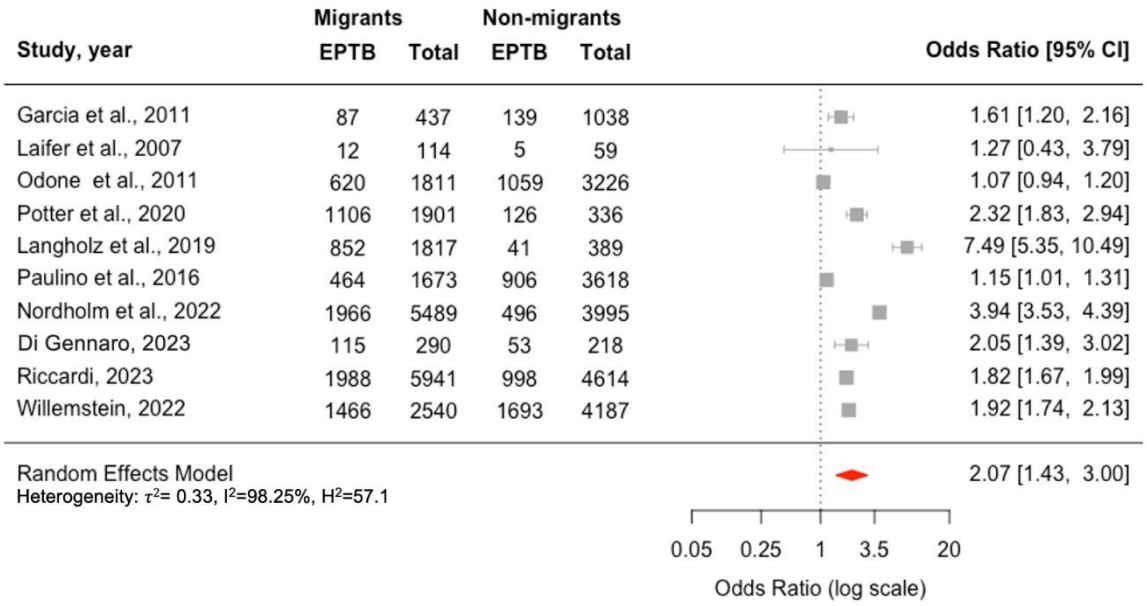
Source: International Organisation of Migration Glossary on migration https://publications.iom.int/system/files/pdf/iml_34_glossary.pdf

Supplement figure S1 Prisma flow diagram

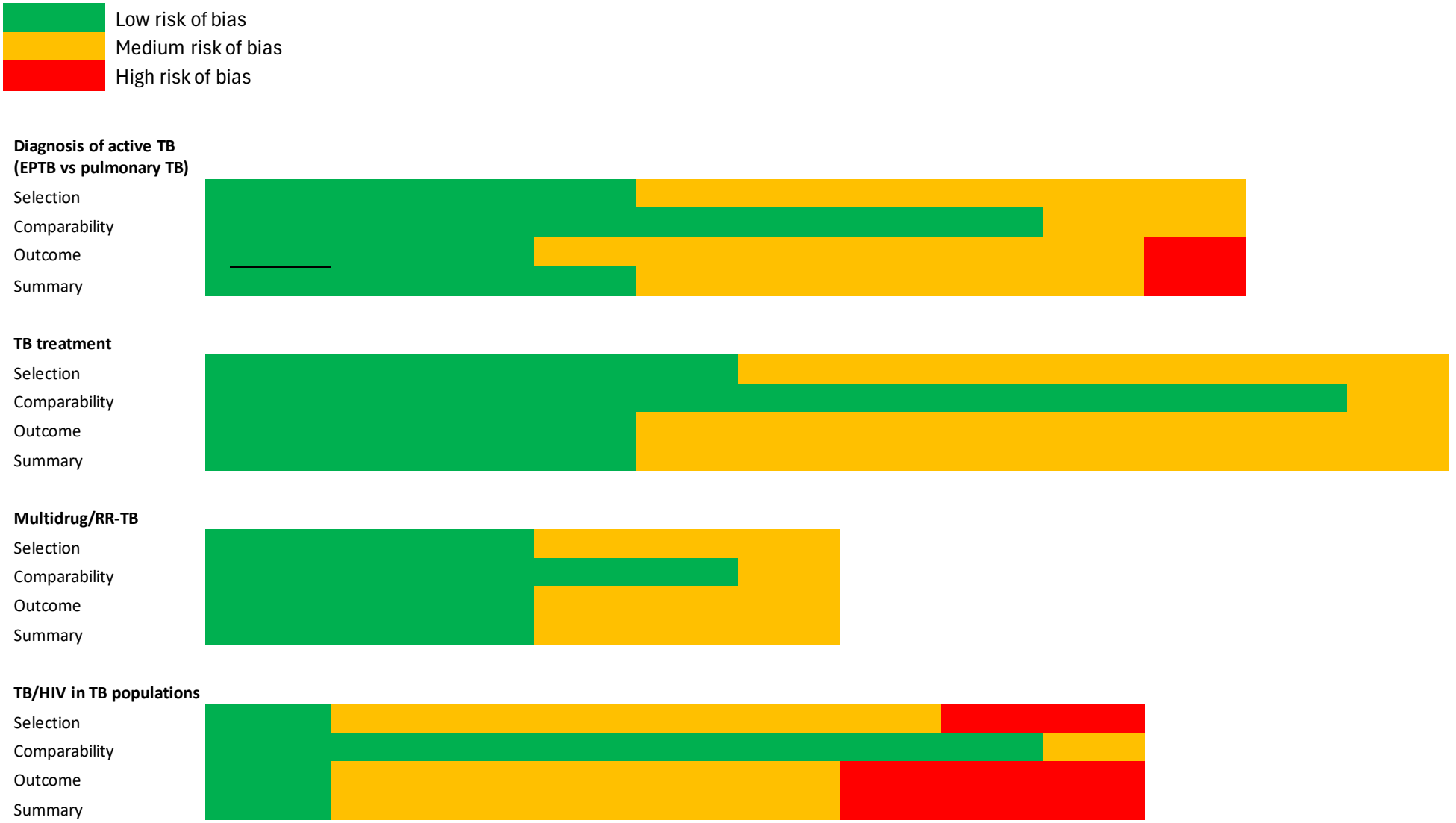


MDR/ RR TB=Multidrug-resistant/ Rifampicin resistant tuberculosis

Supplement figure S2 Sensitivity analysis: Diagnosis of active tuberculosis (extrapulmonary vs pulmonary tuberculosis) studies



Supplement Figure S3 Quality assessment using the Newcastle-Ottawa Scale for risk of bias of studies included in the systematic review



MDR/ RR TB=Multidrug-resistant/ Rifampicin resistant tuberculosis

EPTB = Extrapulmonary tuberculosis

Supplement table S2 PICOs for each expert chapter group

Chapter group	Content	Population	Intervention/ Exposure	Control	Outcome	Studies
Diagnosis of active TB in migrants including the spectrum of clinical presentation **Delay in diagnosis**	Evaluation of migrants vs non-migrants in the diagnosis of active TB including the spectrum of clinical presentation and the delay in diagnosis	Migrants diagnosed with TB in clinical centers in the EU/EAA &UK	Diagnosis of active TB Delay in diagnosis	Non-migrants diagnosed with TB in clinical centers in the EU/EAA &UK	Clinical presentation pulmonary vs extrapulmonary TB Diagnostic delay including patient delay and health system delay	Observational cohort studies
Treatment of TB in migrants including management issues	Evaluation of the treatment of active TB in migrants vs non-migrants Evaluation of management issues	Migrants treated for TB in clinical centers in the EU/EAA &UK	Treatment for drug-susceptible TB Use of migrant-sensitive strategies	Non -migrants treated for TB in clinical centers in the EU/ EAA &UK No use of migrant-sensitive strategies	TB treatment outcome	Observational cohort studies including non-controlled cohort studies Interventional studies.
Treatment of MDR/RR-TB and management issues	Evaluation of the diagnosis and management of MDR/RR TB in migrants vs non-migrants	Migrants treated for MDR/ RR TB in clinical centers in the EU/EAA &UK	Diagnosis of MDR/RR TB Treatment for MDR/RR TB	Non -migrants treated for MDR/ RR TB in clinical centers in the EU/ EAA &UK	Prevalence of MDR/RR TB MDR/RR TB treatment outcomes	Observational cohort studies including non-controlled cohort studies Interventional studies.

			Use of migrant sensitive strategies	No use of migrant sensitive strategies		
Special consideration for TB and HIV co-infection in migrants	Evaluation of the diagnosis and management of TB/HIV coinfection in migrants vs non-migrants in the EU/EAA& UK	Migrants with TB/ HIV co-infection treated in clinical centers in the EU/EAA &UK	Diagnosis of HIV/TB co-infection Treatment for TB	Non -Migrants with TB/ HIV co-infection treated in clinical centers in the EU/EAA&UK	Prevalence of TB/ HIV co-infection TB treatment outcome	Observational cohort studies including non-controlled cohort studies Interventional studies.

Supplement table S3 Diagnosis of active tuberculosis (TB)-Extrapulmonary vs pulmonary TB studies

Author Year Country	**Study design Study period Populations excluded**	**Migrants and non-migrants total**	**Migrants total**	**Non-migrants total**	**PTB in migrants**	**PTB in non-migrants**	**EPTB in migrants**	**EPTB in non-migrants**	**OR [95% CI]**
Paulino [1] 2016 Portugal	Retrospective National TB Surveillance study 2008-2012 Disseminated TB excluded	5291	1673	3618	1209	2712	464	906	1.15 [1.01, 1.31]

Nordholm [2] 2022 Denmark	Nationwide retrospective register-based case control study 1990-2018 .	9484	5489	3995	3523	3499	1966	496	3.94 [3.53, 4.391]
Garcia-Garcia [3] 2011 Spain	Prospective Multicentre cohort-study 2006-2007 Study period 2006-2007 Patients were included in extrapulmonary group if mixed features; unknown site was excluded	1475	437	1038	350	899	87	139	1.61 [1.20, 2.16]
Hayward [4] 2021 Multiple countries	Retrospective multi country Tessy database study 1995-2017	1270896	326987	943909	179173	739296	147814	204613	2.98 [2.96, 3.01]

Laifer [5] 2007 Switzerland	Retrospective hospital-based study 1997-2004 Denominator derived by percentage	173	114	59	102	54	12	5	1.27 [0.43, 3.79]
Odone [6] 2011 Italy	Retrospective regional TB surveillance system 1996-2006 Disseminated TB excluded	5037	1811	3226	1191	2167	620	1059	1.07 [0.94, 1.20]
Potter [7] 2020 UK	Retrospective national database study 2011-2016	2237	1901	336	795	210	1106	126	2.32 [1.83, 2.94]
Langholz [8] 2019 Denmark	Register-based prospective cohort study 1993-2015	2206	1817	389	965	348	852	41	7.49 [5.35, 10.49]
Di Gennaro [9] Italy 2023	Retrospective cohort study 2013- 2021	508	290	218	175	165	115	53	2.05 [1.39-3.02]

	Miliary TB excluded								
Riccardi [10] Italy 2023	Retrospective cohort study 1990-2019 Pulmonary TB data obtained from author	10555	5941	4614	3953	3616	1988	998	1.82 [1.67-1.99]
Willemstein [11] The Netherlands 2022	Retrospective cohort study 2003 and 2018 Pulmonary and extrapulmonary group excluded	6727	2540	4187	1122	2494	1466	1693	1.92 [1.74-2.13]

Supplement table S4. Patient and health system delay studies

Author Year Country	Population Study period	Study design	Total patients	Patient delay migrants Median days (IQR) Number of patients	Patient delay non-migrants Median days (IQR) Number of patients	Health system delay migrants Median days (IQR) Number of patients	Health system delay non-migrants Median days (IQR) Number of patients
Holden [12] 2019 Denmark	EPTB only 2009-2014	Retrospective national database study	N-450	60 (26-120) N=336	30 (9-120) N=61	28 (12-63) N=358	38.5 (14-82) N=70
Quattrocchi [13] 2018 Italy	EPTB and PTB 2014-2016	Prospective cross-sectional study	Patient delay 231 (IQR NA) Health system delay 225 (IQR NA)	30 (14-60) N=NA	15 (7-60) N=NA	8 (4-22) N=NA	21 (7.25-61) N=NA
Zao [14] 2019 Portugal	EPTB and PTB 2010-2014 (Migrants 1162/ Non-migrants 5660)	National surveillance database study	NA	49 (NA)	32 (NA)	13 (NA)	18 9 (NA)

NA: not available

Supplement table S5 Tuberculosis treatment outcome studies

Author Year Country	Study design Study period Population	Definition of favourable treatment outcome	Definition of unfavourable treatment outcome	Total number of migrants	Total number of Non-migrants	Migrants favourable outcome	Migrants unfavourable Outcome	Non-migrants favourable outcome	Non-migrants Unfavourable Outcome	OR [95% CI]
Antoine [15] 2013 France	Retrospective National database 2009	Treatment completed	Potentially unfavourable outcome	680	918	527	153	780	138	1.64 [1.27, 2.12]
Anyama [16] 2007 UK	Prospective National Database Study 2001-2002	Successful treatment completion within 12 months	Treatment not completed or outcome unknown	266	189	215	51	143	46	0.74 [0.47, 1.16]
Borgdorff [17] 2000 Netherlands	Retrospective National Database Study 1993-1997	Cure and treat-ment comple-tion (Inclusive Definition used)	Treatment default	3916	3354	3447	469	3153	201	2.13 [1.80, 2.54]
Cayla[18] 2004 Spain	Prospective Multicentre Cohort study 1999-2000	Cure and treatment completion	Treatment default	92	1114	76	16	1072	42	5.37 [2.89, 10.00]
Cayla [19] 2009 Spain Percentage	Prospective Multicentre Cohort Study 2006-2007	No treatment default, derived from percentage	Treatment default, there was no data on death, loss to follow up and	420	1004	369	51	963	41	3.25 [2.12, 4.98]

	Population derived from percentage		unevaluated by migrant status							
Cegolon [20] UK 2010	Retrospective London TB register-study 2003-2006	Cure and treatment completion	Treatment failure	8519	2136	7604	915	1906	230	1.00 [0.86, 1.16]
Garcia-Garcia [3] Spain 2011	Prospective Multicentre cohort-study 2006-2007	No treatment default	Unfavourable outcome = treatment default and unknown outcome	442	1048	369	73	963	85	2.24 [11.60, 3.13]
Holden [12] 2019 Denmark	Retrospective National Database Study 2009-2014 Extrapulmonary TB only	Treatment success and treatment completion	Unfavourable treatment outcome	330	67	313	17	64	3	1.16 [0.33, 4.07]
Karo [21] 2015 Norway/ Poland/ Romania/Slovenia/ UK	EU/ EAA Surveillance Database study 2002-2011	Treatment success	No treatment success = died, failed, default, transferred out and unknown outcome	37471	202129	29151	8320	159617	42512	1.07 [1.04, 1.10]
Mazza-Stalder[22] 2019 Switzerland	Retrospective Database study 2013-2014	Treatment success	Unsuccessful treatment outcome	288	87	262	26	76	11	0.69 [0.32, 1.45]

Paulino [1] Portugal 2016	Retrospective National TB Surveillance study 2008-2012	Treatment success	Treatment failure	2009	4111	1743	266	3581	530	1.03 [0.88, 1.21]
Di Gennaro [9] Italy 2023	Retrospective cohort study 2013- 2021	Treatment success	Unsuccessful treatment outcome= loss to follow up, death and failure	305	209	137	168	203	6	2.05 [1.39, 3.02]
Mechai [23] France 2022	Observational, prospective, multicenter cohort study 2018-2020.	Favourable treatment outcome	Unfavourable treatment outcome	123	22	100	23	14	8	0.4 [0.15, 1.07]
Riccardi [10] Italy 2023	Retrospective cohort study 1990-2019	Treatment success	Unfavourable treatment outcome = transferred out/ drop-out, died and failure	5941	4614	5358	583	4362	252	1.88 [1.62, 2.19]

Supplement table S6. Multidrug/rifampicin-resistant tuberculosis studies

Author Year Country	Study design Study period	Number of total MDR/RR-TB patients	Number of MDR/RR-TB patients in migrants	Number of MDR/RR-TB patients in non-migrants	Percent of MDR cases in migrants
Bartu [24] 2010 Czech Republic	Retrospective cohort study 2001-2009	50	33	17	66
Bhering [25] 2019 Portugal	Retrospective cohort study 2000-2014	265	93	172	35.1
Flament - Saillour [26] 1999 France	Retrospective nationwide case-control study 1994	51	32	19	62.7
Fattorini [27] 2012 Italy	Retrospective laboratory study 2008-2010	198	162	36	81.8
Gavin [28] 2012 Spain	Retrospective laboratory study 1998-2008	478	202	276	42.3
Ghebremichael [29] 2008 Sweden	Retrospective laboratory study 1995- 2004	400	347	53	86.7
Helbling [30] 2014	Retrospective cohort study	51	46	5	90.2

Switzerland	2003-2010				
Ingen [31] 2008 Netherlands	Retrospective laboratory study 1993-2007	153	135	18	88.2
Ioannidis [32] 2017 Greece	Retrospective laboratory study 2007-2011	54	38	16	70.4
Kanavaki [33] 2006 Greece	Retrospective laboratory study 1993-2002	133	48	85	36.1
Oliveria [34] 2021 Portugal	Retrospective national database study 2000-2016	435	108	327	24.8
Seminari [35] 2020 Italy	Retrospective laboratory study 1998-2017	33	21	12	63.6
Van Altena[36] 2015 Netherlands	Retrospective cohort study 2000-2009	113	108	5	95.6
Vasankari [37] 2012 Finland	Retrospective cohort study 1994-2005	19	14	5	73.7
Vazquez-Gallardo [38] 2007 Spain	Prospective cohort study 1998 and 2004	58	7	51	12.1

Vluggen [39] 2017 Belgium	Retrospective laboratory study 2010-2013	30	28	2	93.3
Di Gennaro [9] Italy 2023	Retrospective cohort study 2013- 2021 MDR TB = MDR TB and RR TB	77	71	6	96.8
Kherabi [40] France 2022	Observational retrospective study 2008 to 2018	65	59	6	90.8

Supplement table S7. Multidrug/rifampicin-resistant vs drug-susceptible tuberculosis studies

Author Year Country	**Study design Study period**	**Number of total migrants**	**Number of total non-migrants**	**Number of MDR/RR-TB patients in migrants**	**Number of MDR/RR-TB patients in non-migrants**	**Number of patients with drug-susceptible TB in migrants**	**Number of patients with drug-susceptible TB in non-migrants**	**OR [95% CI]**
Cannas [41] 2019 Italy	Prospective cohort study 2011-2016	651	206	42	9	609	197	1.51 [0.72, 3.16]
Gaborit [42] 2018 France	Retrospective cohort study 2002-2013	58	76	33	11	25	65	7.80 [3.42, 17.77]

Ferrara [43] 2005 Italy	Retrospective cohort study 1995-1999	1026	2353	39	88	987	2265	1.02 [0.69. 1.49]
Glasauer [44] 2019 Germany	Retrospective national database study 2008-2017	12741	10126	478	70	12263	10056	5.60 [4.35, 7.21]
Jensenius [45] 2016 Norway	Retrospective national database study 1995-2014	36	894	85	4	3448	890	5.49 [2.01, 14.99]
Ruesen [46] 2014 Netherlands	Retrospective national database study 1993-2011	8914	4382	339	27	8575	4355	6.38 [4.30, 9.45]
Riccardi [10] Italy 2023	Retrospective cohort study 1990-2019 MDR TB =MDR and RR TB	4886	505	677	248	4209	2570	1.67 [1.43-1.94]

Supplement table S8. Tuberculosis/ HIV co-infection in Tuberculosis populations studies

Author Year Country	Study design Study period	Total TB cases	Number of migrants	Number of non-migrants	Total TB HIV - co-infection	Total TB /HIV co-infection in migrants	Total TB /HIV co-infection in non-migrants	OR [95% CI]
Fronti [47] 2016 Italy	Observational retrospective cohort study 1998-2013	615	425	190	48	36	12	1.37 [0.70, 2.70]
Iñigo [48] 2006 Spain	Observational study 1994 - 2003	4263	472	3791	1391	62	1329	0.28 [0.21, 0.37]
Robert [49] 2000 France	Prospective study 1995-1997	2253	814	1439	246	89	157	1.00 [0.76, 1.32]
González-García [50] 2017 Spain	Observational retrospective study 1995-2013	1284	304	980	298	30	268	0.29 [0.19, 0.43]
Brindicci [51] 2016 Italy	Retrospective cohort study 2005-2013	129	44	85	11	3	8	0.70 [0.18, 2.80]
Diz Farina [52] 2007 Spain	Retrospective cohort study 1990-2002	1494	98	1397	532	16	516	0.33 [0.19, 0.58]
Paulino- [1] 2016 Portugal	Retrospective case-control study 2008-2012	6040	2009	4131	1123	452	671	1.50 [1.31, 1.71]

Meyssonnier [53] 2012 France	Retrospective cohort study 1995-2008	14610	7129	7481	1270	784	486	1.78 [1.58, 2.00]
Di Gennaro [9] Italy 2023	Retrospective cohort study 2013- 2021	543	323	220	24	21	3	5.03 [1.48, 17.1]
Riccardi [10] Italy 2023	Retrospective cohort study 1990-2019	10555	5941	4614	354	227	127	1.4 [1.13, 1.75]

Supplement table S9: TB/ HIV co-infection in people living with HIV studies

Author Year Country	Study design Study period	Total HIV cases	Number of Migrants	Number of Non-migrants	Total TB HIV - co-infection	Total TB/HIV co-infection in migrants	Total TB/HIV co-infection in non-migrants	OR [95% CI]
Abgrall [54] 2010 France	Retrospective cohort study 1997-2008	72580	14491	58089	2625	1231	1394	3.78 [3.49, 4.09]
Camoni [55] 2013 Italy	Retrospective cohort study 1993-2010	45548	4867	40681	4075	1390	2685	5.66 [5.26, 6.09]
Velasco [56] 2008 Spain	Retrospective cohort study 1987-2006	7761	727	7034	1284	99	1185	0.78 [0.62. 0.97]
Martin-Iguacel [57] 2022 Denmark	Retrospective cohort study 1995–2017	6745	2020	4725	217	145	72	5.00 [3.75, 6.66]
Karo [58] 2014 Germany	Retrospective cohort study 2001-2011	11693	1403	8362	233	134	89	9.82 [7.46, 12.92]
Martin [59] 2011 Spain	Retrospective cohort study 1994–2005	3600	321	3279	1130	119	1011	1.32 [1.04, 1.68]
Suarez [60] 2024	Retrospective cohort study	4673	1290	3383	60	46	14	8.9 {4.87,16.24]

Germany	2006 -2017							

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