UK Health Security Agency

Effectiveness of methods to identify people infected with tuberculosis or people with active tuberculosis disease in refugees or people seeking asylum

A rapid systematic review

Contents

Main messages

1. This rapid systematic review (search up to 3 July 2024) identified and summarised evidence relating to the effectiveness of methods to identify people infected with tuberculosis (TB) or people with active TB disease in refugees or people seeking asylum within countries with low and moderate TB incidence. Low and moderate incidence countries were defined as those with a TB incidence of less than 40 cases per 100,000 people. In total, 7 studies were included (1 to 7).

2. In this review, the term 'active case finding' was defined as any method to diagnose latent TB infection or active TB disease. Passive case finding was defined as detection of TB in people who self-refer with symptoms suggestive of TB. The case finding strategies identified in this review included chest X-ray (CXR), tuberculin skin test (TST), Interferon Gamma Release Assay (IGRA) and symptom-based interview-informed case finding. No studies evaluated methods to identify non-respiratory TB.

3. Two studies provided information on the diagnostic accuracy of active case finding (1, 2), 3 studies reported outcomes informing the number of additional TB cases identified and treated as a result of case finding (3 to 5), and 2 studies reported on the cost-effectiveness of active case finding (4, 6, 7).

4. Two studies provided information on the diagnostic accuracy of active case finding (1, 2). One study reported that TST had moderate sensitivity (50%) and specificity (73.9%) for detecting latent TB infection (LTBI), when compared to IGRA (reference standard). Results varied depending on Bacillus Calmette-Guérin (BCG) vaccination status (1). A second study reported that CXR had 100% sensitivity and 89.6% specificity, and symptom-based interview had 55.2% sensitivity and 96% specificity for detection of active respiratory TB, both compared to culture as the reference standard (2).

5. There was limited and conflicting evidence on the number of additional cases identified by LTBI case finding. One study reported that IGRA identified more cases of LTBI than TST followed by IGRA, but also noted that there were more people lost to follow-up between tests in the 2-stage case finding strategy (3). A second reported that TST identified more LTBI cases compared to IGRA (5), however as TST is a less specific test, this may not accurately reflect true LTBI cases.

6. Cost-effectiveness analyses showed that higher TB incidence thresholds for case finding of LTBI and active TB may be more cost-effective than no case finding threshold. One study showed that introduction of an LTBI case finding at a TB incidence threshold of 150 cases per 150,000 was the most cost-effective strategy, with 11.8 additional quality adjusted life years (QALYs) gained at an incremental cost effectiveness ratio (ICER) of €55,900 (6). Another study showed that higher thresholds for targeted active TB case

finding reduced costs per case but also detected fewer cases. A threshold of 50 per 100,000 was most cost-effective but 20.5% of cases were missed compared to indiscriminate case finding (7). Although higher incidence thresholds reduced the cost per active TB case identified this also decreased the number of cases detected and prevented, compared to no threshold for case finding. The study did not include the downstream costs of cases missed by introducing a case finding threshold.

7. Critical appraisal highlighted several potential biases in the included studies. The studies which measured diagnostic outcomes were at risk of bias due to limitations in the reference standards used for TB case identification, as TST and IGRA may not accurately identify all TB cases. There was also concern about the conduct of the studies as not all participants received both case finding strategies being assessed. The quasi-experimental and retrospective studies were potentially biased by factors that could have confounded the results but were not considered in the analysis. The cost-effectiveness studies were not conducted in the UK, and therefore may have limited generalisability to UK healthcare costs.

8. Limited evidence was found for the effectiveness of active case finding in refugees and people seeking asylum, with only a small number of studies identified. Due to differences in case finding strategies and reference tests across studies, the findings are also not directly comparable between studies and the evidence does not conclusively determine which case finding method was most effective. However, the evidence offers some insights into the accuracy and cost-effectiveness of individual TB case finding methods. These findings should be interpreted with caution, considering the limitations in the evidence.

Purpose

The purpose of this rapid systematic review was to identify and summarise evidence relating to the effectiveness of methods to identify people infected with tuberculosis (TB) or people with active TB disease in refugees or people seeking asylum within countries with a low or moderate TB incidence. In this review, the term ‘active case finding’ was defined as any method to diagnose latent TB infection or active TB disease.

The research question was:

1. What are the effective strategies of case finding for tuberculosis (TB) refugees or people seeking asylum?

Methods

A rapid systematic review was conducted, following streamlined systematic methods to accelerate the review process. A literature search was undertaken to look for relevant studies, published or available as preprint, up to 3 July 2024. The reference lists of relevant guidelines were checked to identify any additional primary studies.

Only studies in populations from countries or territories with low and moderate TB incidence (estimated incidence rate of less than 40 per 100,000 in 2022) that included people seeking asylum or refugees were included (8). The definitions of 'refugee' and 'person seeking asylum' used here are the ones used by the United Nations refugee agency (9):

- refugee – "someone who has been compelled to leave their country and cannot return because of a serious threat to their life, physical integrity or freedom as a result of persecution, armed conflict, violence or serious public disorder"
- person seeking asylum – "someone who intends to seek or is awaiting a decision on their request for international protection"

Studies of other migrants, such as economic migrants, were excluded. Case finding could be at any time after refugees and people seeking asylum enter the country. The outcomes of relevance that would be included in this rapid systematic review are available in Table A1. These included sensitivity and specificity, cost-effectiveness, additional TB cases identified by case finding, and how often individuals refused to participate in case finding.

Screening on title and abstract was undertaken in duplicate by 2 reviewers for 20% of the eligible studies, with the remainder completed by one reviewer. Screening on full text was undertaken by one reviewer and checked by a second. Data extraction was performed by one reviewer and checked by a second.

Critical appraisal was conducted in duplicate by 2 reviewers. A protocol was produced before the literature search was conducted, including the review question, the eligibility criteria, and all other methods. Full details of the methodology are provided in the protocol in Annexe A. There were 2 deviations from the protocol:

1. The National Institute for Health and Care Excellence (NICE) appraisal checklist for economic evaluations, and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool were used to assess risk of bias for economic evaluations and studies with information on accuracy of case finding strategies respectively, whilst the ROBINS-I was used for other non-randomised study designs (10).

2. The World Health Organization (WHO) estimates of TB incidence reported on GOV.UK (11) were used to determine eligibility for inclusion during screening of studies. This list

was withdrawn during the review, therefore the included studies were checked against the Global TB Programme website data to verify TB incidence (12).

The NICE appraisal checklist for cost-effectiveness studies assesses both applicability and study limitations (13). Where studies did not conduct full cost-effectiveness models, this checklist was still applied to assess risk of bias, as the most applicable available tool.

The QUADAS-2 tool assesses 4 domains that could introduce bias into the studies, comprising bias from selection of cases, bias from the conduct or interpretation of the case finding strategy being evaluated (the index test), bias from the reference case finding strategy, its conduct, or its interpretation, and bias from the patient flow (14). There is no overall risk of bias rating from the QUADAS-2 tool, so the domains that were considered high risk for each study are presented in the report.

Glossary of terms

This review includes specific terminology relating to TB, diagnostic accuracy and cost-effectiveness evaluations. These terms are defined below to help with interpretation of the review's findings.

Incremental cost-effectiveness ratio (ICER): a measure of the cost-effectiveness of a healthcare intervention by comparing the additional cost to the additional health benefit it provides, (often expressed in terms of cost per number of QALYs gained).

Quality-adjusted life year (QALY): is a measure that combines the length and quality of life into a single value, with one QALY representing one year of life in perfect health. It's used to evaluate the effectiveness of interventions by considering both how long they extend life and how much they improve its quality.

Positive likelihood ratio: how much more likely a positive test result is to occur in someone with the disease compared to someone without the disease.

Negative likelihood ratio: how much less likely a negative test result is to occur in someone with the disease compared to someone without the disease.
Reference standard: a standard test used to evaluate the accuracy of another test by comparison assumed to have perfect sensitivity and specificity.

Sensitivity: the proportion of people with the disease correctly identified.

Specificity: the proportion of people without the disease correctly identified.

TB infection: a person exposed to TB with immunological evidence of infection but who is well.

TB disease: a person infected with TB who has signs and or symptoms of disease.

Evidence

In total, 4,883 primary studies were screened at title and abstract and 153 studies were screened at full text. Of these, 7 studies met the inclusion criteria (1 to 7). A PRISMA diagram showing the flow of studies through the review is shown in Annexe B, and studies excluded at full text screening are available with the reasons why in Annexe C. Study characteristics are available in Annexe D, and risk of bias assessments are available in Annexe E.

Two studies reported diagnostic accuracy outcomes for TB case finding (1, 2), 3 studies (one quasi-experimental and 2 retrospective cohort studies) reported additional TB cases identified and treated (3 to 5), and 3 studies reported cost-effectiveness outcomes (4, 6, 7). No studies reported other outcomes specified in the protocol.

Diagnostic accuracy of TB case finding strategies

Two studies reported diagnostic accuracy outcomes for TB case finding (1, 2).

Elliot and others tested 212 refugee children (aged less than 15 years old) for latent TB infection (LTBI) with the Tuberculin Skin Test (TST) and Interferon Gamma Release Assays (IGRA) in Australia, between 2007 and 2010 (1). The results were:

- TST negative, IGRA negative: 133 (62.7%)
- TST negative, IGRA positive: 16 (7.5%)
- TST positive, IGRA negative: 47 (22.2%)
- TST positive, IGRA positive: 16 (7.5%)

Sensitivity and specificity of TST was calculated, using IGRA as the reference standard, as this was not directly reported by the study:

- overall sensitivity: 50%
- overall specificity: 73.9%

BCG vaccination can affect TST test results. Sensitivity and specificity of TST (reported by study) was reported for children with and without BCG scars (children without BCG scars were assumed not to have been vaccinated):

- sensitivity for children with BCG scar: 52%
- specificity for children with BCG scar: 73%

- sensitivity for children without BCG scar: 50%
- specificity for children without BCG scar: 88%

The lower specificity in children with a BCG scar suggests TST may detect more false positives in this group.

Critical appraisal of this study identified high potential risk of bias in the reference standard, as IGRA may not accurately identify all latent TB cases.

Schneeberger Geisler and others compared 2 case finding strategies for active TB, in Switzerland (2). Culture confirmation was used as the reference standard. The case finding strategies were:

- CXR (18,465 people screened, between 2004 and 2005)
- targeted interview-informed risk assessment (based on symptoms and incidence of TB in country of origin), followed by CXR if TB suspected (23,402 people screened between 2007 and 2008)

The study reported that culture was conducted on all individuals who underwent either CXR case finding or interviews for case finding to confirm active TB diagnosis, within 90 days of initial case finding.

In the 2004 to 2005 period, 31 cases with abnormal CXR were confirmed as having active TB, with a prevalence of 14.3 per 10,000. In the 2007 to 2008 period, 29 cases were confirmed by culture as active TB, with a prevalence of 12.4 per 10,000. Of these, 16 cases were detected by interview informed case finding (and confirmed by culture), while 13 cases were not suspected during interviews, but later developed symptoms and were confirmed as active TB by culture.

Median time to treatment was faster in cases who received CXR (6 days, range 0 to 79 days) compared to interview informed case finding (25 days, range 0 to 85 days).

For CXR, diagnostic accuracy was reported as:

- sensitivity: 100%
- specificity: 89.6%
- positive likelihood ratio: 9.99 (95% CI: 9.99 to 10)
- negative likelihood ratio: 0.00 (95% CI: 0.00 to infinity)

For interview-informed case finding, diagnostic accuracy was reported as follows:

- sensitivity: 55.2%
- specificity: 96%
- positive likelihood ratio: 13.7 (95% CI: 12.37 to 15.15)

- negative likelihood ratio: 0.5 (95% CI: 0.4 to 0.54)

Critical appraisal of this study highlighted a concern in the timing of when participants received the case finding strategies. The case finding strategies were conducted at 2 different time periods, and different participants received different case finding strategies, which impacts the interpretation of the results of the accuracy of these case finding strategies.

Additional cases identified and treated

Three studies reported outcomes which provided information on the number of additional LTBI cases identified and treated (3 to 5).

Lim and others compared TST followed by IGRA to IGRA alone for detection of LTBI in 471 refugees (54% male, mean age 24.8 years) in Canada between 2017 and 2020 (3). Cases with active TB, as well as children under 2 years old were excluded (as these children are tested by TST). The case finding strategies were:

1. TST followed by IGRA (IGRA conducted only if TST positive, 240 people screened, between August 2017 to December 2018)
2. IGRA (231 people screened, between March 2019 to February 2020)

A positive test result was followed by CXR and referral for LTBI treatment.

When IGRA was used as the only test, 41 cases of LTBI were identified, compared to 20 cases detected by TST followed by IGRA ($p = 0.002$).

There was no difference between case finding strategies in the number of cases who completed treatment (16 cases tested with TST followed by IGRA, and 14 cases tested with IGRA, $p = 0.8929$).

Critical appraisal found this study to be at serious risk of bias. It was noted that although the study adjusted their analysis for gender, refugee status, origin by TB incidence, and case finding test methods, other factors that may have impacted the results had not been accounted for. Additionally, more people were lost to follow up between tests in the 2 step case finding strategy (54% completed both tests) compared to IGRA (85% completed IGRA testing, $p < 0.01$) which would have affected the number of cases that could be identified by the 2-step case finding strategy.

Russo and others compared 2 case finding strategies for detection of LTBI in cases seeking asylum (91.4% male, median age: 26 years old, interquartile range: 22 to 32 years old) in Italy (4). Cases with active TB were excluded. The study authors highlighted that due to a shortage of TST during the study period because of the COVID-19 pandemic, it was not possible to

randomly assign participants to the 2 intervention groups. Cases were assigned to one of 2 case finding strategies:

1. IGRA (358 participants)
2. TST followed by IGRA (237 participants)

If test results were positive, participants received CXR and clinical evaluation to assess the need for preventative treatment for LTBI. Both case finding strategies had similar completion rates (completion defined as result communicated or preventative treatment started).

The initiation of preventative treatment between people identified from each case finding strategy was similar (IGRA, 18.2%, 65 cases and TST followed by IGRA 21.9%, 52 cases, adjusted incidence rate ratio: 0.83, 95% CI: 0.6 to 1.15, p = 0.272).

Critical appraisal found this study to have serious limitations. It was noted that random allocation of case finding strategies was not possible due to a shortage of TST during the COVID-19 pandemic. Although the study adjusted for age at first test, sex, study arm assignment and TB incidence in country of origin, unmeasured confounding from the lack of randomisation may still have impacted the results.

Walters and others compared 2 case finding methods for detection of LTBI in 2,244 refugees (44% female, 32% children [ages 6 to 17 years] and 68% adults [ages 18 to 49 years]) between 2009 and 2012, in the USA (5). People with suspected or active TB were excluded. The case finding methods were:

1. TST (1,125 refugees, screened between November 2009 to April 2011)
2. IGRA (1,029 refugees, screened between May 2011 to October 2012)

People with positive test results were referred for further evaluation at a TB clinic for confirmation of LTBI diagnosis.

Four hundred and twenty (35%) refugees tested positive for LTBI with TST, and 346 (34%) refugees tested positive with IGRA. TST identified more LTBI cases (94%, 393 cases) compared to IGRA (83%, 287 cases), ($p<0.0001$). People tested with IGRA were more likely to start treatment than those tested with TST (odds ratio 1.53; 95% CI: 1.02 to 2.29; $p=0.040$), which may indicate that TST identified more false positive LTBI cases.

Critical appraisal found this study to have moderate limitations. It was noted that although the study adjusted for age, ethnicity, immigration class, and region of birth, other factors that may have influenced the results were not considered. In addition, due to a test kit recall during the IGRA period, 24 participants were excluded, and 2 further participants were excluded as they did not return for a re-test. This missing data may have impacted the study’s findings.

Cost-effectiveness of case finding strategies

Three studies reported on cost-effectiveness of case finding for active and LTBI in people seeking asylum or refugees (4, 6, 7).

Marx and others conducted a cost-effectiveness study of case finding based on different TB incidence thresholds for LTBI in a hypothetical cohort of 30,000 to 45,000 children and young adults (aged 15 to 34 years) seeking asylum in Germany in 2022, using observed data from cohorts between 2017 to 2022 (6).

Children, young adolescents (aged less than 15 years) and pregnant women were assumed to be evaluated with TST or IGRA. People aged 15 years or over (who were not pregnant) were assumed to be screened using clinical examination and CXR. TB incidence thresholds evaluated were no threshold, 20, 50, 100, 150, 200, and 250 cases per 100,000 population. Total costs were estimated under a scenario of no threshold, to include costs of IGRA testing, counselling and provision of preventative TB treatment, and management of preventative TB related adverse events in the German public healthcare system, all calculated from a healthcare payer's perspective. Costs were based on 2020 prices and calculated in euros (€).

The model results showed that introducing case finding at a TB incidence threshold of 250 cases per 100,000 would gain 7.3 QALYs (95% CI: 2.7 TO 14.8 QALYs) at a cost of €51,000 (95% CI: €18,000 to €114,100). Incremental cost effectiveness ratios (ICERs) per additional QALY gained at lower thresholds were:

- 250 cases per 100,000: €51,000 (95% CI: €18,000 to €114,100)
- 200 cases per 100,000: €53,300 (95% CI: €19,100 to €122,500)
- 150 cases per 100,000: €55,900 (95% CI: €20,200 to €128,200)
- 100 cases per 100,000: €62,000 (95% CI: €23,200 to €142,000)
- 50 cases per 100,000: €82,400 (95% CI: €31,600 to €184,700)
- 20 cases per 100,000: €111,800 (95% CI: €42,700 to €251,000)
- No case finding threshold: €156,300 (95% CI: €54,500 to €373,300)

The most cost-effective threshold observed was 150 cases per 100,000, with 11.8 additional QALYS (95% CI: 4.4 to 23.7 QALYs) gained compared to 200 cases per 100,000, detecting 44% (95% CI: 35 to 52%) of all LTBI, and preventing 16% (10 to 23%) of active TB cases. Cost-effectiveness was lowest for thresholds below 100 cases per 100,000. Results from additional analysis indicated that if one secondary TB case was developed for every 5 LTBI cases who progress to active disease, a case finding threshold of 100 TB cases per 100,000 would cost less than €55,200 per additional QALY gained.

Critical appraisal highlighted some applicability concerns as this study was conducted in Germany, and therefore findings may not be applicable to the UK. Future costs were discounted at 3% (rather than 3.5% as recommended by the NICE economic evaluation checklist).

Russo and others (reported above in additional cases identified and treated) compared 2 case finding strategies for detection of LTBI in people seeking asylum (91.4% male, median age: 26 years old [interquartile range: 22 to 32 years old]) in Italy (4). Participants were non-randomly assigned to one of the 2 case finding strategies:

1. IGRA (358 participants)
2. TST followed by IGRA (237 participants)

The study estimated the cost-effectiveness of the 2 case finding strategies as an average cost effectiveness ratio (ACER), which was the ratio between the cost of the intervention and the number of cases who started treatment for LTBI. A smaller ACER indicates the case finding strategy is more cost-effective.

Total costs estimated were direct costs only, including the costs of TST, IGRA, clinical evaluation, CXR, preliminary blood tests for preventive treatment and CXR examinations performed for initial clinical indication of active TB. Total costs were estimated to be €26,792.30 for IGRA (€74.84 per person undergoing case finding) and €13,655.90 (€57.62 per person undergoing case finding) for TST followed by IGRA.

The ACER for each case finding strategies were:

- IGRA: 412.19
- TST followed by IGRA: 262.61

Therefore, TST followed by IGRA was reported to be the most cost-effective case finding strategy, with a lower cost per case treated for LTBI.

Due to previously mentioned shortage of TST during the study period, the groups were unbalanced. The larger number of participants in the IGRA alone strategy likely biased the study's outcomes towards higher costs for the IGRA alone strategy, cases avoided were not calculated as part of their analysis. As the study did not present the detail typical of cost-effectiveness studies, it was critically appraised using the ROBINS-I checklist rather than the NICE economic evaluation checklist (previously discussed above). However, as this study was conducted in Italy, the costs reported may differ from those in the UK.

Wahedi and others conducted a cost-effectiveness study comparing the current strategy of case finding for active and LTBI in all people seeking asylum (referred to as indiscriminate case finding) in Germany, with a hypothetical targeted case finding strategy based on the incidence of TB in the person seeking asylum's country of origin (7).

The indiscriminate case finding strategy was composed of a symptom questionnaire and a CXR for all individuals seeking asylum aged over 16 years old. Data was collected from 84,505 people seeking asylum between 2002 and 2015 (aged 18 and older), which included 73 confirmed TB cases. This data was used to model the cost-effectiveness of targeted case finding based on TB incidence in the person seeking asylum's country of origin. The base-case comparison was countries with TB incidence of 50 active TB cases per 100,000, and 4 different thresholds were considered up to 250 cases per 100,000. Cost-effectiveness of indiscriminate and targeted case finding strategies were also compared to a 'do-nothing' strategy of no case finding, where TB cases were passively detected by self-referral. Passively detected TB cases were assumed to cause 0.5 active TB cases on average (overall transmission rate of 0.78), whereas actively identified cases were assumed to cause no further transmission.

Effectiveness was measured as the cost per case of TB identified and cost per case prevented (presented as ICERs). Costs included the initial case finding methods, diagnostic confirmation of positive results, public health measures including contact tracing and treatment costs, all calculated from a healthcare payer's perspective. Costs were based on 2019 prices in euros (€).

The model results showed that a targeted case finding strategy of people seeking asylum from countries with incidence of active TB cases equal or greater than 50 per 100,000 was more cost effective than indiscriminate case finding but resulted in fewer cases identified and fewer cases prevented. However, the study did not include the downstream costs of cases that were missed. Increasing the TB incidence threshold at which case finding would be implemented, up to 250 cases per 100,000, reduced the ICER for both the cost per TB case found and the cost per TB case prevented but continued to also decrease the number of TB cases identified and prevented (Table 1).

Sensitivity analysis showed that the ICERs for targeted case finding (threshold of 50 TB cases per 100,000) and indiscriminate case finding were influenced most by country-specific TB prevalence, the specificity of chest X-rays, reimbursement schemes, and the frequency of diagnostics and technical costs (this was reported as percentage change in ICERs). In contrast, variations in TB transmission rates had only a minor effect on cost-effectiveness. The sensitivity analysis also suggested that the base-case ICER (TB incidence threshold 50 per 100,000) was a conservative estimate, as varying programme costs showed a less favourable ICER in most cases.

In addition to not considering costs of cases missed by increasing the case finding threshold, critical appraisal highlighted applicability concerns, as the study was conducted in Germany so the findings may not be applicable to the UK. The study also used a fixed model which did not account for the possibility of re-infection with TB.

Table 1: Wahedi and others, cost-effectiveness of TB cases found and prevented

Abbreviations: ICER, incremental cost effectiveness ratio

Case finding strategy	Cases found	ICER (Cost per TB case found)	Cases prevented	ICER (Cost per case prevented)	Total costs*	Costs per case found actively	Number of cases found passively	Costs per case found passively
No strategy	0	Not applicable	0.0	Not applicable	€658,331.90	Not applicable	73	€9,018.25
Indiscriminate case finding	73	€110,050.18	56.9	€141,089.98	€3,046,031.87	€41,726.46	0	Not applicable
Threshold: 50 per 100,000**	58	€15,436.24	45.2	€19,790.05	€1,395,279.10	€21,724.23	15	€9,018.25
Threshold: 150 per 100,000	53	€14,040.22	41.3	€18,000.29	€1,318,097.89	€21,466.66	20	€9,018.25
Threshold: 200 per 100,000	24	€10,980.69	18.7	€14,077.81	€910,931.38	€19,543.22	49	€9,018.25
Threshold: 250 per 100,000	14	€10,199.47	10.9	€13,076.24	€801,124.43	€19,217.71	59	€9,018.25

*Total costs: total cost of initial case finding, diagnostic confirmation of positive results, public health measures and treatment costs
**Threshold is based on the incidence of TB in the country of origin of the person seeking asylum

Health inequalities

This review was focused on refugees and people seeking asylum, both of which are inclusion health groups and populations at risk of a range of health inequalities due to displacement and aligned socio-demographic factors. Displacement is a risk factor for poorer health outcomes in general and these groups are at higher risk of infectious diseases (including TB) and broader issues perpetuated by poor access to healthcare and housing, unemployment, deprivation, and discrimination. In addition, many refugees and people seeking asylum will already be at risk or experiencing poorer health and inequality driven by determinants of health and circumstances in countries of origin.

Many refugees and people seeking asylum originate from countries with a high TB incidence and are therefore at a higher risk of contracting TB. Only one included study specifically modelled the number of additional cases identified by implementing a TB incidence threshold by country of origin. This study showed that a targeted case finding strategy (TB incidence threshold of 50 per 100,000) cost less than indiscriminate case finding, but resulted in fewer cases identified and fewer cases prevented (7).

The included studies did not identify evidence of health inequalities in additional subgroups of refugees or people seeking asylum specified in the protocol: people living with HIV, people with immunosuppression, silicosis (a lung disease caused by breathing in small amounts of silica particles), chronic renal failure, leukaemia, diabetes, mental health illness, and cancers of the head, neck, or lung and people who use alcohol and substances (such as injection drug use), people experiencing homelessness and people who have previously been incarcerated.

The limited evidence identified in on the effectiveness of active case finding for TB in refugees and people seeking asylum, as well as no evidence identified in the additional subgroups at potential further risk of health inequalities, signals a range of gaps in current existing evidence.

Limitations

This rapid systematic review used streamlined systematic methods to accelerate the review process. Sources of evidence searched included databases of peer-reviewed and preprint research, but an extensive search of other sources was not conducted and most article screening was completed without duplication, so it is possible relevant evidence may have been missed.

A number of limitations were identified in the included evidence. Studies that measured diagnostic outcomes were at risk of bias due to limitations in the reference standard for TB case identification as none were considered true gold standards. There were also concerns about reliability of the results in one of the studies as different groups received each of the strategies

being compared, and there was limited detail about timing of the case finding strategies. The quasi-experimental and retrospective studies were potentially biased by factors that could have confounded their results but weren't considered in their analysis. The cost-effectiveness studies were not conducted in the UK, and therefore may have limited generalisability to UK healthcare costs.

This review only identified limited evidence on diagnostic accuracy, additional cases identified and treated and the cost-effectiveness of case finding strategies. No other measures of cost-effectiveness were identified.

The findings should not be directly compared between studies, because the case finding strategies (and their comparator reference tests) considered by each study differed.

Evidence gaps

No evidence was identified for stage of disease identified, incidence of adverse events, health and social care utilisation, length of stay, and mortality.

Limited evidence was identified on the diagnostic accuracy and cost-effectiveness of individual case finding strategies.

Across studies, a range of case finding strategies were reported, including TST, IGRA, CXR, and interview-informed case finding. However, the small number of studies means there was limited information about each case finding strategy and limited evidence which compares each strategy.

Conclusion

This rapid systematic review examined the effectiveness of various latent and active TB case finding strategies in refugees and people seeking asylum, including 6 studies.

Two studies looked at the diagnostic accuracy of case finding strategies. One study reported that TST had moderate sensitivity and specificity compared to IGRA as the reference standard for detection of LTBI. A second study (which used culture as the reference standard) reported that untargeted CXR demonstrated high sensitivity compared to targeted interview-informed case finding for detection of active TB.

There was limited evidence on the number of additional cases identified and treated by LTBI case finding strategies. One study reported that IGRA identified more cases of TB than TST followed by IGRA. A second reported that TST had a higher confirmation rate for LTBI compared to IGRA.

Cost-effectiveness analyses showed that higher TB incidence thresholds for case finding of LTBI and active TB may be more cost-effective than no case finding threshold. One study showed that introduction of a case finding threshold of 150 cases per 150,000 was the most cost-effective with 11.8 additional QALYs gained at an ICER of €55,900. Another study suggested that higher TB incidence thresholds for targeted active TB case finding reduced costs per case but also detected fewer cases. Specifically, a TB incidence threshold for case finding of 50 per 100,000 was most cost-effective but missed 20.5% of cases compared to indiscriminate case finding. However, the study did not include the downstream costs of cases missed by introducing a case finding threshold. Using IGRA for case finding was reported to be more expensive than TST followed by IGRA, though case finding was faster with IGRA.

The evidence does not conclusively determine which case finding strategy was most effective. However, it offers some insights into the accuracy and cost-effectiveness of individual TB case finding methods. These findings should be interpreted with caution, considering the identified limitations in the evidence.

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7. Wahedi K and others. 'Cost-effectiveness of targeted screening for active pulmonary tuberculosis among asylum-seekers: A modelling study with screening data from a German federal state (2002-2015)' PLoS ONE [Electronic Resource] 2020: volume 15, issue 11, page e0241852
8. World Health Organization. 'Global Tuberculosis Report 2023' 2023
9. 'UNHCR. Refugees' 2024
10. Sterne JA and others. 'ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions' BMJ 2016: volume 355, page i4919
11. UK Health Security Agency. 'WHO estimates of tuberculosis incidence by country and territory, 2020' (viewed on 24 October 2023) 2022
12. 'World Health Organisation (WHO) Global TB Programme website' (viewed on 2 December 2024)
13. National Institute for Health and Care Excellence. 'The guidelines manual: Appendix G: Methodology checklist: economic evaluations' 2012
14. Whiting PF and others. 'QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies' Annals of Internal Medicine 2011: volume 155, issue 8, pages 529 to 536
15. Sterne JAC and others. 'RoB 2: a revised tool for assessing risk of bias in randomised trials' British Medical Journal 2019: volume 366, page l4,898

Annexe A. Protocol

Review question

There is one review question:

1. What are the effective strategies of case finding for tuberculosis (TB) in refugees and people seeking asylum?

A search for primary evidence to answer this review question will be conducted up to 3 July 2024.

Only studies in populations from countries or territories with low and moderate TB incidence (estimated incidence rate of less than 40 per 100,000 in 2022) will be included (8).

Only studies examining refugees and people seeking asylum will be included. The definitions of 'refugee' and 'person seeking asylum' used here are the ones used by the UNHCR (The UN refugee agency):

- refugee: "someone who has been compelled to leave their country and cannot return because of a serious threat to their life, physical integrity or freedom as a result of persecution, armed conflict, violence or serious public disorder"
- people seeking asylum: "someone who intends to seek or is awaiting a decision on their request for international protection"

Studies of populations not labelled as refugees or people seeking asylum, but could nonetheless fit the definition of refugees or people seeking asylum, will be included, but reported on separately. Studies of other migrants, such as economic migrants, will be excluded.

Strategies of case finding could be at any time after refugees and people seeking asylum enter the country conducting the case finding.

The effectiveness of case finding could be measured in numerous ways, including cost-effectiveness evaluations, sensitivity and specificity, and any change in onward transmission (full list in Table A.1 below).

Eligibility criteria

Table A.1 Inclusion and exclusion criteria

	Included	Excluded
Population	Refugees and people seeking asylum, defined above	Any other population, including economic migrants
Context	Countries or territories conducting case finding with low and moderate TB incidence (estimated incidence rate less than 40 per 100,000 in 2022)	Countries or territories conducting case finding with high TB incidence (estimated incidence rate at least 40 per 100,000 in 2022)
Settings	Any	
Intervention or exposure	Strategies of case finding for TB, compared to each other or no strategies, either alone or in combination, comprising: • symptom assessment • imaging assessment (for example, X-ray, ultrasound, echocardiogram, CT scan) • TB sampling (mucus, fluid, biopsy) • Mantoux test • interferon gamma release assay (IGRA) test	Any other intervention not listed
Outcomes	Any of the following measures of effectiveness for strategies of TB case finding: • sensitivity and specificity of the case finding strategy • additional cases identified and treated as a result of the case finding strategy • stage of disease identified • refusal of case finding intervention • onward transmission prevented as a result of the case finding strategy • incidence of adverse events, complications, safety, and tolerability	

	Included	Excluded
	• health and social care related quality of life, if considering side effects, including long term harm or disability • health and social care utilisation, including length of stay, planned and unplanned contacts • cost-effectiveness • mortality For observational studies on TB case finding, the outcomes need to occur close in time to the intervention (during the intervention time period or shortly afterwards).	
Language	English	Any other language
Date of publication	Up to 3 July 2024	
Study design	Experimental studies, including but not limited to: • randomised-controlled trials • quasi-experimental studies • cross-over designs • before-and-after studies Observational studies, including but not limited to: • cross-sectional • cohort Any study design for estimating cost-effectiveness	• reviews (all types) • case-control studies • qualitative research • mixed method studies • case reports • case series • ecological studies • modelling studies (other than cost-effectiveness studies)
Publication type	• peer-reviewed published research • preprints	• conference abstracts • editorials • letters • news articles • other grey literature

In this review, countries with a low or moderate TB incidence will be defined as any country or territory with an estimated TB incidence rate of less than 40 per 100,000 people, based on WHO 2022 estimates (8). This includes: Albania, American Samoa, Andorra, Anguilla, Antigua and Barbuda, Argentina, Armenia, Aruba, Australia, Austria, Bahamas, Bahrain, Barbados, Belarus, Belgium, Belize, Bermuda, Bosnia and Herzegovina, British Virgin Islands, Bulgaria, Cabo Verde, Canada, Cayman Islands, Chile, Comoros, Cook Islands, Costa Rica, Croatia, Cuba, Curacao, Cyprus, Czechia, Denmark, Dominica, Egypt, Estonia, Finland, France, French Polynesia, Germany, Greece, Grenada, Guam, Guatemala, Honduras, Hungary, Iceland, Iran (Islamic Republic of), Iraq, Ireland, Israel, Italy, Jamaica, Japan, Jordan, Kuwait, Latvia, Lebanon, Lithuania, Luxembourg, Maldives, Malta, Mauritius, Mexico, Monaco, Montenegro, Montserrat, Netherlands (Kingdom of the), New Caledonia, New Zealand, North Macedonia, Norway, occupied Palestinian territory, including east Jerusalem, Oman, Poland, Portugal, Puerto Rico, Qatar, Republic of Korea, Russian Federation, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Samoa, San Marino, Saudi Arabia, Serbia, Seychelles, Sint Maarten (Dutch part), Slovakia, Slovenia, Spain, Suriname, Sweden, Switzerland, Syrian Arab Republic, Togo, Tokelau, Tonga, Trinidad and Tobago, Tunisia, Turkey, Turks and Caicos Islands, United Arab Emirates, United Kingdom of Great Britain and Northern Ireland, United States of America, Uruguay, Vanuatu, Wallis and Futuna.

Identification of studies

The following databases will be searched for studies published up to 3 July 2024: OVID Medline and Embase, Emcare and Web of Science Preprint Citation Index. The search strategy is presented below. Duplicates from the main database search will be identified and removed using Deduklick.

The TRIP database will be searched for guidance and recommendations from NICE and WHO, and the websites for European Centre for Disease Control and US Centers for Disease Control and Prevention will be searched separately for guidance and recommendations. The reference lists of relevant guidance, recommendations, or guidelines will be searched for relevant primary studies (backwards citation searching).

Screening

Title and abstract screening of the main database search will be undertaken in duplicate by 2 reviewers for at least 20% of the eligible studies, with the remainder completed by one reviewer. Disagreement will be resolved by discussion or with involvement of a third reviewer where necessary.

Screening on full text will be undertaken by one reviewer and checked by a second.

Citation searching of reference lists of guidance, recommendations, and guidelines will be undertaken manually by one reviewer. Potentially relevant studies will be screened by one reviewer.

Data extraction

Summary information for each study will be extracted and reported in tabular form. Information to be extracted will include country, study period, study design, intervention, participants, results, and any relevant contextual data. This will be undertaken by one reviewer and checked by a second.

Risk of bias assessment

Two reviewers will independently complete a risk of bias assessment for included studies, with disagreements resolved by discussion or with a third reviewer. Interventional primary studies will be assessed using the Cochrane Risk of Bias 2 tool (15). Observational primary studies will be assessed using the ROBINS-I tool for non-randomised studies (10). Cost-effectiveness studies will be assessed using the NICE appraisal checklist for economic evaluations (13).

Synthesis

If data is presented in a consistent format between studies, a narrative synthesis will be produced to describe the results from this review. The number of studies, the number of participants in each study, effect size and variance and a summary of the risk of bias across studies will be summarised and presented. The prevalence or assumed prevalence of TB in cost-effectiveness studies will be stated, where possible, as the prevalence of disease affects the cost-effectiveness of screening studies. Results of studies of refugees and people seeking asylum (and any other groups which could be refugees or people seeking asylum, but the study isn't clear) will be presented separately. Alternatively, if data is too heterogeneous, a narrative summary of each study will be provided.

Health inequalities

Variations across the following populations and subgroups will be considered, where evidence is available: people living with HIV, people with immunosuppression, silicosis, chronic renal failure, leukaemia, diabetes, mental health illness, and cancers of the head, neck, or lung, people who use alcohol and substances (such as injection drug use), people from a deprived background, people experiencing homelessness, people who have previously been incarcerated, and people from countries with a high TB incidence.

Search strategy

Ovid MEDLINE(R) ALL (1946 to 2 July 2024)

1. exp Prisoners/ (19029)
2. exp Correctional Facilities/ (12014)
3. Incarceration/ (92)
4. Criminals/ (6572)
5. "Transients and Migrants"/ or Refugees/ or exp Human Migration/ (50889)
6. Deportation/ (31)
7. (immigrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (384)
8. (migrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (2410)
9. (emigrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (93)
10. immigrant*.tw,kf. (31988)
11. migrant*.tw,kf. (27296)
12. emigrant*.tw,kf. (1784)
13. refugee*.tw,kf. (15970)
14. asylum.tw,kf. (4928)
15. asylee*.tw,kf. (58)
16. ((flee* or displace*) adj3 (person* or people* or population* or citizen*)).tw,kf. (2800)
17. (ICE adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (422)
18. (Border* adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (404)
19. (customs adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (119)
20. (deportation* or deported).tw,kf. (840)
21. (prison* or imprison* or detain* or detention or custod* or jail* or gaol* or remand* or internment* or interned or offender* or convict* or criminal*).tw,kf. (73735)
22. (secure adj2 (setting* or facilit* or institut* or estate* or home* or centre* or center* or environment*)).tw,kf. (1146)
23. ((correctional or corrections) adj2 (setting* or facilit* or institut* or estate* or home* or centre* or center*)).tw,kf. (2852)
24. (incarcerat* or carcereal*).tw,kf. (15900)
25. (depriv* adj2 (freedom* or liberty)).tw,kf. (361)
26. (inmate* or penal or penitentiar*).tw,kf. (8221)
27. ((youth or young) adj offender*).tw,kf. (653)
28. ((child* or teen*) adj offender*).tw,kf. (23)
29. ((child* or teen* or youth or young) adj home*).tw,kf. (2114)
30. approved premis#s.tw,kf. (10)
31. probation*.tw,kf. (1996)
32. (halfway hous* or half way hous*).tw,kf. (295)
33. parole*.tw,kf. (1029)

34. or/1-33 (190858)
35. tuberculos#s.tw,kf. (244064)
36. exp Tuberculosis/ (209816)
37. LTBI.tw,kf. (3297)
38. TB.tw,kf. (78817)
39. Mycobacterium tuberculosis/ (59161)
40. or/35-39 (311879)
41. Tuberculin Test/ (14397)
42. ((TB or tubercul*) adj3 (react* or sensitiv* or positiv* or test* or sampl*)).tw,kf. (30428)
43. mantoux.tw,kf. (1724)
44. (tst adj3 (react* or sensitiv* or positiv*)).tw,kf. (1469)
45. (Interferon-Gamma Release Assay or IGRA).tw,kf. (2520)
46. QTF-Plus.tw,kf. (4)
47. QuantiFERON-TB Gold Plus.tw,kf. (193)
48. (case adj3 (find* or identif*)).tw,kf. (31506)
49. Sputum/ (23408)
50. (sputum adj3 (exam* or test* or collect* or sampl* or specimen* or collect*)).tw,kf. (10984)
51. (muc?us adj3 (exam* or test* or collect* or sampl* or specimen* or collect*)).tw,kf. (2109)
52. Swab*.tw,kf. (49776)
53. sputum-smear microscopy.tw,kf. (561)
54. Culture.tw,kf. (716254)
55. Diagnosis/ or Early Diagnosis/ (48330)
56. diagnosis.tw,kf. (2006696)
57. diagnostic.tw,kf. (949328)
58. Mass Screening/ (118414)
59. Diagnostic Services/ or Diagnostic Screening Programs/ (2161)
60. screening.tw,kf. (724346)
61. radiograph*.tw,kf. (283485)
62. (xray* or x-ray*).tw,kf. (457560)
63. exp Radiography, Thoracic/ (40826)
64. Xpert MTB*.tw,kf. (1795)
65. Xpert Ultra.tw,kf. (203)
66. exp Ultrasonography/ (497890)
67. exp Echocardiography/ (151833)
68. (ultrasound* or ultrasonograph*).tw,kf. (435530)
69. echocardiogra*.tw,kf. (189567)
70. echograph*.tw,kf. (10529)
71. echotomograph*.tw,kf. (764)
72. exp Tomography, X-Ray Computed/ (506110)
73. CT scan*.tw,kf. (124447)
74. Comput* tomograph*.tw,kf. (408257)
75. (biopsies or Biopsy).tw,kf. (470194)
76. exp Biopsy/ (312651)

77. Diagnostic Imaging/ (47066)
78. imaging.tw,kf. (1132291)
79. ((clinical* or symptom*) adj3 (evaluat* or assess*)).tw,kf. (368321)
80. Symptom Assessment/ (7134)
81. or/41-80 (6609779)
82. 34 and 40 and 81 (3371)

Embase (1974 to 2 July 2024)

1. prisoner/ (19373)
2. exp correctional facility/ (4059)
3. exp incarceration/ (2459)
4. exp detention center/ or asylum seeker center/ (4230)
5. deportation/ (146)
6. correctional staff/ (226)
7. offender/ (17620)
8. exp migrant/ or exp refugee/ or exp migration/ (97184)
9. (Immigrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (382)
10. (emigrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (86)
11. (migrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (2515)
12. Immigrant*.tw,kf. (36850)
13. Migrant*.tw,kf. (27142)
14. emigrant*.tw,kf. (2293)
15. Refugee*.tw,kf. (17341)
16. Asylum.tw,kf. (5341)
17. asylee*.tw,kf. (64)
18. ((flee* or displace*) adj3 (person* or people* or population* or citizen*)).tw,kf. (2913)
19. (ICE adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (457)
20. (Border* adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (476)
21. (customs adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (136)
22. (deportation* or deported).tw,kf. (936)
23. (prison* or imprison* or detain* or detention or custod* or jail* or gaol* or remand* or internment* or interned or offender* or convict* or criminal*).tw,kf. (89828)
24. (secure adj2 (setting* or facilit* or institut* or estate* or home* or centre* or center* or environment*)).tw,kf. (1686)
25. ((correctional or corrections) adj2 (setting* or facilit* or institut* or estate* or home* or centre* or center*)).tw,kf. (3385)
26. (incarcerat* or carcereal*).tw,kf. (19480)
27. (depriv* adj2 (freedom* or liberty)).tw,kf. (472)
28. (inmate* or penal or penitentiar*).tw,kf. (10239)

29. ((youth or young) adj offender*).tw,kf. (864)
30. ((child* or teen*) adj offender*).tw,kf. (29)
31. ((child* or teen* or youth or young) adj home*).tw,kf. (2352)
32. approved premis#s.tw,kf. (13)
33. probation*.tw,kf. (2424)
34. (halfway hous* or half way hous*).tw,kf. (344)
35. parole*.tw,kf. (1109)
36. or/1-35 (241914)
37. tuberculos#s.tw,kf. (223529)
38. exp tuberculosis/ (232880)
39. LTBI.tw,kf. (4712)
40. TB.tw,kf. (97005)
41. Mycobacterium tuberculosis/ (78506)
42. or/37-41 (323349)
43. tuberculin test/ (19970)
44. interferon gamma release assay/ (5751)
45. ((TB or tubercul*) adj3 (react* or sensitiv* or positiv* or test* or screen* or sampl*)).tw,kf. (39777)
46. mantoux.tw,kf. (2694)
47. (tst adj3 (react* or sensitiv* or positiv*)).tw,kf. (2190)
48. ((Interferon-Gamma Release Assay or IGRA) adj3 positiv*).tw,kf. (1083)
49. QTF-Plus.tw,kf. (6)
50. QuantiFERON-TB Gold Plus.tw,kf. (305)
51. (case adj3 (find* or identif*)).tw,kf. (45283)
52. exp sputum examination/ (34147)
53. (sputum adj3 (exam* or test* or collect* or sampl* or specimen* or collect*)).tw,kf. (16952)
54. (muc?us adj3 (exam* or test* or collect* or sampl* or specimen* or collect*)).tw,kf. (2684)
55. Swab*.tw,kf. (69708)
56. sputum-smear microscopy.tw,kf. (699)
57. Culture.tw,kf. (897198)
58. diagnosis/ or diagnostic reasoning/ or diagnostic test/ or early diagnosis/ (1730130)
59. diagnosis.tw,kf. (2911454)
60. diagnostic.tw,kf. (1332033)
61. mass screening/ (63343)
62. screening/ or screening test/ (280924)
63. screening.tw,kf. (1021657)
64. radiograph*.tw,kf. (334885)
65. (xray* or x-ray*).tw,kf. (519716)
66. exp thorax radiography/ (241169)
67. Xpert MTB*.tw,kf. (2615)
68. Xpert Ultra.tw,kf. (234)
69. exp echography/ (1061053)
70. exp echocardiography/ (461756)

71. (ultrasound* or ultrasonograph*).tw,kf. (669672)
72. echocardiogra*.tw,kf. (339865)
73. echograph*.tw,kf. (13987)
74. echotomograph*.tw,kf. (938)
75. exp x-ray computed tomography/ (113397)
76. CT scan*.tw,kf. (223892)
77. Comput* tomograph*.tw,kf. (522762)
78. (biopsies or Biopsy).tw,kf. (777026)
79. biopsy/ or exp respiratory tract biopsy/ (230123)
80. diagnostic imaging/ (260190)
81. imaging.tw,kf. (1595746)
82. ((clinical* or symptom*) adj3 (evaluat* or assess*)).tw,kf. (559462)
83. symptom assessment/ (12943)
84. or/43-83 (9581253)
85. 36 and 42 and 84 (5357)
86. limit 85 to conference abstract (1085)
87. 85 not 86 (4272)
88. limit 87 to (editorial or letter) (250)
89. 87 not 88 (4022)

Ovid Emcare (1995 to 2 July 2024)

1. prisoner/ (6323)
2. exp correctional facility/ (1341)
3. exp incarceration/ (918)
4. exp detention center/ or asylum seeker center/ (1419)
5. deportation/ (98)
6. correctional staff/ (115)
7. offender/ (15992)
8. exp migrant/ or exp refugee/ or exp migration/ (34398)
9. (Immigrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (177)
10. (emigrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (21)
11. (migrat* adj5 (force* or illegal* or undocument* or involuntar* or irregular*)).tw,kf. (789)
12. Immigrant*.tw,kf. (20444)
13. Migrant*.tw,kf. (13614)
14. emigrant*.tw,kf. (532)
15. Refugee*.tw,kf. (10348)
16. Asylum.tw,kf. (3100)
17. asylee*.tw,kf. (43)
18. ((flee* or displace*) adj3 (person* or people* or population* or citizen*)).tw,kf. (1464)
19. (ICE adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (100)

20. (Border* adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (178)
21. (customs adj3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)).tw,kf. (72)
22. (deportation* or deported).tw,kf. (539)
23. (prison* or imprison* or detain* or detention or custod* or jail* or gaol* or remand* or internment* or interned or offender* or convict* or criminal*).tw,kf. (46722)
24. (secure adj2 (setting* or facilit* or institut* or estate* or home* or centre* or center* or environment*)).tw,kf. (964)
25. ((correctional or corrections) adj2 (setting* or facilit* or institut* or estate* or home* or centre* or center*)).tw,kf. (2078)
26. (incarcerat* or carcereal*).tw,kf. (9874)
27. (depriv* adj2 (freedom* or liberty)).tw,kf. (325)
28. (inmate* or penal or penitentiar*).tw,kf. (4798)
29. ((youth or young) adj offender*).tw,kf. (711)
30. ((child* or teen*) adj offender*).tw,kf. (22)
31. ((child* or teen* or youth or young) adj home*).tw,kf. (1464)
32. approved premis#s.tw,kf. (13)
33. probation*.tw,kf. (1518)
34. (halfway hous* or half way hous*).tw,kf. (92)
35. parole*.tw,kf. (858)
36. or/1-35 (107976)
37. tuberculos#s.tw,kf. (40021)
38. exp tuberculosis/ (30145)
39. LTBI.tw,kf. (1166)
40. TB.tw,kf. (20306)
41. Mycobacterium tuberculosis/ (7516)
42. or/37-41 (52871)
43. tuberculin test/ (2836)
44. interferon gamma release assay/ (643)
45. ((TB or tubercul*) adj3 (react* or sensitiv* or positiv* or test* or screen* or sampl*)).tw,kf. (7781)
46. mantoux.tw,kf. (367)
47. (tst adj3 (react* or sensitiv* or positiv*)).tw,kf. (484)
48. ((Interferon-Gamma Release Assay or IGRA) adj3 positiv*).tw,kf. (195)
49. QTF-Plus.tw,kf. (1)
50. QuantiFERON-TB Gold Plus.tw,kf. (68)
51. (case adj3 (find* or identif*)).tw,kf. (11797)
52. exp sputum examination/ (5161)
53. (sputum adj3 (exam* or test* or collect* or sampl* or specimen* or collect*)).tw,kf. (2562)
54. (muc?us adj3 (exam* or test* or collect* or sampl* or specimen* or collect*)).tw,kf. (299)
55. Swab*.tw,kf. (13235)
56. sputum-smear microscopy.tw,kf. (204)

57. Culture.tw,kf. (143762)
58. diagnosis/ or diagnostic reasoning/ or diagnostic test/ or early diagnosis/ (263342)
59. diagnosis.tw,kf. (582788)
60. diagnostic.tw,kf. (299532)
61. mass screening/ (8811)
62. screening/ or screening test/ (76733)
63. screening.tw,kf. (230639)
64. radiograph*.tw,kf. (114848)
65. (xray* or x-ray*).tw,kf. (76545)
66. exp thorax radiography/ (43749)
67. Xpert MTB*.tw,kf. (693)
68. Xpert Ultra.tw,kf. (75)
69. exp echography/ (165491)
70. exp echocardiography/ (69019)
71. (ultrasound* or ultrasonograph*).tw,kf. (164145)
72. echocardiogra*.tw,kf. (68096)
73. echograph*.tw,kf. (1686)
74. echotomograph*.tw,kf. (35)
75. exp x-ray computed tomography/ (7975)
76. CT scan*.tw,kf. (44961)
77. Comput* tomograph*.tw,kf. (149760)
78. (biopsies or Biopsy).tw,kf. (97959)
79. biopsy/ or exp respiratory tract biopsy/ (28784)
80. diagnostic imaging/ (51591)
81. imaging.tw,kf. (396388)
82. ((clinical* or symptom*) adj3 (evaluat* or assess*)).tw,kf. (141856)
83. symptom assessment/ (1910)
84. or/43-83 (1906850)
85. 36 and 42 and 84 (1224)
86. limit 85 to conference abstract (0)
87. 85 not 86 (1224)
88. limit 87 to (editorial or letter) (36)
89. 87 not 88 (1188)

Web of Science Preprint Citation Index (1990 – current)

Date of search: 2 July 2014

TS=(immigrat* NEAR/5 (force* or illegal* or undocument* or involuntar* or irregular*)) OR
TS=(migrat* NEAR/5 (force* or illegal* or undocument* or involuntar* or irregular*)) OR
TS=(emigrat* NEAR/5 (force* or illegal* or undocument* or involuntar* or irregular*)) OR
TS=(immigrant*) OR TS=(migrant*) OR TS=(emigrant*) OR TS=(refugee*) OR TS=(asylum) OR
TS=(asylee*) OR TS=((flee* or displace*) NEAR/3 (person* or people* or population* OR

citizen*)) OR TS=(ICE NEAR/3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)) OR TS=(Border* NEAR/3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)) OR TS=(customs NEAR/3 (federal or Enforcement or confine* or removal* or detain* or detention or facilit* or institution*)) OR TS=(deportation* or deported) OR TS=(prison* or imprison* or detain* or detention or custod* or jail* or gaol* or remand* OR internment* OR interned OR offender* OR convict* OR criminal*) OR TS=(secure NEAR/2 (setting* or facilit* or institut* or estate* or home* or centre* or center* OR environment*)) OR TS=((correctional or corrections) NEAR/2 (setting* or facilit* or institut* or estate* or home* or centre* or center*)) OR TS=(incarcerat* or carcereal*) OR TS=(depriv* NEAR/2 (freedom* or liberty)) OR TS=(inmate* or penal or penitentiar*) OR TS=((youth or young) NEAR/0 offender*) OR TS=((child* or teen*) NEAR/0 offender*) OR TS=((child* or teen* or youth or young) NEAR/0 home*) OR TS=(“approved premises” OR “approved premisis”) OR TS=(probation*) OR TS=(“half way hous*” OR “halfway hous*”) OR TS=(parole*)

And

TS=(tuberculosis OR tuberculoses) OR TS=(LTBI OR TB)

And

TS=((TB or tubercul*) NEAR/3 (react* or sensitiv* or positiv* or test* OR sampl*)) OR TS=(Mantoux) OR TS=(tst NEAR/3 (react* or sensitiv* or positiv*)) OR TS=(“Interferon-Gamma Release Assay” or IGRA) OR TS=(“QTF-Plus”) OR TS=(“QuantiFERON-TB Gold Plus”) OR TS=(case NEAR/3 (find* or identif*)) OR TS=(sputum NEAR/3 (exam* or test* or collect* or sampl* or specimen* or collect*)) OR TS=((mucus OR mucous) NEAR/3 (exam* or test* or collect* or sampl* or specimen* or collect*)) OR TS=(Swab*) OR TS=(“sputum-smear microscopy”) OR TS=(Culture) OR TS=(diagnosis OR diagnostic) OR TS=(screening) OR TS=(radiograph* OR “x-ray*” OR xray* OR “Xpert MTB*” OR “Xpert Ultra”) OR TS=(ultrasound* or ultrasonograph* OR echocardiogra* OR “CT scan*” OR “Comput* tomograph*” OR echograph* OR echotomography* OR Biopsy OR biopsies OR imaging) OR TS=((clinical* or symptom*) NEAR/3 (evaluat* or assess*))

12 results

TRIP Database

Date of search: 2 July 2024

‘Tuberculosis’ in title

Filter to: Guidelines

117 results

FAIR Database

Date of search: 3 July 2024

Searched in title and abstract:

tuberculosis and (prison OR prisoner OR offender OR convict OR criminal OR asylum OR asylee OR refugee OR migrant OR immigrant OR emigrant)

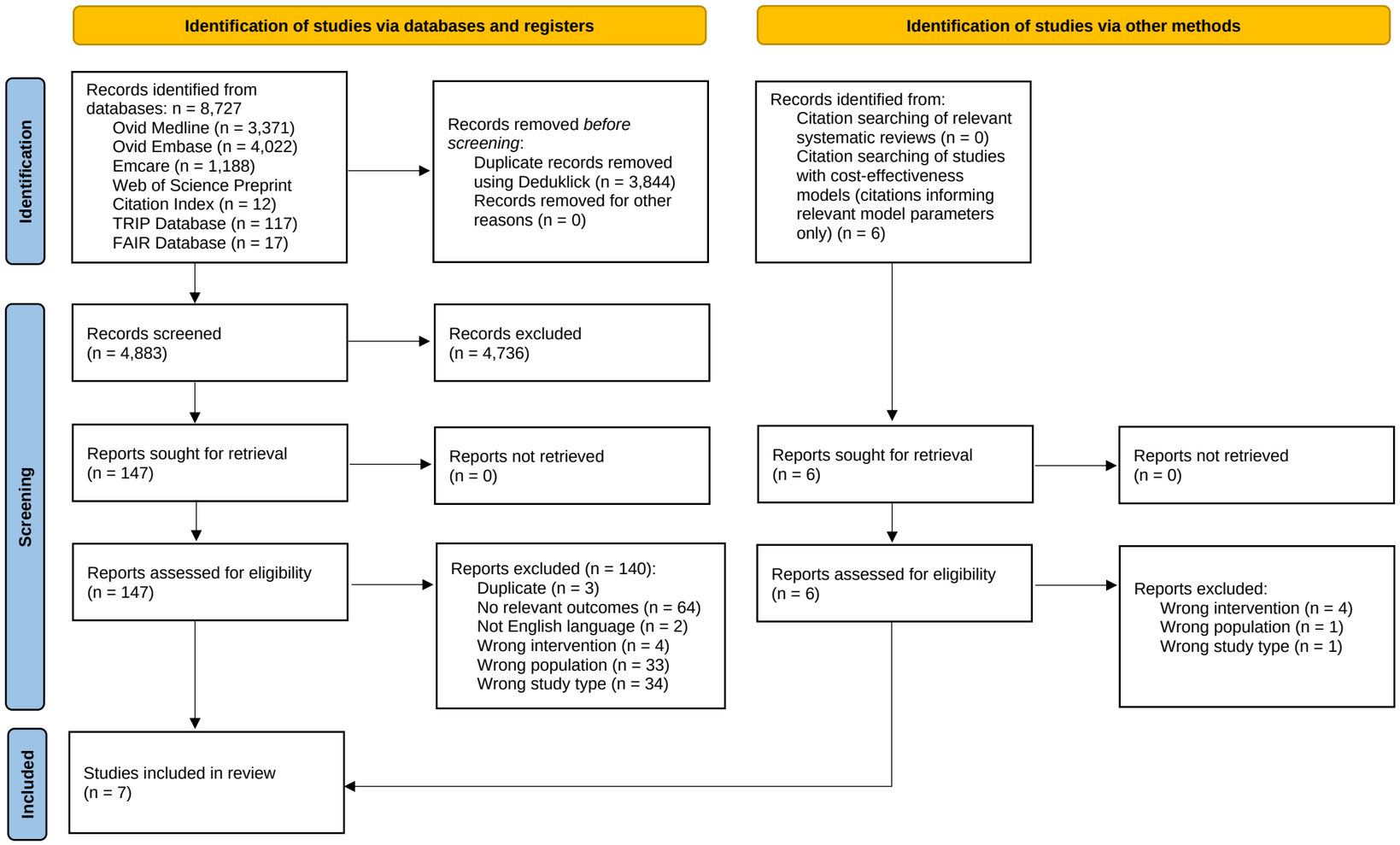
Deviations

There were 2 deviations from the protocol:

1. The NICE appraisal checklist for economic evaluations and the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool were used to assess risk of bias for economic evaluations and diagnostic studies respectively.
2. The World Health Organization (WHO) estimates of TB incidence reported on GOV.UK (11) were used to determine eligibility for inclusion during screening of studies. This list was withdrawn during the review, therefore the included studies were checked against the Global TB Programme website data to verify TB incidence (12).

Annexe B. Study selection flowchart

Figure B.1. PRISMA diagram



Text version of Figure B.1. PRISMA diagram

A PRISMA diagram showing the flow of studies through this review, ultimately including 9 studies.

From identification of studies via databases, n=8,727 records:

- Ovid Medline (n = 3,371)
- Ovid Embase (n = 4,022)
- Emcare (n = 1,188)
- Web of Science Preprint Citation Index (n = 12)
- TRIP Database (n = 117)
- FAIR Database (n = 17)

From these, records removed before screening:

- duplicate records removed using Deduklick (n=3,844)
- records removed for other reasons (n=0)

n=4,883 records screened, of which n=4,736 were excluded, leaving n=147 papers sought for retrieval, of which all were retrieved.

Of the n=147 papers assessed for eligibility, n=140 reports were excluded:

- duplicate (n = 3)
- no relevant outcomes (n = 64)
- not English language (n = 2)
- wrong intervention (n = 8)
- wrong population (n = 34)
- wrong study type (n = 35)

Studies identified via other methods: n=6 studies from citation searching of studies with cost-effectiveness models (citations informing relevant model parameters only), all of which were ineligible:

- wrong intervention (n = 4)
- wrong population (n = 1)
- wrong study type (n = 1)

n=7 papers included in the review.

Annexe C. Excluded full texts

No relevant outcomes (64 studies)

Ackermann N and others. 'Screening for infectious diseases among newly arrived asylum seekers, Bavaria, Germany, 2015' Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2018: volume 23, issue 10, page 3

Banfield S and others. 'Factors associated with the performance of a blood-based interferon-gamma release assay in diagnosing tuberculosis' PLoS ONE [Electronic Resource] 2012: volume 7, issue 6, page e38556

Barcellini L and others. 'App-based symptoms screening with Xpert MTB/RIF Ultra assay used for active tuberculosis detection in migrants at point of arrivals in Italy: The E-DETECT TB intervention analysis' PLoS ONE [Electronic Resource] 2019: volume 14, issue 7, page e0218039

Barry SM and others. 'Outcomes from a national screening program for Ukrainian refugees at risk of drug resistant tuberculosis in Wales' Thorax 2023: volume 79, issue 1, pages 86 to 98

Bennet R, Eriksson M. 'Tuberculosis infection and disease in the 2015 cohort of unaccompanied minors seeking asylum in Northern Stockholm, Sweden' Infectious Diseases 2017: volume 49, issue 7, pages 501 to 506

Bertoncello C and others. 'LTBI among migrants by Mediterranean Sea: assessing prevalence and its variations according with different thresholds and diagnostic tools. A 10-month on-field experience' Journal of Travel Medicine 2018: volume 25, issue 1, page 1

Boyd AT and others. 'An evaluation of a tuberculosis case-finding and treatment program among Syrian refugees-Jordan and Lebanon, 2013-2015' Conflict & Health [Electronic Resource] 2019: volume 13, pages 32

Bozorgmehr K and others. 'Infectious disease screening in asylum seekers: range, coverage and economic evaluation in Germany, 2015' Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2017: volume 22, issue 40

Breuss E and others. 'Screening and treatment for latent tuberculosis infection among asylum seekers entering Switzerland' Swiss Medical Weekly 2002: volume 132, issue 15, pages 197 to 200

Bua A and others. 'Tuberculosis screening among asylum seekers in Sardinia' Journal of Public Health 2016: volume 38, issue 4, pages 760 to 764

Buonfrate D and others. 'Extended screening for infectious diseases among newly-arrived asylum seekers from Africa and Asia, Verona province, Italy, April 2014 to June 2015' Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2018: volume 23, issue 16, page 4

Callister ME and others. 'Pulmonary tuberculosis among political asylum seekers screened at Heathrow Airport, London, 1995-9' Thorax 2002: volume 57, issue 2, pages 152 to 156

Colgan K and others. 'Latent tuberculosis may be missed by current screening practices: Analysis of interferon-gamma release assay results from a paediatric refugee clinic' Journal of Paediatrics and Child Health 2019: volume 55, issue 7, pages 826 to 832

Cuomo G and others. 'Migration and health: A retrospective study about the prevalence of HBV, HIV, HCV, tuberculosis and syphilis infections amongst newly arrived migrants screened at the Infectious Diseases Unit of Modena, Italy' Journal of Infection and Public Health 2019: volume 12, issue 2, pages 200 to 204

Einterz EM and others. 'The impact of a public health department's expansion from a one-step to a two-step refugee screening process on the detection and initiation of treatment of latent tuberculosis' Public Health 2018: volume 159, pages 27 to 30

El-Hamad I and others. 'Screening for tuberculosis and latent tuberculosis infection among undocumented immigrants at an unspecialised health service unit' International Journal of Tuberculosis and Lung Disease 2001: volume 5, issue 8, pages 712 to 716

Eonomopoulou A and others. 'Migrant screening: Lessons learned from the migrant holding level at the Greek-Turkish borders' Journal of Infection and Public Health 2017: volume 10, pages 177 to 184

Evans TB and others. 'Tuberculosis misclassification among resettled refugees in Buffalo, New York, USA' International Journal of Tuberculosis and Lung Disease 2015: volume 19, issue 2, pages 231 to 236

Fiore V and others. 'Infectious diseases screening approach among refugees: results from a single-center study' Journal of Infection in Developing Countries 2021: volume 15, issue 6, pages 847 to 852

Geweniger A and others. 'High diagnostic yield of endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) in the diagnosis of adolescent pulmonary tuberculosis' BMC Infectious Diseases 2021: volume 21, issue 1, page 946

Grecchi C and others. 'Screening program for latent tuberculosis infection in asylum seekers - a single center experience in Pavia, Italy' Annali di Igiene 2020: volume 32, issue 6, pages 682 to 688

Harling R and others. 'Tuberculosis screening of asylum seekers: 1 years' experience at the Dover Induction Centres' Public Health 2007: volume 121, issue 11, pages 822 to 827

Harstad I and others. 'Tuberculosis screening and follow-up of asylum seekers in Norway: a cohort study' BMC Public Health 2009: volume 9, page 141

Harstad I and others. 'Predictive values of QuantiFERON-TB Gold testing in screening for tuberculosis disease in asylum seekers' International Journal of Tuberculosis and Lung Disease 2010: volume 14, issue 9, pages 1,209 to 1,211

Hosten E and others. 'Tuberculosis contact-tracing among Syrian refugee populations: lessons from Jordan' Conflict & Health [Electronic Resource] 2018: volume 12, page 25

King K and others. 'Is premigration health screening for tuberculosis worthwhile?' Medical Journal of Australia 2011: volume 195, issue 9, pages 534 to 537

Langholz Kristensen K and others. 'Tuberculosis screening among newly arrived asylum seekers in Denmark' Infectious Diseases 2022: volume 54, issue 11, pages 819 to 827

Liu Y and others. 'Tuberculosis among Newly Arrived Immigrants and Refugees in the United States' Annals of the American Thoracic Society 2020: volume 17, issue 11, pages 1401 to 1,412

Lucas M and others. 'A prospective large-scale study of methods for the detection of latent Mycobacterium tuberculosis infection in refugee children' Thorax 2010: volume 65, issue 5, pages 442 to 448

Marras TK and others. 'Tuberculosis among Tibetan refugee claimants in Toronto: 1998 to 2000' Chest 2003: volume 124, issue 3, pages 915 to 921

Mor Z and others. 'Chest radiography validity in screening pulmonary tuberculosis in immigrants from a high-burden country' Respiratory Care 2012: volume 57, issue 7, pages 1,137 to 1,144

Mueller-Hermelink M and others. 'Universal screening for latent and active tuberculosis (TB) in asylum seeking children, Bochum and Hamburg, Germany, September 2015 to November 2016' Euro Surveillance: Bulletin Europeen sur les Maladies Transmissibles = European Communicable Disease Bulletin 2018: volume 23, issue 12, page 3

Mulder C and others. 'Role of the QuantiFERON(R)-TB Gold In-Tube assay in screening new immigrants for tuberculosis infection' European Respiratory Journal 2012: volume 40, issue 6, pages 1,443 to 1,449

Mulder C and others. 'Predictive value of the tuberculin skin test among newly arriving immigrants' PLoS ONE [Electronic Resource] 2013: volume 8, issue 3, page e60130

Pacifici LE and others. 'Screening for tuberculosis among asylum seekers: Experience from an immigration centre in Central Italy and literature review' Giornale Italiano di Medicina Tropicale 2010: volume 15, pages 21 to 27

Pampaloni A and others. '"Diagnosis on the Dock" project: A proactive screening program for diagnosing pulmonary tuberculosis in disembarking refugees and new SEI model' International Journal of Infectious Diseases 2021: volume 106, pages 98 to 104

Pontarelli A and others. 'Screening for active and latent tuberculosis among asylum seekers in Italy: A retrospective cohort analysis' Travel Medicine and Infectious Disease 2019: volume 27, pages 39 to 45

Prestileo T and others. 'Tuberculosis among Migrant Populations in Sicily: A Field Report' Journal of Tropical Medicine 2021: volume 2021, page 7856347

Rahman A and others. 'A feasibility study evaluating the uptake, effectiveness and acceptability of routine screening of pregnant migrants for latent tuberculosis infection in antenatal care: a research protocol' BMJ Open 2022: volume 12, issue 4

Raisanen PE and others. 'Tuberculosis screening of asylum seekers in Finland, 2015-2016' BMC Public Health 2020: volume 20, issue 1, page 969

Rennert-May E and others. 'A Step toward Tuberculosis Elimination in a Low-Incidence Country: Successful Diagnosis and Treatment of Latent Tuberculosis Infection in a Refugee Clinic' Canadian Respiratory Journal 2016: volume 2016, pages 7980869

Rysstad OG, Gallefoss F. 'TB status among Kosovar refugees' International Journal of Tuberculosis and Lung Disease 2003: volume 7, issue 5, pages 458 to 463

Sane Schepisi M and others. 'Tuberculosis case finding based on symptom screening among immigrants, refugees and asylum seekers in Rome' BMC Public Health 2013: volume 13, page 872

Sarivalasis A and others. 'Factors associated with latent tuberculosis among asylum seekers in Switzerland: a cross-sectional study in Vaud County' BMC Infectious Diseases 2012: volume 12, page 285

Schepisi MS and others. 'Active Tuberculosis Case Finding Interventions Among Immigrants, Refugees and Asylum Seekers in Italy' Infectious Disease Reports 2016: volume 8, issue 2, page 6594

Schoch and others. 'Diagnostic yield of sputum, induced sputum, and bronchoscopy after radiologic tuberculosis screening' American Journal of Respiratory & Critical Care Medicine 2007: volume 175, issue 1, pages 80 to 86

Serre Delcor N and others. 'Infectious Diseases in Sub-Saharan Immigrants to Spain' American Journal of Tropical Medicine and Hygiene 2016: volume 94, issue 4, pages 750 to 756

Sheikh M and others. 'The epidemiology of health conditions of newly arrived refugee children: A review of patients attending a specialist health clinic in Sydney' Journal of Paediatrics and Child Health 2009: volume 45, issue 9, pages 509 to 513

Smit GS and others. 'Cost-effectiveness of screening for active cases of tuberculosis in Flanders, Belgium' Bulletin of the World Health Organization 2017: volume 95, issue 1, pages 27 to 35

Smock L and others. 'Factors Associated with Development of Tuberculosis Disease Among Refugees, Massachusetts, 2008-2018' Journal of Immigrant & Minority Health 2023: volume 25, issue 1, pages 31 to 37

Staerke NB and others. 'The cascade of care in tuberculosis infection screening and management in newly arrived refugees in Aarhus, Denmark' Travel Medicine and Infectious Disease 2022: volume 49, page 102,388

Tewes S and others. 'Tuberculosis screening during the 2015 European refugee crisis' BMC Public Health 2020: volume 20, issue 1, page 200

Thee S and others. 'Screening and treatment for tuberculosis in a cohort of unaccompanied minor refugees in Berlin, Germany' PLoS ONE [Electronic Resource] 2019: volume 14, issue 5, page e0216234

Tiong AC and others. 'Health issues in newly arrived African refugees attending general practice clinics in Melbourne' Medical Journal of Australia 2006: volume 185, issue 11, pages 602 to 606

Trauer JM, Krause VL. 'Assessment and management of latent tuberculosis infection in a refugee population in the Northern Territory' Medical Journal of Australia 2011: volume 194, issue 11, pages 579 to 582

van Burg JL and others. 'The epidemiology of tuberculosis among asylum seekers in The Netherlands: implications for screening' International Journal of Tuberculosis and Lung Disease 2003: volume 7, issue 2, pages 139 to 144

Van Leent JP, Hopkins PF. 'Report of a mantoux survey of "displaced persons" migrant children' The Medical Journal of Australia 1951: volume 1, issue 19, pages 673 to 676

Villa S and others. 'Tuberculosis among asylum seekers in Milan, Italy: epidemiological analysis and evaluation of interventions' European Respiratory Journal 2019: volume 54, issue 4, page 10

Weinrich JM and others. 'Yield of chest X-ray tuberculosis screening of immigrants during the European refugee crisis of 2015: a single-centre experience' European Radiology 2017: volume 27, issue 8, pages 3,244 to 3,248

Wendorf and others. 'Interferon-gamma Release Assays for Tuberculosis Infection Diagnosis in Refugees <5 Years Old' Pediatrics 2020: volume 146, issue 4, page 10

Wenzel M. 'An alternative to 'two-step' tuberculin skin testing for Southeast Asian refugees' The Nurse practitioner 1991: volume 16, issue 9, pages 25 to 28

Winje and others. 'Screening for tuberculosis infection among newly arrived asylum seekers: comparison of QuantiFERONTB Gold with tuberculin skin test' BMC Infectious Diseases 2008: volume 8, page 65

Zellweger JP, Vejdovsky R. 'Tuberculosis among refugees: study of a population screening at the Tuberculosis Clinic in Lausanne (Switzerland) between 1983 and 1988' Bulletin of the International Union Against Tuberculosis and Lung Disease 1988: volume 63, issue 4, pages 29 to 31

Zuber PL and others. 'Tuberculosis screening for immigrants and refugees. Diagnostic outcomes in the state of Hawaii' American Journal of Respiratory and Critical Care Medicine 1996: volume 154, issue 1, pages 151 to 155

Not English language (2 studies)

Romby A and others. 'Tuberculosis testing and treatment among vulnerable migrants. Survey in comede healthcare centre, France' Bulletin Epidemiologique Hebdomadaire 2013, issue 28, pages 348 to 353

Serre-Delcor N and others. 'Sequential strategy for the LTBI screening of newly-arrived immigrants in vulnerable social situations' Enfermedades Infecciosas y Microbiología Clínica 2018: volume 36, issue 9, pages 550 to 554

Wrong intervention (8 studies)

Armitage AJ and others. 'Description and evaluation of a pathway for unaccompanied asylum-seeking children' Archives of Disease in Childhood 2022: volume 107, issue 5, pages 456 to 460

Barniol J and others. 'Transmission dynamics of pulmonary tuberculosis between autochthonous and immigrant sub-populations' BMC Infectious Diseases 2009: volume 9, issue 1, page 197

Catanzaro A. 'Multiple puncture skin test and mantoux test in Southeast Asian refugees' Chest 1985: volume 87, issue 3, pages 346 to 350

Diel R and others. 'Tuberculosis: cost of illness in Germany' European Respiratory Journal 2012: volume 40, issue 1, page 143

Diel R and others. 'Epidemiology of Tuberculosis in Hamburg, Germany: Long-Term Population-Based Analysis Applying Classical and Molecular Epidemiological Techniques' Journal of Clinical Microbiology 2002: volume 40, issue 2, pages 532 to 539

Gelaw SM and others. 'Diagnostic accuracy of three computer-aided detection systems for detecting pulmonary tuberculosis on chest radiography when used for screening: analysis of an international, multicenter migrants screening study' PLOS Global Public Health 2022: volume 3, issue 7

Glynn JR and others. 'Interpreting DNA fingerprint clusters of Mycobacterium tuberculosis. European Concerted Action on Molecular Epidemiology and Control of Tuberculosis' Int J Tuberc Lung Dis 1999: volume 3, issue 12, pages 1,055 to 1,060

Porco TC and others. 'Cost-effectiveness of tuberculosis evaluation and treatment of newly-arrived immigrants' BMC Public Health 2006: volume 6, pages 157

Wrong population (34 studies)

Al Abri and others. 'Cost-effectiveness of IGRA/QFT-Plus for TB screening of migrants in Oman' International Journal of Infectious Diseases 2020: volume 92, pages S72 to S77

Barcellini and others. 'Latent tuberculous infection among foreign-born individuals applying to shelters in the metropolitan area of Milan' International Journal of Tuberculosis & Lung Disease 2018: volume 22, issue 10, pages 1,160 to 1,165

Boardman and others. 'Pulmonary Tuberculosis Disease Among Immigrant Detainees: Rapid Disease Detection, High Prevalence of Asymptomatic Disease, and Implications for Tuberculosis Prevention' Clinical Infectious Diseases 2021: volume 73, issue 1, pages 115 to 120

Carvalho and others. 'QuantiFERON-TB Gold test in the identification of latent tuberculosis infection in immigrants' Journal of Infection 2007: volume 55, issue 2, pages 164 to 168

Cauthen and others. 'Boosting of tuberculin sensitivity among Southeast Asian refugees' American Journal of Respiratory & Critical Care Medicine 1994: volume 149, issue 6, pages 1,597 to 1,600

Dale and others. 'Modeling the Cost-Effectiveness of Latent Tuberculosis Screening and Treatment Strategies in Recent Migrants to a Low-Incidence Setting' American Journal of Epidemiology 2022: volume 191, issue 2, pages 255 to 270

Donkeng-Donfack and others. 'A cost-benefit algorithm for rapid diagnosis of tuberculosis and rifampicin resistance detection during mass screening campaigns' BMC Infectious Diseases 2022: volume 22, issue 1, page 219

Flynn and others. 'Use of tuberculin skin test, chest radiograph and interferon-gamma release assay to select migrants for treatment of latent tuberculosis' Communicable Diseases Intelligence 2018: volume 42

Hardy and others. 'Cost-effectiveness of the NICE guidelines for screening for latent tuberculosis infection: the QuantiFERON-TB Gold IGRA alone is more cost-effective for immigrants from high burden countries' Thorax 2010: volume 65, issue 2, pages 178 to 180

Haukaas and others. 'Immigrant screening for latent tuberculosis in Norway: a cost-effectiveness analysis' European Journal of Health Economics 2017: volume 18, issue 4, pages 405 to 415

Kik and others. 'Interferon-gamma release assays in immigrant contacts and effect of remote exposure to Mycobacterium tuberculosis' International Journal of Tuberculosis & Lung Disease 2009: volume 13, issue 7, pages 820 to 828

Kik and others. 'Predictive value for progression to tuberculosis by IGRA and TST in immigrant contacts' European Respiratory Journal 2010: volume 35, issue 6, pages 1,346 to 1,353

Levine and others. 'Latent tuberculosis infection in the outpatient general medicine clinic: Efficacy of a nurse-run electronic directly observed treatment program' Preventive Medicine Reports 2023: volume 35, page 102,321

Linas and others. 'Priorities for screening and treatment of latent tuberculosis infection in the United States' American Journal of Respiratory & Critical Care Medicine 2011: volume 184, issue 5, pages 590 to 601

Mathez and others. 'Active screening for pulmonary tuberculosis among immigrants by chest x-ray at the Swiss border' Swiss Medical Weekly 2007: volume 137, issue 45, pages 649 to 654

Medina-Macias and others. 'Latent tuberculosis in migrants travelling through the northeast regions of Mexico' Journal of Clinical Tuberculosis and Other Mycobacterial Diseases 2020: volume 21, page 100,194

Miranda-Schaeubinger and others. 'Frequency of abnormal findings on chest radiograph after positive PPD in children and adolescents in an urban setting in the United States' Clinical Imaging 2024: volume 105

Mor and others. 'The yield of tuberculosis screening of undocumented migrants from the Horn of Africa based on chest radiography' Israel Medical Association Journal: Imaj 2015: volume 17, issue 1, pages 11 to 13

Orlando and others. 'Interferon-gamma releasing assay versus tuberculin skin testing for latent tuberculosis infection in targeted screening programs for high risk immigrants' Infection 2010: volume 38, issue 3, pages 195 to 204

O'Shea and others. 'Tuberculin skin testing and treatment modulates interferon-gamma release assay results for latent tuberculosis in migrants' PLoS ONE [Electronic Resource] 2014: volume 9, issue 5, page e97366

Painter and others. 'Tuberculosis screening by tuberculosis skin test or QuantiFERON-TB Gold In-Tube Assay among an immigrant population with a high prevalence of tuberculosis and BCG vaccination' PLoS ONE [Electronic Resource] 2013: volume 8, issue 12, page e82727

Panchal and others. 'The effectiveness of primary care based risk stratification for targeted latent tuberculosis infection screening in recent immigrants to the UK: a retrospective cohort study' Thorax 2014: volume 69, issue 4, pages 354 to 362

Pang and others. 'Tuberculosis case-finding in Western Australia' Respiratory Medicine 1994: volume 88, issue 3, pages 213 to 217

Pareek and others. 'Screening of immigrants in the UK for imported latent tuberculosis: a multicentre cohort study and cost-effectiveness analysis' The Lancet Infectious Diseases 2011: volume 11, issue 6, pages 435 to 444

Pareek and others. 'Community-based evaluation of immigrant tuberculosis screening using interferon gamma release assays and tuberculin skin testing: observational study and economic analysis' Thorax 2013: volume 68, issue 3, pages 230 to 239

Park and others. 'Comparison of active tuberculosis case finding strategies for immigrants in South Korea: Epidemiology and cost-effectiveness analysis' PLoS ONE [Electronic Resource] 2023: volume 18, issue 4, page e0283414

Smyth and Porter. 'Geographic variations in the prevalence of sensitivity to PPD-S and PPD-B in Western Australia' Tubercle 1967: volume 48, issue 4, pages 273 to 280

Story and others. 'Active case finding for pulmonary tuberculosis using mobile digital chest radiography: an observational study' International Journal of Tuberculosis & Lung Disease 2012: volume 16, issue 11, pages 1,461 to 1,467

Tattersall and others. 'Tuberculosis case-finding in a reception centre' Public Health 1957: volume 269, issue 6979, pages 1,138 to 1,139

Truong and others. 'Tuberculosis among Tibetan immigrants from India and Nepal in Minnesota, 1992-1995' JAMA 1997: volume 277, issue 9, pages 735 to 738

Usemann and others. 'Cost-effectiveness of tuberculosis screening for migrant children in a low-incidence country' International Journal of Tuberculosis & Lung Disease 2019: volume 23, issue 5, pages 579 to 586

van't Hoog AH and others. 'Choosing algorithms for TB screening: a modelling study to compare yield, predictive value and diagnostic burden' BMC Infectious Diseases 2014: volume 14, issue 1, page 532

Walles and others. 'Pregnancy Outcomes in Women Screened for Tuberculosis Infection in Swedish Antenatal Care' Clinical Infectious Diseases 2024: volume 78, pages 125 to 132

Zwerling and others. 'TB screening in Canadian health care workers using interferon-gamma release assays' PLoS ONE 2012: volume 7, issue 8

Wrong study type (35 studies)

Ahmad and others. 'Latent tuberculosis infection among minor asylum seekers in Denmark' European Respiratory Journal 2020: volume 55, issue 1, page 1

Akkerman and others. 'Implementing tuberculosis entry screening for asylum seekers: the Groningen experience' European Respiratory Journal 2016: volume 48, issue 1, pages 261 to 264

Argel and others. 'Screening of refugees from Ukraine for TB: a TBnet survey' International Journal of Tuberculosis & Lung Disease 2024: volume 28, issue 4, pages 202 to 203

Arnesen and others. 'Economic models of LTBI screening in migrants: need for harmonization of approach' International Journal of Tuberculosis & Lung Disease 2017: volume 21, issue 9, page 954

Arrazola de Onate and others. 'Tuberculosis screening yield of asylum seekers in Europe' European Respiratory Journal 2016: volume 48, issue 4, pages 1,253 to 1,254

Bozorgmehr and others. 'Yield of tuberculosis screening in asylum-seekers by country of origin: analysis of screening data in a German federal state (2002-2015)' European Respiratory Journal 2017: volume 49, issue 4, page 4

Bozorgmehr and others. 'Tuberculosis screening in asylum seekers in Germany: a need for better data' The Lancet Public Health 2018: volume 3, issue 8, pages e359 to e361

Bozorgmehr and others. 'Using country of origin to inform targeted tuberculosis screening in asylum seekers: a modelling study of screening data in a German federal state, 2002-2015' BMC Infectious Diseases 2019: volume 19, issue 1, page 304

Coker and van Weezenbeek. 'Mandatory screening and treatment of immigrants for latent tuberculosis in the USA: just restraint?' The Lancet Infectious Diseases 2001: volume 1, issue 4, pages 270 to 276

Cookson and others. 'Impact of and response to increased tuberculosis prevalence among Syrian refugees compared with Jordanian tuberculosis prevalence: case study of a tuberculosis public health strategy' Conflict & Health [Electronic Resource] 2015: volume 9, page 18

de Onate and others. 'High-income countries and latent tuberculosis infection screening for migrants' The Lancet Infectious Diseases 2019: volume 19, issue 7, pages 690 to 691

de Vries and others. 'Tuberculosis screening yield of asylum seekers in Europe' European Respiratory Journal 2016: volume 48, issue 4, pages 1,255 to 1,256

de Vries and others. 'Low yield of screening asylum seekers from countries with a tuberculosis incidence of <50 per 100 000 population' European Respiratory Journal 2016: volume 47, issue 6, pages 1,870 to 1,872

Denholm and others. 'Immigration screening for latent tuberculosis infection' Medical Journal of Australia 2013: volume 199, issue 10, page 654

Ferro and others. 'Tuberculosis Screening of Ukrainian Refugees in Portugal' Acta Medica Portuguesa 2023: volume 36, issue 7, pages 535 to 336

Fiebig and others. 'Tuberculosis screening in asylum seekers in Germany, 2015: characteristics of cases and yield' European Respiratory Journal 2017: volume 50, issue 4, page 10

Griffin and Kelly. 'Immigration screening for latent tuberculosis infection' Medical Journal of Australia 2013: volume 199, issue 10, page 654

Hacker and others. 'TB screening of Ukrainian refugees in Germany' International Journal of Tuberculosis & Lung Disease 2023: volume 27, issue 8, pages 641 to 642

Harwood-Johnson and others. 'Community treatment of latent tuberculosis in child and adult refugee populations: outcomes and successes' Frontiers in Public Health 2023: volume 11, page 1,225,217

Kim and Kim. 'One Step toward a Low Tuberculosis-Burden Country: Screening for Tuberculosis Infection among the Immigrants and Refugees' Tuberculosis & Respiratory Diseases 2020: volume 83, issue 1, pages 104 to 105

Kohler and others. 'Tuberculosis screening in migrants to the EU/EEA and UK' European Respiratory Journal 2023: volume 62, issue 5, page 11

Menzies and others. 'Screening immigrants to Canada for tuberculosis: chest radiography or tuberculin skin testing?' CMAJ Canadian Medical Association Journal 2003: volume 169, issue 10, pages 1,035 to 1,036

Menzies and Schwartzman. 'Management of latent tuberculosis infection in immigrants' New England Journal of Medicine 2003: volume 348, issue 13, pages 1,289 to 1,292; author reply

Ormerod and others. 'Screening immigrants at risk of tuberculosis' British Medical Journal 1994: volume 308, issue 6,930, pages 720 to 721

Ormerod and others. 'Further evidence supporting programmatic screening for, and treatment of latent TB Infection (LTBI) in new entrants to the UK from high TB prevalence countries' Thorax 2013: volume 68, issue 3, page 201

Pareek and others. 'Community-based testing of migrants for infectious diseases (COMBAT-ID): impact, acceptability and cost-effectiveness of identifying infectious diseases among migrants in primary care: protocol for an interrupted time-series, qualitative and health economic analysis' British Medical Journal Open 2019: volume 9, issue 3, page e029188

Ritz and others. 'Tuberculosis in young refugees' Lancet 2015: volume 386, issue 10012, pages 2,475 to 2,476

Sandgren A and others. 'Tuberculosis transmission between foreign- and native-born populations in the EU/EEA: a systematic review' European Respiratory Journal 2014: volume 43, issue 4, pages 1,159

Sanneh and Al-Shareef. 'Effectiveness and cost effectiveness of screening immigrants schemes for tuberculosis (TB) on arrival from high TB endemic countries to low TB prevalent countries' African Health Sciences 2014: volume 14, issue 3, pages 663 to 671

Spruijt and others. 'The identification of prevalent tuberculosis disease through infection screening among high-risk migrants in the Netherlands' European Respiratory Journal 2022: volume 59, issue 5

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Annexe D. Data extraction tables

Abbreviations: BCG: Bacillus Calmette-Guérin, CI: confidence interval, CXR: chest X-ray, ICER: incremental cost-effectiveness ratio, IGRA: interferon gamma release assay, IQR: interquartile range, LTBI: latent TB infection, mL: millilitre, mm: millimetre, QFT: QuantiFERON test, SD: standard deviation, TB: tuberculosis, TST: tuberculin skin test

Table D.1. Studies of diagnostic accuracy

Study	Country, time period	Study type	Population	Case finding intervention(s)	Reference standard	Outcomes
Elliot 2018 (1)	Australia, 2007 to 2010	Diagnostic test accuracy	272 refugee children (under 15 years old) who arrived in the Illawarra-Shoalhaven region of Australia, between 2007 to 2010. 60 participants were excluded since did not have both IGRA and TST results available, leaving 212 (77%) eligible. Of the 272 children: 7% under 2 years old, 18% 2 to 4 year olds, 40% 5 to 9 years old and 35% 10 to 14 years old, 57% from Africa, 35% from Southeast Asia, 6% from Eastern Mediterranean, under 1% from Europe or the Western Pacific, 2% unknown location.	1. TST (intradermal injection of purified protein derivative) considered positive if induration was larger than 10 mm for all age groups. 2. IGRA (QuantiFERON Gold In-Tube) considered positive if interferon-gamma was more than 0.35 international units per mL	IGRA	Number of participants testing positive and negative by test: • TST negative, IGRA negative: 133 (62.7%) • TST negative, IGRA positive: 16 (7.5%) • TST positive, IGRA negative: 47 (22.2%) • TST positive, IGRA positive: 16 (7.5%) Number of participants testing positive and negative by test with BCG scar present: • TST negative, IGRA negative: 118 • TST negative, IGRA positive: 15 • TST positive, IGRA negative: 45 • TST positive, IGRA positive: 15 Number of participants testing positive and negative by test with BCG scar absent: • TST negative, IGRA negative: 15 • TST negative, IGRA positive: 1 • TST positive, IGRA negative: 2 • TST positive, IGRA positive: 1 Sensitivity and specificity: • sensitivity for children with BCG scar: 52% • specificity for children with BCG scar: 73% • sensitivity for children without BCG scar: 50% • specificity for children without BCG scar: 88% • overall sensitivity (calculated, not reported): 50% • overall specificity (calculated, not reported): 73.9% TST: positive in 63 (30%), 149 negative

Study	Country, time period	Study type	Population	Case finding intervention(s)	Reference standard	Outcomes
						IGRA: positive 32 (15%), 180 negative (5 of which tested inconclusive but were included in negative group for analysis, as testing was not repeated and the children were not treated)
Schneeberger Geisler 2010 (2)	Switzerland, 2004 to 2005 and 2007 to 2008	Diagnostic test accuracy	People seeking asylum entering Switzerland who were screened for LTBI, 21,727 from 2004 to 2005 who underwent CXR screening and 23,402 from 2007 to 2008 who underwent interview-based screening. (CXR group: 16,154 were men and 5,573 were women. Interview group 17,648: were men and 5,754 were women. Age range from 0 to over 54 years old. There were no significant differences as to age and sex between the 2 groups). Under 15s and pregnant women were excluded from CXR group. Those with repeat screening examinations were excluded from analysis.	1. CXR: categorised as either normal, abnormal, or not conducted. Individuals with abnormal CXRs were directed to clinics for additional evaluation. 2. Nurse led interviews, where the questions covered estimated TB prevalence in the country of origin (scored from 0 to 10 points), symptoms (up to 11 points), personal and family TB history (up to 2 points), and the overall assessment by the interviewing nurse (0 or 3 points). If the total score exceeded 10, or at the nurse's discretion, the person seeking asylum was referred to a clinician for further examination, which included a CXR, and if the results were abnormal, microbiological testing.	Culture	Number of cases of culture-confirmed pulmonary TB starting treatment within 90 days of screening procedure: CXR screening 2004 to 2005: 31 out of 21,727 (prevalence 14.3 per 10,000) - all 31 had abnormal CXR on screening. Interview-informed screening: 2007 to 2008: 29 of out 23,402 (prevalence 12.4 per 10,000) - only 16 of 29 were identified by screening, the remainder needed medical attention in the weeks that followed when they developed symptoms. Number of cases of culture-confirmed extra-pulmonary TB starting treatment within 90 days of screening procedure: CXR screening 2004 to 2005: 8 out of 21,727 Interview informed screening 2007 to 2008: 8 out of 23,402 CXR led to more diagnoses of pulmonary TB that remained unconfirmed by culture (32 compared to 8 for interview informed screening), meaning more treatment decisions had to be made based on radiographical and clinical findings. Median time from screen to treatment for: CXR screening: 6 days (range: 0 to 79 days). Interview informed screening: 25 days (range: 0 to 85 days). CXR for identifying pulmonary TB Sensitivity: 100% Specificity: 89.6% PLR: 9.99 (95% CI: 9.99 to 10)

Study	Country, time period	Study type	Population	Case finding intervention(s)	Reference standard	Outcomes
						NLR: 0.00 (95% CI: 0.00 to infinity) Interview informed screening for identifying pulmonary TB Sensitivity: 55.2% Specificity: 96% PLR: 13.7 (95% CI: 12.37 to 15.15) NLR: 0.5 (95% CI: 0.4 to 0.54)

Table D.2. Cost-effectiveness study

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
Marx 2021 (6)	Germany, 2017 to 2019	Indiscriminate screening compared to targeted screening thresholds of 20, 50, 150 and 250 cases per 100,000. Children, young adolescents (aged less than 15 years) and pregnant women were evaluated with TST or IGRA. People aged 15 years or over (who are not pregnant) were screened using clinical and CXR examination. Individuals who test positive with IGRA but with no diagnosis of active TB were assumed positive for LTBI and assumed to have received preventative TB treatment (600 milligrams of rifampicin, daily for 4 months).	Probabilistic decision-analytic model sampling from a population of people seeking asylum who were adolescents or young adults (aged 15 to 34 years). Hypothetical cohort of 30,000 to 45,000 people seeking asylum in Germany expected to arrive in Germany in 2022 from cohorts observed between 2017 to 2022. Estimated health system costs included the costs for administering and processing IGRA based tests, counselling, provision of TB preventative treatment and management of related adverse events in the public healthcare system. Costs were based on 2020 prices.. Future costs and health	Sensitivity of IGRA: 80% (95% CI: 75% to 84%) Specificity of IGRA: 98% (95% CI: 87% to 99%) (beta distribution)	Transition probabilities were sampled from published literature on studies conducted in Germany and other countries within the European Union. Assumptions for cases with LTBI: • probability of initiating preventative TB treatment: 70% (95% CI: 60% to 80%) • probability of completing preventative TB treatment: 70% (95% CI: 60% to 80%) • probability of reactivation of untreated LTBI: 5.3% (95% CI: 2.5% to 8.0%) • effectiveness of complete preventative TB treatment: 66% (95% CI: 43% to 89%) • effectiveness of incomplete preventative	Estimated that 17.5% of people seeking asylum entering Germany (95% CI: 14.2% to 21.6%) would have LTBI (6597 individuals, 95% CI: 4874 to 8832 individuals), and of these 346 (95% CI: 159 to 592) were estimated to develop TB due to the reactivation of LTBI post-immigration. Cost-effectiveness by LTBI screening threshold: LTBI screening threshold: ≥ 250 • total costs: €0.31 million (range: €0.20 to €0.42 million) • TB cases prevented: 16 (range: 7 to 32) • QALYs gained: 7.3 (range: 2.7 to 14.8) • incremental costs: €0.31 million (range: €0.20 to €0.42 million) • incremental TB cases prevented: 16 (range: 7 to 32) • incremental QALYs gained: 7.3 (range: 2.7 to 14.8)

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
			benefits were discounted by 3% annually. QALYs were calculated to estimate health impact of LTBI screening and preventative TB treatment. ICERs were calculated for introduction of LTBI screening and preventative TB treatment at different TB incidence thresholds. 1,000 monte carlo simulations were run to account for uncertainty in model parameters. Willingness to pay thresholds were estimated at €81,300 (twice the gross domestic product per capita for Germany) and international benchmarks recommended by the National institute for health and care excellence (NICE) €34,000, and €87,600 often used for health economic analysis in the United States. One-way sensitivity analysis was conducted at an incidence threshold of equal to or more than 150 cases per 100,000, to assess		TB treatment: 25% (95% CI: 15% to 35%) • effectiveness of preventative TB treatment for rifampicin-resistant LTBI: 0% (95% CI: –) • probability of preventative TB treatment drug-toxicity events not requiring hospitalization: 2% (95% CI: 1% to 3%) • probability of preventative TB treatment drug-toxicity events requiring hospitalization: 0.003% (95% CI: 0.0001% to 0.006%) Cost parameters: • cost for performing IGRA including laboratory fees (€): €47.03 (95% CI: €37.62 to €56.43) • cost for counselling an IGRA-positive individual for preventative TB treatment (€): €27.34 (95% CI: €21.87 to €32.80) • cost for physician consultation during preventative TB treatment (fee for 2 quarters of a year, €):	• ICER (per TB case prevented): €22,300 (range: €8,200 to €50,000) • ICER (per QALY gained): €51,000 (range: €18,000 to €114,100) LTBI screening threshold: ≥ 200 • total costs: €0.56 million (range: €0.37 to €0.87 million) • TB cases prevented: 29 (range: 12 to 56) • QALYs gained: 13.2 (range: 4.9 to 26.3) • incremental costs: €0.25 million (range: €0.17 to €0.35 million) • incremental TB cases prevented: 13 (range: 5 to 25) • Incremental QALYs gained: 5.8 (range: 2.1 to 11.6) • ICER (per TB case prevented): €23,300 (range: €8,600 to €52,200) • ICER (per QALY gained): €53,300 (range: €19,100 to €122,500) LTBI screening threshold: ≥ 150 • total costs: €1.10 million (range: €0.74 to €1.52 million) • TB cases prevented: 56 (range: 23 to 105) • QALYs gained: 24.9 (range: 9.3 to 49.9) • incremental costs: €0.54 million (range: €0.37 to €0.74 million) • incremental TB cases prevented: 26 (range: 11 to 50)

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
			additional health benefits accrued from prevention of onward transmission from people seeking asylum with LTBI reactivation (secondary TB would arise in contacts of equal age compared with the index case (average age at LTBI reactivation: 31 years), an average serial interval of 8 to 10 years, and similar reductions in quality of life due to TB, and case fatality compared to those estimated for the index case). Average numbers of secondary cases were assumed to range between 0.1 to 5 per index case of reactivated LTBI.		€34.72 (95% CI: €27.78 to €41.67) • cost for laboratory tests prior to and during preventative TB treatment (€): €16.18 (95% CI: €12.95 to €19.42) • cost for 4-months of rifampicin-based preventative TB treatment (€): €330.39 (95% CI: €322.91 to €337.87) • factor for discounting cost for incomplete preventative TB treatment: 37.5% (95% CI: 25.0% to 50.0%) • in-patient management of drug adverse events of preventative TB treatment (€): €2553.10 (95% CI: €1702.07 to €3404.13) • average costs for managing TB disease (€): €8947.65 (95% CI: €7158.12 to €10,737.17) Quality of life parameters: • quality of life weight for active TB: 0.67 • quality of life weight for LTBI: 1.00 • quality of life weight for preventative TB	• incremental QALYs gained: 11.8 (range: 4.4 to 23.7) • ICER (per TB case prevented): €24,500 (range: €9,200 to €53,700) • ICER (per QALY gained): €55,900 (range: €20,200 to €128,200) LTBI screening threshold: ≥ 100 • total costs: €1.19 million (range: €0.80 to €1.63 million) • TB cases prevented: 60 (range: 24 to 113) • QALYs gained: 26.6 (range: 9.9 to 53.5) • incremental costs: €0.09 million (range: €0.06 to €0.12 million) • incremental TB cases prevented: 4 (range: 2 to 7) • incremental QALYs gained: 1.7 (range: 0.6 to 3.3) • ICER (per TB case prevented): €27,100 (range: €10,500 to €59,800) • ICER (per QALY gained): €62,000 (range: €23,200 to €142,000) LTBI screening threshold: ≥ 50 • total costs: €1.66 million (range: €1.13 to €2.27 million) • TB cases prevented: 75 (range: 31 to 142) • QALYs gained: 33.6 (range: 12.5 to 67.1) • incremental costs: €0.47 million (range: €0.33 to €0.66 million)

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
					treatment-related drug toxicity not requiring hospitalization: 0.75 • quality of life weight for preventative TB treatment-related drug toxicity requiring hospitalisation: 0.50 Other parameters: • average age at immigration: 24 years • life expectancy at immigration (years): 59 years • average time to LTBI reactivation (years): 7.0 years (95% CI: 6.0 to 8.0 years) • TB case-fatality ratio: 1.5% (95% CI: 1.0% to 2.0%) Cost estimates were derived from a published costing study that estimated the cost of non-multidrug-resistant TB disease and contact investigation in Germany.	• incremental TB cases prevented: 16 (range: 6 to 30) • incremental QALYs gained: 6.9 (range: 2.6 to 13.8) • ICER (per TB case prevented): €36,000 (range: €14,700 to €78,400) • ICER (per QALY gained): €82,400 (range: €31,600 to €184,700) LTBI screening threshold: ≥ 20 • total costs: €2.04 million (range: €1.39 to €2.78 million) • TB cases prevented: 84 (range: 34 to 157) • QALYs gained: 37.7 (range: 14 to 74.7) • incremental costs: €0.38 million (range: €0.26 to €0.54 million) • incremental TB cases prevented: 9 (range: 4 to 18) • incremental QALYs gained: 4.1 (range: 1.5 to 8.7) • ICER (per TB case prevented): €48,700 (range: €19,800 to €106,700) • ICER (per QALY gained): €111,800 (range: €42,700 to €251,000) LTBI screening threshold: None • total costs: €2.91 million (range: €2.02 to €4.02 million) • TB cases prevented: 100 (range: 41 to 187) • QALYs gained: 44.8 (range: 16.8 to 88.3)

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
						• incremental costs: €0.87 million (range: €0.6 to €1.25 million) • incremental TB cases prevented: 16 (range: 5 to 35) • incremental QALYs gained: 7.1 (range: 2.2 to 16.3) • ICER (per TB case prevented): €68,000 (range: €26,100 to €158,700) • ICER (per QALY gained): €156,300 (range: €54,500 to €373,300) Secondary analysis estimated that one secondary TB case for every 5 TB reactivations (average number: 0.2), incidence thresholds above 100 (or higher) resulted in less than €55,200 incremental cost per additional QALY gained.
Wahedi 2020 (7)	Germany, 2002 to 2015	1. Indiscriminate screening (84,505 people seeking asylum and 73 cases of TB): all arriving people seeking asylum (excluding persons under the age of 16 years, and pregnant women) undergo a symptom-based questionnaire and CXR. Data was observed from countries with greater than or equal to 5 cases identified during screening or greater than or equal to 5,000	Deterministic decision model (cycle length and horizon time not applicable). The threshold was varied between no threshold, 50, 100, 150, 200, 250 per 100,000 cases of TB in country of origin. Total programme costs consisted of: screening costs, diagnostic work up (doctors appointment, culture, microscopy), public health measures (contact and source tracing) and treatment costs	Specificity of CXR: 0.89 (SE: 0.01276), beta PAS distribution. Sensitivity not reported.	Screening data taken from a German federal state between 2002 to 2015 was used to assume the proportion of culture-positive cases to be 62% and 82% for actively and passively found cases respectively. Proportion of hospitalised cases (as well as rates differentiated by case finding strategy) were assumed to be 73% for actively found and 78% for passively found, derived from the Robert Koch-Institute (a central public health body in Germany).	Introducing a screening threshold of more than or equal to 50 per 100,000 TB cases resulted in 54,468 people seeking asylum from Macedonia, Syria, Kosovo and Iraq not being screened. 30,037 people seeking asylum remained at this threshold, with discriminate screening identifying 79.5% (58) of TB cases and missing 20.5% (15) of TB cases, which with an assumed transmission rate of 0.78 would cause an additional 4 cases of TB. Costs of case finding strategies Indiscriminate Screening Total costs of screening: €2,702,237 Annual cost of screening: €193,017 Costs per identified case: €37,017

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
		cases screened and country-level estimates of TB available in World Health Organisation database. Screening data was only included for persons aged 18 years or older. 2. Targeted screening (hypothetical decision tree model): Varying thresholds of TB incidence per 100,000 in people seeking asylum's home country of original were used to allocate hypothetical people seeking asylum to either the screening or no screening arm with CXR (if CXR is abnormal, it is followed up by clinical examination, microscopy, sputum culture). If in the screening arm and diagnosed with active TB, the person would begin treatment. 3. 'Do nothing' strategy (no screening, passive identification of cases). People seeking asylum with active TB not detected from screening are assumed to become	(medications, inpatient and outpatient costs), covering direct costs only. Treatment costs and public health measures were taken from a German costing study. Technical and diagnostic data unit costs were taken from the statutory insurance scheme. Medication costs were based on standard therapy regimens and German standardised prices. All unit costs were provided in Euros from 2019. Sensitivity analysis was performed to compare between indiscriminate screening and discriminate screening with a threshold of more than or equal to 50/100,000 TB cases: Deterministic Sensitivity Analyses: 1. Univariate Analyses: - assessed variations in transmission rate, specificity of chest X-ray, rates of hospitalisation, and culture positivity. - used 95% confidence intervals or logical approximations (for example, more than or less than 30% of base case values).		Static transmission model using transmission rates from published literature (a clustering study conducted in Germany), calculated by (n-1) method: - undetected cases or cases with long latency periods were excluded - one passively detected case was assumed to infect 5 contacts, of which 5 to 15% are considered to progress to active disease over their lifetime, (causing a further 0.5 cases on average) Other model assumptions: - culture positivity of actively found TB cases: 0.65 (SD 0.0128, beta distribution) - culture positive of passively found TB cases: 0.84 (SD 0.0019, beta distribution) - hospitalisation of actively found TB cases: 0.73 (SD 0.0041, beta distribution) - hospitalisation of actively of passively found TB cases: 0.78 (SD 0.00018, beta distribution) - mean duration of hospital stay: 13.26 days Disease prevalence in study population yields per 1000: Macedonia 0.29 (SD 0.00022, beta distribution) Syria 0.29 (SD 0.00014, beta distribution) Cosovo 0.34 (SD 0.00014, beta distribution)	Costs per newly arrived people seeking asylum: €32 Discriminate screening threshold of greater than or equal to 50 per 100,000 Total costs of screening: €986,853 Annual cost of screening: €70,490 Costs per identified case: €17,015 Costs per newly arrived people seeking asylum: €12 Total programme costs of case finding strategies (includes treatment and public health costs of cases found and missed by screening) No Screening (reference strategy) Cases found: 0 ICER when compared to next higher threshold: Not applicable Cases prevented through screening: 0.0 ICER when compared to next higher threshold: Not applicable Total programme costs: €658,331.90 Total screening costs: Not applicable Costs per case found actively: Not applicable Costs per case found passively: €9,018.25 Number of cases found passively: 73 Indiscriminate Testing Cases found: 73 ICER when compared to next higher threshold: €110,050.18 Cases prevented through screening: 56.9 ICER when compared to next higher threshold: €141,089.98 Total programme costs: €3,046,031.87

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
		symptomatic and detected passively.	2. Multivariate Analyses: - assessed variations in hospitalisation rates, culture positivity, transmission rates, different severity levels of hospitalised cases. - considered changes in reimbursement schemes (private insurance fees) and extreme cost scenarios (maximum or minimum estimates). Probabilistic Sensitivity Analysis: - assigned beta-distributions to the specificity of CXR and TB yields due to their variability between 0 and 1. - used Bayesian Poisson regression to obtain 95% credible intervals for country-specific yield. - applied gamma distribution to length of hospital stay. - created triangular distributions for technical costs due to lack of uncertainty estimates, with minimal and maximal assumptions. - conducted 2 probabilistic scenarios for unit costs, lower-bound estimate based on statutory insurance providers, higher-bound estimate based on private providers.		Iraq 0.10 (SD 0.00012, beta distribution) Russia 1.65 (SD 0.00076, beta distribution) Eritrea 4.64 (SD 0.00157, beta distribution) Gambia 2.58 (SD 0.00061, beta distribution) Afghanistan 0.27 (SD 0.00020, beta distribution) Georgia 2.36 (SD 0.00109, beta distribution) Cameroon 2.00 (SD 0.00092, beta distribution) Pakistan 1.37 (SD 0.00053, beta distribution) Somalia 6.83 (SD 0.00263, beta distribution)	Total screening costs: €110,050.18 Costs per case found actively: €41,726.46 Costs per case found passively: N/A Number of cases found passively: 0 Threshold: 50/100,000 Cases found: 58 ICER when compared to next higher threshold: €15,436.24 Cases prevented through screening: 45.2 ICER when compared to next higher threshold: €19,790.05 Total programme costs: €1,395,279.10 Total screening costs: €15,436.24 Costs per case found actively: €21,724.23 Costs per case found passively: €9,018.25 Number of cases found passively: 15 Threshold: 150/100,000 Cases found: 53 ICER when compared to next higher threshold: €14,040.22 Cases prevented through screening: 41.3 ICER when compared to next higher threshold: €18,000.29 Total programme costs: €1,318,097.89 Total screening costs: €14,040.22 Costs per case found actively: €21,466.66 Costs per case found passively: €9,018.25 Number of cases found passively: 20 Threshold: 200/100,000 Cases found: 24 ICER when compared to next higher threshold: €10,980.69 Cases prevented through screening: 18.7

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
			- medication costs were treated as fixed costs. Effectiveness outcome measured was incremental cost effectiveness (ICER) is measured as cost per case of pulmonary TB found and cost per case prevented.			ICER when compared to next higher threshold: €14,077.81 Total programme costs: €910,931.38 Total screening costs: €10,980.69 Costs per case found actively: €19,543.22 Costs per case found passively: €9,018.25 Number of cases found passively: 49 Threshold: 250/100,000 Cases found: 14 ICER when compared to next higher threshold: €10,199.47 Cases prevented through screening: 10.9 ICER when compared to next higher threshold: €13,076.24 Total programme costs: €801,124.43 Total screening costs: €10,199.47 Costs per case found actively: €19,217.71 Costs per case found passively: €9,018.25 Number of cases found passively: 59 Deterministic Sensitivity Analysis: Largest changes in ICERs were due to changes in: Country-specific prevalence: -60% to +180% Specificity of CXR: -13% to +76% Reimbursement scheme: +42% Modelled frequency of diagnostics and technical costs: 5% to 47% All other parameters had only small effects on the cost-effectiveness of screening. Probabilistic Sensitivity Analysis: Base case represents a conservative estimate; most points show a less favourable ICER.

Study	Country, time period	Case finding intervention(s)	Model method and utilities	Sensitivity and specificity of test(s)	Other model parameters	Outcomes
						Probability for cases to be found at costs below €100,000 per additional case found by screening was low in all scenarios (p=0.12 to 0.35). Different transmission rates had low impact on cost-effectiveness.

Table D.3. Non-randomised, quasi-experimental study

Study	Country, time period	Case finding intervention(s)	Study methods	Outcomes
Russo 2023 (4)	Italy, May 2019 to May 2022	1. IGRA-only strategy (n=358 people seeking asylum and undocumented migrants): Quantiferon-TB Gold Plus kit, performed according to manufacturer's protocol. If positive, participants received CXR and clinical evaluation to assess need for preventative treatment. 2. Sequential strategy (n=237 people seeking asylum and undocumented migrants): TST (intradermal injection of 5 tuberculin units on the volar surface of the forearm, induration evaluation at 48 to 72 hours, positive if 10mm or more), followed by IGRA as above if TST positive, and CXR if IGRA positive. In the case of a positive IGRA and negative CXR, participants received clinical evaluation to assess the need for preventative treatment. .	Non-randomised, quasi-experimental design. A shortage of TST during the study resulted in the loss of randomisation to recruit participants to the TST arm (sequential strategy) and uneven numbers in the 2 study arms. Population: 91.4% male, median age at the time of arrival: 26 years (IQR: 22 to 32 years), 65% were from countries where TB incidence exceeded 150 per 100,000. Participants were excluded if they displayed signs of active TB at initial clinical evaluation, case finding strategies were to identify LTBI only. Only direct individual medical costs were included. Effectiveness was measured as the number of people starting preventative treatment, under the assumption that treating tuberculosis infection is cost-effective. For both study arms, the average cost effectiveness ratio (ACER) was calculated as the ratio between the total cost of the intervention and the number of people who started TB treatment. Total cost included the costs of TST, IGRA, clinical evaluation, CXR, preliminary blood tests for preventive treatment, (from the healthcare tariff list provided by the Lombardy region), CXR examinations performed for clinical indication (presence of cough lasting more than 2 weeks, fever, night sweats, and/or weight loss).	Rate of completing case finding strategy (informs refusal of case finding intervention): IGRA only strategy: 328 out of 358, 91.6% Sequential strategy: 202 out of 237 85.2% adjusted incidence rate ratio for screening completion: 1.08 (95% CI: 1.01 to 1.14, p=0.019). Adjusted for: sex, age at first test, TB incidence in country of origin. Proportion of eligible participants starting preventative treatment similar between the groups (informs additional cases identified and treated): IGRA only strategy: 18.2% (65 cases) Sequential strategy: 21.9% (52 cases) adjusted incidence rate ratio for preventative treatment initiation: 0.83 (95% CI: 0.60 to 1.15, p=0.272). Adjusted for: sex, age at first test, TB incidence in country of origin. Median time to complete screening and evaluation process for those with a positive result IGRA only strategy: 46 days Sequential strategy: 74 days (p=0.002) Total costs were estimated to be €26,792.30 for the IGRA alone strategy (€74.84 per person undergoing screening) and

Study	Country, time period	Case finding intervention(s)	Study methods	Outcomes
			The following costs were not considered in the analysis: societal costs, treatment provision, follow-up, managing side effects. Treatment outcome also was not considered. A multivariable poisson regression analysis was also used to examine the association between initiation of preventative treatment, and screening strategy, sex, age, and TB incidence in country of origin.	€13,655.90 (€57.62 per person undergoing screening) for the TST followed by IGRA strategy. Average cost effectiveness ratio (ACER: ratio between the total cost of the intervention and the number of people who started TB treatment) lower in the sequential strategy (262.61) compared to the IGRA only strategy (412.19), indicating the sequential strategy was more cost effective.

Table D.4. Retrospective cohort studies

Study	Country, time period	Study type	Population	Case finding intervention(s)	Outcomes
Lim 2021 (3)	Canada, August 2017 to February 2020	Retrospective cohort	471 refugees who arrived in Calgary, Alberta, Canada, and were assessed at the Mosaic Refugee Health Clinic. Thirteen participants were excluded (either under 2 years old or had active TB at initial assessment), leaving 458 (97%) eligible. 240 subjects were in the sequential screening cohort received TST and then confirmatory IGRA. 231 subjects within the solo-QFT cohort received IGRA (QuantiFERON-TB Gold Plus) only. (Of the 471 refugees: 54% male, mean age 24.8 years, no significant difference between cohorts. Of the 2 step cohort: 32% Eritrea, 14% Ethiopia, 14% Nigeria, 9% Iraq, 8% Sudan, 6% Venezuela, 5% Syria, 4% Angola, 3% Somalia, 3% Pakistan, 2% Afghanistan; Of the QFT cohort: 30% Eritrea, 16% Sudan, 14% Afghanistan, 9% Somalia, 8% Iraq, 5% Honduras, 5% South Sudan, 4% Democratic Republic of Congo, 4% Myanmar, 3% Ethiopia, 2% Vietnam)	1. 2 step case finding: TST followed by IGRA (QuantiFERON-TB Gold Plus) if the TST was positive. TST considered positive if induration was larger than 10mm. IGRA considered positive according to manufacturer's specifications. 2. IGRA only. Deemed positive as described above. Positive IGRA triggered a CXR in both groups and referral to local TB clinics for further evaluation	Additional cases identified: for the 2 step case finding cohort 20 subjects were diagnosed with LTBI, compared to 41 in the solo-QFT cohort (p=0.002) Additional cases treated: for sequential screening cohort 19 attended TB clinic. 16 individuals began treatment, 14 completed treatment. for the solo-QFT group 35 subjects attended TB clinic, 33 started treatment and 29 completed treatment. No significant difference in treatment completion between cohorts (p=0.8929) Refusal of case finding strategy: difference in the proportion completing screening was 0.31, in favour of IGRA strategy (p<0.01), adjusted OR of 3.74 (95% CI 2.30, 6.09; p<0.001), where 54% (129/240) completed LTBI screening in the sequential screening group and 85% (197/231) of the IGRA group completed screening. Time to completing screening was shorter in the IGRA group (difference 16.5 days, p<0.01, 95% CI: 9.3 to 23.7).
Walters and Sullivan 2016 (5)	US, November 2009 to October 2012	Retrospective cohort	2,244 refugees (44% female, 32% between 6 to 17 years of age, 68% between 18 to 49 years of age, 36% Asian or pacific islander,	1.TST where a positive test was defined as induration more or equal to 10 mm	Of the TST only: 420 of 1,215 (35%) tested positive and were referred to TB clinic, of which 393 (94%) were diagnosed with TB, 333 (85%) were candidates for LTBI

Study	Country, time period	Study type	Population	Case finding intervention(s)	Outcomes
			27% black, 13% Hispanic, 14% white, 10% other/unavailable) met inclusion criteria. 1,215 refugees (mean age 23.8, SD 11.9) were screened for LTBI between November 2009 to April 2011 in the TST only period 1,029 (mean age 25.8, SD 11.3) were screened in the IGRA only period between May 2011 to October 2012. Excluded if suspected or confirmed active TB cases or if failed to return for repeat QFT (IGRA) test during the QFT test recall in October 2012.	2. IGRA (QuantiFERON-TB Gold) Those with a positive test were referred on for additional evaluation at TB clinic.	treatment, 221 (66%) started LTBI treatment, 154 (70%) completed LTBI treatment. Of the IGRA only: 346 of 1,029 (34%) tested positive and were referred to TB clinic of which 287 (83%) were diagnosed with TB, 215 (75%) were a candidate for LTBI treatment, 160 (74%) started LTBI treatment, 107 (67%) completed LTBI treatment. Additional cases found and treated: The proportion of clients diagnosed with LTBI was higher in the TST only period (393 diagnosed/420 evaluated, 94%) than the IGRA only period (287 diagnosed/346 evaluated, 83%) (p<0.0001). The proportion of patients who were candidates for treatment was higher in TST only (333/393, 85%) compared to IGRA only (215/287, 75%), (p=0.001) and those who started treatment: 221/333, 66% in TST only, 160/215, 74% in IGRA only (p=0.046). After controlling for age and immigration class, refugees who were tested with IGRA were more likely to start treatment than those tested with TST (adjusted odds ratio 1.53; 1.02–2.29; p = 0.040). No cases of active TB were identified during the follow up period, therefore measures of diagnostic accuracy such as sensitivity and specificity could not be calculated.

Annexe E. Risk of bias assessments

Table E.1. QUADAS-2 risk of bias assessment

Study	1. Could the selection of patients have introduced bias?	2. Could the conduct or interpretation of the index test have introduced bias?	3. Could the reference standard, its conduct, or its interpretation have introduced bias?	4. Could the patient flow have introduced bias?	Notes
Elliot and others (1)	Low risk	Low risk	High risk	Low risk	Q3: No gold standard for TB testing, IGRA as a reference standard may not accurately identify latent TB cases. Q4: 60 participants excluded due to missing data.
Schneeberger Geisler and others (2)	Low risk	Low risk	Low risk	High risk	Q4: CXR and symptom-based interviews were conducted in 2 separate time periods in 2 different populations.

QUADAS-2 questions:

Domain 1: Patient selection
Was a consecutive or random sample of patients enrolled?
Was a case-control design avoided?
Did the study avoid inappropriate exclusions?
Could the selection of patients have introduced bias?
Is there concern that the included patients do not match the review question?

Domain 2: Index test(s)
Were the index test results interpreted without knowledge of the results of the reference standard?
If a threshold was used, was it pre-specified?
Could the conduct or interpretation of the index test have introduced bias?
Is there concern that the index test, its conduct, or interpretation differ from the review question?

Domain 3: Reference standard
Is the reference standard likely to correctly classify the target condition?
Were the reference standard results interpreted without knowledge of the results of the index test?
Could the reference standard, its conduct, or its interpretation have introduced bias?
Is there concern that the target condition as defined by the reference standard does not match the review question?

Domain 4: Flow and timing
Was there an appropriate interval between index test(s) and reference standard?
Did all patients receive a reference standard?
Did patients receive the same reference standard?
Were all patients included in the analysis?
Could the patient flow have introduced bias?

Table E.2. NICE Economic critical appraisal checklist risk of bias assessment, Section 1: Applicability

Abbreviations: CXR: chest X-ray, ICER: incremental cost effectiveness analysis, IGRA: interferon gamma release assay, NA, not applicable, TST: tuberculin skin test

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Overall judgement	Comments
Marx and others (6)	Yes	Yes	Partly	Yes	Yes	Partly	Yes	Partially applicable	German context, discounting 3% (not NICE 3.5% recommended)
Wahedi and others (7)	Yes	Yes	Partly	Yes	Yes	No	No	Partially applicable	German context, no discounting (but model only looks at one time-point), no QALYs calculated.

Questions for the NICE Economic critical appraisal checklist, Section 1: Applicability

1. Is the study population appropriate for the review question?
2. Are the interventions appropriate for the review question?
3. Is the system in which the study was conducted sufficiently like the current UK context?
4. Is the perspective for costs appropriate for the review question?
5. Is the perspective for outcomes appropriate for the review question?
6. Are all future costs and outcomes discounted appropriately?
7. Are quality-adjusted life years (QALYs), derived using NICE's preferred methods, or an appropriate social care-related equivalent used as an outcome? If not, describe rationale and outcomes used in line with analytical perspectives taken (item Q5 above).

Table E.3. NICE Economic critical appraisal checklist risk of bias assessment, Section 2: Study limitations

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Overall judgement	Comments
Marx and others (6)	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Minor limitations	
Wahedi and others (7)	No	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Potentially serious limitations	Q1 & 2: model is deterministic, not a markov model, does not account for uncertainty in moving between health states (for example does not account for the potential of re-infection) Q6: Does not account for the cost of cases missed by introducing a screening threshold

Questions for the NICE Economic critical appraisal checklist, Section 2: Study limitations

1. Does the model structure adequately reflect the nature of the topic under evaluation?
2. Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?
3. Are all important and relevant outcomes included?
4. Are the estimates of baseline outcomes from the best available source?
5. Are the estimates of relative intervention effects from the best available source?
6. Are all important and relevant costs included?
7. Are the estimates of resource use from the best available source?
8. Are the unit costs of resources from the best available source?
9. Is an appropriate incremental analysis presented or can it be calculated from the data?
10. Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?

11. Has no potential financial conflict of interest been declared?

Note that in the NICE Economic critical appraisal checklist, ‘minor limitations’ is used both for studies that meet all quality criteria, and for studies that fail to meet one or more quality criteria but this is unlikely to change the conclusions about cost effectiveness.

Table E.4: Risk of bias in non-randomised studies of interventions (ROBINS-I)

Abbreviations: not applicable (NA), no information (NI), potential direction (PD), probably no (PN), probably yes (PY), risk of bias (RoB)

Bias due to confounding:

Study	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	RoB	PD	Notes
Lim and others (3)	PY	No	NA	PN	NA	No	NA	NA	Moderate	Unpredictable	Has adjusted for gender, refugee status, origin by TB incidence and case finding test method. Unmeasured confounding may still impact results.
Walters and others (5)	Yes	No	NA	PY	PY	No	NA	NA	Moderate	Unpredictable	The study adjusted for age, race/ethnicity, immigration class and region of birth, however other confounding variables may not have been measured in the analysis (such as changes in healthcare practices over time). Race and ethnicity not a direct measure of socio-economic deprivation (hence PY for 1.5). Unmeasured confounding may still impact results.
Russo and others (4)	Yes	No	NA	PY	PY	No	NA	NA	Serious	Unpredictable	Randomisation not possible in this study due to TST shortage. Confounding variables adjusted for included age at first test, sex, study arm assignment, TB incidence in country of origin. Unmeasured confounding may still impact results.

Bias in selection of participants into the study:

Study	2.1	2.2	2.3	2.4	2.5	RoB	PD	Notes
Lim and others (3)	No	NA	NA	NI	NA	Low	NA	
Walters and others (5)	No	NA	NA	PY	NA	Low	NA	The authors did not explicitly report that the start of follow-up and the start of the intervention coincided for all participants, but this is assumed.
Russo and others (4)	No	NA	NA	Yes	NA	Low	NA	None

Bias in classification of interventions:

Study	3.1	3.2	3.3	RoB	PD	Notes
Lim and others (3)	Yes	Yes	No	Low	NA	
Walters and others (5)	Yes	Yes	No	Low	NA	
Russo and others (4)	Yes	Yes	Yes	Moderate	Unpredictable	Non-randomised assignment due to TST availability could indeed mean that the classification of intervention status might have been influenced by factors related to

Study	3.1	3.2	3.3	RoB	PD	Notes
						the participants' characteristics, however the tests are objective measurements so unlikely to have a large impact.

Bias due to deviations from intended interventions:

Study	4.1	4.2	4.3	4.4	4.5	4.6	RoB	PD	Notes
Lim and others (3)	Yes	Yes	Unclear	No	No	No	Low	NA	54% (129/240) completed LTBI case finding in the 2 step case finding group and 85% (197/231) of the solo-QFT group completed case finding.
Walters and others (5)	No	NA	NA	Yes	Yes	NA	Low	NA	None
Russo and others (4)	No	NA	Yes	No	Yes	Yes	Serious	NA	For Arm 1, the intervention was successfully implemented as planned. For Arm 2, the intervention was partially implemented due to the unavailability of TST. However, study arm was adjusted for in the regression analysis.

Bias due to missing data:

Study	5.1	5.2	5.3	5.4	5.5	RoB	PD	Notes
Lim and others (3)	No	No	No	NA	NA	Low	NA	54% (129/240) completed LTBI case finding in the 2 step case finding group and 85% (197/231) of the IGRA group completed case finding
Walters and others (5)	PY	Yes	PN	No	No	Moderate	NA	24 participants explicitly from the post-QFT period were excluded because of the test-kit recall. 2 participants were excluded because the tests were cancelled and they did not return for a re-test. 156 participants were excluded due to their involvement in early pilot projects (primarily from pre-IGRA assignment group). Missing data is uniformly distributed across the pre-IGRA and post-IGRA periods. No statistical analysis (such as multiple imputation or sensitivity analysis) performed to account for missing data.
Russo and others (4)	Yes	No	No	NA	NA	Low	NA	None

Bias in measurement of outcomes:

Study	6.1	6.2	6.3	6.4	RoB	PD	Notes
Lim and others (3)	PY	Yes	Yes	NI	Serious	Unpredictable	
Walters and others (5)	PY	Yes	Yes	NI	Moderate	Unpredictable	
Russo and others (4)	Yes	Yes	Yes	NI	Moderate	Unpredictable	

Bias in selection of the reported result:

Study	7.1	7.2	7.3	RoB	PD	Notes
Lim and others (3)	No	No	N	Low	NA	
Walters and others (5)	No	No	No	Low	NA	None
Russo and others (4)	No	No	No	Low	NA	None

Overall bias:

Study	RoB	PD
Lim and others (3)	Serious	Bias towards underestimation of 2 step case finding
Walters and others (5)	Moderate	Unpredictable
Russo and others (4)	Serious	Unpredictable

Signalling questions

1.1 Is there potential for confounding of the effect of intervention in this study?
1.2. Was the analysis based on splitting participants' follow up time according to intervention received? If N/PN, answer questions relating to baseline confounding (1.4 to 1.6)
1.3. Were intervention discontinuations or switches likely to be related to factors that are prognostic for the outcome? If Y/PY, answer questions relating to both baseline and time-varying confounding (1.7 and 1.8)
1.4. Did the authors use an appropriate analysis method that controlled for all the important confounding domains?
1.5 If Y/PY to 1.4: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?
1.6. Did the authors control for any post-intervention variables that could have been affected by the intervention?
1.7. Did the authors use an appropriate analysis method that controlled for all the important confounding domains and for time-varying confounding?
1.8. If Y/PY to 1.7: Were confounding domains that were controlled for measured validly and reliably by the variables available in this study?
2.1. as selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention? (If N/PN to 2.1: go to 2.4)
2.2 If Y/PY to 2.1: Were the post-intervention variables that influenced selection likely to be associated with intervention?
2.3 If Y/PY to 2.2: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?
2.4. Do start of follow-up and start of intervention coincide for most participants?
2.5. If Y/PY to 2.2 and 2.3, or N/PN to 2.4: Were adjustment techniques used that are likely to correct for the presence of selection biases?
3.1 Were intervention groups clearly defined?
3.2 Was the information used to define intervention groups recorded at the start of the intervention?
3.3 Could classification of intervention status have been affected by knowledge of the outcome or risk of the outcome?
4.1. Were there deviations from the intended intervention beyond what would be expected in usual practice?
4.2. If Y/PY to 4.1: Were these deviations from intended intervention unbalanced between groups and likely to have affected the outcome?

If your aim for this study is to assess the effect of starting and adhering to intervention, answer questions 4.3 to 4.6
4.3. Were important co-interventions balanced across intervention groups?
4.4. Was the intervention implemented successfully for most participants?
4.5. Did study participants adhere to the assigned intervention regimen?
4.6. If N/PN to 4.3, 4.4 or 4.5: Was an appropriate analysis used to estimate the effect of starting and adhering to the intervention?
5.1 Was outcome data available for all, or nearly all, participants?
5.2 Were participants excluded due to missing data on intervention status?
5.3 Were participants excluded due to missing data on other variables needed for the analysis?

5.4 If PN/N to 5.1, or Y/PY to 5.2 or 5.3: Are the proportion of participants and reasons for missing data similar across interventions?
5.5 If PN/N to 5.1, or Y/PY to 5.2 or 5.3: Is there evidence that results were robust to the presence of missing data?
6.1 Could the outcome measure have been influenced by knowledge of the intervention received?
6.2 Were outcome assessors aware of the intervention received by study participants?
6.3 Were the methods of outcome assessment comparable across intervention groups?
6.4 Were any systematic errors in measurement of the outcome related to intervention received?

Is the reported effect estimate likely to be selected, on the basis of the results, from...
7.1. …multiple outcome measurements within the outcome domain?
7.2 …multiple analyses of the intervention-outcome relationship?
7.3 ... different subgroups?

Acronyms

Acronym	Term
BCG	Bacillus Calmette-Guérin
CI	confidence interval
CXR	chest X-ray
HIV	human immunodeficiency virus
ICER	Incremental cost-effectiveness ratio
IGRA	Interferon Gamma Release Assay
IQR	interquartile range
LTBI	detection of latent TB infection
MDR-TB	multidrug resistant TB
mL	millilitre
Mm	millimetre
NICE	National Institute for Health and Care Excellence
QFT	QuantiFERON test
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies
QUALY(s)	quality-adjusted life year(s)
SD	standard deviation
TB	tuberculosis
TST	tuberculin skin test
USD	US dollars ($)
WHO	World Health Organization

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