

Interventions to improve latent and active tuberculosis treatment completion rates in underserved groups in low incidence countries

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BMJ Open Interventions to improve latent and active tuberculosis treatment completion rates in underserved groups in low incidence countries: a scoping review

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ABSTRACT

Background People in underserved groups have higher rates of tuberculosis (TB) and poorer treatment outcomes compared with people with no social risk factors.

Objectives This scoping review aimed to identify interventions that improve TB treatment adherence or completion rates.

Eligibility criteria Studies of any design focusing on interventions to improve adherence or completion of TB treatment in underserved populations in low incidence countries.

Sources of evidence MEDLINE, Embase and Cochrane CENTRAL were searched (January 2015 to December 2023).

Charting methods Piloted data extraction forms were used. Findings were tabulated and reported narratively. Formal risk of bias assessment or synthesis was not undertaken.

Results 47 studies were identified. There was substantial heterogeneity in study design, population, intervention components, usual care and definition of completion rates. Most studies were in migrants or refugees, with fewer in populations with other risk factors (eg, homelessness, imprisonment or substance abuse). Based on controlled studies, there was limited evidence to suggest that shorter treatment regimens, video-observed therapy (compared with directly observed therapy), directly observed therapy (compared with self-administered treatment) and approaches that include tailored health or social support beyond TB treatment may lead to improved outcomes. This evidence is mostly observational and subject to confounding. There were no studies in Gypsy, Roma and Traveller populations, or individuals with mental health disorders and only one in sex workers. Barriers to treatment adherence included a lack of knowledge around TB, lack of general health or social support and side effects. Facilitators included health education, trusted relationships between patients and healthcare staff, social support and reduced treatment duration.

Conclusions The evidence base is limited, and few controlled studies exist. Further high-quality research in well-defined underserved populations is needed to confirm the limited findings and inform policy and practice in TB management. Further qualitative research should include more people from underserved groups.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Strengths of this scoping review were the comprehensive searches using sensitive search strategies, full-text screening by several reviewers and detailed data extraction.
- ⇒ A further strength was the inclusion of any study design to capture all relevant evidence.
- ⇒ Limitations included the lack of formal risk of bias assessment and lack of formal quantitative synthesis.

INTRODUCTION

Tuberculosis (TB) is the 13th leading cause of death worldwide, with over 80% of cases and deaths in low-income and middle-income countries.¹ In low incidence countries, TB tends to be most prevalent in vulnerable populations such as migrants, people experiencing homelessness or people with substance abuse disorders.² In England, there has been a decline in TB notification rates over the last 10 years, but the rate of decline has slowed, with rates remaining highest in large urban areas with high levels of deprivation and in underserved groups.³ Underserved groups have been defined by the Collaborative Tuberculosis Strategy for England as ‘individuals whose social circumstances, language, culture or lifestyle (or those of their parents or carers) make it difficult to recognise the clinical onset of TB, access diagnostic and treatment services, self-administer treatment (or, in the case of children and young people, have treatment administered by a parent or carer); or attend regular appointments for clinical follow-up’.⁴ Some migrant groups (eg, asylum seekers and refugees), people who experience homelessness, people in contact with the criminal justice system, or with mental health needs, and/or drug and alcohol misuse are all included in this

definition.^{3 5} It can include other groups who share a common feature of being underserved by healthcare services due to a lack of access or other issues.⁵

People in underserved groups not only have higher rates of TB but also poorer treatment outcomes, for example, higher rates of death and/or loss to follow-up in people with at least one social risk factor compared with those without a social risk factor.⁵

This scoping review was undertaken to inform the 2023 update of Tackling TB in Inclusion Health Groups: A toolkit for a multi-agency approach resource,⁶ which aims to provide best practice, shared learning and recommendations to support the design, delivery and improvement of services to tackle TB in underserved groups in England and support the TB Action Plan for England, 2021–2026.⁵ Underserved groups, termed ‘health inclusion groups’ in the recent toolkit update, include those with one or more social risk factors such as current or history of drug misuse, homelessness or imprisonment. The aim of this scoping review was to provide an overview of the recent evidence base for interventions or approaches that could help improve treatment adherence and/or completion rates for both active and latent TB in underserved groups in low incidence countries. This is particularly relevant in a post-COVID-19 context, due to the fragmentation of some services that arose during the pandemic.⁷

An existing systematic review, published in 2018, updated and extended work commissioned by the National Institute for Health and Care Excellence and assessed the effectiveness of service delivery and organisational models to manage TB within these populations.^{8 9} A further systematic review focused on the qualitative literature on barriers and facilitators to TB management in such populations.¹⁰ For this scoping review, it was, therefore, decided to focus on more recent evidence since the publication of these two systematic reviews.

METHODS

Methods for this scoping review were guided by the Joanna Briggs Institute (JBI) Manual for Evidence Synthesis.¹¹ A scoping review approach was chosen to map the availability of evidence in terms of volume, study design/s and type of underserved population; to summarise the evidence for different approaches to improving TB treatment adherence or completion rates in underserved populations; to provide a resource of extracted data from primary studies and to identify gaps in the evidence. We believe our question was suitable for this scoping approach due to the broad nature of the question (any study designs or intervention, active and latent TB, any underserved population), the fact that we anticipated gaps in the literature and were not aiming to use results to answer a defined question on the effectiveness of a specific intervention or to inform guidance or practice.¹² The Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

(PRISMA-ScR) checklist was adhered to (online supplemental material 1).¹³

Searches

Sensitive search strategies using text and index terms relating to TB, underserved populations and treatment completion or adherence were used (online supplemental material 2). The term ‘inclusion health group’, more recently preferred to ‘underserved’ or ‘vulnerable’ group, was not included in the search strategy as preliminary searches did not find this term represented in relevant articles. MEDLINE ALL (Ovid), Embase (Ovid) and Cochrane CENTRAL were searched from January 2015 to December 2023 to identify studies since the previous relevant systematic reviews were published. There were no restrictions by study design, language or intervention. Reference lists of existing systematic reviews were checked for additional studies.

Study selection

Titles and abstracts were screened by one reviewer (JD) and full texts were checked by two or more reviewers (JD, CH, AR and LA). Any disagreements were resolved through discussion with the whole team. The study selection process was documented in a PRISMA flow diagram (figure 1), and reasons for exclusion of full-text studies were recorded. Primary studies of any design were included where they assessed the effect of an intervention on treatment completion and/or adherence rates in underserved groups in low incidence countries (online supplemental material 3 for full inclusion and exclusion criteria). Mixed populations including underserved groups were included providing subgroup analyses were reported for the underserved groups only. Single-arm studies were included to gain an overview of any additional interventions and risk groups they were evaluated in, and to record factors associated with non-completion. Underserved groups included populations described as disadvantaged, underserved, hard-to-reach or vulnerable; prison populations; underserved or undocumented migrants, refugees, asylum seekers, victims of human trafficking/modern slavery or unaccompanied minors; homeless people; sex workers; Gypsy, Roma, Traveller (GRT) groups; people with alcohol and/or drug misuse; people with mental health disorders. Both active and latent TB were included. Any intervention was eligible, including changes to existing services, introduction of new services or comparisons between different treatment approaches providing the focus was on underserved groups. Studies exploring different approaches to screening or testing were included as studies show that there can be significant losses to care at that point.¹⁴ The nature of this initial contact may, therefore, have an effect of retaining people in the cascade of care. Such studies had to report the effect on treatment adherence or completion, studies only reporting screening uptake were excluded. Qualitative evidence was included where this was in the context of treatment approaches to TB in underserved populations.

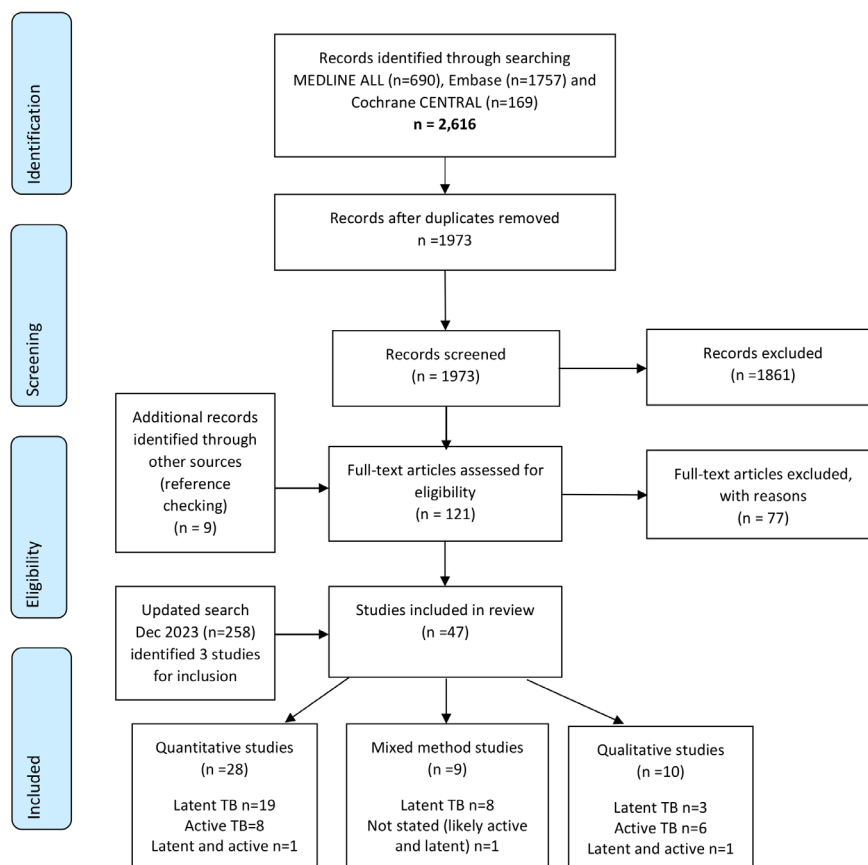


Figure 1 PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Low incidence countries were defined by the WHO estimates of TB incidence by country and territory, 2020 (updated June 2022).¹⁵

Data extraction

A piloted data extraction form was used. For quantitative studies, data items extracted included study design, population characteristics (risk factors, type of TB (latent/active), sample size), details on intervention and comparator (where applicable), completion rates and factors associated with non-completion. For qualitative studies, data items extracted included population characteristics, sample size, data collection and analysis method, method of recruitment and representativeness of sample, intervention and comparator (where applicable), and main facilitators and barriers to adherence and/or treatment completion. Formal risk of bias assessment was not undertaken, but any study limitations as described by the study authors were recorded.

Synthesis

Findings were tabulated and reported narratively. Studies were grouped by type of intervention and further

subgrouped where applicable by population and type of TB (active or latent). Meta-analysis, for example, of completion rate was precluded by substantial heterogeneity in study design, populations, settings, interventions, drug treatment regimen and definition of completion rate. No formal thematic or other synthesis of qualitative findings was undertaken, but the main barriers and facilitators to treatment adherence and/or completion were extracted and narratively summarised.

Patient and public involvement

Patients or the public were not involved in this scoping review.

RESULTS

47 studies were included: 28 quantitative, 9 mixed-methods and 10 qualitative studies (figure 1). Figure 2 shows the volume of evidence by study design, type of underserved population and latent or active TB. Most studies (n=27) were in migrants/refugees (57.4%), six studies (12.8%) were in (predominantly) people experiencing

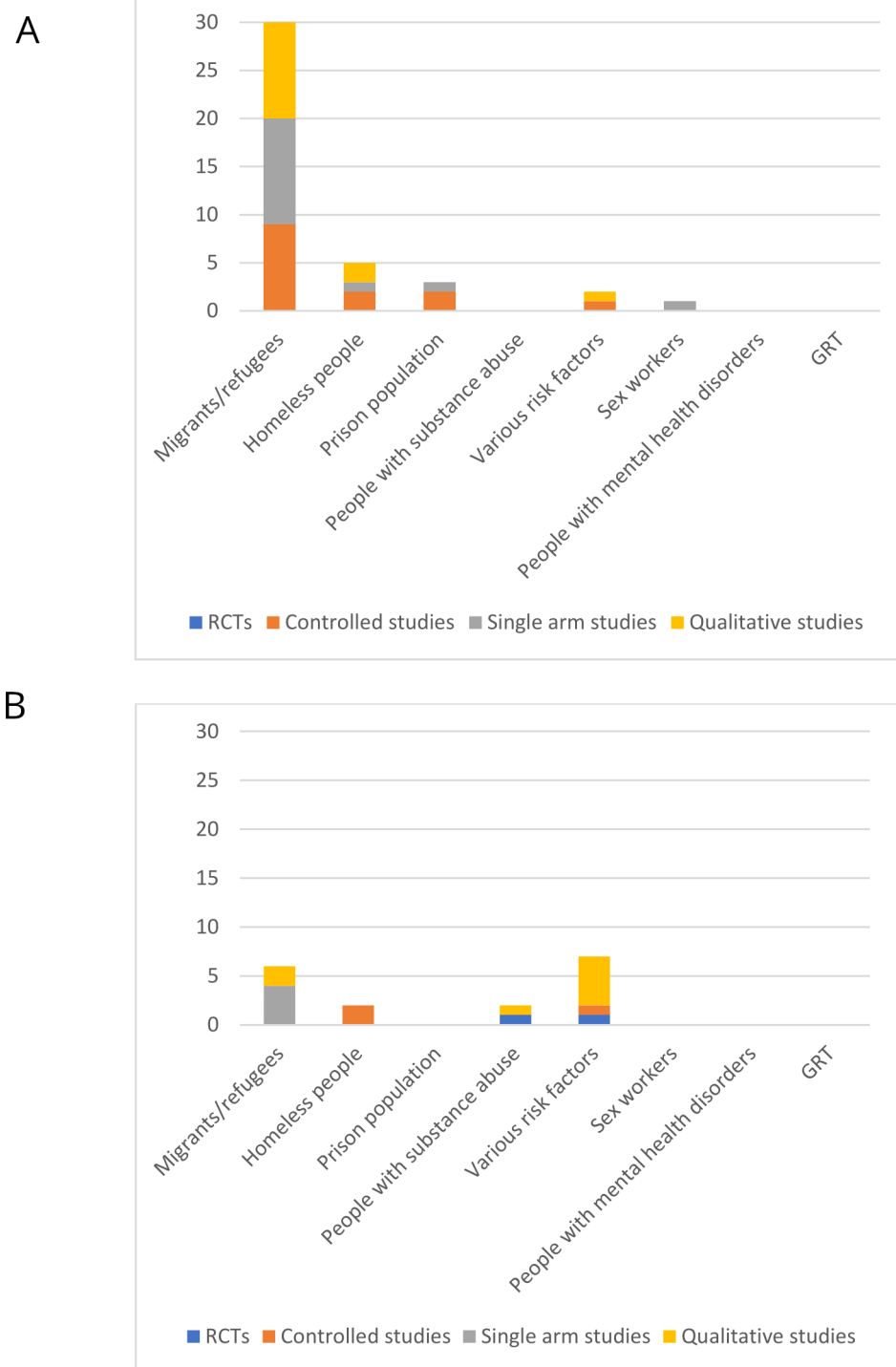


Figure 2 (A) Number and type of studies in different underserved groups—latent TB. (B) Number and type of studies in different underserved groups—active TB. Mixed-methods studies contributed to both qualitative and quantitative study numbers; qualitative studies undertaken either in underserved population or in health care workers; various risk factors include the other categories but are not focused specifically on a single type of underserved population; studies with mixed populations (latent/active) included in both Figure A and B; GRT, Gypsy, Roma, Traveller; RCTs, randomised controlled trials.

homelessness, three (6.4%) in prison populations, two (4.3%) in people with substance abuse, one (2.1%) in sex workers and eight (17.0%) in populations with a variety of risk factors. There were no studies in the GRT population, and no studies focused specifically on those with mental health disorders, although this was an additional

risk factor in some populations. No studies specifically mentioned victims of human trafficking/modern slavery or unaccompanied minors. Thirty (63.8%) were in latent TB, 14 (29.8%) were in active TB and three (6.38%) focused on both active and latent TB. Of the latent TB studies, most (70%) were in migrants/refugees, and of

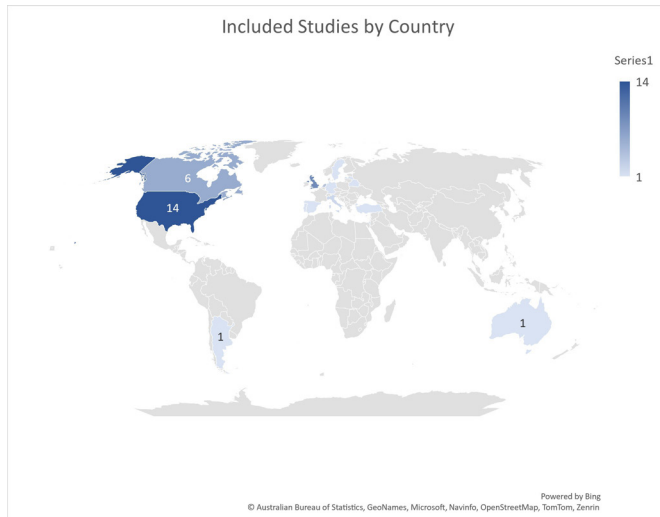


Figure 3 Included studies by country.

the active TB studies, most (71.4%) were in populations with social risk factors (homelessness, prison, substance abuse or a variety of risk factors).

Of the quantitative studies (n=36 including the quantitative component from mixed-methods studies), only 2 (5.5%) were randomised controlled trials (RCTs), 17 (47.2%) were studies including a control group (concurrent, historical or before-and-after study) and 17 (47.2%) were single-arm studies. Nineteen studies contributed to qualitative evidence (10 qualitative studies and 9 mixed-methods studies). Most studies were based in the USA, the UK or Canada (figure 3). The focus of the results reported here is on findings from the RCTs and controlled studies, as single-arm studies are inherently inappropriate for demonstrating a benefit of a certain type of treatment, and comparisons across single-arm studies were not possible due to substantial clinical and methodological heterogeneity. Additional details on single-arm and qualitative studies are in online supplemental materials 4,5.

Different drug regimens and treatment lengths

We identified four studies, all in latent TB. Four observational studies compared 3HP (3 months of once-weekly isoniazid plus rifapentine), or either 3HP or 4R (4 months of daily rifampin) with 6H (isoniazid for 6 months) or 9H (isoniazid for 9 months) (online supplemental material 6 for Table of study characteristics and main findings from RCTs and controlled studies).^{16–19} Study populations were prisoners in two US studies^{17 19}; the general population with subgroup analyses for people experiencing homelessness, ‘irregular’ migrants sent by non-governmental organisations (NB ‘irregular’ not further defined by study authors) and asylum seekers/refugees in an Italian study¹⁸ and government-assisted refugees in a Canadian study.¹⁶ Studies consistently found higher completion rates with the shorter 3HP or 4R regimens compared with the longer 6H or 9H regimens, with statistically significant differences based on unadjusted analyses in two of the four studies ($p < 0.001$ ¹⁷ and $p < 0.0001$ ¹⁸). For the study

that looked at completion rates by subgroup, the shorter treatment regimen was found to have higher completion rates ($p < 0.0001$) in favour in people experiencing homelessness.¹⁸ There was no statistically significant difference for migrants or refugees/asylum seekers (unadjusted analyses).¹⁸ Main reasons for treatment non-completion included parole, discharge or transfer out of prison for the prison populations.^{17 19} One study found that shorter treatment duration and female sex tended to positively affect treatment completion in government-assisted refugees.¹⁶

Different types of treatment administration (directly observed therapy/video-observed therapy/self-administered treatment)

We identified one study in active TB and two studies in latent TB.

An RCT set in the UK compared directly observed therapy (DOT) with video-observed therapy (VOT) in a population with active TB and social risk factors.²⁰ This study found significantly higher completion rates with VOT compared with DOT (adjusted OR (95% CI): 2.52 (1.17 to 5.47), $p = 0.019$ ²⁰). Levels of initial engagement with DOT were substantially lower compared with VOT, with particularly low engagement (with DOT) among younger adults, foreign-born patients and those without social risk factors or mental health problems.²⁰ An Argentinian prospective cohort study in active TB did not directly compare modes of administration but found that self-administered treatment (SAT) was associated with a higher risk of incomplete treatment compared with DOT or mixed DOT/SAT (based on multivariable model, in socioeconomically disadvantaged patients).²¹

A US-based retrospective cohort study compared DOT with SAT in a homeless population with latent TB and found significantly higher completion rates with DOT (adjusted OR (95% CI): 1.40 (1.07 to 1.82), $p = 0.014$).²² A retrospective cohort set in Israel also found slightly lower treatment completion rates with SAT compared with semi-DOT in Ethiopian immigrants with latent TB living in reception centres, though the difference was not statistically significant (adjusted OR (95% CI): 0.54 (0.28 to 1.04), $p = 0.08$).²³ Semi-DOT was defined as once weekly DOT administered by a nurse with the second weekly dose self-administered.

Factors significantly associated with treatment completion in the US cohort were male sex, being black/African American, older age and positive HIV status, while alcohol use was associated with decreased odds of completing treatment.²² The Israeli cohort found that treatment completion was significantly lower in those with side effects.²³

Screening or testing approaches

We identified three studies in latent TB. Two studies in latent TB compared the impact on treatment outcomes of different screening strategies. A Canadian retrospective cohort study compared screening with an interferon gamma release assay (IGRA) test only with a sequential



screening strategy (tuberculin skin test (TST) followed by IGRA if positive TST).²⁴ Treatment completion rates were very similar among those who started treatment, however, screening completion rates were higher with the IGRA only strategy (adjusted OR (95% CI): 3.74 (2.30 to 6.09) $p < 0.001$). A US-based before-and-after study compared a strategy of mainly IGRA (post-2011) with a strategy of mainly TST (pre-2011).²⁵ Treatment completion rates were also similar, but diagnosis of latent TB was higher pre-2011 and treatment initiation was higher post-2011. In both studies, patients were treated in the same way once identified as eligible for treatment though either screening strategy. A study set in the Netherlands looked at six different community strategies, including education sessions, for engaging Eritrean migrants with screening for latent TB and subsequent treatment.²⁶ The treatment completion rate was 97% overall, but there was no analysis by type of community strategy. Uptake of latent TB education differed between strategies from 13% to 75%, and uptake of screening after education sessions was 64%.

Strategies tailored to people experiencing homelessness, social risk factors or substance abuse

We identified three studies in active TB and one study in latent TB.

Among the active TB studies, one was undertaken in a homeless population,²⁷ and one in a population with social risk factors where many were homeless.²⁸ In both, a standard approach to TB treatment was compared with an enhanced approach with provision of additional services (a UK residential respite service²⁷ or integration of a social care team into a UK TB service²⁸). Both included social and mental health support and support for drug/alcohol use, and in one study, accommodation was also provided.²⁷

An RCT set in the USA was undertaken in substance users (drug and/or alcohol) that compared provision of DOT by community outreach staff who were former substance users with standard DOT.²⁹ All three studies found that completion rates were significantly higher in the enhanced arms (RR (95% CI: 2.5 (1.2 to 5.1), p value not reported),²⁹ adjusted OR (95% CI): 2.97 (1.44 to 6.96), p value not reported²⁷ and adjusted OR 2.35 (95% CI 1.41 to 3.91), $p = 0.001$ ²⁸).

A US study in homeless people with latent TB compared a standard approach with a nurse-led, community health worker programme.³⁰ This also included social and mental health support and support for drug/alcohol use and the community health workers were formerly homeless people. Completion rates were higher in the enhanced programme (91.8% in prospective arm compared with 66% in historical control, no summary estimate provided).

Factors for non-completion were variable, for example, non-completion more likely in people aged < 50 (in the intervention group in the latent TB study³⁰); or a more unstable housing situation (regardless of treatment type) in the US-based RCT in active TB.²⁹

Strategies tailored to migrants, refugees and asylum seekers

We identified four studies in latent TB. A US retrospective cohort study compared a refugee health clinic, which included collaborative working between refugee resettlement agencies and refugee health clinics, with a standard clinic.³¹ An Australian retrospective cohort study compared a refugee health and well-being service providing intensive transitional care with a universal primary care clinic.³² Services provided by the clinics included interpreter services, educational material and multidisciplinary healthcare teams. Significantly greater completion rates were reported both in the refugee health clinic compared with the standard clinic (unadjusted OR (95% CI): 9.44 (2.39 to 37.30), p value not reported³¹) and the refugee health and well-being service compared with the universal primary care clinic (OR not reported, $p = 0.0373$ based on unadjusted analysis).^{31 32} Factors associated with non-completion were not reported. One retrospective cohort study compared TB physician and nursing outreach integrated into an Israeli migrant reception centre with a regional TB clinic.³³ Both study arms included nurse-managed semi-DOT and transport to regional clinics was provided free of charge.³³ Completion rates were similar. Factors significantly associated with non-completion were age < 5 years and side effects. A Swedish study compared standard care (up to 2013) with a strategy of all subjects being given prescheduled appointments for nurse visits, assisted by interpreters.³⁴ The completion rate was significantly higher in those initiating treatment after 2013 compared with those initiating treatment earlier (OR not reported, $p < 0.01$ based on unadjusted analysis). Additional factors significantly associated with completion were a regimen of isoniazid treatment for 6 months compared with 9 months and receiving latent TB treatment in connection with immunosuppressive treatment (multivariate analysis).

Conditional cash transfer

We identified one study in active TB. An Argentinian prospective cohort study compared conditional cash transfer (contingent on adherence to health checks and treatment) with standard care in a socioeconomically disadvantaged population.²¹ Treatment success was significantly higher with the conditional cash transfer (adjusted OR 2.91 (95% CI 1.97 to 4.28), $p = 0.001$). Factors associated with incomplete treatment were SAT, younger age, lack of insurance, lower income and use of alcohol and illicit drugs.

Single-arm studies

There were 17 single-arm studies (5 as part of a mixed-methods study, online supplemental material 4). These looked at completion rates after 3HP/DOT (in prisoners³⁵ and people experiencing homelessness³⁶); mandatory screening in asylum seekers³⁷; a migrant focused TB screening programme³⁸; medical examination by civil surgeons for people who were adjusting immigration status to permanent residency³⁹; screening at a sexual

health clinic for sex workers⁴⁰; integrated clinics for migrants, refugees or asylum seekers^{41–46}; other strategies tailored to migrants, refugees or asylum seekers (such as engaging community health workers or TB education)^{47–50} or the effect of the CureTB Programme, a continuity of care programme for patients relocating outside of the USA before completing treatment.⁵¹ Completion rates were not directly comparable due to heterogeneity in populations, settings, approaches to screening and treatment, length and methods of follow-up and definition of completion rate, as well as any differences in intervention components. Nonetheless details on factors associated with non-completion (reported in online supplemental material 4) may be useful for those interested in the feasibility of such approaches.

Qualitative evidence

There were 19 studies contributing evidence on barriers and facilitators to initiating and completing treatment for latent or active TB (online supplemental material 5). There was substantial variability in population characteristics, setting and type of interventions experienced or delivered. Eleven studies (57.9%) focused on providing TB care to migrants or refugees, the remainder on people with social risk factors (homelessness, substance abuse or a combination of risk factors). Eight of the studies (42.1%) included only healthcare workers but also provided data on perceived patient level barriers and facilitators. Some barriers were common across several studies, including: a lack of knowledge particularly around latent TB and TB-associated stigma; fear of disclosure and language barriers (especially for migrants); lack of other (non-TB) health or social support; unstable housing and transience of population; lack of staff resources; lack of connectivity between different services and burden of treatment including side effects. Some common facilitators included health education; building trusted relationships between patients and healthcare staff; collaborative working with other services or community organisations; social support and reduced treatment duration. Some barriers were population specific, for example, coping with withdrawal symptoms while in hospital (people with substance use disorder), inability to safely store medications (people experiencing homelessness) or fear of deportation (asylum seekers). Population-specific facilitators included the use of interpreters (asylum seekers/refugees), hostel workers reminding patients to take medication (people experiencing homelessness) or referral to support for substance abuse.

DISCUSSION

This scoping review identified 47 quantitative, mixed-methods or qualitative studies focusing on TB treatment adherence in underserved populations in low incidence countries. Heterogeneity across studies was high in terms of study design, population, country, intervention components, usual care and outcome definitions. Focusing on

the 19 quantitative controlled studies, higher completion rates were found with VOT compared with DOT (statistically significant finding from one RCT) and with conditional cash transfer compared with standard care alone (statistically significant finding from one observational study, adjusted result) for active TB. For latent TB, higher completion rates were consistently found with shorter treatment regimens compared with longer treatment regimens (statistically significant findings in two of four studies, unadjusted results); DOT or semi-DOT compared with SAT (statistically significant finding in the DOT study, adjusted result); clinics that integrated TB services within primary care compared with standard TB care (statistically significant findings in two studies, unadjusted results); and other refugee focused services (such as prescheduled appointments assisted by interpreters) compared with standard clinics (statistically significant finding in one of two studies, unadjusted result). Enhanced approaches that included social, mental health and drug/alcohol use support compared with standard TB care led to higher completion rates for both active and latent TB (statistically significant findings in three of four studies, results from RCT or adjusted results). Evidence from two studies exploring whether types of screening for latent TB had an impact found little difference in treatment completion rates when comparing IGRA alone versus TST followed by IGRA, or IGRA alone versus TST alone. However, screening completion rates were higher with a one-step screening approach (statistically significant finding from one study, adjusted result), which could affect the overall number of people treated.

Factors associated with non-completion were inconsistently reported in the quantitative studies, but included treatment side effects, instability of housing, transience of population and use of alcohol or drugs; a factor associated with treatment completion was a shorter treatment regimen. This was reflected in the findings from the qualitative evidence where factors such as side effects and unstable housing were also found to be barriers to treatment completion, and reduced treatment duration was found to be a facilitator. Other facilitators identified across the qualitative evidence included health education and social (and language) support, while common barriers include a lack of disease knowledge, stigma and lack of cohesion and resources across different services.

Strengths of this scoping review were the comprehensive searches using sensitive search strategies, full-text screening by several reviewers and detailed data extraction. A further strength was the inclusion of any study design to capture all relevant evidence. Nonetheless the evidence identified was limited: findings from the controlled studies were based on 1–4 (mostly observational) studies for each comparison and should therefore be interpreted cautiously. Evidence from observational studies is likely to be subject to confounding and not all studies adjusted for this. Formal risk of bias assessment was not undertaken, and heterogeneity precluded any formal synthesis. There is a lack of consistency in

the literature around defining vulnerable populations. Despite a sensitive search strategy, it is possible that studies may have been missed where vulnerable populations and/or treatment completion were described using different terminology.

Given the limitations of the published evidence base, the results of this evidence review were combined with several additional sources to inform the Tackling TB in Inclusion Health Groups: A toolkit for a multi-agency approach document.⁶ These included:

- ▶ A rapid consultation exercise with TB nurses and regional TB programme managers and leads on how their services work with inclusion health groups, and their experience of the challenges and enablers.
- ▶ A UK Health Security Agency (UKHSA) Knowledge and Library Service evidence review looking at the impact of the COVID-19 pandemic on TB services for inclusion health groups.
- ▶ Collection of recommendations, exemplars of local and regional good practice from across the country, and tools, links and resources for services to draw on and adapt locally.
- ▶ Comments and contributions from a wide range of stakeholders and also via two task and finish groups.

Improved representation of inclusion health/underserved groups within TB research is still needed to support further steps to improve prevention, detection and control of TB in these populations.

A previous systematic review⁸ evaluated screening and completion rates in underserved populations in low incidence countries. The authors found that adherence or completion rates were increased in drug users with more intensive or tailored approaches compared with standard care: enhanced case management by peers⁵²; mobile screening and treatment service at a convenient community location⁵³; and DOT and active follow-up of non-adherent patients.⁵⁴ A fourth study included in the systematic review found no difference in completion rates in migrants, drug users, homeless people and prisoners when DOT was at a convenient location in the community versus at a health clinic.⁵⁵ This finding of higher completion rates with more enhanced approaches in three out of four studies is consistent with the findings from the more recent studies identified in this scoping review. Some of the barriers (eg, stigma) and facilitators (eg, social support) identified here are also similar to those identified in a 2017 systematic review of qualitative evidence.¹⁰ These findings are also reflected in higher incidence settings. A recent systematic review looking at interventions throughout the TB care cascade for active TB in mainly low-income and middle-income countries found that interventions that included counselling and education were significantly associated with treatment success.⁵⁶ A further systematic review assessing community-based TB interventions (such as electronic medication monitors, community health worker or family direct observation therapy) in low-income and middle-income countries found these approaches may improve

treatment success while also offering convenience to patients.⁵⁷

Evidence on sex workers was limited to one single-arm study, and no studies were identified that focused on GRT populations. There were no studies that focused specifically on people with mental health disorder, though this was an additional risk factor in some studies. No studies specifically mentioned victims of human trafficking/modern slavery or unaccompanied minors. Future studies should focus on these underrepresented groups in particular. While a larger proportion of evidence was in migrants, asylum seekers or refugees, this is not a homogeneous group and there is variation around the terminology and categories used for different groups of migrants. There is no uniform understanding in the literature of what constitutes a 'vulnerable' population. While some groups, for example, incarcerated populations, are reasonably well defined and studied, some groups may have risk factors which align them with more than one (overlapping) category thus making their identity more difficult to capture.⁵⁸ Future studies should consider this when defining populations for research. Given the strong connection between social determinants of health and TB-related vulnerability, future studies should also consider strategies that are linked to alleviation of poverty and social protection.⁵⁸

Only 17 low incidence countries contributed to the evidence base, with much of the evidence originating from the USA, the UK and Canada, which raises questions about generalisability to other countries. Much of the evidence is observational and future studies would benefit from a randomised design, for example, cluster randomisation, to minimise selection bias. Future qualitative research should include more people from underserved groups in addition to healthcare workers, as the former group was often underrepresented in the body of evidence identified here.

CONCLUSION

Evidence in underserved populations is limited, heterogeneous in terms of study design, populations, settings and interventions, and mostly observational in nature. The available evidence from controlled studies suggests that shorter treatment regimens, VOT compared with DOT, DOT compared with SAT, and approaches tailored to specific populations and that include health or social support beyond TB treatment may lead to improved adherence and completion rates. Further research is needed to confirm these findings, ideally in large studies designed to minimise selection bias such as RCTs, and in well-defined populations that include GRT populations, sex workers and individuals with mental health disorders. Further qualitative research should aim to include more people from underserved groups as well as healthcare workers. The purpose of the Tackling TB in Inclusion Health Groups: A toolkit for a multiagency approach resource is to provide local systems with support to lead

the development, improvement and delivery of services to tackle TB in inclusion health groups using an integrated approach across inclusion health groups and the TB pathway. The scoping review findings have been integrated into this toolkit to draw together the best available evidence together with best practice and learning from across the country.

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Patient consent for publication Not applicable.

Provenance and peer review Not commissioned; externally peer reviewed.

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Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) Checklist

SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
TITLE			
Title	1	Identify the report as a scoping review.	Title, p1
ABSTRACT			
Structured summary	2	Provide a structured summary that includes (as applicable): background, objectives, eligibility criteria, sources of evidence, charting methods, results, and conclusions that relate to the review questions and objectives.	Abstract, p2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known. Explain why the review questions/objectives lend themselves to a scoping review approach.	3 rd and 4 th paragraph p4 and paragraph under 'Methods' p 5.
Objectives	4	Provide an explicit statement of the questions and objectives being addressed with reference to their key elements (e.g., population or participants, concepts, and context) or other relevant key elements used to conceptualize the review questions and/or objectives.	3 rd paragraph p 4.
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists; state if and where it can be accessed (e.g., a Web address); and if available, provide registration information, including the registration number.	There was no protocol for this scoping review.
Eligibility criteria	6	Specify characteristics of the sources of evidence used as eligibility criteria (e.g., years considered, language, and publication status), and provide a rationale.	'Study selection' and 'Searches' paragraphs p 5,6'.
Information sources*	7	Describe all information sources in the search (e.g., databases with dates of coverage and contact with authors to identify additional sources), as well as the date the most recent search was executed.	'Searches' paragraph p5
Search	8	Present the full electronic search strategy for at least 1 database, including any limits used, such that it could be repeated.	In supplementary material
Selection of sources of evidence†	9	State the process for selecting sources of evidence (i.e., screening and eligibility) included in the scoping review.	'Study selection paragraph' p5,6
Data charting process‡	10	Describe the methods of charting data from the included sources of evidence (e.g., calibrated forms or forms that have been tested by the team before their use, and whether data charting was done independently or in duplicate) and any processes for obtaining and confirming data from investigators.	'Data extraction' paragraph, p6.



SECTION	ITEM	PRISMA-ScR CHECKLIST ITEM	REPORTED ON PAGE #
Data items	11	List and define all variables for which data were sought and any assumptions and simplifications made.	'Data extraction' paragraph, p6.
Critical appraisal of individual sources of evidence§	12	If done, provide a rationale for conducting a critical appraisal of included sources of evidence; describe the methods used and how this information was used in any data synthesis (if appropriate).	No formal appraisal of evidence. Main limitations of studies as reported by the study authors were noted. Also noted if results were adjusted for confounders or not.
Synthesis of results	13	Describe the methods of handling and summarizing the data that were charted.	'Synthesis' paragraph p 6/7
RESULTS			
Selection of sources of evidence	14	Give numbers of sources of evidence screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally using a flow diagram.	'Results' paragraph p 7 and Figure 1 (flow diagram)
Characteristics of sources of evidence	15	For each source of evidence, present characteristics for which data were charted and provide the citations.	'Results' paragraph p7, Table 1 and supplementary material.
Critical appraisal within sources of evidence	16	If done, present data on critical appraisal of included sources of evidence (see item 12).	Not undertaken.
Results of individual sources of evidence	17	For each included source of evidence, present the relevant data that were charted that relate to the review questions and objectives.	Table 1, supplementary material and last paragraph p7 to first paragraph p11.
Synthesis of results	18	Summarize and/or present the charting results as they relate to the review questions and objectives.	P8 -12.
DISCUSSION			
Summary of evidence	19	Summarize the main results (including an overview of concepts, themes, and types of evidence available), link to the review questions and objectives, and consider the relevance to key groups.	First two paragraphs under 'Discussion', p12/13.
Limitations	20	Discuss the limitations of the scoping review process.	Second paragraph p13.
Conclusions	21	Provide a general interpretation of the results with respect to the review questions and objectives, as well as potential implications and/or next steps.	'Conclusion' paragraph p15.
FUNDING			
Funding	22	Describe sources of funding for the included sources of evidence, as well as sources of funding for the scoping review. Describe the role of the funders of the scoping review.	Included p16.

JB1 = Joanna Briggs Institute; PRISMA-ScR = Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews.

* Where *sources of evidence* (see second footnote) are compiled from, such as bibliographic databases, social media platforms, and Web sites.



† A more inclusive/heterogeneous term used to account for the different types of evidence or data sources (e.g., quantitative and/or qualitative research, expert opinion, and policy documents) that may be eligible in a scoping review as opposed to only studies. This is not to be confused with *information sources* (see first footnote).

‡ The frameworks by Arksey and O'Malley (6) and Levac and colleagues (7) and the JBI guidance (4, 5) refer to the process of data extraction in a scoping review as data charting.

§ The process of systematically examining research evidence to assess its validity, results, and relevance before using it to inform a decision. This term is used for items 12 and 19 instead of "risk of bias" (which is more applicable to systematic reviews of interventions) to include and acknowledge the various sources of evidence that may be used in a scoping review (e.g., quantitative and/or qualitative research, expert opinion, and policy document).

From: Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA ScR): Checklist and Explanation. *Ann Intern Med.* 2018;169:467–473. doi: [10.7326/M18-0850](https://doi.org/10.7326/M18-0850).



St. Michael's
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Inspiring Science.

Search strategies

Database: Ovid MEDLINE(R) ALL <1946 to February 24, 2023>

Search Strategy:

-
- 1 exp tuberculosis/
 - 2 tuberculosis.ti,ab.
 - 3 TB.ti,ab.
 - 4 MTBC.ti,ab.
 - 5 LTBI.ti,ab.
 - 6 1 or 2 or 3 or 4 or 5
 - 7 ((treatment\$ or intervention\$ or therap\$ or medic\$ or drug\$ or dose\$) adj3 (adher\$ or compl\$ or concordan\$ or regimen\$ or uptake)).ti,ab.
 - 8 exp patient compliance/
 - 9 exp medication adherence/
 - 10 ((treatment\$ or therap\$ or intervention\$ or management) adj3 (success\$ or failure\$ or effectiveness or outcome\$)).ti,ab.
 - 11 ((compl\$ or adheren\$ or concordan\$) adj3 rate\$).ti,ab.
 - 12 exp treatment failure/
 - 13 7 or 8 or 9 or 10 or 11 or 12
 - 14 ((disadvantaged or under-served or underserved or hard-to-reach or hard to reach or vulnerable) adj (population\$ or group\$ or patient\$)).ti,ab.
 - 15 exp prisoners/
 - 16 (prison\$ or jail\$ or imprison\$ or penitentiary\$).ti,ab.
 - 17 (offender\$ or convict\$ or detainee\$ or inmate\$ or incarcerat\$).ti,ab.
 - 18 exp correctional facilities/
 - 19 exp custodial care/
 - 20 exp criminals/
 - 21 exp juvenile delinquency/
 - 22 exp jails/
 - 23 exp prisons/
 - 24 (custod\$ or detention or YOI or correctional).ti,ab.
 - 25 criminal justice.ti,ab.
 - 26 (immigrant\$ or migrant\$).ti,ab.
 - 27 exp "Transients and Migrants"/
 - 28 exp refugees/

29 (refugee\$ or asylum seeker\$).ti,ab.
30 exp human trafficking/
31 modern slavery.ti,ab.
32 exp enslaved persons/
33 human trafficking.ti,ab.
34 exp undocumented immigrants/
35 undocumented.ti,ab.
36 (displaced adj (people or person)).ti,ab.
37 (unaccompanied adj (minor\$ or child\$)).ti,ab.
38 exp homeless youth/
39 exp ill-housed persons/
40 homeless\$.ti,ab.
41 exp sex workers/
42 sex worker\$.ti,ab.
43 (escort\$ or prostitute\$).ti,ab.
44 exp Roma/
45 gyps\$.ti,ab.
46 traveller\$.ti,ab.
47 exp substance-related disorders/
48 exp alcoholism/
49 (drug adj2 (misuse\$ or abuse\$ or dependen\$ or inject\$)).ti,ab.
50 (alcohol adj2 (misuse\$ or abuse\$ or dependen\$)).ti,ab.
51 (substance adj2 (misuse\$ or abuse\$ or dependen\$)).ti,ab.
52 exp mental health/
53 mental health.ti,ab.
54 exp mental disorders/
55 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or
29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or
45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54
56 6 and 13 and 55
57 limit 56 to yr="2015 -Current"

.....
Database: Embase <1974 to 2023 February 24>

Search Strategy:

-
- 1 exp tuberculosis/
 - 2 tuberculosis.ti,ab.
 - 3 TB.ti,ab.
 - 4 exp Mycobacterium tuberculosis complex/
 - 5 MTBC.ti,ab.
 - 6 LTBI.ti,ab.
 - 7 1 or 2 or 3 or 4 or 5 or 6
 - 8 ((treatment\$ or intervention\$ or therap\$ or medic\$ or drug\$ or dose\$) adj3 (adher\$ or compl\$ or concordan\$ or regimen\$ or uptake)).ti,ab.
 - 9 exp patient compliance/
 - 10 exp medication compliance/
 - 11 ((treatment\$ or therap\$ or intervention\$ or management) adj3 (success\$ or failure\$ or effectiveness or outcome\$)).ti,ab.
 - 12 ((compl\$ or adheren\$ or concordan\$) adj3 rate\$).ti,ab.
 - 13 exp treatment failure/
 - 14 8 or 9 or 10 or 11 or 12 or 13
 - 15 7 and 14
 - 16 exp medically underserved/
 - 17 ((disadvantaged or under-served or underserved or hard-to-reach or hard to reach or vulnerable) adj (population\$ or group\$ or patient\$)).ti,ab.
 - 18 exp prisoner/
 - 19 (prison\$ or jail\$ or imprison\$ or penitentiary\$).ti,ab.
 - 20 (offender\$ or convict\$ or detainee\$ or inmate\$ or incarcerat\$).ti,ab.
 - 21 exp correctional facility/
 - 22 exp custodial care/
 - 23 exp offender/
 - 24 exp juvenile delinquency/
 - 25 exp detention center/
 - 26 exp prison/
 - 27 (custod\$ or detention or YOI or correctional).ti,ab.
 - 28 exp criminal justice/
 - 29 criminal justice.ti,ab.
 - 30 (immigrant\$ or migrant\$).ti,ab.

- 31 exp migrant/ or exp forced migrant/ or exp migrant worker/
32 exp refugee/
33 exp asylum seeker/
34 (refugee\$ or asylum seeker\$).ti,ab.
35 exp human trafficking/
36 modern slavery.ti,ab.
37 human trafficking.ti,ab.
38 exp undocumented immigrant/
39 undocumented.ti,ab.
40 exp internally displaced person/
41 (displaced adj (people or person)).ti,ab.
42 (unaccompanied adj (minor\$ or child\$)).ti,ab.
43 exp homeless person/
44 homeless\$.ti,ab.
45 exp homelessness/
46 exp sex worker/
47 sex worker\$.ti,ab.
48 (escort\$ or prostitute\$).ti,ab.
49 exp "Romani (people)"/
50 gyps\$.ti,ab.
51 traveller\$.ti,ab.
52 exp drug dependence/
53 exp alcoholism/
54 (drug adj2 (misuse\$ or abuse\$ or dependen\$ or inject\$)).ti,ab.
55 (alcohol adj2 (misuse\$ or abuse\$ or dependen\$)).ti,ab.
56 exp substance abuse/
57 (substance adj2 (misuse\$ or abuse\$ or dependen\$)).ti,ab.
58 exp mental health/
59 mental health.ti,ab.
60 exp mental disease/
61 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or
31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or
47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60
62 15 and 61

63 limit 62 to yr="2015 -Current"

.....

Database: Cochrane CENTRAL

Search strategy:

ID	Search
#1	MeSH descriptor: [Tuberculosis] explode all trees
#2	(tuberculosis):ti,ab,kw
#3	(TB):ti,ab,kw
#4	(MTBC):ti,ab,kw
#5	(LTBI):ti,ab,kw
#6	(OR #1-#5)
#7	((treatment* or intervention* or therap* or medic* or drug* or dose*) NEAR/3 (adher* or compl* or concordan* or regimen* or uptake)):ti,ab,kw
#8	MeSH descriptor: [Patient Compliance] explode all trees
#9	MeSH descriptor: [Medication Adherence] explode all trees
#10	((treatment* or therap* or intervention* or management) NEAR/3 (success* or failure* or effectiveness or outcome*)):ti,ab,kw
#11	((compl* or adheren* or concordan*) NEAR/3 rate*):ti,ab,kw
#12	MeSH descriptor: [Treatment Failure] explode all trees
#13	(OR #7-#12)
#14	MeSH descriptor: [Prisoners] explode all trees
#15	(prison* or jail* or imprison* or penitentiari*):ti,ab,kw
#16	(offender* or convict* or detainee* or inmate* or incarcerat*):ti,ab,kw
#17	MeSH descriptor: [Correctional Facilities] explode all trees
#18	MeSH descriptor: [Custodial Care] explode all trees
#19	MeSH descriptor: [Criminals] explode all trees
#20	MeSH descriptor: [Juvenile Delinquency] explode all trees
#21	MeSH descriptor: [Jails] explode all trees
#22	MeSH descriptor: [Prisons] explode all trees
#23	(custod* or detention or YOI or correctional):ti,ab,kw
#24	(criminal justice):ti,ab,kw
#25	(immigrant* or migrant*):ti,ab,kw
#26	MeSH descriptor: [Transients and Migrants] explode all trees

- #27 MeSH descriptor: [Refugees] explode all trees
 - #28 (refugee* or asylum seeker*):ti,ab,kw
 - #29 MeSH descriptor: [Human Trafficking] explode all trees
 - #30 (modern slavery):ti,ab,kw
 - #31 MeSH descriptor: [Enslaved Persons] explode all trees
 - #32 (human trafficking):ti,ab,kw
 - #33 MeSH descriptor: [Undocumented Immigrants] explode all trees
 - #34 (undocumented):ti,ab,kw
 - #35 (displaced NEXT (people or person)):ti,ab,kw
 - #36 (unaccompanied NEXT (minor* or child*)):ti,ab,kw
 - #37 MeSH descriptor: [Homeless Youth] explode all trees
 - #38 MeSH descriptor: [Ill-Housed Persons] explode all trees
 - #39 (homeless*):ti,ab,kw
 - #40 MeSH descriptor: [Sex Workers] explode all trees
 - #41 (sex worker*):ti,ab,kw
 - #42 (escort* or prostitut*):ti,ab,kw
 - #43 MeSH descriptor: [Roma] explode all trees
 - #44 (gyps*):ti,ab,kw
 - #45 (traveller*):ti,ab,kw
 - #46 MeSH descriptor: [Substance-Related Disorders] explode all trees
 - #47 MeSH descriptor: [Alcoholism] explode all trees
 - #48 (drug NEAR/2 (misuse* or abuse* or dependen* or inject*)):ti,ab,kw
 - #49 (alcohol NEAR/2 (misuse* or abuse* or dependen*)):ti,ab,kw
 - #50 (substance NEAR/2 (misuse* or abuse* or dependen*)):ti,ab,kw
 - #51 MeSH descriptor: [Mental Health] explode all trees
 - #52 (mental health):ti,ab,kw
 - #53 MeSH descriptor: [Mental Disorders] explode all trees
 - #54 ((disadvantaged or under-served or underserved or hard-to-reach or hard to reach or vulnerable) NEXT (population* or group* or patient*)):ti,ab,kw
 - #55 (OR #14-#54)
 - #56 #6 and #13 and #55
- Limit to 2015-2023

Study selection criteria

	Include	Exclude
Study design	Any primary study with n>1 Quantitative, qualitative or mixed methods.	Reviews, commentaries (with no primary study data)
Publication status; language	Fully published articles in any language, published between 2015 and 2023.	Conference abstracts
Population	Active or latent TB (or combination of both), with or without any co-morbidities. Any age-group. Low incidence countries as defined by WHO estimates. Vulnerable* or hard-to-reach population; population where a <i>majority</i> have risk factors that make them vulnerable; population with a vulnerable sub-group providing there is a sub-group analysis for the vulnerable sub-group.	High incidence countries as defined by WHO estimates. General (non-vulnerable) population. Studies that include a population where all or a majority were not born in the country they are living in <i>unless</i> they are deemed to be vulnerable for additional reasons. Exclude if no information in title or abstract to suggest a (partially) vulnerable population.
Intervention	Any, for example, different drug regimens, changes to existing way of delivering services or development of a new service. Can be part of a wider programme that also includes screening, contact tracing etc., providing it includes treatment.	Interventions aimed solely at screening or contact tracing. Usual intervention/standard care where there is analysis of risk factors for success/failure of treatment and/or recurrence of TB.
Comparator	Any or none.	N/A
Outcome	Must include an outcome relating to treatment adherence and/or completion; or facilitators or barriers to adherence/completion for qualitative studies.	Outcomes relating solely to screening or contact tracing rates, diagnosis, or knowledge or awareness of TB treatments. Prevalence rates of TB (in different sub-groups, including vulnerable). Identification of risk factors for TB or TB associated mortality, or risk factors for treatment failure/success/recurrence.

* population described as disadvantaged, under-served, hard-to-reach or vulnerable; prison population, under-served or undocumented migrants, refugees, asylum seekers, victims of human trafficking/modern slavery, unaccompanied minors, homeless people, sex workers, GRT (Gypsy, Roma, Traveller); people with any type of substance misuse (drugs/alcohol), people with mental health disorders

Single arm study findings

a) 3HP/DOT

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Schmit 2019, US ¹	Latent	Single arm prospective	Prisoners from seven Federal Bureau of Prisons facilities; 16.9% with mental health disorder.	3HP/DOT once weekly for 3 months (n=463)	424/463 (92%) completed treatment.	Reasons for discontinuation included symptoms associated with treatment, transfer or release, treatment refusal, and provider error. Asian race was significantly associated with treatment discontinuation due to adverse events or symptoms related to treatment.
Nwana 2019, US ²	Latent	Single arm, retrospective-part of mixed methods study	Homeless during ≥12 months before TB evaluation; alcohol use 15%, injection drug use 2.3%, non-injection drug use 10.7%, inmate at correctional institution during previous year 7.1%.	3HP/DOT* (n=393)	301/393 (76.6%) completed, 92/393 (23.4%) discontinued, of those 55/393 (14.0%) lost to follow-up.	No factors found to be significantly associated in multivariable models. In bivariate analyses those aged ≥65 were more likely to discontinue compared with those aged 31-44; contacts of persons with active TB were less likely to continue.

*DOT: directly observed therapy; 3HP: three months of once-weekly isoniazid plus rifapentine; * some sites variously included resources to improve outreach (e.g., informational brochures, personnel, and mental health or addiction services, emphasis on clear communication, administering medication in local shelters, provision of incentives, partnerships with shelter staff or correctional facilities)*

b) Screening or test focussed approaches

Study	Type of TB	Design	Population/ risk factors	Intervention (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Kuehne 2018, Germany ³	Active	Retrospective data analysis	Newly arrived asylum seekers.	Mandatory screening among <u>asylum seekers</u> (chest X-ray or IGRA or TST for pregnant women and children <15)), n=1,474 Passive case finding (diagnosed after clinical presentation or post-mortem) or through contact tracing in <u>general population</u> , n=39,019 (passive case finding) and n=3,591 (contact tracing).	Significantly higher treatment completion rates where cases were identified through contact tracing compared with passive case finding; significantly higher completion rates where cases were identified through passive case finding compared with screening of asylum seekers. Model A (treatment success vs ALL other outcomes): 74% (passive), 87% (contact tracing), 60% (screening asylum seekers); adjusted OR (95% CI): 0.64 (0.57, 0.71), p<0.001 for contact tracing vs passive case finding; adjusted OR (95% CI): 2.37 (2.11, 2.67), p<0.001 for screening asylum seekers vs passive case finding. Model B (treatment success vs no treatment success): 83% (passive), 96% (contact tracing), 90% (screening asylum seekers) adjusted OR (95% CI): 0.54 (0.45, 0.65), p<0.001 for contact tracing vs passive case finding; adjusted OR (95% CI): 1.38 (1.10, 1.73), p=0.006 for screening asylum seekers vs passive case finding.	Reasons for non-completion not reported.
Bordin 2022, Italy ⁴	Latent	Single arm (retrospective review)	Asylum seekers temporarily residing in the area.	Migrant focussed TB screening programme. Two-step screening strategy. Preliminary clinical examination followed by chest X-ray if signs of active TB. TST if asymptomatic. IGRA (QuantiFERON-TB) if borderline TST result. All participants were informed about screening results and free treatment (three months of rifampicin and isoniazid) offered. Migrants accompanied to each consultation.	578/715 (80.83%) of those diagnosed with LTBI started treatment; 498/715 (69.65%) completed treatment. 2231/2486 (89.74%) invited to screening adhered to the full screening programme.	Factors associated with completion were age ≥24 (OR 1.75, 95% CI 1.05, 2.93) and African origin (OR 2.89, 95% CI 1.46, 5.71), multivariate analysis.
Gustavson 2022, US ⁵	Latent	Single arm (retrospective review) -part of mixed methods study	Non-US born people who adjust their immigration status to permanent residents.	Medical examination by civil surgeons for people who are adjusting immigration status to permanent residency. Includes screening for TB. Civil surgeon may recommend treatment.	59/203 (29%) initiated treatment and (127/203 (62%) "were interested in treatment"; 32/59 (54%) completed treatment (<i>by time article was drafted</i>).	37% of those recommended by civil surgeon to start treatment did so versus 10% of those who were not recommended treatment.

IGRA: Interferon-Gamma Release Assays; TST: tuberculin skin test.

c) Strategies tailored to sex workers

<i>Study</i>	<i>Type of TB</i>	<i>Design</i>	<i>Population/ risk factors</i>	<i>Intervention (n=)</i>	<i>Main findings (note if adjusted)</i>	<i>Reasons/factors associated with non-completion</i>
Daly 2016, UK ⁶	Latent	Single arm prospective	Commercial sex workers (none with alcohol abuse or intravenous drug use), n=21	Screening at sexual health clinic. Follow-up pathway altered during study period to improve accessibility and facilitate weekly DOT. Integration of nurse TB clinic into sexual health clinic. LTBI therapy changed to weekly weight-based regimen of rifapentine and isoniazid with weekly assessment for adverse drug reactions. Availability of Romanian interpreters and support from outreach workers. Multiple attempts made by outreach workers to contact women with positive IGRAs who did not attend appointments.	16/21 (76.2%) completed treatment, 2/21 (9.5%) transferred care and 3/21 (14.3%) defaulted from care.	None reported. Authors speculated that this might be due to transient nature of population (most were Romanian and may have returned to Romania).

d) Strategies tailored to migrants, refugees and asylum seekers

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Benjumea-Bedoya 2019, Canada ⁷	Latent	Single arm retrospective review- part of mixed methods study	Government-assisted refugees	<u>BridgeCare Clinic LTBI program</u> . Primary healthcare facility with integrated TB care for government-assisted refugees; trained interpreter and outreach worker available; monthly follow-up, with active follow-up for those who missed appointments; written information provided in clients' own languages; education sessions on TB in general, LTBI, testing positive for LTBI, its treatment, possible adverse events, and consequences of not treating; n=59.	45/59 (76.3%) eligible and accepted treatment; 34/45 (75.6%) started treatment; 27/34 (79.4%) completed treatment.	Includes: younger age of some clients, language or literacy barriers, adverse events, service resource limitations, lack of familiarity with preventive medicine. <i>See supplementary material on qualitative studies for further detail.</i>
Harwood-Johnson 2023, Canada ⁸	Latent	Single arm retrospective review	Government-assisted refugees, private-sponsored refugees, and refugee claimants	<u>Refugee Engagement and Community Health (REACH) clinic</u> . Housed within a community clinic providing access to care to marginalised populations. Primary and paediatric healthcare provided through multidisciplinary teams (including interpreters, settlement agencies, and other community partners) for a duration of 12–18 months post-arrival to Canada. The clinic is staffed by providers with additional training in refugee health, trauma-informed care, and infectious diseases. Treatment and support provided free of charge regardless of patients' insured status or immigration documentation; n=78.	56/66 (84.8%) accepted treatment of those eligible; 45/56 (80.4%) started treatment; 42/45 (92.3%) completed treatment.	Reasons for declining included concerns about side effects relating to pregnancy or non-specified. Treatment acceptance more common in children compared with adults (p=0.02), but did not vary significantly according to gender, categories of refugees, WHO region of origin or year of arrival.
Rennert-May 2016, Canada ⁹	Latent	Single arm retrospective review	Government-sponsored refugees	<u>Integration of TB services with a general refugee health clinic</u> . Enhanced TB screening program for refugees within two weeks of arrival; variety of medical services available (assessment for LTBI, psychological support, screening for HIV, viral hepatitis, and parasitic infections); telephonic and in-person interpreters; all diagnostic tests and treatments for TB/LTBI free of charge, and transportation subsidies offered; convenient appointment times offered; TB screening was not a mandatory requirement and had no impact on immigration status; settlement counsellor, fluent in the language of the refugee, helped guide clients to appointments when necessary; n=151.	147/151 (97.4%) eligible offered treatment; 141/147 (96%) agreed to start treatment. 103/141 (73%) completed an entire course of LTBI therapy. 103/151 (68%) completed treatment where treatment indicated.	Younger participants (p = 0.039) and those of Sub-Saharan African origin (p<0.005) less likely to complete treatment once started. No significant differences in completion for those taking INH versus RIF (p > 0.1).
Pepin 2022, Canada ¹⁰	Latent	Single arm retrospective review (2 cohorts)	Refugees or asylum claimants	<u>Sherbrooke refugee clinic within a primary care facility</u> . Refugees referred by two community organizations; comprehensive evaluation for detecting and managing LTBI and other diseases; TST provided and chest X-ray, and transfer to infectious disease clinic where indicated; patients experiencing adverse reactions instructed to contact translator to arrange a medical visit; instructions provided in writing at the initial medical visit, in the refugees' own language, in addition to explanations given through the translator; community pharmacists instructed to provide rifampin; n=295 (cohort 1) and n=146 (cohort 2).	Completion rates (of those offered treatment): 2010-2014 cohort 1: 250/295 (85%); 2018-2019 cohort 2: 124/146 (85%).	Reasons for non-completion not stated. Reasons for not initiating treatment: deferral due to pregnancy or other health issues or because patients moved out of area.

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Rogo 2017, US ¹¹	Latent	Single arm retrospective review	Paediatric population with 30% refugees	<u>Paediatric Tuberculosis Clinic at Hasbro Children's Hospital (HCH).</u> Evaluations and treatment for all paediatric patients referred with a positive TB screening test – either TST or IGRA; dental care provided; trauma-informed child psychologist provides mental health care; same nurse for paediatric TB Clinic as for paediatric Refugee Health Program (PRHP) providing continuity; PRHP works with medical interpreters, most of whom are former refugees who provide services as Community Health Workers (CHW); CHWs provide culturally appropriate care coordination and additional social support; continued paediatric primary care support at HCH beyond initial evaluation; follow-up phone calls where patient does not attend scheduled visit; gift card to child's family upon completion of treatment; free parking vouchers or free bus passes; TB treatment provided free of charge, n=120 (n=36 refugees).	Completion rates (of those diagnosed with LTBI): 94/120 (78.3%) (95% CI not reported) total cohort, 31/36 (91.2%) (95% CI 81.6%, 100%) refugees. Patients who missed any doses 83.3% (refugee) vs 86.7% (non-refugee); Percent of scheduled appointments attended 95.4% (refugee) vs 82.3% (non-refugee).	Higher rates of treatment completion among female patients, patients referred internally from other HCH clinics, patients who used an interpreter, and those who did not report side effects.
Carter 2017, US ¹²	Latent	Single arm retrospective review	Refugees	<u>Primary care clinic for refugees with clinical pharmacist-run LTBI clinic.</u> Role of pharmacist was to track patients diagnosed with LTBI, initiate treatment, provide education and counselling (in person), assess for adherence, and arrange follow-up; use of telephonic interpreters; comprehensive medication reconciliations at each visit; other pharmaceutical care needs addressed in collaboration with physicians (e.g., uncontrolled diabetes, smoking cessation, hypertension, vaccinations); n=90.	85/90 (94.4%) completed LTBI treatment (of those referred). Of those, 40% required at least one intervention from the pharmacist to remain adherent.	Not reported, but reasons for requiring pharmacist interventions were refill access issues, barriers at the pharmacy, misunderstanding about disease state and/or initiating treatment, subtherapeutic dose or duration of medication, adverse events, insurance lapse.

e) Other strategies tailored to migrants, refugees and asylum seekers

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Boyd 2019, US, Jordan, Lebanon ¹³	Active	Single arm retrospective review	Syrian refugees to Lebanon and Jordan.	Resources/activities varied slightly between countries but included: engaging community health workers to provide awareness sessions about TB disease and treatment services in refugee camps/community organisations; providing symptom screening at international border entry points or in settlements/shelters; use of mobile medical units; funding of screening, medication and transportation costs to clinic; provision of DOT by community health workers or nurses; n=58 (Jordan), n=139 (Lebanon).	Completion rates: Jordan: 96.2% (in 2013), 94.4% (in 2014), 94.8% (2015). Lebanon: 77.1% (in 2014), 87.8% (in 2015).	No difference in cure or completion by sex, age group, or camp status (Jordan, bivariate analysis). Males had lower odds than females, but age group had no effect on cure or completion (Lebanon).
Essadek, 2018, Spain ¹⁴	Active and latent	Single arm retrospective review	Hard-to-reach immigrants.	Community-oriented programme including health care professionals and community health workers from different cultures; community health workers assigned to cases based on place of origin, culture and other needs; tracing and following up TB cases which were considered lost to follow-up or who had difficulties following treatment, and actively searching for contacts; calls, mediation, on the spot visits, informal meetings, visits to health care centres and group workshops; n=122 (active TB cases), n= 54 (LTBI).	Completion rates: 73% (active cases), 79.6% (LTBI).	Not reported.
Spruijt 2019a, The Netherlands ¹⁵	Latent	Single arm retrospective review -part of mixed methods study.	Immigrants not applying for asylum from non-EU countries.	Information brochure on purpose of LTBI screening by mail or at registration at the Public Health Service (PHS); Medical Technical Assistants gave further explanations about screening procedures; IGRA or TST/IGRA for screening; if eligible for LTBI treatment, TB physicians educated client on the purpose and possible side-effects of LTBI treatment; TB physicians consulted clients on LTBI treatment every month for adverse and treatment adherence; during regular contact moments, TB nurses interviewed, educated and supported the client during treatment in a "demand-driven, tailored way". Information materials in Dutch and English. Treatment offered free of charge, and a minimum intended stay of 6 months was set for screening to ensure continuity of care; n=94 (with LTBI)	Completion rate: 69% of those initiating treatment. Treatment initiated of those diagnosed with LTBI: 52%.	Most common reason for discontinuation of treatment was side-effects. <u>Treatment initiation</u> was associated with PHS, lower age group, longer intended duration of stay in the Netherlands, and lower level of education. Other common reasons reported for not initiating treatment were: no perceived advantages of LTBI treatment by client, and return of the client to country of origin in the foreseeable future.
Spruijt 2019b, The Netherlands ¹⁶	Latent	Single arm retrospective review -part of mixed methods study.	Asylum seekers living in asylum seeker centres.	TBI screening consisted of education, a health questionnaire (filled in by clients) and blood sampling (undertaken by Medical Technical Assistants). IGRA used for LTBI testing. TB physicians confirmed LTBI diagnosis and offered eligible participants treatment free of charge. TB nurses provided LTBI treatment support based on the client's needs. Communication of test result through bilingual letter (in Dutch and mother tongue of client). If necessary, interpreters were used during consultations and other LTBI treatment activities; n=178 (with LTBI)	Completion rate: 91% of those initiating treatment and not lost to follow-up; 86.6% if include those lost to follow up.	Eritreans (versus non-Eritreans) more likely to initiate LTBI treatment, whereas those in higher age groups (versus those aged <24 years) were less likely to start LTBI treatment. Those with higher education more likely to complete treatment.

f) Cure TB programme

Study	Type of TB	Design	Population/ risk factors	Intervention (n=)	Comparator (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Figuero a, 2020, US ¹⁷	Active (verified or possible)	Single arm retrospective review	Migrants relocating outside the US before completing treatment	<u>CureTB Programme</u> . Referral and continuity of care programme for patients relocating outside of the US before completing treatment. Links patients to health care for treatment and diagnostic services at their destination; facilitates exchange of diagnostic, treatment, and outcome information between receiving countries and referring jurisdictions. During telephone interviews, CureTB informs patients how to access TB services in their destination countries and educates them about TB disease and the importance of treatment adherence; n=440.		78% completed treatment or had a bacteriologically confirmed cure.	Significantly higher risk of being lost to follow in patients: who were not interviewed before leaving the US (p<0.001); who were in law enforcement custody (p<0.0001); who did not have diabetes (compared with those who had diabetes) (p=0.022).

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Qualitative studies - main characteristics and findings

a) Different drug regimens and treatment lengths

Study	Type of TB	Population/ risk factors	Data collection and analysis	Intervention/ comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence/completion)
Chevrier 2022, Canada ¹	Latent	BridgeCare* clinical staff and programme managers (n=not reported).	Four structured interviews and constant comparative analysis approach to identify major themes.	3HP or 4R versus 9H* Proportion with DOT not stated.	<p><u>Generally (BridgeCare clinic):</u></p> <ul style="list-style-type: none"> - difficulty in evaluating the actual risk of TB disease (without knowledge of LTBI disease history) - being pregnant or trying to become pregnant <p><u>For 3HP/4R (compared with 9H):</u></p> <ul style="list-style-type: none"> - more interactions with other medication - 3HP DOT more work for nurses 	<p><u>Generally (BridgeCare clinic):</u></p> <ul style="list-style-type: none"> - on-site lab sampling at BridgeCare Clinic - trust, comfort, and familiarity in the relationship between client and clinical staff - easy access to interpreters - most clients come from TB endemic countries and have more knowledge of TB <p><u>For 3HP/4R (compared with 9H):</u></p> <ul style="list-style-type: none"> - reduced duration improved receptivity to treatment and resulted in fewer missed appointments - fewer side effects; suitability for clients with chronic hepatitis; improved ability to complete treatment within the 12 months that clients are followed for at BridgeCare - 3 HP DOT contributed to continuity of care

DOT: directly observed therapy; 3HP: three months of once-weekly isoniazid plus rifapentine; 4R: four months of daily rifampin; 9H: isoniazid for 9 months; *BridgeCare clinic, a primary healthcare facility with integrated TB care for government-assisted refugees.

b) 3HP/DOT

Study	Type of TB	Population/ risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence/completion)
Nwana 2019, US ²	Latent	Health care workers from three programme sites that treated a substantial proportion of study patients experiencing homelessness (n=7).	Two interviews by phone and one in person; three themes considered in analysis (programme related, process of 3HP/DOT implementation and provider perceptions of 3HP/DOT).	3HP/DOT*	<ul style="list-style-type: none"> - 3HP/DOT implementation seen as more costly (staffing and time) compared with 9H - limited staff, and staff had limited experience with this regimen - high pill burden and frequently reported high blood pressure with 3HP/DOT - concerns with triggering psychological feelings of being intoxicated ("high") during blood draws (for substance users) - frequent patient relocation due to instability in housing - frequent treatment interruptions in alcohol and drug users - some patients mistrusted regimen as it was characterised as 'new' 	<ul style="list-style-type: none"> - treating LTBI seen as worthwhile investment to avoid active TB cases - incentives and short duration of 3HP seen as valuable for increasing adherence - one site stated a preference for administering treatment at local shelters
Thomas & Summers 2022, UK ³	Active	People with one or more social risk factors or factors for non-adherence+ (n=8).	Semi-structured interviews and thematic analysis.	Range of supervision styles (daily DOT, DOT three times/week, weekly home or clinic visits, monthly clinic visits, home visits with tablet counts, weekly pill box top ups).	<ul style="list-style-type: none"> - some people felt they weren't trusted, listened to, or included in the decision-making process - perceived wasted time during outpatient appointments (re-explaining diagnosis and treatment progress to new doctors at each appointment) - intentional non-adherence (to SAT) influenced by employment, domestic situation and personal experience affecting daily behavioural health choices - viewing DOT as a mechanism for disclosure, which led to secretive behaviour (e.g. not telling employers) - discrimination from within family - perceived isolation and inability to escape DOT left participants feeling trapped - no psychological support offered to outpatients - medical team's failure in recognising deteriorating mental state contributed to downward spiral of untreated depression, alcoholism and non-adherence 	<ul style="list-style-type: none"> - practical support, social connection and a degree of empowerment (DOT as vehicle to retaking control of health) - experience of TB (and hospital stay) as motivation to endure daily disruption to work and side-effects - using knowledge of behavioural change gained from working as a nurse - DOT visits enabled donations of food and other necessities, and help with benefits applications - deriving comfort from routine of DOT (unemployed participant) - social connection and psychological support through DOT - access to psychological assessment/therapy as an inpatient

* some sites variously included resources to improve outreach (e.g., informational brochures, personnel, and mental health or addiction services, emphasis on clear communication, administering medication in local shelters, provision of incentives, partnerships with shelter staff or correctional facilities); + 3/8 homelessness/drug/alcohol misuse; 2/8 imprisonment current or within 5 years; 1/8 memory disorder; 5/8 previous treatment or treatment failure; 2/8 previous non-adherence to treatment.

c) Screening or test focussed approaches

Study	Type of TB	Population/ risk factors	Data collection and analysis	Intervention and comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
Gustavson 2022, US ⁴	Latent	Non-US born people who adjust their immigration status to permanent residents ('status adjusters'), n=203.	Programme staff contacted 'status adjusters' via phone to solicit their understanding of LTBI and encourage them to seek further evaluation for LTBI. Standardised calling script used, but adapted where needed.	Medical examination by civil surgeons for people who are adjusting immigration status to permanent residency. Includes screening for TB. Civil surgeon may recommend treatment.	<ul style="list-style-type: none"> - lack of understanding of LTBI versus TB and/or belief that a positive IGRA was due to prior BCG vaccination; doubt around having LTBI - concern about treatment costs (particularly if uninsured) - COVID-19 pandemic delayed treatment - concern that having LTBI would affect application for status adjustment - confusion about interest in tracking treatment initiation and completion if treatment is optional - wide variation in LTBI treatment practices and recommendations among civil surgeons 	None reported.
Survey results: 71% aware of their LTBI diagnosis; 48% had some understanding of distinction between LTBI and TB; 6% believed that a positive IGRA was due to prior BCG vaccination; 48% reported that civil surgeon either recommended against treatment or did not discuss LTBI.						
Spruijt 2020a, The Netherlands ⁵	Latent	Health care professionals and Eritrean patients, n=unclear (group interviews), n=10 (individual interviews).	Semi-structured group interviews with project teams and individual interviews plus group interviews with Eritrean participants. Coding scheme used; researchers discussed coding and interpretation of the data in regular meetings.	Six community strategies to encourage screening and treatment, developed with Eritreans from the community. All strategies included 1-3 education sessions in a community setting followed by screening sessions; n=410 (participation in community strategies), n=30 (with LTBI). Screening and treatment offered free of charge. LTBI treatment support by TB nurse and interpreters where necessary.	<ul style="list-style-type: none"> - organisation and execution of strategies seen as time consuming and requiring a flexible attitude from TB care staff - most staff doubted feasibility of activities in regular practice - staff questioned effectiveness of the program because of low LTBI screening uptake - participants felt overloaded by letter/flyers from various organisations and prioritised only compulsory appointments - mistrust and lack of respect (by participants) towards Eritrean key figures (who are often perceived as supporters of the current Eritrean regime from which new generation of migrants fled) - difficult to motivate target population to participate in the program because of competing priorities - lack of understanding of LTBI when participants felt healthy and had normal chest X-ray - some respondents felt stigmatised as the program targeted only Eritreans and not Arabic migrants - some respondents were sceptical about the project's purpose - gossip in the community about Western countries testing medical devices on African refugees, such as vaccines 	<ul style="list-style-type: none"> - education perceived as eye-opening and important by patients - reimbursement of screening and treatment costs - active face-to-face outreach seen by participants/key community figures as more effective than letters, flyers or posters - key community figures crucial in approaching and reaching the target population

d) Strategies tailored to people experiencing homelessness, social risk factors or substance abuse

Study	Type of TB	Population/risk factors	Data collection and analysis	Intervention/comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
Salem 2020, US ⁶	Latent	Homeless people who experienced at least one mental illness, substance use or received medical care while homeless, n=11	Focus groups using semi-structured interview guides; line-by-line coding to generate major themes.	<i>NB participants have not experienced this intervention –study to inform future intervention.</i> 3HP LTBI Nurse and Community Health Worker (CHW) 6-month intervention; CHW conducts a weekly 20-min case management session over 12 weeks; each week, the CHW will deliver all components of the program as well as assess 3HP side effects, track missed doses, and provide health-related support. Focus of case management sessions varies, e.g. education, support for mental health problems, dangers of substance abuse, facilitating access to stable housing, identifying triggers for non-adherence.	<ul style="list-style-type: none"> - lack of LTBI treatment 'readiness' - accessing the population (e.g. safety of research staff, high risk populations) - lack of paperwork related to identification or health insurance - lack of physical and mental chronic healthcare access and mental and physical self-care - lack of institutional trust - concurrent use of medications (fear of side effects) - lack of education on medication side effects, administration, compliance issues - fear of TB disease and taking LTBI medication - language barriers - lack of respect and being stigmatised - being forced to take medication - concurrent substance abuse - transience of homeless population - lack of incentives 	<ul style="list-style-type: none"> - LBTI treatment 'readiness' (i.e. "catch people at the right time") - LBTI and TB health education (particularly on side effects) - characteristics of research staff (e.g. gender, personality, communication and bilingual proficiency, ability to earn trust) - familiarity with homeless population (research team "who know the streets") - timing of intervention (e.g. less likely to engage at weekends) - importance of being involved in care - having a friendly provider - providing compensation and incentives - a comprehensive and holistic social and health services approach - keeping in contact with participants, building trust, keeping them engaged, location details
Harrison 2022, Belarus ⁷	Active	Patients with suspected alcohol use disorder or harmful alcohol use; n=12 (patients), n=20 (health-care workers)	In-depth interviews with patients and focus group discussion with healthcare workers; thematic analysis.	Person-centred, multidisciplinary, psychosocial support and harm reduction programme (PCMPS) delivered by TB doctors, counsellors, psychiatrists, health-educators, and social workers. Includes individual and group counselling, patient education, mental health support, psychiatric care, and social support around 1–3 times per week in person or by phone. DOT or VOT. Tailored to risk, i.e. patients more at risk of non-adherence received more intensive counselling or harm reduction packages, mandatory assessment by a psychiatrist, and anti-craving medication where appropriate.	<ul style="list-style-type: none"> - approaches where doctors only care about adherence to TB treatment, and were not interested in other aspects of a patients' health - some practitioners perceived patients who had a substance abuse and imprisonment history as problematic - programme psychiatric staff said that patients with other drug use or untreated personality disorders could be the hardest to engage 	<ul style="list-style-type: none"> - being able to build a trusting relationship - for those in isolation, counsellors represented relationships they otherwise might not have had - referral to social worker for patients with employment or other social issues - referral for other medical problems - counselling to help patients deal with conflict with partners, financial or administrative stressors, or fears surrounding TB - counselling meant patients were treated 'as human beings' - teamwork and integration of health workers' differing specialties (e.g. to help manage crises) - patient resilience and determination - importance of trust in loved ones, and, in some instances, in practitioners who treated them humanely and with care

Study	Type of TB	Population/ risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
Kielmann 2018, Latvia ⁸	Active	<p>Patients with social risk factors (n=10) and health care professionals or social workers (n=14).</p> <p>Patients: 5/10 history of alcohol or substance abuse; 4/10 unstable employment or unemployed; 1/10 refugee from Eritrea.</p>	<p>Semi-structured interviews and qualitative observations</p> <p>. Open coding around broad topic of 'organisation of TB care for underserved patients' leading to a framework focusing on four different dimensions of care.</p>	<p>Intervention designed to improve adherence of patients to TB treatment: two-day training workshop to strengthen staff-patient communication skills; development of psychosocial risk screening tool to identify those patients likely to struggle with adherence; patients identified by the screening tool provided with additional adherence support meeting with head ambulatory nurse; these patients closely followed up and offered help with finding suitable housing, referral to a psychologist and financial support to cover travel costs, where needed.</p>	<ul style="list-style-type: none"> - history of alcohol/narcotics abuse, social isolation, dual burden of disease (e.g. diabetes, HIV), unstable housing, job insecurity, avoidance of doctors when feeling unwell to avoid missing work, inability to negotiate the (health) "system", vulnerability in terms of domestic violence - long/delayed diagnostic process, poor communication of disease status in hospital, little resource for patient education, dehumanising hospital environment (staff and patients), missed opportunities for education on treatment impact - social support can't easily be accessed by homeless people registered in a different city - applying for social assistance cumbersome, relies on phone calls to make contact, patients often resistant to being called and reluctant to provide information about their whereabouts or social contacts - financial assistance limited/not enough to buy food - lack of family members willing to act as treatment supporters - referral for psychological support services not readily accepted by patients (due to sensitivity of issues and cost) and not always available - lack of TB NGOs in the city - low status of social workers in clinical settings, lack of awareness of their (potential) roles - limited assistance for substance abuse, immigration issues and lack of integration of health and social services, view that care for TB patients is foremost the domain of clinicians and prioritisation of medical over social aspect - lack of flexibility in staff attitudes and DOT treatment schedule - DOT as constraint on ability to work - home visits where patients have missed DOT time consuming, tiring and ineffective (e.g. locating and accessing buildings) - gaps in workforce 	<ul style="list-style-type: none"> - initial consultations (for initiation of treatment) with doctor and nurse experienced as positive by patients (often contrasted with the confusion and distress experienced at time of diagnosis) - head nurse eliciting information about the patients' social circumstances, and spends time gauging their understanding of the condition and the course of treatment - gaining patients' trust over progressive meetings - patients felt nurses showed interest in how they felt and that treatment at the Centre for Tuberculosis and Lung Diseases was "civilised" (compared with hospital) - nurses can facilitate social support (financial, psychological, or referral to a 'narcologist') - courier to follow-up on patients who have missed DOT

Study	Type of TB	Population/ risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
Craig & Zumla 2015, UK ⁹	Active	Patients with complex social and/or medical needs (most homeless, many with drug and alcohol use or immigration problems, history of imprisonment); n=17.	Semi-structured interview; theoretical thematic analysis involving both deductive (top down) and inductive (bottom up) coding and linking codes.	Appears to be standard care, with some receiving DOT. The study formed part of a wider service development project conducted in London, UK, which aimed to develop a social outreach model of care for marginalised groups with TB and generate an evidence base for the need of a TB caseworker in supporting clients with complex needs.	<ul style="list-style-type: none"> - lack of social support, e.g. for medication reminders - lack of training /funding for hostel workers to assist with healthcare - lack of material or practical assistance (job, housing, money to buy 'good' food, assistance with shopping, coming off drugs, someone to talk to) - fear of disclosure related to the threat of eviction and rejection by the wider Somali community - under-prescription of opioid substitution therapy while in hospital, withdrawal symptoms - conflict in hospital between meeting patient needs and adhering to prescribing protocols (e.g. some wards have a zero tolerance policy relating to drugs and alcohol) - refusal to treat patients unless they modified their behaviour - coercion to comply with treatment to avoid compulsory detention - distance to Drug Dependency Unit for DOT or inability to attend for drug users as they had used or intended to obtain drugs - resentment where DOT was administered in an authoritarian atmosphere - difficulty of taking the prescribed regimen when trying to maintain daily routines (especially where also taking medication for HIV) - difficulty in storing medication or having medication stolen - difficulty in having control over availability of food to comply with when medication should be taken - adverse effects of therapy - difficulty in distinguishing between symptoms of TB, adverse events, other co-morbidities, alcohol use and withdrawal symptoms 	<ul style="list-style-type: none"> - hostel workers or friends reminding patients to take medication or accompanying them to clinic appointments - hospital seen as "welcome break" from homelessness - hospital as safety net (with delayed discharge until accommodation was provided by Social Services) - receiving DOT as opportunity for social interaction and structure - more routine and stable lifestyles and using reminders such as alarm clocks or charts.

Study	Type of TB	Population/ risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
Karat 2021, UK ¹⁰	Active	Patients with previous or current active TB, or caregivers. Included migrants and some participants with high levels of alcohol use, incarceration, emergency migration, or homelessness. Identified as 'high risk' for non-adherence.	In-depth interviews using a topic guide. Information categorised into a matrix to compare and contrast data on five key themes (personal, social, structural, health systems, and treatment-related) until theme saturation was reached.	Standard care	<ul style="list-style-type: none"> - 'chaotic lifestyle' (e.g. high alcohol intake, unstable employment) - social isolation (e.g. due to homelessness) - fragmented care or mixed health care messages (e.g. due to complex co-morbidities) - perception of risk as low (e.g. if in denial of diagnosis) - absence or loss of faith in the health care system (e.g. due to delayed entry into care) - poor understanding of the need to take medication (e.g. due to language barrier) - treatment side effects (especially in complex/severe disease) - mental health issues (could be exacerbated by treatment side effects). 	<ul style="list-style-type: none"> - well-established medication routine (e.g. established through early admission to hospital) - at least one close/caring relationship (e.g. married or cohabiting) - role as breadwinner/carer - good understanding of the need to take medication (e.g. though previous experience of disease) - supportive employer/regular employment - sense of progression towards end of treatment (e.g. clinical improvement such as weight gain) - good relationship with/trust in TB nurse - perception of risk as high (e.g. if severe symptoms).

e) Refugee specific clinics (integrated care)

Study	Type of TB	Population/ risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
Kunin 2022, Australia ¹¹	Latent	Health care workers from the Monash Health Refugee Health and Wellbeing (MHRHW) service and the universal primary care clinic (includes GPs, nurses, infectious disease physicians); n=15	Two focus group discussions (face-to-face or via phone in) and qualitative exploratory descriptive analysis.	Intervention: MHRHW service. Integrated primary care and specialist services providing intensive transitional care to refugees experiencing high levels of vulnerability, complex health needs and restricted access to Medicare. Includes use of interpreting services, a multi-disciplinary team, a training module for health care workers, and a Patient Education Resource Pack Comparator: universal primary care clinic	- limited motivation of patients to engage with LTBI treatment - asymptomatic nature of the condition and the extended duration of treatment - patients struggled to process diagnosis-related information (active TB versus latent TB) - competing priorities (having other things to worry about) - low confidence of GPs in responding to medication related adverse reactions - Medicare billing model not adequate in renumeration time spent "to call, to follow-up and chase [patients] up" - short consultation time - limitations of isoniazid (adverse reactions and the length of treatment)	- routine patient education, including "teach-back" technique, distributing information about LTBI across several education sessions and visual aids - comprehensive LTBI training and ongoing support to primary care providers from MHRHW infectious diseases physicians and availability of infectious disease physicians for consultations as required - initiative evolved through a process of codesign and established relationships - cultural competency and familiarity with refugee health - communication in patients' first language and access to interpreters - resource availability (extended consultations and staffing resources) - dedicated resource for patient education and follow-up - importance of free medication
Benjumea-Bedoya 2019, Canada ¹²	Latent	Senior BridgeCare Clinic and Winnipeg Regional Health Authority staff; n= not reported	Document reviews and five in-person semi-structured Interviews. interviews categorised according to levels of a social ecological model.	BridgeCare Clinic LTBI program. Primary healthcare facility with integrated TB care for government-assisted refugees; trained interpreter and outreach worker available; monthly follow-up, with active follow-up for those who missed appointments; written information provided in clients' own languages; education sessions on TB in general, LTBI, testing positive for LTBI, its treatment, possible adverse events, and consequences of not treating.	<u>Intrapersonal</u> : younger age of some clients; pregnancy and family planning; unknown age; unknown medical history; language barriers; low literacy levels; concern regarding side effects; long duration of treatment <u>Institutional</u> : lab services availability; staff and resources limitations; communications across facilities and between providers. <u>Socio-cultural/community</u> : lack of familiarity with prophylactic/preventive medicine. <u>Structural/Policy</u> : temporary nature of clinic services; lack of material incentives for treatment completion; limited staff and resources.	<u>Intrapersonal</u> : absence of side effects with first line treatment; low prevalence of alcohol dependence/issues among refugee populations. <u>Interpersonal</u> : strong relationships with clients. <u>Institutional</u> : significant focus on client health education; nurses in central program management roles; clients assigned to a regular primary care physician; accessible and well utilised interpreter service; multipurpose contacts with clients; patient-centred approach to care; improved efficiency and accessibility of laboratory services. <u>Socio-cultural/community</u> : personal experience with active TB patients and fearing disease consequences. <u>Structural/Policy</u> : availability and accessibility of IGRA testing; comprehensive health care coverage; region-wide clinical rounds specific to LTBI

f) Other strategies tailored to migrants, refugees and asylum seekers

Study, type of TB	Type of TB	Population/risk factors	Data collection and analysis	Intervention/comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
Spruijt 2019a, The Netherlands ¹³	Latent	Health care professionals, n=unclear	Semi-structured group interviews using a topic guide. Coding scheme used; two researchers discussed coding and interpretation of the data in regular meetings.	Information brochure on LTBI screening; Medical Technical Assistants gave further explanations about screening procedures; IGRA or TST/IGRA for screening; if eligible for LTBI treatment, TB education by physicians (including on side-effects); monthly consultations with TB physicians; regular contact and support from TB nurses ("demand-driven, tailored way". Information materials in Dutch and English. Treatment free of charge, minimum intended stay of 6 months set.	<ul style="list-style-type: none"> - information brochures not sent out - wrong belief that screening would include chest X-ray - LTBI screening was more time-intensive than the expected chest X-ray - misunderstanding that screening outcomes would affect residence permit - screening health questionnaire not always completed accurately by Medical Technical Assistant - some TB physicians sceptical about offering LTBI treatment to immigrants with a short-intended duration of stay (and high risk of re-infection in home country) - some higher educated clients could not believe they had been diagnosed with LTBI (perceived TB as a disease of the poor) - unfamiliarity with LTBI treatment - lack of trust in the Dutch TB control system; some patients consulted physicians in their home country who advised against LTBI treatment - TB nurses said that clients with lower levels of education need more intensive treatment support - clients were hard to reach during office hours for phone appointments - staff experienced the LTBI screening and treatment program as more time-intensive than chest X-ray screening - costs of LTBI treatment (free in this study) 	<ul style="list-style-type: none"> - higher initiation of treatment where Public Health Service had an attitude of "intention to screen is intention to treat" - TB physicians perceived clients with difficulties understanding the concept of LTBI and who confused their diagnosis with TB disease, and clients with fear of developing TB disease were more inclined to initiate LTBI treatment - clients who understand prevention and the benefits of LTBI treatment more inclined to initiate LTBI treatment - LTBI screening with only IGRA would be a more efficient pathway compared with TST followed by confirmatory IGRA
Spruijt 2019b, The Netherlands ¹⁴	Latent	Health care professionals and Eritrean patients, n=unclear	Semi-structured group interviews using a topic guide. Coding scheme used; two researchers discussed coding and interpretation of the data in regular meetings.	TBI screening consisted of education, a health questionnaire and blood sampling. IGRA used for LTBI testing. Treatment free of charge for eligible participants. TB nurses provided treatment support based on the client's needs. Communication of test result through bilingual letter (in Dutch and mother tongue of client). Use of interpreters where needed.	<ul style="list-style-type: none"> - relocation of clients between asylum seeker centres (ASC) or from the ASC to the municipalities - gossip in the ASC about the amount of blood collected for the blood test - poor understanding of health-related topics and need for help to fill in the health questionnaire using a professional interpreter - most clients did not read the information brochure because of negligence, the perceived difficult content or illiteracy - some clients who did not use week boxes felt overwhelmed with the number of tablets when given all at once for 1 or 2 months - clients missing appointments, not knowing how to reschedule appointments, financial or practical difficulties travelling (unfamiliar with public 	<ul style="list-style-type: none"> - planning the screening in collaboration with the ASC-COA (Asylum Seeker Centre and Central Agency for the Reception of Asylum Seekers) personnel during weekly mandatory reporting ensured the client's presence - ASC-COA personnel could help locate clients in case of no-show - allowing clients to call and invite friends or family eligible for LTBI screening - screening seen as important for own health - in-person verbal education about TB and LTBI prior to the blood sampling

Study, type of TB	Type of TB	Population/ risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
					transportation or (Google) maps, illiteracy and dependence on the help of others to travel, problems asking for help because of language barriers) - language a barrier for some clients experiencing side-effects: they could not reach out to staff.	- education seen as essential for informed decision making for participation in screening - TB physicians believed that most Eritrean clients initiated LTBI treatment because they did not distinguish TB disease from LTBI - use of professional interpreters - LTBI treatment support by TB nurses, of which the intensity was comparable to that of TB disease treatment support - use of alarms on mobile phones, WhatsApp contact between nurses and clients (using emoticons, spoken messages and very simple text messages), and week boxes for medication - collaboration with the ASC health services (help filling the week boxes or function as a contact person for clients with queries concerning the treatment).
Sprijit 2020b, The Netherlands ¹⁵	Latent	Eritrean asylum seekers and refugees, n=31 (individual interviews, n=unclear for focus groups).	Semi-structured group and individual interviews. Coding scheme used for coding transcripts. Three researchers discussed coding and interpretation of the data in regular meetings.	Participants received TB and LTBI group education before LTBI testing. Education, included posters and PowerPoint slides, in participants' mother tongue, using professional interpreters. Participants with an LTBI diagnosis received further education by TB physicians and nurses throughout the care cascade, also with use of a professional interpreter.	- community members told stories of 'poisonous' medication given in the Netherlands - concealing of LTBI due to fear (of gossip and isolation) - too difficult to explain the difference between the treatment for infection and disease to others - cultural beliefs and fear of disease transmission (of LTBI) persisted over new information from TB professionals - TB and LTBI education provided throughout the cascade of care improved knowledge, however, did not prevent stigma	- health education created more awareness and consciousness about severity of TB disease - some participants said they received good support because their friends also participated in the TB education session, which contributed to treatment adherence and completion.
Yasin 2015, Turkey ¹⁶	Latent or active	Leading stakeholders who took part in running the Tuberculosis	Field notes and semi-structured interviews conducted face-to-face and over	Tuberculosis Aid Program (ITAP), a community-based screening and treatment programme, which ran from 2005-2008.*	- language barrier between dispenser staff and migrants - difficulty in reaching "irregular" migrants (potentially) infected with TB after ITAP ceased (IPTA staff were only subsequently able to help those who seek help by themselves).	- collaboration with non-governmental aid and support organisations (including faith-based), which already had contacts to "irregular" migrants

Study, type of TB	Type of TB	Population/risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
		Aid Program (ITAP), a community-based programme for "irregular" migrants in Istanbul, n=10.	email. Thematic analysis.			<ul style="list-style-type: none"> - importance of livelihood support (access to food, clothing, shelter/housing and medications) - removing language barriers (though interpreters or multi-lingual staff) - community involvement for supporting treatment and adherence - ensuring follow-up at every stage of treatment (supported by community leaders and home visits) - confidentiality increased trust (e.g. no obligation to present a valid ID, less fear of deportation) - no fee for screening/treatment
Tavares 2019, Portugal ¹⁷	Active	Health professionals involved in TB care for migrants, n=17 (interviews), n=120 (survey)	Online survey with 19 multiple choice items; semi-structured interviews using topic guide. Thematic analysis.	Standard care	<ul style="list-style-type: none"> - unawareness of TB disease and its symptoms as factor for presentation with advanced disease stage - referral at an advanced stage of disease due to being tested first for other pathologies - experience of social and economic adversities in the host country as a factor for delayed presentation - mobility of patients, social isolation and lack of family support as reason for non-adherence and difficulties in follow-up - difficulties in understanding the treatment plan - side effects, high pill burden and long treatment period - side effects and initial relief of symptoms resulting in self-perception of cure and futility of continuing treatment - incompatibilities of DOT appointments with working hours - having HIV co-infection - having a non-cooperating personality or addictions (i.e. drugs, alcohol) - religious constraints (e.g. treatment during fasting hours of Ramadan) - transportation costs (especially if HIV-TB co-infection) - costs related to work absences or becoming unemployed while on sick leave - absence of social support mechanisms preventing unemployment and loss of income - difficulties with bureaucratic procedures during registration for primary health care in Portugal - lack of knowledge on rights to health care 	<ul style="list-style-type: none"> - increasing training initiatives for healthcare workers to improve cross-cultural competencies and knowledge on migrants' social and health contexts - training on HIV and TB integrated care - language training in order to assure providers' proficiency in at least one foreign language - willingness to know more about institutions and public services to which they can refer migrant patients for support.

Study, type of TB	Type of TB	Population/risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
					<ul style="list-style-type: none"> - needless fear of being reported to Immigration Services or being deported - communication barriers with migrant patients - social and cultural perceptions of the disease, and stigma towards TB disease among patients and the community - workload and understaffing (particularly for home visits) - increasing barriers for the provision of social protection to TB patients and the need for more social workers placed at the healthcare units - inefficient organisation of healthcare services and low problem-solving capacity - communication problems between hospitals and primary care centres - need for more psychological support services for migrant patients, especially for those with HIV-TB co-infection - lack of pulmonologists and adapted in-patient facilities - scientific update and training initiatives considered costly, non-sponsored, and often restricted to certain professional groups- usually the superiors rather than routine service providers in close contact with the patients. 	

**Developed as a collaborative effort between two social entrepreneurs and the Istanbul anti-TB association (IVSD), a quasi-governmental association with 11 clinics running across the city. Included raising awareness about the causes and consequences of TB and encouraged "irregular" migrants to be screened without fear of reprisal. Free treatment in a clinic regardless of legal or economic status. Also specific strategies like house visits (for engagement with screening) and constant contact with the patient in order to encourage him/her to remain in Istanbul until the end of treatment. Included DOT observers. Despite the absence of any funding, all services and facilities were offered voluntarily and free of charge. Formal identification not often demanded (even if TB positive), ITAP community mediators served as contacts for follow-up. Educational materials on TB and nutrition in seven different languages.*

g) Evaluations in context of the Collaborative Tuberculosis Strategy 2015-2020 for England

Study	Type of TB	Population/ risk factors	Data collection and analysis	Intervention /comparator	Main barriers (treatment initiation and/or adherence/completion)	Main facilitators (treatment initiation and/or adherence or completion)
Berrocal-Almanza 2019, UK ¹⁸	Latent	Stakeholders from community, community-based organisations (CBO) and public sector stakeholders. Includes health care professionals and local community organisation staff; n=23	Three stakeholder meetings and five focus group discussions. Topic guide used. Thematic analysis.	Focus on 2015–2020 Collaborative Tuberculosis Strategy for England for voluntary LTBI testing, counselling and treatment in migrants. LTBI testing provided through primary care services. Rates of LTBI testing, treatment acceptance and completion are suboptimal. Discussions focused on interventions that facilitate collaboration to improve health care outreach and delivery.	<ul style="list-style-type: none"> - perception that the public sector may occasionally consider itself superior to the voluntary sector (a barrier to collaborative work) - capacity of the NHS to accommodate itself to the service users' needs is limited, NHS timings and locations can create barriers to interaction - rigid timelines in commissioning cycles, which do not consider the real time involved in making such interventions happen in a meaningful way - voluntary sector comprised of many small organisations with different agendas-can be difficult to manage - users may have other priorities (e.g. staying in the country) - fear that encounter with health services may lead to deportation - frontline staff in primary care services, as well as underserved populations (e.g. undocumented migrants) sometimes lack clarity about legality and rights to health care access - conflict between need to collect information on immigration status and confidentiality - mandatory public health notification of active TB can cause shame and social exclusion in certain communities 	<ul style="list-style-type: none"> - collaboration (of the NHS) with CBOs, who meet their users on their terms, opens more opportunities for user engagement (while NHS has specialist knowledge, CBOs can motivate people to access/use services and have less strict rules of engagement) - routine discussions about difficult health issues and building trust in relationships may help reduce stigma - making tests routine could reduce stigma - CBOs could support education about the disease and social stigma as they already have community trust.
Berrocal-Almanza 2023, UK ¹⁹	Not stated (likely active and latent TB)	Individuals from diverse backgrounds who had experienced diagnostic delay or poor treatment outcome; n=9 (4 with country of origin outside UK) Health care professionals (5 chest physicians, 5 TB nurses, 2 lead TB nurses, 2 nurses, 1 support worker, 1 cultural link worker); n=16	25 semi-structured interviews using topic guides. Thematic analysis. <i>NB mixed methods study but only qualitative data extracted</i>	Topic guides informed by goals of 2015–2020 Collaborative Tuberculosis Strategy for England. Discussions focused on healthcare priorities, barriers for healthcare access, additional services and interventions needed to improve healthcare delivery and the factors that contribute to poor treatment outcome.	<ul style="list-style-type: none"> -structural barriers surrounding work and access to welfare support create situations where people (with TB) would be left without money to live on -some TB patients have complex lives with issues such as immigration status, access to housing, and co-morbidities, which challenge their abilities to address TB -groups considered especially vulnerable by healthcare professionals: those with drugs and alcohol use disorder, elderly patients, low-paid workers, those with mental health disorders, with chaotic lifestyles, under prolonged stress and some foreign-born individuals - some healthcare professionals thought the term 'underserved' did not adequately reflect the range of services available and the effort and commitment devoted to engaging and supporting patients - patients and healthcare professionals agreed that timing and location of services represent barriers for access, and once services are reached, there is often poor primary healthcare responsiveness - diagnostic delay within primary care (as TB often not immediately diagnosed) leading to progression of the disease prior to treatment - treatment duration, side effects, amount of tablets and difficulties to cope with the direct observation of therapy (DOT) programme 	<ul style="list-style-type: none"> - health promotion with a wider focus, not exclusive to TB, and better networking between services, including social support and social workers within the TB team - supplemental services through drop-in clinics and community and peer advocates - connectivity of medical records through technology would also make for improved healthcare access and provision - regarding models of care, practitioners wished for more control over patients and patients wanted to maintain a sense of normal life

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Table 1 Study characteristics and main findings from RCTs and controlled studies

a) Different drug regimens and treatment lengths

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings	Reasons/factors associated with non-completion
Juarez-Reyes 2015, US ¹	Latent	Single arm (prospective) compared with historical control	Both groups: inmates of Santa Clara Jail (California). Large proportion also with history of alcoholism and/or drug use (in the prospective group).	3HP by DOT (prospective group, n=91)	9H by DOT (historical control, n=154)	3HP: 77/91 (85%) completed versus 9H: 28/154 (18%) completed, p<0.001 (unadjusted comparison). Complete AEs reported only for 3HP arm.	Main reason for non-completion was transfer out of jail; other reasons included discontinuation due to rash, unrelated illness/declined further treatment, no identifiable reason.
Wheeler & Mohle-Boetani 2019, US ²	Latent	Single arm prospective and single arm retrospective (NB not designed as comparative study)	Patients entering California state prisons (prospective group); patients from the California Correctional Health Care Services registry (retrospective group). Additional risk factors not reported.	3HP by DOT (prospective group, n=122)	9H by DOT (retrospective group, n=92)	3HP:110/122 (90%) versus 9H: 39/92 (42%). Higher completion rate in 3HP prospective cohort compared with 9H retrospective cohort but not designed as comparative study.	Main reason was parole, discharge or transfer out of system, discontinuation by providers or refusal to complete treatment.
Villa 2019, Italy ³	Latent	Retrospective cohort study	General population, with sub-group analysis for homeless people, "irregular" migrants and asylum seekers and refugees.	3HP or 4R (not stated if DOT, n=4065)	6H (not stated if DOT, n=15,605)	Overall: 85.6% (3HP or 4R) completed versus 77.8% (6H), p<0.0001 (unadjusted comparison). Based on those without treatment changes only (n=17,859): Homeless people: 55.6% (6H) versus 76.8% (3HP or 4R), p<0.0001; "irregular" migrants: 73.0% (6H) versus 70.8% (3HP or 4R), p=0.54; asylum seekers or refugees: 100% (6H) versus 93.3% (3HP or 4R), p=1. More frequent AEs in 6H vs 3HP/4R.	Main reason was loss to follow-up (did not return for follow-up visits), other reasons were patient default, suspension, unknown or death. Not reported separately for sub-groups.
Chevrier 2022, Canada ⁴	Latent	Before and after study - part of mixed methods study	Government assisted refugees from a TB endemic country.	3HP or 4R (post 2015, n with DOT not stated, n=115)	9H (pre 2015, n with DOT not stated, n=74)	3HP or 4R: 104/115 (90.4%) completed versus 9H: 61/74 (82.4%), p=0.170. No differences in adherence reported by staff between clients receiving 3HP (DOT) versus SAT with 4R (no numerical data presented).	Multinomial regression models found that the short treatment regimen, and female sex tended to positively affect the treatment completion proportion.

DOT: directly observed therapy; SAT: self-administered therapy; 3HP: three months of once-weekly isoniazid plus rifapentine; 4R: four months of daily rifampin; 3HR: three months of daily isoniazid plus rifampin; 6H: isoniazid for 6 months; 9H: isoniazid for 9 months.

b) Different types of treatment administration (DOT/VOT/SAT)

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings	Reasons/factors associated with non-completion
Bishara 2023, Israel ⁵	Latent	Retrospective cohort study	Ethiopian immigrants living in reception centres	semi-DOT provided once weekly by nurse with second dose self-administered (n=231)	SAT with medication provided during monthly follow-up visits (n=224)	Slightly lower treatment completion rate with SAT compared with DOT (87.9% vs 93%) but no statistically significant difference (non-adjusted OR 0.54 (95% CI 0.28, 1.04)).	Treatment completion rate significantly lower in those with side effects; no statistically significant difference for sex or age group (though slightly higher completion rate in males).
Story 2019, UK ⁶	Active	Randomised controlled trial	58% with social risk factor (history of homelessness, imprisonment, drug use, alcohol problems, or mental health problems).	DOT provided 3-5 times/week (n=114)	VOT provided by a centralised service and patients trained to send videos using a smartphone app (n=112)	VOT significantly improved odds of successful completion of 80% or more scheduled treatment observations over 2 months compared with DOT (ITT analysis). Partially adjusted OR (95% CI) 5.48 (3.10, 9.68), p<0.0001 (ITT analysis). Fully adjusted OR (95% CI) 2.52 (1.17, 5.47), p=0.019 (restricted analysis which excluded patients with <1 week in observation arm).	Less initial engagement with DOT compared with VOT –particularly among younger adults, foreign-born patients and those without social risk factors or mental health problems. Similar rates of engagement with VOT across all subgroups.
Onwubiko 2019, US ⁷	Latent	Retrospective cohort study	Homeless people who were current residents of an emergency shelter at time of treatment initiation. Higher proportions of current alcohol use (25% vs 8%), illicit drug use (11% vs 3%) and a mental health disorder (12% vs 2%) in the DOT group.	4R DOT provided 5 days/week (n=181)	4R SAT - pill box with 30 doses provided each month (n=93)	DOT significantly improved the odds of treatment completion compared with SAT. Adjusted OR (parsimonious weighted model): OR: 1.30 (1.01, 1.67), p = 0.045. Adjusted OR (fully weighted and adjusted model): OR: 1.40 (1.07, 1.82), p = 0.014.	Male sex, Black/African American, age (50–59, 60 years and older) and positive HIV status significantly associated with increased odds of treatment completion while alcohol use was associated with decreased odds of completing treatment (fully adjusted analysis).

DOT: directly observed therapy; VOT: video observed therapy; SAT: self-administered therapy; 4R: four months of daily rifampin

c) Screening or test focussed approaches

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings	Reasons/factors associated with non-completion
Lim 2021, Canada ⁸	Latent	Retrospective cohort study	Privately sponsored refugees, government-assisted refugees or refugee claimants.	IGRA only screening (QuantiFERON-TB Gold Plus (QFT)). Positive QFT triggered chest x-ray and referral for Treatment* at the local TB clinic (n=41 with LTBI).	Sequential screening: initial TST, followed by confirmatory IGRA if the TST was positive. Positive QFT triggered a chest x-ray and referral for LTBI treatment* at the local TB clinic (n=20 with LTBI).	IGRA: 29/33 (87.9%) who started treatment completed. Sequential: 14/16 (87.5%) who started treatment completed. Screening completion rates (85% IGRA vs 54% sequential). Adjusted OR (95% CI) 3.74 (2.30, 6.09) < 0.001.	Not reported for completion rates. In the adjusted analysis, IGRA only screening and privately sponsored refugees were predictors of screening completion (adjusted analysis).
Walters 2016, US ⁹	Latent	Before and after study	Newly arrived refugees	Post 2011: widespread introduction of IGRA (QuantiFERON-TB Gold Plus (QFT)), n=287 with LTBI	Pre 2011: mainly TST, n=393 with LTBI	Post-QFT: 215/287 (75%) candidate for treatment; 160/215 (74%) started treatment; 107/160 (67%) completed treatment. Pre-QFT: 333/393 (85%) candidate for treatment; 221/333 (66%) started treatment; 154/221 (70%) completed treatment. Significantly greater proportion of refugees diagnosed with LTBI pre-2011, and a significantly greater proportion initiated treatment post 2011.	Reasons for non-completion mostly loss to follow-up and patients stopping treatment (both time periods). 4R or 6R was significantly associated with greater completion rate compared with 6H or 9H; refugees from South Asia had higher odds of treatment completion than refugees from sub-Saharan Africa (bivariate analyses). Age group was not found to be a significant predictor of treatment completion.
Spruijt 2020a, The Netherlands ¹⁰	Latent	Prospective comparison of six strategies - part of mixed methods study.	Eritrean migrants	Six community strategies ^b to encourage screening and treatment, developed with Eritreans from the community. All strategies included 1-3 education sessions in a community setting followed by screening sessions*; n=410 (participation in community strategies), n=30 (with LTBI). Screening and treatment offered free of charge. LTBI treatment support by TB nurse and interpreters where necessary.	Completion rate: 28 of 29 (97%) of those initiating LTBI treatment after diagnosis. Not reported by community strategy arm. Uptake of LTBI education differed between strategies from 13% to 75% (overall 44%). Uptake of screening of those who participated in education session was 64%.	Includes: participants prioritising only compulsory appointments, lack of motivation due to competing priorities, lack of understanding of LTBI and scepticism about the project's purpose. <i>See qualitative studies in supplementary material for further detail.</i>	

IGRA: Interferon-Gamma Release Assays; TST: tuberculin skin test; * treatment with 3HP, 4R or 9H according to local practice and patient factors; a standard treatment 6H or 9H or 4R or 6R depending on age and risk factors. b Strategy 1: invitation by email, Facebook group and WhatsApp church group (education session at community centres); strategy 2: face-to-face promotion through PHS staff (Dutch language classes, libraries, the church, and the gym), education at local community centre; strategy 3: Dutch language classes for promotion by teacher or key community figures, flyers and displaying posters, education session at the PHS; strategy 4: education session in community space of group housing (education session at the house); strategy 5: Education after sports club (football), education session at sports club; strategy 6: promotion of education/screening after church service.

d) Strategies tailored to people experiencing homelessness, social risk factors or substance abuse

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings	Reasons/factors associated with non-completion
Crosby 2023, UK ¹¹	Active	Comparative cross-sectional	Homeless TB patients with complex social needs; proportion with history of drug use, prison, alcohol use or need for DOT.	Residential respite service for homeless TB patients (facilitates timely/safe discharge from hospital, provides accommodation, DOT, psychological help and support for drug and alcohol dependency and support for finding work, living independently and reconciling with families or communities), n=89	Standard community treatment, n=24,092	Greater odds of treatment completion with residential; respite service, adjusted OR 2.97 (95% CI 1.44, 6.96). Adjusted for demographic, social and clinical variables, including drug resistance, history of homelessness, drug or alcohol use and need for DOT.	Strong association between missing data and treatment failure - covariate data may be less likely to be recorded in non-completers.
Nyamathi 2021, US ¹²	Latent	Single arm (prospective) compared with historical control	Homeless person defined as anyone who spent the previous night in a public or private shelter or on the streets, proportion with history of drug or problematic alcohol use.	Tailored nurse-led, community health worker (RN/CHW) program across the LTBI pathway (screening, diagnosis, treatment); CHWs were formerly homeless adults; each RN/CHW assigned 7-8 participants; weekly meetings and provision of DOT; weekly one-on-one case management sessions (coaching support, education, support for drug/alcohol use and mental health issues); health and social service referrals; tracking of participants who missed a dose; n=50	3HP LTBI treatment in historical control (no RN/CHW program), n=56	Greater proportion of people completed in the intervention group compared with the historical control group: 91.8% (95% CI 80.8, 96.8) in intervention group versus 66% (CI not reported) in historical control group.	Younger age (<50) significantly associated with non-completion in intervention group; men less likely to complete than women (not statistically significant). No association found with drug or alcohol use or anxiety/depression.
Izzard 2021, UK ¹³	Active	Retrospective cohort study	Social risk factors, mainly homelessness. Also included a proportion on benefits, immigrants, people with financial issues or drug/alcohol misuse.	North Central London TB network re-configured to include a social care team (SCT). Provision of (additional) dedicated specialist support; intensive individualised casework support for homelessness, housing, benefits, employment, immigration and financial issues such as debt, referrals to other services including drug and alcohol and mental health. Can include regular phone calls, administrative support, and accompanying patients to appointments (e.g. Job Centre, Council, Citizens Advice Bureau, solicitors, or for GP registration); 48% DOT/VOT; n=170	Standard care without access to SCT (i.e. patients who had not been referred); 12% DOT/VOT; n=734	Patients referred to SCT significantly more likely to complete planned treatment. 88.2% (SCT) versus 77.7% (comparison cohort) completed. Adjusted OR 2.35 (1.41, 3.91), p=0.001 (in favour of social care team).	Increased completion rate remained when patients stratified by DOT/VOT or no DOT/VOT, with a stronger association in those not receiving DOT/VOT.
Ricks 2015, US ¹⁴	Active	Randomised controlled trial	Substance users (illicit drug use and/or daily consumption of at least 2 alcoholic drinks during the 6 months before enrolment). Proportion with history of incarceration or unstable housing.	Enhanced arm: use of trained and experienced community (HIV prevention) outreach staff who were former substance users to perform DOT; two-person mixed-sex team to provide DOT.	Standard arm: standard DOT provided by trained and experienced communicable disease investigators.	Patients in standard treatment arm at significantly greater risk of failing to complete treatment (RR 2.5 (95% CI 1.2, 5.1)).	Nine covariates significantly associated with failure to complete treatment: Hispanic ethnicity, primary residence not own or partner's, shelter stay in past 6 months, ≥1 night in rented room, ≥1 night in shelter, ≥1 night in abandoned building, non-cavitary TB, previous TB diagnosis, HIV positive (multivariate model using imputed data).

e) Refugee specific clinics (integrated care)

Study	Type of TB	Design	Population/ risk factors	Intervention (n=) and comparator (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Subedi 2015, US ¹⁵	Latent	Retrospective cohort study	Newly arrived refugees	Intervention: Philadelphia Refugee Health Collaborative (PRHC) clinics. Collaborative working between refugee resettlement agencies and refugee health clinics; includes outpatient paediatric, internal medicine, and family medicine programmes; led by physicians with expertise in primary care for new immigrants; services reimbursed during first 8 months; refugees reminded of appointments; bilingual services and pre-set visit schedule; provision of regular, culturally appropriate refugee orientation meetings, follow-up patient education meetings and educational materials. Multidisciplinary approach by doctors, nurses, social workers and case workers from volunteer agencies and Department of Public Health; n=38. Comparator: non-PRHC clinics. Health screening and follow-up appointments left to patient. No cross-clinic referral system or logistical support from resettlement agencies; n=19.	Significantly greater proportion completed in the PRHC clinic group (89.5%) compared with the non-PRHC clinic group (47.4%). Unadjusted OR (95% CI) 9.44 (2.39, 37.30). Time to initial screening shorter, and greater proportion of follow-up appointments completed in PRHC group compared with non-PRHC-group.	Not reported.
Kunin 2022, Australia ¹⁶	Latent	Prospective cohort study - part of mixed methods study	Asylum seekers and refugees	Intervention: Monash Health Refugee Health and Wellbeing (MHRHW) service. Integrated primary care and specialist services; intensive transitional care to asylum seekers/refugees experiencing high levels of vulnerability, complex health needs and restricted access to Medicare. Includes refugee health assessments; use of interpreting services; delivery of capacity building and community development strategies. Multi-disciplinary team, including GPs, GP refugee health fellows, refugee health nurses, infectious diseases physicians, paediatricians, bicultural workers, community development workers, psychiatrists, counsellors and pharmacists. Development of comprehensive training module for primary care providers, GPs, and nurses, and a Patient Education Resource Pack; n=15.. Comparator: universal primary care clinic. Includes onsite pharmacy; consultations subsidised through Medicare; multi-lingual staff; n=16.	Significantly higher completion rate at MHRHW compared with universal care: 93% (MHRHW) versus 56% (universal care), p=0.0373 (unadjusted analysis).	MHRHW: 1 opted out; Universal care: 1 opted out, 3 adverse reactions, 1 relocated, 2 discontinued collecting medication at less than 6 months (also AEs).

f) Other strategies tailored to migrants, refugees and asylum seekers

Study	Type of TB	Design	Population/risk factors	Intervention (n=)	Comparator (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Bishara, 2015, Israel ¹⁷	Latent	Retrospective cohort study	'Hard-to-reach' Ethiopian immigrants	<u>Intervention:</u> Nurse-managed semi-DOT and TB clinic at migrant centre. Semi-DOT was two weekly doses, one supervised, one self-administered; team outreach programme consisted of physician and nursing outreach at the migrant reception centre (onsite) TB clinic. Professional interpreter (veteran Ethiopian immigrant) available throughout study. All services free of charge, n=297. <u>Comparator:</u> Nurse-managed semi-DOT and regional TB clinic. No team outreach programme, evaluation and follow-up provided at regional TB clinic to which transport was provided free of charge, n=366.		Similar completion rates. On-site clinic: 96.0% versus regional clinic: 93.7%. Similar number of physician follow-up visits in both groups.	Age < 5 years and side effects were each significantly associated with treatment non-completion (p = 0.03 and p< 0.001, respectively).
Olsson 2018, Sweden ¹⁸	Latent	Before-and-after study	Asylum seekers with or without residence permits	<u>Intervention:</u> Standard care + change of strategy introduced in June 2013. Since then, all subjects were given pre-scheduled appointments for nurse visits, assisted by interpreters; n=297. <u>Comparator:</u> standard care -specialised nurses responsible for distribution of drugs and follow-up during treatment; drugs dispensed at outpatient clinic every 1–2 months where nurses inquire about adherence and side effects and register the number of tablets dispensed; people who fail to show up for the collection of medication are contacted by telephone and mail; n=not stated.		Completion rate significantly higher in those initiating treatment after June 2013 (90%) compared with those initiating therapy earlier (69%), p<0.01 (unadjusted analysis).	Factors significantly associated with completion (multivariate analysis): starting treatment after 30th June 2013; isoniazid treatment for 6 months as compared to 9 months; and receiving LTBI treatment in connection to treatment with immunosuppressive treatment as compared to contacts.

g) Conditional cash transfer

Study	Type of TB	Design	Population/ risk factors	Intervention (n=)	Comparator (n=)	Main findings (note if adjusted)	Reasons/factors associated with non-completion
Klein 2019, Argentina ¹⁹	Active	Prospective cohort	Socio-economically disadvantaged patients. Between 45%-55% with current/past drug use and between 21%-23% with current/recent alcohol use.	Registration for conditional cash transfer (CCT). Payment of a monthly amount to eligible patients identified and incorporated into the Provincial TB Control Program (PTP); recipients have to adhere to health checks, treatments, and other conditions established by the PTP; failure to do so may result in the loss of the benefit. Process initiated by a health professional; a social worker and a physician evaluate each case, taking into account the severity, the socioeconomic situation, the community risks, and the most susceptible age groups. Registration into the program was considered present if the administrative procedures to get the cash transfer were started during treatment (intention to treat) and absent otherwise; n=337.	Standard care (not registered for CCT); n=564	83% treatment success (completed 6 months of treatment or cure) with CCT versus 69% (control). Crude OR (95% CI) for treatment success 2.08 (1.49, 2.92); adjusted OR (95% CI) 2.91 (1.97, 4.28, p=0.001)	Variables associated with a higher risk of incomplete treatment were self-administered treatment, younger age, lack of insurance, lower income, and use of alcohol and illicit drugs.

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