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Series: Tuberculosis in hard-to-reach populations

Title:

Barriers and facilitators for the uptake of tuberculosis diagnostic and treatment services by hard-to-reach populations in low- and medium-incidence countries: A systematic review of qualitative literature

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Abstract

Tuberculosis (TB) disproportionately affects hard-to-reach populations such as people who are homeless, migrants, refugees, prisoners, or drug users. These people often face challenges in accessing quality healthcare services. To identify barriers to, and facilitators for, the uptake of TB diagnostic and treatment services by people from hard-to-reach populations in all EU, EEA, EU candidate, and OECD countries, we performed a systematic review of the qualitative literature, following PRISMA guidelines. The twelve studies included in this review focused mostly on migrants. Views on perceived susceptibility to and severity of TB varied widely and included many misconceptions. Stigma and challenges with accessing healthcare were identified as barriers for TB diagnosis and treatment uptake, whereas nurse, family, and friends' support were facilitators to treatment adherence. Further studies are required to identify barriers and facilitators for improved identification and management of TB cases in hard-to-reach populations in order to inform recommendations for more effective TB control programs.

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Introduction

Tuberculosis (TB), together with malaria and HIV, causes the largest loss of disability-adjusted life years worldwide.¹ In 2014, there were an estimated 9.6 million incident cases of TB worldwide of which 5.4 million were men, 3.2 million women and 1.0 million children.² In the European Union (EU) and European Economic Area (EEA), one third of 65 thousand notified TB cases occurred in 18 low-TB incidence countries (i.e. notification rate <10 TB cases per 100 000 population).³ In these countries, TB cases are disproportionately concentrated in big cities linked with an over-representation of TB among a variety of hard-to-reach and susceptible populations, such as people who are homeless, migrants, refugees, prisoners, drug users, sex workers, and people living with human immunodeficiency virus (HIV).^{4,5} While not all people living with HIV can be called “hard-to-reach”, many hard-to-reach populations are more likely to acquire or carry an HIV infection.⁶⁻¹²

Limited surveillance and survey data are available on TB in hard-to-reach populations.^{13,14} It is known that in the EU and EEA, 28% of new TB cases occur in individuals of foreign origin, with thirteen countries reporting >50% of their TB cases in individuals of foreign origin.³ Except for information on TB in individuals of different origin, age, and sex, there is limited information available on TB in hard-to-reach groups, information on other risk factors or social determinants is not readily available, which hampers policy and guideline development required to optimize TB control efforts. The global ‘End TB Strategy’ and the action framework for low-incidence countries ‘Towards TB elimination’ highlighted this and identified the most vulnerable and hard-to-reach (under-served) populations as a priority area for action.^{5,15,16}

Hard-to-reach populations often have specific risk factors which render them more exposed and vulnerable to infection with *Mycobacterium tuberculosis* and for developing active TB disease.¹⁷ These risk factors include living in crowded and poorly ventilated areas, co-morbidities, substance abuse, HIV infection, and malnutrition. In addition, hard-to-reach populations face major challenges in accessing health care and in adhering to TB treatment, which include reduced awareness and knowledge of the signs and symptoms of TB, unstable accommodation, and difficulties with transportation and access to healthcare, limited opening hours of testing centres, the cost of testing and the lengthy duration of treatment.¹⁸⁻²⁷

The European Centre for Disease Prevention and Control (ECDC) initiated guidance for controlling TB in hard-to-reach and vulnerable populations.²⁸ To provide the latest evidence base, we conducted a systematic review of qualitative literature focusing on the barriers and facilitators for the uptake of TB diagnostic and treatment services in hard-to-reach populations, covering all EU, EEA, EU candidate, and Organisation for Economic Co-operation and Development (OECD) countries. Information on barriers and facilitators is often best assessed with qualitative research methods aimed at the perspectives of patients or health care workers. In addition, qualitative methods allow for obtaining a more in-depth understanding of barriers and facilitators compared and in addition to quantitative research methods.²⁹ Synthesized qualitative research findings thus aid the development of new theories, interventions, and policy-making.

The primary review question of our systematic review was, “What factors help or hinder the uptake of TB diagnostic and treatment services by people from hard-to-reach populations in EU, EEA, EU candidate, and OECD countries, and how can those barriers be overcome?” Secondary review questions were: (i) “How do views vary between different hard-to-reach populations?” and (ii) “What are the views of service providers?”.

The findings served as the evidence base for the development of guidance for controlling TB in hard-to-reach and vulnerable groups.

Methods

In 2010, the Matrix Knowledge Group, commissioned by the National Institute for Health and Clinical Excellence (NICE), conducted a systematic review on barriers and facilitators for the uptake of TB diagnostic and treatment services by people from hard-to-reach populations in OECD countries.³⁰ We updated and extended this review, following standards described by the Cochrane Collaboration³¹ and NICE.³² Results are reported according to the PRISMA guidelines for systematic reviews.³³

Search and Eligibility criteria

Medline, Medline In-Process, Embase, PsycInfo, Centre for Reviews and Dissemination database (for DARE, NHS, EED, and HTA databases); The Cochrane Library; Cumulative Index to Nursing and Allied Health Literature, were searched using the same search strategies as used in the NICE review (which covered the period 1990 up to September 2010).³⁰ We updated the search (from September 2010 onwards) and expanded geographical coverage to include all EU/EEA and EU candidate countries. In addition to the hard-to-reach populations covered by the NICE review; migrants, homeless people, people who abuse substances, prisoners, sex workers, and people living with HIV,³⁰ we included children within hard-to-reach populations. Definitions of hard-to-reach groups were used as defined by the respective papers. We limited the search to TB excluding latent TB infection (LTBI). The search performed for the NICE review was updated, covering the period 2010 to 10 April 2015. We included qualitative studies related to either the views of hard-to-reach people regarding perceptions of or attitudes towards TB services, qualitative descriptions of the variation of views between different hard-to-reach populations, or the views of service providers. (See **Supplementary Material I** for PICOS - Population-Intervention-Comparator-Outcome-Study design).

The search for the newly included countries and hard-to-reach populations covered the period 1990 to 10 April 2015. Additionally, all included studies were checked for relevant references and all identified systematic reviews were checked for relevant references, but not included (see **Supplementary Material II** for comprehensive search strategy details).

Selection of studies and data management

Citations identified by the search were imported to an EndNote database and duplicate records were removed (EndNote X7.1, Thomson Reuters 2014). Records were screened on title and/or abstract by three authors (SdV, CCH, BJV) independently and in parallel using pre-specified criteria (**Box 1**). One author screened 100% of the records; the other two authors screened 50% each. Any disagreement was resolved by discussion. Full texts of all articles identified in the initial screening were retrieved. Authors were contacted in case of incomplete data or irretrievable articles. If the article was irretrievable (not accessible from any source, or from authors), the study was excluded. The full text of selected articles was screened by three independent authors (SDV 100%, CCH and ALC 50% each) using a full text assessment inclusion checklist, derived from the previous review performed by NICE.³⁰ Inter-reviewer agreement before reconciliation for the abstract screening was 98.1%, the inter-rater reliability (Cohen's kappa) was $\kappa = 0.627$.

Data extraction, data items and synthesis

Data was extracted by using the data extraction forms used for the previous NICE review.³⁰ For a random 10% of included studies, data extraction was performed by two independent reviewers. For the remaining studies, one reviewer conducted data extraction that was checked by a second reviewer; any disagreement was resolved by discussion.

To structure the data synthesis, we used the Health Belief Model (HBM),³⁴ which explains and predicts health-related behaviours. Two reviewers independently conducted thematic and content analysis.³⁵ Data was coded into meaning units, and categorized into potential determinants of health behaviours within five themes of the HBM framework: (i) perceived susceptibility (risk); (ii) perceived severity (consequences, such as mortality and morbidity); (iii) perceived facilitators (predisposing factors); (iv) perceived barriers (factors that hinder); (v) cues to action (motivating or precipitating forces, such as contact with someone else who has TB).

Risk of bias in individual studies and the overall strength of the evidence

Studies were assessed for quality and risk of bias using the modified NICE Quality Assessment Tools for qualitative research.³⁰ Two reviewers assessed ten percent of included studies independently; the remaining 90% were assessed by one reviewer and checked by a second reviewer. Any disagreement was resolved by discussion. Each study was given a quality rating based on the quality assessment: high quality [++], medium quality [+] or low quality [-]. We did not investigate publication bias. The evidence was graded and reported as described before³⁰ (**Box 2**).

Results

Study selection

Database searches identified 5,915 records. Citation searching of included studies and relevant (but excluded) reviews identified fifteen records. Of the total 5,930 abstracts, 1,810 duplicate records were removed (**Figure 1**). In all, twelve studies were included in this review.^{19,36-46} Detailed descriptions of the characteristics of included studies are given in **Table 1** and **Supplementary Material III**. Of ten studies evaluating the views of individuals belonging to hard-to-reach populations on TB and TB services, seven were views of migrants,^{19,37,39,42,43,45,46} one of a mixed group of homeless people, migrants and drug users,³⁶ one of homeless people,⁴⁰ and one study reported on views of a Roma population.⁴⁴ Two studies focusing on views of healthcare providers on barriers or facilitators for hard-to-reach populations were identified.^{38,41} Studies were conducted in the United Kingdom (UK),^{36,38,39,42} the United States of America (USA),^{13,37,46} Sweden,⁴¹ Norway,⁴³ Serbia,⁴⁴ Canada⁴⁵ and Japan.⁴⁰ The results of quality assessment are presented in **Table 2**. Detailed evidence statements on all themes, combined with the findings of the previous NICE review³⁰ are provided in **Supplementary Material IV** and in the discussion section in short. Here, we present the findings of the update and extension of the NICE review.

Perceived susceptibility

If hard to reach groups view themselves as susceptible for TB, they are more inclined to get tested if they have TB symptoms. Five studies focused on migrant populations,^{19,37,39,42,46} one on a Roma population,⁴⁴ and one on a mixed population of homeless people, drug users and migrants.³⁶ **Table 3** shows an overview of findings on views on susceptibility through reported concepts of causes and modes of transmission. **Supplementary Material V** provides an overview of illustrative quotations identified per theme.

Migrant and traveller populations

A frequent misconception among migrant students and teachers at an adult education centre in the USA was that TB was not present in the USA.¹⁹ Mexican-American TB-patients talked about being vulnerable to TB because of the proximity to Mexico.³⁷ In a Somali community in Sheffield, UK, community leaders generally showed accurate knowledge, but among community members, there was great variation. There were some relatively accurate views calling it “*an airborne disease whereby people became infected by ‘breathing in the germ’ and once infected, they could pass it on to others*”.⁴²

Other hard-to-reach populations

In a mixed group of homeless, drug using and migrant TB patients in London, UK, knowledge of TB was generally limited, and a wide variety of causes was mentioned.³⁶

Perceived severity

The way communities perceive the severity of TB, such as symptoms, health consequences, and treatability, influences people’s health care seeking behaviour. Three studies reported on the views of migrant populations,^{19,37,42} one on a Roma population,⁴⁴ and one on a variety of urban risk populations in London.³⁶

Migrant and traveller populations

Migrant populations in studies reporting on perceived severity consisted of migrants and refugees in the USA,¹⁹ Mexican Americans,³⁷ and Somali migrants in the UK.⁴² One was exclusively reporting on the views of TB patients,³⁷ one reported on views of non-TB patients,^{19,44} and one on both.⁴²

Two studies reported good knowledge of the TB symptoms, persistent (bloody) cough, weight loss, fever and night sweats.^{37,42} Somali TB patients had little knowledge about extra-pulmonary TB, but most were aware of the long duration of treatment with antibiotics, and the prospect for good recovery. Some thought, however, due to the belief that TB is hereditary, that TB could not be cured. There were various beliefs about the length of time a patient remained infectious.⁴² Similarly, a Roma population in Belgrade had accurate knowledge of symptoms. However, views on severity and the effectiveness of treatment varied, ranging from TB being a very serious and lethal disease to a long-lasting, but curable disease.⁴⁴ A mixed group of migrants in the USA reported fear of TB, which consisted mainly of fear of dying from an incurable disease.¹⁹

Other hard-to-reach populations

A group of predominantly homeless people, and drug users, people living with HIV, and migrants, with (suspected) TB infection in London, reported on common symptoms for TB; recognition of symptoms had

not always been accurate in this study; miscellaneous explanations for (common) symptoms were reported.³⁶ Symptoms were often attributed to other (undiagnosed) illnesses, poor diet, or to drug/alcohol abuse.

Perceived barriers to testing and treatment

Eight studies elaborated on the barriers that influence health care-seeking behaviour and treatment adherence of TB patients, hindering effective implementation of TB prevention and control measures; seven reported on migrant populations,^{19,37,39,42,43,45,46} and one on mixed urban risk groups in London.³⁶

Migrant populations

Difficulties with access - In various migrant populations in the USA, there were difficulties with transport to the testing centre, opening hours of testing centres, or the duration and cost of testing.¹⁹

Signs, symptoms and adverse effects of medication - The challenges of TB symptoms combined with TB treatment side effects were described by TB patients of Mexican American³⁷ and Somali¹⁹ origin in the USA. They experienced mental and physical problems, affecting their treatment adherence.

Stress and depression - Two studies^{37,39} commented on stress and depression due to delay in diagnosis and treatment challenges. Somali patients in the UK³⁹ felt stressed, anxious, and powerless, especially if the diagnosis took long, and when they had the feeling that they were not being taken seriously. They felt the “system” let them down and they did not trust their general practitioners. Other patients felt relieved after TB was diagnosed.³⁹ Depression and feelings of sadness were described by Mexican Americans during TB treatment, often related to (self-chosen) social isolation at home and lack of activities, in order to prevent wider infection.³⁷

Loss of privacy/lack of confidentiality - Loss of privacy and lack of confidentiality were identified as important barriers to treatment adherence in two studies.^{43,46} The actions of TB health care services and outreach workers were perceived as revealing a patient’s TB status to others, this was mentioned by both Haitians in the USA⁴⁶ and by Ethiopian and Somali migrants in Norway.⁴³ They worried about DOT health workers aggravating the stigma of TB and being unaware of the consequences of exposing their TB status to others.

Threat of hospitalisation/paternalistic DOT - Three studies described negative attitudes or fear of patients towards DOT that made people reluctant to get tested.^{37,43,46} American Haitians associated TB treatment with incarceration; moreover, they feared loss of employment.⁴⁶ Some Somali and Ethiopian patients in Norway questioned the necessity of DOT, feeling humiliated or discriminated by the frequent home visits. They felt unable to voice any criticism because of their migrant status, a lack of alternative TB services, and the threatening attitudes of nurses in cases of non-cooperation. Some did not understand why nurses suspected them of not being compliant with treatment. They argued that DOT should only be used where people needed assistance with managing their treatment.⁴³ DOT was perceived as imprisoning, forcing the patient into a subservient and confined position hindering work responsibilities and consequently, complicating treatment adherence.^{37,43}

Inadequate service provision - The lack of continuity among health personnel was described by Somali and Ethiopian migrants in Norway as hindering the establishment of a secure and trustful patient-nurse

relationship whilst being on treatment. Some patients described that some health workers tried to limit patient contact as much as they could. Patients often did not know which health worker was coming and at what time, potentially causing feelings of stress and humiliation.⁴³

Economic factors - Economic hardship due to TB diagnosis was mentioned among the Somali patients in the UK.^{39,42} A Somali, homeless patient described how hard management of the disease was without adequate accommodation, social support, and with a poor diet.³⁹ Mexican American migrants reported economic hardship, losing their job or being unable to work.³⁷ Mixed migrant populations in the USA reported that knowledge about TB medication being free of charge reduced financial constraints to accessing TB care.¹⁹

Issues of Stigma - TB patients experiencing TB-related stigma posed a multifaceted problem for both seeking health care and treatment adherence. This topic was covered by seven articles.^{19,37,39,42,43,45,46} We identified five themes: face masks; stigma of association with HIV; self-stigma; consequences of stigma; stigma due to lack of knowledge.

Face masks - Mexican American TB patients associated wearing masks with physical discomfort and stigma.³⁷ They were afraid the mask would reveal their TB status. Most patients stayed at home, or avoided crowded places out of fear of disclosing their TB status and being discriminated. Similarly, migrants in Canada referred to the mask as an 'identifier of TB' and described the impact of face masks on losing friends, jobs, or being unable to find employment.⁴⁵

Stigma of association with HIV - Many Haitian community members in Florida assumed HIV-infection in TB patients aggravating stigma.⁴⁶ In this study, the TB and HIV clinics were located together in a single building contributing to this assumption.

Self-stigmatisation - Four studies described TB self-stigmatisation.^{19,37,39,42} Mexican patients in the USA felt depressed and guilty about having TB; they were afraid of being a burden for family or friends. Negative feelings seemed to be intensified by non-disclosure and self-chosen social isolation. Five of 18 participants did not disclose their TB status, because of shame, not wanting to be a burden, protecting family from TB stigma, or protecting themselves from being stigmatized by family, friends or community members. Some patients only disclosed to their families and hid their TB status from friends, colleagues and community members.³⁷ A few Somali patients in the UK disclosed their TB status, because they understood the importance of contact tracing, whilst others concealed their TB diagnosis to avoid distress and discrimination, and maintain levels of isolation.⁴² Similarly, mixed migrant populations in the USA¹⁹ mentioned patients would shy away from their family members and other social contacts. Somali migrants in the UK and Mexican Americans perceived self-stigmatisation as a barrier to seeking TB care and support while being on treatment.^{37,39,42}

Stigma due to lack of knowledge - Four studies focusing on migrant populations in the USA,¹⁹ Somali migrants in the UK,^{39,42} and Haitians in the USA⁴⁶ found that TB stigma was most likely caused by a lack of knowledge of the community. Haitians in the USA reported being seen as a disadvantaged and socially marginalized group that brought TB and other diseases to the USA.⁴⁶

Stigmatization by the community - Many Mexican American patients felt they were stigmatized by family and friends who stayed away, did not want to share drinks or food, or slept separately. Consequently, most

patients felt depressed, but accepted their situation; understanding that people wanted to protect themselves from TB.³⁷ Consequences of stigma in the Haitian community in Florida were discrimination, avoidance of TB patients by others, and negative effects on relationships with family members.⁴⁶ Many Somali patients in Sheffield were supported by friends and family, but faced socio-cultural consequences in their wider social network.³⁹ In Somalia, where TB treatment was not available, TB was considered shameful for the whole family⁴² and sometimes the whole family was socially isolated and discriminated. Some patients said community members still did not know that TB was curable. Moreover, the idea that TB is hereditary implies that the entire family will face stigma, which could affect employment and marriage prospects.⁴²

Other hard-to-reach populations

Difficulties with access - For drug using TB patients in the UK, the fear of opiate withdrawal symptoms resulted in most people seeking health care only when they had reached a crisis point.³⁶

Threat of hospitalisation/paternalistic DOT - Fear of hospitalisation was also a barrier to seeking care among drug users in the UK, especially if they were unaware of the availability of methadone to prevent withdrawal symptoms.³⁶

Perceived facilitators to testing and treatment

Seven studies reported on the facilitators that influence health care-seeking behaviour and treatment adherence of TB patients; five reported on migrant populations,^{37-39,43,45} one on homeless people in Japan⁴⁰ and one on mixed urban risk groups in London.³⁶

Migrant populations

Nurse support - The importance of the nurse role in TB treatment was emphasised for Somali and mixed migrant populations.^{39,45} Somali patients in the UK appreciated support of Somali health workers and TB specialist nurses.³⁹ For migrant TB patients in Canada nurses played an important role in supporting treatment adherence.^{37,39} Somali TB patients in the UK were mostly supported by their family and friends.³⁹ Mexican American TB patients who had disclosed their diagnosis of TB to their families received support and were accepted; however, those who did not disclose were not able to access this support.³⁷

Hospitalisation, DOT, and care - Two studies noted hospitalisation as a facilitator for health care seeking behaviour and/or adherence in migrants.^{37,43} Some female Somalian and Ethiopian TB patients in Norway described directly observed treatment (DOT) as an expression of genuine care, and reducing their isolation.⁴³ In one study, a majority of Mexican Americans with TB were unable to work and limited other activities to prevent transmission of TB, making the hospital or nursing home visit “*the outing for the day*”.³⁷

Other hard-to-reach populations

Nurse support - A strong relationship of trust between care-workers and patients with care beyond a drug treatment focus was considered important by homeless patients in Tokyo, Japan. At the end of each successfully completed treatment course, the nurses organized a small ceremony, which was deemed important by patients.⁴⁰ These types of support, beyond normal TB care, made the patients generally feel more cared for and helped them adhere to treatment.

Hospitalisation, DOT, and care - Three studies noted hospitalisation as a facilitator for health care seeking behaviour and/or adherence.^{36,38,40} A homeless drug user in the UK viewed hospitalisation as “*a welcome break from the street*”. Some drug users turned to creative and strategic approaches to get hospital admission, thus avoiding opiate withdrawal symptoms.³⁶ Kawatsu and colleagues identified five sub-categories of characteristics of homeless patients in Tokyo that improved after DOT. These included mental health, health behaviour, living environment, personal relationships and attitudes towards society.⁴⁰ A London ex-TB patient, and peer educator, noted the positive effects of DOT on treatment adherence.³⁸

Cues to action for accessing TB care

Three studies mentioned cues to action to access TB care (testing).^{36,39,44}

Migrant and traveller populations

Roma people in Belgrade indicated that Roma people often do not visit a doctor until the symptoms of the disease are so severe that they are unable to work.⁴⁴ Somali TB patients in the UK were reported to all have presented in general practice shortly after initially feeling unwell.³⁹

Other hard-to-reach populations

Several participants (homeless, migrants) in a mixed group in London delayed access to medical care, because they had been trying to self-manage and attribute symptoms to other factors, or sought help only after reaching a crisis point.³⁶

Variation of views between hard-to-reach populations

No studies directly comparing the views between hard-to-reach populations were identified.

Views of service providers

Five studies presented views of TB health care/service providers, involved in the care of migrants in Canada,⁴⁵ Somali migrants in the UK,³⁹ Somali and Ethiopian migrants in Norway,⁴³ HIV infected patients in Sweden,⁴¹ and homeless and drug users in London.³⁸

Service providers' views of service barriers

Migrant populations

Service providers mentioned (fear of) stigma,^{39,45} the use of khat resulting in late presentation of Somali migrant populations,³⁹ atypical presentation of the disease due to different cultural perspectives, language barriers (and the lack of professional translators), paucity of TB cases seen per year,³⁹ negative psychological

effects of wearing masks and isolation,⁴⁵ and an aversion for DOT⁴³ as factors that created difficulties in patients' diagnosis and treatment adherence. Norwegian service providers acknowledged the existence of institutional barriers to treatment adherence.⁴³ Whilst DOT was generally seen as effective, most were aware of the implications of DOT on patients' lives, given they had little standing in society.⁴³ Service providers of Somali TB patients in the UK³⁹ and Norway⁴³ noted that most patients accepted and complied to treatment, non-adherence was sometimes due to the chaotic situation a patient was in, such as applying for asylum.

TB-HIV co-infected patients

HIV and TB specialised physicians and nurses in Sweden were interviewed concerning the challenges in their work regarding TB-HIV co-infection.⁴¹ They reported a number of barriers to access to TB care and treatment adherence. These included (i) reduced continuity among physicians; (ii) staff shortages; (iii) difficulties in monitoring and managing the treatment process; (iv) insufficient networking between the HIV and TB specialties; (v) need for more collaboration; (vi) uncertainty about division of tasks between HIV and TB clinics; and (vii) insufficient communication between team members.

Service providers' views of service facilitators

Migrant populations

Service providers identified facilitators supporting treatment adherence: (i) the use of persuasion based on subtle threats;⁴³ (ii) assisting patients with needs beyond the administration of tablets;^{43,45} (iii) support by TB specialist nurses and Somali service providers,³⁹ (iv) acknowledging difficulties of being an immigrant,⁴⁵ and; (v) support from close family.³⁹

Homeless and/or drug/alcohol dependent patients

Peer educators who had received treatment for active TB and experienced being homeless and/or drug/alcohol dependent in London mentioned that their support could be motivational and have a personal impact on other TB patients in similar situations.³⁸

Discussion

Our review provides evidence-based qualitative information on several important barriers to, and facilitators for, the uptake of TB diagnostic and treatment services by people from hard-to-reach populations regarding TB care in low- and medium TB-incidence EU(-candidate), EEA, and OECD countries. We identified twelve studies, in addition to 25 studies⁴⁷⁻⁷¹ included in the previous NICE review.³⁰ In this latter review,³⁰ twelve studies reported on migrants,^{47,48,54,55,57,58,60,63-67} four on homeless people,^{51,52,62,70} two on a mixture of hard-to-reach populations (migrant, homeless, prisoners),^{53,56} one on drug users,⁷¹ one on people living with HIV,⁶⁹ and five on the views of healthcare professionals.^{49,50,59,61,68} Combining the findings of the current review with those of the previous review³⁰ (see **Supplementary Material IV**) provides a body of evidence which informs important gaps in provision of TB care in low- and medium-incidence countries.

Limited perceived susceptibility can be a barrier, as individuals who do not consider themselves susceptible to TB may not access health care when they develop symptoms. We found strong evidence that many misconceptions existed regarding susceptibility to TB among all investigated hard-to-reach populations in

our review and the previous review.^{19,36,37,39,42,44,46-48,52,53,55-58,60,65,67,70} Regarding TB severity, migrants, prisoners, drugs users, and homeless populations were generally aware of untreated TB being potentially fatal.^{19,47,52,54,56} Previous studies have shown the importance of being aware of the variety of perceptions on illness and health care,^{72,73} and many have stressed the importance of cultural-sensitive programmes.^{74,75} Thus in specific settings, it is relevant to introduce awareness-raising programmes that acknowledge and appropriately address the variety of local perceptions with the aim of enhancing early case-finding and reducing delay in health care seeking.

Ample barriers to treatment seeking and adherence for migrant populations were identified.^{19,37,39,42,46-48,53,54,56-58,60,62,65-67,70} We found strong evidence that TB-related stigmatisation was perceived as a major barrier in almost all studies on migrant populations and some on homeless people.^{37,39,43,45-47,51,53,57,58,60,67} Stigma can be described as a discrediting attribute negatively affecting social status and position and often leading to rejection and/or exclusion.⁷⁶ Self-stigmatisation can be defined as “*a reduction of an individual’s self-esteem or self-worth caused by the individual self-labelling herself or himself as someone who is socially unacceptable*”⁷⁷ and can lead to denial of diagnosis, or hiding of TB status. Stigma and its social consequences is one of the major factors hindering TB diagnosis and treatment adherence.^{22,78,79} Various interventions exist, such as family and community sensitizations, treatment supporter programs, and counselling. However, stigma is often embedded in a cultural context with deep-seated beliefs⁸⁰ and should therefore not solely be ascribed to a knowledge deficit as knowledgeable people may also stigmatize. Therefore, it is necessary to organize interactive sensitization programs at community level specifically targeted at stigmatizing attitudes and actions. Notwithstanding the amount of literature on this topic,⁸¹ TB stigma is still prevalent and therefore a focus for international TB control efforts.^{79,82}

Institutional barriers, such as poor health infrastructure, unavailable diagnostic facilities, incorrect diagnosis, little health care provider training, and lack of follow-up routines,²² were reported to delay TB diagnosis.^{19,36,43,47,48,54,56,57} Additionally, structural barriers were mentioned across studies.^{19,37,39,42,43,46,47,52,54,60,65,69,71} Hard-to-reach groups in low and medium-incidence countries often search for TB care or take TB treatment under challenging circumstances, such as uncertain migrant status, undocumented immigration status, homelessness, addiction to alcohol or drugs, or vulnerable economical and social positions.^{78,83} Countries should critically reflect upon their immigration policies and how this may hamper TB control.⁸³ Evidence on the effect of incentives is conflicting.⁸⁴⁻⁸⁶

No strong evidence on perceived facilitators of TB diagnosis or treatment adherence could be found across the hard-to-reach populations.^{36,37,40,43,45-47,51,54,57,66,69} Possible approaches to improve access to healthcare in general are support and social networks, multidisciplinary teams, care and transportation for free, use of outreach services, and gender- and culture-sensitive trained care providers. A patient-centred approach plays a key role in improving treatment adherence.⁷⁸ For many migrants, there is a need to use interpreters and/or bilingual staff.⁸⁷ In drug use and homelessness services, strong collaborations that integrate existing (social) services with TB care could be useful.⁸⁸ Furthermore, structural barriers need to be tackled.

No strong evidence on ‘cues to action’ motivating or precipitating healthcare seeking could be identified. Delay in health care seeking is often cited as a more complicated obstacle among hard-to-reach populations than treatment adherence, as people who delay care seeking are not yet in the health care system and therefore

difficult to reach. Discontinuity in (primary) care may also cause diagnostic delays.^{48,89-91} Diagnostic delay may be reduced with awareness training of health professionals about atypical TB symptoms, patients' history, and patients' interpretation of TB symptoms.⁴⁸ Moreover, there is a need to improve the accessibility of TB services for hard-to-reach populations.⁹¹

Main challenges identified by service providers with giving care to migrant TB patients were cultural and language barriers,^{39,41,43,45,47,54,59} and regarding TB care in general a lack of specialist services and coordination of care,^{39,41,43,47,49,59,68} and complex social and clinical interactions.^{49,50,53} In low-TB-incidence settings, poor TB awareness and expertise among (primary) care providers is a problem, causing considerable treatment delays and distrust in the health system. There is a need for continuous training of health-care providers on TB and its diagnosis; computer-based decision support has been postulated to improve clinical practice.^{41,92} Language and cultural barriers are considerable obstacles;^{87,93-98} care providers should have unlimited access to high-quality translation services; currently, those are not readily available in many of the studied countries.⁸⁷ Cross-cultural training of health care providers and the availability of bilingual, multidisciplinary teams have been associated with better health outcomes.⁹⁶

Our systematic review highlights the limited number of studies that have been conducted on hard-to-reach populations in EU (candidate), EEA, and OECD countries specifically, and in medium and low-incidence countries in general. Many studies focused on Somali migrants; the majority of findings are therefore quite specific for this migrant population and may not be transferrable to other migrant hard-to-reach populations. Children are not mentioned in the studies included in both our and the previous systematic review, and yet the World Health Organization (WHO) estimated 10% of the TB notification worldwide to be children.² Moreover, two pathogen-related factors that complicate TB care are multidrug resistance and HIV co-infection; the latter exacerbating mortality and facilitating the development of drug resistance.⁹⁹ Multidrug-resistant TB (MDR-TB) is not cited in any of the identified studies, despite the fact that MDR-TB is a growing problem also in Europe.^{100,101} The lengthy duration of treatment with toxic drugs with potentially serious side effects complicates adherence to treatment.¹⁰² Only two studies about TB-HIV co-infection were identified. Thus, more qualitative, large scale, multi-country studies are needed to obtain evidence for operational factors that affect access and delivery of effective TB services, especially for MDR-TB and TB-HIV co-infected patients.

There were several limitations to our study. Thematic analysis is, given its subjective nature, prone to bias; with many views expressed in qualitative literature being interpretable in different ways. We aimed for keeping this limited by following PRISMA guidelines resulting in a critically appraised and structured analysis of the qualitative literature. The quality of the studies was generally moderate-to-high (for grading of qualitative research); aspects in which studies were lacking were the clarity of the role of the researcher, the description of the context, reliability of the data collection methods, and reporting of the approach of the data-analysis. Our evidence is limited as relatively few studies, especially on non-migrant groups, were identified. Additionally, the majority of studies have a focus on (Somalian) migrant populations hindering the formulation of health care recommendations for other hard-to-reach populations.

Conclusions

Whilst medium- and low-TB incidence countries may give lower priority to TB control and research activities, TB has re-emerged as a significant problem.^{16,103} Striving for equitable access to TB care, there is a need for increased investments so that an evidence base on TB knowledge, stigma, DOT, and economic constraints is available to carefully tailor TB programs to specific risk groups.¹⁰⁴ This is especially of importance for making progress towards TB elimination globally. The recent arrival of millions of refugees into Europe from high TB endemic regions of Asia, Middle East and Africa may increase the numbers of hard-to-reach populations with TB. The gaps in knowledge and the new migrant refugees, provide an opportunity to conduct future studies. A focus on patient autonomy, shared decision-making, support systems, and support particularly for patients from hard-to-reach groups can improve uptake of diagnosis and adherence to treatment. The influence of poverty and gender on patients and their treatment adherence are factors which require further study.⁷⁸ Future research should cover the wide variety of hard-to-reach populations in EU, EEA, and OECD countries in order to make realistic recommendations to render TB control programs most effective. Unfortunately, many countries, especially those where TB is concentrated in hard-to-reach populations, do not have a national TB programme that can take up the coordination.^{28,82}

Conflict of interest

The authors have no conflict of interest to disclose.

Authors' contribution

SGdV, CCH and BJV conceived the protocol. RS conducted the literature search. SGdV, CCH and BJV performed the study selection. SGdV, ALC and CCH collected the data and performed quality/risk assessment. SGdV and ALC synthesised the data, created the tables and figures and prepared the manuscript and supplementary files. MPG and MvdW supervised the whole process. All authors were involved in interpretation of the data and revising the manuscript.

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Figure 1: Study selection process

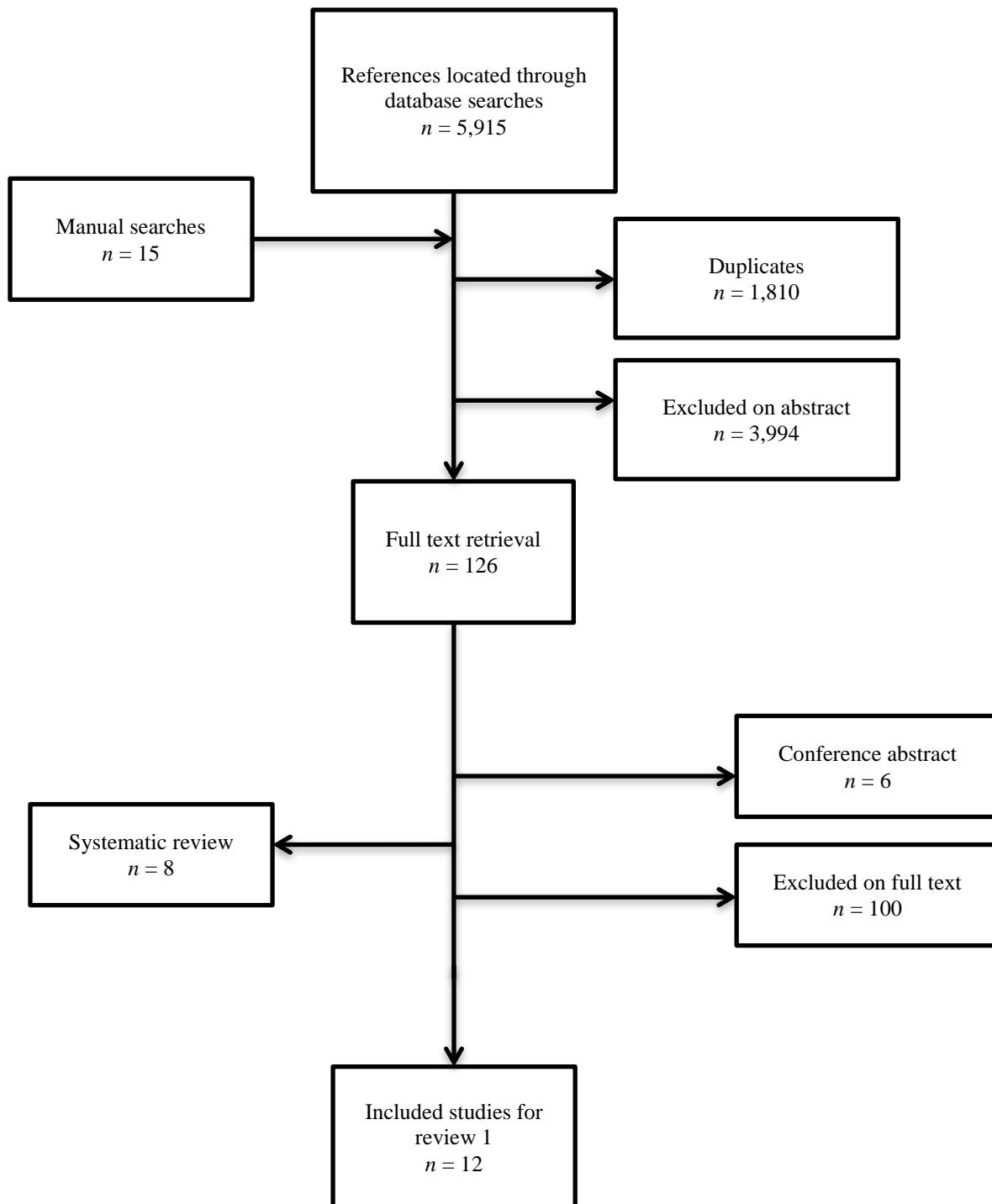


Table 1. Characteristics of included studies

Year	First author	Aim(s)	Method	Number of participants	Location	Study respondents	Quality score
2010	Bender et al. ⁴⁵	To analyse how the experience of client displacement shapes the relational work of TB nurses.	Observations of the usual contacts between nurses and migrant clients (TB patients currently receiving DOT). Additionally, interviews with nurses and some of the observed clients were held.	N = 33 Nurses: 9 TB patients: 24	Toronto, Canada	Migrants and service providers	-
2010	Coreil et al. ⁴⁶	To identify the components of stigma perceived as important within non-affected community samples in the two study populations (Haitians in Haiti and Haitian migrants in California); and second, to understand the contextual influences on these stigma components across sites (including affected members as well). For this review, only the views from participants in Florida are considered.	Participant observation at clinics, interviews, focus group discussions, and media monitoring	N = 128 47 in focus groups 81 in interviews	Broward County and in Palm Beach County, California, USA	Migrants and service providers	+
2011	Vukovic and Nagorni-Obradovic ⁴⁴	Exploring the knowledge and beliefs about TB transmission, symptoms and treatment, opinions on appropriate preventive measures, and attitudes towards people with TB among the Roma population.	Focus group discussions with the Roma population in Belgrade, living in selected Roma communities in different conditions (Living in the worst conditions (slums)/ living in conditions similar to the general population in Belgrade / living in conditions between the previous two).	N = 24	Belgrade, Serbia	Migrants	+
2012	Gerrish et al. ⁴²	To ascertain the socio-cultural meaning and consequences of TB among people of Somali origin living in the UK.	Focus groups and interviews with community leaders (CL) from Somali organizations and TB patients (in the Somali community); interviews and focus groups with members of the wider Somali community (CM).	N = 104 CL: 10 CM: 80 Patients: 14	Sheffield, UK	Migrants	++
2012	Sagbakken et al. ⁴³	To explore experiences of being diagnosed with TB and DOT among migrants in Norway, with a view to identify factors associated with diagnostic delay.	Interviews with health-care professionals and TB patients from Ethiopia and Somalia who had been diagnosed in a hospital and for whom TB treatment had been initiated.	N = 42 Patients: 22 HPs: 20	Oslo, Norway	Migrants and service providers	++
2012	Wieland et al. ¹⁹	To understand the perceptions and misperceptions about TB among students and staff at an adult education centre. To understand how relationships and social structures influence the perceptions of TB. To understand what the perceived barriers and benefits to health seeking behaviour for TB are.	Separate focus groups at the adult education centre with students (from Somalia, Sudan, Vietnam, Cambodia, Laos, China, Pakistan, Ukraine, Russia, Turkey, Mexico, Colombia and Puerto Rico) and their teachers (from Somalia, Sudan, Asia, US).	N = 83 Students: 54 Teachers: 29	Rochester, USA	Migrants	++
2013	Croft et al. ³⁸	To understand the motivation and personal impact of being a peer educator on people with experience of anti-tuberculosis treatment, homelessness and addiction.	Interviews with peer educators who had had treatment for active TB and have experience with homelessness and/or drug/alcohol dependency, and have been a peer educator within the last 3 years of the project (Find & Treat)	N = 6	London, UK	Service care providers - Homeless and drug users	+

2013	Gerrish et al. ³⁹	To explore experiences with the diagnosis and management of tuberculosis from the perspective of Somali patients and healthcare professionals involved in their care.	Interviews with Somali TB patients who had received treatment for TB in the UK and with healthcare practitioners with experience in caring for Somali TB patients (GPs, TB specialists, nurses).	N= 32 Patients: 14 HPs: 18	Sheffield, UK	Migrants and service providers	+
2013	Kawatsu et al. ⁴⁰	To explore the changes experienced by homeless TB patients, and to discuss the possible role of PHC-based DOT treatment in effecting these changes.	Interviews with homeless patients who had received and completed DOT at Shinjuku PHC.	N = 18	Shinjuku, Tokyo, Japan	Homeless	+
2013	Wannheden et al. ⁴¹	To understand the challenges faced by nurses and physicians in the treatment of patients co-infected with the HIV and TB, with special focus on opportunities for information and communication technology.	Interviews with physicians and nurses of each speciality (HIV & TB), working with HIV/TB co-infected patients.	N = 9 Physicians: 4 Nurses: 5	Stockholm, Sweden	Service providers of HIV and TB co-infected patients, including migrants	+
2014	Craig et al. ³⁶	To analyse patients' knowledge of TB, their experiences of symptoms, and their health care seeking behaviours.	Interviews with TB patients with health and social risk factors likely to complicate adherence to treatment (such as homelessness and drug use) attending a major TB centre.	N = 17	London, UK	Homeless, migrants, drug- and alcohol users, people living with HIV	++
2014	Zuñiga et al. ³⁷	Experiences of TB treatment among Mexican Americans living in the Lower Rio Grande Valley.	Interviews with Mexican American adults who were currently receiving DOT treatment.	N = 18	Lower Rio Grande Valley, Texas, USA	Migrants	+
Studies identified by the previous NICE review:³⁰							
1994	Curtis et al. ⁷¹	To examine the responses of injecting drug users (IDUs) to current TB management strategies and to explore the implications of these responses for the implementation of Directly Observed Therapy (DOT).	Ethnographic interviews and observations in locations where drugs were sold and taken. Male and female IDUs were interviewed; Latino, black and white.	N = 68	Brooklyn, New York, USA	Drug users	-
1995	Kitazawa ⁷⁰	To gather the knowledge and views of homeless people living in group shelters concerning tuberculosis, tuberculosis medical care and health education.	Interviews with men and women in homeless shelters who were English and/or Spanish speaking.	N = 20	San Francisco, USA	Homeless	+
1996	Kelly-Rossini et al. ⁶⁹	To understand the experiences of respiratory isolation for HIV-infected patients with TB.	Interviews with males and females with a history of HIV infection or HIV risk behaviour, AFB positive sputum smears and confined to respiratory isolation; 30–51 years old.	N = 18	New York, USA	People living with HIV	+
1997	Jackson & Yuan ⁶⁸	To identify the non clinical barriers family physicians may face in managing TB among patients and suggestions for overcoming these barriers.	Focus groups with primary care physicians, infectious disease specialists and respiratory physicians who work with TB patients.	N = 15	Toronto, Canada	Service providers	+
1999	Ito ⁶⁶	To investigate elements of 'health culture' which affect adherence with preventive treatment for inactive TB among Vietnamese refugees.	Individual interviews and observations with Vietnamese refugees; included individuals who were compliant with treatment and those who were non compliant. Interviews conducted with clinic staff and various community members who were apparently not receiving TB services.	N = 24 (individual who received treatment); others NR)	California, USA	Migrants	+

1999	Yamada et al. ⁶⁷	To understand what Filipino immigrants to the USA know about TB and examine their attitudes and practices concerning TB.	Focus groups with male and female Filipino immigrants in two locations.	N = 21	Hawaii and California, USA	Migrants	++
2000	Fujiwara ⁶⁵	To explore the development of culturally appropriate marketing campaigns for TB awareness, testing and treatment for immigrants from China.	To explore the development of culturally appropriate marketing campaigns for TB awareness, testing and treatment for immigrants from China.	N = 47	New York, USA	Chinese migrants	-
2002	Houston et al. ⁶⁴	To identify the cultural health beliefs regarding TB and barriers to completion of TB prevention programmes among the Vietnamese population.	Individual interviews and observations with Vietnamese refugees; included individuals who were compliant with treatment and those who were non compliant. Interviews conducted with clinic staff and various community members who were apparently not receiving TB services.	N = 67 (53 in focus groups, 14 individual)	California, USA	Migrants	+
2003	Chemtob et al. ⁶³	To identify the barriers to diagnosis, prevention and treatment of TB among immigrants.	Interviews with immigrant Ethiopian families (ranging in size from 2 to 13 members); traditional healers and Israeli health and absorption professionals.	N = 36 (12 families, 3 traditional healers, 21 health professionals)	Israel	Ethiopian migrants and service providers	-
2004	Joseph et al. ⁶¹	To identify the factors that influence healthcare workers' adherence to policies for routine tuberculin skin tests and treatment of latent TB infection.	Focus groups with healthcare workers from a range of occupations including clinical, janitorial, administrative, clerical and security staff; US and foreign- born.	N = 106	USA	Service providers	+
2004	Swigart & Kolb ⁶²	To examine the factors that homeless people report as influencing their decisions to accept or reject TB screening.	Interviews with homeless men and women who either resided in or were visiting shelters.	N = 55	North-Western USA	Homeless	+
2005	Gibson et al. ⁵⁸	To examine socio-cultural factors influencing behaviour related to TB prevention and treatment in high-risk cultural populations.	Interviews with immigrants from Hong Kong, China, Philippines, Vietnam, Punjab, Eastern Europe and Aboriginal populations; included those with active TB, those who had taken directly observed treatment (DOT), those who had been offered DOT and refused and those with past history of TB, or a relative with TB.	N = 133	Canada	Migrants	++
2005	Moro et al. ⁵⁹	To explore chest and infectious disease physicians' views of the barriers to effective tuberculosis control.	Focus groups with chest and infectious disease physicians offering TB care.	N = 49	Emilia Romagna region, Italy	Service providers	++
2005	Van der Oest et al. ⁶⁰	To explore the opinions of refugee and minority group representatives about the significance of TB for their community and perceptions of TB services.	Community representatives were interviewed from the largest community populations, including Maori and Pacific Island groups, as well as immigrants from China, The Philippines, Somalia, and Kampuchea (Cambodia).	N = unclear ('several groups')	New Zealand	Migrants	-
2006	Brewin et al. ⁵⁵	To understand how acceptable tuberculosis screening is to immigrant populations and to explore immigrants' understandings of TB in relation to screening.	Interviews with adult immigrants from a variety of ethnicities who had been offered TB screening.	N = 53	East London, UK	Migrants	+
2006	Johnson ⁵⁶	To explore how specific cultural health beliefs regarding TB affect the awareness and understanding of the disease among at-risk communities.	Focus groups and interviews with members of the following at-risk populations: Chinese, Nigerian, women refugees, Vietnamese, substance misusers, HIV-positive people, homeless people and prisoners.	N = 67	South East London, UK	Migrants, people living with HIV, drug users, homeless, prisoners	-

2006	Nnoaham et al. ⁵⁷	To describe the perceptions and experiences of African patients with TB, particularly relating to diagnosis, adherence and stigma.	Interviews with patients attending a TB clinic, either for preventive therapy or to receive a diagnosis; African-born; over 18 years.	N = 16	London, UK	Migrants	++
2007	Mahmoud ⁵³	To examine the level of knowledge, attitudes and perceptions of TB among populations at high risk of social exclusion and deprivation. To identify barriers that different populations face in accessing treatment, and understand how the cultural context of TB affects their lives.	Focus groups with participants from different ethnicities including refugees and asylum seekers, people who are HIV positive, homeless, and prisoners; male and female. Focus groups with healthcare professionals providing TB services to the same communities. One in-depth interview with a tuberculosis patient	N = 120 (104 migrants, 15 service providers, 1 tuberculosis patient)	Brent, UK	Migrants, PLHIV, homeless, prisoners and healthcare professionals	++
2007	Marais ⁵⁴	To identify the structural influences which operate across community and sector levels within the local context which may influence TB risk, healthcare access and outcome in migrant black African communities. To identify the resources to improve TB control which exist or could be strengthened within the sectors and within these migrant black African communities themselves.	Multi-method participatory research using questionnaires, in-depth interviews, community consultations and observations; migrant black Africans over 18 years old who had been in the UK for less than 10 years; key stakeholders including individuals and representatives of populations, organisations or institutions, which could significantly influence public health interventions for TB control.	N = 329 (312 African migrants, 17 stakeholders)	London, UK	Migrants	++
2008	Belling et al. ⁴⁹	To conduct an audit of TB services in relation to the range of services and expertise required to control and treat TB in London.	Interviews with TB service users and TB service lead professionals. Focus groups with TB nurses and external respiratory physicians/epidemiology professionals.	N = 33	London, UK	Service providers	++
2008	Craig et al. ⁵⁰	To explore how a social outreach model of care, including a TB link worker, can be best implemented for marginalised populations with TB.	To explore how a social outreach model of care, including a TB link worker, can be best implemented for marginalised populations with TB.		UK	Service providers	-
2008	West et al. ⁵²	To explore the knowledge, attitudes and beliefs about TB among homeless shelter residents and persons attending a drug/alcohol rehabilitation centre.	Focus groups of homeless participants at homeless shelters and people with drug/alcohol abuse problems attending a rehabilitation facility.	11 focus groups of 52 participants	USA	Homeless and alcohol abusers	+
2008	Whoolery ⁵¹	To explore what it means for homeless people to have TB and how this impacts their opportunities to complete treatment.	Semi-structured interviews with homeless persons, some of who were also drug users, commercial sex workers or HIV positive.	N = 16	UK	Homeless	++
2010	Gerrish et al. ⁴⁷	To identify socio-cultural influences on the prevention, diagnosis, and treatment of TB within the Somali community and to gain insight into healthcare practitioners' perceptions of and experiences with TB among the Somali community. To identify ways in which culturally appropriate health promotion initiatives regarding TB can reach the Somali community. To identify ways of supporting healthcare practitioners to provide culturally appropriate care in regard to the screening, diagnosis and management of TB within the Somali community.	Interviews with Somali community leaders. Interviews and focus groups with members of the Somali community including those with personal experience of TB. Interviews with healthcare practitioners including GPs, consultants, TB nurses and Somali nurses with experience of working with the Somali community.	N = 122 (N=56 for focus groups; N=66 for individual interview)	Sheffield, UK	Somalian Migrants	++
2010	Sagbakken et al. ⁴⁸	To identify the factors associated with diagnostic delay for TB among immigrants in Norway	Interviews with male and female immigrants from Somalia and Ethiopia who had been diagnosed with TB.	N = 22	Norway	Migrants	+

List of Abbreviations

CL: Community Leaders; CM: Community Members; DOT: Directly Observed Therapy; GP: General Practitioner; HIV: Human Immunodeficiency Virus; HPs: Healthcare Professionals; N = Number of participants; PHC: Public Health Centre; TB: Tuberculosis; UK: United Kingdom; USA: United States of America

Table 2. Quality assessment of included studies

Year	Author	Quality score	1. Is a qualitative approach appropriate?	2. Is the study clear in what it seeks to do?	3. How defensible/rigorous is the research design / methodology?	4. How well was the data collection carried out?	5. Is the role of the researcher clearly described?	6. Is the context clearly described?	7. Were the methods reliable?	8. Is the data analysis sufficiently rigorous?	9. Is the data 'rich'?	10. Is the analysis reliable?	11. Are the findings convincing?	12. Are the findings relevant to the aims of the study?	13. Conclusions	14. How clear and coherent is the reporting of ethics?
2010	Bender et al. ⁴⁵	-	Y	Y	Y	NS	NS	N	Y	Y	Y	NS	Y	Y	P	N
2010	Coreil et al. ⁴⁶	+	Y	Y	Y	Y	N	NS	Y	Y	Y	NS	Y	Y	Y	Y
2011	Vukovic and Nagorni-Obradovic ⁴⁴	+	Y	Y	P	P	Y	Y	N	Y	Y	Y	Y	Y	P	Y
2012	Gerrish et al. ⁴²	++	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2012	Sagbakken et al. ⁴³	++	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
2012	Wieland et al. ¹⁹	++	Y	Y	Y	Y	Y	P	Y	Y	Y	Y	Y	Y	Y	Y
2013	Croft et al. ³⁸	+	Y	Y	Y	Y	NS	N	Y	Y	Y	Y	Y	Y	Y	Y
2013	Gerrish et al. ³⁹	+	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y
2013	Kawatsu et al. ⁴⁰	+	Y	Y	Y	Y	NS	NS	Y	Y	Y	NS	Y	Y	Y	Y
2013	Wannheden et al. ⁴¹	+	Y	Y	Y	Y	NS	NS	Y	Y	Y	Y	Y	Y	Y	Y
2014	Craig et al. ³⁶	++	Y	Y	Y	Y	Y	Y	M	Y	Y	Y	Y	Y	Y	Y
2014	Zuninga et al. ³⁷	+	Y	Y	Y	Y	N	Y	Y	Y	NS	Y	Y	Y	P	Y
<i>Studies identified by the previous NICE review:³⁰</i>																
1994	Curtis et al. ⁷¹	-	Y	M	N	NS	N	NS	Y	N	NS	N	Y	Y	Y	N
1995	Kitazawa ⁷⁰	+	Y	Y	Y	Y	N	Y	NS	N	N	N	Y	Y	Y	Y
1996	Kelly-Rossini et al. ⁶⁹	+	Y	Y	Y	NS	N	NS	Y	Y	Y	Y	Y	Y	Y	Y
1997	Jackson & Yuan ⁶⁸	+	Y	Y	Y	Y	N	Y	Y	Y	N	Y	N	M	Y	Y
1999	Ito ⁶⁶	+	Y	Y	Y	Y	NS	Y	NS	NS	Y	NS	Y	Y	Y	NS
1999	Yamada et al. ⁶⁷	++	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	NS
2000	Fujiwara ⁶⁵	-	Y	Y	Y	Y	N	N	N	N	N	N	N	P	N	N
2002	Houston et al. ⁶⁴	+	Y	Y	Y	Y	Y	NS	Y	Y	N	NS	Y	M	Y	NS
2003	Chemtob et al. ⁶³	-	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N
2004	Joseph et al. ⁶¹	+	Y	Y	Y	Y	NS	N	Y	Y	Y	Y	Y	Y	Y	Y
2004	Swigart & Kolb ⁶²	+	Y	Y	Y	Y	N	Y	Y	Y	NS	Y	Y	Y	Y	N
2005	Gibson et al. ⁵⁸	++	Y	Y	Y	Y	Y	Y	Y	Y	NS	Y	Y	Y	Y	Y
2005	Moro et al. ⁵⁹	++	Y	Y	Y	Y	NS	Y	Y	Y	Y	Y	Y	Y	Y	NS
2005	Van der Oest et al. ⁶⁰	-	Y	Y	Y	Y	N	N	NS	N	Y	N	N	Y	Y	N
2006	Brewin et al. ⁵⁵	+	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
2006	Johnson ⁵⁶	-	Y	N	N	N	N	Y	Y	N	N	N	N	Y	Y	NS
2006	Nnoaham et al. ⁵⁷	++	Y	Y	Y	Y	NS	NS	NS	Y	Y	NS	Y	Y	Y	Y
2007	Brent Refugee Forum ⁵³	++	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2007	Marais ⁵⁴	++	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
2008	Belling et al. ⁴⁹	++	Y	Y	Y	Y	NS	Y	Y	NS	M	Y	Y	Y	Y	Y
2008	Craig et al. ⁵⁰	-	Y	Y	N	NS	N	N	Y	N	N	N	N	Y	Y	Y
2008	West et al. ⁵²	+	Y	Y	Y	NS	N	Y	Y	Y	N	Y	Y	M	N	N
2008	Whoolery ⁵¹	++	Y	Y	Y	Y	Y	Y	Y	Y	Y	NS	NS	Y	Y	Y
2010	Gerrish et al. ⁴⁷	++	Y	Y	Y	Y	Y	Y	Y	Y	Y	NS	Y	Y	Y	Y
2010	Sagbakken et al. ⁴⁸	+	Y	Y	Y	Y	N	Y	Y	Y	N	Y	Y	Y	Y	Y

++	well designed study, minimal risk of bias
+	study may not have addressed all potential sources of bias
-	significant risk of bias
N	No
Y	Yes
NS	Not sure (not reported or inadequately reported)
M	Mostly relevant
P	Partially relevant

Table 3. Views on susceptibility: reported concepts of causes and modes of transmission across 20 studies (this update and the previous NICE review³⁰)

Cause	Total Mentions	Mixed populations*	Homeless	Migrants - mixed	Migrants - African: Somali & Ethiopian	Migrants - Asian incl. Chinese, Vietnamese & Filipino	Migrants - Roma	Migrants - Mexican, Haitian
<i>Smoking</i>	10	1 ⁵³	2 ^{52,70}	3 ^{19,55,58}	2 ^{47,48}	2 ^{56,65}		
<i>Food-related</i>	9	1 ³⁶	2 ^{52,70}	2 ^{19,55}	2 ^{48,56}	1 ⁵⁶	1 ⁴⁴	
<i>Heredity</i>	9	1 ⁵⁶	1 ⁵⁶	2 ^{58,60}	4 ^{39,42,47,57}		1 ⁴⁴	
<i>Other illnesses</i>	8	1 ³⁶ (HIV)	1 ⁵² (AIDS)		3 influenza & pneumonia ⁴² asthma ⁴⁷ pneumonia ⁵⁵	1 ⁵⁶ (low immunity)	1 ⁴⁴ (influenza, pneumonia)	1 ⁴⁶ (HIV)
<i>Environment (typically "dirty" or weather)</i>	8	1 ⁵³	1 ⁵²	1 ⁵⁸	2 ^{47,56}	3 ^{56,65,67}		
<i>Poverty</i>	8	1 ³⁶	1 ⁵²	1 ⁵⁵	3 ^{42,47,48}	1 ⁶⁴	1 ⁴⁴	
<i>Lack of self-care, health imbalance</i>	7	1 ⁵³	1 ⁵²	2 ^{55,58}	2 ^{47,48}	1 ⁶⁷		
<i>Sharing (e.g., cigarettes, cutlery)</i>	6	1 ⁵⁶	2 ^{52,70}	1 ⁵⁵	2 ^{42,57}			
<i>Sexual contact / Saliva</i>	4	1 ⁵⁶		2 ^{19,55}			1 ⁴⁴	
<i>Stress</i>	4				1 ^{42,47}	1 ⁶⁴	1 ⁴⁴	
<i>God</i>	3	1 ³⁶			2 ^{19,42}			
<i>Lifestyle factors</i>	3	1 ³⁶		1 ¹⁹	1 ⁴²			
<i>Blood (type)</i>	2			1 ¹⁹			1 ⁴⁴	
<i>Touch</i>	2			1 ¹⁹			1 ⁴⁴	
<i>Geographical localisation</i>	2			1 ¹⁹ (not in USA)				1 ³⁷ (proximity Mexico)
<i>Airborne</i>	1				1 ⁴²			
<i>Vectors (rats)</i>	1						1 ⁴⁴	

Box 1. In- and exclusion criteria for this review

1. Having a focus on TB services of any kind (any study examining TB or a TB service delivered to a hard-to-reach population);
2. Having been conducted in any of the EU/EEA countries, the candidate countries* and the other OECD countries**;
3. Having been published in 2010 or later for the OECD countries;
4. Having been published in 1990 or later for the EU/EEA countries and candidate countries* not being one of the OECD countries**;
5. Present data on the views of hard-to-reach people regarding perceptions of or attitudes to TB services;
6. Present original qualitative data (no systematic reviews);
7. Include data from any hard-to-reach population:
 - homeless people
 - people with alcohol or other drug addictions
 - sex workers
 - prisoners or people with a history of imprisonment
 - vulnerable migrant populations such as asylum seekers and refugees, but also recent migrants and travellers (including the Roma population)
 - children within vulnerable and hard-to-reach populations
 - people living with HIV
8. Respondents do not necessarily have to be diagnosed with TB;
9. Do not exclusively focus on latent TB infection (LTBI);
10. No language restrictions

EU/EEA: European Union, European Economic Area; OECD: Organisation for Economic Co-operation and Development.

**EU candidate countries = Albania, Montenegro, Serbia, the former Yugoslav Republic of Macedonia and Turkey*

*** OECD countries = Australia, Austria, Belgium, Canada, Chile, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Korea, Luxembourg, Mexico, the Netherlands, New Zealand, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, United Kingdom, United States*

Box 2. Grading of evidence

No evidence – no evidence or clear conclusions from any studies;

Weak evidence – no clear or strong evidence/conclusions from high quality studies and only tentative evidence/conclusions from moderate quality studies or clear evidence/conclusions from low quality studies;

Moderate evidence – tentative evidence/conclusions from multiple high quality studies, or clear evidence/conclusions from one high quality study or multiple medium quality studies, with minimal inconsistencies across all studies;

Strong evidence – clear conclusions from multiple high quality studies.

Supplementary Materials Legend

Supplementary Material I: PICOS (Population-Intervention-Comparator-Outcome-Study design)

Supplementary Material II: Search strategy

Supplementary Material III: Evidence tables

Supplementary Material IV: Evidence statements

Supplementary Material V: Illustrative quotes per theme