

Article 1 of 2:

Series: Tuberculosis identification and management in hard-to-reach and vulnerable populations

Title:

Barriers and facilitators for the uptake of tuberculosis diagnosis and treatment services by hard-to-reach populations: A systematic review of qualitative literature

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Abstract

Tuberculosis (TB) disproportionately affects hard-to-reach populations, such as the homeless, migrants, refugees, prisoners, substance misusers, people living with HIV. These people face important challenges in accessing and receiving quality health care services. To identify barriers to, and facilitators for, the uptake of TB diagnosis and treatment services by people from those hard-to-reach populations we performed a systematic review of the qualitative literature following PRISMA guidelines, . Twelve studies were included in this review; most focussed on migrants. Views on perceived susceptibility to and severity of TB varied widely and included misconceptions. Stigma and challenges with accessing health care were identified as barriers for TB diagnosis and treatment uptake whereas nurse, family, and friends' support were facilitators to treatment compliance. Addressing barriers and facilitators may improve identification of potential TB cases and treatment in hard-to-reach populations.

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Introduction

Tuberculosis (TB), malaria, and HIV are the three infectious diseases that cause the largest loss of disability adjusted life years in the world.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-incidence countries (i.e. notification rate <10 TB cases per 100 000 population).³ In these countries, TB cases are disproportionally accumulated in big cities linked with an over-representation of TB among a variety of hard-to-reach populations, consisting of prisoners, migrants, people living with HIV, homeless people, sex workers, and substance abusers.^{4,5} In the EU/EEA, 28% of the TB patients are diagnosed in foreign born individuals, and males are over-represented in almost every country.³ Except for information on origin, age, and sex, there is limited accurate and comparable surveillance data available on TB in hard-to-reach populations.^{6,7} The lack of data hampers policy and guideline development which is needed to achieve TB elimination. 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.^{5,8,9}

Individuals belonging to hard-to-reach populations often have risk factors that make them vulnerable for being exposed to, and being infected with, *Mycobacterium tuberculosis* and for developing active TB disease after infection.¹⁰ 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.^{11,12} Delay in health care seeking can be related to reduced awareness and knowledge of the signs and symptoms of TB, difficulties with transportation, limited opening hours of testing centres, or the duration and cost of testing.¹³⁻¹⁵ When individuals from hard-to-reach populations are diagnosed with TB, adherence to a treatment of at least six months duration can be extremely difficult without stable accommodation,^{11,16} or while dealing with substance addictions, co-morbidities, HIV, or social and economic problems.^{17,18} Thus, risk factors, delay in health care seeking, and difficulties with treatment adherence fuel TB infection and the ongoing transmission of TB, especially within the hard-to-reach populations.^{19,20}

The European Centre for Disease Prevention and Control (ECDC) set out to develop guidance for controlling TB in hard-to-reach and vulnerable populations.²¹ To provide the latest evidence, a systematic review of qualitative literature was conducted focussing on the barriers and facilitators for the uptake of TB diagnostic and treatment services in a wide range of hard-to-reach populations, covering all EU, EEA, EU candidate, and Organisation for Economic Co-operation and Development (OECD) countries.

The primary review question of our systematic review was: ‘What factors help or hinder the uptake of TB diagnosis and treatment services by people from hard-to-reach populations, 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?’.

Methods

In 2010, the Matrix Knowledge Group conducted a systematic review on barriers and facilitators for the uptake of TB diagnosis and treatment services by people from hard-to-reach populations in OECD countries (see **Box 1**). This review was commissioned by the National Institute for Health and Clinical Excellence (NICE).²² We updated and extended the NICE review,²² using the same methodology to ensure inclusion of the most up-to-date and relevant evidence.

This review was conducted following standards described by Cochrane²³ and NICE.²⁴ Results are reported according to the PRISMA guidelines for reporting of systematic reviews.²⁵ The review protocol was registered in the database of prospectively registered systematic reviews in health and social care, PROSPERO (CRD42015019450).

Eligibility criteria and search

The databases Medline, Medline In-Process, Embase, PsychInfo, Centre for Reviews and Dissemination-University of York; 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).²² 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 and sex workers)²² we included people living with HIV and children within vulnerable and hard-to-reach populations, and limited the search to TB, i.e. not covering latent TB infection (LTBI). The search performed for the NICE review was not repeated but updated, covering the period 2010 up to 10 April 2015. The search for the newly included countries and hard-to-reach populations covered the period 1990 up to 10 April 2015. Three searches were carried out (with the final one performed on 10 April 2015). Additionally, all included studies and all systematic reviews identified in the screening phase were checked for relevant references; identified systematic reviews were reviewed for relevant references and were not included (see **Supplementary Material II** for comprehensive search strategy details). 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, were included. See **Supplementary Material I** for PICOS (Population-Intervention-Comparator-Outcome-Study design).

Study selection and data management

Records identified by the search were imported to an Endnote database and duplicate records were removed (EndNote X7.1, Thomson Reuters 2014). Studies were screened on title and/or abstract by three authors (SdV, CCH, BJV) independently and in parallel using the inclusion criteria (**Box 1**). 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. The full text of selected studies was screened by three independent authors (SdV, ALC, CCH) using a full text assessment inclusion checklist,

derived from the previous review performed by NICE.²² 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.²² For a random 10% of included studies, data extraction was performed by two independent reviewers. For the remaining studies, one reviewer conducted data extraction, checked by a second reviewer; any disagreement was resolved by discussion. To structure the data synthesis, we used the Health Belief Model (HBM),²⁶ as done in the previous review.²² The model explains and predicts health-related behaviours, particularly with regard to the uptake of health services. Two reviewers separately conducted thematic and content analysis.²⁷ Data was screened multiple times, 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 benefits (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). The syntheses for the secondary research questions did not follow the HBM.

We present the evidence resulting from the NICE review together with the evidence from our update in the discussion section and in supplementary material.

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.²² 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 before²² (**Box 2**).

Role of the funding source

The funder of the study was involved in study design, data interpretation, and reporting.

Results

Study selection

Database searches identified 5,915 records. Citation chasing of included studies and applicable excluded reviews identified fifteen records. In total, 5,930 abstracts were entered into the database; 1,810 duplicate records were removed. See **Figure 1** for details of the flow through the literature. Twelve studies were included in this review.^{15,28-38}

Study characteristics and quality

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,^{15,29,31,34,35,37,38} one a mixed group of homeless people, migrants and drug users,²⁸ one of homeless people,³² and one study reported on views of a Roma population.³⁶ No studies were found on views of prisoners, sex-workers and children living in hard-to-reach populations. Two studies focussing uniquely on views of healthcare providers on barriers or facilitators for hard-to-reach populations were identified.^{30,33} Studies were conducted in the United Kingdom (UK),^{28,30,31,34} the United States of America (USA),^{13,29,38} Sweden,³³ Norway,³⁵ Serbia,³⁶ Canada³⁷ and Japan.³² The results of quality assessment are presented in **Table 2**.

Factors that help or hinder the uptake of TB diagnosis and treatment services by people from hard-to-reach populations

Detailed evidence statements on all themes, combined with the findings of the previous NICE review²² are provided in **Supplementary Material IV**. Here we present the findings of the update and extension of the NICE review.

Perceived susceptibility

Individuals who do not consider themselves susceptible to a disease may not access health care if they develop symptoms. We included seven studies that reported views of hard-to-reach people regarding TB susceptibility, such as concepts of causes, risk factors, and modes of transmission.^{15,28,29,31,34,36,38} Six studies focused exclusively on migrant populations,^{15,29,31,34,36,38} and one on a mixed population of homeless people, drug users and migrants.²⁸

Smoking and ‘other illnesses’ were the most frequently mentioned perceived causes or risk factors for TB.^{13,28,34,36} Other frequently perceived causes mentioned by individuals from hard-to-reach populations were: (i) food-related causes (usually ‘bad’, or a lack of food);^{15,28,36} (ii) the misconception that TB ‘is in the blood’ and hereditary (present among Somali migrants and Roma populations);^{31,34,36} (iii) poverty (e.g., poor living conditions);^{28,34,36} (iv) sexual contact;^{15,36} (v) stress;^{34,36} (vi) causes related to God/religion^{28,34} or a punishment of God for past ill deeds;¹⁵ (vii) lifestyle factors;^{15,28,34} and (viii) other illnesses such as HIV;^{28,38} flu, common cold, or pneumonia.^{34,36}

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.¹⁵ Zuñiga et al.²⁹ reported that some of the interviewed Mexican-American TB-patients talked about being vulnerable to TB because of the proximity to Mexico. 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. Only one study demonstrated knowledge of airborne transmission, in a Somali community in Sheffield, UK.³⁴ Community leaders generally showed accurate knowledge and some community members gave relatively accurate views calling TB “*an airborne disease whereby people became infected by ‘breathing in the germ’ and once infected, they could pass it on to others*”.³⁴ **Table 3** shows an overview of findings on views on susceptibility through reported concepts of causes and modes of transmission. **Table 4** provides an overview of illustrative quotations identified per theme.

Perceived severity

The way communities perceive the severity of tuberculosis influences people's health care seeking behaviour. Five studies reported on the views of hard-to-reach people on the severity of TB, such as symptoms, health consequences, and treatability of TB.^{15,28,29,34,36} Hard-to-reach populations in studies reporting on perceived severity consisted of migrants and refugees in the USA, a variety of urban risk populations in London, Mexican Americans, Somali migrants in the UK, and Roma in Belgrade. Two were exclusively reporting on the views of TB patients,^{28,29} whereas the others reported on views of the wider community.^{15,34,36}

Three studies reported good knowledge of the TB symptoms, persistent (bloody) cough, weight loss, fever and night sweats.^{28,29,34} Gerrish et al. described that 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 Somali TB patients 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.³⁴ 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.³⁶ A mixed group of migrants in the USA reported fear of TB, which consisted mainly of fear of dying from an incurable disease.¹⁵ Erroneous explanations for (common) symptoms were reported by a mixed hard-to-reach group in the UK.²⁸ Symptoms were often attributed to other (undiagnosed) illnesses, poor diet, or to drug/alcohol abuse.

Generally, knowledge of symptoms was good and TB patients reported their symptoms accurately, although these had not always been (immediately) recognized. Views on treatability and treatment were very mixed and often inaccurate.

Perceived barriers and benefits to testing and treatment

Nine studies elaborated on the barriers and facilitators that influence health care-seeking behaviour and treatment compliance of TB patients, hindering effective implementation of TB prevention and control measures.^{15,28,29,31,32,34,35,37,38}

Perceived barriers

Difficulties with access

Two studies noted the problem of access to health care facilities.^{15,28} 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.²⁸ 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.¹⁵

Signs, symptoms and adverse effects of medication

The challenges of TB symptoms combined with TB treatment side effects were described in TB patients of Mexican American²⁹ and Somali¹⁵ origin in the USA, affecting their treatment compliance. They experienced mental and physical problems.

Stress and depression

Two studies^{29,31} commented on stress and depression due to delay in diagnosis and treatment challenges complicating seeking care and treatment compliance. Somali patients in the UK³¹ 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.³¹ 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.²⁹

Loss of privacy/lack of confidentiality

Loss of privacy and lack of confidentiality were identified as important barriers to treatment compliance in two studies.^{35,38} The actions of TB health care services and outreach workers were perceived as revealing a patient’s TB status to others mentioned by both Haitians in the USA³⁸ and by Ethiopian and Somalian migrants in Norway.³⁵ 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

Four studies described negative attitudes or fear of patients towards DOT that made people reluctant to get tested.^{28,29,35,38} American Haitians associated TB treatment with incarceration; moreover, they feared loss of employment.³⁸ Fear of hospitalisation was also present among drug users in the UK, especially if they were unaware of the availability of methadone to prevent withdrawal symptoms.²⁸ 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 be only applied for those who needed assistance with managing their treatment.³⁵ DOT was perceived as imprisoning, forcing the patient into a subservient and confined position hindering work responsibilities and consequently, complicating treatment compliance.^{29,35}

Inadequate service provision

The lack of continuity among health personnel was described by Somalian and Ethiopian migrants in Norway as hindering the building of a secure and trustful patient-nurse relationship while being on treatment. Some patients described that health workers limited patient contact as much as they could. They would often not know which health worker was coming and at what time. This caused feelings of stress and humiliation.³⁵

Economic struggles

Economic hardship due to their TB diagnosis was mentioned among the Somali patients in the UK.^{31,34} A homeless patient described how hard management of the disease was without adequate accommodation, social support, and with a poor diet.³¹ Mexican American migrants reported economic hardship, losing their

job or being unable to work.²⁹ Mixed migrant populations in the USA reported that knowledge about TB medication being free of charge reduced financial constraints to accessing TB care.¹⁵

Stigma

TB patients experiencing TB-related stigma seemed a multifaceted problem for both seeking health care and treatment compliance that was covered by most articles.^{15,28,29,31,32,34,35,37,38} We identified five themes: face masks; stigma of association with HIV; self-stigma; consequences of stigma; stigma due to lack of knowledge.

Stigma - face masks

Mexican American TB patients associated wearing masks with physical discomfort and stigma.²⁹ 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 their large impact on losing friends, jobs, or being unable to find employment.³⁷

Stigma of association with HIV

Many Haitian community members in Florida assumed HIV-infection in TB patients.³⁸ In this study, the TB and HIV clinics were located together in a single building thus contributing to this assumption.

Self-stigmatisation

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"*.³⁹ Four studies described TB self-stigmatisation.^{15,29,31,34} 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.²⁹ 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.³⁴ Similarly, mixed migrant populations in the USA¹⁵ 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.^{29,31,34}

Stigma due to lack of knowledge

Four studies focusing on migrant populations in the USA,¹⁵ Somali migrants in the UK,^{31,34} and Haitians in the USA³⁸ 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.³⁸

Stigma by 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. The patients felt depressed because of this, but accepted their situation, understanding that people in their close social environment wanted to protect themselves from TB.²⁹ 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.³⁸ Many Somali patients in Sheffield were supported by friends and family, but faced socio-cultural consequences in their wider social network.³¹ It was explained that when TB treatment was not available in Somalia, TB was considered shameful for the whole family³⁴ 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.³⁴

Perceived benefits (predisposing factors)

Nurse support

The importance of the nurse role in TB treatment was emphasised for migrant populations^{31,37} and homeless people.³² Somali patients in the UK appreciated support of Somali health workers and TB specialist nurses.³¹ A strong relationship of trust between care-workers and patients, with care not only focussed on drug treatment, was deemed very relevant by homeless patients in Tokyo, Japan. At the end of each successfully completed treatment course, the nurses organized a small ceremony, which was considered important by patients.³² These types of support, beyond normal TB care, made the patients generally feel more cared for and helped them adhere to treatment.

Family and friend support

Two articles mentioned the importance of family support during TB treatment.^{29,31} Somali TB patients in the UK were mostly supported by their family and friends.³¹ Mexican American TB patients who disclosed their diagnosis of TB to their families received support and were accepted, but those who did not disclose were not able to access this support.²⁹

Hospitalisation, DOT, and care

Five studies identified hospitalisation as a facilitator for health care seeking behaviour and/or compliance.^{28-30,32,35} 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.²⁸ Some female Somalian and Ethiopian TB patients in Norway described directly observed treatment (DOT) as an expression of genuine care, and reducing their isolation.³⁵ 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*”.²⁹ Kawatsu and colleagues identified five sub-categories of homeless patients’ empowerment in Tokyo that improved after DOT, i.e. mental health, health behaviour, living environment, personal

relationships and attitudes towards society.³² A London ex-TB patient, and peer educator, noted the positive effects of DOT on treatment compliance.³⁰

Cues to Action

Three studies touched on cues to action to access TB care.^{28,31,36} Conflicting evidence arose: 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.³⁶ Somali TB patients in the UK were reported to all have presented in general practice shortly after initially feeling unwell.³¹ 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.²⁸

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 were identified containing views of TB health care/service providers on the experiences and views of people in hard-to-reach populations, such as homeless and drug users in London,³⁰ Somali migrants in the UK,³¹ HIV infected patients in Sweden,³³ migrants in Norway,³⁵ and migrants in Canada.³⁷

Service providers' views of service barriers and facilitators

Service providers caring for Somali patients in the UK acknowledged diagnostic delay and reported that 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, and patient delay contributed to diagnostic delay.³¹ Furthermore, service providers identified facilitators of treatment compliance: (i) the use of persuasion based on subtle threats;³⁵ (ii) assisting patients with needs beyond the administration of tablets;^{35,37} (iii) support by TB specialist nurses and Somali service providers,³¹ (iv) acknowledging difficulties of being an immigrant,³⁷ and; (v) support from close family.³¹

Norwegian service providers acknowledged the existence of institutional barriers to treatment compliance.³⁵ 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.³⁵

Service providers' views of service users' attitudes, cultural values and circumstances

Service providers mentioned delayed presentation of patients to health care, because of (fear of) stigma,^{31,37} late presentation of TB symptoms associated with the use of khat in Somali migrant populations,³¹ psychological effects of wearing masks and isolation,³⁷ and an aversion for DOT,³⁵ as patient-related factors that created difficulties in diagnosis and treatment adherence.

Service providers of Somali TB patients in the UK³¹ and Norway³⁵ noted that most patients accepted the diagnosis, adhered to treatment, and had a positive treatment outcome. If they were non-adherent to treatment, this was more often due to the chaotic situation a patient was in, such as applying for asylum.

Peer educators

Peer educators who had received treatment for active TB and experienced being homeless and/or drug/alcohol dependent in London, understood that they could be motivational and have a personal impact on other TB patients in similar situations.³⁰

TB-HIV co-infection

HIV and TB specialised physicians and nurses in Sweden were interviewed concerning the challenges in their work regarding TB-HIV co-infection.³³ They mentioned a number of barriers to access to TB care and treatment compliance, such as (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.

Discussion

We identified twelve studies, in addition to the 25 studies⁴⁰⁻⁶⁴ included in the previous NICE review,²² that reported qualitative data on barriers and facilitators for the uptake of TB diagnostic and treatment services in EU, EEA, and OECD countries. All these countries are low- or intermediate TB incidence countries in which TB is mostly carried by a variety of hard-to-reach populations. Nevertheless, considering the infectiousness of the disease, the airborne transmission, and in some countries rising incidences of TB, the importance of advanced and strong TB programs is evident.⁶⁵

Of the 12 included studies, seven studies focused on migrants, two on homeless people, two on drug users, one study on a Roma population; five studies focused on views of service providers. No studies were identified on views of prisoners, sex-workers, people living with HIV, and children living in hard-to-reach populations. In the previous NICE review,²² twelve studies reported on migrants,^{40,41,47,48,50,51,53,56-60} four on homeless people,^{44,45,55,63} two on a mixture of hard-to-reach populations (migrant, homeless, prisoners),^{46,49} one on illicit drug users,⁶⁴ one on people living with HIV,⁶² and five on the views of healthcare professionals.^{42,43,52,54,61} Combining the findings of the current review with those of the previous review²² provides a large body of evidence and raises important points of attention regarding TB care in low- and middle-incidence countries which are discussed below. For a complete overview of all combined evidence, see the evidence statements in Supplementary Material IV.

Both the current and previous review²² provide strong evidence that erroneous or incomplete knowledge about TB susceptibility was reported by the studied hard-to-reach populations (see table 3). Limited perceived susceptibility can be a barrier as individuals who do not consider themselves susceptible to a disease may not access health care when they develop symptoms.

Migrants, prisoners, drugs users and homeless populations were generally aware of untreated TB being potentially fatal.^{15,40,45,47,49} The evidence on understanding the general symptoms of TB in these populations was graded as moderate.^{34,36,41,45,49,63} Some individuals within migrants populations were aware of preventive measures and the dangers of TB disease.^{15,36}

Previous studies have shown the importance of being aware of the variety of perceptions on illness and health care,^{66,67} and many scholars have stressed the importance of cultural-sensitive sensitization programs.^{68,69} Thus in specific settings, it may be relevant to introduce awareness raising programs 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.

In many studies, TB-related stigmatisation appeared as a barrier to TB testing and treatment and as an important concern for people diagnosed with TB and their families (in various migrant populations, and homeless people). It often resulted in discrimination, avoidance of TB patients, and affecting the relationship with family members.^{29,31,35,37,38,40,44,46,50,51,53,60} Some studies referred to TB-related taboos causing stigmatizing attitudes among community members^{15,31,38} or stressed the perception of a link between TB and HIV increasing concerns about stigmatisation.^{38,47,49,50} Stigma may result in a delay in seeking health care,¹³ in not initiating treatment and/or non-adherence to treatment.⁷⁰ Stigma is one of the major social factors hindering TB diagnosis and treatment compliance.⁷¹ It can be described as a discrediting attribute negatively affecting social status and position and often leading to rejection and/or exclusion.⁷² Notwithstanding the amount of literature on this topic,⁷³ TB stigma is still prevalent and therefore included in the international TB control efforts.^{71,74}

Other important barriers to help- and treatment seeking and compliance mentioned by migrants were: side effects of TB treatment;^{15,29,51,59} a lack of biomedical TB knowledge;^{15,31,34,38} a lack of information or awareness about service availability or access;^{46,47,58} language barriers;^{40,47,53} and lacking confidence in, or being concerned about, misdiagnoses or delayed diagnosis by healthcare professionals.^{40,41,47,49,50} Various hard-to-reach populations felt that fear of death caused by TB was a barrier to wanting to be screened.^{40,46,55,60,63}

No strong evidence was found regarding perceived facilitators of TB testing or treatment. Moderate evidence exists for the benefits of nurse/health worker support^{31,32,37} and culturally-sensitive and appropriate care^{32,44,47,50} regarding patient access and treatment compliance of migrants and homeless people. Evidence on family and friend support^{29,31,59,62} and hospitalisation and DOT^{28,29,35,38} is conflicting.

For migrant populations, possible approaches to improve access to healthcare are: support- and social networks, multidisciplinary teams, free care and transportation, use of outreach services, the use of interpreters, bilingual staff and gender-sensitive care providers.⁷⁵ In drug- and homeless services, strong collaborations that integrate existing services with TB care could be useful, combined with a patient centred approach and social care.⁷⁶

No strong evidence on 'cues to action' could be identified. Conflicting evidence arose from three studies concerning the timing of healthcare seeking behaviour, with Somali migrants in the UK reporting early access,³¹ and Roma in Serbia³⁶ and drug users in the UK²⁸ reporting delayed access to health care after symptom onset.

No studies comparing the different views between hard-to-reach populations were identified. Nevertheless, we would like to stress the most notable similarities and differences regarding facilitators and obstacles of TB care between migrants on the one hand and homeless and/or drug users on the other hand. Nurse

support was deemed important for both populations,^{31,37} but family support was not mentioned in the latter group.^{31,37} Access and economic barriers were mentioned in both populations.^{15,28,30,32,35} whereas TB-related stigma,^{15,28,29,31,32,34,35,37,38} depression/stress,^{29,31} cultural and language barriers^{31,33,35,37,40,47,52} were mostly cited as problematic in migrant populations. The main difficulty for drug users was a real or perceived likelihood of opiate withdrawal while seeking and receiving TB care.²⁸ Only one article described that DOTS empowered homeless TB patients and (re-)connected them to society, in Japan in contrast to more negative experiences of DOTS.³² This shows how the diversity between and within hard-to-reach populations calls for a careful tailored approach to take into account group-specific facilitators and obstacles.

Main challenges identified by service providers with giving care to migrant TB patients were cultural and language barriers,^{31,33,35,37,40,47,52} and regarding TB care in general a lack of specialist services and coordination of care,^{31,33,35,40,42,52,61} and complex social and clinical interactions were mentioned.^{42,43,46}

In low-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.^{33,77} It is known that language and cultural barriers are considerable obstacles in the access to health care.^{75,78-83} Therefore, care providers should have unlimited access to high-quality translation services; those are not readily available in many of the studied countries now.⁷⁵ Cross-cultural training of health care providers and the availability of bilingual, multidisciplinary teams may also be considered as these are associated with better health outcomes.⁸¹

This systematic review provides information regarding TB diagnosis and control in EU, EEA, and OECD countries, but mostly highlights the limited number of studies that have been conducted for specific hard-to-reach populations. We identified knowledge gaps within the available qualitative literature on TB in EU, EEA, and OECD countries, and in middle and low-incidence countries in general. Children are not mentioned once in the studies included in both our and the previous systematic review, yet the World Health Organization (WHO) estimated 10% of the TB notification worldwide to be children.² Also MDR-TB is not cited in any of the identified studies. TB drug resistance is present in Europe^{84,85} and the harsh medication required leading to serious side-effects complicates treatment compliance.⁸⁶ Therefore, more qualitative studies are needed to explore patients' experience and ways to improve MDR-TB care. Vice versa, the development of TB drug resistance can also be a result of existing barriers to treatment adherence; effort should be done to overcome the barriers and improve adherence. Incentives are not proven to be effective;⁸⁷ a focus on patient autonomy, shared decision-making, support systems, patient support; and the influence of poverty and gender on patients and their treatment adherence is needed.⁷⁰

Most studies focused on migrants, and then specifically on Somali migrants; the majority of findings are therefore quite specific for these migrant populations and may not be transferrable to other hard-to-reach populations. Moreover, it is striking that included studies with a focus on mixed hard-to-reach populations do not compare views between hard-to-reach populations. Another important aspect was that most studies

focused on treatment rather than on testing. This is particularly interesting, because health care delay is often cited as a more complicated obstacle among hard-to-reach populations than treatment compliance. It is known that discontinuity in care can cause diagnostic delays,^{41,88-90} this is a barrier that can be targeted.

Whereas major initiatives to control TB happen in high-incidence countries, in medium- and low-incidence countries interest in both research and interventions regarding TB has been given lower priority. However, much work remains to be done, specifically on TB knowledge, stigma, the paternalistic nature of DOT, economic constraints, and carefully to the specific group tailored TB programs, e.g. with attention for cultural communication regarding migrant populations, and drug-withdrawal for drug users.

We acknowledge several limitations of this report. Data-synthesis was structured around the Health Belief Model themes, because of their applicability in TB-care. Theme-encoding was done by two authors in order to minimize reporting bias. However, thematic analysis is, given its subjective nature, prone to a form of bias, with many views expressed in qualitative literature being multi-interpretable. We tried to keep this to a limit 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; 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 were identified, possibly due to a publication bias in low-incidence settings. Only the low-incidence countries of the region were covered, except for Serbia as a middle-incidence country. Additionally, the majority of studies have a focus on (Somalian) migrant populations hindering the formulation of health care recommendations for hard-to-reach populations in general. Moreover, the whole concept of hard-to-reach populations is challenging, as this category is constructed by researchers, and great variation exists within these populations. Future research should cover the wide variety of hard-to-reach populations in EU, EEA, and OECD countries in order to make realistic health care recommendations to render TB control programs most effective.

Conclusions

With this systematic review we updated and extended the work done for the NICE review and developed the evidence base for the ECDC guidance document for controlling TB in hard-to-reach and vulnerable populations.²¹ The combined evidence for EU, EEA, OECD and EU-candidate countries shows that knowledge of hard-to-reach populations of the causes, risk factors and mode of transmission of TB is in general limited; however, there is awareness of the symptoms and severity of the disease. In addition, TB related stigma appears to be common, particularly in migrant populations. Efforts should be made to increase knowledge and awareness of TB among hard-to-reach populations, not only in order to improve identification and treatment of TB, but also to reduce associated stigma and its implications.

This review also showed that service providers experience barriers in providing treatment to hard-to-reach populations. At a (migrant) patient level, these are mainly culture and language related; with problems in coordination of care and a lack of specialist services identified at a healthcare provider level. Providers of services for TB patients from hard-to-reach populations should be trained in addressing cultural differences; service structures should accommodate and meet the complex needs of hard-to-reach

populations. These tasks can be performed by national TB programmes. 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.^{21,74}

Conflict of interest

The authors have no conflict of interest to disclose.

Authors contribution

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

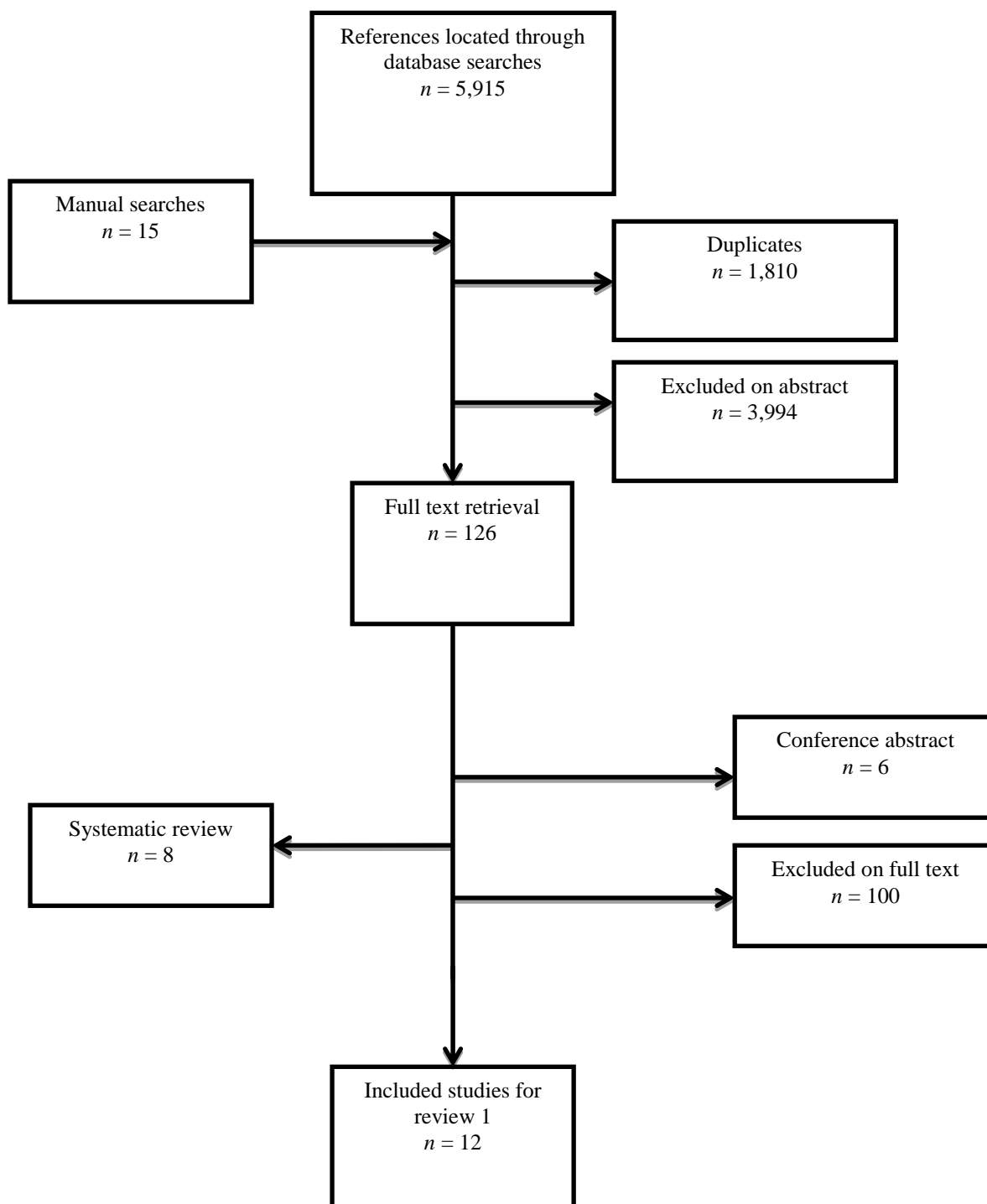


Table 1. Characteristics of included studies

Year	First author	Aim(s)	Method	Number of participants	Location	Study respondents	Quality score
2010	Bender et al. ³⁷	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. ³⁸	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.	Interviews and observations at clinics with community members of Haitian origin.	N = 81 CM: 24 HPs: 24 Patients: 33	Broward County and in Palm Beach County, California, USA	Migrants and service providers	+
2011	Vukovic and Nagorni-Obradovic ³⁶	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. ³⁴	To ascertain the socio-cultural meaning and consequences of TB among people of Somali origin living in the UK.	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. ³⁵	To explore experiences of being diagnosed with TB among migrants in Norway, with a view to identify factors associated with diagnostic delay.	Interviews with 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. ¹⁵	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. ³⁰	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. ³¹	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. ³²	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. ³³	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 TBco-infected patients, including migrants	+
2014	Craig et al. ²⁸	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. ²⁹	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:²²							
1994	Curtis et al. ⁶⁴	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 ⁶³	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. ⁶²	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 ⁶¹	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 ⁵⁹	To investigate elements of 'health culture' which affect compliance 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. ⁶⁰	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 = 36	Hawaii and California, USA	Migrants	++

2000	Fujiwara ⁵⁸	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. ⁵⁷	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. ⁵⁶	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. ⁵⁴	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 ⁵⁵	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. ⁵¹	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. ⁵²	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. ⁵³	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. ⁴⁸	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 ⁴⁹	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. ⁵⁰	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	Brent Refugee Forum ⁴⁶	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.	N = 119 (104 migrants, 15 service providers)	Brent, UK	Migrants, PLHIV, homeless, prisoners and healthcare professionals	++
2007	Marais ⁴⁷	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. ⁴²	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. ⁴³	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. ⁴⁵	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 ⁴⁴	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. ⁴⁰	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 = 120 (N=56 for focus groups; N=64 for individual interview)	Sheffield, UK	Somalian Migrants	++
2010	Sagbakken et al. ⁴¹	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. ³⁷	-	Y	Y	Y	NS	NS	N	Y	Y	Y	NS	Y	Y	P	N
2010	Coreil et al. ³⁸	+	Y	Y	Y	Y	N	NS	Y	Y	Y	NS	Y	Y	Y	Y
2011	Vukovic and Nagorni-Obradovic ³⁶	+	Y	Y	P	P	Y	Y	N	Y	Y	Y	Y	Y	P	Y
2012	Gerrish et al. ³⁴	++	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2012	Sagbakken et al. ³⁵	++	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
2012	Wieland et al. ¹⁵	++	Y	Y	Y	Y	Y	P	Y	Y	Y	Y	Y	Y	Y	Y
2013	Croft et al. ³⁰	+	Y	Y	Y	Y	NS	N	Y	Y	Y	Y	Y	Y	Y	Y
2013	Gerrish et al. ³¹	+	Y	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y
2013	Kawatsu et al. ³²	+	Y	Y	Y	Y	NS	NS	Y	Y	Y	NS	Y	Y	Y	Y
2013	Wannheden et al. ³³	+	Y	Y	Y	Y	NS	NS	Y	Y	Y	Y	Y	Y	Y	Y
2014	Craig et al. ²⁸	++	Y	Y	Y	Y	Y	Y	M	Y	Y	Y	Y	Y	Y	Y
2014	Zuninga et al. ²⁹	+	Y	Y	Y	Y	N	Y	Y	Y	Y	NS	Y	Y	P	Y
<i>Studies identified by the previous NICE review.²²</i>																
1994	Curtis et al. ⁶⁴	-	Y	M	N	NS	N	NS	Y	N	NS	N	Y	Y	Y	N
1995	Kitazawa ⁶³	+	Y	Y	Y	Y	N	Y	NS	N	N	N	Y	Y	Y	Y
1996	Kelly-Rossini et al. ⁶²	+	Y	Y	Y	NS	N	NS	Y	Y	Y	Y	Y	Y	Y	Y
1997	Jackson & Yuan ⁶¹	+	Y	Y	Y	Y	N	Y	Y	Y	N	Y	N	M	Y	Y
1999	Ito ⁵⁹	+	Y	Y	Y	Y	NS	Y	NS	NS	Y	NS	Y	Y	Y	NS
1999	Yamada et al. ⁶⁰	++	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	NS

2000	Fujiwara ⁵⁸	-	Y	Y	Y	Y	N	N	N	N	N	N	N	P	N	N
2002	Houston et al. ⁵⁷	+	Y	Y	Y	Y	Y	NS	Y	Y	N	NS	Y	M	Y	NS
2003	Chemtob et al. ⁵⁶	-	Y	Y	N	N	N	N	N	N	N	N	N	N	N	N
2004	Joseph et al. ⁵⁴	+	Y	Y	Y	Y	NS	N	Y	Y	Y	Y	Y	Y	Y	Y
2004	Swigart & Kolb ⁵⁵	+	Y	Y	Y	Y	N	Y	Y	Y	NS	Y	Y	Y	Y	N
2005	Gibson et al. ⁵¹	++	Y	Y	Y	Y	Y	Y	Y	Y	NS	Y	Y	Y	Y	Y
2005	Moro et al. ⁵²	++	Y	Y	Y	Y	NS	Y	Y	Y	Y	Y	Y	Y	Y	NS
2005	Van der Oest et al. ⁵³	-	Y	Y	Y	Y	N	N	NS	N	Y	N	N	Y	Y	N
2006	Brewin et al. ⁴⁸	+	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y
2006	Johnson ⁴⁹	-	Y	N	N	N	N	Y	Y	N	N	N	N	Y	Y	NS
2006	Nnoaham et al. ⁵⁰	++	Y	Y	Y	Y	NS	NS	NS	Y	Y	NS	Y	Y	Y	Y
2007	Brent Refugee Forum ⁴⁶	++	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
2007	Marais ⁴⁷	++	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y
2008	Belling et al. ⁴²	++	Y	Y	Y	Y	NS	Y	Y	NS	M	Y	Y	Y	Y	Y
2008	Craig et al. ⁴³	-	Y	Y	N	NS	N	N	Y	N	N	N	N	Y	Y	Y
2008	West et al. ⁴⁵	+	Y	Y	Y	NS	N	Y	Y	Y	N	Y	Y	M	N	N
2008	Whoolery ⁴⁴	++	Y	Y	Y	Y	Y	Y	Y	Y	Y	NS	NS	Y	Y	Y
2010	Gerrish et al. ⁴⁰	++	Y	Y	Y	Y	Y	Y	Y	Y	Y	NS	Y	Y	Y	Y
2010	Sagbakken et al. ⁴¹	+	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 review²²)

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 ⁴⁶	2 ^{45,63}	3 ^{15,48,51}	2 ^{40,41}	2 ^{49,58}		
<i>Food-related</i>	9	1 ²⁸	2 ^{45,63}	2 ^{15,48}	2 ^{41,49}	1 ⁴⁹	1 ³⁶	
<i>Heredity</i>	9	1 ⁴⁹	1 ⁴⁹	2 ^{51,53}	4 ^{31,34,40,50}		1 ³⁶	
<i>Other illnesses</i>	8	1 ²⁸ (HIV)	1 ⁴⁵ (AIDS)		3 flu&pneumonia ³⁴ asthma ⁴⁰ pneumonia ⁴⁸	1 ⁴⁹ (low immunity)	1 ³⁶ (flu, pneumonia)	1 ³⁸ (HIV)
<i>Environment (typically "dirty" or weather)</i>	8	1 ⁴⁶	1 ⁴⁵	1 ⁵¹	2 ^{40,49}	3 ^{49,58,60}		
<i>Poverty</i>	8	1 ²⁸	1 ⁴⁵	1 ⁴⁸	2 ^{34,40,41}	1 ⁵⁷	1 ³⁶	
<i>Lack of self-care, health imbalance</i>	7	1 ⁴⁶	1 ⁴⁵	2 ^{48,51}	2 ^{40,41}	1 ⁶⁰		
<i>Sharing (e.g., cigarettes, cutlery)</i>	6	1 ⁴⁹	2 ^{45,63}	1 ⁴⁸	1 ^{34,50}			
<i>Sexual contact / Saliva</i>	4	1 ⁴⁹		2 ^{15,48}			1 ³⁶	
<i>Stress</i>	4				1 ^{34,40}	1 ⁵⁷	1 ³⁶	
<i>God</i>	3	1 ²⁸			2 ^{15,34}			
<i>Lifestyle factors</i>	2	1 ²⁸		1 ¹⁵	1 ³⁴			
<i>Blood (type)</i>	2			1 ¹⁵			1 ³⁶	
<i>Touch</i>	2			1 ¹⁵			1 ³⁶	
<i>Geographical localisation</i>	2			1 ¹⁵ (not in USA)				1 ²⁹ (proximity Mexico)
<i>Airborne</i>	1				1 ³⁴			
<i>Vectors (rats)</i>	1						1 ³⁶	

Table 4. Quotes per theme

Perceived susceptibility	<p>"It starts with flu and then gets worse and becomes a chest infection. If the infection is not treated, it will change to TB."³⁴ "TB is acquired from bad food, nervousness and worries. Yes it is; when you worry too much then disease appears."³⁶ "There is inherited TB, it will stay with you forever, your grandfather had it, then your father, then you."³⁴ "There's a lot of people that come over from Mexico, here in the border towns, and that's probably what makes us susceptible to tuberculosis . . . We're so close to the border. We come into contact with people from Mexico every day."²⁹ "(TB is a) curse or punishment by God for dishonest conducts."⁴⁵ "...there are two kinds of TB: psychological TB and physical TB. Psychological TB is due to too much work, too much worry and stress, which causes TB. Psychological TB does not have microbes ... For psychological TB, we need a cure for the mind. For physical TB, we need medicines [antibiotics] and good food"⁵⁷ "We used the same utensils, shared the same toilet, bathroom, cups and glasses. And we weren't using disinfectants."⁵⁰ "I thought... he passed it on to me through sex, like HIV."⁵⁰</p>		
	<p>"Somali people think that anyone who has TB is infectious until he dies."³⁴ "TB is dangerous but curable. You take antibiotics, doctor tells you what to do, and then you can be cured. It is easier nowadays than it was before."³⁶ "It's a killer disease"¹⁵ "I didn't have a clue.... sweating at night I put down to alcohol, the coughing down to smoking and um feeling unwell, down to withdrawal from um, the heroin."²⁸ "You get isolated, people they look at you like you are going to die you cannot getting treated. It is a lack of knowledge obviously that it can get cured."⁴⁷</p>		
Perceived barriers	Difficulties with access	<p>"I need accommodation and an address first before I register with a GP."⁴⁶ "It's that once you get to the [shelter], you have to stay there, because if you don't stay there and stand in line, you're not going to get in. And food_s the same way. You have to go stand in line for a couple hours, just so you can get something to eat. So you have to budget your time."⁶³</p>	
	Signs, symptoms and adverse effects of medication	<p>"I felt that that wasn't a very good treatment for me because I felt that it started affecting parts of my body. I felt nauseous . . . I started feeling the fatigue. My finger started to feel really stiff. The bone ache, the tiredness . . . I blame the pill treatment. It was all happening because of that because I was fine when I was released [from the hospital]. After that treatment I started feeling all those symptoms."²⁹</p>	
	Stress, depression	<p>"I was treated again for 9 months. I still got one more month to go. . . . And I feel good. The only problem is that sometimes you feel bad . . . when you first get it. . . the family have to go through all this . . . and it's bad, it's real bad . . . Because at that time, my daughter was living with me, two grandsons and my wife and. . . I used to feel real bad because of me they were going through that."²⁹ "Some doctor told me I have TB ... nightmare ... months I am sad, I am cry not in the eye my heart cry [sic]."⁴⁴</p>	
	Loss of privacy/lack of confidentiality	<p>"They call and say 'where are you living, we can't find you?' They move around on the block, going to the wrong floors, looking at all the doors..."³⁵</p>	
	Threat of hospitalization/paternalistic DOT	<p>"People feel that this is not their country and then it is hard to protest. This [DOT] only applies for people coming from the third world."³⁵ "You feel... you feel a bit strange... first of all because people... they are different. And I felt that I... I am a grown-up and you take responsibility, right? At home, with children and family and everything... But... you feel like someone who is a suspect."³⁵</p>	
	Inadequate service provision	<p>"Every day there is a new person [...] They keep ringing on the neighbour's door... they open and then, 'Here you are, your tablets, goodbye.' [The neighbour says] 'I don't expect any tablets' [...] Ah; it's... such a shame."³⁵ "I was coughing lots at night, could not sleep. I went to GP and for 6 months prescribing antibiotics but did not work. After more than 6 months GP sent me to hospital and in examination they said TB."⁴⁷ "I had chest pain . . . I was brought to the emergency . . . the doctor examined me and gave me a painkiller. As I was about to leave, I coughed and, it was all blood."⁵⁰</p>	
	Economic struggles	<p>"I was very ill. It is everything to get back to normal life, to feel fit and strong. It took three years to get back to normal, to find a job."³¹ "Well, London is hard. Even when I'm at work it's still hard. And now I've been off work with TB it is difficult because like, this month, all my sick pay that they paid me is going to go towards my rent. So this will be a difficult month for me, I must say, it's going to be so difficult."⁴⁷</p>	
	Stigma	Face masks	<p>"I didn't like it but I had to wear it . . . I felt like I couldn't breathe. I felt that everybody looked at me sort of saying, oh, she's infected, she's going to infect me. That's why I tried not to go out."²⁹ "I'm scared... It makes me feel miserable. Makes me feel as if I'm being punished for something that I've done, I don't know what I've done ... To start with I didn't really know much about it (TB)... when they started putting masks and that on your face, I never thought I would survive that."⁴⁴</p>
		Self-stigma / non-disclosure	<p>"People are only human. When they feel they are going to be treated like this, they will hide the disease. If they experience stigma, it might affect them mentally. If you're isolated and everyone keeps a distance from you because you have TB, then you get depressed."³⁴</p>

		<p>“You have to understand—in our culture (Somali), TB is a very sensitive issue [...]. They do not want to tell people that they have it or they might have had it at one point in their life. They like to be quiet about it.”¹⁵</p> <p>“I will never tell them. I haven’t told my brothers. I told them I didn’t want them to come and visit me. My sister’s son used to come here and stay in a room back there, . . . but I told him I didn’t want him to stay here any longer. My sons . . . were disappointed because I told him not to come, but I would never tell them the disease I had.”²⁹</p>
	Lack of knowledge	<p>“The media portray us as last class, bad people that we have nothing to offer, because this is all they can reflect to the community, which is false because they don’t get to know us. The themes that are emphasized are that we carry all kinds of diseases and we come here to take away people’s job.”³⁸</p>
	Consequences	<p>“[I]t can be treated, . . . but if you don’t treat it in time, it is pretty contagious. I guess people are kind of right to be cautious . . . If I was in there, I wouldn’t wanna go near somebody I know who has something that might kill me . . . No.”²⁹</p> <p>“Even when he’s had treatment for TB, when he coughs they think he has TB again. They’re fearful, they’ll keep away.”³⁴</p> <p>“When I said I had TB he was shocked, he stopped eating with us.”³⁴</p> <p>“My nephew, who used to come and see me, when he heard that I had TB, started staying away. He thought that if he came close to me, he will contract it and will start dying.”⁵⁰</p> <p>“Your family member don’t come around because they feel you are dirty, and they are afraid that they will be infected by you. They don’t want to talk to you.”⁶⁰</p>
Perceived benefits	Nurse support	<p>“Coming here was such a relief . . . I could let it all out, and they (the nurses) would listen. It was so good. They would never look down on me, but were always so kind, so polite. Coming here really gave me strength to continue the treatment. You know, many people just give up (the treatment). But they made me feel I could do it . . .”³²</p>
	Family and friend support	<p>“In the treatment for tuberculosis, . . . they did make a difference. Not my friends, but my family present here . . . And they have been a really good support because they have helped me to do my best, take my pills, finish the treatment because otherwise, you know, you relapse and it will be harder.”²⁹</p> <p>I read the Bible. My husband comes and visits and that helps.⁶²</p>
	Hospitalization and care	<p>“I had the money to score my heroin to be able to keep me, in, the A & E Department until I was to be admitted and to get my methadone. You see that was my main concern. I didn’t want to be in a situation where, I’d maybe be in there mayb’, I dunno, maybe ten or twelve hours and start withdrawing, not have any heroin and not have any money to score it. Which would then mean I wasted twelve hours.”²⁸</p>
Cues to action	<p>“We Roma do not go to see a doctor while we can work; only when we lay in bed do we ask for doctor’s help.”³⁶</p> <p>“Anyway this w’ when was it Tuesday night and I just. I had the money to score my heroin to be able to keep me, in, the A & E Department until I was to be admitted and to get my methadone. You see that was my main concern. I didn’t want to be in a situation where, I’d maybe be in there mayb’, I dunno, maybe ten or twelve hours and start withdrawing, not have any heroin and not have any money to score it. Which would then mean I wasted twelve hours.”²⁸</p> <p>“My sister had it [TB] one time. She died from it. She used to smoke, then she had a half a lung . . . and she got TB and she died. I thought I better be checked.”⁵⁵</p> <p>“Um, I figured that since I was passing through, and you know, that I would want to see, that I really didn’t pick up nothing from being here.”⁵⁵</p>	
Service providers	<p>“It can be hard to diagnose TB. Patients can present with vague symptoms, it may be difficult for them to explain what’s wrong and it’s harder when there are communication difficulties and different cultural perspectives.”³¹</p> <p>“But above all, we should have more collaboration across, I think. Regardless of how it is solved, because we don’t know . . . I have no idea who has tuberculosis there [at the HIV clinic]. I don’t know how they manage [tuberculosis]. And that’s not good.”³³</p> <p>“I think that there are too many people involved in the management of tuberculosis cases.”⁵²</p> <p>“If you see one case of TB every 3 years, does it make a lot of sense for you to invest a huge amount of energy into knowing about this disorder?”⁶¹</p> <p>“Some ethnic minorities are particularly difficult to communicate with: we need cultural mediators.”⁵²</p> <p>“You can’t always know everything. You might be used to dealing with Somalians and then get a group of Rwandans, whose health needs are different. I feel fairly comfortable with the Muslims who say, it’s Ramadan, I can’t take my tablets. I know exactly what to say and I can point to the passage in the Koran where it says it’s OK to take tablets if you’re ill. But somebody from Vietnam, I know nothing about their health beliefs. And you can’t just send people on courses to find out because you just don’t know what you’re going to get. I’ve got a middle class mother who won’t bring her child in because she doesn’t believe in anything. And she’s white, middle class. She lives in my suburb and her health beliefs are not available to me.”⁴²</p> <p>“I am sure there [are lots] of TB cases in Canada just treating themselves with Tylenol and cold medicine.”⁶¹</p>	

List of Abbreviations

A&E = Accident & Emergency; DOT = Directly Observed Therapy; HIV = Human Immunodeficiency Virus; TB = Tuberculosis

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 travelers (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