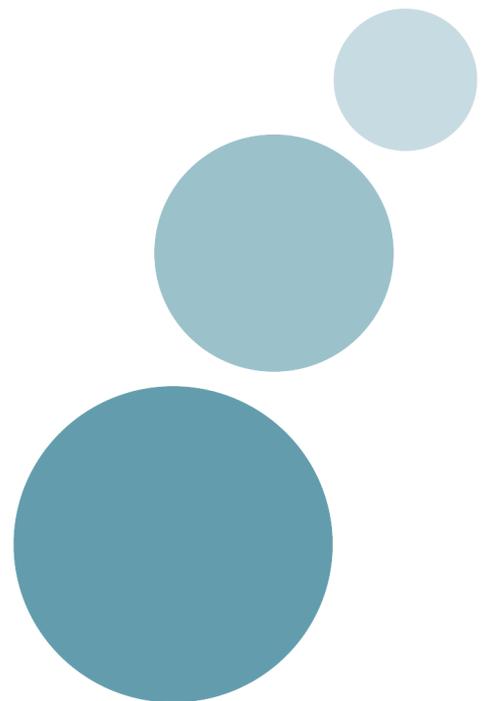# matrix
evidence

National Institute for Health and
Clinical Excellence (NICE)

Evidence review on the
effectiveness and cost-
effectiveness of service models
or structures to manage
tuberculosis in hard-to-reach
groups

July 2011

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Confidentiality

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Declaration of authors' competing interests

No authors have competing interests.

Contents

1.0   Executive summary

1.1   Introduction

This evidence review is the fourth of four commissioned by NICE to inform the guideline on the identification and management of tuberculosis (TB) in hard-to-reach groups. The review examines the effectiveness and cost-effectiveness of service structures aimed at identifying and/or managing TB in hard-to-reach groups. For the purpose of this review, the service structures explored were the type of healthcare worker (any person who was used to deliver the intervention) and setting used to identify and manage TB in hard-to-reach groups. Previous reviews in this series have focused on interventions to identify and/or manage TB that used individual elements of a service model, such as case management, so this review will focus on the comparative effects of alternative service provision used to deliver care and support for hard-to-reach groups at risk of, or being treated for, TB infection. In particular, this review will focus on who delivers interventions to identify and manage TB in hard-to-reach groups and the setting used to deliver these interventions.

We identified only a small number of comparative studies for this review on service structures (N=8) that could illustrate how services should be structured to deliver services to manage people with TB in hard-to-reach groups. We therefore also summarised the non-comparative descriptions of the type of healthcare worker and setting reported in the literature included in the previous two quantitative reviews conducted for NICE on the identification and management of tuberculosis (TB) in hard-to-reach groups.

1.2   Methods

To locate evidence, a range of databases and websites indexing relevant literature were searched. Study reports were included if they:

1. had a focus on TB services of any kind; and
2. were published in 1990 or later; and
3. were written in English; and
4. were conducted in an OECD country; and
5. included data from any hard-to-reach group; and
6. presented quantitative empirical data; and
7. discussed an intervention relating to one of the following: identifying TB cases; managing TB cases; design of service models; and
8. was an effectiveness or cost-effectiveness study; or
9. any other type of quantitative primary research; or
10. a systematic review.

A total of eight studies were identified for this review, seven of which were also included in the previous quantitative reviews on the identification and management of tuberculosis (TB) in hard-to-reach groups.

1.3   Findings

> **Evidence statement 1: The effectiveness of active case finding by healthcare worker in hard-to-reach groups.**
>
> ES1.0 **Moderate evidence** from one RCT (Ricks, 2008 [++]) suggests that peers who were former drug users were more likely to encourage identification of contacts by **drug users** with active TB (40/53, 75%) than were healthcare workers (23/49, 47%; p=0.03). The findings were limited because the peer-led intervention also used enhanced case management compared to the control group that only used limited case management. Therefore, it was unclear whether the positive outcomes in contact identification were due to the healthcare worker leading the identification process or due to the intensity of case management approach.
>
> *Applicability*
> One study was identified that compared the type of healthcare worker delivering contact tracing in the USA in drug users. It is not known how the effectiveness of different healthcare workers conducting contact tracing translate to a UK setting and in other hard-to-reach groups.

> **Evidence statement 2: The effectiveness of active case finding by setting in hard-to-reach groups.**
>
> **ES2.0 Weak evidence from one** before-and-after study (Mor et al., 2008 [-]) found that screening in a pre-immigration setting may reduce the risk of developing TB in **new entrants** from Ethiopia to Israel compared with post-immigration screening, with a shortened detection period from entry into Israel and TB diagnosis (OR=0.72, 95% CI 0.59 to 0.89; p=0.002). The findings were limited because the study did not address the potential differences in TB incidence in the two time periods in which screening occurred.
>
> **ES2.1 Weak evidence from one** prospective cohort study (El-Hamad et al., 2001 [+]) found that **new entrants** may be more likely to complete screening if active case finding was conducted in a specialist TB clinic compared with a non-specialist primary care facility (OR=2.57; 95% CI 1.92 to 3.42). However, there were statistically significant differences between the groups at baseline that were not adjusted for in the analysis.
>
> **ES2.2 Weak evidence from one** cost-comparison study (Bothamley et al., 2002 [-]) found that use of the symptom questionnaire was lowest at the POA clinic (15.8%, 199/1,262) for **new entrants**, compared with a **homeless** centre (98.1%, 262/267); the coverage of the symptom questionnaire among **new entrants** registered for the first

time in a GP setting was not known. For those screened with a symptom questionnaire, the coverage of TST screening was 100% (267/267) in the homeless centre, 90.9% (181/199) in the POA clinic and 86.6% (39/45) in the GP setting. The yield of active TB was three cases in the POA clinic, while no cases of active TB were identified in the other two settings. The study findings were limited because the study compared two different populations in addition to two different settings.

ES2.3 Weak evidence from one study (Miller et al. 2006 [+]) found that there was no statistically significant difference in the coverage of TST screening in the **homeless** centre (94.7%, 778/822) compared with a **prison** setting (95%, 21,778/22,920; p=0.179), however, there was a significantly higher yield of positive TST results in the homeless setting (15.5%, 127/819) compared with the prison setting (2%, 303/15,150; p<0.001). There were also statistically more people prescribed treatment for LTBI or active TB in the homeless setting (LTBI treatment = 22%, 181/822; active TB treatment = 1.2%, 10/833) compared with the prison setting (LTBI treatment = 0.9%, 211/23,444; active TB treatment = 0.03% 7/2,333; p<0.001). The study findings were limited because it was difficult to determine whether the differences in outcome were due to the different settings evaluated or due to the different populations' targeted in each setting including differences in the prevalence of TB.

Applicability
All four studies were conducted in different counties (UK, Italy, USA and Israel) with only one conducted in the UK. In addition, various settings were compared in different populations including prisoners, immigrants/new entrants and the homeless, limiting the applicability of the findings to other hard-to-reach groups such as drug users.

Evidence statement 3: The cost-effectiveness of active case-finding by setting in hard-to-reach groups.

ES3.0 Weak evidence from one study (Mor et al., 2008 [-]) found that screening in a pre-immigration setting would result in net direct savings of $449,817 in a five year time horizon (assuming that 98 more individuals would be free of TB screening in this setting) compared with screening in a post-immigration setting among Ethiopian **immigrants**. No further cost outcomes were reported. The study had several limitations including that the costs of resources used in this analysis came from different sources, with the costs of post-immigration screening more reliable than the costs of pre-immigration screening.

ES3.1 Weak evidence from one study (Miller et al., 2006 [+]) suggests that the cost per active TB case prevented by identifying and treating each person with LTBI was lower in a **homeless** setting ($14,350) compared with a **prison** setting ($34,761). The study findings were limited because the study compared two different populations in two different settings.

ES3.2 Weak evidence from one study (Bothamley et al. (2002 [-]) found that the total costs of screening in three different settings was £22,646 for 199 people screened in a

clinic as part of the POA scheme among **new entrants**, £3,452 for 262 people screened in **homeless** centres, and £938 for 45 people screened in general practice for new patient registrations who were **new entrants**. However, as the POA yielded more cases of active TB (N=3), this resulted in £12.70 cost-savings per person screened in the POA clinic, compared with an additional cost of £0.50 per person screened in the homeless centres and £7.00 per person screened in general practice. The study was limited because in addition to comparing different settings, it also compared different populations which may have different prevalence of active TB.

Applicability
Three studies were identified that were conducted in the UK, Israel and the USA in the homeless, new entrants and prisoners. Although one study was conducted in the UK, it is not known how the evidence found in the other studies on effective service components relates to the UK context. It is also not known how these findings apply to other hard-to-reach groups such as drug users.

Evidence statement 4: **The effectiveness of managing LTBI by setting in hard-to-reach groups.**

ES4.0 Moderate evidence from one RCT (Malotte et al., 2001 [++]) found that treatment completion for managing LTBI among **drug users** was 52.8% (28/53) when it was conducted in an outreach setting at a site convenient for the participant compared with 60% (33/55) when it was conducted onsite in a drug services facility. These differences were not statistically compared, limiting the study findings, but suggest that there was no added benefit in adherence to treatment when it was delivered in an outreach setting.

ES4.1 Moderate evidence from one RCT (Umbricht-Schneiter et al., 1994 [+]) found that the proportion of **intravenous drug users** who enrolled and complied with medical treatment (including treatment for TB) was 92% (23/25) for those treated onsite at a methadone clinic compared with 32% (9/26) for those treated offsite at a medical centre (p<0.001). The proportion of drug users with positive PPT tests who received a chest X-ray was 75% (6/8) for those who received medical treatment onsite compared with 24.4% (3/14) for those treated offsite. The number of patients with positive PPD tests who received chemoprophylaxis was 12.5% (1/8) for people treated onsite compared with 7.1% (1/14) for those treated offsite. Statistical significance was not calculated for either of these differences.

Applicability
Two studies were identified, both conducted in the USA in drug users. The applicability of the findings to the UK context and to other hard-to-reach groups is not known.

Evidence statement 5: The effectiveness of managing active TB by healthcare workers in hard-to-reach groups.

ES5.0 Moderate evidence from one RCT (Ricks, 2008 [++]) found that the probability of completing treatment was statistically greater when peers delivered enhanced case management to **drug users** compared with limited case management delivered by a healthcare worker (RR=2.68, 95% CI 1.24 to 5.82; p=0.01). The conclusions drawn

from these findings were limited because the peer-led intervention also had enhanced case management. It is therefore not known how much of the positive treatment outcomes were due to the healthcare worker who delivered the service or the intensity of case management.

Applicability
The study was conducted in the USA in drug users; it is not known how these findings translate to a UK setting or for other hard-to-reach groups.

Evidence statement 6: The effectiveness of managing active TB by setting in hard-to-reach groups.

ES6.0 Weak evidence from one retrospective cohort study found that there was statistically no significant difference in the management of active TB if it occurred onsite at a healthcare service or in the community at a site convenient for people with active TB, in **mixed hard-to-reach groups** (Deruaz & Zellweger, 2004 [-]).The conclusions that can be drawn from this study were limited because there were systematic differences between groups in how treatment outcomes were collected as well as potential selection bias between groups.

Applicability
One study was identified and was conducted in Switzerland in mixed hard-to-reach groups. It is not known how these findings translate to the UK context and to specific hard-to-reach groups.

1.4   Discussion

There was moderate evidence from one RCT (Ricks, 2008 [++]) that peers who were former drug users were more likely to encourage the identification of contacts by drug users with active TB and could promote greater adherence to treatment compared with 'standard' healthcare workers. There was also some support from moderate and weak evidence that more specialist settings might be associated with better outcomes, such as drug users being managed in drug clinics and/or alongside methadone treatment; homeless people managed in centres for the homeless; and immigrants managed at TB clinics (compared with more general medical settings such as GP surgeries).

1.4.1   Evidence gaps

There was a limited number of comparative studies that explored the effectiveness and cost-effectiveness of different service structures to manage TB in hard-to-reach groups, and only one of these was conducted in the UK. No studies reported on the type of person responsible for commissioning TB services, or on the theoretical or conceptual models that underpin service design.

The studies identified in the review compared different service structures in different hard-to-reach groups, therefore, the results could not be synthesised across studies.

The majority of studies included in the review were also of poor quality. There were no strong evidence statements supported by the review and only three evidence statements were of moderate quality, all of which were in drug users, limiting the applicability of the review to other hard-to-reach groups.

1.4.2 Conclusions

There were a limited number of studies, all of which had multiple variables involving different hard-to-reach groups and different comparisons, which did not allow for a synthesis across studies. In addition, the majority of the evidence was weak. The results of the individual studies with moderate evidence suggest that it is effective to use peers compared with health professionals to encourage patients to identify contacts and to manage active TB among drug users; and to treat intravenous drug users for co-morbid medical problems (including TB) in a methadone clinic or other drug services facility. However, more research is needed in the UK on the effectiveness and cost-effectiveness of different service structures to manage TB in hard-to-reach groups.

2.0   Aims and background

2.1   Objectives

The National Institute for Health and Clinical Excellence (NICE) has been asked by the Department of Health (DH) to develop public health programme guidance aimed at identifying and managing tuberculosis (TB) among hard-to-reach groups. The guidance will provide recommendations for agencies in the health sector, local authorities and other public, private or third-sector bodies, particularly those working with hard-to-reach groups.

This report is the fourth of four systematic reviews that have been undertaken to inform the guidance. It examines the effectiveness and cost-effectiveness of service structures aimed at identifying and/or managing TB cases in hard-to-reach groups. For the purpose of this review, the service structures explored were the type of healthcare worker and setting used to identify and manage TB in hard-to-reach groups. Other aspects of service delivery, such as case management, have been covered in previous reviews, and we identified no studies that assessed the effects of other ways of delivering care to hard-to-reach groups at risk of, or being treated for, TB infection. This report systematically reviews and synthesises relevant research to inform this topic by providing the results on the effectiveness and cost-effectiveness of different healthcare workers and settings to manage TB in hard-to-reach groups. The healthcare worker and setting was the primary focus of this review due to the overlap of studies in the other quantitative reviews, in particular, management interventions that used elements of a service model such as case management, which have already been covered in the third review on effective interventions to manage TB in hard-to-reach groups.

We found very few comparative studies (N=8) that reported on the service structures for hard-to-reach groups with TB. To maximise the ability of the evidence reported in previous reviews to explain the structures needed to deliver services to manage people with TB in hard-to-reach groups, this report also summarises the non-comparative data on the type of professional and setting found in all the studies included in the previous two quantitative reviews conducted in this series for NICE. The output of this summary is a map of the evidence that illustrates the healthcare worker and type of setting found in the literature to identify and manage TB in different hard-to-reach groups.

2.2   Rationale

In 2009 in the UK, a total of 9,040 cases of tuberculosis were reported resulting in a rate of 14.6 cases per 100,000 population (95% confidence interval (CI) 14.3 to 14.9; Health Protection Agency, 2010). Compared with 2008, this was a 9% increase in the number of cases and a 4.2% increase in the rate of TB (Health Protection Agency,

2010). In certain geographic areas of the UK the incidence may be much higher, up to 40 per 100,000 (Department of Health, 2007). Certain populations are at particularly high risk, since TB infection is strongly associated with social risk factors including homelessness, imprisonment, drug use, and immigration (Story et al., 2007). Social risk factors can complicate the treatment of TB including extended treatment, missed appointments and referral requirements to other agencies (Craig et al., 2007). Although overall rates of TB in high-income countries have steadily fallen, prevalence remains high among these typically hard-to-reach groups (Fujiwara, 2000). The association of TB with poverty is well documented (Lönnroth et al., 2009), and individuals with social risk factors for TB that are linked to poverty, such as homelessness and drug abuse, are typically unwilling or unable to seek and comply with medical care, and are therefore hard to reach. These high-risk groups are, therefore, not only much more likely to contract TB, but are also more likely to be diagnosed at a late stage of the disease, and less likely to adhere to treatment, which typically lasts for six months or more (Health Protection Agency, 2009). This reduces the efficacy of antituberculosis therapy, and contributes to the development of drug-resistant forms of the disease, which are much more difficult and costly to treat.

The central challenge to the control and surveillance of TB is therefore identifying and targeting these hard-to-reach, high-risk groups. Individuals or groups who face barriers to accessing health services may benefit from targeted screening to promote early diagnosis of TB (Health Protection Agency, 2007). Ensuring compliance with treatment is also a key aspect of TB control. The Health Protection Agency has found that only 79% of people with TB in the UK complete treatment, below the World Health Organization target of 85% (Health Protection Agency, 2009). Currently 6.8% of cases in the UK are resistant to at least one first-line drug, and 1.1% have multi-drug resistant infection (Health Protection Agency, 2009).

While the highest proportion of cases of TB occur in foreign-born patients (75% of people with TB in London were born abroad [Health Protection Agency, 2009]), evidence from a large outbreak of drug-resistant tuberculosis points to ongoing active transmission among marginalised groups (Antoine et al., 2006). Studies of the spread of TB in prisons have concluded that improving prison conditions is a priority for any effective programme to control TB and reduce its spread back into the hard-to-reach communities from which prisoners are disproportionately derived (Levy et al., 2000). There is also evidence of substantial transmission within UK-born minority ethnic populations (French et al., 2007).

The impact of TB is exacerbated when it occurs in people concurrently infected with HIV, in particular, in groups at high risk of both infections such as drug users (Rodwell et al., 2010) and immigrants (World Health Organization, 2010). Globally, TB is a leading cause of death among people with HIV, and it is estimated that one third of the 40 million people living with HIV worldwide are co-infected with TB (World Health Organization, 2010). In the UK, Ahmed et al.'s (2007) study found that 5.7% of people with TB were infected with HIV, with a substantial year-on-year increase over the

period of their study (from 3.1% in 1999 to 8.3% in 2003). A further serious problem is the stigma connected with HIV and AIDS, which also leads to delayed treatment-seeking and poor adherence to treatment (Grange et al., 2001). Programmes that aim to increase the identification and management of TB must, therefore, address hard-to-reach groups at risk of HIV, such as intravenous drug users (IDUs), prisoners, and sex workers.

In recent years, the emphasis has moved away from a traditional top-down model of TB control to community- and patient-centred health services, which are based on analysis of local factors affecting case-finding and adherence to treatment (Grange et al., 2001), and from a reactive model to one emphasising proactive approaches to locating and treating cases and managing TB. For example, the Department of Health established the Find and Treat service which supports the detection, diagnosis and treatment of TB in hard-to-reach groups in London using mobile digital X-ray machines, advice and support services and follow-up care (Health Protection Agency, 2007).

2.3 Research questions

The primary research question for this review was:

- Which service models and service structures are most effective and cost-effective at supporting TB identification and management of hard-to-reach groups?

The evidence identified for this review focused on service structures, which were defined as the type of healthcare worker and setting used to identify and manage TB in hard-to-reach groups. We identified no study for this review that specifically explored the effectiveness of different service models of care to identify or manage hard-to-reach groups with TB. However, the third review on the management of TB in hard-to-reach groups explored the evidence for individual interventions that are components within a larger service model approach including, for example, case management.

Secondary research questions were:

- Who is responsible for the commissioning and delivery of TB services?
- What (if any) theories or conceptual models underpin the service models/organisational structures?
- What specific individuals or populations are targeted by the interventions?
- How does engagement in various service models/organisational structures differ by group/subgroup (in terms of hard-to-reach group, age, or gender)?

3.0 Methods

The review was conducted in accordance with the methodology laid out in the second edition of *Methods for the development of NICE public health guidance* (NICE, 2009).

In addition to the usual procedures outlined in the public health guidance, this review conducted one large search across the three quantitative reviews on identification, management and service models to control TB in hard-to-reach groups. This review also combined the evidence tables for quantitative and economic evaluation studies (Appendix C).

3.1   Searching

The following databases were searched for this review and for the other two quantitative reviews from 1990 to October 2010:

- Assia
- British Nursing Index
- CRD (DARE, HTA, NHS EED)
- CINAHL
- Cochrane Library (for systematic reviews)
- Current Contents
- ECONLIT
- EMBASE
- ERIC
- HMIC
- Medline
- Medline In-Process
- PsycINFO
- SPP
- Soc Abs
- Social Services Abstracts
- Web of Science

The full search strategy and the results of the searches can be found in Appendix A. The search strategy was written to locate references relevant across the three quantitative effectiveness reviews.

The following websites and databases were searched manually for relevant literature:

- Action - Advocacy to Control TB Internationally
- British Infection Association
- Centers for Disease Control and Prevention (resources on TB)
- Centers for Disease Control TB-Related News and Journal Items Weekly Update mailing list archives
- Centers for Disease Control National Prevention Information Network
- NICE, including former Health Development Agency
- NHS Evidence
- Stop TB Partnership
- TB Alert

- UK Coalition to Stop TB
- World Health Organization
- WHO Global Health Atlas
- Health Protection Agency
- British Thoracic Society
- Public Health Observatories
- BL Direct
- Community Abstracts via Oxmill
- Google Scholar
- National Research Register archive site
- UK Clinical Research Network

To supplement the database and website searches, the review also identified additional potential relevant records using the following methods:

- scanning of citation lists of included studies obtained through database searching;
- 'forward' citation chasing of included studies using ISI Web of Knowledge, locating studies which cited them;
- scanning lists of included studies from all systematic reviews which met the inclusion criteria at the full text screening stage; and
- a call for evidence from all stakeholders, organised by NICE.

3.2   Screening

All records identified by the searches were uploaded into a database and duplicate records were removed. Inclusion criteria were developed (see below) to identify relevant studies for the three reviews. Initially, the records were screened on title and abstract. Where no abstract was available, a web search was first undertaken to locate one; if no abstract could be found, records were screened on title alone. A round of pilot screening was conducted on a random sample of ten abstracts to test and refine the inclusion criteria. Once the inclusion criteria were agreed upon, records were screened by four reviewers independently using the abstract inclusion checklist in Appendix B. Double screening was conducted on 10% of the records; any differences were resolved by discussion and, if necessary, with the input of a third reviewer. Agreement before reconciliation for the abstract screening was 96.48% (N=2,165) and inter-rater reliability (Cohen's kappa) was κ=0.535 (95% CI 0.432 to 0.637).[1]

The inclusion criteria across the three quantitative reviews were the following:
- the study has a focus on TB services of any kind, and

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[1]It has been argued that Cohen's kappa or similar measures may under-rate reliability where scores are highly asymmetrical, i.e. numbers for one code (e.g. exclude) are much higher than for the other(s) (e.g. include) (Feinstein and Cicchetti,1990). This is the case here, because inclusion rates were fairly low and, hence, there were many more studies excluded than included. For this reason, the kappa score is slightly lower than standard guidance would indicate is acceptable, even though rates of agreement were high.

- was published in 1990 or later, and
- is written in English, and
- was conducted in an OECD country, and
- includes data from any hard-to-reach group, and
- presents quantitative empirical data, and
- discusses an intervention relating to one of the following: identifying TB cases; managing TB cases; design of service models, and
- is a (cost)-effectiveness study, or
- any other type of quantitative primary research, or
- a systematic review.

For this review, we focused on studies that discussed service structures or models.

The review also included studies where 50% or more of the participants had characteristics that met the review's definition of hard to reach.

3.3   Quality assessment

All included studies were quality-assessed using the tools in Appendix F (effectiveness studies) and Appendix I (cost-effectiveness) of the *Methods for the development of NICE public health guidance* (NICE, 2009). On the basis of the answers to the questions within these tools, and in line with the NICE guidance manual, each study was given an overall quality rating: [++] for high quality; [+] for medium quality; or [-] for low quality. The tool was completed independently by two reviewers for a randomly selected sample of 10% of records relevant to the management review (n=2). For the other records, the tool was completed by one reviewer and checked by another, with any disagreements resolved by discussion. The results of the quality assessment are presented in section 4.3 below; two examples of completed quality assessment forms are presented in Appendix E.

3.4   Data extraction

Data were extracted from included studies using combined (cost)-effectiveness evidence tables (see Appendix K, NICE, 2009). The tool was completed independently by two reviewers for a randomly selected sample of 10% of records. Three of the eight included studies were independently data extracted for the previous reviews on identification and/or management. For the other records, the tool was completed by one reviewer and checked by another, with any disagreements resolved by discussion or reference to a third researcher. Data for each included study were extracted and are presented in the evidence tables (Appendix C).

3.5   Data synthesis and presentation

In addition to assessing the quality of the individual studies, the overall strength of the evidence statements took into account the quality, quantity, and consistency of the evidence. The evidence statements reflect the strength of the conclusions made by the

studies, the quality of the studies (as determined in the quality assessment), and any inconsistencies in the findings across studies. The summaries used are those described in NICE (2009):

- **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 that are not contradicted by other high quality or moderate quality studies; and
- **inconsistent evidence** – mixed or contradictory evidence/conclusions across studies.

4.0 Summary of included studies

4.1 Flow of literature through the review

Database searches were conducted to locate references relevant for the three reviews, and 31,469 records were found. A further 32 records were located through manual searching. Of these, 16,136 were duplicate records and were removed. The remaining 15,333 abstracts were screened for inclusion in the three reviews.

A total of 15,225 references were excluded following screening of titles and abstracts. After conversation with NICE, non-comparative studies were excluded from the reviews. Full texts of the remaining 140 references were ordered. Four references were irretrievable and 76 excluded, the remaining 60 studies were included across the three reviews.

For this review, one systematic review met the inclusion criteria and was collected for citation chasing and not included in the review. A further eight studies were also identified that met the inclusion criteria, seven of which were also reported in the previous quantitative reviews in either the identification and/or management review. Backward and forward citation-chasing from the included studies yielded no additional references, for a total of eight included references. The flow of literature across the three quantitative reviews is illustrated in Figure 1, and Section 7 has the citation details of all included studies.

Figure 1. Flow of literature

References located through database searches
N=31,469

Manual searches
N=32

Duplicates
N=16,136

Excluded on abstract
N=15,225

Non-comparative effectiveness studies
N=322

Full text retrieval across three reviews
N=140

Irretrievable
N=4

Excluded on full text
N=76

References included in identification review
N=32 *

References included in management review
N=28 *

References included in service review
N=9*

Citation chasing
N=0

Systematic Reviews
N=1

Included studies
N=8 *

* Some articles were relevant for more than one review

4.2   Summary of the included studies

There were eight included studies for this review which have been summarised below by country, population and by type of study.

By country:
- 4 USA;
- 1 UK;
- 1 Israel;
- 1 Switzerland; and
- 1 Italy.

By population (two studies compared more than one population):
- 3 drug users;
- 2 homeless persons;
- 2 undocumented migrants/new entrants
- 1 prisoners; and
- 1 mixed hard-to-reach groups (immigrants, drug and alcohol abusers, homeless, prisoners, HIV positive and people with drug-resistant disease)

By type of studies:
- 5 effectiveness studies; and
- 3 economic evaluations.

A summary of the included studies is provided in Table 1. Full study details are presented in the evidence tables (Appendix C).

Table 1. Summary of included studies

Study id	Aim	Study design	HTR group/s	Identification or management of TB	Location	Quality score
Bothamley et al. (2002)	To compare the yield and costs of TB screening in three settings: a new entrants' clinic within the port of arrival (POA) scheme; a large general practice; and centres for the homeless.	Cost analysis	New entrants; homeless	Identification; Active/LTBI	UK	-
Déruaz & Zellweger (2004)	To evaluate the effect of duration/intensity and location of DOT on clinical outcomes.	Retrospective cohort	Mixed hard-to-reach	Management; Active TB	Switzerland	-
El-Hamad et al. (2001)	To compare the completion rates of screening procedures for TB infection among undocumented migrants at specialised TB units and non-specialised health clinics.	Prospective cohort	Undocumented migrants	Identification; Active/LTBI	Italy	+
Malotte et al. (2001)	To compare the independent and combined effects of monetary incentives and outreach worker provision of DOT (for LTBI) in active drug users.	RCT	Drug users	Management; LTBI	USA	++
Miller et al. (2006)	To evaluate and compare the efficiency of a non-state-law-mandated TB screening programme for homeless persons with a state-law-mandated TB screening programme for prisoners.	Cost analysis	Homeless; prisoners	Identification; Active/LTBI	USA	+
Mor et al. (2008)	To examine the effectiveness and cost-effectiveness of screening before entry with screening at POA.	Cost-effectiveness	New entrants	Identification; Active/LTBI	Israel	-
Ricks (2008)	To compare the effectiveness of the Indigenous Leader Outreach Model (ILOM) versus standard TB control among substance users.	RCT	Drug users	Management; Active TB	USA	++
Umbricht-	To evaluate the efficacy of providing medical care at a methadone	RCT	Intravenous	Management;	USA	+

Schneiter et al. (1994)	clinic versus referral to another site.		drug users	LTBI		

HTR = hard-to-reach; LTBI = latent TB infection; POA = port of arrival; RCT = randomised controlled trial

4.3   Quality of the included studies

The results of quality assessment are presented in Tables 2 and 3.

Two studies were judged to be of high quality [++]:
- Malotte et al. (2001); and
- Ricks (2008).

Three were of medium quality [+]:
- El-Hamad et al. (2001);
- Miller et al. (2006); and
- Umbricht-Schneiter et al. (1994).

Three were of low quality [-]:
- Bothamley et al. (2002);
- Déruaz & Zellweger (2004);
- Mor et al. (2008).
  .

Table 2. Quality of the included studies (effectiveness)

First author	Population					Method of allocation to intervention/comparison									Outcomes								Analysis				Summary		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28
Deruaz (2004)	++	+	+	-	+	-	-	+	-	NR	++	+	+	-	++	++	++	++	++	-	-	NR	-	++	+	-	+	-
El-Hamad 2001	++	+	++	+	++	NA	NA	++	++	NR	++	+	+	++	++	+	++	++	++	++	NA	NR	++	+	++	+	+	+
Malotte (2001)	++	+	+	+	++	++	NA	++	++	NR	++	+	+	++	++	++	++	++	++	++	++	NR	++	++	++	++	+	++
Ricks (2008)	++	+	++	++	++	++	NA	++	++	NR	++	+	+	+	++	++	++	++	++	++	++	+	++	++	++	++	+	++
Umbricht-Schneiter (1994)	-	+	+	+	+	NR	NA	-	-	-	++	+	+	+	+	++	+	-	-	++	-	++	-	+	++	+	++	+

Key: ++ The study has been designed/conducted in such a way as to minimise the risk of bias; + Either the answer to the checklist question is not clear from the way the study is reported, or the study may not have addressed all potential sources of bias; - Significant sources of bias may persist; NR The study fails to report this particular question; NA given the study design.

Key to questions:
1. Is the source population or source area well described?
2. Is the eligible population or area representative of the source population or area?
3. Do the selected participants or areas represent the eligible population?
4. How was confounding minimised?
5. Were interventions (and comparisons) well described and appropriate?
6. Was the allocation concealed?
7. Were participants and/or investigators blind to exposure and comparison?
8. Was the exposure to the intervention and comparison adequate?
9. Was contamination acceptably low?
10. Were other interventions similar in both groups?
11. Were all participants accounted for at study conclusion?
12. Did the setting reflect usual UK practice?
13. Did the intervention or control comparison reflect usual UK practice?
14. Were the outcome measures reliable?
15. Were all outcome measurements complete?
16. Were all important outcomes assessed?
17. Were outcomes relevant?
18. Were there similar follow-up times in exposure and comparison groups?
19. Was follow-up time meaningful?
20. Were exposure and comparison groups similar at baseline? If not, were these adjusted?
21. Was Intention to Treat (ITT) analysis conducted?
22. Was the study sufficiently powered to detect an intervention effect (if one exists)?
23. Were the estimates of effect size given or calculable?
24. Were the analytical methods appropriate?
25. Was the precision of intervention effects given or calculable? Were they meaningful?
26. Are the study results internally valid? (i.e. unbiased)
27. Are the study results generalisable to the source population? (i.e. externally valid)
28. Final quality score.

Key to answers 26-27:
++ All or most of the checklist criteria have been fulfilled; where they have not been, the conclusions are very unlikely to alter
+ Some of the checklist criteria have been fulfilled, where they have not, or not adequately described, the conclusions are unlikely to alter
- Few or no checklist criteria have been fulfilled and the conclusions are likely to alter

Table 3. Quality of the included studies (economic evaluations)

First Author	Applicability (relevance to the specific topic)									Study limitations (level of methodological quality)											
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Bothamley (2002)	PA	Y	Y	N	PA	N	N	PA	D/A	PA	U/C	PA	N	N	Y	N	N	Y	PA	N	Very serious limitations [-]
Mor (2008)	PA	Y	PA	N	PA	N	N	PA	PA	PA	PA	PA	N	PA	PA	U/C	U/C	Y	N	N	Very serious limitations [-]
Miller (2006)	Y	Y	PA	N	PA	N	N	PA	PA	PA	PA	PA	PA	PA	PA	PA	PA	Y	Y	N	Potentially serious limitations [+]

Y=Y; N=no; PA=partially; U/C=unclear ; D/A=Directly Applicable

Key to questions:

1. Is the study population appropriate for the topic being evaluated?
2. Are the interventions appropriate for the topic being evaluated?
3. Is the system in which the study was conducted sufficiently similar to the UK context?
4. Were the perspectives clearly stated?
5. Are all direct health effects on individuals included, and are all other effects included where they are material?
6. Are all future costs and outcomes discounted appropriately?
7. Is the value of health effects expressed in terms of quality adjusted life years (QALYs)?
8. Are costs and outcomes from other sectors fully and appropriately measured and valued?
9. Overall judgment (no need to continue if NA).
10. Does the model structure adequately reflect the nature of the topic under evaluation?
11. Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?
12. Are all important and relevant outcomes included?
13. Are the estimates of baseline outcomes from the best available source?
14. Are the estimates of relative "treatment" effects from the best available source?
15. Are all important and relevant costs included?
16. Are the estimates of resource use from the best available source?
17. Are the unit costs of resources from the best available source?
18. Is an appropriate incremental analysis presented or can it be calculated from the data?
19. Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?
20. Is there any potential conflict of interest?
21. Overall assessment.

4.4   Applicability

There was a limited number of studies included in this review (N=8), with only one study conducted in the UK. Half the studies were conducted in the USA (4/8); the remaining studies were conducted in Italy (N=1), Israel (N=1) and Switzerland (N=1). This raises some issues regarding the applicability of findings to the UK, particularly as this review focuses on service structures which are likely to be different in each country. For example, the type of professional or setting used to identify and manage TB may differ by country.

In regards to the hard-to-reach groups included in this review, a range of populations were evaluated with more than one population compared in two studies. This resulted in three studies in drug users; two in homeless groups; two in undocumented migrants/new entrants; one in prisoners; and one in mixed hard-to-reach groups (immigrants, drug and alcohol abusers, homeless, prisoners, HIV positive and people with drug-resistant disease).

Due to the limited number of studies included in the review and the variety of service structures explored, this raises some issues on the applicability of the evidence on some service structures in different hard-to-reach groups. The applicability of the evidence to the UK context and hard-to-reach groups is discussed in more detail in the evidence statements.

5.0   Study findings

This section first provides a map of the evidence of the service structures (healthcare worker and setting) which were found in the literature from the previous two quantitative reviews conducted for NICE on the identification and management of TB among hard-to-reach groups. This contributes to the understanding of structures used to deliver services to manage TB in different hard-to-reach groups and provides a context when providing recommendations on how to identify and manage TB in hard-to-reach groups.

Following the mapping of service structures, the findings of the current review on effectiveness and cost-effectiveness of different service models are summarised. Studies included in the current review directly compared two or more components of a service structure that aimed to identify, or manage, TB in hard-to-reach groups. This furthers our understanding of the most effective way to deliver services for hard-to-reach groups with TB.

5.1   Identification

The only studies that reported details of the type of healthcare worker or setting for the service to identify people with TB were investigating active case finding. The identification review identified no studies that explored the service structures for conducting passive case finding in hard-to-reach groups. Passive case finding was defined as the process of identifying clinical cases of TB among those who present to health services because of symptoms relating to TB.

5.1.1   Active case-finding

Active case finding: is the process of identifying clinical cases of TB at the earliest possible stage in people who are not seeking medical attention for TB. For example, systematically offering chest X-rays to individuals, regardless of symptoms of TB.

Mapping of service structures from the identification review

Healthcare worker
Table 4 displays the type of healthcare workers that were used to conduct active case-finding in the quantitative review on the identification of TB in hard-to-reach groups. Only those studies that clearly reported the healthcare worker used to identify TB were included in the table. Some studies used more than one healthcare worker to identify TB in hard-to-reach groups.

Table 4: Studies from the identification review that reported on the type of healthcare worker who conducted active case finding

	Homeless	Immigrants	Drug users	Prisoners
Nurse	Citron et al. (1995[+])	Brassard et al. (2006[+])	Malotte et al. (1998[++]) Malotte et al. (1999[++])	
Health educators			Perlman et al. (2001[++])	
General chest clinic staff		Dasgupta et al. (2000[+])		Puisis et al. (1996[-])
GP or non-specialist doctor	Citron et al. (1995[+])	Lavender et al. (1997[-])		Puisis et al. (1996[-])
Consultants (radiologist or chest physician)	Citron et al. (1995[+])	Dasgupta et al. (2000[+])		Puisis et al. (1996[-])
Peer health advisers	Pilote et al. (1996 [++])			

The evidence map demonstrates that a range of healthcare workers were used to conduct active case finding, from nurses to consultant radiologists and chest physicians. In most cases, a team of healthcare workers were used to identify TB in hard-to-reach groups.

The type of healthcare worker used to conduct active case finding may reflect the tool used to identify TB in hard-to-reach groups. For example:

- A consultant radiologist or chest physician were used in studies where part of their identification process incorporated chest X-ray screening (Citron et al., 1995[+]; Dasgupta et al., 2000[+]; Puisis et al., 1996[-]);
- Nurses (with no input from another healthcare worker) and peer health advisers were used in studies that conducted TST and provided incentives (Malotte et al., 1998[++]; Malotte et al., 1999[++];Pilote et al., 1996[++]);
- Medical doctors were used in studies that conducted a medical examination (Citron et al., 1995[+]; Lavender et al., 1997[-]; Puisis et al., 1996[-]).

Setting

Table 5 displays the setting used to conduct active case finding in the quantitative review on the identification of TB in hard-to-reach groups. Only those studies that clearly reported the type of setting that was used have been included in the table.

Table 5: Studies from the identification review that reported on the setting where active case finding occurred

	Homeless	Immigrants/Foreign-born/New entrants	Drug users	Prisoners	Mixed hard-to-reach

General practice or primary care clinic		Bothamley et al. (2002[-]) El-Hamad et al. (2001[+])			
Hospital		Laifer et al. (2007[+])			
TB Clinic	Pilote et al. (1996[++])	Dasgupta et al. (2000[+]) El-Hamad et al. (2001[+]) Verver et al. (2001[+])			
School		Brassard et al. (2006[+])			
Mobile X-ray unit					Watson et al. (2007[++])
Homeless centre	Bothamley et al. (2002[-]) Citron et al. (1995[+]); Miller et al. (2006[+])				
Pre-immigration screening		Mor et al. (2008[-]) Schwartzman et al. (2005[++]) Sciortino et al. (1999[+])			
Port of arrival		Bothamley et al. (2002[-]) Lavender et al. (1997[-]) Monney & Zellweger (2005[+]) Mor et al. (2008[-]) Ormerod (1998[-]) Schwartzman et al. (2005[++])			

Needle Exchange Programme			Fitzgerald et al. (1999[+]) Perlman et al. (2001[++]) Perlman et al. (2003[++])	
Prison				Jones & Shaffner (2001[+]) Miller et al. (2006[+]) Yates et al. (2009[-]) Puisis et al. (1996[-])	

For many studies, the setting was specific to the hard-to-reach group targeted. These population-specific settings included:
- pre-immigration screening for immigrants;
- port of arrival centres for immigrants;
- needle exchange programmes for injecting drug users;
- homeless centres; and
- prisons.

Immigrants were also targeted in a variety of other settings including:
- general practice;
- hospital;
- TB clinic; and
- school.

In the remaining studies, a mobile X-ray unit was used in a mixed population of hard-to-reach groups (Watson et al., 2007[++]) and a TB clinic was used for the homeless, where incentives were provided to encourage adherence to appointments (Pilote et al., 1996 [++]).

Effectiveness review of service structures to identify TB

The evidence map above illustrates the type of healthcare worker who conducted active case finding, and the setting where it took place among different hard-to-reach populations found in the literature from the identification review. However, it is not known which healthcare worker and setting is most effective and cost-effective compared to others in identifying TB. The studies below specifically compared the different healthcare workers and/or different settings used for active case finding to see

which service components are most effective for conducting active case finding in hard-to-reach groups.

Healthcare worker
Table 6 displays details of one study that directly compared the type of healthcare worker who led the identification of TB in drug users.

Table 6: Studies that compared the type of healthcare worker who conducted active case finding

Study id	Study design	Country	Population	Comparisons	Setting	Approach
Ricks (2008 [++])	RCT	USA	Drug users	Peer outreach worker Health worker and nurse case manager	TB clinic	Contact tracing

Ricks (2008 [++]), in a RCT in the USA, examined the effectiveness of contact tracing when it was conducted by former drug users (N=48) compared with a standard (non-peer) healthcare worker (N=46). Those in the intervention (peer) group also received enhanced case management (reported in more detail in the section on management), while those in the control (healthcare worker) group received limited case management.

The study found that peers who delivered enhanced case management were significantly more likely to encourage patients to identify contacts (40/53, 75%) than healthcare workers who provided limited case management (23/49, 47%; p=0.03). Contacts of people in the peer-led intervention were significantly more likely to agree to become 'extensively interviewed contacts' (EIC; 23%, compared with 12% of the control group contacts, p=0.001). EICs were also adults who had used illegal drugs or alcohol in the past six months and agreed to complete a questionnaire and be regularly tested for HIV, but who did not have active TB. In both the intervention and control group, the contacts who were identified were equally likely to be a high (OR 1.06, 95% CI 0.47 to 2.38), medium (OR 0.95, 95% CI 0.51 to 1.78), or an unknown (OR 0.92, 95% CI 0.45 to 1.86) priority for contact tracing.

The conclusions drawn from the study are limited because it was unclear whether the positive outcomes were due to the intervention being led by a peer or due to the enhanced case management involved in the peer-led intervention. This is because enhanced case management is most likely to involve greater time spent in the co-ordination of care by the professional working with the drug users who are accessing

services. This would have allowed for more opportunities to identify cases and to develop a collaborative relationship between the service user and professional. The authors also noted other limitations including small sample sizes and high dropout rates, which may have prevented other small but significant changes from being detected. However, the study suggests that an effective service model approach to identify contacts in drug users may be a combined peer-led and enhanced case-management approach.

Evidence statement 1: The effectiveness of active case finding by healthcare worker in hard-to-reach groups.

ES1.0 **Moderate evidence** from one RCT (Ricks, 2008 [++]) suggests that peers who were former drug users were more likely to encourage identification of contacts by **drug users** with active TB (40/53, 75%) than were healthcare workers (23/49, 47%; p=0.03). The findings were limited because the peer-led intervention also used enhanced case management compared to the control group that only used limited case management. Therefore, it was unclear whether the positive outcomes in contact identification were due to the healthcare worker leading the identification process or due to the intensity of case management approach.

Applicability
One study was identified that compared the type of healthcare worker delivering contact tracing in the USA in drug users. It is not known how the effectiveness of different healthcare workers conducting contact tracing translate to a UK setting and in other hard-to-reach groups.

Setting
Table 7 summarises four studies that directly compared the setting used to identify TB in hard-to-reach groups. However, in all four studies, both the population and the setting differed in each study arm. This limits the conclusions which can be drawn from these studies on the most effective setting to conduct active case finding, because it is unclear how much of the difference in outcomes is caused by the different settings and how much is because of baseline differences in the different population groups.

Table 7: Studies that compared the setting where active case finding was conducted

Study id	Study design	Coun-try	Popul-ation	Comp-arisons	Health-care worker	Approach
Bothamley et al. (2002[-])	Cost-comparison	UK	Homeless New entrants	New entrants' clinic at port of arrival (POA)	Unclear	Symptom questionnaire and TST

				Homeless centre		
				General Practice (GP)		
El-Hamad et al. (2001[+])	Prospective cohort	Italy	Immigrants	Specialised TB unit; Primary care clinic.	Unclear	TST and CXR screening.
Miller et al. (2006[+])	Cost comparison	USA	Homeless Prisoners	Homeless centres; Prison.	Unclear	TST, CXR and medical evaluation; legally mandated screening vs optional screening
Mor et al. (2008[-])	Cost-savings	Israel	Immigrants (Ethiopian)	Pre-immigration screening	Unclear	Unclear
				Post-immigration screening		

Bothamley et al. (2002[-]) compared the effectiveness (and cost outcomes, reported in the economic section) of three different screening strategies in different settings in the UK. The three settings included active screening at a new entrants' clinic/hospital, where identification of TB was part of the port of arrival (POA) scheme; passive screening at a large general practice, where screening for TB was part of the initial health check for new entrants who chose to register as patients; and active screening at centres for the homeless including hostels, an emergency accommodation centre or a drop-in centre. In all three settings, screening was first conducted using a symptom questionnaire; all those with positive symptoms indicative of active TB, or considered high risk, were also tested using a TST.

The study found that the coverage of the symptom questionnaire was low at the POA hospital: 15.8% (199/1,262) of new entrants were screened with the questionnaire, 90.9% of those (181/199) were then screened with a TST, of which 3 (1.6%) had active TB. In the homeless centre, 98.1% (262/267) of individuals were screened with a symptom questionnaire, 100% of those were then screened with a TST, none of whom had active TB. In the GP setting, 45 new patients were screened with a symptom questionnaire; the coverage of passive screening was not known as it was unclear how

many people were eligible for screening. Of these, 86.6% (39/45) were screened with a TST, but none had active TB. No statistical significance calculations were reported.

The study findings were limited because the populations in the three groups were not comparable as they came from different source populations (homeless and new entrants). Therefore, it is difficult to ascertain whether the findings were due to the different settings in which active case finding occurred or due to baseline differences between the population groups, including the difference in prevalence of active TB.

El-Hamad et al. (2001[+]), in a prospective cohort study, compared completion rates for screening undocumented immigrants into Italy at specialist TB centres (N=749) compared with non-specialist primary care facilities targeted at immigrants (N=483). Undocumented immigrants were defined as foreign-born persons with no residence permit and limited access (emergency interventions only) to public medical care services. The selected participants were from countries with a TB prevalence of at least 50/100,000, who had arrived within the previous five years without a residence permit and who were assessed for TB in either a specialist TB clinic or in a general primary care clinic where they sought care; participants self-referred to the services. The active case finding approach used in the specialist TB clinic was chest X-ray screening plus TST conducted at the first visit and read at a second visit. In the general primary care clinic, active case finding used a TST plus physical examination at the first visit, with chest X-ray conducted subsequently off site at a nearby TB clinic; and the TST result was read at a third visit. In both cases, screening was considered to be complete if both chest X-ray and TST were conducted and read, however, this involved more processes and visits in the general primary care clinic.

The study found that, for those who attended the specialist TB clinic, 85.6% (648/749) completed screening, compared with 71.4% (345/483) in the primary care clinic (p-value not reported). The yield of active TB was similar in both settings: 6.7/1,000 at the specialist TB clinic and 6.2/1,000 at the primary care clinic. In a multivariate logistic regression analysis, more people were likely to complete screening if they were enrolled in the specialist TB site compared to those enrolled in the primary care clinic (OR=2.57, 95% CI 1.92 to 3.42). However, as individuals self-referred to the different services, there may be other confounding factors that determined both the choice of service sought and their willingness to complete the screening process. Other limitations included statistically significant differences at baseline between the two groups, which may have contributed to the differences in the results. These differences included more males, Africans and Christians in the primary care group (p<0.001), and more alcohol users (p<0.01), drug users (p<0.001), and individuals living in their own apartment (p<0.001) in the specialist TB clinic group. Despite these limitations, the findings suggest that a service model that conducts a two-stage active case-finding approach onsite in a TB clinic may be more effective than a three-stage approach in a primary care clinic that requires referral to a nearby TB clinic for chest X-ray.

Miller et al. (2006 [+]) compared the effectiveness and costs of active case finding in a prison setting (N=22,920) with a homeless setting (N=822) in the USA. In the prison setting, active case finding was conducted using TST as part of a state-law mandated programme. This was compared with a non-state-law-mandated screening programme implemented in a homeless centre setting that used TST plus chest X-ray to identify TB as well as providing incentives to participants to attend every clinic appointment. Each setting targeted a different hard-to-reach group where there were no statistical comparisons conducted to examine how comparable these samples were at baseline.

The study found that there was no statistically significant difference in the coverage of TST screening in the homeless centre where screening was optional (94.7%, 778/822) compared with a prison setting where screening was mandatory (95%, 21,778/22,920; p=0.179). There was, however, a significantly higher yield of positive TST results in the homeless setting (15.5%, 127/819) compared with the prison setting (2%, 303/15,150; p<0.001). The treatment outcomes for active case finding demonstrated that there were also statistically more people prescribed treatment for LTBI or active TB in the homeless setting (LTBI treatment=22%, 181/822; active TB treatment =1.2%, 10/833) compared with the jail setting (LTBI treatment=0.9%, 211/23,444; active TB treatment=0.03% 7/2,333; p<0.001).

The study was limited because each setting used different methods to conduct active case finding. This included the use of incentives in the homeless setting, which were found to be an effective approach to improve adherence to screening procedures in the first of the quantitative reviews on identification of TB in hard-to-reach groups. Therefore, it is not clear how much of the difference in outcomes is because of the setting where identification occurred, or the different methods used to conduct active case finding, or to differences in prevalence of the disease in the different populations.

Mor et al. (2008[-]) used a before-and-after study design to investigate the effectiveness (and cost-effectiveness, reported in the economic review) of pre-immigration screening of new entrants from Ethiopia before entry into Israel between 2001 and 2005, compared with the previous practice of post-immigration screening, conducted between 1998 and 2001. The pre-immigration screening consisted of TST followed by CXR, and people diagnosed with TB after this screening were treated in Ethiopia; any infected person who was not identified by the pre-immigration screening, and those not infected, entered Israel. Upon arrival in Israel, a public health nurse performed a second TST on all those whose first reading was 10 mm induration in size or more. Further details of the screening methods used in the historical comparison group were not provided. Only those entrants who were not diagnosed with TB within the first two weeks were included in the study.

The study found that proportionally fewer people developed TB among those who were screened before immigration (in 2001 to 2005, 267 cases per 100,000 person-years) compared with those screened post-immigration (in 1998 to 2001, 324 cases per 100,000 person-years). This rate ratio for developing TB was significantly lower for

those screened pre-immigration, compared with post-immigration (rate ratio = 0.82, p<0.01). The detection period (mean number of days between entry into Israel and TB diagnosis) was also lower in the pre-immigration group (mean = 193 days, standard deviation (SD) = 260 days) compared with the post-immigration group (mean = 487 days, SD = 640 days). Survival analysis found a significantly shorter time to diagnosis over the five-year follow-up period for the pre-immigration group compared with the post-immigration group (OR =0.72, 95% CI 0.59 to 0.89; p=0.002).

The study was limited because the use of a historical control group means that the differences in TB incidence in the two groups may have been caused by changes in disease epidemiology over time, rather than differences in detection rates between the two screening strategies. In addition, the pre-immigration screening groups had a shorter follow-up period than the post-immigration group which may also have contributed to the lower prevalence of TB detected in the pre-immigration screening group. The annual TB incidence rate found in this study was also higher than those found in the literature for other hard-to-reach groups in other countries, which may decrease the generalisability of the results.

Evidence statement 2: The effectiveness of active case finding by setting in hard-to-reach groups.

ES2.0 Weak evidence from one before-and-after study (Mor et al., 2008[-]) found that screening in a pre-immigration setting may reduce the risk of developing TB in **new entrants** from Ethiopia to Israel compared with post-immigration screening, with a shortened detection period from entry into Israel and TB diagnosis (OR=0.72, 95% CI 0.59 to 0.89; p=0.002). The findings were limited because the study did not address the potential differences in TB incidence in the two time periods in which screening occurred.

ES2.1 Weak evidence from one prospective cohort study (El-Hamad et al., 2001[+]) found that **new entrants** may be more likely to complete screening if active case finding was conducted in a specialist TB clinic compared with a non-specialist primary care facility (OR=2.57; 95% CI 1.92 to 3.42). However, there were statistically significant differences between the groups at baseline that were not adjusted for in the analysis.

ES2.2 Weak evidence from one cost-comparison study (Bothamley et al., 2002[-]) found that use of the symptom questionnaire was lowest at the POA clinic (15.8%, 199/1,262) for **new entrants**, compared with a **homeless** centre (98.1%, 262/267); the coverage of the symptom questionnaire among **new entrants** registered for the first time in a GP setting was not known. For those screened with a symptom questionnaire, the coverage of TST screening was 100% (267/267) in the homeless centre, 90.9% (181/199) in the POA clinic and 86.6% (39/45) in the GP setting. The yield of active TB was three cases in the POA clinic, while no cases of active TB were identified in the other two settings. The study findings were limited because the study compared two

different populations in addition to two different settings.

ES2.3 Weak evidence from one study (Miller et al. 2006[+]) found that there was no statistically significant difference in the coverage of TST screening in the **homeless** centre (94.7%, 778/822) compared with a **prison** setting (95%, 21,778/22,920; p=0.179), however, there was a significantly higher yield of positive TST results in the homeless setting (15.5%, 127/819) compared with the prison setting (2%, 303/15,150; p<0.001). There were also statistically more people prescribed treatment for LTBI or active TB in the homeless setting (LTBI treatment = 22%, 181/822; active TB treatment = 1.2%, 10/833) compared with the prison setting (LTBI treatment = 0.9%, 211/23,444; active TB treatment = 0.03% 7/2,333; p<0.001). The study findings were limited because it was difficult to determine whether the differences in outcome were due to the different settings evaluated or due to the different populations' targeted in each setting including differences in the prevalence of TB.

Applicability
All four studies were conducted in different counties (UK, Italy, USA and Israel) with only one conducted in the UK. In addition, various settings were compared in different populations including prisoners, immigrants/new entrants and the homeless, limiting the applicability of the findings to other hard-to-reach groups such as drug users.

Economic review of service structures to identify TB

Healthcare worker
No study was identified that reported on the cost-effectiveness of identifying TB using different healthcare workers.

Setting
Table 8 summarises three studies that compared the costs of active case finding conducted in different settings.

Table 8: Studies that compared the setting where active case finding was conducted

Study id	Study design	Coun-try	Popul-ation	Compar-isons	Health-care worker	Approach
Bothamley et al. (2002[-])	Cost-comparison	UK	Homeless New entrants	New entrants clinic (POA) Homeless centre GP (passive	Unclear	Symptom questionnaire and TST

				screening)		
Miller et al. (2006[+])	Cost comparison	USA	Homeless; Prisoners.	Homeless centres; Prison.	Unclear	TST, CXR and medical evaluation; legally mandated screening vs optional.
Mor et al. (2008[-])	Cost-savings	Israel	Immigrants (Ethiopian)	Pre-immigration screening Post-immigration screening	Unclear	Unclear

Bothamley et al. (2002[-] (also reported in this review in the section: 'Effectiveness review of service structures to identify TB') compared the costs of three different screening strategies in different settings in the UK: active screening at a new entrants' clinic/hospital where identification of TB was part of the POA scheme; a large general practice where passive screening for TB was part of the initial health check for new entrants who chose to register as patients; and active screening in homeless centres. The study modelled the cost per case of active TB prevented for each group.

The total costs of screening in the different settings were £22,646 for 199 people screened in the hospital as part of the POA scheme, £3,452 for 262 people screened in homeless centres, and £938 for 45 people screened in general practice as part of new patient registrations. However, as the only cases of active TB identified were in the hospital (N=3), this setting resulted in the greatest cost-savings for active case finding based on cases of active TB prevented: £25,621 for 9.5 cases of active TB prevented, or £12.70 saved per person screened. The cost-savings in the other settings were estimated to be £1,618 for 0.6 cases of active TB prevented when testing in homeless centres, at an additional cost of £0.50 per person screened; and £594 for 0.2 cases of active TB prevented when testing in general practice, at a cost of £7.00 per person screened. The cost per person screened for every case prevented was £10.00 in hospital setting, £23.00 in the homeless centre and £6.32 in general practice. However, the cost per person screened would have been cost saving for all three settings if one additional case had been detected in each: £33 (savings) for testing in hospital, £6 (savings) for testing in general practice and £11 (savings) for testing in homeless centres. The study was limited because in addition to comparing different settings, it also compared different populations which may have different prevalence of active TB. This is particularly pertinent as the economic analysis was sensitive to the number of cases of active TB detected. In addition, the analysis did not report on the economic perspective used and it did not discount the costs of identification.

Miller et al. (2006 [+] (also reported in this review in the section: 'Effectiveness review of service structures to identify TB') compared the estimated costs of active case finding in a homeless centre compared with a prison setting. Costs were derived from the national average of Medicare charges and were adjusted to the 2003 US dollar. The study found that the cost per active TB case prevented by identifying and treating each person with LTBI was $14,350 in the homeless setting and $34,761 in the prison setting. However, these costs were based on the differences in the yield of positive TST results found in the two groups, which may have been caused by population differences rather than the effectiveness of screening in different settings, limiting the conclusions which can be drawn from this study.

Mor et al. (2008[-] (also reported in this review in the section: 'Effectiveness review on service structures to identify TB') used a before-and-after study design to investigate the cost-effectiveness of pre-immigration screening of new entrants from Ethiopia before entry into Israel (between 2001 and 2005) compared with the previous practice of post-immigration screening (conducted between 1998 and 2001). Details on the effectiveness of the different strategies are reported in the section 'Effectiveness review of service structures to identify TB'. The study calculated that pre-immigration screening would result in net direct savings of $449,817 in a five-year time horizon, assuming that 98 more individuals would be free of TB if they were screened in a pre-immigration setting compared with screening at a post-immigration setting. No further cost outcomes were reported. The study had several limitations, including that the costs of resources used in this analysis came from different sources, with one more reliable than the other. For example, the costs of post-immigration screening came from a national published source, while the costs of pre-immigration screening were based on expert opinion. In addition, the study did not explore the uncertainties around the cost of pre-immigration screening in a sensitivity analysis, nor did it use a discount rate to allow for the changes in cost over time. However, the study suggests that screening in a pre-immigration setting may have better effectiveness (reported in the 'Effectiveness review of service structures to identify TB') and cost-effectiveness outcomes compared with screening in a post-immigration setting.

Evidence statement 3: The cost-effectiveness of active case-finding by setting in hard-to-reach groups.
ES3.0 Weak evidence from one study (Mor et al., 2008[-]) found that screening in a pre-immigration setting would result in net direct savings of $449,817 in a five year time horizon (assuming that 98 more individuals would be free of TB screening in this setting) compared with screening in a post-immigration setting among Ethiopian **immigrants**. No further cost outcomes were reported. The study had several limitations including that the costs of resources used in this analysis came from different sources, with the costs of post-immigration screening more reliable than the costs of pre-immigration screening. **ES3.1 Weak evidence from one** study (Miller et al., 2006[+]) suggests that the cost

per active TB case prevented by identifying and treating each person with LTBI was lower in a **homeless** setting ($14,350) compared with a **prison** setting ($34,761). The study findings were limited because the study compared two different populations in addition to two different settings.

ES3.2 Weak evidence from one study (Bothamley et al. (2002[-]) found that the total costs of screening in three different settings was £22,646 for 199 people screened in a clinic as part of the POA scheme among **new entrants**, £3,452 for 262 people screened in **homeless** centres, and £938 for 45 people screened in general practice for new patient registrations who were **new entrants**. However, as the POA yielded more cases of active TB (N=3), this resulted in £12.70 cost-savings per person screened in the POA clinic, compared with an additional cost of £0.50 per person screened in the homeless centres and £7.00 per person screened in general practice. The study was limited because in addition to comparing different settings, it also compared different populations which may have different prevalence of active TB.

Applicability
Three studies were identified that were conducted in the UK, Israel and the USA in the homeless, new entrants and prisoners. Although one study was conducted in the UK, it is not known how the evidence found in the other studies on effective service components relates to the UK context. It is also not known how these findings apply to other hard-to-reach groups such as drug users.

5.2   Management

5.2.1   Management of latent TB infection (LTBI)

Mapping of service structures from the management review on LTBI

Healthcare worker
Table 9 details the type of healthcare worker who conducted an intervention to manage LTBI in hard-to-reach groups. The studies that did not clearly report the type of healthcare worker used to manage LTBI were not included in the table.

Table 9: Studies from the management review that reported on the type of healthcare worker who conducted an intervention to manage LTBI

	Homeless	Immigrants	Drug users	Prisoners	Mixed hard-to-reach
Peers	Tulsky et al. (2000 [+])	Kominski et al. (2007[+]) McCue & Afifi (1996[-])	Chaisson et al. (2001[+])		
Nurse/ outreach worker	Nyamathi et al. (2008[++])		Chaisson et al. (2001[+]) Gourevitch et al. (1998[+]) Malotte et al.		

				(2001[++])		
Health workers					Rodrigo et al. (2002[-])	
General chest clinic staff					White et al. (1998[+])	
Multidisciplinary team						White et al. (2003[+])
Prison discharge planners					White et al. (2005[+])	
Lay research workers	Tulsky et al. (2000[+]) Tulsky et al. (2004[+])				White et al. (2002[+])	

Peers led a variety of interventions including:
- peer-support (Chaisson et al., 2001[+]; Kominski et al., 2007[+]; McCue & Afifi, 1996[-]);
- peer support plus incentives (Kominski et al., 2007[+]); and
- Directly Observed Preventive Therapy (DOPT) (Tulsky et al., 2000 [+]).

Other healthcare workers who delivered DOPT were:
- nurse and/or outreach workers (Chaisson et al., 2001 [+]; Gourevitch et al., 1998 [+]);
- health workers (Rodrigo et al., 2002[-]); and
- pharmacists (Juan et al., 2006[+]).

Other healthcare workers who led an intervention to manage LTBI were general chest clinic staff who provided incentives to adhere to treatment (White et al., 1998 [+]); prison discharge planners who delivered an educational intervention (White et al., 2005 [+]); and a multidisciplinary team who delivered a service model approach/social care support programme (White et al., 2003[+]).

Setting
Table 10 reports the setting used to manage LTBI in hard-to-reach groups. All the studies in the quantitative review clearly reported the type of setting where management occurred.

Table 10: Studies from the management review that reported the setting used to manage LTBI.

	Homeless	Immigrants	Drug users	Prisoners	Mixed hard-to-reach
General health clinic/hospital	Nyamathi et al. (2008[++])	Kominski et al. (2007[+]) McCue & Afifi (1996[-])	Batki et al. (2002[+])		

Chest clinic				Bandyopadhyay et al. (2002[-])	
TB clinic	Tulsky et al. (2000[+])	Matteelli et al. (2000[+])	Chaisson et al. (2001[+])	White et al. (2002[+]) White et al. (1998[+])	White et al. (2003[+])
Outreach (site chosen by participant)			Chaisson et al. (2001[+]) Malotte et al. (2001[++])		
Community storefront	Tulsky et al. (2004[+])				
Drug service/ methadone clinic			Gourevitch et al. (1998[+])		
Prison				White et al. (2005[+]) White et al. (2002[+])	
Pre-immigration		Schwartzman et al. (2005[++])			

The setting most often used to manage LTBI was a TB clinic, followed by a general health clinic or hospital.

There were, however, two studies that provided Directly Observed Preventive Therapy (DOPT) in a mutually convenient location in order to encourage adherence to treatment (Chaisson et al., 2001[+]; Malotte et al., 2001[++]).

Four other studies chose settings that were specifically targeted at the hard-to-reach population, which included a pre-immigration setting (Schwartzman et al., 2005 [++]), prison (White et al., 2005 [+], White et al., 2002 [+]) and a methadone clinic (Gourevitch et al., 1998 [+]).

Effectiveness review of service structures to manage LTBI

The evidence map above illustrates the type of healthcare worker who conducted an intervention to manage LTBI and the setting where it took place among different hard-to-reach populations. However, it is not known which healthcare worker and setting is most effective and cost-effective compared to others in managing LTBI. The studies below specifically compared the different healthcare workers or different settings used to manage LTBI to see which service components are most effective in hard-to-reach groups.

Healthcare worker

No studies were identified that compared the effectiveness of different healthcare workers to manage LTBI in hard-to-reach groups.

Setting
Two studies directly compared the setting used to manage LTBI in drug users and are summarised in Table 11.

Table 11: Studies that compared the setting used to manage LTBI

Study id	Study design	Country	Population	Comparisons	Healthcare worker	Approach
Malotte et al. (2001 [++])	RCT	USA	Drug users	Outreach: at a site chosen by the participant. No outreach: onsite at drug users' service.	Outreach worker	DOPT with a $5 monetary incentive
Umbricht-Schneiter et al (1994[+])	RCT	USA	Intravenous Drug users	Onsite: immediate treatment at methadone clinic. Offsite: referred to medical service where they had to initiate treatment.	Unclear	Unclear

Malotte et al. (2001[++]) compared the management of LTBI in either an outreach setting or a non-outreach setting for a population of drug users with LTBI in the USA. Outreach involved providing DOPT plus incentives in a location chosen by the participant (N=53) compared with DOPT plus incentives delivered in a non-outreach setting onsite at a drug users' service in the community (N=55). DOPT included 900 mg isoniazid twice weekly for six months for those without HIV and 12 months for those with a positive HIV status. Incentives included $5 cash for each appointment attended. The study also had a third comparison arm which was not relevant to this service model review (N=55).

The study found that when the intervention to manage LTBI (DOPT plus incentives in both comparison groups) was conducted in an outreach setting at a site convenient for the participant, 52.8% (28/53) completed treatment compared with 60% (33/55) when it

was conducted onsite in a drug services facility. These differences were not statistically compared limiting the study findings, but suggest that there were was no added benefit in adherence to treatment when the intervention occurred at a site chosen by the participant compared to when it was delivered onsite at a drug services facility. These findings may be because the drug services facility was specifically designed to be convenient for the hard-to-reach group explored in the study.

Umbricht-Schneiter et al (1994[+]), in a RCT in the USA, compared treating intravenous drug users for their co-morbid medical condition (which could include TB) onsite at a methadone clinic (N=25) or offsite at a medical centre to which they were referred (N=26). The medical conditions explored in this study were LTBI, hypertension, HIV infection and acute sexually transmitted disease. For those treated onsite at a methadone clinic, their medical condition was either treated immediately or a follow-up appointment was arranged, after they were assessed for methadone treatment. A counsellor at the methadone clinic co-ordinated the care received for their drug use and co-morbid medical condition. Participants treated offsite were assessed for methadone treatment, then referred to a medical centre, so that the participants were responsible for initiating treatment and obtaining an appointment. Participants received written instructions describing the medical clinic, the location, and contact details. The treatment participants received across settings to manage LTBI was not clearly reported but the outcomes suggest that participants were screened with a purified protein derivative (PPD) and chest X-ray, and those with a positive PPD received chemoprophylaxis treatment.

The study found that for all medical conditions, the proportion of drug users who enrolled and complied with medical treatment was 92% (23/25) in the onsite treatment group and 32% (9/26) for those in the offsite treatment group (p<0.001). The proportion of drug users seen one or more times was 100% (25/25) for those who received medical treatment onsite at a methadone clinic and 30.8% (8/26) for those who were referred for treatment offsite (p<0.001). The mean number of visits per patient was also statistically significantly higher with medical treatment onsite in a methadone clinic (mean=3.1, SD=1.8; p<0.001) compared with the control group (mean=0.4, SD=0.6).

For those outcomes relating to TB treatment only, the number of participants with positive PPD tests who received a chest X-ray was 75% (6/8) among those treated onsite a methadone clinic and 24.4% (3/14) for those referred to treatment offsite. The number of patients with positive PPD tests who received chemoprophylaxis to manage TB was 12.5% (1/8) in the onsite treatment group and 7.1% (1/14) in the offsite treatment group. The differences in outcomes for TB were not statistically compared, perhaps due to the small numbers included in each group. However, the finding suggests that there were more favourable treatment outcomes when services for managing TB (and other medical conditions) were conducted onsite at a methadone clinic for intravenous drug users compared with referring participants to other offsite medical services.

Evidence statement 4: **The effectiveness of managing LTBI by setting in hard-to-reach groups.**

ES4.0 Moderate evidence from one RCT (Malotte et al., 2001[++]) found that treatment completion for managing LTBI among **drug users** was 52.8% (28/53) when it was conducted in an outreach setting at a site convenient for the participant compared with 60% (33/55) when it was conducted onsite in a drug services facility. These differences were not statistically compared, limiting the study findings, but suggest that there was no added benefit in adherence to treatment when it was delivered in an outreach setting.

ES4.1 Moderate evidence from one RCT (Umbricht-Schneiter et al., 1994[+]) found that the proportion of **intravenous drug users** who enrolled and complied with medical treatment (including treatment for TB) was 92% (23/25) for those treated onsite at a methadone clinic compared with 32% (9/26) for those treated offsite at a medical centre (p<0.001). The proportion of drug users with positive PPT tests who received a chest X-ray was 75% (6/8) for those who received medical treatment onsite compared with 24.4% (3/14) for those treated offsite. The number of patients with positive PPD tests who received chemoprophylaxis was 12.5% (1/8) for people treated onsite compared with 7.1% (1/14) for those treated offsite. Statistical significance was not calculated for either of these differences.

Applicability
Two studies were identified, both conducted in the USA in drug users. The applicability of the findings to the UK context and to other hard-to-reach groups is not known.

Cost-effectiveness review of service structures to manage LTBI

No study was identified that explored the cost-effectiveness of different service components to manage LTBI in hard-to-reach groups.

5.2.2 Managing active TB

Mapping of service structures from the management review on active TB

Healthcare worker
Table 12 details the healthcare workers who conducted an intervention to manage active TB in hard-to-reach groups. The studies that did not clearly report the type of healthcare worker who conducted the intervention were not included in the table[3].

Table 12: Studies from the management review that reported on the type of healthcare worker that conducted an intervention to manage active TB.

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[3] The remaining studies in the management review were not included in the table because it was unclear which professional conducted the intervention to manage active TB (Bock et al. (2001 [+]); Chemtob et al. (2003 [-]); Oscherwitz et al. 1997[-]).

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	Homeless	Immigrants	Drug users	Prisoners	Mixed hard-to-reach
Nurse			Alwood (1994 [-])		Deruaz & Zellweger (2004[-])
Health worker			Ricks (2008[++])	Rodrigo et al. (2002[-])	
Pharmacist					Juan et al. (2006[+])
Peer			Ricks (2008[++])		
Family member		MacIntyre et al. (2003[+])			
Multidisciplinary team (MDT)	Diez et al.(1996[-])				

The main intervention evaluated in the management of active TB was DOT which was delivered by various healthcare workers including:
- nurses (Alwood, 1994 [-];Deruaz & Zellweger, 2004[-]);
- health workers (Rodrigo et al., 2002[-]);
- pharmacists (Juan et al., 2006 [+]); and
- family members (MacIntyre et al., 2003 [+]).
- peer (Ricks, 2008 [++])

In the remaining study (Diez et al., 1996[-]), a MDT was used to deliver a service model or social outreach approach which included various intervention components, such as DOT, outreach work and the provision of medical and social care

Setting
Table 13 details the setting used to conduct an intervention to manage active TB in hard-to-reach groups. Only those studies that clearly reported the type of setting where management of active TB occurred were included in the table.

Table 13: Studies from the management review that reported the setting used to manage active TB.

	Homeless	Immigrants	Drug users	Prisoners	Mixed hard-to-reach
Chest clinic			Alwood (1994[-])		
TB Clinic		Chemtob et al. (2003[-])	Ricks (2008[++])		Deruaz & Zellweger (2004[-])
Pharmacy					Juan et al. (2006[+])

Outreach (at a site chosen by the participant or at a social service location)					Deruaz & Zellweger (2004[-])
Prison				Rodrigo et al. (2002[-])	
Residential facility	Diez et al. (1996[-])				
Participant's home		MacIntyre et al. (2003[+])			

The most common setting used to manage active TB was a TB clinic where approaches such as DOT (Chemtob et al., 2003[-]; Deruaz & Zellweger, 2004[-]) and case management (Ricks, 2008[++]) were delivered. Other settings used to conduct DOT were a chest clinic (Alwood, 1994[-]), pharmacy (Juan et al., 2006[+]), prison (Rodrigo et al., 2002[-]) and in the participant's home (MacIntyre et al., 2003[+]). The remaining intervention, service model approach/social care support was conducted in a residential facility in the community for the homeless (Diez et al., 1996[-]).

Effectiveness review of service structures to manage active TB

The evidence map above illustrates the type of healthcare worker who conducted an intervention to manage active TB and the setting where it took place among different hard-to-reach populations. However, it is not known which healthcare worker and setting is most effective and cost-effective in managing active TB. The studies below specifically compared the different healthcare workers or different settings used to manage active TB to see which service components are most effective in hard-to-reach populations.

Healthcare worker
One study was identified that compared the effectiveness of different healthcare workers in the management of active TB in hard-to-reach groups and is summarised in Table 14. This study was reported elsewhere in the identification section of the report.

Table 14: Studies that compared the healthcare worker used to manage LTBI

Study id	Study design	Country	Population	Comparisons	Setting	Approach
Ricks (2008 [++])	RCT	USA	Drug users	Peer outreach worker Health worker and nurse case manager	TB clinic	Enhanced or limited case management

Ricks (2008[++], also reported in this review in section 5.1.1 on active case finding) compared the effectiveness of an intervention to manage active TB when it was delivered by peer outreach workers who were former drug users (N=48) compared with healthcare workers (N=46) in an RCT in the USA. In the peer-led intervention, peer outreach workers delivered DOT and also provided enhanced case management. In the comparison group, a health worker delivered DOT but with limited case management. The study did not report further details on what constituted enhanced versus limited case management.

The study found that treatment completion, defined by the physician and based on the percentage of doses taken and the timing (typically defined as 80% of medication taken by the end of treatment), was 85% (41/48) for those who received enhanced case management delivered by a peer and 61% (28/46) for those who received limited case management delivered by healthcare worker. The probability of completing treatment was statistically greater with the peer-led intervention compared with health worker-led intervention (RR=2.68, 95% CI 1.24 to 5.82; p=0.01). There was also a statistically significant difference found for treatment compliance defined as taking 80% of medication while undergoing treatment. For those in the peer-led intervention 84% (38/48) complied with treatment compared with 68% (25/46) in the health worker-led intervention (RR=2.51, 95% CI 1.15 to 5.48, p=0.016). The mean number of missed DOT appointments was not statistically significant (limited case management=7.64; enhanced case management=4.11; p=0.13).

The conclusions which can be drawn from this study regarding effectiveness of service components in managing active TB were limited because the peer-led intervention also contained enhanced case management. Therefore, it is difficult to determine whether the positive outcomes regarding adherence to treatment was due to the type of healthcare worker or due to the intensity of the management approach. However, the findings suggest that an effective service model approach to manage active TB in hard-to-reach groups may be a combination of a peer-led enhanced case-management approach, which also led to greater identification of contacts of hard-to-reach groups (reported in the identification section).

Evidence statement 5: The effectiveness of managing active TB by healthcare workers in hard-to-reach groups.

ES5.0 Moderate evidence from one RCT (Ricks, 2008[++]) found that the probability of completing treatment was statistically greater when peers delivered enhanced case management to **drug users** compared with limited case management delivered by a healthcare worker (RR=2.68, 95% CI 1.24 to 5.82; p=0.01). The conclusions drawn from these findings were limited because the peer-led intervention also had enhanced case management. It is therefore not known how much of the positive treatment outcomes were due to the healthcare worker who delivered the service or the intensity of case management.

Applicability

The study was conducted in the USA in drug users; it is not known how these findings translate to a UK setting or for other hard-to-reach groups.

Setting
Table 15 summarises the one study identified that directly compared the effectiveness of the setting used to manage active TB.

Table 15: Studies that compared the setting used to manage active TB

Study id	Study design	Country	Population	Comparisons	Healthcare worker	Approach
Deruaz & Zellweger (2004[-])	Retrospective cohort	Switzerland	Mixed hard-to-reach	Outreach: at a site chosen by the participant. No outreach: onsite at drug users' service.	Nurses	DOT

Deruaz & Zellweger (2004[-]), in a retrospective cohort study, compared the effectiveness of managing active TB onsite at a TB clinic (N=27) compared with delivering the same intervention in a social outreach site (N=27) in mixed hard-to-reach groups in Switzerland (immigrants, drug and alcohol abusers, homeless, prisoners, HIV positive and people with drug-resistant disease). The social outreach site consisted of various locations depending on the needs of the participants but included a social care centre where patients with additional needs could be cared for, the patient's home, or at any other location convenient for the participant. The onsite setting was a dispensary unit for TB; asylum seekers received a bus fare to attend the clinic. The intervention delivered at all sites was DOT to manage active TB, however, in each group participants either received a full course of DOT or partial DOT which consisted of only two months of direct observation. Assignment to either full or partial DOT was based on the needs of the patients and was decided by the medical supervisor. Those who were assigned to a full course of DOT were typically refugees, asylum seekers or illegal immigrants; people receiving re-treatment for drug resistant disease; or those with a history of non-adherence. Those who were assigned to partial DOT were typically considered compliant with stable social conditions. DOT was conducted by a nurse and the medication consisted of daily doses of isoniazid, rifampicin, pyrazinamide and ethambutol for two months and continuation therapy with isoniazid and rifampicin for four months.

The study found that for those who received treatment onsite, 55% (15/27) completed treatment and 38% (10/27) were cured of active TB at end of treatment (confirmed by bacteriological confirmation). For those who received treatment in a social outreach setting, 60% (16/27) completed treatment and 26% (7/27) were cured of active TB.

There were no statistically significant differences in all successful treatment outcome (completed treatment and cured) when management occurred onsite (92.6%, 25/27) compared to an outreach setting (85.2%, 23/27; p=0.67).

The conclusions that can be drawn from this study on effective components of service delivery were limited because there were systematic differences between groups in how treatment outcomes were collected. When DOT was conducted onsite, adherence to treatment was recorded systematically by the nurse, but when it was conducted via social outreach, adherence was not routinely recorded. In order to collect the data, information was provided orally by healthcare workers who conducted DOT via social outreach at least six months after treatment completion. This reduces the validity of the findings as it may have been subject to observer and/or recall bias. The findings were further limited as it was not reported how many people in each setting received full or partial DOT; patients who were assigned to full DOT were more likely to have problems with adherence, and may also be those who would receive DOT via social outreach, as allocation to treatment setting was based on the needs of participants. These potential differences between groups may have underestimated the effectiveness of delivering an intervention to manage active TB in a social outreach setting.

Evidence statement 6: The effectiveness of managing active TB by setting in hard-to-reach groups.

ES6.0 Weak evidence from one retrospective cohort study found that there was statistically no significant difference in the management of active TB if it occurred onsite at a healthcare service or in the community at a site convenient for people with active TB, in **mixed hard-to-reach groups** (Deruaz & Zellweger, 2004[-]).The conclusions that can be drawn from this study were limited because there were systematic differences between groups in how treatment outcomes were collected as well as potential selection bias between groups.

Applicability
One study was identified and was conducted in Switzerland in mixed hard-to-reach groups. It is not known how these findings translate to the UK context and to specific hard-to-reach groups.

Cost-effectiveness review of service structures to manage active TB

No evidence was identified that compared the cost-effectiveness of different service model approaches to manage active TB.

6.0   Discussion and summary

The primary research question for this review was:

Which service models and service structures are most effective and cost-effective at supporting TB identification and management of hard-to-reach groups?
The eight comparative studies identified for this review primarily answered this research question and are summarised in the section on key findings. There was no study, however, that specifically addressed the effectiveness of different service models to identify and manage TB. The management review includes individual interventions that can be found in a service model approach, including, for example, case management.

The secondary research questions for this review were:

Who is responsible for the commissioning and delivery of TB services?
The person responsible for the commissioning of service was not reported, however, the type of healthcare worker delivering the TB service was reported. The evidence map of the studies included in the first two quantitative reviews demonstrates that a range of healthcare workers were used to conduct the identification and management of TB in hard-to-reach groups.

The healthcare workers responsible for the identification of TB included:
- nurses (for example Malotte et al., 1998[++]);
- peer health advisers (for example, Pilote et al., 1996[++]);
- health educations (for example, Perlman et al. (2001[++]);
- general chest clinic staff (for example, Dasgupta et al., 2000[+]);
- GPs and non-specialist medical doctors (for example, Lavender et al., 1997[-]); and
- consultant radiologist or chest physician (for example, Citron et al., 1995[+]).

In most cases more than one type of healthcare worker was used to conduct active case finding and the type of healthcare worker responsible reflected the identification approach used, for example, a consultant radiologist or chest physician were used in studies that delivered chest X-ray screening (Citron et al., 1995[+]); Dasgupta et al., 2000[+]; Puisis et al. (1996[-]).

The healthcare workers', the people responsible for the management of LTBI and active TB included:
- lay research workers (White et al., 2002[+]);
- family members (for example, MacIntyre et al., 2003[+]);
- peers (for example, Tulsky et al., 2000[+]; Ricks (2008[++]);
- nurse/ outreach workers (for example, Nyamathi et al., 2008[++]);
- health workers (for example, Rodrigo et al., 2002[-]);
- general chest clinic staff (for example, White et al., 1998[+]);

- prison discharge planners (for example, White et al., 2005[+]);
- pharmacists (for example, Juan et al., 2006[+]); and
- MDT (for example, White et al. (2003 [+]); Diez et al., 1996[-]).

The effectiveness of services by the type of healthcare worker responsible for the identification and/or management of TB in hard-to-reach groups is reported in the section on key findings.

What (if any) theories or conceptual models underpin the service models/organisational structures?
The theories which underpinned the service models/organisation structure were not reported in the studies. This information would have been helpful in understanding the theory behind the service components and how they might be expected to bring about change and improve outcomes in hard-to-reach groups.

What specific individuals or populations are targeted by the interventions?
In the evidence map of the type of healthcare worker and setting covered in the first two quantitative reviews on the identification and management of TB in hard-to-reach groups, the population groups evaluated were:

	Drug users	Homeless groups	Immigrants/new entrants/foreign-born	Prisoners	Mixed hard-to-reach groups
Identification review	8	5	19	5	0
Management review	7	5	6	4	4

The populations targeted in this review that specifically compared effectiveness and cost-effectiveness of different services structures were:

	Drug users	Homeless groups	Immigrants/new entrants/foreign-born	Prisoners	Mixed hard-to-reach groups
Service structure review	3	2	2	1	1

How does engagement in various service models/organisational structures differ by group/subgroup (in terms of hard-to-reach group, age, or gender)?
No study was identified in this review that explored the differences in outcome by population. However, two studies compared the effectiveness and/or cost-effectiveness of different organisational structures in different hard-to-reach groups (Bothamley et al.,

2002[-]; Miller et al., 2006[+]). It was difficult to determine in these studies whether the differences found in the identification of TB were due to population characteristics such as the engagement of the different populations or due to the differences in setting, limiting any conclusions which can be made.

6.1 Key findings

There were a limited number of studies identified for this review that compared the effectiveness or cost-effectiveness of service structures to manage TB in hard-to-reach groups, all of which included a different hard-to-reach group and explored a different service structure, meaning that the effects of each variable were difficult to clarify, and preventing a synthesis of data across studies. Despite this, the key findings of the included studies are reported below. In addition, a summary of the service structures found in the literature from the previous two quantitative reviews on the identification and management of TB are provided below.

6.1.1 Key findings by healthcare worker

The evidence map of the literature from the identification review demonstrated that a range of healthcare workers were used to conduct active case finding, from nurses to consultant radiologists and chest physicians and, in most cases, with more than one healthcare worker used to identify TB in hard-to-reach groups. There was also some suggestion that the type of healthcare worker used may have reflected, or determined, the tool used to identify TB in hard-to-reach groups. For example, a consultant radiologist or chest physician was used in studies that delivered chest X-ray screening (Citron et al., 1995[+]; Dasgupta et al., 2000[+]; Puisis et al., 1996[-]); while nurses (with no input from another healthcare worker) and peer health advisers were used in studies that conducted TST and provided incentives (Malotte et al., 1998[++]; Malotte et al., 1999[++]; Pilote et al., 1996[++]).

The evidence map of the literature from the management review found that several management interventions were led by peers, including peer support (Chaisson et al., 2001[+]; Kominski et al., 2007[+]; McCue & Afifi, 1996[-]); peer support plus incentives (Kominski et al., 2007[+]); and Directly Observed Preventive Therapy (DOPT; Tulsky et al., 2000 [+]). The other healthcare workers who delivered DOPT were nurse and/or outreach workers (Chaisson et al., 2001 [+]; Gourevitch et al., 1998 [+]); health workers (Rodrigo et al., 2002[-]); and pharmacists (Juan et al., 2006[+]). Other healthcare workers who led an intervention were general chest clinic staff, who provided incentives to adhere to treatment (White et al., 1998 [+]); prison discharge planners, who delivered an educational intervention (White et al., 2005 [+]); and a multidisciplinary team, who delivered a service model approach/social care support programme (White et al., 2003[+]).

The evidence maps illustrate the type of healthcare worker that was used to identify and manage TB found in the literature from the previous two quantitative reviews;

however, this final review found only one study that explored the effectiveness of different healthcare professionals to identify and manage TB in hard-to-reach groups. There was moderate evidence from one RCT (Ricks, 2008[++]) that peers who were former drug users were more likely to encourage the identification of contacts by drug users with active TB compared with 'standard' healthcare workers (p=0.03). However, the findings were limited because the peer-led intervention also had enhanced case management compared to the control group that had limited case management. The study also found that the probability of completing treatment was statistically greater when peers delivered enhanced case management to drug users compared with limited case management delivered by a healthcare worker (RR=2.68, 95% CI 1.24 to 5.82; p=0.01; Ricks, 2008[++]).

6.1.2   Key findings by setting

The evidence map of the literature from the identification review on the setting used to identify TB demonstrated that for many studies, the setting was specific to the hard-to-reach group targeted. These population-specific settings included:
* pre-immigration screening for immigrants;
* port of arrival centres for immigrants;
* needle exchange programmes for injecting drug users;
* homeless centres; and
* prisons.

Similarly, the evidence map of the literature from the management review on the setting used to manage LTBI also found settings that were specific to the hard-to-reach group targeted, including:
* pre-immigration setting for immigrants;
* prisons; and
* methadone clinics.

However, across the literature to manage latent and active TB, the setting most often used was a specialist TB clinic.

There was a suggestion from moderate and weak evidence conducted for this review on effective service structures that more specialist settings might be associated with better outcomes, such as drug users being managed in drug clinics and/or alongside methadone treatment; homeless people managed in centres for the homeless; and immigrants managed at specialists TB clinics (compared with more general medical settings such as GP surgeries).The studies which support this are described in further detail below.

Moderate evidence from one RCT (Malotte et al., 2001[++]) suggests that adherence to treatment for LTBI was similar among drug users when DOPT was conducted onsite in a drug services facility (60%, 33/55) or in an outreach setting at a site chosen to be convenient for the participant (52.8%, 28/53); however, these differences were not

statistically compared. There was also weak evidence that there was statistically no significant difference in the management of active TB if DOT occurred onsite at a healthcare service or in the community at a site convenient for people with active TB, in mixed hard-to-reach groups (Deruaz & Zellweger, 2004[-]). However, the conclusions that can be drawn from this study were limited because there were systematic differences between groups in how treatment outcomes were collected and potential selection bias between groups.

Moderate evidence from one RCT (Umbricht-Schneiter et al., 1994[+]) found that a greater proportion of intravenous drug users who were managed onsite at a methadone clinic enrolled and complied with medical treatment (including treatment for TB; p<0.001); were seen one or more times (p<0.001); and had a greater mean number of visits per patient (p<0.001) compared with those referred to an offsite medical service. The outcomes relating to TB treatment alone were not statistically compared, however, the study suggests that there were more favourable treatment outcomes when services for managing TB (and other medical conditions) were conducted onsite at a methadone clinic for intravenous drug users compared with referring participants to other offsite medical services.

There was weak evidence from one prospective cohort study (El-Hamad et al., 2001[+]) that suggests that a service model that conducts a two-stage active case-finding approach onsite in a TB clinic may be more effective than a three-stage approach in a primary care clinic that requires referral to a nearby TB clinic for chest X-ray in new entrants (OR=2.57; 95% CI 1.92 to 3.42). However, there were statistically significant differences between the groups at baseline that were not adjusted for in the analysis.

There was weak evidence from one study (Bothamley et al., 2002[-]) regarding the effectiveness of active case finding conducted in three settings: POA clinic; homeless centre and GP setting for new entrants (who registered for the first time to the GP practice). For the coverage of a symptom questionnaire, the homeless centre (98.1%, 262/267) had the most favourable outcomes compared with the POA clinic (15.8%, 199/1,262; the coverage in the GP setting was not known). However, the yield of active TB was highest in the POA clinic (N=3) compared with the other two settings (N=0). There was also weak evidence that the POA clinic result in cost-savings while in the other settings, screening was not cost-saving. The study findings were limited due to the differences in populations targeted in each group.

There was weak evidence from one before-and-after study (Mor et al., 2008[-]) that found that screening in a pre-immigration setting may reduce the risk of developing TB in new entrants from Ethiopia to Israel compared with post-immigration screening, with a shorted detection period from entry into Israel and TB diagnosis (OR=0.72, 95% CI 0.59-0.89; p=0.002). There was also weak evidence that screening Ethiopian immigrants in a pre-immigration setting would result in net direct savings of $449,817 in a five-year time horizon (assuming that 98 more individuals would be free of TB

screening in this setting) compared with screening in a post-immigration setting (Mor et al., 2008[-]). The findings are limited because the study did not address the potential differences in TB incidence between the two time periods that screening occurred.

Weak evidence from one study (Miller et al. 2006[+]) found that overall there were more favourable outcomes when active case finding occurred in a homeless setting compared with a prison setting, with a higher yield of positive TST (p<0.001) and prescription of treatment for LTBI or active TB (p<0.001). However, there was no statistically significant difference in the coverage of TST between the two settings (p=0.179). There was also weak evidence that the costs per active TB case prevented by identifying and treating each person with LTBI was lower in the homeless setting ($14,350) compared with a prison setting ($34,761). The study findings are limited because each setting targeted a different population making it difficult to determine whether the outcomes are due to the setting and/or the population targeted.

6.2   Strengths and weaknesses of the review

This evidence review was conducted in accordance with NICE's methods manual for public health reviews. Searches were highly sensitive and encompassed a wide range of sources, and safeguards to ensure reliability were in place throughout the process of screening, data extraction and quality assessment, and data synthesis.

For the effectiveness review, the inclusion criteria regarding study methodology were inclusive. Studies that used either a comparison or control group (randomised or non-randomised), or presented data from before-and-after the intervention, was included. Studies that were limited to both a single group and a single time point were excluded on the grounds of methodology. This allowed the review to focus on the effectiveness and cost-effectiveness of service components to identify and manage TB in hard-to-reach groups.

The main weaknesses of the review were that only one study was conducted in the UK, and that there was only a limited number of studies that explored effective service model and/or structures to identify and manage TB in hard-to-reach groups. Half the studies were from the USA, limiting the applicability of the review to the UK. In addition, half the studies were of weak quality (4/8) and there were no strong evidence statements. For evidence statements to be classified as strong there needs to be clear conclusions from multiple high quality studies that are not contradicted by other high quality or moderate quality studies. Due to the paucity of studies (N=8) all comparing different service structures in different hard-to-reach groups, it was not possible to combine studies in an evidence statement. More research is needed on effective service structures for identifying and managing TB in hard-to-reach groups.

6.3 Gaps in the evidence

The main gap in the evidence is that there was a limited number of comparative studies that explored the effectiveness and cost-effectiveness of different service structures to manage TB in hard-to-reach groups. Owing to this, there are limited conclusions which could be drawn from these studies. In addition, the studies identified in the review compared different service structures and different hard-to-reach groups, therefore, the results could not be synthesised across studies.

Another gap in the evidence is the limited number of high quality studies. Half the studies included in the review were of poor quality (4/8). In addition, the review did not include any strong evidence statements. The three evidence statements that were considered moderate quality were relevant to drug users, reducing the applicability of the findings to other hard-to-reach groups.

6.4 Conclusions

The conclusions which can be drawn from this review are limited as the majority of the evidence is weak and the results could not be synthesised across studies. The results of the individual studies with moderate evidence suggest that it is effective to use peers to identify contacts and manage active TB compared with healthcare workers among drug users; and to treat intravenous drug users for co-morbid medical problems (including TB) in a methadone clinic or other drug services facility. However, more research is needed in the UK on the effectiveness and cost-effectiveness of different service structures to manage TB in hard-to-reach groups.

6.5 Implications identified by the review team

The first qualitative review of barriers and facilitators in the identification and management of TB found that members of hard-to-reach groups viewed professionals to be both potential barriers and facilitators to care. The barriers included: negative attitudes of staff; lack of confidence in or misdiagnoses by healthcare professionals; stigma from healthcare workers; and language and culture where communication barriers arise. Professionals were found to be facilitators to care when the standard of care was of high quality and professionals were respectful, and when services were adapted to the cultural needs of hard-to-reach groups. Although it is clear that the healthcare worker plays a key role in hard-to-reach groups accessing services, the only study identified in this review that explored the effectiveness of using different types of staff was focused on the use of peers from the same hard-to-reach group to identify and manage TB in substance users. This study found that peers may be more effective in identifying contacts of hard-to-reach groups and promoting treatment adherence than professional healthcare workers, possibly by breaking down these barriers. These results are supported by the other quantitative reviews in this series, which found some evidence to support the use of peers to lead the identification of TB in the homeless

and for peer-support interventions to manage LTBI in drug users, although the evidence was inconsistent in immigrants.

The management review found mixed results regarding the effectiveness of DOPT/DOT to manage LTBI/active TB. The evidence map of the literature from the management review demonstrates that a range of healthcare workers and other support 'staff' were used to provide DOPT/DOT, including pharmacists, peers and family members. Due to the variability in results, it is important to understand which service structures, including the type of healthcare professionals used, are most effective at managing TB in order to explain the variability between studies and to improve outcomes for hard-to-reach groups. We know from this review that for drug users, conducting DOPT/DOT via outreach may have no added benefit compared with conducting DOPT/DOT onsite at a drug service facility (although better high quality studies are needed), but we do not know if the type of professional group who delivers the intervention makes an impact on treatment outcomes. Therefore, further research is needed into the effectiveness and cost-effectiveness of such service structures to understand which are the most beneficial TB service structures for hard-to-reach groups.

Although the evidence found in this review was weak, it suggests that specialist settings including those of relevance to the hard-to-reach group may be an effective location to identify and manage TB including drug treatment clinics for drug users who may also be undergoing methadone maintenance and homeless centres for the homeless. Other specialist settings that may be effective are TB clinics compared with more general health services. We also found weak evidence that providing outreach services that takes the treatment to these hard-to-reach groups at convenient settings for the participant may not lead to any greater treatment outcomes compared with treatment provided at a central location. In addition, peers may be effective in identifying contacts and managing TB compared with other standard healthcare professionals.

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8.0 Glossary

Active case finding: is the process of identifying clinical cases of TB at the earliest possible stage in people who are not seeking medical attention for TB. For example, systematically offering chest X-rays to individuals, regardless of symptoms of TB.

Active TB: TB that is symptomatic and may be contagious, typically confirmed by sputum cultures.

B notification: is a screening programme in the USA where new entrants are tested for TB prior to entry into the USA. Those with X-ray signs of active TB but a negative culture are given a B1 notification; those with X-ray signs of inactive infection are given a B2 notification.

Case management: involves an individual healthcare professional taking responsibility for the co-ordination of care of a patient.

Chest X-ray: are used to check for lung abnormalities that indicate the presence of current or previous TB infection. They cannot determine, however, whether the infection is latent or active.

Coverage uptake: of screening refers to the number of people who were eligible for screening that were screened.

DOPT —Directly Observed Preventive Therapy: any intervention that involves the observation of participants ingesting their prescribed doses for LTBI.

DOT—Directly Observed Therapy: any intervention that involves the observation of patients ingesting their prescribed doses for active TB. NICE (2006) currently recommend the use of DOT for active TB in patients at risk for non-adherence to treatment using a thrice-weekly dosing regimen. None of the studies identified for this review used this dosing regimen.

Drug users: individuals who take any illegal recreational drug including intravenous drugs such as heroin and non-intravenous drugs such as cocaine.

Foreign-born: includes those who were born outside of the country in which they are currently living. It includes both permanent residents and temporary visitors on a work or student visa.

Hard-to-reach-groups: any group that has difficulty accessing or remaining in services for TB.

Intravenous Drug Users (IDU): includes drug users who primarily take intravenous drugs.

ILOM—Indigenous Leader Outreach Model: services delivered by a peer who is or was a member of the hard-to-reach group, who actively identifies other members of the group and offers care in the community.

Immigrant: a person who has come into a foreign country to live there permanently, not as a tourist or visitor.

Incentives: any intervention that uses cash or a voucher with a monetary value to encourage desired behaviour in the patient. These can be one-off incentives at the start or end of treatment, or offered at regular intervals throughout the duration of the intervention.

Latent Tuberculosis Infection (LTBI): TB that is asymptomatic, but can convert to active disease over time. Identification based on active or passive screening, usually with TST, QFT-G.

MDT—Multi-Disciplinary Team: a team involving members of more than one health or social service profession.

NA—Not Applicable

NR—Not Reported

New entrants: people recently arriving in or newly returning to a country.

Peer support: any intervention, individual- or group-based, that is led by a member of the same hard-to-reach group as the patient's own, with the emphasis on providing support to the patient, and may include sharing of information about TB.

Passive case finding: is the process of identifying clinical cases of TB among those who present to health services because of symptoms relating to TB.

Port of arrival: the entry point at which new entrants arrive into a country, which can be used as a site to actively screen people for TB.

Post-immigration screening: involves screening for TB among new entrants once they have arrived in the country.

Prisoners: people residing in a prison for either a remand period or for a convicted offence. This population also overlaps with other hard-to-reach groups due to prisoners being disproportionately derived from hard-to-reach communities, for example, drug users.

PPD—Purified Protein Derivative

RCT—Randomised Controlled Trial

RR—Relative Risk

SAT—Self-Administered Therapy

QuantiFERON-TB Gold (QFT-G): is an *in vitro* test to diagnose TB, typically LTBI, by collecting a sample of blood to quantify the interferon gamma released from lymphocytes to measure a person's immune reactivity to TB.

Service model approach/social care support: any intervention that goes beyond the treatment of TB to also offer, for example, access to other medical and mental health services and social care support. Social care support can include, but is not limited to, social work referrals, food and clothing, and housing and financial support.

Sputum culture: is used to identify TB by growing colonies of bacteria indicative of TB from sputum samples.

Sputum smears: are used to identify TB by examining a sample of sputum for bacteria indicative of TB.

TAU—Treatment as Usual

TB contacts: people in close contact with someone diagnosed with active TB. These individuals are at increased risk for developing TB and are therefore targeted for screening.

Tuberculin Skin Test (TST): are tests used to identify TB, typically LTBI, based on a delayed hypersensitivity response to the injection of purified protein antigen into the skin, occurring within 48 to 72 hours.

Yield of screening: refers to the number of cased of TB (latent or active) identified by a test.

9.0 Appendix A: Search strategies and results

9.1 Database searches

The search strategy was written at the Centre for Evidence and Policy, King's College, London, in partnership with Matrix Reviews, Dr Gill Craig of City University, London, and NICE. All results were imported into a bibliographic management tool for screening and management.

The search approach was systematic and exhaustive. One comprehensive strategy was written to locate references relevant to the three quantitative reviews (see section 8.1.1 below). Additional, targeted searches were conducted subsequently in four databases (see section 8.1.2 below).

Table A1. Database searches results

Database	Hits
Assia*	658
British Nursing Index	48
CRD (DARE, HTA, NHS EED)	200
CINAHL	2,023
Cochrane Library (Reviews)	683
Current Contents	3,147
ECONLIT	99
EMBASE*	10,359
ERIC	58
HMIC	171
Medline*	7,574
Medline In-Process	352
PsycINFO	373
SPP	50
Soc Abs*	431
Social Services Abstracts	102
Web of Science	5,141
Total	*31,469*

*Additional searches were conducted in these databases.

Note: After de-duplication, there were a total of 15,354 unique studies.

9.1.1 Searching of electronic databases: strategy

1. exp Tuberculosis/ or (tuberculosis or tb).ti,ab.
2. ((hard$ adj2 reach) or (hard$ adj2 locate) or (hard$ adj2 find) or (hard$ adj2 treat) or (difficult adj2 locate) or (difficult adj2 engage) or social$ exclu$ or

social inequalit$ or (difficult$ adj2 reach) or (difficult$ adj2 find) or (difficult$ adj2 treat)).ti,ab.

3. (geograph$ or transport$ or physical and (barrier$)).ti,ab.
4. (low$ or poor$ or negative and (quality adj2 life)).ti,ab.
5. ((vulnerable or disadvantaged or at risk or high risk or low socioeconomic status or neglect$ or affected or marginal$ or forgotten or non-associative or unengaged or hidden or excluded or transient or inaccessible or underserved or stigma$ or inequitable) and (people or population$ or communit$ or neighbourhood$1 or neighborhood$1 or group$ or area$1 or demograph$ or patient$ or social$)).ti,ab. or Vulnerable populations/
6. poverty area/
7. (refuser$1 or nonuser$1 or non-user$1 or non user$1 or discriminat$ or shame or prejud$ or racism or racial discriminat$).ti,ab.
8. social support/ or *social conditions/ or stigma/ or Social Isolation/ or *quality of life/ or Prejudice/ or Socioeconomic Factors/
9. prisoner$1.ti,ab.
10. (recent$ adj2 release$ adj2 (inmate$ or prison$ or detainee$ or felon$ or offender$ or convict$ or custod$ or detention or incarcerat$ or correctional or jail$ or penitentiar$)).ti,ab.
11. ((prison$ or penal or penitentiar$ or correctional facilit$ or jail$ or detention centre$ or detention center$) and (guard$1 or population or inmate$ or system$ or remand or detainee$ or felon$ or offender$1 or convict$ or abscond$)).ti,ab.
12. (parole or probation).ti,ab.
13. *prisoners/
14. ((custodial adj (care or sentence)) or (incarceration or incarcerated or imprisonment)).ti,ab.
15. (immobile or (disabled and (house bound or home bound)) or (house or home adj3 (bound))).ti,ab. or Homebound Persons/
16. ((hous$ and (quality or damp$ or standard$ or afford$ or condition$ or dilapidat$)) or (emergency or temporary or inadequate or poor$ or overcrowd$ or over-crowd$ or over-subscribed and (hous$ or accommodation or shelter$ or hostel$ or dwelling$))).ti,ab. or housing/ st
17. (rough sleep$ or runaway$1 or (homeless$ or street or destitut$ and (population or person$1 or people or group$ or individual$1 or shelter$ or hostel$ or accommodation$1))).ti,ab. or exp homeless persons/
18. (drug$ or substance and (illegal or misus$ or abuse or intravenous or IV or problem use$ or illicit use$ or addict$ or dependen$ or dependant or delinquency)).ti,ab. or *Substance-Related Disorders/ or Drug users/ or Substance Abuse, Intravenous/
19. ((alcohol$ and (misus$ or abuse or problem$ use$ or problem drink$ or illicit use$ or addict$ or dependen$ or dependant or delinquency)) or alcoholic$1).ti,ab. or *Alcohol-Related Disorders / or Alcoholics/
20. (prostitution or sex work$ or transactional sex$ or prostitute$1).ti,ab. or Prostitution/

21. (poverty or deprivation or financial hardship$).ti,ab.
22. (low-income or low income or low pay or low paid or poor or deprived or debt$ or arrear$ and (people or person$1 or population$1 or communit$ or group$ or social group$ or neighbourhood$1 or neighborhood$1 or famil$)).ti,ab.
23. poverty/
24. (low$ and (social class$)).ti,ab.
25. (traveller$1 or Gypsies or Gypsy or Gipsy or Romany or Roma).ti,ab. or gypsies/
26. (mental$ and (health or ill or illness)).ti,ab. or *mental health/ or Mentally Ill Persons/
27. (health care worker$1 or (health care adj2 service provi$) or (health-care adj2 provi$)).ti,ab.
28. (complex adj2 (patient$ or Need$)).ti,ab.
29. (outreach adj2 worker$1).ti,ab. or Community health aides/
30. (support adj2 worker$1).ti,ab.
31. (case adj2 worker$1).ti,ab.
32. (social adj2 worker$1).ti,ab.
33. social care professional$1.ti,ab.
34. ((social care adj2 service provi$) or (social-care adj2 provi$)).ti,ab.
35. ((language$ or communicat$ and (barrier$ or understand$ or strateg$ or proficien$)) or translat$ or interpret$ or (cultur$ and (competen$))).ti,ab. or Communication Barriers/ or *Language/
36. (immigrant$ or migrant$ or asylum or refugee$ or undocumented or foreign born or UK born or non-UK born or non UK born or (born adj overseas) or (displaced and (people or person$1))).ti,ab. or "Emigration and Immigration"/ or refugees/
37. "Transients and Migrants"/
38. "Emigrants and Immigrants"/
39. or/2-38
40. (Intervention$).ti,ab. or Crisis Intervention/
41. ((early or primary) adj2 Intervention$).ti,ab.
42. (person$ or individual or local$ or community or cultural or structural or supported or indicated or target$ or multi?component or comprehensive or pilot or media and (Intervention$)).ti,ab.
43. ((midstream or mid-stream) and intervention$).ti,ab.
44. (Identify$ or find or finding or locat$ or trac$ or contact$ or discover$ or detect or recruit$ or attract$).ti,ab.
45. (case finding or (active or passive adj3 (case finding))).ti,ab.
46. (program$ or scheme$1 or service$1 or campaign$ or mobili?ation or strateg$ or measure or policy or policies and (tuberculosis or tb)).ti,ab.
47. ((case adj3 management) or case-managed).ti,ab. or Case Management/ or Patient Care Planning/ or Managed Care Programs/ or Patient care management/
48. (case adj3 manag$ adj3 strategy).ti,ab. or continuity of patient care/

49. (treat$ or diagnosis and (management)).ti,ab.
50. (active or passive and (Case adj3 Management)).ti,ab.
51. (risk assess$ or risk profile or risk Indicator or care plan$).ti,ab.
52. ((service and (model$ or deliver$))).ti,ab. or delivery of health care/ or *health services/ or Urban health services/
53. ((primary adj3 healthcare) or (primary adj3 health$ or care)).ti,ab. or exp Primary Health Care/
54. (nurse or ((general or family) adj3 (practice$ or practitioner$ or physicians$ or doctor$))).ti,ab. or Nurses/ or 1/ or Family practice/ or Physicians, Family/
55. ((health or extension or multi-disciplinary or multidisciplinary) and (professional$ or personal$ or practitioner or worker$ or partner$ or promot$ or provider or care team or care provider or unit or casework$ or (case adj2 work$))).ti,ab. or *Health Personnel/ or Nurses' Aides/
56. (social adj2 (work$ or Support$ or Outreach)).ti,ab. or social work/ or Social Support/
57. (lay or allied or link and (professional$ or practitioner$1 or worker$1 or advocate$1 or personnel)).ti,ab. or Allied Health Personnel/
58. (volunteer$ or voluntary or charit$ or third sector).ti,ab. or Voluntary Workers/ or exp Voluntary health agencies/
59. (health adj1 (center$1 or centre$1 or facilit$ or service$ or clinic$1 or hospital$1 or program$1)).ti,ab or Community Health/ or "Catchment Area (Health)"/
60. ((day adj2 (care or hospital$ or patient$)) or workshop$).ti,ab. or day care/
61. (rehab$).ti,ab. or rehabilitation centers/
62. (dedicated or permanent or rapid access or fixed or TB or tuberculosis and (clinic$1 or centre$1 or center$1 or program$)).ti,ab.
63. (((drug adj2 dependency) or substance abuse or HIV) and (unit$ or clinic$1 or centre$1 or center$1 or program$) and (tuberculosis or tb))).ti,ab. or Substance Abuse Treatment Centers/
64. (pharmac$ or dispensary).ti,ab. or Pharmacies/ or Community Pharmacy Services/
65. (communit$ or (support$ adj2 communit$)).ti,ab. or *Community Health Services / or *Community Networks / or Community Health Aides/ or *Community-Institutional Relations/ or community hospital/ or Community Health Nursing/
66. (directly observed treatment or directly observed therapy or (supervised adj2 treatment) or (coerc$ adj2 (treat$ or therapy))).ti,ab. or Directly Observed Therapy/
67. (ambulatory adj2 care).ti,ab. or ambulatory care/ or Ambulatory Care Facilities/
68. ((mobile or travel$ or transport$ or workplace or work-place or tertiary) and (health adj3 (care or work$ or practitioner$ or professional$ or service$ or center$1 or centre$1 or unit$1 or program$))).ti,ab. or Mobile Health Units/
69. ((mobile or travel$ or transport$ or workplace or work-place or tertiary) and (nurs$ or doctor$)).ti,ab.

70. ((out adj3 hours) or (after adj3 hours) or telephone or telemedicine).ti,ab. or after-hours care/ or Telemedicine/
71. ((walk-in or walkin or walk in) adj2 (center$1 or centre$1 or service or program$ or Clinic$1 or Session or Assesment$1)).ti,ab.
72. ((drop$ adj1 in) adj2 (center$1 or centre$1 or service or program$ or clinic$1 or session or meeting or assesment$1)).ti,ab.
73. (((health or home$ or house$) and (call$ or visit$)) or (home-care or home-based or (support$ adj1 hous$))).ti,ab. or Home Health Aides/ or home care services/ or *House Calls/
74. ((early adj2 discharge) or (recent$ adj2 discharged) or (out adj2 patient)).ti,ab. or patient care/ or outpatient clinics, hospital/ or patient care team/
75. (counselling or counseling or counsellor or counselor or (integrated counselling adj1 testing centre$1) or (integrated counselling adj1 testing center$1) or ICTC).ti,ab. or Counseling/ or Directive Counseling/
76. ((help adj2 group$) or (self adj2 help) or support$ or (peer adj2 peer)).ti,ab. or Self-Help Groups/
77. (collaborat$ or shared or (integrated adj1 care$) or ICP or network$ or co-locat$ or (one adj1 stop)).ti,ab. or "delivery of health care, integrated"/
78. ((health adj2 education) or (skill adj2 mix) or (role adj2 develop$) or leadership or (interdisciplinary or inter-team or Professional or team adj2 (communicate$))).ti,ab. or exp Health Education/ or Interdisciplinary Communication/ or Leadership/
79. (outreach or mobile$ or satellite$ or hub or spoke or rural or urban or street or pavement$1 or sidewalk$1 or corner or shelter or hostel or sanatorium or sanitorium or sanitarium and (tuberculosis or tb)).ti,ab.
80. or/40-79
81. (test$).ti,ab.
82. (examination$1 or assessment$1 or identification or assay$ or detection).ti,ab.
83. (diagnosi$).ti,ab. or *diagnostic tests, routine/
84. ((chest adj2 x?ray) or chest radiograph or MXU).ti,ab. or Mass Chest X-Ray/
85. (screen$ or (new$ adj1 screen$)).ti,ab.
86. (monitor$ or sampling).ti,ab.
87. (target$ or focus$ or community or population or individual$ or person$ or opportunistic or coerc$ or voluntary or initiated and (test$ or diagnosis or screen$ or assay$ or detection)).ti,ab.
88. PIT.ti,ab.
89. provider initiated test$.ti,ab.
90. ((rapid or prompt or quick$ or earl$ or (point adj2 care)) and (test$ or screen$ or diagnosi$ or assay$ or detection)).ti,ab.
91. ((provider or anonymous or accurate or support$ or incentiv$ or counsel$) and (test$ or diagnosis or screen$ or assay$)).ti,ab. or Anonymous Testing/
92. (test$ adj2 (center$1 or centre$1 or unit$1 or setting)).ti,ab.
93. or/81-92

94. (acceptability or acceptable or attend$ or access$ or availab$ or non-attend$ or increas$ or promot$ or opt$ or particip$ or adhere$ or involvement or uptake or take-up or utiliz$ or utilis$ or refus$ or referr$ or self-referr$ or self-report$ or barrier$ or decreas$ or isolation or interven$ or aware$ or opportunit$ or advice or information or incentiv$ or recruit$ or find or finding or compliance or comply or retain or retention or provision or encour$ or usage).ti,ab.

95. (socio sanitary support or reimburs$ or (social adj2 support) or (cash or financial or money or monetary or economic or voucher or credit or drug$1 or methadone or telephone adj2 (benefit$ or support or incentive or assist$ or credit))).ti,ab. or Reimbursement, Incentive/

96. (((lifestyle or behavio?r) adj2 (therapy or modif$ or chang$ or adapt$ or adopt$)) and (tuberculosis or tb)).ti,ab. or social marketing/

97. "Marketing of Health Services"/

98. Attitude to health/

99. Health Services Accessibility/

100. Access to information/

101. Confidentiality/

102. Health education/

103. Health promotion/

104. Patient acceptance of health care/

105. Patient compliance/

106. Motivation/

107. Stigma.ti,ab.

108. prevalence/

109. *Consumer Participation/

110. or/94-109

111. (treat$).ti,ab. or Treatment Outcome/

112. (directly observed treatment or directly observed therapy or (supervised adj2 treatment) or (coerc$ adj2 (treat$ or therapy))).ti,ab. or Directly Observed Therapy/

113. (disease management or (treat$ and (management or control))).ti,ab.

114. ((adherence or compli$ or non-compli$ or default$ or finish$ or Retention or attrition or (drop adj1 out) or disappear$ or abscond$) and (treat$)).ti,ab. or exp Patient Compliance/

115. ((referr$ or self-referr$ or (self adj diagnos$)) and (treat$)).ti,ab.

116. ((suitab$ or eligib$) and (treat$)).ti,ab.

117. ((follow adj1 up) or (discharge)).ti,ab. or Follow-Up Studies/

118. ((positive or negative) and (test)).ti,ab.

119. ((interrupt$ or relapse$ or stop$ or cessation or with?ld$ or avoidance or (lost adj2 follow)) and (treat$)).ti,ab. or *Withholding Treatment/

120. ((medicine$1 or drug or treat$) and (regimen or adherence)).ti,ab.or exp self care/

121. (treat$ and (appointment$ or Schedule$)).ti,ab. or "Appointments and Schedules"/

122. ((care adj2 seeking) and (pathway$)).ti,ab.
123. (case adj3 management or case-managed).ti,ab. or Case Management/ or Patient Care Planning/ or Managed Care Programs/ or Patient care management/
124. (case adj3 manag$ adj3 strategy).ti,ab. or continuity of patient care/
125. ((case or treat$ or diagnosis) and (management)).ti,ab.
126. ((active or passive) and (case adj3 management)).ti,ab.
127. ((risk assessment or care plan$) and (case adj3 management)).ti,ab.
128. or/111-127
129. (1 AND 39 AND (80 OR (93 AND (110 OR 128))))
130. limit 129 to yr="1990 -Current"
131. limit 130 to "English Language"
132. (animal$ or badger$ or Cow$ or Cattle or bovine).ti,ab. or (animals/ not humans/)
133. 131 not 132

9.1.2 Additional searches: strategy

Additional searches were conducted in PubMed, Medline, ASSIA and SocAbs, following discussion on an earlier review with the PDG. These searches specifically targeted four topics:

1. religion/religious groups as a hard-to-reach group;
2. illiteracy and benefits as a poverty term;
3. engaging community leaders/champions/advocates; and
4. patient and professional relationships.

The following clusters were added to the tuberculosis line described above (exp Tuberculosis/ or (tuberculosis or tb).ti,ab.):

For topic 1:

(christian* or church* or chapel* or priest* or vicar* or catholic* or catholicism or protestant* or methodist* or baptist* or Jehovah* or presbyterian* or anglican* or pentecostal*).ti,ab.
(muslim* or islam* or mosque* or imam*).ti,ab.or jews/ or (jew* or judaism* or synagogue*).ti,ab.
exp religion/ or (christian* or church* or chapel* or priest* or vicar* or catholic* or catholicism or protestant* or methodist* or baptist* or Jehovah* or presbyterian* or anglican* or pentecostal*).ti,ab.
jews/ or (jew* or judaism* or synagogue*).ti,ab.
(sikh* or hindu* or buddhis* or temple*).ti,ab.
((religion* or religious* or faith*) and (people* or person* or group* or population or neighbour* or neighbor* or patient* or communit*)).ti,ab.

For topic 2:

(illitera$ or welfare benefit$ or social benefit$)

For topic 3:

(community adj1 leader$ or community adj1 Manag$ or advocat$ or champion$) and (engag$ or involv$)

For topic 4:

professional-family relations/ or professional-patient relations/ or nurse-patient relations/ or physician-patient relations/ or patient relationships

9.2   Website searches

The following websites and databases were searched manually for relevant literature:

Table A2. Website searching details

Website	Web-link	Notes	Included on abstract
Action - Advocacy to Control TB Internationally	www.action.org	-	0
British Infection Association	www.britishinfection.org	-	0
Centers for Disease Control and Prevention	www.cdc.gov/tb	Searched for resources on TB	4
Centers for Disease Control TB-Related News and Journal Items Weekly Update mailing list archives	www.cdcnpin.org/lyris/ui/listservs.aspx	-	0
Centers for Disease Control National Prevention Information Network	www.cdcnpin.org/scripts/tb/index.asp	-	0
NICE, including former Health Development Agency	www.nice.org.uk	Searched for (TB or tuberculosis)	0
NHS Evidence	www.evidence.nhs.uk	Searched for (TB or tuberculosis)	2
Stop TB Partnership	www.stoptb.org	-	0
TB Alert	www.tbalert.org	-	0
UK Coalition to Stop TB	www.stoptbuk.org	-	0
World Health Organization	http://www.who.int/tb/en/	Searched the WHO Library database	0
WHO Global Health Atlas	http://apps.who.int/globalatlas/dataQuery/default.asp	-	0
Health Protection Agency	www.hpa.org.uk	Tuberculosis (publications)	0
British Thoracic Society	www.brit-thoracic.org.uk	Tuberculosis (all fields)	2
Public Health Observatories	www.apho.org.uk/resource/searchoptions.aspx	Tuberculosis (all fields)	0
BL Direct*	Database	tuberculosis (all fields; one week date limit)	0
Community Abstracts via Oxmill*	Database	Tuberculosis (all fields)	3
Google Scholar*	Database	tuberculosis AND (identifying OR managing OR "at risk" OR "hard to reach" OR "service models" OR immigrant OR migrant OR prisoner OR asylum OR refugee OR "drug use" OR homeless)	22
National Research Register archive site*	Database	Tuberculosis (all fields)	1
UK Clinical Research Network*	Database	Tuberculosis	0

*These databases were treated as hand-searching

9.3 Other sources

We requested recommendations from our expert advisor, Dr Gillian Craig, and the PDG Chair, Andrew Hayward. As part of the guidance development process, NICE also carried out a call for evidence (see section 8.4, below).

9.4 Call for evidence

Table A3. Additional studies included after the call for evidence

Full Reference (E.g. Author, date of publication, full title of paper/report and where a copy can be obtained)	Screening code
Bodenmann, P., Vaucher, P., Wolff, H., Favrat, B., Tribolet, F., Masserey, E., Zellweger, J. P. (2009). Screening for latent tuberculosis infection among undocumented migrants in Swiss healthcare centres; a descriptive exploratory study. *BMC Infect Dis*, *9*(1):34.	Non-comparative
Carr, R., & Dukes, R. (2009). *Report, findings and recommendations from a consultation with newly arrived people focused on ways to improve uptake of and increase general awareness of Tuberculosis and Tuberculosis screening in Leeds*.	Non-comparative
Peterborough TB Awareness Pilot Programme 2008/09 Report; produced by McGuire C and Pankhania G, Public Health, NHS Peterborough, April 2009.	Non-comparative

9.5 Citation chasing

After full-text screening was completed, the citation lists of included studies and relevant systematic reviews were scanned for relevant titles, which were then screened

for inclusion. This yielded no new included studies. Forward citation-chasing was conducted for all included studies using Google Scholar. This yielded 165 references, of which no new study was included in this review.

10.0 Appendix B. Screening checklist

Table B1. Screening checklist

Q	Question	Hierarchy	Code	Notes
1.	Does the study have a focus on **TB services** of any kind?	YES/ UNCLEAR – go to Q2	NO – exclude **1_EX.TB**	Studies need not focus on TB services exclusively, but must present data relating to TB services (preventing, screening, treating). Abstracts regarding infectious diseases in general, which do not mention TB, should be excluded. Studies on the following should also be excluded: • epidemiological research (prevalence of TB, mapping of spread); • the microbiology of TB; • the pharmacology of specific treatments; without reference to services; • preventive TB vaccine (e.g. BCG); • the effectiveness of different tests for diagnosing active and latent TB; • drug treatment regimens (drugs used, dosage, frequency, and duration); and • clinical effectiveness of drug treatment and/or surgery.
2.	Was the study published in **1990 or later**?	YES/ UNCLEAR – go to Q3	NO – exclude **2_EX.DATE**	
3.	Is the study report in **English**?	YES/ UNCLEAR – go to Q4	NO – exclude **3_EX.NON-ENG**	
4.	Was the study conducted in an **OECD country**?	YES/ UNCLEAR – go to Q5	NO – exclude **4_EX.OECD**	OECD countries are taken to include: Australia; Austria; Belgium; Canada; Chile; Czech Republic; Denmark; Finland; France; Germany; Greece; Hungary; Iceland; Ireland; Israel; Italy; Japan; Luxembourg; Mexico; the Netherlands; New Zealand; Norway; Poland; Portugal; South Korea; Slovakia; Slovenia; Spain; Sweden; Switzerland; Turkey; the UK; and the USA.
5.	Does the study include data from any **hard-to-reach group**?	YES/ UNCLEAR – go to Q6	NO – exclude **5_EX.POP**	Hard-to-reach groups at risk of TB: children, young people and adults whose social circumstances or lifestyle, or those of their parents or carers, make it difficult to: • recognise the clinical onset of tuberculosis; • access diagnostic and treatment services; • self-administer treatment (or, in the case of children and young people, have treatment administered by a parent or carer); or • attend regular appointments for clinical follow-up. Hard-to-reach groups include, but are not limited to: prisoners; problem drug users or people with alcohol

				problems; homeless people or people in temporary accommodation; asylum-seekers, refugees, and recent immigrants; Gypsies/travellers/Romas; and sex workers. Groups such as Aboriginal peoples or migrant populations that are not particularly relevant in the UK setting (e.g., Latino/Hispanic samples in the USA) are not considered hard-to-reach for this review. This criterion should be applied inclusively at abstract stage, i.e. any paper not specifically excluding such groups should be included.
6.	Does the study present any **quantitative empirical data**?	YES/ UNCLEAR – go to Q7	NO – exclude **6_EX.NON-EMP**	Include studies with quantitative empirical data. Exclude think pieces, policy documents, practice guidelines, non systematic reviews, etc.
7.	Does the study discuss an **intervention** relating to one of the following**:** **Identifying** **Managing** **Service models**	YES/ UNCLEAR - go to next section *Note which review using the tick boxes*	NO – exclude **7_EX.TOPIC**	IF INCLUDED, ALWAYS TICK A BOX. Exclude studies about interventions on the prevention of TB for people who do not have TB (latent or active). **Interventions** regarding **raising awareness** of TB or **identifying** people with TB (diagnosis/ screening). Include: • interventions aiming to increase the uptake of diagnostic services, such as advice and information from clinicians or other professionals, or educational interventions to raise awareness of the symptoms of TB or of the availability of diagnostic services; • outreach services targeted at particular groups, such as mobile clinics or diagnosis (e.g., mobile X-ray units) and referral services; • diagnostic completion (that is, that once TB is suspected, the diagnosis is confirmed). Exclude studies of the effectiveness of different tests for diagnosing active and latent TB. **Interventions** regarding **managing** TB, including **case management** and treatment compliance. Include: • interventions aiming to increase the uptake of treatment services, such as advice and information from clinicians or other professionals, or educational interventions to raise awareness of treatment services; • outreach treatment services targeted at particular groups, such as mobile clinics; • interventions aiming to identify people in need of additional support, or to support people to complete TB treatment. This may include, for example: case management approaches led by clinicians, multidisciplinary teams or specialist caseworkers; educational or psychosocial interventions to promote treatment adherence; interventions with professionals or patients to promote directly observed therapy (DOT); or interventions to identify people who have commenced

				treatment in the past, but are not known to have completed the full course of treatment. **Interventions** regarding **service models** and service structures for supporting TB identification and management. Include any organisational-level intervention aimed at improving TB diagnosis or treatment among hard-to-reach groups. This may include, for example: • the provision of new services, such as outreach clinics; • changes to service delivery or accessibility to reduce barriers to accessing TB services; • the provision of services in new settings or by different providers; • the adoption of new information or knowledge management schemes to facilitate service delivery; and • professional development and education; or • other interventions to raise clinicians' and other professionals' awareness of TB.
8	Is it a **(cost)-effectiveness study**?	YES/ UNCLEAR – 8_IN.EFF	NO – go to next section	Include if study presents effectiveness or cost-effectiveness data, which comes from one or more of the following study designs: • RCTs, non-randomised controlled trials; • one-group (pre-test – post-test), or two-groups designs (other than RCT or non-RCT); • any economic analysis (cost-benefit, cost-effectiveness, cost-utility analyses, cost evaluation or other cost analyses). If the study does not compare the intervention group with another group or time point, go to Q9. If the study is a systematic review or meta-analysis, go to Q10.
9	Is it **any other** type of quantitative primary research?	YES/ UNCLEAR – 9_IN.OTHER	NO – go to next section	
10	Is the study a **systematic review**?	YES/ UNCLEAR – 0_IN.SR	END	Include if the study is a systematic review or meta-analysis.
Flag	What hard-to-reach population is it?	Tick all boxes that apply		IF INCLUDED, ALWAYS TICK A BOX. • recent immigrant/asylum-seeker/refugee; • homeless; • drug misuse; • prisoner; • all other (e.g., Sex worker, Gypsy/traveller/Roma) – please note; • unclear/undefined.

For cases where inclusion is unclear, code as **Q_QUERY** and save to discuss with screening team.

11.0   Appendix C: Evidence tables

Study details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Bothamley et al. **Year:** 2002 **Citation:** Bothamley, G. H., Rowan, J. P., Griffiths, C. J., Beeks, M., McDonald, M., Beasley, E., Bosch, C. van den, et al. (2002). Screening for tuberculosis: the port of arrival scheme compared with screening in general practice and the homeless. *Thorax*, *57*(1), 45-49. **Aim of study:** To compare	**Source population/s:** New entrants into the UK and the homeless. **Eligible population:** New entrants and homeless in Hackney, London. **Selected population:** All new entrants who were contacts of TB cases and without a visible BCG scar, or symptomatic individuals under 35 years of age; all the homeless. **Excluded population:** Individuals who had no symptoms, were not new	**Method of allocation:** Self-allocation. **Intervention/s description:** 1) Tuberculin (Heaf) testing offered in general practice as part of the registration health check. 2) Tuberculin (Heaf) testing offered in centres for the homeless (three hostels, an emergency accommodation centre, and a drop-in centre). **Comparator/control/s description:** POA scheme, in which new entrants are offered Tuberculin (Heaf) testing in a clinic/hospital. Note: all patients across groups were	**Primary outcomes:** Cost per individual screened. Cost per individual per case of TB prevented. **Secondary outcomes:** Cases of TB, tuberculin reactors requiring chemoprophylaxis and BCG vaccinations [not extracted]. **Method of analysis:** comparisons were made using the chi-square test; 95% CI for the incidence of TB were calculated using the direct standardisation method described by Morris and Gardner. **Modelling method and assumptions:**	**Primary results:** Number screened with questionnaire: Hospital = 199/1262. Homeless = 262/267. GP = 45/unknown. Number screened with questionnaire who were eligible for TST: Hospital = 181/199. Homeless = 262/262. GP = 39/45. Number of active TB cases: Hospital = 3. Homeless = 0. GP = 0. Total costs: Hospital = £22,646. Homeless = £3,452. GP = £938. Savings (number of cases prevented): Hospital = £25,621 for 9.5 cases prevented. Homeless = £1,618 for	**Limitations identified by author:** The authors stated that there was still enough uncertainty around the data that recommendations cannot yet be made to replace the POA scheme by an assured registration health check in primary care. **Limitations identified by review team:** Groups are not comparable and no attempt was made to analyse or report baseline differences. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** None

the yield and costs of TB screening for new entrants in three settings: a new entrants' clinic within the port of arrival scheme; a large general practice; and centres for the homeless. **Study design:** Economic evaluation. **Type of economic analysis:** Cost analysis. **Economic perspective:** NR **Quality appraisal effectiveness studies:** **Internal validity:** NA **External**	entrants and had a BCG scar; those who had no symptoms or contact with TB and were over 35 years of age; those who had already been screened. **Setting:** Three venues in Hackney, London: a new entrants' clinic in Homerton Hospital; a large general practice with academic affiliations; and centres for the homeless (three hostels, an emergency accommodation centre, and a drop-in centre). **Sample characteristics:** 2,840 persons who visited one of the three venues. 1,434 were new entrants, of whom 416 were screened for TB. No socio-	first screened with a TB symptom questionnaire before a TST to determine if further testing was required. **Sample sizes:** **Total** 2,840. **Intervention** 1,578. **Control** 1,262. **Baseline comparisons:** NR **Study sufficiently powered?** NR	The study modelled the cost per case of TB prevented and assumed that a patient with a positive TST had a 10% risk of developing TB within the first 2 years of the test due to the effectiveness of chemoprophylaxis and estimates of HIV infection in the new entrant population. Includes nursing costs (calculated as time and % salary); medical equipment and material costs (disposable Heaf gun heads, tuberculin costs); clerical costs (time and % of salary, including stationery); treatment costs (chemoprophylaxis, outpatient visits, drugs, contact investigations, patient stay); and BCG vaccination costs. Calculation of cases prevented assumes that each case of TB	0.6 cases prevented. GP = £594 for 0.2 cases prevented. Cost per person screened: Hospital = £12.70 (savings). Homeless = £0.50. GP = £7.00. Cost per person screened for each case prevented: Hospital = £10.00. Homeless = £23.00. GP = £6.32. Sensitivity analysis: results were sensitive to cases detected; if a further case was detected at each location, the total cost per screened individual would be cost savings of £33 for hospital screening, £6 for GP and £11 for homeless. **Secondary results:** Not extracted. **Attrition details:** NR	

| validity: NA

Quality appraisal economic studies: **Quality score:** -
Applicability: ++ | demographic characteristics are provided for the sample as a whole.

Economic analysis data sources: Published literature. | | gives rise to three others.

Time horizon: NR | | |

Study details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Déruaz &. Zellweger **Year:** 2004 **Citation:** Dèruaz, J., & Zellweger, J., P. (2004). Directly-observed therapy for tuberculosis in a low	**Source population/s:** Mixed hard-to-reach groups with active TB, Switzerland. **Eligible population:** All the patients who started in the DOT programme from October 1997 to March 2000 and had ended treatment by March	**Method of allocation:** Natural allocation conducted retrospectively. Patients were assigned by the medical supervisor to management onsite at a TB centre (onsite DOT); or via social outreach, in a convenient location for the participant or in a centre that could address their social needs (outreach DOT).	**Primary outcomes:** <u>Treatment outcome:</u> Successful outcomes were those *cured* (with bacteriological confirmation) and those who had *completed* a full course of treatment (without bacteriological confirmation of cure). Unsuccessful	**Primary results:** <u>Treatment outcome by intensity of DOT:</u> *Full DOT:* Cured = 38% (14/36); Treatment completed = 50% (18/36); Default = 5% (2/36); Transfer out = 5% (2/36); Death = 0% (0/36); Failure = 0% (0/36). *Partial DOT:* Cured = 17% (3/18); Treatment completed =	**Limitations identified by author:** There was a problem with communicating with the non-French speaking patients about the treatment regimen. In addition, there was a lack of communication between the TB dispensary unit and the external structures. For example, 1 pharmacy did not report bad adherence to the dispensary and 1 patient was lost to follow-up. There may have been a

prevalence region: first experience at the Tuberculosis Dispensary in Lausanne. *Swiss Medical Weekly*, *134*, 552–558. **Aim of study:** The aim of the study was to evaluate a DOT programme for outcomes given the location of DOT. **Study design:** Retrospective cohort **Type of economic analysis:** NA **Economic perspective:** NA	2001. **Selected population:** Immigrants or patients with severe psychiatric comorbidities (psychosis etc.), alcohol or drug abusers, patients presenting with social problems (homeless, illegal immigrants, prison inmates), HIV-infected patients; and retreatment cases, intermittent treatment cases and all drug-resistant TB. **Excluded population:** NR **Setting:** Onsite at a TB dispensary unit or outreach in a social health service or convenient location for the patient, Canton of Vaud,	**Intervention/s description:** Onsite DOT: DOT occurred entirely on site, at a single institution where TB medication was dispensed. Patients visited the site daily to take their medication. Asylum seekers received bus fare reimbursement to attend the dispensary. Social outreach DOT: DOT occurred either in a social care centre so patients with additional needs could be cared for, with nurses visiting the patients at home or patients coming to the centre. Social centres included health centres for refugees and asylum seekers, shelters with nurses or social workers supervising treatment, general practitioner surgeries, pharmacies. Daily	outcomes were presented as *failure* (sputum still positive after 5 months of treatment); *defaulters* (interruption of treatment for more than 2 months); *death* (whatever the cause); *transfer* (patient transferred out of the health care system and lost to follow-up); and *relapse* (new diagnosis of TB in a patient who was declared cured or who had completed a full course of treatment). **Secondary outcomes:** NA **Method of analysis:** Comparison of results between different subgroups was calculated by Fisher's exact test. **Modelling method**	72% (13/18); Default = 5% (1/18); Transfer out = 0% (0/18); Death = 5% (1/18); Failure = 0% (0/18). There was no statistically significant difference in successful treatment outcomes (89.5% in both groups) for full DOT (32/36) versus partial DOT (16/18; p=1.00). Outcome by type of supervision: *On site (only) DOT:* Cured = 38% (10/27); Treatment completed = 55% (15/27); Default = 4% (1/27); Transfer out = 0% (0/27); Death = 4% (0/27); Failure = 0% (0/27). *Outreach, DOT:* Cured = 26% (7/27); Treatment completed = 60% (16/27); Default = 7% (2/27); Transfer out = 8% (2/27); Death = 0% (0/27);	measurement bias as outcomes for patients who received DOT on site were recorded systematically by the nurse. However for those who received DOT via social outreach efforts, this was not always recorded and therefore information was given orally by professionals. As data was collected at least 6 months after treatment completion, the accuracy of the outcomes is uncertain, reducing the validity of the findings. **Limitations identified by review team:** In addition to the limitations noted above, the study was unable to provide interpreters for non-French speaking patients (which accounted for the majority of participants), which may have affected the results. Intervention groups have been contaminated, as many treatments were started in the dispensary and later moved to another supervision structure. For example, 10 patients received DOT on site at the

Quality appraisal non-economic studies: **-** **Internal validity: -** **External validity:** **+** **Quality appraisal economic studies:** NA **Quality score applicability:** NA	Switzerland. **Sample characteristics:** Males =5 7.4%; Females = 42.6%; Swiss nationality = 5.6%; foreign-born residents = 24.1%; asylum seekers and refugees = 62.9%; illegal immigrants 7.4%. **Economic analysis data source:** NA	supervision could also be by a family member, with the patient collecting the drugs weekly from the dispensary, or drug distribution in prison. Where possible, patients were seen at a site located near the patient's home or workplace. Female patients with small children were usually visited at home by a nurse. Note: across settings treatment consisted of either partial DOT (2-months of directly observed treatment) or full DOT (for the whole course of the treatment). The medication used was 2-month intensive phase with isoniazid, rifampicin, pyrazinamide, plus ethambutol) followed by a 4-month continuation phase with isoniazid and	**and assumptions:** NA **Time horizon:** Data was collected retrospectively, at least 6 months after completion of treatment.	Failure = 0% (0/27). There was no statistically significant difference in successful treatment outcomes for DOT delivered on site (92.6%, 25/27) versus when it was delivered by outreach (85.2%, 23/27; p=0.67). Note: results are extracted from graphs and therefore only an approximation. **Secondary results:** NA **Attrition details:** 1 patient was lost to follow-up.	TB dispensary centre as well asin a social outreach location (pharmacy, family, prison, social health structures). Allocation to treatment group was based on factors associated with the outcomes. For instance, those who were assigned to partial DOT were more likely to be compliant and a treatment outcome was compliance to treatment. Likewise those administered a full course of DOT were more likely to be non-compliant. In addition, it is not known within each group (i.e. full DOT and partial DOT) how many patients were treated on site or via social outreach. The effects attributable to DOT by duration/intensity are not precisely known as the results may have been confounded by the distribution of social outreach or onsite TB administration. **Evidence gaps and/or**

| | | rifampicin, and was adapted if necessary according to drug sensitivity, side effects and contra-indications.

The mean duration of treatment was 6.5 months.

Patients were observed taking all medication by a nurse.

Comparator/control/s description:
NA

Sample sizes:
Total: N=54
Intervention:
Full DOT: N=36
Partial DOT: N=18
Onsite DOT: N=27
Social outreach DOT: N=27.

Note: sub-group analyses were carried out by splitting the total study population first into those who received full or partial DOT, and second by whether it occurred on site or via social | | | **recommendations for future research:**
NR

Source of funding:
NR |

		outreach. **Control:** NA **Baseline comparisons:** NR **Study sufficiently powered?** NR			

Study details	Population and setting	Method of allocation to intervention/control	Outcomes and methods of analysis:	Results	Notes
Authors: El-Hamad et al. **Year:** 2001 **Citation:** El-Hamad, I., Casalini, C., Matteelli, A., Casari, S., Bugiani, M., Caputo, M., Bombana, E., et al. (2001). Screening for tuberculosis and latent tuberculosis infection among	**Source population/s:** Undocumented immigrants to Italy without appropriate visa, evaluated between April 1996-October 1997. **Eligible population:** Undocumented immigrants were defined as foreign-born persons with no residence permit and limited access (emergency interventions only)	**Method of allocation:** Not allocated. Participants were recruited from each health clinic. **Intervention/s description:** TBU: full-time TB screening site for contacts and people applying to enter dormitories. This service is considered 'specialised'. Screening included: TST and CXR performed at the first consultation and the TST result was read at a second consultation. Screening was	**Primary outcomes:** Completion rate (CXR and TST performed and read). **Secondary outcomes:** NR **Methods of analysis:** Continuous data was compared by Student's *t*-test and categorical data were analysed with	**Primary outcomes:** 392 participants had a TST of >10 mm. The calculated prevalence of LTBI was 39.4%. Eight cases of active TB were detected, five with extra-pulmonary and three with pulmonary disease. The calculated prevalence of TB disease in this population was 650/100,000. Active TB cases: The TBU clinic and	**Limitations identified by author:** NR **Limitations identified by review team:** There are differences in baseline characteristics between the study groups. These are controlled for in the multivariate logistic regression statistical analyses. However, as individuals self-referred to one of the two types of service, there may be other confounding factors that determined the choice of service sought, as well as the willingness to

undocumented immigrants at an unspecialised health service unit. *International Journal of Tuberculosis & Lung Disease*, *5*(8), 712-716. **Aim of study:** This study aimed to compare the completion rates of screening procedures for TB infection and disease among undocumented immigrants at both specialised TB and unspecialised health services. **Study design:** Prospective cohort. **Type of economic analysis:** NA	to public medical care services. **Selected population:** Participants eligible for screening: 1) arrived in Italy from countries with a TB prevalence of 50/100 000 or more; and 2) had migrated less than 5 years previously. In total, 2,611 people were evaluated for participation in the screening programme;1,318 (50.4% of the evaluated population) were eligible for TB screening. **Excluded population:** N=1293:1) migrated more than 5 years previously (N=1042); 2) previous screening	considered completed if the CXR and TST had been performed and read. **Control/comparison/s description:** MHCU: first-level medical care to immigrants only, during limited opening hours. This is considered an unspecialised health service. Screening includes: physical examination and TST performed at the first consultation; and the chest X-ray at the second consultation, and was conducted at a nearby TB clinic. The TST result was read at a third consultation. Screening at this service was considered completed if the CXR and TST had been performed and read. **Sample sizes:** **Total:** N=1,232. **Intervention:** N=749. **Control:** N=483. **Baseline comparisons:** There were more males,	Mantel-Haenszel stratified analysis. Univariate and multivariate logistic regression analyses (Wald test) were conducted using either the completion of screening procedures or the TST result as dependent variables. P value of <0.05 was considered significant. **Modelling method and assumptions:** NA **Time horizon:** NA	the MHCU clinic identified similar numbers of active TB cases. TBU = 5/749, or 6.7/1000; MHCU = 3/483, or 6.2/1000). <u>Completion rates:</u> Among the TBU group, 85.6% completed screening (648/749). 101 individuals did not return for the interpretation of the TST. Among the MHCU group, 71.4% completed screening (345/483). 138 individuals either did not attend for CXR (117 individuals) or for TST (21 individuals). <u>Probability of completing screening according to subject characteristics:</u> The only variable that increased the	complete the screening process. **Evidence gaps and/or recommendations for future research:** The authors suggest that future studies should evaluate the efficacy of short-term multidrug regimens delivered through outreach directly observed preventive therapy to undocumented immigrants in industrialised countries. **Source of funding:** Italian Tuberculosis Projects I (1995) and II (1997) of the Istituto Superiore di Sanità.

| **Economic perspective:** NA **Quality appraisal non-economic studies:** + **Internal validity:** + **External validity:** + **Quality appraisal economic studies:** **Quality score:** NA **Applicability:** NA | or treatment for TB (N=171); 3) pregnancy (N = 40); 4) expecting to move away from the study area in less than 6 months (N =31); 5) migrated from a country with low prevalence of TB (N =9). **Setting:** health care unit (MHCU) in Brescia and TB clinic (TBU) in Turin, Italy. **Sample characteristics:** MHCU: Male = 362 (75%); <35 years = 393 (82%); Married = 192 (40%); Stable work = 131 (27%). Living in: own apartment = 121 (25%); with friends = 318 (66%); | Africans and Christians in the MHCU group, and more Eastern European, alcohol and drug abusers, and individuals living in their own apartment in the TBU group. **Study sufficiently powered?** NR | | probability of completing screening was being enrolled in the TBU group (odds ratio 2.5; 95% CI 1.8–3.5, p<0.001). **Secondary outcomes:** NR **Attrition details:** NR | |

homeless/dorm = 33 (7%); NR = 11 (2%). Religion: Christian = 339 (70%); Muslim = 131 (27%); Other = 13 (3%). Country of origin: Sub-Saharan Africa = 222 (46%); North Africa = 75 (16%); Indian subcontinent = 129 (26%); Eastern Europe = 48 (10%); Other = 9 (2%). Substance use: Alcohol = 21 (4%); Drugs = 6 (1%). TBU: Male = 357 (48%); <35 years = 616 (82%); Married = 310 (41%); Stable work = 238 (32%). Living in: own apartment = 292 (39%);				

staying with friends = 236 (32%); homeless/dorm = 46 (6%); NR = 175 (23%). Religion: Christian = 290 (39%); Muslim = 395 (53%); Other = 64 (8%). Country of origin: sub-Saharan Africa = 272 (36%); North Africa = 121 (16%); Indian subcontinent = 6 (1%); Eastern Europe = 235 (32%); Other = 115 (15%). Substance use: Alcohol = 76 (10%); Drugs = 26 (3%). **Economic analysis data source:** NA				

Study details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors:	**Source**	**Method of allocation:**	**Primary outcomes:**	**Primary results:**	**Limitations identified by**

Malotte et al. **Year:** 2001 **Citation:** Malotte, C. K., Hollingshead, J. R., & Larro, M. (2001). Incentives vs outreach workers for latent tuberculosis treatment in drug users. *American Journal of Preventive Medicine*, *20*(2), 103–107. **Aim of study:** To compare the independent and combined effects of monetary incentives and outreach worker provision of DOT (for LTBI) treatment in a sample of active drug users.	**population/s:** Drug users with LTBI, USA. **Eligible population:** Participants with a positive tuberculin skin test and no evidence of active disease or major contraindications to isonazid. **Selected population:** 169 participants agreed to participate. **Excluded population:** **Setting:** Community, storefront facility that housed both research and service programmes for drug users, California, USA. **Sample**	Randomisation to one of three groups within blocks of 18. Allocation concealment using numbered, opaque, sealed envelopes. **Intervention/s description:** Outreach DOPT plus monetary incentives (Condition 1): twice-weekly DOPT supplied by an outreach worker at a location chosen by the participant, plus a $5 per visit incentive. Outreach DOPT (Condition 2): twice-weekly DOT by an outreach worker at a site chosen by the participant but with no monetary incentive. Note: this comparison arm was not reported in this current review on service models. DOPT plus monetary	Percentage of medication taken on time: number of doses taken on time divided by the total number of doses taken on time, late and/or missed. Minimum number of doses in the denominator was 52 (two per week for 26 weeks) unless the medication was stopped by a health professional. Those lost to follow-up were assumed to have missed doses (all doses from the last dose taken up to 52 doses were counted as missed). Completion of treatment: no further definition provided. Did not include those whose medication was stopped for medical reasons. **Secondary**	Completion of treatment: Outreach DOPT plus monetary incentives (Condition 1) = 28/53 (52.8%). Outreach DOPT (Condition 2) = 2/55 (3.6%). DOPT plus monetary incentives (Condition 3) = 33/55 (60%). Adjusted Odds Ratio (AOR) for outreach DOPT plus incentive compared with outreach DOPT alone = 29.7 (95% CI 6.4-137.5), p<0.0001. AOR (for DOPT plus incentive compared with outreach DOPT alone = 45.5 (95% CI 9.7-214.6); p<0.0001. Percentage of medication taken on time: Outreach DOPT plus	**author:** None. **Limitations identified by review team:** In the comparisons of the different treatment groups, condition 1 and condition 3 were only compared with condition 2. It was not clear from the methods that condition 2 was the 'control condition'. Comparisons should have also been conducted between condition 1 and 3 to understand whether the inclusion of an outreach worker to administer DOPT improved treatment completion compared with standard DOPT. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** National Institute on Drug Abuse.

Study design: RCT	**characteristics:** Mean age: 42 years, range 23 to 69 years); male: 82%; crack cocaine use: 68%; IDUs: 13%; alcohol consumption: 81%. living in own home: 41.7%.	incentives (Condition 3): twice-weekly DOPT, conducted at the study's community site. Participants in this group were paid $5 per scheduled visit attended.	**outcomes:** NA	monetary incentives (Condition 1) = 72%; p<0.001 compared with condition 2. Outreach DOPT (Condition 2) = 12%. DOPT plus monetary incentives (Condition 3) = 69%; p<0.001 compared with condition 2.	
Type of economic analysis: NA			**Method of analysis:** Baseline differences were assessed using analysis of variance (ANOVA) for continuous variables and contingency table analysis (x^2) for categorical variables.		
Economic perspective: NA		Note: all participants were prescribed INH, 15 mg/kg, with a maximum dose of 900 mg, twice per week (Monday and Thursday or Tuesday and Friday).		Note: absolute numbers were not reported for this outcome, only percentages.	
Quality appraisal non-economic studies: ++ **Internal validity:** ++	**Economic analysis data source:** NA		Univariate relationships of treatment completion with treatment condition, demographic characteristics, and drug use characteristics were tested using x^2 analyses with continuity correction where appropriate.	**Secondary results:** Variables associated with increased treatment completion: No binge drinking in the past 30 days compared with some: AOR = 2.1 (95% CI 0.9-4.4, p=0.07).	
External validity: +		Length of treatment was 6 months or 12 months depending on HIV status.			
Quality appraisal economic studies: NA		All participants were informed of the importance of treatment completion and possible side effects of medication.	Intervention effects were tested in both univariate and multivariate logistic regression analyses,	Recruitment status Prior study participants compared with newly recruited participants: AOR = 2.5 (95% CI 1.1-5.7, p=0.03).	
Quality score applicability: NA		Participants were observed swallowing			

| | | all medications. If the participant did not appear or could not be found, medication could be given the following day. If the dose was not provided the following day, it was considered missed.

Comparator/control/s description:
NA
Sample sizes:
Total =
163
Intervention:
Outreach DOPT plus monetary incentives (Condition 1): N=53;

Outreach DOPT (Condition 2): N=55;

DOPT plus monetary incentives (Condition 3): N=55.

Control = NA

Baseline | on an intention-to-treat basis. In addition to treatment condition, the multivariate analysis included as covariates all variables that were related (p<0.10) to treatment completion in univariate comparisons.

Analysis on treatment completion did not include those whose medication was stopped for clinical reasons (N=6).

If a participant was lost to follow-up (moved or imprisoned), all doses after the last dose taken were counted as missed.

Modelling method and assumptions:
NA

Time horizon:
NA | **Sample selection and attrition details:**
202 were eligible, 169 consented to take part in the study.

14 individuals were not eligible for INH due to evidence of potential active disease or medical contraindications, 2 were followed by the health department and 6 did not return for assessment results.

6 individuals were not included in the analysis: 2 had a previous history of INH therapy; 3 had prolonged elevated liver function tests; and 1 was referred to the health department for multiple medications due to a positive sputum test. | |

| | | comparisons: No statistically significant differences at baseline.

Study sufficiently powered?
NR | | | |

Study details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Miller et al. **Year:** 2006 **Citation:** Miller, T. L., Hilsenrath, P., Lykens, K., McNabb, S. J., Moonan, P. K., & Weis, S. E. (2006). Using cost and health impacts to prioritize the targeted testing of tuberculosis in the United	**Source population/s:** Homeless and jailed populations in the USA. **Eligible population:** NA **Selected population:** NA **Excluded population:** NA **Setting:** Jail and homeless centre, Texas, USA. **Sample characteristics:**	**Method of allocation:** NA **Intervention/s description:** Jail programme: state-law-mandated Mantoux TST screening programme for all inmates in jails with a population greater than 100 (except those with a clearly documented previous positive test). All individuals with a positive TST result or TB symptoms undergo additional medical evaluation, and treatment of LTBI is	**Primary outcomes:** Cost of screening. Cost of treatment. Cost per case. **Secondary outcomes:** NA **Method of analysis:** NA **Modelling method:** Costs and activities associated with the detection and treatment of TB were estimated for patients with uncomplicated active TB and LTBI and adjusted for	**Primary results:** <u>Screening results:</u> TST placed: 778/822 (94.7%) homeless programme; 21 778/22,920 (95%) jail programme (p=0.179). Positive TST results (from those read): 127 (15.5%) homeless programme; 303 (2%) jail programme (p<0.001). Treatment prescribed for LTBI: 181 (22%) homeless programme; 211 (0.9%) jail programme (p<0.001). Note: treatment for	**Limitations identified by author:** Costs do not include contact investigations, secondary transmission and patient costs. Therefore total costs are underestimated, as are full savings per TB case averted. Some differences between the jail and homeless groups may affect comparability. **Limitations identified by review team:** none in addition to the above. **Evidence gaps and/or recommendations for future research:** NR

States. *Annals of Epidemiology*, *16*(4), 305-312. **Aim of study:** To evaluate and compare the efficiency of a non state-law-mandated TB screening programme for homeless persons and a state-law-mandated TB screening programme for jail inmates. **Type of economic analysis:** Cost comparison **Economic perspective:** NR **Quality appraisal effectiveness studies:**	22,920 jailed inmates; 822 homeless persons. **Economic analysis data sources:** Collected by researchers (homeless programme); monthly reports compiled by the Tarrant County Public Health Department (jail programme); available statistics (additional cost data).	offered as appropriate. Medically licensed staff directly observed all TB therapy. Homeless programme: outreach effort which includes on-site TB symptom check, CXR, TST and medical evaluation. Tarrant County Public Health Department staff (who had completed TB training and were experienced in working with homeless people but without medical license) observed treatment on site. In addition, personnel were supervised by public health nurses and physicians. Patients received an incentive for keeping medication appointments, such as dietary supplements or fast-food coupons. **Comparator/control/s description:** NA **Sample sizes:**	current TB treatment recommendations. Treatment and professional costs were estimated at the midpoint of Medicare's national average, mean fee for non-Medicare charges, and average wholesale price for drugs. All costs were adjusted to 2003 US dollars; hospitalisation rates and costs were adjusted to the region. Costs for contact investigations, patient expenses, facilities, administration, or other programme costs were not considered. **Time horizon:** NR	LTBI may have been prescribed for other reasons than a positive TST result. Treated for active TB: 10 (1.2%) homeless programme; 7 (0.03%) jail programme (p<0.001). TST lost or unread: 245 (29.8%) homeless programme; 6760 (31.1%) jail programme (p=0.356). Number screened per LTBI case: 4.5 homeless programme; 108.7 jail programme. Number screened per active TB case: 82.2 homeless programme; 3274 jail programme. Number of screenings required to initiate one treatment: 5.7 homeless programme; 140 jail programme. Number of screenings to prevent 1 active TB case: 69 homeless	**Source of funding:** Center for Disease Control and Prevention.

				programme; 2,142 prison programme.
Internal validity: NA **External validity:** NA **Quality appraisal economic studies: Quality score:** ++ **Applicability:** +		**Total:** N=23,740. **Intervention:** N=22,920 (inmates) and 822 (homeless). **Control**: NA **Baseline comparisons:** NR **Study sufficiently powered?** N/R		Homeless programme Cost ofscreening = $54,334. Cost of treatment per patient diagnosed with active TB = $5,433. Cost of screening per patient diagnosed with LTBI = $300. Cost of screening and treatment per active TB case prevented (by treating LTBI cases) = $14,350. Jail programme: Cost for screening = $245,244. Cost of treatment per patient diagnosed with active TB = $35,035. Cost of screening per patient diagnosed with LTBI = = $1,163. Cost of screening and treatment per active TB case prevented (by treating LTBI cases) = $34,761. Note: The sums of screening and treatment costs were

				used for comparison of programs, and costs of negative screening results were adjusted proportionally to the number of LTBI and TB diagnoses made. **Secondary results:** NR **Attrition details:** NR	

Study details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Mor, et al. **Year:** 2008 **Citation:** Mor, Z., Lerman, Y., & Leventhal, A. (2008). Pre-immigration screening process and pulmonary tuberculosis among	**Source population/s:** Ethiopian immigrants to Israel. **Eligible population:** All Ethiopian immigrants with TB who migrated to Israel and were located on various national registers. **Selected**	**Method of allocation:** by historical exposure to pre-immigration screening or post-immigration screening. **Intervention/s description:** pre-immigration screening in Addis Ababa before immigrants arrived in Israel, which occurred between June 2001 and December 2005. The screening	**Primary outcomes:** Rate ratio for TB. Detection period (time between immigration date and diagnosis date). Net direct cost savings. **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method**	**Primary results:** TB incidence Pre-immigration: 267 cases per 100,000 person-years Post-immigration: 324 cases per 100,000 person-years. The disease OR between study and comparison groups was 0.4 (no confidence intervals provided). The number of TB cases and disease rates were lower in	**Limitations identified by author:** The authors state that there was a limited time period for following up the groups, 4.5 years for the study group and 7 years or less for the comparison group. A longer time period may have been able to capture important health outcomes for this population with TB. In addition, as the groups were not studied concurrently, the better

Ethiopian migrants in Israel. *European Respiratory Journal*, *32*(2), 413-418. **Aim of study:** To examine the effectiveness and cost-effectiveness of pre-immigration screening before entry to Israel with post-immigration screening at point of entry among Ethiopian immigrants in Israel. **Study design:** NA **Type of economic analysis:** cost-savings.	**population:** Those who migrated to Israel between January 1998 and December 2005 who were diagnosed with TB at least 2 weeks after arriving. **Excluded population:** Those diagnosed with extrapulmonary TB (N=183); migrated between 1975 and 1997 (N=441) and; who were diagnosed within the first 2 weeks of arrival in Israel (N=65). **Setting:** not reported. **Sample characteristics:** Intervention group: mean age at immigration was 27.4 years (SD 20.1 years), mean age at diagnosis was 28.7 years (SD 20.3 years), sex	procedure in Ethiopia included TST followed by CXR (for immigrants >6 months old. Diagnosed cases were treated in Ethiopia and all other cases entered Israel. Upon arrival in Israel, a public health nurse visited absorption centres where immigrants were placed and performed a second TST on all those whose first reading was 10 mm indurations in size. **Comparator/control/s description:** post-immigration screening when immigrants arrive to Israel, which occurred between January 1998 and May 2001. **Sample sizes:** **Total:** N=267. **Intervention:** N=162. **Control:** N=105. **Baseline comparisons:** no	**and assumptions:** Non-economic assumptions such as morbidity trends based on this study's findings. Cost assumptions of diagnosis, treatment and follow-up of each individual PTB case in Israel was estimated at $60,100 (US dollars). The costs of maintaining a health station during the same period was $7,619. **Time horizon:** 5 years.	pre-immigration group compared with post-immigration; rate ratio for TB: 0.82 (p<0.01). <u>Detection period</u>: the difference between the mean number of days between immigration and TB diagnosis for the pre-immigration group was 193 days (SD 260) and for the post-immigration group was 487 days (SD 640). The difference between the groups was statistically significant in favour of pre-immigration screening (p<0.01). Survival analysis found an increasing difference in time to diagnosis between the two groups over the 5-year follow-up period (OR =0.72, 95% CI 0.59 – 0.89; p=0.002). <u>Net direct savings</u> in cost for pre-immigration screening was $449,817 for 5 years assuming that	identification of TB in the pre-immigration group may have been confounded by better treatment, as it occurred at a later time period where staff had better training and experience with TB. **Limitations identified by review team:** The difference in TB incidence in the two groups may be caused by changing disease epidemiology over time, rather than differences in detection rates with the two screening strategies. The study had different follow-up periods for the two groups. There may have been differences in outcomes between the two groups due to the different length of time that the groups were followed-up. The costing of resources came from different sources, with one more reliable than the other. The costing of healthcare in Israel came from a national published source, the Ministry of Health Tariff, while the costing of the

Economic perspective: NR **Quality appraisal non-economic studies:** NA **Internal validity:** NA **External validity:** NA **Quality appraisal economic studies:** **Quality score:** + **Applicability:** +	ratio M:F was 1.04 and 13.8% were HIV positive. Control group: mean age at immigration was 28.8 years (SD 22.4 years), mean age at diagnosis was 29.4 years (SD 22.5 years), sex ratio M:F was 1.04 and 14.2% were HIV positive. **Economic analysis data source:** operational costs (including salaries, rent and costs of drugs and equipment used for diagnosis and treatment) of the pre-immigration infrastructure at Addis Ababa were taken from professionals. Costs of resources in Israel were from the Ministry of Health Tariff figures in 2008.	statistically significant differences. **Study sufficiently powered?** NR		98 individuals would be free of TB using this screening approach (and based on the cost assumptions of each screening group). **Secondary results:** NR **Attrition details:** NA	station in Addis Ababa came from expert opinion amongst professionals. A discount rate was not used to allow for the changes in cost over time, and a sensitivity analysis was not performed to explore the uncertainties around the cost of the services, in particular the costs of the health station in Addis Ababa. The annual TB incidence rate found in this study was higher than those found in the literature for other HTR groups in other countries. This may decrease the generalisability of the results. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** NR

Study details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Ricks **Year:** 2008 **Citation:** Ricks, P. M. (2008). *Tuberculosis control among substance users: The indigenous leadership outreach model vs. standard care (PhD Thesis).* Chicago, Illinois: University of Illinois at Chicago. **Aim of study:** To compare the effectiveness of the	**Source population/s:** Drug users with active TB, USA. **Eligible population:** Substance users undergoing TB treatment in Chicago. **Selected population:** Inclusion criteria: 1) was assigned to West Garfield TB nursing station, which was where the primary Chicago Department of Public Health (CDPH) case management nurse was located, 2) was at least 18 years of age, 3) had used an illicit drug in the	**Method of allocation:** Participants randomly assigned to intervention/control using a random number sequence and allocated using sequentially numbered envelopes. **Intervention/s description:** <u>Enhanced model</u>: two person mixed-gender team of Indigenous Leader Outreach Workers (ILOWs) (former substance users) who provided DOT. Patients were seen every 30 days for medical evaluation. ILOWs facilitated client attendance at scheduled medical exam appointments by reminding clients of their appointments, providing incentives	**Primary outcomes:** *Identification review:* <u>Contact tracing:</u> proportion becoming "extensively interviewed contacts" (EICs). *Management review:* <u>TB treatment completion</u>: decided by the physician and based on the percentage of doses taken and the timing. This was typically defined as the patient taking 80% of their medication from the DOT worker. <u>Treatment compliance</u>: having taken at least 80% of prescribed doses of TB medication, *whilst under*	**Primary results:** *Identification review:* <u>Contact tracing</u>: 40/53 (75%) of participants in the intervention group listed names of contacts (for a total N=431). 23/49 (47%) of participants in the control group provided contacts (total N=230) (p=0.03). Contacts in the intervention group were significantly more likely to be go on to become "extensively interviewed contacts" (EICs) than contacts in the standard arm (23% vs. 12%, p=.001). Overall, there were 99 EICs in the intervention group, of whom 47completed follow-up interviews, and 27	**Limitations identified by author:** small sample size and high dropout rate limited the ability to detect changes that may have been small but significant. However, the study did manage to find some statistically significant differences. **Limitations identified by review team:** The aim of the study was to examine whether using peers from similar hard-to-reach groups was more effective than using non-peer health workers. However, in the treatment group participants also received intensive case management. This made it difficult to determine which component of the intervention led to improved outcomes. **Evidence gaps and/or recommendations for future research:** NR

Indigenous Leader Outreach Model (ILOM) vs standard TB management among substance users. **Study design:** RCT **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal effectiveness studies:** ++ **Internal validity:** ++ **External validity:** + **Quality**	6 months prior to enrolment and/or daily use of alcohol in the 6 months prior to enrolment, 4) had active TB and DOT was ordered by the CDPH physician, 5) agreed to complete baseline and follow-up interviews, 6) agreed to provide blood samples for HIV-testing after each interview. **Excluded population:** Potential participants who failed to meet one of the criteria above. **Setting:** Chicago, October 1996 to July 2000 **Sample characteristics:** 61% African	(monetary and non-monetary, such as tokens), providing transportation, and advocating/translating for clients with the healthcare provider at the appointment. The ILOWs also provided the client with comprehensive health information regarding infectious diseases, strategies for reducing specific risk behaviours, and prevention materials. **Comparator/control/s description:** Standard CDPH approach: one public health worker who performed DOT, with limited case management provided by a nurse case manager. Patients were seen every 30 days for medical evaluation. The nurses were responsible for all case-management	*treatment*. People who missed taking medication from their DOT worker may have been considered compliant, if it was verified that they received treatment from another source, such as a hospital or jail. Missed DOT appointments: missing a scheduled DOT appointment. Consecutively missed appointments. **Secondary outcomes:** Changing HIV and TB risk behaviours, TB knowledge, and sense of TB stigmatisation among adult substance users with TB in Chicago.	EICs in the standard arm, of whom 15 completed follow-up interviews. Cases in both arms were equally as likely to identify contacts whose priority for contact tracing was high, OR 1.06 (95% CI 0.47-2.38), medium, OR 0.95 (95% CI 0.51-1.78), or unknown OR 0.92 (95% CI 0.45-1.86). Note: Inclusion criteria for becoming an EIC were as follows: 1) were a contact of a case that was enrolled in the study, 2) were at least 18 years of age 3) had used an illegal substance and/or daily alcohol consumption, during the preceding 6 months, 4) completed a baseline questionnaire, 5) agreed to have their	**Source of funding:** NR

appraisal economic studies: NA **Quality score applicability:** NA	American male; 58% had never been married; 61% lived with other people; 3% had private insurance; 57% spent most nights in the preceding 6 months at their own or partner's house or apartment; leading source of income (20%) was benefits from the Veterans Affairs, disability, and Supplemental Security Income; mean monthly income from all sources was $746 (median $511); 56% had a chest X-ray at time of diagnosis that was consistent with active TB; injecting drug use was low (5%), freebasing cocaine or crack, smoking marijuana,	services, and for developing referral relationships with social service and health care providers. The CDPH was able to provide monetary incentives and tokens for transportation to patients with adherence issues. **Sample sizes:** **Total** 94 **Intervention** 48 **Control** 46 **Baseline comparisons:** No significant differences in gender, race, education, risk behaviours, TB knowledge, or TB stigma. **Study sufficiently powered?** The final sample had 76% power to detect a 20% difference in completion rates	[not extracted] **Method of analysis:** Modified intention-to-treat analysis (participants who after randomisation were found to not have TB were excluded from analysis); Fishers t-test; Wilcoxon rank-sum tests. **Modelling method and assumptions:** NA **Time horizon:** NA	blood drawn for HTV-testing, and 6) did not have active TB. *Management review* Treatment completion: intervention group = 41/48 (85%); control group = 28/46 (61%); RR=2.68, 95% CI 1.24 - 5.82 (p=0.01). Treatment compliance: intervention group = 38/48 (84%); control group = 25/46 (68%) (RR=2.51, 95% CI 1.15-5.48, p=0.016). Missing DOT appointments: control group = 7.64 (mean); treatment group = 4.11 (p=0.13). Consecutively missed DOT appointments: comparison group = 3.82 (mean); treatment group = 3.96 (p=0.57). **Secondary results:**	

	and non-injecting heroin use were the three most frequently used illicit drugs; 74% reported multiple drug use; alcohol use was the most common (70%); 45% had a regular sexual partner. **Economic analysis data sources:** NA	between the two groups.		NA. **Sample selection and attrition details:** 100/549 suspected cases were eligible and consented to participate. Of these, 6 were found after randomisation to not have active TB and thus were removed from the analysis. Among the remaining 94, 6 died or were transferred before DOT, 2 withdrew from the study and 7 refused to be interviewed. Overall, 36/46 (78%) cases completed the study in the control group, and 43/48 in the intervention group (90%).	

Study details	Population and setting	Method of allocation to intervention/	Outcomes and methods of	Results	Notes

		comparator	analysis:		
Authors: Umbricht-Schneiter et al. **Year:** 1994 **Citation:** Umbricht-Schneiter A., Ginn D.H., Pabst K.M., Bigelow G.E. (1994) Providing medical care to methadone clinic patients: referral vs. on-site care. *Am J Public Health. 84*(2):207-210. **Aim of study:** To evaluate the efficacy of providing medical care at a methadone clinic versus referral to another site.	**Source population/s:** Injecting drug users (IDUs) with LTBI, USA. **Eligible population:** Opioid-dependent drug users seeking methadone treatment. **Selected population:** Drug users with no primary care physicians, needing care for one of the following conditions: Hypertension Tuberculosis exposure HIV+ (asymptomatic) Acute sexually transmitted disease. **Excluded population:** NR	**Method of allocation:** Participants randomized to treatment and control group following medical examination at methadone clinic. Participants were either randomised to treatment onsite (at methadone clinic) or referred to medical clinic (where participants needed to seek treatment). Randomisation method not reported. No details on allocation concealment. **Intervention/s description:** On-site treatment at methadone clinic: Patients were treated for their medical condition (including TB) immediately onsite after examination at methadone clinic, or a follow-up appointment was arranged. Counsellors co-	**Primary outcomes:** Enrolment to medical treatment rate: the number of patients who enrolled for medical treatment and complied with recommendations. Number of medical visits: number of patients seen one or more times; two or more times; mean number of visits per patient (not necessarily complied with treatment recommendations). **Secondary outcomes:** N/A **Follow-up period:** 4 and 8 weeks. **Method of analysis:** T-tests for continuous and z-tests for dichotomous	**Primary results:** *For all medication conditions (including TB):* Enrolment to medical treatment: Onsite treatment = 23/25 (92%); Control= 9/26 (32%); p<0.001. Number of patients seen one or more times: Onsite treatment = 25/25 (100%); Control = 8/26 (30.8%); p<0.001 Number of patients seen two or more times: Onsite treatment = 19/25 (76%) Control = 1/26 (3.8%); p<0.001. Number of visits per patient, mean (SD): Onsite treatment = 3.1 (1.8);Control = 0.4 (0.6); =p<0.001 *For TB medical treatment only:*	**Limitations identified by author:** NR **Limitations identified by review team:** It is not clear what management interventions occurred on each site therefore it is not known whether there were any differences in treatment between the two sites which may have led to differences in adherence to treatment. The numbers of patients with TB in this study small limiting the generalisability to the source population. **Evidence gaps and/or recommendations for future research:** Additional study (e.g., assessments of emergency room visits or hospitalizations) to evaluate the cost-effectiveness of providing medical care at addiction treatment sites is recommended. **Source of funding:**

		ordinated the care between the addiction unit and medical services.	variables.	Number of patients with positive PPD tests who received chest X-rays: Onsite treatment = 6/8; Control = 3/14; Differences not statistically tested.	NR
Study design: RCT	**Setting:** Hospital-based methadone treatment research clinic in South-eastern Baltimore.		**Modelling method and assumptions**: N/A		
Type of economic analysis: N/A		**Comparator/control/s description:** Referred treatment to a medical centre: Patients were instructed to contact a medical clinic located on the same campus as the methadone treatment clinic. They received written instructions describing the clinic location, and were given the telephone number of the clinic.	**Time horizon:** N/A		
Economic perspective: N/A	**Sample characteristics:** *Male*: Intervention: N=17; Control N=20.			Number of patients with positive PPD tests who received chemoprophylaxis: Onsite treatment = 1/8; Control = 1/14; Differences not statistically tested.	
Quality appraisal non-economic studies: + **Internal validity: -** **External validity: +**	*Non whites*: Intervention: N=16; Control N=19.				
	Distribution of diagnoses Hypertension: Intervention: N=4; Control: N=3. PPD positive: Intervention: N=8; Control: N=14. HIVpositive: Intervention: N=7; Control: N=4. Sexually transmitted disease: Intervention: N=9;	They were responsible for obtaining an appointment at the medical clinic, where a physician was available twice weekly; there was no waiting list, and appointments could be obtained within 4 days. **Sample sizes:** **Total:** N=51 **Intervention:** N=25		**Secondary results:** N/A **Attrition details:** 161 methadone treatment patients evaluated; 75 had at least one of the relevant conditions; 51 agreed to participate and were randomized. In the intervention group, 2 did not enroll and/or did not comply to medical treatment. In the control group, 15 did receive medical treatment.	
Quality appraisal economic studies: N/A **Quality score Applicability:** N/A					

	Control=13. **Economic analysis data source:** N/A	**Control:** N=26 **Baseline comparisons:** No significant differences in the characteristics of participants in the study groups. **Study sufficiently powered?** NR			

12.0 Appendix D. Studies excluded at full text stage

Table D1. Studies excluded after full text screening (N=76)

Reference details	Abstract	Exclusion Code
Andre, M. et al. (2007). Transmission network analysis to complement routine tuberculosis contact investigations. *American Journal of Public Health*, *97*(3), 470-477.	OBJECTIVE: We examined the feasibility and value of network analysis to complement routine tuberculosis (TB) contact investigation procedures during an outbreak. METHODS: We reviewed hospital, health department, and jail records and interviewed TB patients. Mycobacterium tuberculosis isolates were genotyped. We evaluated contacts of TB patients for latent TB infection (LTBI) and TB, and analyzed routine contact investigation data, including tuberculin skin test (TST) results. Outcomes included number of contacts identified, number of contacts evaluated, and their TST status. We used network analysis visualizations and metrics (reach, degree, betweenness) to characterize the outbreak. RESULTS: secondary TB patients and more than 1200 contacts. Genotyping detected a 21-band pattern of a strain W variant. No HIV-infected patients were diagnosed. Contacts prioritized by network analysis were more likely to have LTBI than nonprioritized contacts (odds ratio=7.8; 95% confidence interval=1.6, 36.6). Network visualizations and metrics highlighted patients central to sustaining the outbreak and helped prioritize contacts for evaluation. CONCLUSIONS: A network-informed approach to TB contact investigations provided a novel means to examine large quantities of data and helped focus TB control.	5_EX.POP
Badiaga, S., Raoult, D., & Brouqui, P. (2008). Preventing and controlling emerging and reemerging transmissible diseases in the homeless. *Emerging Infectious Diseases*, *14*(9), 1353-1359.	Homelessness is an increasing public health problem. Because of poor living conditions and limited access to healthcare systems, homeless persons are exposed to many communicable infections. We summarize the intervention measures reported to be efficient for the control and the prevention of common transmissible infections among homeless populations. Evidence suggests that appropriate street- or shelter-based interventions for targeted populations are the most efficient methods. Depending on the populations targeted, these interventions may include education, free condom distribution, syringe and needle prescription programs, chest radiography screening for tuberculosis, directly observed therapy for tuberculosis treatment, improvement of personal clothing and bedding hygiene, and widespread use of ivermectin for scabies and body louse infestation. Systematic vaccination against hepatitis B virus, hepatitis A virus, influenza, Streptococcus pneumoniae, and diphtheria is strongly recommended. National public health programs specific to homeless populations are required.	6_EX.NON-EMP
Barnes, P. F., & Barrows, S. A. (1993). Tuberculosis in the 1990s. *Annals of Internal Medicine*, *119*(5), 400-410.	PURPOSE: To summarize major recent developments in tuberculosis and current approaches to its treatment and prevention. DATA IDENTIFICATION: Articles published since 1987 that addressed important issues in tuberculosis were identified by searching the MEDLINE database and bibliographies of relevant articles. STUDY SELECTION: One hundred one references were selected that were judged by the authors to contain information most relevant to practicing internists. RESULTS: Recent increases in tuberculosis morbidity in the United States are concentrated in racial and ethnic minorities, the foreign-born, and persons with human immunodeficiency virus infection. Amplification of Mycobacterium tuberculosis DNA by polymerase chain reaction allows rapid	6_EX.NON-EMP

	diagnosis of tuberculosis, and "DNA fingerprinting" of individual M. tuberculosis strains allows delineation of patterns of tuberculosis transmission. These techniques are available in research laboratories and are promising clinical tools for the future. Treatment regimens for drug-susceptible tuberculosis yield cure rates of more than 95%. Failure to ensure compliance with antituberculosis medications has resulted in an increasing prevalence of multiple-drug-resistant tuberculosis that responds poorly to therapy. Guidelines for isoniazid chemoprophylaxis have been modified in the past 5 years and are summarized. CONCLUSION: Control of tuberculosis in the United States will require improved implementation of established techniques to diagnose, treat, and prevent tuberculosis, with renewed emphasis on ensuring compliance with therapy. [References: 102]	
Burgos, J. L. et al., 2009. Targeted screening and treatment for latent tuberculosis infection using QuantiFERON - TB Gold is cost-effective in Mexico. *International Journal of Tuberculosis & Lung Disease*, *13*(8),.962-968.	OBJECTIVE: To assess the cost-effectiveness of screening for latent tuberculosis infection (LTBI) using a commercially available detection test and treating individuals at high risk for human immunodeficiency virus (HIV) infection in a middle-income country. DESIGN: We developed a Markov model to evaluate the cost per LTBI case detected, TB case averted and quality-adjusted life year (QALY) gained for a cohort of 1000 individuals at high risk for HIV infection over 20 years. Baseline model inputs for LTBI prevalence were obtained from published literature and cross-sectional data from tuberculosis (TB) screening using QuantiFERON-TB Gold In-Tube (QFT-GIT) testing among sex workers and illicit drug users at high risk for HIV recruited through street outreach in Tijuana, Mexico. Costs are reported in 2007 US dollars. Future costs and QALYs were discounted at 3% per year. Sensitivity analyses were performed to evaluate model robustness. RESULTS: Over 20 years, we estimate the program would prevent 78 cases of active TB and 55 TB-related deaths. The incremental cost per case of LTBI detected was US$730, cost per active TB averted was US$529 and cost per QALY gained was US$108. CONCLUSIONS: In settings of endemic TB and escalating HIV incidence, targeting LTBI screening and treatment among high-risk groups may be highly cost-effective.	5_EX.POP
Burgos, M., et al. (2005). Treatment of multidrug-resistant tuberculosis in San Francisco: an outpatient-based approach. *Clinical Infectious Diseases*, *40*(7), 968-975.	BACKGROUND: Treatment of patients with multidrug-resistant tuberculosis requires prolonged therapy, often involving long hospital stays. Despite intensive and costly therapy, cure rates are relatively low. METHODS: We reviewed the outcomes for all patients with multidrug-resistant tuberculosis treated in San Francisco, California, during 1982-2000 and identified billing charges for patients treated during 1995-2000. Mycobacterium tuberculosis isolates were genotyped by IS6110-based restriction fragment-length polymorphism analysis. RESULTS: Forty-eight cases were identified with resistance to a median of 3 drugs (range, 2-9 drugs). The median age of the patients was 49.5 years (range, 22-78 years); 36 (75%) of 48 patients were foreign born, 11 (23%) were human immunodeficiency virus (HIV) seropositive, and 45 (94%) had pulmonary tuberculosis. Thirty-two (97%) of the 33 HIV-seronegative patients were cured, with only 1 relapse occurring 5 years after treatment. All 11 HIV-seropositive patients died during observation. Twenty-one patients (44%) required hospitalization, with a median duration of stay of 14 days (range, 3-74 days). The estimated inpatient and outpatient aggregate cost for the 11 patients treated after 1994 was $519,928, with a median cost of $27,752 per patient. No secondary cases of multidrug-resistant tuberculosis were identified through population-based genotyping. CONCLUSIONS: Treatment of multidrug-resistant tuberculosis in HIV-seronegative patients largely on an outpatient basis was feasible and was	7_EX.TOPIC

	associated with high cure rates and lower cost than in other published studies. Patients with underlying HIV infection had very poor outcomes.	
Burns, A. D., & Harrison, A. C. (2007). Costs of investigating and managing non-residents with possible tuberculosis: New Zealand experience of an international problem. *Respirology*, *12*(2), 262-266.	BACKGROUND AND OBJECTIVE: This study's aims were to identify the diagnoses, the public hospital costs and payments for non-New Zealand (non-NZ) patients referred because of possible tuberculosis (TB). There have been no previous financial studies in this area. Funding arrangements for these patients were also reviewed. METHODS: A systematic, retrospective review was performed to identify the costs of investigating and managing non-NZ patients referred to the adult TB unit of a large, teaching hospital in Auckland, NZ. Patients were enrolled between 1 July 2002 and 30 June 2003. RESULTS: Forty-five non-NZ patients were studied. The mean age was 33.8 (+/-13.4) years. Thirty-four (75.5%) were managed under compulsion through Section 9 of the NZ TB Act. Thirty-two (71%) patients received TB treatment: 11 (24%) had infectious pulmonary TB and four had active extra-pulmonary TB. There were no multi-drug-resistant isolates. Three TB cases accounted for 250 (39%) inpatient days. One patient with rifampicin-resistant TB was responsible for 117 (29%) day-patient ward visits. Four (13%) infectious TB cases were managed as inpatients for more than 6 weeks. The total cost of services (US dollars) for the 45 patients was 350,236 dollars. The cost range was 544-43,513 dollars per patient. Four patients incurred costs over 25,000 dollars. CONCLUSIONS: TB in non-residents is a costly problem in NZ. Current policy applying to this area and the ability to determine its cost-effectiveness are in need of review.	7_EX.TOPIC
Carr, T. (1998). Return of school forms and nurse home visits increased adherence with follow up reading of tuberculosis tests in children [commentary on Cheng TL, Ottolini MC, Baumhaft K, et al. Strategies to increase adherence with tuberculosis test reading in a high- risk population. *Pediatrics*, 100, 210-213.] *Evidence-Based Nursing*, *1*(3), 78.	Question: In high risk children, can strategies of verbal and written instructions, telephone follow up, transportation tokens and a toy, education, or withholding school forms (proof of immunisation status) improve the rate of adherence with follow up reading of tuberculosis tests? Design: Randomised controlled trial. Setting: Outpatient department of an urban children's hospital in Washington, DC, USA. Participants: 627 consecutive children aged 1 to 12 years (91% African American, 74% Medicaid recipients) who were healthy and had no recent history of tuberculosis contact. 45% of participants had >/= 1 risk factor for tuberculosis (born in a country with a high prevalence of tuberculosis or contact with people who were homeless, street drug abusers, incarcerated, from high prevalence areas, or had HIV infection). Intervention: Participants and their families were given routine verbal and written instructions and randomised by day of the week to 1 of 5 strategies to improve adherence to follow up tuberculosis test reading at 48-72 hours after the Mantoux test: (1) no additional intervention (control group) (n = 121); (2) a reminder telephone call (n = 125); (3) transportation tokens and toy on return (positive reinforcement) (n = 121); (4) withholding of school forms until time of reading and information that the test would be repeated if not read within 48-72 hours (negative reinforcement) (n = 162); (5) parents taught to read the induration and a nurse home visit was scheduled to verify the results (n = 98). All children did not have school forms to complete; and for those who did, the form was not necessary for school attendance. Main outcome measure: Rate of adherence with follow up reading of tuberculosis test Main results: The adherence rates in the 5 groups were 58%, 70%, 67%, 70%, and 72%, respectively. Withholding school forms and advising parents that the test would be repeated (group 4, p = 0.03) and nurse home visits (group 5, p = 0.04) improved adherence for test reading compared with routine instructions alone (group 1). A reminder telephone call (group 2)	5_EX.POP

	showed a trend towards improvement and transportation tokens plus a toy (group 3) did not increase adherence for test reading compared with routine instructions alone. Conclusion: Withholding school forms until the time of tuberculosis test reading and nurse home visits were effective strategies for increasing the rate of adherence with follow up reading of tuberculosis tests in high risk children.	
Casal, M., et al. (2005). A case-control study for multidrug-resistant tuberculosis: risk factors in four European countries. *Microbial Drug Resistance-Mechanisms Epidemiology & Disease*, *11*(1), 62-67.	The aim of this study was to detect risk factors for multidrug resistance in patients with pulmonary tuberculosis in four European Union countries: France, Germany, Italy, and Spain. A prospective epidemiological case control study was conducted, made up of patients with clinically diagnosed and microbiologically confirmed pulmonary tuberculosis in the four countries between 1997 and 2000. A total of 138 cases and 276 controls were studied. Considering the four countries as a whole, the most statistically significant risk factors were as follows: intravenous drug use (OR 4.68); asylum-seeker support (OR 2.55) as income factor; living in a nursing home (OR 2.05); previous tuberculosis (OR 2.03) with pulmonary location; prison (OR 2.02); known tuberculosis contacts (OR 2.01); immunosuppression other than human immunodeficiency virus (HIV) (OR 1.96); acquired immunodeficiency syndrome (AIDS) (OR 1.96); current tuberculosis with pulmonary location (OR 1.77); and health-care worker (OR 1.69). These risk factors will have to be taken into account in the European Union as a whole, as well as in each individual country, to establish a health policy of monitoring and control for these cases of multidrug resistance. Although rare, their seriousness makes them particularly important.	1_EX.TB
Chang, S., Wheeler, L. S. M., & Farrell, K. P. (2002). Public health impact of targeted tuberculosis screening in public schools. *American Journal of Public Health*, *92*(12), p.1942.	Not available	9_IN.OTHER
Chaulk, C. P., et al. (1995). Eleven years of community-based directly observed therapy for tuberculosis. *JAMA*, *274*(12), 945-951.	OBJECTIVE: To evaluate community-based directly observed therapy (DOT) for tuberculosis (TB) control. DESIGN: Ecological study. METHODS: Three comparisons were made in this descriptive study. (1) An 11-year retrospective comparison of TB case rates, sputum conversion rates (SCRs), rates of therapy completion, and confounding factors (acquired immunodeficiency syndrome [AIDS], immigration, unemployment, and poverty) in Baltimore, Md, with those of the five major US cities having the highest TB incidence in 1981 but which did not have comprehensive DOT programs. (2) An 11-year trend of TB in Baltimore and the 19 major US cities with the highest TB incidence in 1981. (3) A 7-year trend in TB in both city groups between 1985 and 1992. SETTING: Twenty US metropolitan cities with more than 250,000 residents. RESULTS: Since 1981, Baltimore experienced the greatest decline in TB incidence (35.6 cases per 100,000 population, 1981; 17.2 cases per 100,000 population, 1992 [-51.7%]), and city rank for TB (sixth in 1981, 28th in 1992). Conversely, the average incidence of TB increased 2.1% in the five-city cohort and increased 1.8% in the 19-city cohort. Since 1985, TB incidence increased 35.3% in the five-city cohort and 28.5% in the 19-city cohort, but declined 29.5% in Baltimore. From 1986 through 1992, Baltimore's DOT-managed cases had the highest annual SCRs at 3 months (mean, 90.7%), and the highest completion rates for standard anti-TB therapy (mean, 90.1%) when compared with the five cities. These trends could not be attributed to differentials in AIDS, immigration, poverty, or unemployment.	5_EX.POP

	Increasingly, more Baltimore cases were treated under DOT (86.5%, 1993) over time. Disease relapse rates remained low, even among HIV-infected patients. Within Baltimore, the documented SCR was significantly higher among DOT-managed cases compared with non-DOT-managed cases (P < .05); multidrug resistance remains rare (0.57%). Within Maryland, Baltimore accounted for 44.4% of all TB cases in 1981, compared with 28.7% in 1992 (P < .001). CONCLUSIONS: In contrast to the national TB upswing during the 1980s, Baltimore experienced a substantial decline in TB following implementation of community-based DOT, despite highly prevalent medicosocial risk factors. Directly observed therapy facilitated high treatment completion rates and bacteriologic evidence of cure. Directly observed therapy could help reduce TB incidence in the United States, particularly in cities with high case rates.	
Chaulk, C. P., Friedman, M., & Dunning, R. (2000). Modeling the epidemiology and economics of directly observed therapy in Baltimore. *International Journal of Tuberculosis & Lung Disease*, *4*(3), 201-207.	SETTING: From 1958 to 1978, Baltimore maintained one of the highest pulmonary tuberculosis (TB) rates in the US. But, from 1978 to 1992 its TB rate declined by 64.3% and its ranking for TB fell from second highest among large US cites to twenty-eighth. This TB trend coincided with the implementation of an aggressive directly observed therapy (DOT) program by Baltimore's Health Department. OBJECTIVES: We used modeling to estimate the range of TB cases prevented in Baltimore under DOT. Case estimates equal the difference between the observed number of TB cases in Baltimore versus the expected number if Baltimore's TB trend was replaced by the TB trend for the US (low estimate) or the TB trend for all US cities with over 250,000 residents (high estimate). Economic savings are estimated. RESULTS: Without DOT we estimate there would have been between 1,577 (53.6%) and 2,233 (75.9%) more TB cases in Baltimore, costing $18.8 million to $27.1 million. Cases prevented and expenditures saved increased with increased DOT participation. CONCLUSION: Our model predicts that Baltimore's TB decline accompanying DOT resulted in health care savings equal to twice the city's total TB control budget for this period. These results are most plausibly due to DOT, since it was the only major change in Baltimore's TB control program, and rising TB risk factors-AIDS, injection drug use, poverty-in a city where TB had been epidemic should have triggered a TB increase as in comparable US cities, rather than the observed decline. As national TB rates continue to decline it will be important to identify ways to capture and reinvest these savings to support effective TB control programs.	5_EX.POP
Clark, P. M., et al. (2007). Effect of pharmacist-led patient education on adherence to tuberculosis treatment. *American Journal of Health-System Pharmacy*, *64*(5), 497-506.	PURPOSE: The purpose of this study was to assess the effect of a clinical pharmacist-directed patient education program on the therapy adherence of first-time tuberculosis (TB) patients and to identify the major pharmaceutical care needs and issues of first-time TB and multidrug-resistant (MDR)-TB patients. METHODS: In the first part of the study, first-time TB patients were randomized either to the No EDU group (n = 58) where patients received routine medical and nursing care or to the EDU group (n = 56) where patients were also provided with clinical pharmacist-directed patient education. The patient's adherence to treatment was evaluated by attendance at scheduled visits, medication counting, and urine analysis for the presence of isoniazid metabolites. In the second part of the study, the pharmaceutical care needs and issues were determined for first-time TB patients and for MDR-TB patients (n = 40). RESULTS: The adherence of patients who received pharmacist-directed patient education was greater than that of patients who did not. The attendance at scheduled visits and urine analysis for the presence of isoniazid metabolites yielded better results in respect to adherence for the EDU group (p < 0.05), while medication counting did not differ	5_EX.POP

	between the two groups. The major pharmaceutical care needs of first-time TB patients were for pain control, nutrient replacement, appropriate prescribing, respiratory control, and diabetic control. Similar findings were recorded for MDR-TB patients. CONCLUSION: Patients' adherence to TB treatment improved when a pharmacist provided patient education on medication use and addressed patients' pharmaceutical care issues.	
Clark, R. C., & Mytton, J. J. (2007). Estimating infectious disease in UK asylum seekers and refugees: a systematic review of prevalence studies. *Journal of Public Health*, *29*(4), 420-428.	BACKGROUND: The prevalence of infectious diseases such as tuberculosis (TB), HIV and hepatitis B in the UK asylum seeker and refugee population is currently uncertain. METHODS: Systematic review of published and unpublished studies. RESULTS: Five studies met the inclusion criteria. Three studies reported the prevalence of TB with rates ranging from 1.33 to 10.42 per 1000. The three studies reporting hepatitis B estimated rates from 57 to 118 per 1000. One study reported a prevalence rate for HIV of 38.19 per 1000. CONCLUSION: A small number of studies have been identified reporting prevalence rates for TB, hepatitis B and HIV that vary widely where comparisons are available. These differences may reflect true variation in risk between study populations, but are likely to be affected by sampling difficulties encountered when researching these population groups. Efforts are required to improve these difficulties which are currently limiting the validity of prevalence findings and generalizability to comparable asylum seeker and refugee populations. [References: 29]	1_EX.TB
Codecasa, L. R., & Besozzi, G. (1998). Acceptance of isoniazid preventive treatment by close contacts of tuberculosis cases: a 692-subject Italian study. *International Journal of Tuberculosis & Lung Disease*, *2*(3), 208-212.	SETTING: Villa Marelli Institute, Lombardy Regional Reference Centre for Tuberculosis. OBJECTIVE: To evaluate acceptance of and adherence to isoniazid preventive treatment (IPT) of close contacts of contagious tuberculosis (TB) cases (CC); comparison of Italian and immigrant patients. METHODS: A retrospective study of a consecutive series of 692 subjects (474 Italians and 218 immigrants from developing countries) exposed to contagious TB cases, who were offered IPT after tuberculin skin testing and chest X-ray, according to the Lombardy Regional Protocol for TB control. RESULTS: Of 692 CCs, 36 (5.2%) subjects refused IPT, 522 (75.5%) completed the treatment as prescribed, 23 (3.3%) suspended IPT because of adverse effects, 14 (2.0%) spontaneously discontinued IPT against our advice, 93 (13.4%) were lost to follow up, and seven (0.6%) were still in treatment when the present data were evaluated. Italian CCs had a completion rate significantly higher than the immigrants (81.0% vs 63.3%, P < 0.01). CONCLUSION: The rate of acceptance and completion of IPT in our population proved higher than many previously reported data, and the better results among Italian subjects reflect the importance of a complete comprehension of IPT that may not always be achieved with immigrant patients.	9_IN.OTHER
Coker, R. J. (2003). Public health impact of detention of individuals with tuberculosis: systematic literature review. *Public Health*, *117*(4), 281-287.	As the world witnesses ever-increasing rates of tuberculosis, particularly of drug-resistant strains affecting some of society's most marginalized individuals, policy makers and Legislators may again visit the statute books in order to strengthen their armamentarium of tools to protect public health. This paper assesses the evidence in support of the sanction to detain those with tuberculosis who are perceived as posing a public heath threat, and shows that Little research has been conducted to inform policy, probably because traditional epidemiological methods used to assess the impact of interventions are not feasible.	6_EX.NON-EMP
Davidson, B. L. (1998). A controlled comparison of directly observed therapy vs self-administered	STUDY OBJECTIVES: To compare treatment completion rates at 8 and 12 months after treatment initiation for patients with active TB treated with either directly observed therapy (DOT) or self-administered therapy (SAT). DESIGN: Retrospective comparison	5_EX.POP

therapy for active tuberculosis in the urban United States. *Chest*, (5), 1239-43.	study of DOT and SAT concurrent patient cohorts. SETTING: Urban Tuberculosis Control Program within a Department of Public Health. PATIENTS: Three hundred nineteen patients confirmed to have active TB between July 1, 1994, and June 30, 1995, who began outpatient drug therapy. INTERVENTIONS: Patients and/or their physicians chose to receive their anti-TB drug therapy by DOT (n=113) or SAT (n=206) and were assessed for treatment completion at prospectively determined times, 8 and 12 months. MEASUREMENTS AND RESULTS: Proportions of patients who completed treatment at 8 and 12 months without crossing over to the other group were compared. At 8 months, 52% of DOT and 35% of SAT patients had completed treatment (relative superiority of DOT, 49%; p=0.003). At 12 months, completion rates were 70% for DOT patients and 53% for SAT patients (relative superiority of DOT, 30%; p=0.006). CONCLUSIONS: In our setting, patients receiving DOT were much more likely to complete treatment earlier than those receiving SAT. Even with DOT, only 52% of patients had completed treatment by 8 months.	
Diel, R., & Niemann, S. (2003). Outcome of tuberculosis treatment in Hamburg: a survey, 1997-2001. *International Journal of Tuberculosis & Lung Disease*, *7*(2), 124-131.	SETTING: Federal State of Hamburg, Germany, 1997-2001. OBJECTIVE: To determine risk factors affecting the treatment outcome for tuberculosis according to the WHO/IUATLD classification. DESIGN: Prospective evaluation among patients with culture-confirmed pulmonary disease due to Mycobacterium tuberculosis during the period 1997-1999. RESULTS: Five hundred and eighteen (467 new and 51 re-treatment) cases started a course of treatment (average duration 36.1 +/- 15.5 weeks), resulting in cure for 416 (80.3%) and treatment completed for three (0.6%) patients; 449 patients (86.7%) initially received a three-drug regimen. Treatment interruption occurred in 54 (10.4%), and failure in 12 (2.3%) cases; 32 (6.2%) patients died (irrespective of cause). Alcohol dependence appeared to be the strongest risk factor for persistence of disease, followed by homelessness and unemployment. The risk of treatment interruption was six times higher among alcoholics (OR = 6.0), five times higher among drug abusers (OR = 5.2) and three times higher among the homeless (OR = 3.0) than in other patients. CONCLUSION: Although the current treatment management in Hamburg is considered to be effective, a further improvement in the proportion of patients who complete treatment can be achieved by increased public health surveillance of subpopulations with the above-mentioned risk factors.	7_EX.TOPIC
Elk, R., et al. (1993). Compliance with tuberculosis treatment in methadone-maintained patients: Behavioral interventions* 1. *Journal of Substance Abuse Treatment*, *10*(4), 371–382.	Tuberculosis has increased dramatically in the United States. Noncompliance with treatment is high. The purpose of this investigation was to achieve compliance with prophylactic TB treatment and simultaneously decrease drug use in a high-risk group of intravenous drug users. Two studies were conducted. Study 1: Subjects were 9 chronic opiate users who tested positive for tuberculosis and were placed on isoniazid (INH) and methadone. Methadone was dispensed contingent upon INH ingestion throughout. A within-subject, A-B design with contingency management interventions on drug use was implemented. Results: Compliance with INH was 100% in 8 patients. Cocaine use remained high. Study 2: Two patients, meeting same criteria as Study 1, participated in a within-subject A-B multiple baseline design. Methadone was dispensed contingent upon INH ingestion throughout. Successive decreases in cocaine use were reinforced in the contingent phase. Results: Compliance with INH was high. During contingency, both patients had over 40% cocaine-free urine samples compared with 0% at baseline. This investigation serves as a model for achieving compliance with TB treatment in opiate users.	9_IN.OTHER

Fallab-Stubi, C. L., et al. (1998). Electronic monitoring of adherence to treatment in the preventive chemotherapy of tuberculosis. *International Journal of Tuberculosis & Lung Disease*, 2(7), 525-530.	SETTING: Non-adherence to treatment is a frequent problem in the preventive chemoprophylaxis of tuberculosis. OBJECTIVE: To evaluate the usefulness of the Medication Event Monitoring System (MEMS) for following and improving patient adherence to 6-month treatment with isoniazid. DESIGN: Three methods of monitoring compliance, MEMS, pill count and a urine test for isoniazid, were compared prospectively in 30 patients. The efficacy of a combined intervention by the physician and the pharmacist was evaluated in non-compliant patients. RESULTS: According to the MEMS data, overall adherence to isoniazid therapy was 91.5%, and 86% of the patients were considered compliant throughout the period of observation. The pill count and the urine test tended to overestimate the overall compliance when compared to the MEMS. The combined intervention of the physician and pharmacist allowed drug adherence to be enhanced in non-compliant patients, but the effect was only transient if this was not repeated every month. CONCLUSION: Our results suggest that the MEMS system is a useful approach for monitoring and improving compliance with preventive chemotherapy for tuberculosis.	5_EX.POP
Faustini, A., Hall, A. J., & Perucci, C. A. (2005). Tuberculosis treatment outcomes in Europe: a systematic review. *European Respiratory Journal*, 26(3), 503-510.	In order to facilitate the control of tuberculosis (TB), the World Health Organization (WHO) has defined a standardised short-course chemotherapy and a strategy, directly observed therapy. In 2000, WHO surveillance of TB treatments in Europe recorded a successful outcome rate of 77%. The aim of this report is to estimate treatment outcomes in European countries based on published studies and to identify their determinants. A systematic review was conducted of published reports of TB treatment outcomes in Europe. Meta-analysis, meta-regression and subgrouping were used to pool treatment outcomes and analyse associations with mean age, sex, immigration status and multidrug resistance. Of the 197 articles identified in the search, 26 were eligible for the review; 74.4% of outcomes were successful, 12.3% were unsuccessful and 6.8% of patients died. Heterogeneity was high for all outcomes. National estimates were possible for six countries. Multidrug resistance was inversely associated with successful outcome, which were fewer in populations with >9% multidrug-resistant TB, and in patients aged <44 yrs. Successful tuberculosis treatment outcomes were below the 85% threshold suggested by the World Health Organization. There was an inverse association with levels of multidrug-resistant tuberculosis. The unexplained heterogeneity between the studies for unsuccessful outcomes seems to be due to differing interpretations given to World Health Organization definitions. [References: 45]	7_EX.TOPIC
Floyd, K. (2003). Costs and effectiveness: the impact of economic studies on TB control (Brief record). *Tuberculosis*, (1-3), 187-200.	This paper assesses the impact of economic studies on TB control during the period 1982–2002, with a focus on cost and cost-effectiveness studies. It begins by identifying broad categories of economic study relevant to TB control, and how economic studies can, theoretically, have an impact on TB control. The impact that economic studies of TB control have had in practice is then analysed through a systematic review of the literature on cost and cost-effectiveness studies related to TB control, and three case studies (one cost study and two cost-effectiveness studies). The results show that in the past 20 years, 66 cost-effectiveness studies and 31 cost studies have been done on a variety of important TB control topics, with a marked increase occurring after 1994. In terms of numbers, these studies have had most potential for impact in industrialized countries, and within industrialized countries are most likely to have had an impact on policy and practice related to screening and preventive therapy. In developing countries with a high burden of tuberculosis, far fewer studies have been undertaken.	5_EX.POP

	Here, the main impact of economic studies has been influencing policy and practice on the use of short-course chemotherapy, justifying the implementation of community-based care in Africa, and helping to mobilize funding for TB control based on the argument that short-course treatment for TB is one of the most cost-effective health interventions available. For the future, cost and cost-effectiveness studies will continue to be relevant, as will other types of economic study.	
Fraser, A., et al. (2006). Treatment of latent tuberculosis in persons at risk for multidrug-resistant tuberculosis: systematic review. *International Journal of Tuberculosis & Lung Disease*, *10*(1), 19-23.	SETTING: The emergence and spread of multidrug-resistant tuberculosis (MDR-TB), caused by Mycobacterium tuberculosis resistant to at least isoniazid (INH) and rifampicin, is a threat to global TB control. OBJECTIVE: To appraise evidence of the effectiveness of treatment of latent TB infection (LTBI) in people at risk for developing active MDR-TB. DESIGN: Systematic review of comparative studies of people treated and not treated for LTBI following exposure to MDR-TB. DATA SOURCES: PubMed, EMBASE, LILACS and the Cochrane Library (December 2004). RESULTS: Two observational studies met inclusion criteria. A prospective cohort study found individualised tailored treatment to be effective for preventing active TB in children (OR = 0.20, 95%CI 0.04-0.94), while a retrospective cohort study found INH not to be effective (OR = 0.46, 95%CI 0.07-2.32). CONCLUSION: Evidence of the effects of treatment of LTBI in people exposed to MDR-TB is extremely limited in both quantity and quality. The increasing global spread of MDR-TB and the difficulties in treating it emphasise the need for effective preventive measures. Ideally, this issue should be addressed in a randomised controlled trial. Until such a trial is conducted, routine clinical data collected as part of existing TB control programmes could be useful and can be generated relatively easily.	1_EX.TB
Furin, J. (2007). The clinical management of drug-resistant tuberculosis. *Current Opinion in Pulmonary Medicine*, *13*(3), 212-217.	PURPOSE OF REVIEW: Drug-resistant tuberculosis is a growing problem, with almost half a million cases worldwide. In spite of the difficulty in its management, drug-resistant tuberculosis can be successfully treated, even in poor settings. RECENT FINDINGS: This article will review key findings in the areas of epidemiology, diagnosis and management of drug-resistant tuberculosis, including new antituberculous drugs. The issue of extensively drug-resistant tuberculosis will also be reviewed and discussed. Finally, novel approaches to the management of drug-resistant tuberculosis in populations with HIV, as well as in pediatric populations, among pregnant women, and among patients requiring surgical therapy, will be reviewed. SUMMARY: New advances in the diagnosis and management of drug-resistant tuberculosis allow for excellent clinical outcomes to be achieved, even in difficult-to-treat populations. This is possible with timely diagnosis of disease and rapid initiation of appropriate therapy in supported settings. [References: 44]	6_EX.NON-EMP
Gonzalez-Ochoa, E., et al. (2009). Pulmonary tuberculosis case detection through fortuitous cough screening during home visits. *Tropical Medicine & International Health*, *14*(2), pp.131-135.	OBJECTIVE: To compare the yield of active tuberculosis (TB) case detection among risk groups during home visits with passive detection among patients at health services. METHODS: In April 2004, in a first phase, we introduced, active screening for coughing among all family members of patients that were visited at home by their family doctor or nurse for other reasons. Subsequently, from October 2004 onwards, active screening was restricted to family members belonging to groups at risk of TB. RESULTS: The overall detection rate of TB increased from 6.7/100,000 during passive detection at health services before the intervention to 26.2/100,000 inhabitants when passive detection was complemented by active case finding. Active screening among risk groups yielded 35 TB cases per 1000 persons screened compared to 20 TB cases per	4_EX.OECD

	1000 persons passively screened at health services. Active case finding was particularly efficient in those coughing for 3 weeks or more (107/1000 screened). CONCLUSION: This study demonstrates that active case finding in groups at risk during home visits increases the case detection rate in the population and permits the identification of cases that may not be detected through passive case finding at health facility level.	
Gourevitch, M. N., et al. (1996). Successful adherence to observed prophylaxis and treatment of tuberculosis among drug users in a methadone program. *Journal of Addictive Diseases*, *15*(1), 93–104.	Incomplete antituberculous chemoprophylaxis and treatment are major causes of the resurgence of tuberculosis, often drug-resistant, among drug users. We offered directly observed antituberculous chemoprophylaxis (n = 102) or treatment (n = 12) to tuberculous chemoprophylaxis (n = 102) or treatment (n = 12) to eligible methadone maintenance treatment patients. Methadone dosing was not contingent upon ingestion of antituberculous medication(s). No material incentives were provided. Ninety (88%) prophylaxis and 9 (75%) treatment patients were administered > or = 5 weekly doses of antituberculous medications during > or = 80% of 4740 patient-weeks. The majority of patients were HIV-seropositive. Active substance abuse was not associated with diminished adherence. Over 80% of patients completed or were still receiving therapy at the end of the study. Adherence to and completion of directly observed antituberculous therapy can thus be attained by drug users in treatment, despite ongoing drug misuse. Substance abuse treatment programs provide opportunities for enhanced compliance, and should thus be viewed as critical components of strategies to address the tuberculosis epidemic in drug users.	9_IN.OTHER
Gruber, V. A. et al. (2008). A randomized trial of 6-month methadone maintenance with standard or minimal counseling versus 21-day methadone detoxification. *Drug & Alcohol Dependence*, *94*(1-3), 199-206.	BACKGROUND: Important questions remain regarding the necessary duration and intensity for methadone treatment to be effective. METHODS: As part of a clinical trial of tuberculosis chemoprophylaxis [Batki, S.L., Gruber, V.A., Bradley, J.M., Bradley, M., Delucchi, K., 2002. A controlled trial of methadone treatment combined with directly observed isoniazid for tuberculosis prevention in injection drug users. Drug Alcohol Depend. 66 283-293. doi:10.1016/S0376-8716(01)00208-3], patients with opioid dependence were recruited from an outpatient 21-day methadone detoxification program and were randomly assigned to one of three treatment conditions: (1) continuation in 21-day methadone detoxification; (2) transfer to 6-month methadone maintenance with only minimal counseling; or (3) transfer to 6-month methadone maintenance with standard twice monthly counseling and as-needed social work and psychiatric services. Both the 6-month maintenance treatments were followed by 1.5 months of detoxification. Urine drug tests and self-report measures were collected at baseline, months 1-6, and month 8.5. RESULTS: Compared to 21-day methadone detoxification, 6-month methadone maintenance with either minimal or standard counseling resulted in fewer opiate positive urine tests and days of self-reported heroin and alcohol use. There was no change in cocaine use or other outcome measures. The increased counseling available in the standard counseling condition did not appear to reduce heroin use further than the minimal counseling condition, in contrast to the effect found for more structured counseling in long-term methadone maintenance (McLellan et al., 1993). CONCLUSIONS: Six months of methadone maintenance, even with minimal counseling, reduces heroin and alcohol use more than 21-day methadone detoxification.	7_EX.TOPIC
Guzman-Montes, G. Y., Ovalles, R. H., & Laniado-Laborin, R. (2009). Indirect patient	BACKGROUND: One of the main problems faced by the Mexican National Tuberculosis Program is the high rate of patients abandoning treatment. This study aimed to determine the magnitude of unaccounted costs of tuberculosis (TB) treatment in Tijuana,	7_EX.TOPIC

expenses for antituberculosis treatment in Tijuana, Mexico: is treatment really free? *Journal of Infection in Developing Countries*, *3*(10), 778-782.	Mexico. METHODOLOGY: Subjects were recruited at 21 health centres. Patients had confirmed active pulmonary TB, had been on treatment for more than 12 weeks, and were aged 18 years and older. The questionnaire provided information about demographics, past and current episodes of TB, and various categories of expenses. RESULTS: The study included 180 patients as follows: 48 had been diagnosed with tuberculosis in the past (26.6%) and had either currently relapsed or failed treatment; 160 (88.8%) were under directly observed therapy (DOT); 131 (72.8%) attended a health centre; and the rest received directly observed treatment at home. The daily cost of transportation to the health centre was MXN $25.88 +/- 3.22 (1 USD = 13 MXN). Thirty-two patients (17.8%) had to buy medication at least once, with a monthly medication expense of MXN $440.5 +/- 40.3. Patients receiving DOT at the health centre reported daily food and beverages expenses, spending MXN $56.5 +/- 10.1. Forty-two patients reported laboratory testing expenses, on average MXN $558.8 +/- 85.8 per month. Eighty patients (42.4%) reported expenses on radiographic/ultrasound studies, on average MXN $562.9 +/- 72.1 per six-month regimen. Conclusions TB diagnosis and treatment posed a significant economic burden on patients in terms of both cost and affordability; clinic-based DOT may contribute disproportionately to the costs incurred by patients.	
Haynes, R. B., et al. (2008). Interventions for enhancing medication adherence. *Cochrane Database of Systematic Reviews*, (2), p.CD000011.	Background People who are prescribed self- administered medications typically take less than half the prescribed doses. Efforts to assist patients with adherence to medications might improve the benefits of prescribed medications, but also might increase their adverse effects. Objectives To update a review summarizing the results of randomized controlled trials (RCTs) of interventions to help patients follow prescriptions for medications for medical problems, including mental disorders but not addictions. Search strategy We updated searches of The Cochrane Library, MEDLINE, CINAHL, EMBASE, International Pharmaceutical Abstracts (IPA), PsycINFO (all via OVID) and Sociological Abstracts (via CSA) in January 2007 with no language restriction. We also reviewed bibliographies in articles on patient adherence and articles in our personal collections, and contacted authors of relevant original and review articles. Selection criteria Articles were selected if they reported an unconfounded RCT of an intervention to improve adherence with prescribed medications, measuring both medication adherence and treatment outcome, with at least 80% follow- up of each group studied and, for long- term treatments, at least six months follow- up for studies with positive initial findings. Data collection and analysis Study design features, interventions and controls, and results were extracted by one review author and confirmed by at least one other review author. We extracted adherence rates and their measures of variance for all methods of measuring adherence in each study, and all outcome rates and their measures of variance for each study group, as well as levels of statistical significance for differences between study groups, consulting authors and verifying or correcting analyses as needed. The studies differed widely according to medical condition, patient population, intervention, measures of adherence, and clinical outcomes. Therefore, we did not feel that quantitative analysis was scientifically justified; rather, we conducted a qualitative analysis. Main results For short- term treatments, four of ten interventions reported in nine RCTs showed an effect on both adherence and at least one clinical outcome, while one intervention reported in one RCT significantly improved patient adherence, but did not enhance the clinical outcome. For long- term treatments, 36 of 81 interventions reported in 69 RCTs were associated with improvements in adherence, but only 25 interventions led to	5_EX.POP

	improvement in at least one treatment outcome. Almost all of the interventions that were effective for long-term care were complex, including combinations of more convenient care, information, reminders, self- monitoring, reinforcement, counseling, family therapy, psychological therapy, crisis intervention, manual telephone follow- up, and supportive care. Even the most effective interventions did not lead to large improvements in adherence and treatment outcomes. Authors' conclusions For short- term treatments several quite simple interventions increased adherence and improved patient outcomes, but the effects were inconsistent from study to study with less than half of studies showing benefits. Current methods of improving adherence for chronic health problems are mostly complex and not very effective, so that the full benefits of treatment cannot be realized. High priority should be given to fundamental and applied research concerning innovations to assist patients to follow medication prescriptions for long-term medical disorders.	
Horsburgh, C. R., et al. (2010). Latent TB infection treatment acceptance and completion in the United States and Canada. *Chest*, *137*(2), 401-409.	BACKGROUND: Treatment of latent TB infection (LTBI) is essential for preventing TB in North America, but acceptance and completion of this treatment have not been systematically assessed. METHODS: We performed a retrospective, randomized two-stage cross-sectional survey of treatment and completion of LTBI at public and private clinics in 19 regions of the United States and Canada in 2002. RESULTS: At 32 clinics that both performed tuberculin skin testing and offered treatment, 123 (17.1%; 95% CI, 14.5%-20.0%) of 720 subjects tested and offered treatment declined. Employees at health-care facilities were more likely to decline (odds ratio [OR], 4.74; 95% CI, 1.75-12.9; P = .003), whereas those in contact with a patient with TB were less likely to decline (OR, 0.19; 95% CI, 0.07-0.50; P = .001). At 68 clinics starting treatment regardless of where skin testing was performed, 1,045 (52.7%; 95% CI, 48.5%-56.8%) of 1,994 people starting treatment failed to complete the recommended course. Risk factors for failure to complete included starting the 9-month isoniazid regimen (OR, 2.08; 95% CI, 1.23-3.57), residence in a congregate setting (nursing home, shelter, or jail; OR, 2.94; 95% CI, 1.58-5.56), injection drug use (OR, 2.13; 95% CI, 1.04-4.35), age >or= 15 years (OR, 1.49; 95% CI, 1.14-1.94), and employment at a health-care facility (1.37; 95% CI, 1.00-1.85). CONCLUSIONS: Fewer than half of the people starting treatment of LTBI completed therapy. Shorter regimens and interventions targeting residents of congregate settings, injection drug users, and employees of health-care facilities are needed to increase completion.	7_EX.TOPIC
Jasmer, R. M., et al. (2000). Twelve months of isoniazid compared with four months of isoniazid and rifampin for persons with radiographic evidence of previous tuberculosis: an outcome and cost-effectiveness analysis. *American Journal of Respiratory & Critical Care Medicine*, *162*(5), 1648-1652.	Isoniazid taken daily for 12 mo and isoniazid and rifampin taken daily for 4 mo are both recommended options for patients with radiographic evidence of previous tuberculosis and positive tuberculin skin tests who have not had prior treatment. We compared the completion rates, number of adverse effects, and cost effectiveness of these two regimens. Patients were treated at the San Francisco Tuberculosis Clinic from 1993 through 1996. A Markov model was developed to assess impact on life expectancy and costs. One thousand twenty-two patients, with a mean age of 52 yr, and > 90% foreign born, were treated; 545 received isoniazid and 477 received isoniazid and rifampin. For isoniazid, 79.8% completed 12 mo of therapy and 4.9% had adverse effects versus 83.6% completion, 6.1% adverse effects for isoniazid and rifampin (p > 0.05 for all between-group comparisons). Both regimens increased life expectancy by 1.4-1.5 yr. Compared with isoniazid, isoniazid and rifampin produced net incremental savings of $135 per patient treated. In patients with radiographic evidence of prior tuberculosis who have not been previously treated, isoniazid for 12 mo and	7_EX.TOPIC

	isoniazid and rifampin for 4 mo have similar rates of completion and adverse effects, and both increase life expectancy compared with no treatment. Isoniazid and rifampin for 4 mo is cost saving compared with isoniazid alone. This advantage was maintained even when compared with 9 mo of isoniazid, the new American Thoracic Society/Centers for Disease Control (ATS/CDC) recommendation for treatment with isoniazid alone.	
Jasmer, R. M. et al. (2004). Tuberculosis treatment outcomes: directly observed therapy compared with self-administered therapy. *American Journal of Respiratory & Critical Care Medicine*, *170*(5), 561-566.	Effective treatment of tuberculosis requires adherence to a minimum of 6 months treatment with multiple drugs. To improve adherence and cure rates, directly observed therapy is recommended for the treatment of pulmonary tuberculosis. We compared treatment outcomes among all culture-positive patients treated for active pulmonary tuberculosis (n = 372) in San Francisco County, California from 1998 through 2000. Patients treated by directly observed therapy at the start of therapy (n = 149) had a significantly higher cure rate compared with patients treated by self-administered therapy (n = 223) (the sum of bacteriologic cure and completion of treatment, 97.8% versus 88.6%, p < 0.002), and decreased tuberculosis-related mortality (0% vs. 5.5%, p = 0.002). Rates of treatment failure, relapse, and acquired drug resistance were similar between the two groups. Forty-four percent of patients who received self-administered therapy had risk factors for nonadherence and should have been assigned to directly observed therapy. We conclude that treatment plans that emphasize directly observed therapy from the start of therapy have the greatest success in improving tuberculosis treatment outcomes.	5_EX.POP
Khan, K., et al. (2002). Global drug-resistance patterns and the management of latent tuberculosis infection in immigrants to the United States. *New England Journal of Medicine*, *347*(23), 1850-1859.	BACKGROUND: In the United States, an increasingly disproportionate burden of tuberculosis among the foreign-born population has led to calls for improvements in the detection and treatment of latent infection in new immigrants. Current treatment guidelines do not take into account global differences in drug-resistance patterns or their implications for the treatment of immigrants. The use of multinational surveillance systems to guide the management of latent infection according to region-specific drug-resistance profiles could improve the efficiency of efforts to reduce the burden of tuberculosis in immigrants to the United States. METHODS: We constructed a decision-analysis model by using a hypothetical cohort of all documented immigrants entering the United States from developing nations. Region-specific drug-resistance profiles were derived from data on 30,388 cases of infection. The model examined the effectiveness and cost effectiveness of four strategies: no intervention or tuberculin skin testing followed by treatment with isoniazid, treatment with rifampin, or treatment with rifampin plus pyrazinamide for those with a positive test result. RESULTS: A strategy of detecting and treating latent tuberculosis infection was cost-saving among immigrants from Mexico, Haiti, sub-Saharan Africa, South Asia, and developing nations in East Asia and the Pacific. This strategy was highly cost effective among immigrants from other developing nations. Rifampin plus pyrazinamide was the preferred strategy for treating latent infection in immigrants from Vietnam, Haiti, and the Philippines. CONCLUSIONS: For new immigrants to the United States from developing nations, a strategy of detecting and treating latent tuberculosis infection would lead to substantial health and economic benefits. Because of the high prevalence of resistance to isoniazid, treatment with a rifampin-containing regimen should be strongly considered for immigrants from Vietnam, Haiti, and the Philippines. Copyright 2002 Massachusetts Medical Society	7_EX.TOPIC

Kimerling, M. E. et al. (1999). Spot sputum screening: evaluation of an intervention in two homeless shelters. *The International Journal of Tuberculosis and Lung Disease*, *3*(7), 613–619.	SETTING: Two homeless shelters in Birmingham, Alabama. OBJECTIVE: To interrupt tuberculosis transmission and evaluate the utility of spot sputum screening. DESIGN: Two shelters participated in the study between May 1996 and February 1997. A spot sputum specimen was collected on a given evening from each overnight client. Information was obtained regarding symptoms and tuberculin skin test (TST) status. There were four screenings during two rounds, with TST in round one only. RESULTS: Of 127 persons involved in the study, 120 (95%) provided specimens, and four tuberculosis cases were identified (4/127, 3.1%). Symptoms were infrequently reported. RFLP analysis (IS6110) confirmed a two-band cluster in three of the four cases; another matching two-band strain was found in a drug rehabilitation client staying in one shelter. Secondary RFLP typing (pTBN12) confirmed the homeless cluster. Costs were $1311 per case identified. Among 92 clients with a prior TST, 40% reported a positive result (37/92). Of 21 PPD tests read, 11 were > or =10 mm (52%). CONCLUSION: Spot sputum screening is effective in identifying unsuspected tuberculosis cases in shelters. It has acceptable costs, is logistically simple and efficient. Symptom screening was not useful in this general homeless population. RFLP analysis showed cloning of the two-band strain. Given the evidence for ongoing transmission, sputum screening should be considered in shelter settings.	9_IN.OTHER
Kong, P.M. et al. (2002). Skin-test screening and tuberculosis transmission among the homeless. *Emerging Infectious Diseases*, *8*(11), 1280-1284.	We describe the implementation of a mandatory tuberculosis (TB) screening program that uses symptom screening and tuberculin skin testing in homeless shelters. We used the results of DNA fingerprinting of Mycobacterium tuberculosis isolates to evaluate the effect of the program on TB incidence and transmission. After the program was implemented, the proportion of cases among homeless persons detected by screening activities increased, and the estimated TB incidence decreased from 510 to 121 cases per 100000 population per year. Recent transmission, defined by DNA fingerprinting analysis as clustered patterns occurring within 2 years, decreased from 49% to 14% (p=0.03). Our results suggest that the shelter-based screening program decreased the incidence of TB by decreasing its transmission among the homeless.	9_IN.OTHER
Kranzer, K., et al. (2010). Yield of HIV-associated tuberculosis during intensified case finding in resource-limited settings: a systematic review and meta-analysis. *The Lancet Infectious Diseases*, *10*(2), 93-102.	Intensified case finding is the regular screening for evidence of tuberculosis in people infected with HIV, at high risk of HIV, or living in congregate settings. We systematically reviewed studies of intensified case finding published between January, 1994, and April, 2009. In 78 eligible studies, the number of people with tuberculosis detected during intensified case finding varied substantially between countries and target groups of patients. Median prevalence of newly diagnosed tuberculosis was 0.7% in population-based surveys, 2.2% in contact-tracing studies, 2.3% in mines, 2.3% in programmes preventing mother-to-child transmission of HIV, 2.5% in prisons, 8.2% in medical and antiretroviral treatment clinics, and 8.5% in voluntary counselling and testing services. Metaregression analysis of studies that included only people with HIV showed that for each increment in national prevalence of tuberculosis of 100 cases per 100 000 population, intensified case finding identified an additional one case per 100 screened individuals (p=0.03). Microbiological sputum examination of all individuals without prior selection by symptom screening yielded an additional four cases per 100 individuals screened (p=0.05). Data on the use of serial screening, treatment outcomes in actively identified cases of tuberculosis, and cost-effectiveness, however, were lacking. Concerted action is needed to develop intensified case finding as an important method for control of tuberculosis. [References: 117]	4_EX.OECD

Lincoln, T., et al. (2004). Completing tuberculosis prophylaxis in jail: targeting treatment and comparison of rifampin/pyrazinamide with isoniazid regimens. *International Journal of Tuberculosis & Lung Disease*, *8*(3), 306-311.	SETTING: A county jail. OBJECTIVE: To characterize the treatment of latent tuberculosis infection and the impact on treatment completion of the 2-month rifampin and pyrazinamide regimen as compared to the traditional 6- to 12-month isoniazid regimen among persons incarcerated at a county correctional facility. DESIGN: Retrospective review of tuberculosis records from January 1998 to December 2000. RESULTS: Of 2127 inmates who were tuberculin skin test positive, 146 were started on treatment. This was generally limited to those expected to remain incarcerated long enough to complete the course of treatment. Completion rates were 88% (67/76) for the 2-month and 74% (51/69) for the 6- to 12-month courses (P = 0.03), and 82% overall. The two regimens were similarly tolerated, but inmates on isoniazid were more likely to be released (despite longer projected incarceration) and not complete treatment once in the community. Thirty-seven per cent of persons for whom treatment was not indicated by the previous guidelines should have had treatment by the new guidelines. CONCLUSION: The 2-month rifampin/pyrazinamide regimen had a higher completion rate than the longer isoniazid regimen, without additional toxicity, and allowed more patients to be treated. Latent tuberculosis treatment targeted to those able to complete the regimen in jail yields high completion rates.	7_EX.TOPIC
Long, R., et al. (2002). The emergency department is a determinant point of contact of tuberculosis patients prior to diagnosis. *International Journal of Tuberculosis and Lung Disease*, *6*(4), 332-339.	SETTING: Metropolitan Edmonton, Canada. OBJECTIVES: To determine 1) the pre-diagnosis emergency department utilization history of urban tuberculosis patients, and 2) the resource and outcome implications of emergency department utilization by tuberculosis patients pre-diagnosis. DESIGN: Nested case (emergency department attendee) control (non-emergency department attendee) study of a retrospective cohort of tuberculosis patients. PATIENTS: All tuberculosis notifications, 1994 through 1998. MAIN OUTCOME MEASURES: Emergency department utilization during the 6 months antedating the diagnosis and emergency department attendee characteristics; for those notified in 1997 and 1998, hospitalizations, nosocomial infectiousness time, and health care costs. RESULTS: Of 250 cases of tuberculosis, 117 (47%) made a total of 258 pre-diagnosis emergency department visits. Emergency department use increased the nearer the patient was to diagnosis. Emergency department attendees were more likely to be older, to have smear and/or culture positive respiratory disease, to have a risk factor for progression of infection to disease, and to have a fatal outcome. In 1997 and 1998, emergency department throughput accounted for 70% of all hospitalization days, 95% of all source case nosocomial infectiousness time, and most health care costs of tuberculosis patients pre-diagnosis. CONCLUSIONS: The emergency department is heavily utilized by urban tuberculosis patients pre-diagnosis. Emergency department throughput of tuberculosis patients pre-diagnosis has major resource and outcome implications. The emergency department may present an opportunity for earlier diagnosis.	1_EX.TB
Lorvick, J., et al. (1999). Incentives and accessibility: a pilot study to promote adherence to TB prophylaxis in a high-risk community. *Journal of Urban Health*, *76*(4), 461–467.	SETTING: A community-based directly observed preventive therapy (DOPT) program for treatment of latent tuberculosis infection among injection drug users (IDUs) in an inner-city neighborhood. OBJECTIVE: To test adherence to a 6-month course of DOPT using cash incentives and an easily accessible neighborhood location. DESIGN: Street-recruited IDUs (N = 205) were screened for Mycobacterium tuberculosis (TB) infection using the Mantoux test and two controls. Subjects who had a purified protein derivative (PPD) reaction of > or =5 mm, were anergic, or had a history of a positive PPD received clinical evaluation at a community field site,	9_IN.OTHER

	provided in collaboration with the San Francisco Department of Public Health Tuberculosis Clinic. Twenty-eight subjects were considered appropriate candidates for prophylaxis with isoniazid, and 27 enrolled in the pilot study. Participants received twice-weekly DOPT at a community satellite office, with a $10 cash incentive at each visit. RESULTS: The 6-month (26-week) regimen was completed by 24/27 (89%) participants. The median time to treatment completion was 27 weeks (range 26 to 34 weeks). The median proportion of dosing days attended in 6 months was 96%. CONCLUSION: Community-based DOPT using cash incentives resulted in high levels of adherence and treatment completion among drug users.	
Lucas, G. M., et al. (2007). Adherence, drug use, and treatment failure in a methadone-clinic-based program of directly administered antiretroviral therapy. *AIDS Patient Care & STDS*, *21*(8), 564-574.	Supervised dosing is a cornerstone of tuberculosis treatment. HIV treatment strategies that use directly administered antiretroviral therapy (DAART) are increasingly being assessed. In a prospective single-arm clinical trial, we enrolled methadone-maintained, HIV-infected participants to receive supervised doses of antiretroviral therapy (ART) on days when they received methadone. Other ART doses were self-administered. In this analysis we examined factors associated with retention to DAART, adherence to supervised doses, and virologic failure. Factors associated with retention to DAART were assessed with the Kaplan-Meier method and Cox proportional hazards models. Factors associated with nonadherence with supervised dosing and with virologic failure were assessed by logistic regression and techniques for longitudinal data analysis. A total of 16,453 supervised doses were administered to 88 participants over a median follow-up of 9.4 months. The median participant adherence with supervised dosing was 83%. Active drug use, determined by urine drug screens, was associated twofold increased risks of both intervention dropout and nonadherence with supervised doses. Adherence with supervised doses was strongly associated with virologic failure. Because DAART was administered only on methadone dosing days, fewer than half of the total ART doses were scheduled to be supervised in most participants. The percent of doses that was scheduled to be supervised was not associated with either adherence or with virologic failure. Given that a relatively small proportion of the total ART doses were supervised in many patients, future studies should assess how DAART affects adherence with nonsupervised doses and retention to ART.	1_EX.TB
MacIntyre, C. R., & Plant, A. J. (1998). Preventability of incident cases of tuberculosis in recently exposed contacts. *International Journal of Tuberculosis & Lung Disease*, *2*(1), 56-61.	SETTING: Contacts of tuberculosis (TB) cases are at risk for TB. If contact screening and intervention are effective, one would expect a reduced incidence of TB in contacts who have been screened. OBJECTIVE: To measure the incidence of TB in contacts during a 2-year follow up, and to estimate the preventability of incident cases. METHODS: A retrospective cohort study of 783 contacts screened in Victoria, Australia, in 1991. Contacts were matched with the TB registry for the following 2 years. Screening records were reviewed. RESULTS: The rate of TB in contacts was 511/100,000 population/year for the first 2 years. In Poisson regression models the only significant variable predicting disease was skin test reaction size. Six of eight incident cases were potentially preventable, with a lowest achievable incidence rate of 128/100,000/year. CONCLUSION: Contacts who underwent screening for TB through a state screening programme had a high incidence of TB during the 2 year follow up. Published rates of TB of 425-670/100,000 in untreated contacts suggests that the Victorian screening programme had minimal impact on the natural history of disease progression. Intrinsic programme factors such as the appropriateness of the guidelines, adherence to guidelines and rates of preventive therapy	5_EX.POP

	need to be evaluated. The devolution of the TB programme in the 1980s also reduced its efficacy. Systematic assessment of screening programmes for efficacy and outcome is part of good public health practice.	
MacIntyre, C. R., & Plant, A. J. (1998). Tuberculosis in South-East Asian refugees after resettlement – can prevention be improved by better policy and practice? *Preventive Medicine*, *27*(6), 815-820.	OBJECTIVE: This study aimed to determine whether incident cases of tuberculosis (TB) in a cohort of South-East Asian refugees followed for 5 years after resettlement were potentially preventable and whether prevention of TB was optimal in a state refugee TB screening program in Victoria, Australia. DESIGN: A retrospective cohort study of 1,101 refugees from Laos, Cambodia, and Vietnam screened for TB in the 6-month period from July 1989 to January 1990 was conducted. Incident cases of TB were identified by matching each refugee with the TB notification database for 5 years from the date of initial screening. Preventability was assessed for incident cases by reviewing medical records. Screening guidelines and practice were reviewed. RESULTS: The main outcome was the preventability of cases of active tuberculosis that developed in the study population in the first 5 years after resettlement. The incidence of active TB was 363/100,000 during the first year and 109/100,000/year during the first 5 years. Five of six incident cases were assessed as potentially preventable, which if prevented would have resulted in an annual incidence of 18/100,000 over the first 5 years. Use of a more sensitive skin test definition of infection would have made an additional 245 refugees eligible for prevention and potentially prevented an additional 25 cases of TB over a lifetime. CONCLUSIONS: There is a high incidence of tuberculosis among SE Asian refugees, particularly in the first year after resettlement. A large proportion of TB may be preventable. Improvement in case prevention may be possible with updated guidelines and better implementation of screening policy.	9_IN.OTHER
MacIntyre, C. R., et al. (2000). No evidence for multiple-drug prophylaxis for tuberculosis compared with isoniazid alone in Southeast Asian refugees and migrants: completion and compliance are major determinants of effectiveness. *Preventive Medicine*, *30*(5), 425-432.	BACKGROUND: The use of multiple-drug prophylaxis for tuberculosis (TB) has not been shown to be more effective than prophylaxis with isoniazid alone. The boundary between inactive pulmonary TB (class 4 TB) and culture-negative "active" pulmonary TB (class 3 TB) is often unclear, as is the intention to treat such patients as a preventive measure or as a curative measure. METHODS: We compared the effectiveness of single drug preventive therapy with isoniazid to the effectiveness of multiple drug preventive therapy for patients with asymptomatic, inactive TB, in a retrospective cohort study of 984 Southeast (SE) Asian migrants and refugees who received prophylaxis between 1978 and 1980. RESULTS: The rate of TB developing in this cohort was 122 per 100,000 person-years. There was no significant difference in development of TB between people who received isoniazid only and those who received multiple drugs. The only significant predictor of TB was noncompletion of prophylaxis [relative risk (RR) = 62, 95% confidence interval (CI) = 20-194]. Subgroup analysis on people who had completed therapy showed noncompliance as a significant predictor of TB (RR = 16, 95% CI = 1.4-179). The risk of noncompletion (RR = 4.7, 95% CI = 2.37-9.39, P < 0.0001) and noncompliance (RR = 2.2, 95% CI = 1.03-4.7, P = 0.03) was higher for patients who received multiple drugs compared with isoniazid alone. Multiple-drug therapy cost 30 times more than isoniazid alone. CONCLUSIONS: We did not find evidence in support of the empirical practice of giving multiple drugs for prevention of TB. This practice is also more costly and more likely to result in noncompliance and adverse drug reactions.	7_EX.TOPIC
MacNeil, J. R., Lobato, M. N., & Moore, M.	OBJECTIVES: We sought to describe disparities and trends in tuberculosis (TB) risk factors and treatment outcomes between	1_EX.TB

(2005). An unanswered health disparity: tuberculosis among correctional inmates, 1993 through 2003. *American Journal of Public Health*, *95*(10), 1800-1805.	correctional inmate and noninmate populations. METHODS: We analyzed data reported to the national TB surveillance system from 1993 through 2003. We compared characteristics between inmate and non-inmate men aged 15-64 years. RESULTS: Of the 210976 total US TB cases, 3.8% (7820) were reported from correctional systems. Federal and state prison case rates were 29.4 and 24.2 cases per 100000 inmates, respectively, which were considerably higher than those in the noninmate population (6.7 per 100000 people). Inmates with TB were more likely to have at least 1 TB risk factor compared with noninmates (60.1% vs 42.0%, respectively) and to receive directly observed therapy (65.0% vs 41.0%, respectively); however, they were less likely to complete treatment (76.8% vs 89.4%, respectively). Among inmates, 58.9% completed treatment within 12 months compared with 73.2% of noninmates. CONCLUSIONS: Tuberculosis case rates in prison systems remain higher than in the general population. Inmates with TB are less likely than noninmates to complete treatment.	
Malmborg, R. et al. (2006). Can public-private collaboration promote tuberculosis case detection among the poor and vulnerable? *Bulletin of the World Health Organization*, *84*(9), 752-758.	Private-public mix (PPM) DOTS is widely advocated as a DOTS adaptation for promoting progress towards the international tuberculosis (TB) control targets of detecting 70% of TB cases and successfully treating 85% of these. Private health care plays a central role in health-care provision in many developing countries that have a high burden of TB. It is therefore encouraging that PPM projects are being set up in various countries around the world to explore possible interaction between the national TB programmes and other partners in the fight against TB. The objective of this review was to use the published literature to assess the range of providers included in PPMs for their ability to provide case-detection services for the vulnerable. From a case-detection perspective, we identify the essential elements of a pro-poor PPM model, namely, cost-effectiveness from a patient perspective, accessibility, acceptability and quality. The review revealed that a very large part of the total spectrum of potential PPM-participating partners has not yet been explored; current models focus on private-for-profit health-care providers and non-governmental organizations. We conclude that it is important to think critically about the type of private providers who are best suited to meeting the needs of the poor, and that more should be done to document the socioeconomic status of patients accessing services through PPM pilots. [References: 49]	7_EX.TOPIC
McNabb, S. J. et al. (2004). Applying a new conceptual framework to evaluate tuberculosis surveillance and action performance and measure the costs, Hillsborough County, Florida, 2002. *Annals of Epidemiology*, *14*(9), 640-645.	PURPOSE: Tuberculosis (TB) elimination is an important US public health goal and improving the performance of TB surveillance and action and reducing the costs will help achieve it. But, there exists the need to better evaluate the performance and measure the costs. METHODS: We pilot tested an evaluation strategy in Hillsborough County, Florida using a conceptual framework of TB surveillance and action with eight core and four support activities. To evaluate performance, we developed indicators and validated their accuracy, usefulness, and measurability. To measure the costs, we obtained financial information. RESULTS: In 2001, Hillsborough County reported 78 (7%) of the 1145 Florida TB cases. Nineteen (24%) were previously arrested. While 13 (68%) of the 19 were incarcerated during the 2 years prior to being reported, only 1 (5%) of 19 was reported from the jail. From 111 TB suspects, 219 (25%) of 894 sputum specimens were inadequately collected. Of the $1.08 million annual budget, 22% went for surveillance, 29% for support, and 49% for action. CONCLUSIONS: This conceptual framework allowed measurement of TB surveillance and action performance and cost. The evaluation performed using it revealed missed opportunities for detection of TB cases and wasted resources. This conceptual	7_EX.TOPIC

	framework could serve as a model for evaluation of TB surveillance and action.	
Menendez, E., White, M. C., & Tulsky, J. P. (2001). Locating study subjects: predictors and successful search strategies with inmates released from a U.S. county jail. *Controlled Clinical Trials*, *22*(3), 238-247.	Minimizing loss to follow-up in longitudinal studies is critical. The purpose of this study was to examine the ability to locate subjects recently released from jail, identify predictors of being able to find a subject, and describe effective search strategies for this unique population. The sample for this cohort study included study subjects who were sought for interview after release from jail. Inmates in the San Francisco City and County Jail were enrolled in a randomized trial of incentives to improve follow-up for tuberculosis therapy after release from jail. Sociodemographic, health-related, and extensive locating information was collected during baseline interviews in jail. The main outcome was successful location of the subject. Study personnel recorded data on the number and nature of attempts made to find subjects in order to describe successful search strategies. Of 254 persons sought for the postrelease interview, 188 (74.0%) were found. Primary English speakers were more likely than Spanish speakers to be found (relative risk: 3.2, 95% confidence interval: 1.5-6.7, p = 0.002). Nearly one quarter of subjects (24%) were found back in jail, and the remainder were found in the community. Phone calls and letters to the subjects, and personal contacts to family and friends were successful strategies for 53% of the subjects. Seeking persons in programs, such as shelters and drug and alcohol programs, was successful in finding 18% of English-speaking subjects. Outreach efforts in sections of the city where Latinos spent time, including popular restaurants and community gathering places, were successful in finding 13% of Spanish-speaking subjects. We conclude that study subjects released from jails can be successfully located using well-defined search protocols tailored to the ethnicity of the sample and including a variety of strategies. Employment of bilingual personnel is important when a large proportion of subjects is monolingual and non-English speaking.	1_EX.TB
Mohle-Boetani, J. C. et al. (2002). Tuberculosis outbreak in a housing unit for human immunodeficiency virus-infected patients in a correctional facility: transmission risk factors and effective outbreak control. *Clinical Infectious Diseases*, *34*(5), 668-676.	In 1995, an outbreak of tuberculosis (TB) occurred among residents of a correctional-facility housing unit for inmates infected with human immunodeficiency virus (HIV). We isolated and treated patients who were suspected to have TB. To determine risk factors for in-prison transmission of TB, we conducted a case-control study to compare inmate case patients infected with a distinct outbreak strain of TB with control subjects who resided in the HIV unit. We identified 15 case patients during a 4-month period. Among inmates with a CD4 count of /=20 hours per week in a communal day room (odds ratio, 42; P=.002) and were less likely to have a television in their single-person room (odds ratio, 0.10; P=.003). The communal day room was a likely site of transmission. Successful collaboration between the correctional system and public health departments halted the outbreak.	1_EX.TB
Moore, R. D. et al. (1996). Cost-effectiveness of directly observed versus self-administered therapy for tuberculosis. *American Journal of Respiratory and Critical Care Medicine*, *154*(4), 1013.	Decision analysis was used to compare three alternative strategies for a 6-mo course of treatment for tuberculosis: directly observed drug therapy (DOT), self-administered fixed-dose combination drug therapy, and self-administered conventional individual drug therapy. Estimates of effectiveness were obtained from the published literature. Estimates of costs were obtained from the literature and the Baltimore City Health Department. Both DOT and fixed-dose combination therapy were less costly and more effective than conventional therapy, although DOT was most cost-effective. In total, the average cost per patient treated was $13,925 for DOT, $13,959 for fixed-dose combination therapy, and $15,003 for conventional therapy. Per 1,000 patients treated, 31 relapses and three deaths could be expected for DOT, 96 relapses and eight deaths for fixed-	5_EX.POP

	dose combination therapy, and 133 relapses and 13 deaths for conventional therapy. The marginal cost-effectiveness of DOT relative to fixed-dose combination therapy was most sensitive to variability in the direct cost of DOT and less sensitive to relapse rates for DOT and fixed-dose combination therapy. The inferior cost-effectiveness of conventional therapy was not sensitive to plausible variability in cost or effectiveness. Both DOT and fixed-dose combination therapy were cost-effective relative to conventional therapy, although DOT is probably most cost-effective.	
Morisky, D. E. et al. (1990). A patient education program to improve adherence rates with antituberculosis drug regimens. *Health Education & Behavior*, *17*(3), 253.	An incentive scheme to reward positive health behaviours plus targeted educational counselling sessions was implemented in a randomised clinical controlled trial. Patients with active tuberculosis or preventive patients were randomly assigned to a special intervention (SI) group or a usual care (UC) control group. Results demonstrate the positive effects of a structured health education programme. (Abstract amended)	5_EX.POP
NoY, J., & Popay, J. (2007). Directly observed therapy and tuberculosis: how can a systematic review of qualitative research contribute to improving services? A qualitative meta-synthesis. *Journal of Advanced Nursing*, *57*(3), 227-243.	AIM: This paper reports the findings from a qualitative meta-synthesis concerning people with, or at risk of, tuberculosis, service providers and policymakers and their experiences and perceptions of tuberculosis and treatment. BACKGROUND: Directly observed therapy is part of a package of interventions to improve tuberculosis treatment and adherence. A Cochrane systematic review of trials showed an absence of evidence for or against directly observed therapy compared with people treating themselves. METHOD: Qualitative systematic review methods were used to search, screen, appraise and extract data thematic analysis was used to synthesize data from 1990 to 2002, and an update of literature to December 2005. Two questions were addressed: 'What does qualitative research tell us about the facilitators and barriers to accessing and complying with tuberculosis treatment?' and 'What does qualitative research tell us about the diverse results and effect sizes of the randomized controlled trials included in the Cochrane review?' Findings help explain the diverse trial results in a Cochrane systematic review of directly observed therapy and tuberculosis and consider implications for research, policy and practice. FINDINGS: Five themes emerged from the 1990 to 2002 synthesis: socio-economic circumstances, material resources and individual agency; explanatory models and knowledge systems in relation to tuberculosis and its treatment; the experience of stigma and public discourses around tuberculosis; sanctions, incentives and support, and the social organization and social relationships of care. Two additional themes emerged from the 2005 update. CONCLUSION: The qualitative meta-synthesis improved the relevance and scope of the Cochrane review of trials. The findings make a major contribution to the development of theory concerning global WHO-branded disease control and the practicality of local delivery to people. [References: 86]	6_EX.NON-EMP
Orlando, G., et al. (2010). Interferon-gamma releasing assay versus tuberculin skin testing for latent tuberculosis infection in targeted screening programs for high risk immigrants. *Infection*, *38*(3), 195-204.	BACKGROUND: Recent immigrants from developing countries (20 mM (k = 0.47), in subjects aged 40-50 years (k = 0.41) and in unvaccinated persons (k = 0.40). In a multiple logistic regression model continent of origin, class of TB prevalence in the country of origin and contacts with TB patients were found to be significantly associated with the probability of TST and QFT-IT positive result. Low education levels were associated only to an increased risk of TST positive results. CONCLUSIONS: The drawback of the TST screening strategy in recent immigrants from highly endemic countries is due to low sensitivity/specificity of the test and to high drop-out rate with an overall significant lowering in strategy	7_EX.TOPIC

	efficacy/efficiency. The higher QFT-IT specificity prevents unnecessary overload of the health care system and, although more expensive, might represent a cost-effective alternative to TST in targeted screening programs directed to high risk populations.	
Oxlade, O., Schwartzman, K., & Menzies, D. (2007). Interferon-gamma release assays and TB screening in high-income countries: a cost-effectiveness analysis. *The International Journal of Tuberculosis and Lung Disease*, *11*(1), 16–26.	OBJECTIVE: Interferon-gamma release assays (IGRA) are now available alternatives to tuberculin skin testing (TST) for detection of latent tuberculosis infection (LTBI). We compared the cost-effectiveness of TST and IGRA in different populations and clinical situations, and with variation of a number of parameters. METHODS: Markov modelling was used to compare expected TB cases and costs over 20 years following screening for TB with different strategies among hypothetical cohorts of foreign-born entrants to Canada, or contacts of TB cases. The less expensive commercial IGRA, Quanti-FERON-TB Gold (QFT), was examined. Model inputs were derived from published literature. RESULTS: For entering immigrants, screening with chest radiograph (CXR) would be the most and QFT the least cost-effective. Sequential screening with TST then QFT was more cost-effective than QFT alone in all scenarios, and more cost-effective than TST alone in selected subgroups. Among close and casual contacts, screening with TST or QFT would be cost saving; savings with TST would be greater than with QFT, except in contacts who were bacille Calmette-Guerin (BCG) vaccinated after infancy. CONCLUSIONS: Screening for LTBI, with TST or QFT, is cost-effective only if the risk of disease is high. The most cost-effective use of QFT is to test TST-positive persons.	7_EX.TOPIC
Pillaye, J., & Clarke, A. (2003). An evaluation of completeness of tuberculosis notification in the United Kingdom. *BMC Public Health*, *3*, 31.	BACKGROUND: There has been a resurgence of tuberculosis worldwide, mainly in developing countries but also affecting the United Kingdom (UK), and other Western countries. The control of tuberculosis is dependent on early identification of cases and timely notification to public health departments to ensure appropriate treatment of cases and screening of contacts. Tuberculosis is compulsorily notifiable in the UK, and the doctor making or suspecting the diagnosis is legally responsible for notification. There is evidence of under-reporting of tuberculosis. This has implications for the control of tuberculosis as a disproportionate number of people who become infected are the most vulnerable in society, and are less likely to be identified and notified to the public health system. These include the poor, the homeless, refugees and ethnic minorities. METHOD: This study was a critical literature review on completeness of tuberculosis notification within the UK National Health Service (NHS) context. The review also identified data sources associated with reporting completeness and assessed whether studies corrected for undercount using capture-recapture (CR) methodology. Studies were included if they assessed completeness of tuberculosis notification quantitatively. The outcome measure used was notification completeness expressed between 0% and 100% of a defined denominator, or in numbers not notified where the denominator was unknown. RESULTS: Seven studies that met the inclusion and exclusion criteria were identified through electronic and manual search of published and unpublished literature. One study used CR methodology. Analysis of the seven studies showed that undernotification varied from 7% to 27% in studies that had a denominator; and 38%-49% extra cases were identified in studies which examined specific data sources like pathology reports or prescriptions for anti-tuberculosis drugs. Cases notified were more likely to have positive microbiology than cases not notified which were more likely to have positive histopathology or be surgical in-patients. Collation of prescription data of two or more anti-tuberculosis drugs increases case ascertainment of tuberculosis.	7_EX.TOPIC

	CONCLUSION: The reporting of tuberculosis is incomplete in the UK, although notification is a statutory requirement. Undernotification leads to an underestimation of the disease burden and hinders implementation of appropriate prevention and control strategies. The notification system needs to be strengthened to include education and training of all sub-specialities involved in diagnosis and treatment of tuberculosis. [References: 35]	
Porco, T. C. et al. (2006). Cost-effectiveness of tuberculosis evaluation and treatment of newly-arrived immigrants. *BMC Public Health*, *6*(1), *p.*157.	BACKGROUND: Immigrants to the U.S. are required to undergo overseas screening for tuberculosis (TB), but the value of evaluation and treatment following entry to the U.S. is not well understood. We determined the cost-effectiveness of domestic follow-up of immigrants identified as tuberculosis suspects through overseas screening. METHODS: Using a stochastic simulation for tuberculosis reactivation, transmission, and follow-up for a hypothetical cohort of 1000 individuals, we calculated the incremental cost-effectiveness of follow-up and evaluation interventions. We utilized published literature, California Reports of Verified Cases of Tuberculosis (RVCTs), demographic estimates from the California Department of Finance, Medicare reimbursement, and Medi-Cal reimbursement rates. Our target population was legal immigrants to the United States, our time horizon is twenty years, and our perspective was that of all domestic health-care payers. We examined the intervention to offer latent tuberculosis therapy to infected individuals, to increase the yield of domestic evaluation, and to increase the starting and completion rates of LTBI therapy with INH (isoniazid). Our outcome measures were the number of cases averted, the number of deaths averted, the incremental dollar cost (year 2004), and the number of quality-adjusted life-years saved. RESULTS: Domestic follow-up of B-notification patients, including LTBI treatment for latently infected individuals, is highly cost-effective, and at times, cost-saving. B-notification follow-up in California would reduce the number of new tuberculosis cases by about 6-26 per year (out of a total of approximately 3000). Sensitivity analysis revealed that domestic follow-up remains cost-effective when the hepatitis rates due to INH therapy are over fifteen times our best estimates, when at least 0.4 percent of patients have active disease and when hospitalization of cases detected through domestic follow-up is no less likely than hospitalization of passively detected cases. CONCLUSION: While the current immigration screening program is unlikely to result in a large change in case rates, domestic follow-up of B-notification patients, including LTBI treatment, is highly cost-effective. If as many as three percent of screened individuals have active TB, and early detection reduces the rate of hospitalization, net savings may be expected.	9_IN.OTHER
Rendleman, N. J. (1999). Mandated tuberculosis screening in a community of homeless people. *American Journal of Preventive Medicine*, *17*(2), 108–113.	BACKGROUND: To examine the effects of a community program on tuberculosis incidence, prevalence, and transmission requiring users of public facilities to carry cards certifying their compliance with a tuberculosis screening, prophylaxis, and treatment program. Community knowledge of tuberculosis and costs and benefits of the program are described. SETTING: A West Coast "skid row" community with historically high rates of tuberculosis, homelessness, poverty, and use of drugs and alcohol. DESIGN: Analysis of tuberculosis activity in communities in Oregon using Oregon Health Division Tuberculosis Data Bank data. Description of community response and cost considerations. MAIN OUTCOME MEASURES: Rates of active disease, mortality, and skin-test response. Compliance with card use and understanding of tuberculosis control measures. Program expenditures. RESULTS: An 89% drop in active disease in the highest-risk community in Oregon occurred over the	9_IN.OTHER

	first 10 years of the program. Compliance with the program permitting the use of public facilities, based on cooperation with skin testing, radiology, sputum collection, and therapy has been between 33% of converters completing prophylaxis in the worst year to 100% of active cases completing 4-drug therapy in the best. Facilities that provide services have been almost universal in requiring cooperation for participants. Costs have been reduced. CONCLUSION: A program of mandated compliance with tuberculosis skin testing, radiologic and sputum examination and treatment, coupled with education and outreach, succeeded in drastically reducing active tuberculosis, transmission, deaths, and cost in a homeless community.	
Rose, D. N. (2000). Benefits of screening for latent Mycobacterium tuberculosis infection. *Archives of Internal Medicine*, *160*(10), 1513-1521.	BACKGROUND: The benefits of screening for latent Mycobacterium tuberculosis infection are unknown for most people, because screening has not been studied in clinical trials and preventive therapy has not been tested in all risk groups for whom it is recommended. METHOD: A MEDLINE search was performed to determine tuberculosis risk. A Markov model was used to analyze tuberculin skin test screening and preventive therapy for 3-year-old and 30-year-old persons with positive test results. Outcome measures were lifetime and 10-year tuberculosis risk, including spread to others, life expectancy extension, and number needed to screen and number needed to treat to prevent 1 case and 1 death during 10 years. RESULTS: The benefits of screening and preventive therapy outweigh the risks for all groups tested, although the benefits range from large to small. The number needed to screen to prevent 1 case is 10 to 6888, and the number needed to treat is 2 to 179. Persons with human immunodeficiency virus infection, intravenous drug abuse, or end-stage renal disease treated with transplantation and children exposed to high-risk adults have the highest tuberculosis rates and the lowest number needed to screen and number needed to treat to prevent cases and deaths. The range of risks found in the literature for some risk groups, such as persons with silicosis, leukemia or lymphoma, end-stage renal disease treated with dialysis, or prolonged corticosteroid therapy, is wide and, as a result, the benefits of screening are uncertain. CONCLUSIONS: The benefits of screening and preventive therapy vary widely, although the benefits outweigh the risks for all risk groups. The benefits are large for some risk groups and uncertain for others.	6_EX.NON-EMP
Rozovsky-Weinberger, J. et al. (2005). Delays in suspicion and isolation among hospitalized persons with pulmonary tuberculosis at public and private US hospitals during 1996 to 1999. *Chest*, *127*(1), 205-212.	BACKGROUND: While prior studies have shown that public and private hospitals differ in their rates of suspicion and isolation of patients who are at risk for tuberculosis (TB), no study has investigated whether this variation is due to differences in the impact of patient case-mix on hospitals or to variations attributable to specific hospital practice patterns. OBJECTIVE: To investigate patient-level and hospital-level factors associated with delays in TB suspicion and isolation among inpatients with pulmonary TB disease. DESIGN: Retrospective cohort study of patients hospitalized with culture-positive pulmonary TB during 1996 to 1999. SETTING: Patients with culture-proven pulmonary TB treated at three public hospitals (765 patients) and seven not-for-profit private hospitals (172 patients) in Chicago, Los Angeles, and southern Florida that provided care for five or more patients with TB per year during the study period. MEASUREMENTS: Two-day rates (within 48 h from admission) of acid-fast bacilli (AFB) smear orders and 1-day rates (within 24 h from admission) of TB isolation. RESULTS: Two-day rates of ordering AFB smears were > 80% at three public and two private hospitals vs 65 to 75% at five private hospitals. One-day rates of TB isolation at the three public hospitals were 64%, 79%, and	5_EX.POP

	86%, respectively, vs 39 to 58% at the seven private hospitals. Delays of > 2 days in ordering AFB smears were associated with patient-level factors: absence of cough (adjusted odds ratio [AOR], 6.02; 95% confidence interval [CI], 3.82 to 9.52), cavitary lung lesion (AOR, 5.17; 95% CI, 1.98 to 13.50), night sweats (AOR, 3.38; 95% CI, 1.90 to 5.99), chills (AOR, 1.70; 95% CI, 1.01 to 2.88), and female gender (AOR, 1.66; 95% CI, 1.06 to 2.60). Delays of > 1 day in ordering pulmonary isolation were associated with patient-level factors: absence of cough (AOR, 3.40; 95% CI, 2.31 to 5.03), cavitary lung lesion (AOR, 2.66; 95% CI, 1.57 to 4.50), night sweats (AOR, 1.98; 95% CI, 1.35 to 2.92), and history of noninjecting drug use (AOR, 1.86; 95% CI, 1.16 to 2.99) and one hospital-level factor: receiving care at a nonpublic hospital. Even after adjustment for patient-level factors, TB patients at private hospitals were half as likely as those at public hospitals to be placed in pulmonary isolation (AOR, 0.47; 95% CI, 0.30 to 0.72), while odds of suspecting TB in these same patients were similar at both hospitals. CONCLUSION: Private hospitals should order TB isolation for all patients for whom AFB smears are ordered, a policy that has been instituted previously at public hospitals in our study.	
Schumann, A., Nyamathi, A., & Stein, J. A. (2007). HIV risk reduction in a nurse case-managed TB and HIV intervention among homeless adults. *Journal of Health Psychology*, *12*(5), 833-843.	This study evaluated a six-month nurse case-managed intervention against a standard care control program among 295 sheltered homeless adults from Los Angeles, USA. The primary aim of the intervention was encouraging latent tuberculosis infection treatment completion. The secondary aim was reducing HIV risk, the focus of this report. A longitudinal path model revealed that the intervention impacted cognitive factors of AIDS Knowledge, Perceived AIDS Risk and Self-efficacy for Condom Use, but did not impact substance use and risky sexual behaviors. The dual intervention program for HIV and TB provided promising synergistic effects by targeting risk factors common to both infections.	7_EX.TOPIC
Selwyn, P. A., et al. (1993). Utilization of on-site primary care services by HIV-seropositive and seronegative drug users in a methadone maintenance program. *Public Health Reports*, *108*(4), 492-500.	The feasibility of on-site primary care services and their use by human immunodeficiency virus HIV-seropositive and seronegative injecting drug users within an outpatient methadone maintenance program are examined. A 16-month prospective study was conducted within an ongoing cohort study of HIV infection at a New York City methadone program with on-site primary care services. The study group consisted of 212 seropositive and 264 seronegative drug injectors. A computerized medical encounter data base, with frequencies of primary care visits and with diagnoses for each visit, was linked to the cohort study data base that contained information on patients' demographic characteristics, serologic status, and CD4+ T-lymphocyte counts. Eighty-one percent of the drug injectors in the study voluntarily used on-site primary care services in the methadone program. Those who were HIV-seropositive made more frequent visits than those who were seronegative (mean annual visits 8.6 versus 4.1, P < .001), which increased with declining CD4+ T-lymphocyte counts; 79 percent of those who were seropositive with CD4 counts of less than 200 cells per cubic millimeter received on-site zidovudine therapy or prophylaxis against Pneumocystis carinii pneumonia, or both. Common primary care diagnoses for patients seropositive for HIV included not only conditions specific to the human immunodeficiency virus but also bacterial pneumonia, tuberculosis, genitourinary infections, asthma, dermatologic disease, psychiatric illness, and complications of substance abuse; those who were seronegative were most frequently seen for upper respiratory infection, psychiatric illness, complications of substance abuse, musculoskeletal disease, hypertension, asthma, and diabetes mellitus. Vaginitis and cervicitis, other gynecologic diseases, and	7_EX.TOPIC

	pregnancy were frequent primary care diagnoses among both seropositive and seronegative women.	
Smieja, M. J. et al. (2000). Isoniazid for preventing tuberculosis in non-HIV infected persons. *Cochrane Database of Systematic Reviews*, (2), 001363.	BACKGROUND: Although isoniazid (INH) is commonly used for treating tuberculosis (TB), it is also effective as preventive therapy. OBJECTIVES: The objective of this review was to estimate the effect of 6 and 12 month courses of INH for preventing TB in HIV-negative people at increased risk of developing active TB. SEARCH STRATEGY: We searched the Cochrane Infectious Diseases Group trials register, the Cochrane Controlled Trials Register, Medline, Embase and reference lists of articles. We hand-searched Science Citation Index and Index Medicus. SELECTION CRITERIA: Randomised trials of INH preventive therapy for 6 months or more compared with placebo. Follow-up for a minimum of 2 years. Trials enrolling patients with current or previously treated active TB, or with known HIV infection, were excluded. Criteria were applied by two reviewers independently. DATA COLLECTION AND ANALYSIS: Trial quality was assessed by two reviewers independently, and data extracted by one reviewer using a standardized extraction form. MAIN RESULTS: Eleven trials involving 73,375 patients were included. Trials were generally of high quality. Treatment with INH resulted in a relative risk (RR) of developing active TB of 0.40, (95% confidence interval (CI) 0.31 to 0.52), over two years or longer. There was no significant difference between 6 and 12 month courses (RR of 0.44, 95% CI 0.27 to 0.73 for six months, and 0.38, 95% CI 0.28 to 0.50 for 12 months). Preventive therapy reduced deaths from TB, but this effect was not seen for all cause mortality. INH was associated with hepatotoxicity in 0.36% of people on 6 months treatment and in 0.52% of people treated for 12 months. REVIEWER'S CONCLUSIONS: Isoniazid is effective for the prevention of active TB in diverse at-risk patients, and six and 12 month regimens have a similar effect. [References: 15]	5_EX.POP
Snyder, D. C. et al. (1999). Tuberculosis prevention in methadone maintenance clinics. Effectiveness and cost-effectiveness. *American Journal of Respiratory & Critical Care Medicine*, *160*(1), 178-185.	To determine the effectiveness and cost-effectiveness of a program to provide screening for tuberculosis infection and directly observed preventive therapy (DOPT) in methadone maintenance clinics, we determined completion rates of screening for tuberculosis infection, medical evaluation, and preventive therapy, as well as the number of active tuberculosis cases and tuberculosis-related deaths prevented, in five clinics in San Francisco, California. Between 1990 and 1995, a total of 2,689 clients (of whom 18% were HIV-seropositive) were screened at least once. Of eligible clients, 99% received tuberculin skin tests, 96% received a medical examination, 91% began isoniazid preventive therapy, and 82% completed preventive therapy. Program effectiveness was enhanced by close collaboration between public health and methadone maintenance programs and the use of incentives and enablers. Over a 3-yr follow-up period, only one verified case of tuberculosis was reported among clients with a positive tuberculin skin test, thereby preventing as much as 95% of expected tuberculosis cases. Over 10 yr, we estimate the program would prevent 30.0 (52%) of 57.7 expected cases of tuberculosis, and 7.6 (57%) of 13.4 expected tuberculosis-related deaths. The program cost $771,569, but averted an estimated $876,229, for a net savings of $104,660 (average of $3, 724 per case prevented). Our study demonstrates that when effectively implemented, screening for tuberculosis infection and DOPT in methadone maintenance clinics is a highly cost-effective approach to prevent tuberculosis.	7_EX.TOPIC
Solsona, J., et al. (2001). Screening for tuberculosis upon admission to shelters	BACKGROUND: The homeless are at very high risk of suffering tuberculosis (TB). The aims of this study were to determine the prevalence and risk factors for tuberculosis infection and disease among the homeless in Barcelona and to evaluate the roles of case	9_IN.OTHER

and free-meal services. *European journal of epidemiology, 17*(2), 123–128.	finding and contact investigation. METHODS: Observational prevalence study carried out between 1997 and 1998. PARTICIPANTS: 447 homeless patients (394 men and 53 women) were evaluated before admission to shelters and free-meal services. At the same time, 48 co-residents with smear-positive TB patients in 2 long-term shelters were evaluated too. A chest X-ray and Tuberculin Skin Test were performed on all subjects. Sputum smears were processed by the Ziehl-Neelsen and Lowenstein-Jensen procedures in patients with radiographic findings consistent with pulmonary TB. RESULTS: Of the 447 homeless examined, 335 (75%) were infected with Mycobacterium tuberculosis. Active pulmonary TB was diagnosed in five persons (1.11%), and 62 (13.8%) had radiographic evidence of inactive pulmonary TB. Tuberculosis infection was associated with age and smoking, but not with sex or alcohol abuse. No significant differences in infection rates were found between the main group and 48 homeless co-residents of smear-positive subjects. Only 16.9% of the homeless with active TB in Barcelona in the same period were diagnosed through active case-finding, the remainder being mainly detected in hospitals (69.8%) and other several centres (13.3%). CONCLUSIONS: Homeless individuals have a very high risk of TB infection and disease and contact investigation requires specific methods for them. Programmes of screening and supervised treatment should be ensured in this group.	
Spyridis, P., et al. (2003). The impact of Greece's childhood tuberculosis screening programme on the epidemiological indexes in the greater Athens area. *International Journal of Tuberculosis & Lung Disease, 7*(3), 248-253.	SETTING: A hospital referral centre for childhood tuberculosis in Athens. OBJECTIVE: To evaluate the effectiveness of the screening programme implemented for childhood tuberculosis, through its impact on the epidemiological index. DESIGN: In Greece, tuberculosis has been systematically screened for in children since 1991 using the tuberculin skin test. The epidemiological and clinical profiles of all tuberculous children who attended the TB clinic were compared. The children were divided into those who attended in 1982-1990 and those who did so in 1991-1999. RESULTS: A total of 1122 TB patients were screened. In the second period there was an increase in numbers of immigrant children (3% vs. 28%, P = 0.0001), the rate of extra-pulmonary TB decreased (16% vs. 7.6%, P = 0.0001), patients identified by the screening programme increased (19% vs. 57%, P = 0.0001) and the number of symptomatic children fell (51% vs. 16%, P = 0.0001). The proportion of children who failed to attend for regular follow-up was lower during the second period (20% vs. 7%, P = 0.0001). CONCLUSIONS: Our study suggests that the screening programme applied in Greece during the last decade has contributed to the early identification of tuberculosis, and the limitation of symptomatic patients and extrapulmonary TB cases.	5_EX.POP
Sreeramareddy, C. T., et al. (2009). Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. *BMC Infectious Diseases, 9*, 91.	BACKGROUND: Delay in diagnosis of pulmonary tuberculosis results in increasing severity, mortality and transmission. Various investigators have reported about delays in diagnosis of tuberculosis. We aimed at summarizing the data on these delays in diagnosis of tuberculosis. METHODS: A systematic review of literature was carried out. Literature search was done in Medline and EMBASE from 1990 to 2008. We used the following search terms: delay, tuberculosis, diagnosis, and help-seeking/health-seeking behavior without language restrictions. In addition, indices of four major tuberculosis journals were hand-searched. Subject experts in tuberculosis and authors of primary studies were contacted. Reference lists, review articles and text book chapters were also searched. All the studies were assessed for methodological quality. Only studies carried out on smear/culture-positive tuberculosis patients and reporting about total, patient and health-care system	7_EX.TOPIC

	delays were included. RESULTS: A total of 419 potential studies were identified by the search. Fifty two studies qualified for the review. The reported ranges of average (median or mean) total delay, patient delay, health system delay were 25-185 days, 4.9-162 days and 2-87 days respectively for both low and high income countries. Average patient delay was similar to health system delay (28.7 versus 25 days). Both patient delay and health system delay in low income countries (31.7 days and 28.5 days) were similar to those reported in high income countries (25.8 days and 21.5 days). CONCLUSION: The results of this review suggest that there is a need for revising case-finding strategies. The reported high treatment success rate of directly observed treatment may be supplemented by measures to shorten the delay in diagnosis. This may result in reduction of infectious cases and better tuberculosis control. [References: 68]	
Stevens, A., et al. (1992). The public health management of tuberculosis among the single homeless: is mass miniature x ray screening effective? *British Medical Journal*, *46*(2), 141.	STUDY OBJECTIVE – The aim was to test the assumption that mass miniature x ray screening of the single homeless (hostel residents) is a cost-effective means of controlling pulmonary tuberculosis. DESIGN – The study was a prospective experimental screening exercise to identify new cases of active tuberculosis completing treatment. SETTING – The setting was eight hostels in south London. A mobile x ray screening facility was set up outside the hostels. SUBJECTS – Subjects were 547 single homeless residents in the hostels. They were encouraged to attend for chest x ray, and for active follow up of abnormal x rays. MAIN RESULTS – No new cases of active tuberculosis were found. CONCLUSIONS – Mass miniature x ray is ineffective in controlling tuberculosis because of its unacceptability and increasing inaccessibility to this population.	9_IN.OTHER
Storla, D. G., Yimer, S., & Bjune, G. A. (2008). A systematic review of delay in the diagnosis and treatment of tuberculosis. *BMC Public Health*, *8*, 15.	BACKGROUND: Early diagnosis and immediate initiation of treatment are essential for an effective tuberculosis (TB) control program. Delay in diagnosis is significant to both disease prognosis at the individual level and transmission within the community. Most transmissions occur between the onset of cough and initiation of treatment. METHODS: A systematic review of 58 studies addressing delay in diagnosis and treatment of TB was performed. We found different definitions of, for example, debut of symptoms, first appropriate health care provider, time to diagnosis, and start of treatment. Rather than excluding studies that failed to meet strict scientific criteria (like in a meta-analysis), we tried to extract the "solid findings" from all of them to arrive on a more global understanding of diagnostic delay in TB. RESULTS: The main factors associated with diagnostic delay included human immunodeficiency virus; coexistence of chronic cough and/or other lung diseases; negative sputum smear; extrapulmonary TB; rural residence; low access (geographical or sociopsychological barriers); initial visitation of a government low-level healthcare facility, private practitioner, or traditional healer; old age; poverty; female sex; alcoholism and substance abuse; history of immigration; low educational level; low awareness of TB; incomprehensive beliefs; self-treatment; and stigma. CONCLUSION: The core problem in delay of diagnosis and treatment seemed to be a vicious cycle of repeated visits at the same healthcare level, resulting in nonspecific antibiotic treatment and failure to access specialized TB services. Once generation of a specific diagnosis was in reach, TB treatment was initiated within a reasonable period of time. [References: 57]	7_EX.TOPIC
Tanke, E. D., & Leirer, V. O. (1994). Automated telephone reminders in tuberculosis care. *Med*	This study assessed the impact of automated telephone reminders in a population of 2,008 patients scheduled for appointments in a public health tuberculosis clinic. Overall, remainders increased appointment attendance from 52% to 62%. Reminders were more effective for	5_EX.POP

Care, (4), 380-389.	some applications than others, but the effectiveness of reminders did not differ significantly across patient age, sex, or ethnicity. Counter to theoretical predictions, neither attribution of the reminder message to an authority nor a statement stressing the importance of the appointment significantly increased the effectiveness of the reminder above the level obtained without these enhancements.	
Taylor, Z., et al. (2000). Causes and costs of hospitalization of tuberculosis patients in the United States. *International Journal of Tuberculosis & Lung Disease*, *4*(10), 931-939.	OBJECTIVE: To examine the costs, lengths of stay and patient characteristics associated with tuberculosis (TB) hospitalizations. METHODS: A prospective cohort study of 1493 TB patients followed from diagnosis to completion of therapy at 10 public health programs and area hospitals in the US. The main outcome measures were the following: 1) occurrence, 2) cost, and 3) length of stay of TB-related hospitalizations. RESULTS: There were 821 TB-related hospitalizations among the study participants; 678 (83%) were initial hospitalizations and 143 (17%) were hospitalizations during the treatment of TB. Patients infected with human immunodeficiency virus (HIV) (OR 1.8, 95% CI 1.2-2.6), and homeless patients (OR, 1.7 95% CI 1.1-2.8) were at increased risk of being hospitalized at diagnosis. Homeless patients (RR 2.5, 95%CI 1.5-4.3), patients who used alcohol excessively (RR 1.9, 95% CI 1.2-3.0), and patients with multidrug-resistant TB (RR 5.7, 95% CI 2.7-11.8) were at increased risk of hospitalization during treatment. The median length of stay varied from 9 to 17 days, and median costs per hospitalization varied from $6441 to $12968 among the sites. CONCLUSION: Important social factors, HIV infection, and local hospitalization practice patterns contribute significantly to the high cost of TB-related hospitalizations. Efforts to address these specific factors are needed to reduce the cost of preventable hospitalizations.	7_EX.TOPIC
Thomas, R. E. (1997). Mantoux (tuberculosis) testing. Evaluation of guidelines for testing in Canadian institutions. *Canadian Family Physician*, *43*, 933-938.	OBJECTIVE: To evaluate the guidelines for Mantoux testing and isoniazid (INH) prophylaxis in various institutions and shelters for the homeless in Canada in light of research in Canada and other industrialized countries. DATA SOURCES: MEDLINE searches from January 1980 to June 1996 yielded 219 articles, some of which were case reports. The bibliographies of these articles were searched for relevant titles. A further search adding the words randomized, controlled trial and controlled clinical trial yielded two citations, neither of which was a randomized, controlled trial. DATA EXTRACTION: Studies were included if they described the incidence, screening, diagnosis, or prophylaxis of tuberculosis (TB), in institutions in Canada. DATA SYNTHESIS: Studies of staff patients in institutions tend to be incomplete in reporting exposure to TB, extent of Mantoux testing, and whether INH prophylaxis was completed. CONCLUSIONS: Institutions admitting patients with TB should follow the 1996 recommendations of the Canadian Thoracic Society (CTS). The best way to implement the recommendations is to have a TB control officer who administers protocols to identify staff and patients at risk for TB and a committee that regularly monitors implementation of CTS guidelines. [References: 40]	7_EX.TOPIC
Underwood, B. R., et al. (2003). Contact tracing and population screening for tuberculosis--who should be assessed?. *Journal of Public Health Medicine*, *25*(1), 59-61.	BACKGROUND: The aim of the study was to investigate the relative effectiveness of four strategies in detecting and preventing tuberculosis: contact tracing of smear-positive pulmonary disease, of smear-negative pulmonary disease and of non-pulmonary disease, and screening new entrants. METHODS: An analysis of patient records and a TB database was carried out for an NHS Trust-based tuberculosis service in a socio-economically deprived area. Subjects were contacts of all patients treated for TB between 1997 and 1999. New entrants were screened in 1999. Outcomes measured were	9_IN.OTHER

	numbers of cases of active tuberculosis detected and numbers of those screened given chemoprophylaxis. RESULTS: A total of 643 contacts of 227 cases of active TB were seen, and 322 new entrants to the United Kingdom. The highest proportion of contacts requiring full treatment or chemoprophylaxis were contacts of smear-positive index cases (33 out of 263 contacts; 12.5 per cent). Tracing contacts of those with smear-negative pulmonary tuberculosis (12 out of 156; 7.7 per cent) and non-pulmonary disease (14 out of 277; 6.2 per cent) was significantly more effective in identifying individuals requiring intervention (full treatment or chemoprophylaxis) than routine screening of new entrants (10 out of 322; 3.1 per cent). CONCLUSIONS: Screening for TB of new entrants to the United Kingdom is part of the national programme for control and prevention of TB, whereas tracing contacts of those with smear-negative and non-pulmonary disease is not. This study demonstrates that, in our population, the contact-tracing strategy is more effective than new entrant screening. It is not likely that the contacts have caught their disease from the index case, but rather that in high-incidence areas such as ours such tracing selects extended families or communities at particularly high risk.	
Walker D, M. R. (2000). An incremental cost-effectiveness analysis of the first, second and third sputum examination in the diagnosis of pulmonary tuberculosis. *International Journal of Tuberculosis and Lung Disease*, *4*(3), 246-251.	This record was compiled by CRD commissioned reviewers according to a set of guidelines developed in collaboration with a group of leading health economists.	4_EX.OECD
Weis, S. E., et al. (1994). The effect of directly observed therapy on the rates of drug resistance and relapse in tuberculosis. *New England Journal of Medicine*, *330*(17), 1179-1184.	BACKGROUND: Tuberculosis has re-emerged as an important public health problem, and the frequency of drug resistance is increasing. A major reason for the development of resistant infections and relapse is poor compliance with medical regimens. In Tarrant County, Texas, we initiated a program of universal directly observed treatment for tuberculosis. We report the effect of the program on the rates of primary and acquired drug resistance and relapse among patients with tuberculosis. METHODS: We collected information on all patients with positive cultures for Mycobacterium tuberculosis in Tarrant County from January 1, 1980, through December 31, 1992. Through October 1986, patients received a traditional, unsupervised drug regimen. Beginning in November 1986, nearly all patients received therapy under direct observation by health care personnel. RESULTS: A total of 407 episodes in which patients received traditional treatment for tuberculosis (January 1980 through October 1986) were compared with 581 episodes in which therapy was directly observed (November 1986 through December 1992). Despite higher rates of intravenous drug use and homelessness and an increasing rate of tuberculosis during this 13-year period, the frequency of primary drug resistance decreased from 13.0 percent to 6.7 percent (P < 0.001) after the institution of direct observation of therapy, and the frequency of acquired resistance declined from 14.0 percent to 2.1 percent (P < 0.001). The relapse rate decreased from 20.9 percent to 5.5 percent (P < 0.001), and the number of relapses with multidrug-resistant organisms decreased from 25 to 5 (P < 0.001). CONCLUSIONS: The administration of therapy for M. tuberculosis infection under direct observation leads to significant reductions in the frequency of primary drug resistance, acquired drug resistance, and relapse.	5_EX.POP

White, M. C., et al. (2003). Strategies for effective education in a jail setting: the Tuberculosis Prevention Project. *Health Promotion Practice*, *4*(4), 422-429.	Jails are a unique setting for health education. The Tuberculosis (TB) Prevention Project was designed to improve completion of care for latent TB infection in released inmates. As part of an ongoing clinical trial to improve rates of completion, educators provided TB-focused educational sessions to 1,027 inmates. This article describes the educational sessions and illustrates some of the barriers to working in a jail setting and strategies to overcome them. The nature of the jail itself, inmate characteristics, the characteristics of educators, and the educational sessions themselves interacted in different ways to enhance or impair the interaction. Jail is a setting in which the population is at high risk for a number of health problems and health education is increasingly important.	7_EX.TOPIC
White, M. C., et al. (2005). Incidence of TB in inmates with latent TB infection: 5-year follow-up. *American Journal of Preventive Medicine*, *29*(4), 295-301.	BACKGROUND: Inmates are a high-risk population for tuberculosis (TB) control efforts, including treatment for latent tuberculosis infection (LTBI). Completion of therapy after release has been poor. The goal of this study was to evaluate therapy completion and active disease over 5 years in a cohort of inmates. METHODS: The sample was from a completed randomized trial in 1998-1999 of education or incentive versus usual care to improve therapy completion after release from the San Francisco County Jail. Records from the jail, the County Tuberculosis Clinic, and the California TB Registry were used to measure therapy completion and development of active TB. Analyses were conducted in 2005. RESULTS: Of a total 527 inmates, 31.6% (n=176) completed therapy, of whom 59.7% (n=105) completed it in jail. Compared with the U.S.-born, foreign-born inmates residing in the United States for < or =5 years were less likely to complete the therapy (adjusted odds ratio [AOR]= 0.49, 95% confidence interval [CI]=0.28-0.85), and those with more education were more likely to complete the therapy (AOR=1.06, 95% CI=1.01-1.12). Three subjects developed active TB in the 5 years of follow-up, resulting in an annual rate of 108 per 100,000. Compared with California rates, subjects were 59 times as likely to develop active TB (standardized morbidity ratio of 59.2, 95% CI=11.2-145.1). None had completed therapy, none were new immigrants, and two were known to be HIV-positive at diagnosis. CONCLUSIONS: Completion of therapy for LTBI is a challenge, but the active TB seen in this jail cohort emphasizes the importance of continued efforts to address TB risk in this population.	9_IN.OTHER
White, M. C., Cuttler, S., & Zhao, X. (2007). Linking released inmates to TB clinic for treatment of latent tuberculosis infection: Why is it so difficult? *Journal of Correctional Health Care*, *13*(3), 206-215.	Released inmates who are infected with Mycobacterium tuberculosis are at high risk for not completing therapy. This study describes reasons for postrelease behavior in a cohort of participants from a randomized trial. We interviewed 230 participants after the primary trial endpoint (visit to the tuberculosis [TB] clinic within 30 days of release) had occurred. Those participants who, in jail, thought they would have social support for continuing therapy but after jail indicated they did not have such support were half as likely to have gone to the TB clinic (odds ratio 0.5, 95% confidence interval 0.2 to 0.9), controlling for drug/alcohol problems and factors significant in the original randomized trial (study group and recent immigrant status). The disruption of incarceration alters postrelease life, and inmates who find social support has changed after release may be nonadherent. Information gathered from incarcerated persons may not predict postrelease reality. (PsycINFO Database Record (c) 2010 APA, all rights reserved) (journal abstract)	6_EX.NON-EMP
Winje, B. A., et al. (2008). Screening for tuberculosis infection among newly arrived asylum seekers:	BACKGROUND: QuantiFERONTB Gold (QFT) is a promising blood test for tuberculosis infection but with few data so far from immigrant screening. The aim of this study was to compare results of QFT and tuberculin skin test (TST) among newly arrived asylum seekers in Norway and to assess the role of QFT in routine diagnostic screening	1_EX.TB

comparison of QuantiFERONTB Gold with tuberculin skin test. *BMC Infectious Diseases*, *8*, 65.	for latent tuberculosis infection. METHODS: The 1000 asylum seekers (age > or = 18 years) enrolled in the study were voluntarily recruited from 2813 consecutive asylum seekers arriving at the national reception centre from September 2005 to June 2006. Participation included a QFT test and a questionnaire in addition to the mandatory TST and chest X-ray. RESULTS: Among 912 asylum seekers with valid test results, 29% (264) had a positive QFT test whereas 50% (460) tested positive with TST (indurations > or = 6 mm), indicating a high proportion of latent infection within this group. Among the TST positive participants 50% were QFT negative, whereas 7% of the TST negative participants were QFT positive. There was a significant association between increase in size of TST result and the likelihood of being QFT positive. Agreement between the tests was 71-79% depending on the chosen TST cut-off and it was higher for non-vaccinated individuals. CONCLUSION: By using QFT in routine screening, further follow-up could be avoided in 43% of the asylum seekers who would have been referred if based only on a positive TST (> or = 6 mm). The proportion of individuals referred will be the same whether QFT replaces TST or is used as a supplement to confirm a positive TST, but the number tested will vary greatly. All three screening approaches would identify the same proportion (88-89%) of asylum seekers with a positive QFT and/or a TST > or = 15 mm, but different groups will be missed.	

13.0 Appendix E. Example quality assessment forms

13.1 Quantitative study

Malotte et al. 2001	
1. Is the source population or source area well described?	**Comments**
++	Demographics of participants are thoroughly reported (Table 1); country is indicated; study setting well described.
2. Is the eligible population or area representative of the source population or area?	**Comments**
+	The place and time of recruitment (recruited from an initial study on TB skin test adherence, April 1994-September 1997) was identified; The study describes eligibility clearly and provides the criteria by which this was assessed, as well as the population number that was subsequently ineligible for participation. The eligible group however may not be representative of all drug users in California, USA.
3. Do the selected participants or areas represent the eligible population?	**Comments**
+	Inclusion/exclusion criteria were explicitly stated. Since the selected population was a volunteer sample of the eligible population it may not be fully representative.
4. How was confounding minimised?	**Comments**
+	Allocation to exposure and comparison was randomised.
5. Were interventions (and comparisons) well described and appropriate?	**Comments**
++	Described in detail/replicable.
6. Was the allocation concealed?	**Comments**
++	Numbered, opaque, sealed envelopes containing the assigned treatment condition was administered to study nurses to ensure concealment

7. Were participants and/or investigators blind to exposure and comparison?	**Comments**
NA	
8. Was the exposure to the intervention and comparison adequate?	**Comments**
++	Exposure level does not impact on outcomes. The exposure is adequate in both groups.
9. Was contamination acceptably low?	**Comments**
++	No participant from either group was exposed to the other.
10. Were other interventions similar in both groups?	**Comments**
NR	
11. Were all participants accounted for at study conclusion?	**Comments**
++	Treatment completion rates was the outcome being measured and drop-out rates have been described with reasons for drop-out.
12. Did the setting reflect usual UK practice?	**Comments**
+	Drug users in the UK have similar access to 'storefront' clinics. However, since this is a US study, it is not certain whether provision of services and research conducted at these clinics appropriately reflects UK practice.
13. Did the intervention or control comparison reflect usual UK practice?	**Comments**
+	Directly observed treatment, the use of an outreach worker and the provision of incentives (treatments provided in this study) for TB adherence for a drug using population is common in the UK.
14. Were the outcome measures reliable?	**Comments**

++	The primary outcome measure was the percentage of medication taken as prescribed; and completion of medication regimen. This was objectively verified by observation (participants were observed swallowing all medications).
15. Were all outcome measurements complete?	**Comments**
++	All were accounted for.
16. Were all important outcomes assessed?	**Comments**
++	All important outcomes assessed, including reasons for drop-out/default.
17. Were outcomes relevant?	**Comments**
++	The outcomes assessed are all relevant in order to find the independent and combined effects of monetary incentives and outreach worker provision of DOT.
18. Were there similar follow-up times in exposure and comparison groups?	**Comments**
++	Equal time.
19. Was follow-up time meaningful?	**Comments**
++	8-12 month follow up, depending on prescribed duration of treatment (based on HIV status).
20. Were exposure and comparison groups similar at baseline? If not, were these adjusted?	**Comments**
++	No demographic or drug use variable was significantly related to intervention groups.
21. Was intention to treat (ITT) analysis conducted?	**Comments**
++	Intervention effects were also tested in both univariate and multivariate logistic regression analyses, on an intention-to-treat basis.
22. Was the study sufficiently powered to detect an intervention effect (if one exists)?	**Comments**
NR	Not reported.
23. Were the estimates of effect size given or calculable?	**Comments**

++	Reported thoroughly.
24. Were the analytical methods appropriate?	**Comments**
++	Appropriate.
25. Was the precision of intervention effects given or calculable? Were they meaningful?	**Comments**
++	P value, and CI and AOR are all reported.
26. Are the study results internally valid? (i.e., unbiased)	**Comments**
++	The baseline characteristics were not significantly different between groups. There were no significant flaws in the study design.
27. Are the study results generalisable to the source population? (i.e. externally valid)	**Comments**
+	Not statistically.

13.2 Economic evaluation

Kominski et al. 2010	
1. Is the study population appropriate for the topic being evaluated?	**Comments**
Partly	Only 80% of the participants in the study are foreign-born and thus not completely appropriate for an understanding of this hard-to-reach group (new entrants).
2. Are the interventions appropriate for the topic being evaluated?	**Comments**
Yes	
3. Is the system in which the study was conducted sufficiently similar to the UK context?	**Comments**
Partly	US study.
4. Were the perspectives clearly stated?	**Comments**
Yes	Societal perspective.
5. Are all direct health effects on individuals included, and are all other effects included where they are material?	**Comments**
Yes.	
6. Are all future costs and outcomes discounted appropriately?	**Comments**
Partly.	3% discounting rate is used in this study rather than the best accepted annual rate of 3.5%.
7. Is the value of health effects expressed in terms of quality adjusted life years (QALYs)?	**Comments**
Yes.	
8. Are costs and outcomes from other sectors fully and appropriately measured and valued?	**Comments**
Yes	Costs occurring in other sectors have been reported. One example is the cost of letters sent to adolescents.
9. Overall judgement (no need to	**Comments**

continue if not applicable)	
Partly applicable	Although relevant to NHS context & NICE guidelines, the study is conducted in the USA and not all selected participants are considered hard-to-reach for the purposes of developing this particular guideline.
10. Does the model structure adequately reflect the nature of the topic under evaluation?	**Comments**
Yes	The model design and its structural elements appropriately reflect the nature of the topic: the study identified treatment pathways; used quality adjusted life year; provided incremental analysis; and reported predicators of compliance. The assumptions underlying the method were also sufficiently informed: obtained from an actual study conducted, published literature or Medicare records.
11. Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	**Comments**
Yes.	Lifetime TB-related costs.
12. Are all important and relevant outcomes included?	**Comments**
Yes.	Relevant outcomes reported: adherence to isoniazid preventive therapy; total cost of LTBI treatment; average lifetime TB-related costs; ICER/QALYs.
13. Are the estimates of baseline outcomes from the best available source?	**Comments**
Partly.	Baseline outcomes have not been identified from a recent well-conducted systematic review of the literature. However, the estimates of baseline outcomes do appear from a natural sample from a previous study, published literature and Medicare records, that are likely to reflect outcomes for the relevant for the purposes of this review.
14. Are the estimates of relative 'treatment' effects from the best available source?	**Comments**
Partly	The study did not use treatment effects from a published systematic review. Instead, they used

	outcomes from a cohort of people in their own trial, which is considered a good available estimate.
15. Are all important and relevant costs included?	**Comments**
Yes.	
16. Are the estimates of resource use from the best available source?	**Comments**
Partly.	Not derived from a systematic review but are considered the best available estimates.
17. Are the unit costs of resources from the best available source?	**Comments**
Partly.	Unit costs of resources included charges made to Medicare (USA), which may differ from current UK NHS/PSS unit costs.
18. Is an appropriate incremental analysis presented or can it be calculated from the data?	**Comments**
Yes.	
19. Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	**Comments**
Yes.	
20. Is there any potential conflict of interest?	**Comments**
Unclear.	The article does not indicate whether or not there are financial conflicts of interest.
21. Overall assessment	**Comments**
Minor limitations	The study only fails to meet a few of the quality criteria presented here, but this is unlikely to change the conclusions about cost-effectiveness.