National Institute for Health and Clinical Excellence (NICE)

Evidence review on the effectiveness and cost-effectiveness of interventions aimed at identifying people with tuberculosis and/or raising awareness of tuberculosis among hard-to-reach groups.

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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 second of four commissioned by NICE to inform the guideline on the identification and management of tuberculosis (TB) in hard-to-reach groups. The focus of this review is on the effectiveness and cost-effectiveness of strategies to identify TB in these populations. Other reviews in the series cover the management of TB in hard-to-reach groups, the best service models to identify and manage these groups, and barriers and facilitators to screening and treatment of TB.

The primary research question for this review was:

- Which interventions are effective and cost-effective at identifying TB and/or raising awareness about screening for TB among hard-to-reach groups?

The secondary research questions were:

- What factors impact on the effectiveness of the interventions? For example, does the efficacy of the intervention vary by the:
    a) theories or conceptual models underpinning the interventions?
    b) diversity of the population (in terms of hard-to-reach group, age, or gender)?
    c) persons/organisations commissioning/delivering the interventions?
    d) way in which the intervention is delivered (for example, one-to-one or group-based)?
    e) involvement of the target population in the planning, design, or delivery of the intervention?
    f) content of different interventions?
    g) frequency, intensity, and duration of the intervention?
    h) time and place that the intervention is delivered?
- How transferable are the findings regarding effectiveness to other hard-to-reach populations, other settings, or other times? (for example, how representative is the sample; what are the key characteristics of the sample compared with other hard-to-reach groups; and how appropriate is the analysis in terms of generalisability?).
- What are the adverse or unintended effects (for example, increased stigma) of interventions to identify those individuals with TB from hard-to-reach groups, if any?

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 a (cost)-effectiveness study, or
9. any other type of quantitative primary research, or
10. a systematic review.

A total of 31 studies met all these inclusion criteria and reported comparative effectiveness or economic data, and were included in the review. An additional 39 studies were identified that did not report comparative data but met all the other inclusion criteria. Data from these non-comparative studies on screening completion rates and rates of latent and active TB infection are reported in Appendix F.

1.3 Findings

Evidence statement 1: Effectiveness evidence on the coverage and yield of screening and active case finding of TB in immigrant groups

Four comparative effectiveness studies were identified that reported data on active case finding of TB in the foreign-born, immigrants and new entrants (Laifer et al., 2007 [+]; Monney and Zellweger, 2005 [+]; Sciortino et al., 1999 [+]; Verver et al., 2001 [+]). A further two studies were identified in this topic area that reported both comparative effectiveness and economic data (Bothamley et al., 2001 [-]; Mor et al., 2008 [-]). The effectiveness data for all six studies has been used to inform the following evidence statements.

ES1.1 **Moderate evidence from three** retrospective cohort studies suggests that active screening is associated with a reduction in the severity or infectivity of identified cases, with a lower proportion of cases who were symptomatic or smear or culture-positive (Laifer et al., 2007 [+]; Monney and Zellweger, 2005 [+]; Verver et al., 2001 [+]). However, the studies did not adjust for baseline differences between cohorts of immigrants being actively screened and other groups of passively-screened foreign-born residents who were usually workers, students or tourists, or undocumented migrants.

ES1.2 **Weak evidence from** one retrospective cohort study is inconclusive about the effectiveness of pre-immigration screening using B notification to identify TB among immigrants to the USA compared with not providing B notifications (Sciortino et al., 1999 [+]).

ES1.3 **Weak evidence from one** before-and-after study suggests that pre-immigration

screening may reduce the risk of developing TB in immigrants 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 0.59-0.89; p = 0.002) (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.

ES1.4 **Weak evidence from one** study meant that conclusions could not be drawn on the comparative effectiveness of screening in either a hospital as part of the POA programme; in general practice as part of a new patient registration health check; or at homeless centres, because the differences in coverage and yield of screening were not statistically compared (Bothamley et al., 2001 [-]).

Applicability
Only one of the six studies identified in this section was from the UK, the rest originating from a range of European and North American countries with different immigration policies and screening strategies for new entrants, and which are targeted by new entrants from different countries with different demographics and prevalence of TB and other infections such as HIV. This limits the applicability of the findings in this section to the UK. However, the findings are reasonably consistent across countries, and we found no evidence of a national difference in effectiveness of different strategies.

Evidence statement 2: Economic evidence on the coverage and yield of screening and active case finding of TB in immigrant groups

Seven comparative economic studies were identified that provided evidence on the coverage and yield of screening and active case finding of TB in immigrant and new entrant groups (Brassard et al., 2006 [+]; Dasgupta and Menzies, 2005 [-]; Dasgupta et al., 2000 [+]; Hardy et al., 2010 [-]; Pareek et al., 2009 [-]; Schwartzman and Menzies, 2000 [++]; Schwartzman et al., 2005 [++]). A further two comparative studies were identified in this topic area that provided effectiveness and economic data (Bothamley et al., 2001 [-]; Mor et al., 2008 [-]). All nine studies were used to inform the evidence statements below:

ES2.1 **Moderate evidence from three** economic studies suggests that screening with chest X-rays among immigrants is less costly than TST per case identified (Schwartzman and Menzies, 2000 [++]; Dasgupta and Menzies, 2005 [-]) and cost-saving when secondary transmission of TB disease is taken into account (Schwartzman and Menzies, 2000 [++]). Adding TST to screening with a chest X-ray did not result in cost-savings for new entrants (Schwartzman et al., 2005 [++]). Although the studies are of varying quality, they all supported the same conclusions.

ES2.2 **Weak evidence from one** cost-comparison study suggests that the total cost of screening in immigrants may be less when using Quantiferon- Gold (QFT-G) as a first-line screening tool, compared with the strategy supported by NICE (2006) of chest X-

ray followed by TST for high-risk people, with QFT-G for positive TST results (Hardy et al., 2010 [-]).The findings are limited due to its narrow perspective on costs and no direct comparison of costs such as ICERs.

ES2.3 **Inconsistent evidence from two** cost-effectiveness studies suggests that the cost-effectiveness of active screening of immigrants compared with passive case-detection depends on the assumptions used in the economic model (Brassard et al., 2006 [+]; Dasgupta et al., 2000 [+]). Dasgupta et al., 2000 [+]) found that active case finding had an incremental cost of $20,328 for treating active TB compared with passive case detection and would have only been cost-saving is the future risk of TB was higher than the baseline estimate of 0.05%. Brassard et al. (2006 [+]), using different assumptions, found that actively screening immigrant children would have resulted in annual net savings of around $20,000.

Applicability
Only three of the nine studies identified in this section were from the UK, the rest originating from a range of European and North American countries with different immigration policies and screening strategies for new entrants, and which are targeted by new entrants from different countries with different demographics and prevalence of TB and other infections such as HIV. This limits the applicability of the findings in this section to the UK. However, the findings are reasonably consistent across countries, and we found no evidence of a national difference in cost-effectiveness of different strategies.

Evidence statement 3: Effectiveness evidence on the coverage and yield of screening and active case finding of TB in homeless groups

ES3.1 **Weak evidence** from one study (Miller et al., 2006 [+]) found that the yield of positive TST results and the number who were prescribed treatment for LTBI and active TB was statistically greater in a non-state-law-mandated homeless screening programme compared with a state-law-mandated prison screening programme. However, the two screening groups were not from comparable source populations and therefore any differences found may not be solely attributable to the different screening programmes.

Applicability
There was one study that informed this evidence statement and it was conducted in the USA. Due to the weakness of the evidence only a few conclusions can be drawn. The study targeted homeless people who attended shelters or other services for the homeless, so there is no evidence on how best to target other homeless groups such as rough sleepers who do not use these services.

Evidence statement 4: Economic evidence of the coverage and yield of screening and active case finding of TB in homeless groups

ES4.1 **Weak evidence** from one cost-comparison study that did not carry out direct cost comparisons is insufficient to draw conclusions about the cost-effectiveness of screening for TB in the homeless compared within prisons (Miller et al., 2006 [+]).

Applicability
There was one study that informed this evidence statement and it was conducted in the USA. Due to the weakness of the evidence only a few conclusions can be drawn. The study targeted homeless people who attended shelters or other services for the homeless, so there is no evidence on how best to target other homeless groups such as rough sleepers who do not use these services.

Evidence statement 5: Effectiveness and cost-effectiveness evidence on the coverage and yield of screening and active case finding of TB in drug users

ES5.1 No studies were identified that reported effectiveness and/or cost-effectiveness data on the coverage and yield of screening and/or active case finding of TB specifically in drug users.

Evidence statement 6: Effectiveness evidence on the coverage and yield of screening and active case finding of TB in prisoners

Two studies were identified that reported comparative effectiveness data on the coverage and yield of screening or active case-finding of TB among prisoners (Puisis et al., 1996 [-]; Yates et al., 2009 [-]). A further one study (evidence statement also reported elsewhere) provided both effectiveness and economic data for a screening programme conducted in prison compared within homeless centre. All three studies informed the evidence statements below.

ES3.1 **Weak evidence** from one study (Miller et al., 2006 [+]) reported in evidence statement 3, found that the yield of positive TST results and the number who were prescribed treatment for LTBI and active TB was statistically greater in a non-state-law-mandated homeless screening programme compared with a state-law-mandated prison screening programme. However, the two screening groups were not from comparable source populations and therefore any differences found may not be solely attributable to the different screening programmes.

ES6.1 **Weak evidence** from one before-and-after study found that the yield for identifying active TB was comparable when using chest X-rays (0.056%) and TST (0.069%) among prisoners, however, this was not compared using a statistical test and as such the findings are limited (Puisis et al., 1996 [-]). In addition, the study did not compare for baseline differences between the groups.

ES6.2 **Weak evidence** from one retrospective cohort suggests that screening with MXU should be offered to all prisoners regardless of symptoms of TB, since limiting

screening to those with symptoms would have missed a substantial number of cases (Yates et al., 2009 [-]). The conclusions drawn from this study are limited as it looked retrospectively at collected data to calculate how many cases would have been missed if screening had been limited in such a way.

Applicability
One of the three studies identified was from the UK, the other studies were from the USA. The overall findings were similar, and we have no reason to believe that the results from US studies are not applicable to the UK prison population. However, the strength of the evidence for the three studies is weak which means that only limited conclusions can be drawn.

Evidence statement 7: Cost-effectiveness evidence on the coverage and yield of screening and active case finding of TB in prisoners

One study was identified, which reported economic data on the cost of the coverage and yield of screening of TB in prisoners (Jones and Schaffner, 2001 [+]). A further one study (evidence statement also reported elsewhere) provided both effectiveness and economic data for a screening programme conducted in prison compared within homeless centre. Both studies informed the evidence statements below.

ES4.1 **Weak evidence** from one cost-comparison study, also reported in evidence statement 4, did not carry out direct cost comparisons and so is insufficient to draw conclusions about the cost-effectiveness of screening for TB in the homeless compared with prisoners (Miller et al., 2006 [+]).

ES7.1 **Weak evidence from one** cost-comparison study suggests that the cost per case of active TB would be lowest if the screening of prisoners was conducted by CXR ($9,600) compared with TST ($32,100) and using a symptom questionnaire ($54,100) (Jones and Schaffner, 2001 [+]). The findings are limited as the study did not directly compare the costs of screening in, for example, an ICER. In addition the study did not take into account the start-up costs of implementing screening with CXR.

Applicability
There were no comparative studies identified from the UK, only one study from the USA. There is no suggestion that the result from this US study is not applicable to the UK prison population.

Evidence statement 8: Effectiveness evidence on the coverage and yield of screening and active case finding of TB in mixed hard-to-reach groups of people with TB.

ES8.1 **Moderate evidence from one** case-control study suggests that using mobile X-ray units (MXU) to screen for TB reduced diagnostic delay among hard-to-reach

groups in the UK (including the homeless, drug users and prisoners) compared with passive case detection (adjusted hazard ratio for delay = 0.35, 95% CI 0.21 to 0.59, p < 0.0001). People identified as having TB by MXU screening were less likely to be symptomatic on diagnosis compared with those identified by passive case-detection (adjusted OR 0.35, 95% CI 0.15 to 0.81, p < 0.001) (Watson et al., 2007 [++]).

Applicability
The one study identified in this section was from the UK. The effectiveness evidence on the benefits of MXU is relevant to the UK, but the results for the specific hard-to-reach groups included in the study cannot be determined.

Evidence statement 9: Economic evidence on the coverage and yield of screening and active case finding of TB in mixed hard-to-reach groups of people with TB.

ES9.1 **Moderate evidence from one** case-control study found that screening with a MXU would have been cost-saving when compared with passive case detection in the UK if the cost of TB treatment was assumed to be £10,000 (cost-saving ICER of £1,912.33). This was not the case if the cost of TB treatment was assumed to be £5,000 (ICER = £2,180; cost per QALY = £3,206, ranging from £1,398 to £15,572) (Watson et al., 2007 [++]).

Applicability
The one study identified in this section was from the UK. The economic evidence on the benefits of MXU is relevant to the UK, but the results for the specific hard-to-reach groups included in the study cannot be determined.

Evidence statement 10: Economic evidence on the coverage and yield of screening and active case finding of TB in hard-to-reach contacts of people with TB.

Two economic studies identified that reported comparative data on the coverage and yield of screening/active case finding among foreign-born contacts of cases (Marra et al., 2008 [++]; Tan et al., 2008 [++]), and one additional cost-benefit study on screening close associates of immigrant children with LTBI (Brassard et al., 2006 [+]).

ES10.1 **Weak evidence** from one cost-benefit study suggests that it is cost-saving to screen contacts of immigrant children with LTBI identified using active screening methods compared with passive case-detection (Brassard et al., 2006 [+]).

ES10.2 **Moderate evidence** from one cost-effectiveness study suggests that people who are foreign-born who have a household contact with active TB should be tested and treated, but that it is not cost-effective for those who are not household contacts to be screened (Tan et al., 2008 [++]).

ES10.3 **Weak evidence from one** cost-effectiveness study suggests that the most cost-effective strategy might be to use Quantiferon-G as first-line screening in all foreign-born, aboriginal and BCG-positive contacts and TST in all others (Marra et al., 2008 [++]). The applicability of the results to hard-to-reach groups is limited as the strategies were not explored for foreign-born residents alone.

Applicability
All three studies identified for this section were from Canada, and reported on identifying new entrant contacts of people with TB, which limits their applicability to the UK situation. There is no reason to believe that these studies are not at least partially applicable to the UK, but the lack of high-quality evidence on identifying hard-to-reach contacts means that few conclusions can be drawn.

Evidence statement 11: Effectiveness of interventions to improve coverage and uptake of screening or active case-finding using more convenient locations

ES11.1 **Weak evidence** from one prospective cohort study suggests that undocumented immigrants may be more likely to complete screening if this was conducted in a specialised TB clinic compared with a general health clinic (OR = 2.57; 95% CI 1.92 to 3.42). However, the study did not adjust for known differences between the groups at baseline (El-Hamad et al., 2001 [+]).

Applicability
The one study we identified was on undocumented immigrants in Italy, where the health services available to immigrants are different from the UK. These findings are therefore of only partial applicability to the UK.

Evidence statement 12: Economic data on interventions to improve coverage and uptake of screening or active case-finding using more convenient locations

ES12.1 The review found no economic studies on the cost of screening in more convenient locations to improve the coverage/uptake of screening.

Evidence statement 13: Effectiveness of interventions to improve coverage and uptake of screening or active case-finding using peers or staff from the same hard-to-reach group

ES13.1 **Moderate evidence** from two RCTs suggest that using peers from the same hard-to-reach group as part of the screening programme can improve screening outcomes for drug users (Ricks, 2008 [++]) and the homeless (Pilote et al., 1996 [++]). Ricks, 2008 [++] found that problem drug users with peers as case managers were more likely to identify contacts than those without such case managers ($p = 0.03$). However, it is not known how much of this difference was due to the staff being former

drug misusers or due to the extra case management received (Ricks, 2008 [++]). Pilote et al. (1996 [++]) found that the homeless with a peer health adviser were more likely to complete screening than those given usual care (p = 0.004).

Applicability
Two studies were identified that were conducted in the USA, one on the homeless and one on drug users. These findings are only partially applicable as there were no studies identified from the UK. However, there is no reason to suggest that these hard-to-reach groups in the UK would respond differently to the impact of peer health workers.

Evidence statement 14: Economic evidence on interventions to improve coverage and uptake of screening or active case-finding using peers or staff from the same hard-to-reach group

ES14.1 The review found no cost-effectiveness studies on using peers or staff from the same cultural background to improve the coverage/uptake of screening.

Evidence statement 15: Effectiveness of interventions to improve coverage and uptake of screening or active case-finding using monetary incentives

Six comparative studies were identified that provided effectiveness data exclusively on the use of incentives to improve the coverage/uptake of screening. There was a further one study that provided both effectiveness and cost-effectiveness data. Five studies were on drug misusers (Chaisson et al., 1996 [+]; Fitzgerald et al., 1999 [+]; Malotte et al., 1998 [++]; Malotte et al., 1999 [++]; Perlman et al., 2003 [++]) and two on the homeless (Citron et al., 1995 [+]; Pilote et al., 1996 [++]). The effectiveness data from these five studies have been used to inform the following evidence statements.

ES15.1 **Strong evidence** from five studies, two RCTs (Malotte et al., 1998 [++]; Malotte et al., 1999 [++]) and three before-and-after studies (Chaisson et al., 1996 [+]; Fitzgerald et al., 1999 [+]; Perlman et al., 2003 [++]) shows that drug misusers who are provided with small monetary incentives are statistically more likely to complete screening compared with no incentives (p = 0.004, Chaisson et al., 1996 [+]; p < 0.001, Fitzgerald et al., 1999 [+]; Malotte et al., 1998 [++]; Malotte et al., 1999 [++]; Perlman et al., 2003 [++]).

ES15.2 **Strong evidence** from two RCTs found that providing drug misusers with a brief educational programme alone is unlikely to increase the proportion who complete screening compared with no incentives or education (p = 0.786, Malotte et al., 1998 [++]; p = 0.547, Malotte et al., 1999 [++]).

ES15.3 **Moderate evidence** from two studies, one RCT (Malotte et al., 1998 [++]) and one before-and-after study (Chaisson et al., 1996 [+]) suggests that drug misusers who were provided with monetary incentives and a brief educational programme were

statistically more likely to complete screening compared with providing no monetary incentives or education (p = 0.001, Chaisson et al., 1996 [+]; p < 0.001, Malotte et al., 1998 [++]).

ES15.4 **Moderate evidence** from two studies, one RCT (Pilote et al.,1996 [++]) and one before-and-after study, suggests that providing monetary incentives increases the uptake of screening (from 23% with no incentive to 62% with a £1.50 incentive and 45% with a £3.00 incentives, Citron et al., 1995 [+]; and from 53% with no incentive to 84% for $5.00 incentives, p<.001, Pilote et al., 1996 [++]).Although the quality of the studies varied, both studies supported the same findings.

Applicability
One of the seven studies in this section was from the UK, the rest being from the USA and Canada. The UK study found similar benefits from incentives offered to the homeless as seen in the North American studies on the homeless and with drug users. The applicability of these studies to the UK for all hard-to-reach groups is limited, but we have no evidence to suggest that drug users in the UK would not also respond to monetary incentives. There is no evidence on whether incentives make a difference to response rates in new entrant groups in the UK or elsewhere.

Evidence statement 16: Economic evidence for interventions to improve coverage and uptake of screening or active case-finding using monetary incentives

ES16.1 **Weak evidence** from one cost-benefit study suggests that, under the most conservative assumptions, providing IDUs identified at a needle exchange programme with a $25 cash incentive to return for TST readings might result in greater net savings of $54,770 compared with a net saving of $46,226 from offering screening with no cash incentives (Perlman et al., 2001 [++]). However, this was not directly compared in a cost-effectiveness analysis.

Applicability
The study identified was on drug users in the USA. The applicability of this study to the UK for all hard-to-reach groups is limited, but we have no evidence to suggest that drug users in the UK would not also respond to monetary incentives.

Evidence statement 17: Effectiveness of interventions to improve coverage and uptake of screening or active case-finding by identifying more members of hard-to-reach groups

Two studies were identified on the effectiveness of increasing the detection of immigrants to improve the coverage/uptake of screening (Lavender et al., 1997 [-]; Ormerod, 1998 [-]).

ES17.1 Weak evidence from two studies, one prospective (Ormerod, 1998 [-]) and one retrospective cohort (Lavender, 1997 [-]) suggests that using a health service register of patients could identify a further group of individuals who were not identified on entry to the country by the POA scheme; however the benefit of these different identification systems on the coverage and yield of screening is inconclusive. Only 6% of immigrants identified via the health service register who were not identified by the POA form were screened for TB (Lavender, 1997 [-]) and the yield of active TB was significantly greater among those identified via the POA process compared with those identified via the health service register (Ormerod, 1998 [-]). Both studies had limitations as they did not assess for baseline differences between the two groups.

Applicability
Both studies identified were from the UK and therefore relevant to UK practice today, although they both used registers from the now obsolete FHSAs. There is no evidence on any intervention to increase detection of members of other hard-to-reach groups, in the UK or elsewhere.

1.4 Discussion

1.4.1 Evidence gaps

The aims of this review were to identify the evidence on effective and cost-effective interventions to identify people with TB and to increase awareness about TB among hard-to-reach groups. After a comprehensive and exhaustive search, which identified over 15,000 unique studies, we found 32 studies that provided unique comparative data on the topic. Most of these studies focused on immigrants and foreign-born residents as the hard-to-reach group; and most sought to identify people with TB rather than to increase awareness of the disease in high-risk groups. As such, this review presents data on strategies to identify people with latent or active TB infection, but has little to report on strategies to increase awareness about TB in at-risk people, in the healthcare staff who are instrumental in screening and testing at-risk people, or in other personnel who could be influential in encouraging at-risk individuals for seeking help or attending for screening.

Although passive case-detection was a common comparator in the studies on active interventions, we identified no studies that focused on how to improve passive case-detection in hard-to-reach groups.

A number of other evidence gaps were indentified. As two thirds of the studies were focused on immigrants, there was a relative lack of evidence on other hard-to-reach groups. We found few studies that evaluated the effectiveness of contact tracing among hard-to-reach groups. About one quarter of the studies were from the UK, and many of the others are likely to be applicable to the UK context, but we found no UK studies for some types of interventions or groups, in particular:

- the effects of offering screening at different locations;

- the use of peer workers from the same group;
- the use of incentives; and
- specific data on homeless groups, drug users, and hard-to-reach contacts of people with TB.

1.4.2 Conclusions

A few general conclusions can be drawn from the evidence in this review.

- Active screening seems to increase identification of latent and active TB infection among immigrants and contacts of foreign-born people who are at high risk of infection, compared with passive case-detection, and leads to earlier diagnosis and reduced infective periods in those with active TB. The cost-effectiveness of active screening compared with passive case-detection is less certain, and more research is needed to confirm the economic benefits of such strategies in the UK.
- Screening with chest X-rays seems to be more effective than TST in immigrants and prisoners, but there is no clear evidence about whether this is also true for other hard-to-reach groups.
- Tracing household contacts of foreign-born cases appears to be cost effective.
- Using peers from the same hard-to-reach group as part of the screening programme seems to improve outcomes in the homeless and drug users.
- Offering small monetary incentives or vouchers is an effective and cost-effective strategy to increase the proportion of people who attend for TST test reading or for further investigation or management, in drug users, and seems to be effective in the homeless.
- Educational interventions about TB have not been shown to increase return rates for screening results without an additional monetary incentive, in drug users.

Other strong conclusions could not be drawn from the literature due to the limited number of studies and/or due to the quality of the evidence provided. More high quality comparative studies are needed on screening among hard-to-reach groups, in particular, those that address any baseline differences between the intervention groups where RCT studies cannot be done.

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 second of four systematic reviews that will be undertaken to inform the guidance. It examines the effectiveness and cost-effectiveness of interventions aimed at identifying TB cases and/or raising awareness of TB among hard-to-reach groups. This report systematically reviews and synthesises relevant research to inform this topic. The outcomes of interest include (but are not limited to) the uptake of screening services, the number of TB cases identified and the quality adjusted life years (QALYs), for cost-effectiveness studies. The remaining two reviews will explore quantitative evidence in relation to managing TB in hard-to-reach groups, and appropriate models for TB services for these populations.

2.2 Rationale

The incidence of TB in England increased from 12.3 cases per 100,000 people in 2000 to 15.5 per 100,000 in 2008 (Health Protection Agency, 2009). 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). Although overall rates of TB in high-income countries have steadily fallen, there remain high prevalences 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 Organisation 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. 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 interventions are effective and cost-effective at identifying TB and/or raising

awareness about screening for TB among hard-to-reach groups?

The secondary research questions were:

- What factors impact on the effectiveness of the interventions? For example, does the efficacy of the intervention vary by the:
    i) theories or conceptual models underpinning the interventions?
    j) diversity of the population (in terms of hard-to-reach group, age, or gender)?
    k) persons/organisations commissioning/delivering the interventions?
    l) way in which the intervention is delivered (for example, one-to-one or group-based)?
    m) involvement of the target population in the planning, design, or delivery of the intervention?
    n) content of different interventions?
    o) frequency, intensity, and duration of the intervention?
    p) time and place that the intervention is delivered?
- How transferable are the findings regarding effectiveness to other hard-to-reach populations, other settings, or other times? (For example, how representative is the sample; what are the key characteristics of the sample compared with other hard-to-reach groups; and how appropriate is the analysis in terms of generalisability?)
- What are the adverse or unintended effects (for example, increased stigma) of interventions to identify those individuals with TB from hard-to-reach groups, if any?

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, as some economic studies reported both effectiveness and cost-effectiveness data.

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:

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

For this review we focused on interventions relating to identifying TB cases.

The review also included studies where 50% or more of the participants had characteristics that met the review's definition of hard-to-reach. A further group of studies that did not report comparative data but otherwise met all the inclusion criteria have been summarised (from abstract only) in Appendix F.

[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.

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 (n = 3). 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 (n = 3). 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

The studies of effectiveness did not support meta-analysis and were synthesised narratively, as were the cost-effectiveness studies.

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

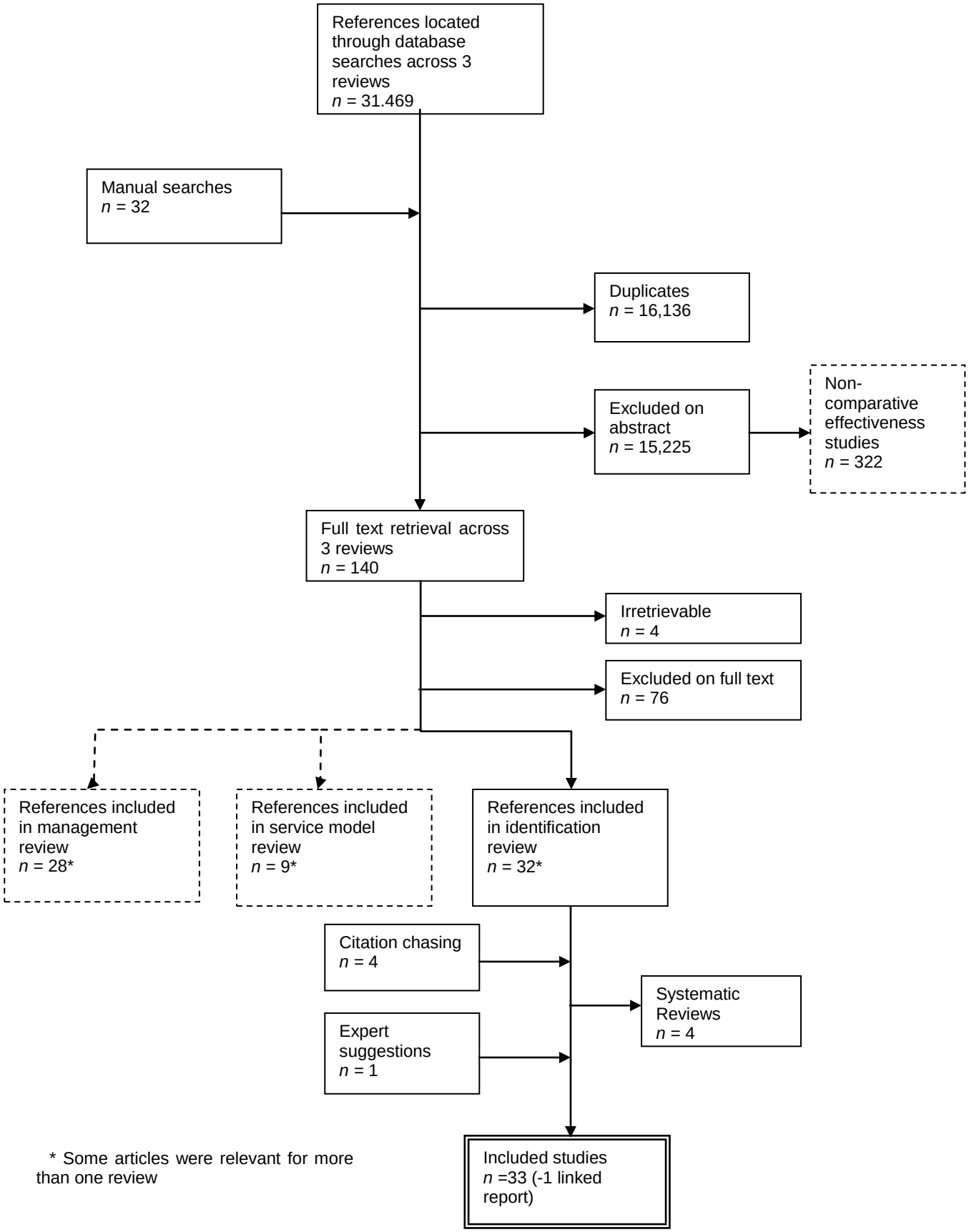
4.1 Flow of literature through the review

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. However, Appendix F briefly summarises the results of 39 non-comparative studies that were identified from the search but these were not included in the main report. 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, 32 studies were relevant of which four were systematic reviews that were checked for relevant references but were not included in the review. A further four studies were identified from forward citation chasing and a one study was identified by an expert of the Programme Development Group (PDG). These yielded 33 included papers with two reports linked (Citron et al., 1995; Kumar et al., 1995) and treated as one included study (Citron et al., 1995). The flow of literature through the review is illustrated in Figure 1, and Section 7 has the citation details of all included studies.

Figure 1. Flow of literature



* Some articles were relevant for more than one review

4.2 Summary of included studies

The 32 included papers report studies conducted in the following countries:

- 12 in the USA;
- 8 in the UK;
- 7 in Canada;
- 2 in Switzerland;
- 1 in Israel;
- 1 in Italy; and
- 1 in the Netherlands.

Study population characteristics consisted of the following (some studies reported data on more than one hard-to-reach group):

- 19 on immigrants, new entrants, foreign-born residents and/or refugees;
- 8 on drug users;
- 5 on prisoners; and
- 5 on homeless and sheltered individuals.

The types of study were as follows:

- 17 non-economic evaluations;
- 15 economic evaluations;
- of which 5 evaluations reported effectiveness and cost-effectiveness data.

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

	Aim	Study design	HTR group/s	Location	Quality score
Bothamley et al. (2001)	To compare the yield and costs of TB screening in three settings: a new entrants' clinic within the port of arrival scheme; a large general practice; and centres for the homeless.	Cost analysis	New entrants; homeless	UK	-
Brassard et al. (2006)	To evaluate the cost-effectiveness of a school-based screening programme targeting children at high risk of TB infection and close associates of children with LTBI compared with passive case-finding.	Cost-benefit analysis	Immigrants	Canada	+
Chaisson et al. (1996)	To determine the impact of a food voucher incentive and patient education programme on return rates for TST.	Before and after	IDUs	US	+
Citron et al. (1995) and Kumar et al. (1995)	To assess the prevalence of TB; the feasibility and effect of incentives and education; and the effects of targeting higher-risk age groups, on uptake of screening.	Before and after	Homeless	UK	+
Dasgupta et al. (2000)	To evaluate the impact and cost-effectiveness of two screening programmes compared with passive case-detection.	Cost-effectiveness	Immigrants	Canada	+
Dasgupta and Menzies (2005)	To examine the impact of migration from high TB-prevalence countries to low TB-prevalence countries, and to compare the cost-effectiveness of different TB control strategies.	Cost-effectiveness	Immigrants	Canada	-
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 immigrants	Italy	+
FitzGerald et al. (1999)	To evaluate the effect of giving a small financial incentive on compliance with TST screening.	Before and after	IDUs	Canada	+

Hardy et al. (2010)	To assess the cost-effectiveness of the QuantiFERON-TB Gold (QFT-G) test for screening new entrants from high-risk countries.	Cost-effectiveness	Immigrants	UK	-
Jones and Schaffner (2001)	To evaluate the cost-effectiveness of miniature chest radiography to screen new inmates for TB, compared with symptom-based and TST-based screening.	Cost-comparison	Prisoners	USA	+
Laifer et al. (2007)	To compare active screening of new entrants at POA with passive screening of foreign-born residents.	Retrospective cohort study	Immigrants	Switzerland	+
Lavender (1997)	To investigate the effects of screening at POA plus identifying new entrants using the FHSA new patient register, compared with screening at POA alone.	Retrospective cohort study	Immigrants	UK	-
Malotte et al. (1998)	To assess the effects of different monetary incentives and an educational intervention on completion of TST screening.	RCT	Drug users	USA	++
Malotte et al. 1999	To compare the effects of monetary versus nonmonetary incentives and an educational intervention on completion of TST screening.	RCT	Drug users	USA	++
Marra et al. (2008)	To assess the cost-effectiveness of QuantiFERON-TB Gold (QFT-G) test compared with TST to diagnose LTBI in contacts of active TB cases.	Cost-effectiveness	Immigrants	Canada	++
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	USA	+
Monney and Zellweger (2005)	To compare the effects of active screening at the POA with passive screening on bacteriological and clinical presentation of TB and the outcomes of treatment.	Retrospective cohort study	Foreign-born residents and new entrants	Switzerland	+
Mor et al. (2008)	To examine the effectiveness and cost-effectiveness of screening before entry with screening at POA.	Cost-effectiveness	Immigrants	Israel	-

Ormerod (1998)	To investigate the effects of screening at POA plus identifying new entrants using the FHSA new patient register, compared with screening at POA alone.	Prospective cohort	Immigrants	UK	-
Pilote et al. (1996)	To assess the effectiveness of providing monetary incentives or peers from the same hard-to-reach group to improve adherence to screening compared with usual care.	RCT	Homeless	USA	++
Pareek et al. (2009)	To assess the health impact and cost-effectiveness of screening for LTBI.	Cost-effectiveness	New entrants	UK	-
Perlman et al. (2001)	To test whether the costs of TB screening (and directly observed preventative therapy, DOPT) at a syringe exchange programme are lower than costs of identifying and treating the averted cases of active TB.	Cost-effectiveness	IDUs	USA	++
Perlman et al. (2003)	To compare adherence to referral for CXRs before and after the introduction of monetary incentives.	Before and after	IDUs	USA	++
Puisis et al. (1996)	To evaluate the effects of high-speed CXR screening compared with TST screening.	Before and after	Prisoners	USA	-
Ricks (2008)	To compare the effectiveness of the Indigenous Leader Outreach Model with standard TB control on contact tracing and treatment outcomes.	RCT	Drug users	USA	++
Schwartzman et al. (2005)	To investigate the health-related outcomes and costs of adding pre-immigration directly observed treatment, short-course (DOTS) or a TST to the standard CXR screening at POA.	Cost-analysis	Legal and undocumented Immigrants	USA	++
Schwartzman and Menzies (2000)	To model the cost-effectiveness of CXR and TST for TB prevention.	Cost-effectiveness	Immigrants	Canada	++
Sciortino et al. (1999)	To assess the effectiveness of the B notification programme for detecting TB among recent foreign-born entrants.	Retrospective cohort study	Immigrants	USA	+

Tan et al. (2008)	To examine the cost-effectiveness of LTBI screening and treatment for various subgroups, using a hypothetical cohort.	Cost-effectiveness	Foreign-born contacts	Canada	++
Verver et al. (2001)	To evaluate the impact of TB screening on the severity of the disease at diagnosis and on the length of the infectious period.	Retrospective cohort study	Immigrants	Netherlands	+
Watson et al. (2007)	To evaluate the clinical and cost- effectiveness of a digital mobile X-ray unit (MXU) compared with passive case-identification.	Case-control; cost-effectiveness	Homeless; prisoners; IDUs; refugee and asylum seekers.	UK	++
Yates et al. (2009)	To assess the impact on case-detection of limiting CXR to individuals with symptoms of TB.	Cohort study	Prisoners	UK	-

HTR = hard-to-reach; LTBI = latent TB infection; TST = tuberculin skin test; CXR = chest x-ray; POA = port of arrival; FHSA = family health service authority; IDU = injection drug user; RCT = randomised controlled trial; nRCT = non-randomised controlled trial.

4.3 Quality of the included studies

The results of quality assessment are presented in Tables 2 and 3. Eleven studies were judged to be of high quality [++], twelve of medium quality [+], and nine of low quality [-], as follows:

- High quality [++]:
  - Malotte et al. (1998) Malotte et al. (1999); Marra et al. (2008); Perlman et al. (2003); Perlman et al. (2001); Pilote et al. (1996) ; Ricks (2008); Schwartzman and Menzies (2000); Schwartzman et al. (2005); Tan et al. (2008); Watson et al. (2007);
- Medium quality [+]:
  - Brassard et al. (2006); Chaisson et al. (1996); Citron et al. (1995) / Kumar et al. (1995); Dasgupta et al. (2000); El-Hamad et al. (2001); FitzGerald et al. (1999); Jones and Schaffner (2001); Laifer et al. (2007); Miller et al. (2006); Monney and Zellweger (2005); Sciortino et al. (1999); Verver et al. (2001);
- Low quality [-]:
  - Bothamley et al. (2001); Dasgupta and Menzies (2005); Hardy et al. (2010); Lavender (1997); Mor et al. (2008); Ormerod (1998); Pareek et al. (2009); Puisis et al. (1996); Yates et al. (2009).

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
Chaisson, 1996	++	+	++	+	++	NA	NA	++	++	NR	+	+	+	++	+	++	++	++	++	++	NR	NR	++	++	++	++	+	+
El-Hamad, 2001	++	+	++	+	++	NA	NA	++	++	NR	++	+	+	++	++	+	++	++	++	++	NA	NR	++	+	++	+	+	+
FitzGerald, 1999	+	+	NR	+	++	NA	NA	+	NR	NR	++	+	+	++	+	++	++	++	+	+	++	NR	++	-	++	+	+	+
Kumar, 1995 and Citron, 1995	++	++	+	+	++	NA	NA	+	+	NR	++	++	++	++	++	++	++	+	++	+	+	NR	-	-	+	+	+	+
Laifer, 2007	++	++	++	-	++	NA	NA	+	++	NR	++	+	+	++	++	+	++	NR	NR	-	NA	NR	-	++	+	-	+	+
Lavender, 1997	+	+	+	+	+	NA	NA	+	++	NR	NA	+	+	++	+	+	++	NR	+	NR	NA	NR	-	++	-	-	+	-
Malotte, 1999	++	++	+	++	+	+	NA	++	++	NR	++	+	+	++	++	++	++	++	++	++	NA	NR	++	++	++	++	+	++
Malotte, 1998	++	++	+	++	++	+	NA	++	++	NR	++	+	+	++	++	++	++	++	++	+	NA	NR	++	++	++	++	+	++
Monney, 2005	++	+	NR	-	++	NA	NA	++	++	NR	++	+	+	+	+	+	++	++	++	-	NR	NR	+	-	+	-	+	+
Ormerod, 1998	+	++	NR	+	-	NA	NA	NR	++	NR	++	++	++	++	++	+	++	NR	NR	-	NR	NR	++	-	++	-	+	-
Perlman, 2003	++	+	++	+	++	NA	NA	++	+	NR	++	+	+	++	++	++	++	++	++	++	NA	NR	++	++	++	++	+	++
Pilote, 1996	+	++	+	++	++	NR	NA	++	NR	+	+	++	+	+	++	++	+	++	NR	NA	+	NA	NR	++	++	++	+	++
Puisis, 1996	++	+	++	-	+	NA	NA	++	++	NR	+	+	+	+	+	+	++	NR	NR	-	-	NR	++	-	-	-	-	-
Ricks, 2008	++	+	++	++	++	++	NA	++	++	NR	++	+	+	+	++	++	++	++	+	++	++	NR	++	++	++	++	+	++
Sciortino, 1999	+	+	++	+	-	NA	NA	++	NR	NR	+	+	+	++	++	++	++	++	++	++	NA	NR	++	++	++	++	+	+
Verver, 2001	++	++	+	-	+	NA	NA	++	NR	NR	++	+	+	++	+	++	++	++	++	-	++	NR	++	+	++	+	+	+
Yates,2009	++	+	+	+	+	NA	NA	++	++	NR	NR	++	++	-	+	++	++	NA	+	-	NR	NR	-	+	-	+	-	-

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 Not applicable 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, 2001	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 [-]
Brassard, 2006	Y	Y	PA	N	PA	PA	N	PA	PA	PA	Y	PA	N	PA	PA	PA	PA	N	Y	PA	Potentially serious limitations [+]
Dasgupta, 2000	Y	Y	PA	N	PA	PA	N	PA	PA	Y	Y	Y	PA	N	PA	PA	PA	Y	Y	U/C	Potentially serious limitations [+]
Dasgupta, 2005	Y	Y	PA	N	PA	N	N	PA	PA	PA	U/C	PA	PA	PA	N	PA	PA	N	N	N	Very serious limitations [-]
Hardy, 2010	PA	Y	Y	N	N	N	N	N	PA	PA	PA	N	U/C	PA	N	U/C	Y	N	N	N	Very serious limitations [-]
Jones, 2001	PA	Y	PA	Y	PA	Y	N	PA	PA	Y	Y	Y	PA	Y	Y	PA	PA	Y	Y	U/C	Potentially serious limitations [+]
Marra, 2008	PA	Y	PA	Y	PA	PA	Y	N	PA	Y	Y	Y	Y	PA	Y	PA	PA	PA	Y	Y	Minor 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 [+]
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 [-]
Pareek, 2009	Y	Y	Y	N	PA	N	N	N	PA	N	Y	U/C	U/C	U/C	U/C	U/C	U/C	Y	N	N	Very serious limitations [-]
Perlman, 2001	Y	Y	PA	Y	Y	Y	N	PA	PA	Y	Y	Y	Y	Y	Y	PA	PA	Y	Y	U/C	Minor limitations [++]
Schwartzman, 2000	Y	Y	PA	Y	PA	Y	N	PA	PA	Y	Y	Y	PA	PA	Y	PA	PA	Y	Y	N	Minor limitations [++]
Schwartzman, 2005	Y	Y	PA	Y	Y	PA	N	Y	PA	PA	Y	Y	PA	PA	Y	PA	PA	N	Y	N	Minor limitations [++]
Tan, 2008	Y	Y	PA	Y	Y	PA	Y	PA	PA	Y	PA	Y	PA	PA	Y	PA	PA	Y	Y	U/C	Minor limitations [++]
Watson, 2007	Y	Y	Y	Y	PA	Y	Y	PA	D/A	PA	PA	PA	PA	PA	Y	PA	PA	Y	Y	N	Minor limitations [++]

Y= yes; 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 not applicable).
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

As noted above, one quarter (n = 8) of the 32 included studies were carried out in the UK. The remaining studies came predominantly from the USA and Canada, with five from other OECD countries, all of which are likely to offer different types of TB services to hard-to-reach groups compared with the UK. As such, although the non-UK studies cover similar interventions and population groups to those in the UK studies, differences in clinical and cost-effectiveness may be related to differences in services provided. In other words, the review group consider that the findings presented here should be transferable to the UK setting.

5.0 Study findings

5.1 Approaches to screening for latent infection and active TB in different populations

Latent infection, by definition, is asymptomatic, but can convert to active disease over time. Identification is therefore based on active or passive screening, usually with tuberculin skin tests (TST), or quantiferon-gold (QFT-G). Some studies also used chest X-ray to identify people with lesions that may or may not have appeared to be active.

Active case finding is the identification of people with active disease, who may or may not be symptomatic. Diagnosis is based on typical chest X-ray findings, which may be done after a positive TST, plus a positive sputum smear for acid-fast bacilli, or positive sputum culture.

Most of the studies we identified for hard-to-reach populations were concerned with screening for active or latent TB infection (LTBI), but yields were much higher for latent than active disease. The majority of the studies did not focus on only identifying latent or active TB.

The screening approaches covered in the review to identify latent and/or active TB among new entrants were as follows:

Hard-to-reach group	TST	Chest X-ray	In-vitro and QTF-G	Sputum smears/culture	Serology	Symptom questionnaire
Immigrants/ new entrants/ foreign-born residents	Bothamley et al., 2001 [-]; El-Hamad et al., 2001 [+]; Hardy et al., 2010 [-]; Lavender et al., 1997 [-]; Marra et al., 2008 [++]; Monney and Zellweger (2005 [+];Mor et al., 2008 [-];Ormerod,	Dasgupta et al., 2000 [+]; Dasgupta and Menzies, 2005 [-]; El-Hamad et al., 2001 [+]; Hardy et al., 2010 [-]; Laifer et al., 2007 [+]; Lavender et al., 1997 [-]; Monney and Zellweger, 2005 [+];	Hardy et al., 2010 [-] Pareek et al., 2009 [-] Dasgupta and Menzies, 2005 [-].	Dasgupta and Menzies, 2005 [-]; Sciortino et al., 1999 [+]; Verver et al., 2001 [+]	Dasgupta and Menzies, 2005 [-].	

	1998 [-]; Pareek et al., 2009 [-]; Schwartzman et al., 2005 [++].	Mor et al., 2008 [-] Ormerod, 1998 [-]; Schwartzman et al., 2005 [++]; Schwartzman and Menzies, 2000 [++];Sciortino et al., 1999 [+]; Verver et al., 2001 [+].				
Homeless	Miller et al., 2006 [+].	Citron et al., 1995 [+]; Miller et al., 2006 [+]; Watson et al., 2007 [++].				
Drug users	Chaisson et al., 1996 [+]; Fitzgerald et al., 1999 [+]; Malotte et al., 1998 [++]; Malotte et al., 1999 [++]; Perlman et al. (2001 [++].	Fitzgerald et al., 1999 [+]; Perlman et al., 2003 [++]; Pilote et al., 1996 [++]); Watson et al., 2007 [++].		Pilote et al., 1996 [++].		
Prisoners	Jones and Shaffner, 2001 [+]; Miller et al., 2006 [+]; Puisis et al. (1996 [-].	Jones and Shaffner, 2001 [+]; Puisis et al., 1996 [-]; Watson et al., 2007 [++]; Yates et al. (2009				Jones and Shaffner, 2001 [+]; Yates et al. (2009 [-]).

		[-].				
Hard-to-reach contacts	Brassard et al., 2006 [+];Marra et al., 2008 [++]; Tan et al., 2008 [++].		Marra et al., 2008 [++].			

5.2 Approaches to improve passive case finding aimed at awareness-raising in high risk groups, those working with high groups and maximising service accessibility

The review found two studies that included an educational component (among other factors), on the hard-to-reach population themselves (Citron et al., 1995 [+]) and/or in workers at homeless shelters to increase identification of TB (Citron et al., 1995 [+]; Miller et al., 2006 [+]) to increase the identification of TB. However, these studies were concerned with active case finding and not passive case detection.

5.3 Coverage uptake and yield from screening / active case finding in different population groups

This section is concerned with ascertaining effective and cost-effective strategies for identifying TB for each hard-to-reach group. The review found 20 studies relevant to this section, which evaluated the following hard-to-reach groups:

Hard-to-reach group	Effectiveness studies	Economic studies	Effectiveness/economic studies
Immigrants/ new entrants/ foreign-born residents	Laifer et al. (2007 [+]); Switzerland Monney and Zellweger (2005 [+]); Switzerland Verver et al. (2001 [+]); Netherlands Sciortino et al. (1999 [+]); USA	Pareek et al. (2009 [-]); UK Hardy et al. (2010 [-]); UK. Dasgupta et al. (2000 [+]); Canada Dasgupta and Menzies (2005 [-]); Canada Schwartzman and Menzies (2000 [++]); Canada Schwartzman et al.	Bothamley et al. (2001 [-]); UK Mor et al., (2008 [-]); Israel

		(2005 [++]); Canada Brassard et al. (2006 [+]); Canada	
Homeless	None identified	None identified	Miller et al., 2006 [+]; USA
Drug users	None identified	None identified	
Prisoners	Puisis et al. (1996 [-]); USA Yates et al. (2009 [-]); UK	Jones and Shaffner (2001 [+]); USA	Miller et al. (2006 [+]; USA
Mixed populations	None identified	None identified	Watson et al., 2007 [++]); UK
Hard-to-reach contacts	None identified	Brassard et al., 2006 [+]; Canada Marra et al., 2008 [++]; Canada Tan et al., 2008 [++]; Canada	

5.3.1 Immigrants, new entrants and foreign-born residents

Thirteen relevant studies were identified; four studies reported comparative effectiveness data, seven studies reported comparative cost data and two studies reported both effectiveness and cost-effectiveness data on the uptake and yield of screening among immigrants and new entrants.

In the four effectiveness studies:

- Three studies assessed the effectiveness of active post-immigration screening of immigrants and new entrants compared with passive case-detection:
    - Laifer et al., (2007 [+]) in Switzerland;
    - Monney and Zellweger (2005 [+]) in Switzerland; and
    - Verver et al, (2001 [+]) in the Netherlands.

- One study explored the association between receiving a B-notification at pre-immigration screening compared with not receiving a B-notification on outcomes relating to TB:
    - Sciortino et al. (1999 [+]) in the USA.

In the seven economic studies:

- Four studies compared different screening tools with each other to ascertain which are the most cost-effective:
    - Dasgupta and Menzies, (2005 [-]) in Canada;
    - Pareek et al., (2009 [-]) in the UK;

    - Schwartzman and Menzies, (2000 [++]) in Canada; and
    - Schwartzman et al. (2005 [++]), in Canada.

- One study compared the different sequencing of the screening tools to investigate which strategy is the most cost-effective:
    - Hardy et al., (2010 [-]), in the UK.

- Two studies compared the cost-effectiveness of actively screening for TB compared with passive case detection:
    - Dasgupta et al., (2000 [+]) in Canada; and
    - Brassard et al., (2006 [+]), in Canada.

In the two studies that reported both effectiveness and economic data:

- One study explored active post-immigration screening of new entrants at a hospital via the port of arrival, compared with subsequent screening in general practice as part of the registration health check, or screening at centres for the homeless:
    - Bothamley et al., (2001 [-]) in the UK.

- One study explored the effectiveness of pre-immigration screening compared with post-immigration screening:
    - Mor et al., (2008 [-]), in Israel.

Effectiveness studies

There were four effectiveness studies that reported outcomes relating to the uptake and yield from screening and/or active case finding in immigrants. Three studies assessed the effects of active screening of immigrants, foreign-born residents or new entrants on the subsequent severity and infectivity of TB infection (Laifer et al., 2007 [+]; Monney and Zellweger (2005 [+]); Verver et al, 2001 [+]).

Laifer et al. (2007 [+]) carried out a retrospective cohort study of all patients admitted with suspected TB to a hospital isolation unit in Switzerland between 1997 and 2004 (n = 02). Patients were categorised as foreign-born residents who had work permits or were tourists or students, who were identified by passive case detection after referral from their GP (n = 59); or new entrants, who were actively screened by chest X-ray at the border and referred if they had abnormalities (n = 43). A third group (n = 54), of native Swiss, are not reported here as they are not defined as hard to reach. The active screening group were statistically more likely to be younger (mean age of 30.6 years compared with 35.1 years in the passive case-detection group); more likely to have a history of prior TB (14%, compared with 1.7%) and less likely to have HIV co-infection (0%, compared with 12.5%). Although not statistically significant, the proportion of men was higher in the active screening group (90.7%, compared with 61% in the passive case-detection group) and almost two thirds of new entrants were from Eastern Europe (62.8%) compared with one third (32.2%) of foreign-born residents, with similar numbers from Africa (18.6% of new entrants compared with 15.3% of foreign-born

residents).

New entrants were significantly less likely than foreign-born residents to have active disease, positive smears, or to die in hospital. These results reflect the fact that foreign-born residents were referred by their GP when they presented with a problem, while screening of new entrants occurred whether or not they had symptoms. About one third (34.9%) of the 43 new entrants had active disease and at least one positive acid-fast smear, compared with 76.2% of the 59 foreign-born residents ($p < 0.05$); 76.7% of the new entrants had active disease and at least one positive sputum culture compared with 100% of the foreign-born residents ($p < 0.05$); and none of the new entrants died in hospital, compared with 1.7% of the foreign-born residents. However, new entrants who had TB were significantly more likely to have resistant disease: one fifth (21.9%) had isoniazid-resistant infections compared with 10.2% of the foreign-born resident group ($p < 0.05$); and 6.3% had multidrug-resistant disease, compared with 1.7% of the foreign-born residents ($p < 0.05$).

It is difficult to compare active screening directly with passive case-detection from this study, since the foreign-born residents had different baseline characteristics and may have come from countries with different demographic characteristics and TB prevalence. The study does not report the proportion of all new entrants who had abnormal chest X-rays.

Monney and Zellweger (2005 [+]) also retrospectively compared active screening with passive case detection among foreign-born entrants and residents to Switzerland in 2001 and 2002. The screening policy in Switzerland at the time was to actively screen all adult asylum seekers and other migrant groups from countries other than the European Union, the USA, Canada, Australia or New Zealand using TST and chest X-ray. Foreign-born workers from the same countries were also actively screened but with a chest X-ray only. All other foreign-born residents such as students, tourists or undocumented migrants were not actively screened and identification of TB was conducted by passive case-detection when they sought medical treatment for TB symptoms.

One fifth (21%) of the 71 actively-screened entrants were female with a mean age of 26 years, in contrast with the 108 foreign-born residents, 37% of whom were female with a mean age of 34 years, or the 34 passively-screened group, 56% of whom were female with a mean age of 31 years. The actively-screened group were significantly more likely to be free of symptoms at diagnosis than the passively-screened groups, 49.3% were asymptomatic; 95% CI 37.4% to 61.2%, compared with 17.6% of the passive-screened group; 95% CI 10.3 to 24.9%. Of the passively-screened groups, 91% of foreign-born workers and 71% of other foreign-born residents had symptoms at diagnosis. Two thirds (63.4%) of the actively-screened group had a positive smear or culture compared with 74% of foreign-born workers and 65% of passively-screened foreign-born residents (significance not reported).

This study reports on clinical and microbiological presentations of people already diagnosed with TB. As such, it does not allow a comparison of different strategies for the initial identification of people with TB. However, it suggests that active screening facilitates the diagnosis of active TB before it becomes symptomatic, and may therefore help to reduce the delay to treatment and help reduce transmission in undiagnosed cases.

Verver et al. (2001 [+]) also carried out a retrospective cohort study to assess the effects of active screening of immigrants to the Netherlands on the severity of TB and length of the infectious period. Active screening was mandatory for would-be immigrants from at-risk countries who intended to stay for longer than three months, and took place at a TB clinic by chest X-ray or TST, followed by sputum smear and culture for those with positive results. Outcomes for the 454 immigrants who were actively screened between 1993 and 1998 were compared with those of 822 foreign-born residents, screened or not screened, who sought medical care for symptoms of TB. The two groups were similar demographically, 64% of the actively-screened group and 63% of the passively-screened group were male; 78% of the active screening group and 77% of the passive screening group were aged less than 35 years; 46% of the active screening group were from Africa including Morocco and Somalia, compared with 55% of the passive screening group. However, 16% of the passive screening group did not have legal resident status, compared with 3% of the actively-screened group.

Among the 708 (86%) of patients for whom there was information, those who participated in active screening were diagnosed earlier and had a shorter duration of symptoms than those detected passively ($p = 0.001$); the mean duration of symptoms was 10.5 weeks (median 7.5 weeks) for passive case-detection compared with a mean of 4.2 (median of 0) weeks for actively-screened patients, only 37% of whom had symptoms. The odds ratio for being smear positive at diagnosis with active screening compared with passive case-detection was 0.5 (95% CI 0.3 to 0.8). Overall, it was estimated that six-monthly screening would have reduced the infectious period prior to diagnosis from a total of 3,379 to 2,355 weeks for the 322 patients identified by passive case-detection, a reduction of 30% in the total infectious period, and a reduction of 34% for those who were smear-positive.

Detection of cases through screening was less likely with increasing duration of stay. 302/454 (66%) of the actively-screened group had been in the Netherlands for less than six months, compared with 114/368 (31%) of passively-detected cases. In contrast, 26% of passively-detected group had been resident for 24-30 months, compared with 6% of actively-screened patients. However, the retrospective design may have led to recall bias and inaccuracy about the true duration of symptoms, and the duration of symptoms was assumed to be similar to the infectious period, which may not be accurate.

One study investigated the association between B notification of Latent TB Infection

(LTBI) from pre-immigration screening and likelihood of presenting with active TB in the following year, in immigrants to California in the USA arriving between 1992 and 1995. Immigrants from high-risk countries were screened before departure to the USA with chest X-rays, and sputum culture if abnormalities were detected. Those with X-ray signs of active TB but a negative culture were given a B1 notification; those with X-ray signs of inactive infection were given a B2 notification; both sets of notifications were included in this study to determine the conversion rate to active TB. Children under 15 years were tested if they were close contacts of a case with active TB or had symptoms of TB. Those with B notifications were allowed entry into the USA but were required to report to a local health department for evaluation of TB (Sciortino et al., 1999 [+]).

Of 27,412 immigrants with a B notification on arrival, 970 were subsequently diagnosed with active TB. These cases were compared with those from a second database of foreign-born entrants to the USA who had been diagnosed with active TB, 970 of whom had a prior B notification. New entrants with a B notification were largely of immigrant status (20,760 out of the 27,412) and 4,971 were refugees. Slightly more than half were male (14,621) and most were aged 45 and older (18,323). Most (24,834) were from Asia or the Pacific Islands, in particular the Philippines (9,975) and Vietnam (9,365). Recent entrants with TB infection were slightly younger and from a wider range of countries: 1,528 out of the 2,547 identified in this way were male; 1,126 were aged 45 and over;1,714 were from Asia or the Pacific Islands, with 727 from the Philippines, 598 from Mexico, 586 from Vietnam, 149 from China and 487 from other countries. Overall, 28.3% of immigrants were from Latin America, but only 1.7% entered with a B notification.

The conversion rate to active TB in people entering with a B notification was 3.5% (95% CI 3.3% to 3.8%) within one year of arrival. However, of all 2,547 foreign-born individuals diagnosed with active TB within one year of arrival, only 38.1% had a B notification. Among the 2,210 recent arrivals with TB who were adults (>15 years), those with a B notification were more likely to have pulmonary TB (prevalence ratio [PR] = 1.12, 95% CI 1.10 to 1.15), less likely to have smear-positive pulmonary disease (PR=0.32, 95% CI 0.26 to 0.39) and were reported to have TB sooner after their arrival in the USA compared with those with no B notification (mean of 3.2 months, compared with 4.7 months without B notification, $p = 0.001$). The B notification programme failed to identify 87% of the smear-positive pulmonary TB cases in adults, and 99% of highly infectious cases among Latin Americans. There was limited evidence to support the use of B notification to identify TB among new entrants in the USA.
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The retrospective design of this study limits the conclusions that can be drawn from the results. In particular, it is unclear whether the cases of active TB diagnosed in new entrants were acquired after entry to the USA, or were pre-existing active or latent infections and whether participants received treatment for their TB infection. It is also unclear how many of the cases without B notification were actually screened prior to arrival in the USA. It is therefore difficult to be sure how effective the B notification

programme was at detecting active or latent TB prior to immigration.

Economic studies

Seven studies were identified that reported comparative cost data on the coverage uptake and yield of screening in immigrants and new entrants. Four studies compared different screening tools with each other to ascertain which tools are most cost-effective for screening for TB among new entrants (Dasgupta and Menzies, 2005 [-]; Pareek et al., 2009 [-]; Schwartzman and Menzies, 2000 [++]; Schwartzman et al. (2005 [++]).

Dasgupta and Menzies (2005 [-]) compared different tools for identifying active cases of TB among immigrants entering Canada from countries with a high prevalence of TB, based on a literature review. The identification tools tested were TST, sputum TB culture, sputum TB polymerase chain reaction (PCR) tests, serology, and *in vitro* tests of cell-mediated immunity (such as Quantiferon (QFT), an interferon-γ release assay [IGRA] test). These were compared with chest X-ray to identify active cases of TB. The study estimated that chest X-ray would detect 7 cases of active TB at a total cost of $69,285, amounting to $9,898 per case of active TB detected (based on Canadian dollars). More cost-effective strategies included culture of one sputum sample per person, which was estimated to detect 8.2 cases of active TB at a total cost of $55,404, or $6,757 per case of active TB detected. Serology was also cost-effective, with an estimated 5.5 cases of active TB detected at a total cost of $39,169, or $7,122 per case of active TB detected, including the cost of drawing blood samples. The remaining screening strategies (TST, sputum TB PCR and Quantiferon) were more expensive than the current strategy of testing with a chest X-ray. The study has limitations in that it does not report sufficient detail about the study's economic perspective and did not use discount rates to take into account the increasing costs over time. In addition, sensitivity analyses were not conducted to test the uncertainty surrounding the assumptions and the study did not calculate the incremental cost-effectiveness ratio (ICER) of the different screening strategies.

Pareek et al. (2009 [-]) compared three strategies for screening for TB among new entrants into the UK: TST-alone; Quantiferon-Gold (QFT-G), an *in vitro* test for cell-mediated immunity; and using both a TST and QFT-G. There was no detail on the assumptions and data sources used in the economic model. Screening for LTBI with TST or QTF-G was estimated to have reduced annual TB incidence by 9.45%. Implementing a three-yearly TST plus QFT-G strategy would have prevented 25,538 cases of TB in the first 20 years. This would have resulted in savings of £8,345,291. Screening annually with TST and QFT-G would have produced an ICER of £1,298 per case of TB prevented and screening annually with QFT-G alone would have produced an ICER of £25,072. The results suggest that adding QFT-G to TST for detecting LTBI among new entrants into the UK would improve the cost-effectiveness of screening. However, as the study was a brief report presented at a conference, the authors did not report the economic perspective used, or other important factors such as whether all future outcomes and costs were discounted appropriately. In addition, it was unclear

what sources were used to identify outcomes, treatment effects, resource use and costs, which limits the confidence with which any conclusions can be drawn.

Schwartzman and Menzies (2000 [++]) modelled screening for TB using chest X-ray or TST compared with no active screening (but passive detection of cases of active TB) among three different at-risk populations of immigrants into Canada over a 20-year time horizon. Effectiveness assumptions were based on pre-existing epidemiological and effectiveness research, epidemiological approximation methods, or on arbitrary choices when no data was available. All immigrants were assumed to be 20 years of age and a 3 per cent discount rate was used. The highest risk cohort were immigrants from sub-Saharan Africa, with an assumed 50% TB prevalence and 10% HIV prevalence. The next highest risk cohort was immigrants from South-East Asia, with 50% TB and 1% HIV prevalence. The lowest risk cohort was from Western Europe, with 5% TB and 1% HIV prevalence.

Screening using a chest X-ray was estimated to detect 35.8 cases of active TB per 1,000 tested in the highest risk cohort, at a total cost of $338,310. Compared with no screening, this was an incremental cost of $3,943 per active TB case prevented over a 20-year time period. In the next highest risk cohort, chest X-ray screening was estimated to detect 23.4 cases of active TB per 1,000 screened, at a total cost of $231,430. Compared with no screening, this was an incremental cost of $10,627 per case of active TB prevented. In the lowest risk cohort, chest X-ray was estimated to detect 2.3 cases of active TB per 1,000 tested, at a total cost of $51,170. Compared with no screening, this was an incremental cost of $236,496 per case of active TB prevented. Screening using TST was more costly than screening with chest X-ray, and estimated to detect 32.8 cases of active TB per 1,000 tested in the highest risk cohort at a total cost of $436,390. Compared with chest X-rays, this was an incremental cost of $32,601 per case of active TB prevented. In the second highest risk cohort, screening with TST was estimated to detect 21.7 cases of active TB at a total cost of $342,730. Compared with chest X-rays, this was an incremental cost of $66,759 per case of active TB prevented. In the lowest risk cohort, TST was estimated to detect 2.2 cases of active TB per 1,000 screened, at a total cost of $62,640. Compared with chest X-rays this was an incremental cost of $68,799 per case of active TB prevented. However, for the lowest risk population, TST had extended dominance over chest X-ray screening but at an ICER of $140000, TST is not necessarily cost effective.

In a secondary analysis, which included secondary active cases of TB in the economic model, the incremental cost per case of active TB detected using chest X-rays was cost-saving compared with no screening for the two highest risk populations, but TST screening retained its extended dominance over chest X-rays in this secondary analysis for the lowest risk population. The results suggest that for high-risk cohorts of immigrants, screening with chest X-ray is more cost-effective than screening with TST. The study only included minor limitations.

Schwartzman et al. (2005 [++]) explored adding TST to chest X-ray screening compared with screening using chest X-rays alone to identify active TB among legal immigrants, undocumented migrants and temporary visitors from Mexico entering the USA. There was also a third comparison arm which was not explored here as it was relevant to the treatment of TB. The screening programmes used a hypothetical cohort to investigate screening in Mexico before entry into the USA. Based on published sources, the study estimated that 35,400,000 new entrants would enter the USA over a 20-year period and that testing with a chest X-ray would identify 47,610 cases of active TB. The study also estimated that there would be 5,245 TB-related deaths.

The total direct costs of active screening using chest X-ray was estimated to cost $1,985,000,000 over the 20-year period and the total indirect costs were estimated to be $632,000,000 (in 2003 US dollars). Compared with screening using chest X-ray alone, the study estimated that 401 cases of active TB would be prevented if TST was also used. The total direct costs of screening with TST plus chest X-ray was estimated at $2,245,000,000 over a 20-year period, an added cost of $260,000,000 compared with screening using a chest X-ray alone. The total indirect costs of this screening programme were estimated to be $701,000,000, an added cost of $69,000,000 compared with screening using a chest X-ray alone. The results demonstrate that adding TST to screening with a chest X-ray did not result in cost-savings.

The authors note that there are several uncertainties around some of the assumptions used in their economic model, for example that the incidence of TB would decrease 6% annually (this figure was taken from the rate of decline found in Peru after expansion of a DOT programme), and that the patterns of migration would remain constant over 20 years. However, the authors tested these uncertainties in several sensitivity analyses and demonstrated that these did not impact on the findings.

One study was identified that compared different sequencing of screening tools to investigate which procedure is most cost-effective for identifying TB among immigrants (Hardy et al., 2010 [-]).

Hardy et al. (2010 [-]) investigated using Quantiferon Gold (QFT-G, an *in vitro* IGRA test to detect interferon-gamma) as a frontline screening tool when screening for latent TB among immigrants into the UK from countries with a high incidence of TB. The screening procedure tested was first-line QFT-G with subsequent chest x-ray if the QFT-G was positive. This was compared with the strategy recommended by NICE (2006) of using a chest X-ray for first-line screening, plus TST for new entrants from countries with a high prevalence of TB, and subsequent QFT-G for people with positive TST. Based on actual outcomes of screening 280 immigrants using QFT-G as first-line screening, the total screening cost was £9,781.82 (£34.94 per new entrant) to identify 105 cases of LTBI, at a cost of £93.16 per case identified. The study estimated that following the NICE (2006) strategy in 280 new entrants would have cost £13,346.75 (£47.67 per immigrant) and would have identified 83 cases of LTBI at a cost of £160.81 per case identified. The study findings are limited, as the costs only included the cost of

the screening tool and not other important costs and resources use, such as the need to offer treatment for LTBI..

Two studies compared the cost-effectiveness of actively screening for TB compared with passive case detection (Dasgupta et al. (2000 [+]; Brassard et al., 2006 [+]).

Dasgupta et al. (2000 [+]) investigated active applicant immigrant screening to identify active cases of TB. Chest X-rays were offered to all immigrants into Canada who applied for permanent residence, or individuals coming to Canada on a work or study visa for longer than six months. This was compared with medical surveillance for immigrants to Canada who were identified as having LTBI following screening, and with a hypothetical cohort of immigrants who underwent passive case-detection; no further details were provided on the assumptions used for passive case-detection.

Among the active screening group, there was an incremental cost of $20,328 (Canadian dollars) for treating active TB and of $39,409 for preventing active TB compared with passive case-detection. Including only the marginal costs of LTBI treatment (that is, only those additional costs directly attributable to therapy for LTBI), active screening had a net savings of $1,967 compared with passive case-detection. In a sensitivity analysis, active screening would have been even more cost-effective if the future risk of TB was higher than the baseline estimate of 0.05%. In addition, restricting screening to applicants from countries with a high incidence of TB did not significantly change the results.

Among the immigrants who underwent medical surveillance after being identified with LTBI, there was an incremental cost of $24,225 per case of active TB treated, and of $65,126 for each case of active TB prevented, compared with passive case-detection. Including only the marginal costs for LTBI treatment, passive case detection by medical surveillance had an incremental cost of $3,770 compared with passive case-detection.

The authors noted some limitations in their cost analysis including that the cost of outpatient treatment for passive case detection was lower than those estimated in other studies ($1,006 compared with $2,305). In addition, the model assumed that treatment for less than six months would not have resulted in any benefit; this would have underestimated the benefits of screening.

Brassard et al. (2006 [+]) reported the cost-effectiveness of actively screening for TB among schoolchildren who were immigrants into Canada, and screening the contacts of those children identified as having LTBI, compared with passive screening. Immigrant children aged between 4 and 18 years who attended schools with high numbers of pupils from highly-endemic TB countries were screened with TST. Of the 3,710 eligible children, 2,524 (68%) were screened, of whom 542 (41%) had a positive TST measuring >10mm. Of these, 484 (89%) presented for treatment; 375 started isoniazid for LTBI and 2 active cases were diagnosed. An additional 99 children had a TST of 5-9mm, 9 of whom were diagnosed and treated for LTBI. Five hundred and

ninety-nine close contacts were identified for the 484 TST-positive children, of whom 555 were tested and 211 (38%) of these were positive. Of these, 108 were children who were started treatment for LTBI and one active case of TB was diagnosed.

The model estimated that screening these high-risk schoolchildren would have prevented 36.1 active cases of TB, which would have cost $557,384 to treat. The total cost of screening the children and their contacts was $193,461, so the programme had net savings of $363,923 over five years ($19,106 per year); $268,393 net savings were generated by the school screening alone, and the contact tracing contributed $95,530 of savings. If the proportion of children treated in hospital fell from 76% to 50%, the screening programme would generate reduced savings but would still be cost-effective, with annual net savings of $23,068. The results suggest that it is cost-saving to actively screen for TB among immigrants and to supplement this with the screening of contacts of LTBI cases. Some limitations of the study were that it did not state the economic perspective used in the economic analysis.

Studies reporting effectiveness and economic data

Two studies reported both effectiveness and economic data on the coverage uptake and yield from screening and/or active case finding among immigrants and new entrants.

Mor et al. (2008 [-]) used a before-and-after study design to investigate the effectiveness and cost-effectiveness of pre-immigration screening of immigrants from Ethiopia before entry into Israel between 2001 and 2005, compared with the previous practice of post-immigration screening, done between 1998 and 2001. No further details on the screening methods used were provided. Only those immigrants 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 5-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 calculated that pre-immigration screening would result in net direct savings of $449,817 for five years, assuming that 98 more individuals would be free of TB using this screening approach compared with post-immigration screening.

The study had several limitations. The use of a historical control meant that 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. 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 higher than those found in the literature for other hard-to-reach groups in other countries; this may have decreased the generalisability of the results. The costs of resources used in this analysis came from different sources, with one more reliable than the other - the costs of post-immigration screening came from a national published source, while the costs of pre-immigration screening were based on expert opinion. 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.

Bothamley et al. (2001 [-]) compared the effectiveness and cost outcomes for 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; 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 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, also being tested using a TST. The study modelled the cost per case of active TB prevented for each group.

The study found that use of the symptom questionnaire was low at the POA hospital, with only 15.8% (199/1,262) of new entrants being screened with the questionnaire, of whom 181 were given TST and 3 had active TB. In contrast, 98.1% (262/267) of individuals at the homeless shelter were screened with the questionnaire, all of whom were testing using TST but none of whom had active TB. Forty-five new patients who registered with the GP practice were screened with the questionnaire, but the total number of new registrations who were eligible for screening using the initial symptom questionnaire was not known. Of these 45, 39 were given a TST, but none had active TB. No statistical significance calculations were reported.

The total costs of screening in the different settings were £22,646 in the hospital as part of the POA scheme, £3,452 in homeless centres, and £938 in general practice at 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 a

further case was detected in each: £33 (savings) for testing in hospital, £6 (savings) for testing in general practice and £11 (savings) for testing in homeless centres.

One of the main limitations of this study was that the populations in the three groups were not comparable as they came from different source populations (homeless and new entrants) with some active and some passive screening. Therefore, it is difficult to ascertain how far the different outcomes were due to the different settings in which the testing occurred or due to baseline differences between the population groups. 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, it did not discount the costs of identification, and did not report QALYs which all limited the study's applicability to the review question.

Evidence statement 1: Effectiveness evidence on the coverage and yield of screening and active case finding of TB in immigrant groups

Four comparative effectiveness studies were identified that reported data on active case finding of TB in the foreign-born, immigrants and new entrants (Laifer et al., 2007 [+]; Monney and Zellweger, 2005 [+]; Sciortino et al., 1999 [+]; Verver et al., 2001 [+]). A further two studies were identified in this topic area that reported both comparative effectiveness and economic data (Bothamley et al., 2001 [-]; Mor et al., 2008 [-]). The effectiveness data for all six studies has been used to inform the following evidence statements.

ES1.1 **Moderate evidence from three** retrospective cohort studies suggests that active screening is associated with a reduction in the severity or infectivity of identified cases, with a lower proportion of cases who were symptomatic or smear or culture-positive (Laifer et al., 2007 [+]; Monney and Zellweger, 2005 [+]; Verver et al., 2001 [+]). However, the studies did not adjust for baseline differences between cohorts of immigrants being actively screened and other groups of passively-screened foreign-born residents who were usually workers, students or tourists, or undocumented migrants.

ES1.2 **Weak evidence from** one retrospective cohort study is inconclusive about the effectiveness of pre-immigration screening using B notification to identify TB among immigrants to the USA compared with not providing B notifications (Sciortino et al., 1999 [+]).

ES1.3 **Weak evidence from one** before-and-after study suggests that pre-immigration screening may reduce the risk of developing TB in immigrants 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) (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.

ES1.4 **Weak evidence from one** study meant that conclusions could not be drawn on the comparative effectiveness of screening in either a hospital as part of the POA programme; in general practice as part of a new patient registration health check; or at homeless centres, because the differences in coverage and yield of screening were not statistically compared (Bothamley et al., 2001 [-]).

Applicability
Only one of the six studies identified in this section was from the UK, the rest originating from a range of European and North American countries with different immigration policies and screening strategies for new entrants, and which are targeted by new entrants from different countries with different demographics and prevalence of TB and other infections such as HIV. This limits the applicability of the findings in this section to the UK. However, the findings are reasonably consistent across countries, and we found no evidence of a national difference in effectiveness of different strategies.

Evidence statement 2: Economic evidence on the coverage and yield of screening and active case finding of TB in immigrant groups

Seven comparative economic studies were identified that provided evidence on the coverage and yield of screening and active case finding of TB in immigrant and new entrant groups (Brassard et al., 2006 [+]; Dasgupta and Menzies (2005 [-]; Dasgupta et al. (2000 [+]; Hardy et al., 2010 [-]; Pareek et al., 2009 [-]; Schwartzman and Menzies (2000 [++]; Schwartzman et al., 2005 [++]). A further two comparative studies were identified in this topic area that provided effectiveness and economic data (Bothamley et al., 2001 [-]; Mor et al., 2008 [-]). All nine studies were used to inform the evidence statements below:

ES2.1 **Moderate evidence from three** economic studies suggest that screening with chest X-rays among immigrants is less costly than TST per case identified (Schwartzman and Menzies (2000 [++]; Dasgupta and Menzies (2005 [-]) and cost-saving when secondary transmission of TB disease is taken into account (Schwartzman and Menzies (2000 [++]). Adding TST to screening with a chest X-ray did not result in cost-savings for new entrants (Schwartzman et al., 2005 [++]). Although the studies are of varying quality, they all supported the same conclusions.

ES2.2 **Weak evidence from one** cost-comparison study suggests that the total cost of screening in immigrants may be less when using Quantiferon- Gold (QFT-G) as a first-line screening tool, compared with the strategy supported by NICE (2006) of chest X-ray followed by TST for high-risk people, with QFT-G for positive TST results (Hardy et al., 2010 [-]).The findings are limited due to its narrow perspective on costs and no direct comparison of costs such as ICERs.

ES2.3 **Inconsistent evidence from two** cost-effectiveness studies suggests that the

cost-effectiveness of active screening of immigrants compared with passive case-detection depends on the assumptions used in the economic model (Brassard et al., 2006 [+]; Dasgupta et al., 2000 [+]). Dasgupta et al. (2000 [+]) found that active case finding had an incremental cost of $20,328 for treating active TB compared with passive case detection and would have only been cost-saving is the future risk of TB was higher than the baseline estimate of 0.05%. Brassard et al. (2006 [+]), using different assumptions, found that actively screening immigrant children would have resulted in annual net savings of around $20,000.

Applicability
Only three of the nine studies identified in this section were from the UK, the rest originating from a range of European and North American countries with different immigration policies and screening strategies for new entrants, and which are targeted by new entrants from different countries with different demographics and prevalence of TB and other infections such as HIV. This limits the applicability of the findings in this section to the UK. However, the findings are reasonably consistent across countries, and we found no evidence of a national difference in cost-effectiveness of different strategies.

5.3.2 Homeless

One study compared the effectiveness and cost-effectiveness of screening prisoners with TST as part of a state-law-mandated programme in the USA, with a non-state-law-mandated screening programme for the homeless using TST plus chest X-ray (as well as providing incentives) (Miller et al. 2006 [+]). The study found that TST was conducted on 94.7% (778/822) of the eligible population in the homeless programme, a similar proportion compared with prisoners. However, there was a significantly higher proportion of positive TST results (among those read) in the homeless screening programme (15.5%) than the jail screening programme (2%; $p < 0.001$). A significantly higher proportion of people were prescribed treatment for LTBI and active TB in the homeless group (22% and 1.2%, respectively) compared with the jail programme (0.9% and 0.03% respectively; $p < 0.001$). However, it is unclear whether this is because of a different prevalence of the disease in the different populations, or because of different efficiencies of the screening programme.

The study also compared the estimated costs of the different programmes based on the national average of Medicare charges and found that, although the cost per treatment per patient was substantially less for the homeless programme than the prison population, the cost per patient diagnosed with active or latent TB was less for the prison programme compared with the homeless programme. The cost per active TB case prevented by treating each person with LTBI was estimated at $14,350 for the homeless programme and $34,761 for the prison programme. Although the findings suggest that the costs are higher for the prison programme compared with the homeless programme, these were based on the differences in effectiveness outcomes

found in the two groups, which may have been caused by population differences rather than the screening programme. Therefore, the conclusions drawn from this study are limited. In addition, the authors did not consider the costs of contact investigations and secondary transmission of the disease.

Evidence statement 3: Effectiveness evidence on the coverage and yield of screening and active case finding of TB in homeless groups

ES3.1 **Weak evidence** from one study (Miller et al. 2006 [+]) found that the yield of positive TST results and the number who were prescribed treatment for LTBI and active TB was statistically greater in a non-state-law-mandated homeless screening programme compared with a state-law-mandated prison screening programme. However, the two screening groups were not from comparable source populations and therefore any differences found may not be solely attributable to the different screening programmes.

Applicability
There was one study that informed this evidence statement and it was conducted in the USA. Due to the weakness of the evidence only a few conclusions can be drawn. The study targeted homeless people who attended shelters or other services for the homeless, so there is no evidence on how best to target other homeless groups such as rough sleepers who do not use these services.

Evidence statement 4: Economic evidence of the coverage and yield of screening and active case finding of TB in homeless groups

ES4.1 **Weak evidence** from one cost-comparison study that did not carry out direct cost comparisons is insufficient to draw conclusions about the cost-effectiveness of screening for TB in the homeless compared within prisons (Miller et al., 2006 [+]).

Applicability
There was one study that informed this evidence statement and it was conducted in the USA. Due to the weakness of the evidence only a few conclusions can be drawn. The study targeted homeless people who attended shelters or other services for the homeless, so there is no evidence on how best to target other homeless groups such as rough sleepers who do not use these services.

5.3.3 Drug Users

No study was identified that reported effectiveness or cost-effectiveness data on the coverage and yield of screening specifically in drug users. One study, reported in section 5.3.5, reported the results of screening with a mobile chest X-ray unit (MXU) compared with passive screening on a variety of hard-to-reach groups including drug

users. However, there was no evidence reported separately for this group.

Evidence statement 5: Effectiveness and cost-effectiveness evidence on the coverage and yield of screening and active case finding of TB in drug users

ES5.1 No studies were identified that reported effectiveness and/or cost-effectiveness data on the coverage and yield of screening and/or active case finding of TB specifically in drug users.

5.3.4 Prisoners

Four comparative studies were identified that provided evidence on the coverage uptake and yield of screening in prisoners. Two studies reported effectiveness data (Puisis et al., 1996 [-]; Yates et al., 2009 [-]), one reported economic data (Jones and Shaffner (2001 [+]) and a further one study reported both effectiveness and economic data (Miller et al., (2006 [+]).

In the two comparative effectiveness studies:

- One study compared chest X-ray with TST screening in prisoners:
  - Puisis et al. (1996 [-]) in the USA.
- One study compared the likely detection rates with mobile X-ray screening of prisoners based on different symptoms of TB:
  - Yates et al. (2009 [-]) in the UK.

One economic study compared screening with chest X-ray with TST and a symptom questionnaire:

- Jones and Shaffner (2001 [+]) in the USA.

One study that reported effectiveness and economic data compared a state-law-mandated programme of screening prisoners using TST with a non-state-law-mandated programme of screening the homeless using TST plus chest X-rays:

- Miller et al. (2006 [+]) in the USA.

Effectiveness

Puisis et al. (1996 [-]) compared chest X-ray screening with TST to identify active cases of TB among prisoners in the USA using a before-and-after study design. TST carried out between 1991 to 1992 identified 26 cases of active TB out of 46,711 tests conducted (0.056%) while chest X-ray, carried out between 1992 and 1994, identified 67 cases of active TB out of 126,608 tests conducted (0.053%) and a further 19 cases were identified by diagnostic work-up of prisoners with normal chest X-rays, a total of 86 cases of active TB identified (0.068%). The study estimated the cost of active case-finding using chest X-ray was $5,700 per case of active TB identified and $10,800 per new case identified.

The study did not conduct statistical comparisons between outcomes; therefore it is not

known whether significantly more active cases of TB were identified using chest X-rays compared with TST. The use of historical controls means that it is unclear how much of the difference in prevalence is caused by the different screening strategies and how much reflects different baseline disease prevalence. In addition, the study did not report the cost of screening using TST; therefore the costs of the programmes cannot be compared. Also, two different follow-up periods were used, allowing for more time for active cases of TB to be detected in the chest X-ray group (two years) compared with the TST group (one year).

Yates et al. (2009 [-]), in a retrospective cohort study, compared the potential impact of limiting screening with MXU to prisoners in the UK with symptoms of TB, compared with universal screening regardless of symptoms. This was done by looking retrospectively at symptoms present in prisoners screened with a MXU. Of the number of people with TB found overall by MXU, 19 out of 30 (63.3%) had at least one of the symptoms present at screening: cough for more than three weeks; night sweats; fever; weight loss; and coughing-up blood (haemoptysis) . Restricting screening just to prisoners with any of the five symptoms would have missed 36.7% of TB cases. More cases of TB would have been missed if screening was limited to a smaller range of symptoms. The study is limited because although these symptoms may have been present at the time of screening, it is not known if professionals would have screened for TB based on these symptoms in real practice.

Economic

Jones and Shaffner (2001 [+]) used a hypothetical cohort of US prisoners to investigate the cost for every case of TB identified using miniature chest X-rays compared with TST and a symptom questionnaire. The study used published sources for their assumptions and estimated that chest X-rays would identify the most cases of active TB (0.68 cases per 1,000 tested, at a cost of $9,600 per case), followed by TST (0.25 cases per 1,000 tested, at a cost of $32,100 per case), followed lastly by a symptom questionnaire (0.09 cases per 1,000 tested, at a cost of $54,100 per case, all based on 1998 US dollars).

This cost-comparison study only took into account the cost of testing and then treatment for active cases of TB and preventive therapy for close contacts, but did not consider the start-up costs of implementing the miniature CXR in the prison setting, such as the cost of the technology and training needed to deliver the testing. The study also did not directly compare the costs of screening, such as by calculating an ICER.

Studies reporting effectiveness and economic data

As reported in the section on homeless groups, above, Miller et al. (2006 [+] compared the effectiveness and cost-effectiveness of screening prisoners in the USA with TST with a screening programme for the homeless using TST and chest X-ray plus incentives. The study found that the cost per active TB case prevented by treating each person with LTBI was estimated at $14,350 for the homeless screening programme and $34,761 for the prison screening programme. Although the findings suggest that

the costs are higher for the prison programme compared with the homeless programme, these were based on the differences in effectiveness outcomes found in the two groups, which may have been caused by population differences rather than the screening programme. Therefore, the conclusions drawn from this study are limited.

Evidence statement 6: Effectiveness evidence on the coverage and yield of screening and active case finding of TB in prisoners

Two studies were identified that reported comparative effectiveness data on the coverage and yield of screening or active case-finding of TB among prisoners (Puisis et al. (1996 [-]; Yates et al. 2009 [-]). A further one study (evidence statement also reported elsewhere) provided both effectiveness and economic data for a screening programme conducted in prison compared within homeless centre. All three studies informed the evidence statements below.

ES3.1 **Weak evidence** from one study (Miller et al. 2006 [+]) reported in evidence statement 3, found that the yield of positive TST results and the number who were prescribed treatment for LTBI and active TB was statistically greater in a non-state-law-mandated homeless screening programme compared with a state-law-mandated prison screening programme. However, the two screening groups were not from comparable source populations and therefore any differences found may not be solely attributable to the different screening programmes.

ES6.1 **Weak evidence** from one before-and-after study found that the yield for identifying active TB was comparable when using chest X-rays (0.056%) and TST (0.069%) among prisoners, however, this was not compared using a statistical test and as such the findings are limited (Puisis et al. (1996 [-]). In addition, the study did not compare for baseline differences between the groups.

ES6.2 **Weak evidence** from one retrospective cohort suggests that screening with MXU should be offered to all prisoners regardless of symptoms of TB, since limiting screening to those with symptoms would have missed a substantial number of cases (Yates et al. 2009 [-]). The conclusions drawn from this study are limited as it looked retrospectively at collected data to calculate how many cases would have been missed if screening had been limited in such a way.

Applicability
One of the three studies identified were from the UK, the other studies were from the USA. The overall findings were similar, and we have no reason to believe that the results from US studies are not applicable to the UK prison population. However the strength of the evidence for the three studies is weak which means that only limited conclusions can be drawn.

Evidence statement 7: Cost-effectiveness evidence on the coverage and yield of screening and active case finding of TB in prisoners

One study was identified, which reported economic data on the cost of the coverage and yield of screening of TB in prisoners (Jones and Schaffner, 2001 [+]). A further one study (evidence statement also reported elsewhere) provided both effectiveness and economic data for a screening programme conducted in prison compared within homeless centre. Both studies informed the evidence statements below.

ES.1 **Weak evidence** from one cost-comparison study, also reported in evidence statement 4, did not carry out direct cost comparisons and so is insufficient to draw conclusions about the cost-effectiveness of screening for TB in the homeless compared with prisoners (Miller et al., 2006 [+]).

ES7.1 **Weak evidence from one** cost-comparison study suggests that the cost per case of active TB would be lowest if the screening of prisoners was conducted by CXR ($9,600) compared with TST ($32,100) and using a symptom questionnaire ($54,100) (Jones and Schaffner, 2001 [+]). The findings are limited as the study did not directly compare the costs of screening in, for example, an ICER. In addition the study did not take into account the start up costs of implementing screening with CXR.

Applicability
There were no comparative studies identified from the UK, only one study from the USA. There is no suggestion that the result from this US study is not applicable to the UK prison population.

5.3.5 Mixed hard-to-reach groups

One comparative study was identified that explored the coverage uptake and yield of screening among a mixed group of hard-to-reach populations. Watson et al. (2007 [++]) compared the effectiveness and cost-effectiveness of a digital mobile X-ray unit (MXU) with passive case-detection for hard-to-reach groups including the homeless, drug users and prisoners. The study design was a case-control study where cases were those who started treatment for active TB following screening via the MXU, and controls were patients who received treatment for active TB at the same locations but who were identified by passive case-detection. The study found that MXU screening reduced diagnostic delay compared with passive case-detection (adjusted hazard ratio for delay =0.35, 95% CI 0.21 to 0.59, $p < 0.0001$). In addition, people with TB who were screened by the MXU were less likely to be contagious on diagnosis (44% were smear-positive) compared with passive case-detection (66% smear-positive; adjusted OR 0.35, 95% CI 0.15 to 0.81, $p < 0.001$).

The economic analysis assumed that the follow-up of the homeless would be 63% and prisoners 73%, and estimated that, over 10 years, 553.73 more cases would be averted using the MXU compared with passive case-detection, and the total cost of the screening programme would be £3,473,275. The study estimated that if each case

averted was valued at £5,000 then the total value of averted cases would be £2,266,090; the net cost would be £1,207,184; the ICER was estimated at £2,180.11 and estimated cost per QALY was £3,206.05 (ranging from £1,397.51 to £15,572.24). If each case averted was valued at £10,000, the total value of averted cases would rise to £4,532,180, with net cost-savings of £1,058,906, thus dominating passive case-detection.

The main limitation of this study is that results for different sub-populations were not reported separately, so it remains unclear whether any one hard-to-reach group benefited significantly from MXU screening. The authors noted that there may have been recall bias, as is common in case-control studies, as participants were required to recall their date of onset of TB symptoms. However; this is unlikely to differ by group. As the study was not an RCT there may have been additional differences between the groups that were not identified at baseline, which may also have influenced the results.

Evidence statement 8: Effectiveness evidence on the coverage and yield of screening and active case finding of TB in hard-to-reach groups of people with TB.

ES8.1 **Moderate evidence from one** case-control study suggests that using mobile X-ray units (MXU) to screen for TB reduced diagnostic delay among hard-to-reach groups in the UK (including the homeless, drug users and prisoners) compared with passive case detection (adjusted hazard ratio for delay = 0.35, 95% CI 0.21 to 0.59, $p < 0.0001$). People identified as having TB by MXU screening were less likely to be symptomatic on diagnosis compared with those identified by passive case-detection (adjusted OR 0.35, 95% CI 0.15 to 0.81, $p < 0.001$) (Watson et al., 2007 [++]).

Applicability
The one study identified in this section was from the UK. The effectiveness evidence on the benefits of MXU is relevant to the UK, but the results for the specific hard-to-reach groups included in the study cannot be determined.

Evidence statement 9: Cost-effectiveness evidence on the coverage and yield of screening and active case finding of TB in hard-to-reach groups of people with TB.

ES9.1 **Moderate evidence from one** case-control study found that screening with a MXU would have been cost-saving when compared with passive case detection in the UK if the cost of TB treatment was assumed to be £10,000 (cost-saving ICER of £1,912.33). This was not the case if the cost of TB treatment was assumed to be £5,000 (ICER = £2,180; cost per QALY = £3,206, ranging from £1,398 to £15,572) (Watson et al., 2007 [++]).

Applicability
The one study identified in this section was from the UK. The economic evidence on

the benefits of MXU is relevant to the UK, but the results for the specific hard-to-reach groups included in the study cannot be determined.

5.3.6 Hard-to-reach contacts

Three comparative economic studies were identified for screening hard-to-reach contacts of people with TB:

- One study compared supplementing active screening of new entrant children with screening of contacts of children identified with LTBI, compared with passive case detection:
    - Brassard et al., 2006 [+], Canada.

- One study investigated using QuantiFERON-Gold (QFT-G) to screen foreign-born contacts of active TB cases, or TST screening then QFT-G for those testing positive; compared with TST screening alone:
    - Marra et al., 2008 [++], Canada.

- One study explored test-and-treat strategy for new entrant contacts compared with a treat-all strategy, or with no active intervention:
    - Tan et al., 2008 [++], Canada.

Effectiveness

We found one economic study (Brassard et al., 2006 [+]) that reported some effectiveness data on screening for TB in new entrant contacts of schoolchildren with LTBI, which has also been reported in the section on new entrants, above. However, the study did not report comparative data for effectiveness of different screening strategies, and so is only reported in the economic study section, below.

Economic

Brassard et al. (2006 [+]), already reported on page 51, also evaluated the cost-benefit of screening immigrants to Canada who were pupils attending schools with high intakes of children from countries with high prevalence of TB, as well as screening close associates of these children who had been identified with LTBI, compared with passive case-finding. The model used costs and adherence data from the study itself, plus data from published research on the likely number of contacts per case, costs of interventions, test sensitivity and specificity and conversion rates from LTBI to active disease. Sensitivity analyses adjusted the rates of hospitalisation for cases, and a 3% discount rate was used for the 20-year horizon.

The study found that 599 close associates were identified from 484 TST-positive children, of whom 211 (38%) also tested positive on TST. Of these, 211 were under 18 years, 131 attended the TB clinic, 108 started treatment for LTBI and one active case of TB was identified. The model estimated that the total cost of screening the children and their contacts was $193,461, and that the programme had net savings of $363,923 over five years ($19,106 per year); $268,393 net savings were generated by the school

screening alone, and the associate investigation contributed $95,530 of savings. If the proportion of children treated in hospital fell from 76% to 50%, the screening programme would generate reduced savings but would still be cost-effective, with annual net savings of $23,068. The results suggest that it is cost-saving to actively screen for TB among immigrants and to supplement this with the screening of contacts of LTBI cases. However, the study did not report on the cost-effectiveness of the contact-screening component alone, nor did it state the economic perspective used in the economic analysis and did not report QALYs or ICERs.

Two studies by the same group in Canada (Marra et al., 2008 [++]; Tan et al., 2008 [++]) used a hypothetical cohort of high-risk people, including foreign-born residents, to evaluate the cost-effectiveness of different screening strategies for contacts of people with active TB.

Marra et al. (2008 [++]) assessed the likely cost-effectiveness of using QuantiFERON-Gold (QFT-G) to screen foreign-born contacts of active TB cases in Canada, compared with TST screening alone, or TST screening followed by QFT-G for those testing positive. The modelling was based on different hypothetical sub-populations of foreign-born, aboriginal and Canadian-born people, with or without BCG vaccination, over 20 years. Contacts who tested positive would have been offered isoniazid treatment, and those with clinical or X-ray signs of active infection would have been further evaluated for anti-TB therapy. Data on prevalence of TB infection and adherence to treatment were taken from a provincial population-based database, and efficacy of isoniazid treatment for LTBI, and test performance for TST and QFT-G were taken from published literature. Only direct medical costs were included in the model, which was carried out from a third party payer perspective. TST and QFT-G were assumed to have a sensitivity of 99%, but a sensitivity analysis modelled different sensitivities for QFT-G to detect LTBI.

The cost of performing one QFT-G test was almost twice that of administering and reading one TST. The model found that the incremental QALY for each alternative strategy compared with TST screening alone was very low, between 0.0000 and 0.0002 for strategies that specifically targeted foreign-born residents. The most cost-effective of these strategies, as measured by the INMB (incremental net monetary benefit, calculated as the gain in health outcome multiplied by change in costs), was to use QFT-G in all foreign-born, aboriginal and BCG-positive contacts and TST in others, with an INMB of $2.83, and a cost per case averted (ICER) of $137,320. Using a combination of TST followed by QFT-G for foreign-born, aboriginal and BCG-positive contacts and TST alone for the rest, had an INMB of $1.05 and was dominant for cost per case averted. QFT-G alone was more cost-effective than TST alone only in people who were BCG-positive. The study did not evaluate the cost-effectiveness of different screening strategies in foreign-born residents alone, making it difficult to determine the best strategy for hard-to-reach populations.

Tan et al. (2008 [++]) compared a test-and-treat strategy with a treat-all strategy, or

with no screening or treatment, for a hypothetical series of contacts of people with active TB in Canada, including foreign-born residents. Risk of acquiring TB, utility values and some costs were based on data from the British Columbia Centre for Disease Control; other cost data came from health insurers and hospitals in Canada. The model took into account the risk of contacts developing TB infection, harms of treatment for LTBI and secondary transmission of TB, and used a 3% discount rate for a six-year time horizon.

For foreign-born contacts who were *not* household contacts of the active case, with or without prior BCG vaccination, the most cost-effective strategy was not to screen or treat, with a cost of $32 to $39 Canadian dollars for 4.62 QALYs gained and 0.003 to 0.004 active TB cases prevented. For foreign-born contacts who *were* household contacts of the active case, the most cost-effective strategy was to test with TST and treat those with positive results (test and treat), at a cost of $247 for those with prior BCG, for 4.61 QALYs gained and 0.015 TB cases averted, and $495 for those without prior BCG, for 4.61 QALYs gained and 0.04 TB cases prevented. The most cost-effective strategy for all household contacts under 10 years of age was to treat without screening (however data are not presented separately for foreign-born children). Tan et al. (2008 [++]) reported results for foreign-born subgroups separately, but did not separate out those from countries with high prevalence of TB. However, they only modelled the effect for six years, and used a TST cut-off of 5mm to indicate a positive result, which has a high sensitivity but low specificity.

Evidence statement 10: Economic evidence on the coverage and yield of screening and active case finding of TB in hard-to-reach contacts of people with TB.

Two economic studies identified that reported comparative data on the coverage and yield of screening/active case finding among foreign-born contacts of cases (Marra et al., 2008 [++]; Tan et al., 2008 [++]), and one additional cost-benefit study on screening close associates of immigrant children with LTBI (Brassard et al., 2006 [+]).

ES10.1 **Weak evidence** from one cost-benefit study suggests that it is cost-saving to screen contacts of immigrant children with LTBI identified using active screening methods compared with passive case-detection (Brassard et al., 2006 [+]).

ES10.2 **Moderate evidence** from one cost-effectiveness study suggests that people who are foreign-born who have a household contact with active TB should be tested and treated, but that it is not cost-effective for those who are not household contacts to be screened (Tan et al., 2008 [++]).

ES10.3 **Weak evidence from one** cost-effectiveness study suggests that the most cost-effective strategy might be to use Quantiferon-G as first-line screening in all foreign-born, aboriginal and BCG-positive contacts and TST in all others (Marra et al., 2008 [++]). The applicability of the results to hard-to-reach groups is limited as the

strategies were not explored for foreign-born residents alone.

Applicability
All three studies identified for this section were from Canada, and reported on identifying new entrant contacts of people with TB, which limits their applicability to the UK situation. There is no reason to believe that these studies are not at least partially applicable to the UK, but the lack of high-quality evidence on identifying hard-to-reach contacts means that few conclusions can be drawn.

5.4 Effectiveness of interventions to improve coverage or uptake of screening and active case-finding

This section of the report is focused on interventions that have been shown to be effective or cost-effective at improving the uptake of screening or case-detection among hard-to-reach groups. We identified 11 studies relevant to this section, which evaluated the following topics:

Screening at a more convenient location:
- One effectiveness study was identified that explored screening for TB in different settings among undocumented immigrants in Italy (El-Hamad et al. (2001 [+]).
- No economic studies were identified.

Using peers or staff from the same hard-to-reach group:
- One effectiveness study was identified investigating the use of professionals who were former drug users to improve the coverage uptake of identification among current drug users in the USA (Ricks (2008 [++]).
- No economic studies were identified.

Offering incentives:
- Six comparative studies were identified that explored offering incentives to hard-to-reach groups to improve the coverage uptake of screening. The study types included:

Effectiveness studies	Economic studies	Effectiveness/economic studies
Chaisson et al. (1996 [+]) drug users, USA; Malotte et al (1998 [++]); drug users, USA; Malotte et al. (1999 [++]); drug users, USA; Fitzgerald et al. (1999 [+]); drug users, Canada. Citron et al. (1995 [+]);	None	Perlman et al. (2003 [++]); drug users, USA

homeless, UK.

Increasing detection of hard-to-reach group members prior to screening:

- Two comparative effectiveness studies were identified, which investigated strategies to increase detection of immigrants in the UK (Lavender et al. (1997 [-]); Ormerod (1998 [-]).
- No economic studies were identified.

5.4.1 Conducting screening or active case-finding at a convenient location

We found one effectiveness study that compared screening completion rates at a specialist TB centre compared with general medical clinics for undocumented immigrants:

- El-Hamad et al. (2001 [+]), Italy.

Effectiveness studies

El-Hamad et al. (2001 [+]) carried out a prospective cohort study to compare completion rates for screening undocumented immigrants into Italy at specialist TB centres compared with non-specialist health services targeted at immigrants. Of 1,318 immigrants from countries with a TB prevalence of at least 50/100,000, who had arrived within the previous five years without a residence permit, 749 were assessed at a specialist TB clinic and 483 at a general health clinic offering primary care to new entrants. The two groups were comparable in the proportion under 35 years (82%), married (40 to 41%), and homeless or living in a shelter (6 to 7%). However, there were substantial baseline differences in other characteristics. Those presenting to the TB clinic were more likely to be female (52%), in stable work (32%), living in their own apartment (39%), and to take alcohol or drugs (13%). They originated mainly from Africa (52%) or Eastern Europe (32%). Those presenting to the general medical clinic were more likely to be male (75%), living with friends (66%), and mainly originated from Africa (62%) or the Indian subcontinent (26%). Five percent took alcohol or drugs (5%), and 27% were in stable work.

Screening at the TB clinic involved chest X-ray plus TST done at the first visit and read at a second visit. The general clinic carried out TST and physical examination at the first visit, with chest X-ray done subsequently at the TB clinic. The TST was read at a third visit. In both cases, screening was considered to be complete if both chest X-ray and TST had been done and read.

Overall, 392 of the 1,318 immigrants (39.4%) who were screened had a positive TST >10mm indicative of LTBI. Similar prevalences of active TB were found at the two sites, 6.7/1,000 at the TB clinic and 6.2/1,000 at the general clinic. Among the TB clinic attendees, 85.6% completed screening, compared with 71.4% of those attending the general clinic. In a multivariate logistic regression analysis, the only variable that significantly increased the likelihood of completing screening was being enrolled at the

TB clinic (OR = 2.57, 95% CI 1.92–3.42). 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 complete the screening process.

Economic studies
No economic study was identified on the costs of screening in different locations.

Evidence statement 11: Effectiveness of interventions to improve coverage and uptake of screening or active case-finding using more convenient locations

ES11.1 **Weak evidence** from one prospective cohort study suggests that undocumented immigrants may be more likely to complete screening if this was conducted in a specialised TB clinic compared with a general health clinic (OR = 2.57; 95% CI 1.92 to 3.42). However, the study did not adjust for known differences between the groups at baseline (El-Hamad et al., 2001 [+]).

Applicability
The one study we identified was on undocumented immigrants in Italy, where the health services available to immigrants are different from the UK. These findings are therefore of only partial applicability to the UK.

Evidence statement 12: Economic data on interventions to improve coverage and uptake of screening or active case-finding using more convenient locations

ES12.1 The review found no economic studies on the cost of screening in more convenient locations to improve the coverage/uptake of screening.

5.4.2 Use of peers or staff from the same hard-to-reach group

Two effectiveness studies were identified that investigated the use of peers or staff from the same hard-to-reach group to improve the coverage and uptake of screening:

- One effectiveness study explored the use of peers as case managers to improve contact identification rates compared with standard public health staff in drug users:
    - Ricks (2008 [++]), USA.

- One effectiveness study explored the use of peer health advisers compared with usual care to increase completion of TB screening among the homeless:
    - Pilote (1996 [++]), USA.

Effectiveness
Ricks (2008 [++]) carried out a RCT to compare the effects of using indigenous outreach leaders (defined as indigenous as they were former substance users) to coordinate TB treatment and contact identification, with standard public health workers

for problem drug users in the USA. Participants were adults who had been referred to a TB nursing station in Chicago between 1996 and 2000, with a history of illicit drug use and/or alcohol use in the previous six months, with diagnosed active TB who were prescribed directly-observed treatment, and who agreed to regular testing for HIV. The intervention group were randomised to have case-management from a mixed-gender team of indigenous care workers. The control group received standard DOT and limited case-management from a nurse care worker. The two groups had no significant differences at baseline.

Indigenous case managers were recruited from former members of the target population, with the aim of increasing access to drug and alcohol users, increase awareness in this group about TB, assist clients to assess their risk, reinforce behaviour change and encourage preventive behaviour among group members. Outreach members worked in the community to offer education and medical care.

The intervention group were significantly more likely to identify contacts than the control group. Forty of the 53 participants in the intervention group (75%) listed a total of 431 contacts, compared with 23 of the 49 (47%) in the control group (a total of 230), p = 0.03. 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). Contacts of people in the intervention group 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 6 months and agreed to complete a questionnaire and be regularly tested for HIV, but who did not have active TB. Overall, 90% of the intervention group and 78% of the control group completed the study. The small sample size and high drop-out rates were considered by the author to have limited the ability of the study to detect small but significant differences between the two groups. It is unclear how much of the difference in contact identification was because of the use of indigenous staff, and how much was due to the use of case-management itself.

Pilote et al. (1996 [++]) in a RCT explored the use of peer health advisers who were currently homeless or in unstable living conditions to improve the adherence of the homeless to attendance at a TB clinic to complete screening for TB in the USA, compared with usual care. Peer health advisers were responsible for escorting the participants to their TB clinic for screening. Participants in both groups also received bus tokens to attend their appointment. Nothing further was provided to those participants in usual care. A third comparison arm was also explored which investigated the use of monetary incentives to improve adherence, and is reported in Section 5.4.3.

All participants who were included in the study had a positive TST result but were required to attend a TB clinic to be further screened with a chest X-ray and sputum spear in order to confirm the diagnosis. The primary outcome was attendance at the TB

clinic to complete screening. The study found that of the 83 participants randomised to the peer adviser group, 62 (75%) adhered to their clinic appointment. This was significantly more than in the usual care arm, where 42 of the 79 participants (53%) adhered to their clinic appointment, (p = 0.004). The odds for completing screening was 2.6 (95%CI 1.3-5.1) for the peer health adviser group compared with usual care.

The authors note that a minor limitation of the study is that the sample may not be generalisable to the source population of the homeless in the USA as the participants had already demonstrated adherence with initial TST screening and then randomisation into the RCT.

Economic

No comparative economic study was identified that explored the effects of peers or staff from the same hard-to-reach group on screening uptake or active case-finding.

Evidence statement 13: Effectiveness of interventions to improve coverage and uptake of screening or active case-finding using peers or staff from the same hard-to-reach group

ES13.1 **Moderate evidence** from two RCTs suggest that using peers from the same hard-to-reach group as part of the screening programme can improve screening outcomes for drug users (Ricks, 2008 [++]) and the homeless (Pilote et al., 1996 [++]). Ricks, 2008 [++] found that problem drug users with peers as case-managers were more likely to identify contacts than those without such case-managers (p = 0.03). However, it is not known how much of this difference was due to the staff being former drug misusers or due to the extra case management received (Ricks, 2008 [++]). Pilote et al. (1996 [++]) found that the homeless with a peer health adviser were more likely to complete screening than those given usual care (p = 0.004).

Applicability

Two studies were identified that were conducted in the USA, one on the homeless and one on drug users. These findings are only partially applicable as there were no studies identified from the UK. However, there is no reason to suggest that these hard-to-reach groups in the UK would respond differently to the impact of peer health workers.

Evidence statement 14: Economic evidence on interventions to improve coverage and uptake of screening or active case-finding using peers or staff from the same hard-to-reach group

ES14.1 The review found no cost-effectiveness studies on using peers or staff from the same cultural background to improve the coverage/uptake of screening.

5.4.3 Use of incentives

We identified four studies that provided data solely on the effectiveness of using incentives to improve completion of screening in drug users:

- Chaisson et al. (1996 [+]), USA;
- Malotte et al (1998 [++]), USA;
- Malotte et al. (1999 [++]), USA; and
- Fitzgerald et al. (1999 [+]), Canada.

We identified two studies on the effectiveness of incentives on homeless groups:

- Citron et al. (1995 [+]), UK;
- Pilote et al. (1996 [++]), UK.

We identified one additional study that reported both effectiveness and economic data on providing incentives in drug users:

- Perlman et al. (2001 [++]), USA.

We found no other studies comparing the effects of incentives on screening uptake and completion rates for other hard-to-reach groups.

Effectiveness studies

Chaisson et al. (1996 [+]) investigated the effectiveness of adding a food voucher incentive and/or a brief patient education programme to a screening programme using TST among individuals seeking care at a HIV clinic in the USA. Of the sample used, 50% acquired HIV from IDU. The study was a before-and-after study design and found that the proportion of patients who returned for the TST reading was 35% (96/272) in the group without incentives or education messages compared with 48% (111/229) in those who received food vouchers; this difference was statistically significant (p = 0.004). The proportion of patients who returned for their TST reading was significantly higher at 61% (96/158) among those who received food vouchers plus a brief education programme compared with those in the no-incentive or education group (p = 0.0001).Those who received food vouchers were 1.69 times more likely to return for their TST reading compared with those in the no incentive or education group (95% CI 1.18 to 2.45). Those who received monetary incentives plus a brief education message were 2.98 times more likely to return to get their TST readings compared with those who received screening only (95% CI 1.97 to -4.15). The study also found that 2% of participants had a positive TST result with no statistically significant differences between groups (screening-only programme 5/ 272; voucher-only programme: 6/229; and voucher plus education programme: 3/158).

The study also found that being a resident in the city and being male were significantly associated with returning for a TST reading (city resident: adjusted OR = 1.89, 95% CI 1.32 to 2.72; male gender: adjusted OR 1.54, 95% CI, 1.09 to 2.19). The study is limited in its design such that it is a before-and-after study, therefore, there may be differences between the groups other than the different screening programmes that

may have influenced the differences in treatment outcomes that were not tested for in the study.

In a RCT, Malotte et al (1998 [++]) compared the effectiveness of providing brief educational programmes and/or different ranges of monetary incentives ($5 or $10) to encourage 1,004 drug misusers to return for TST reading in the USA, compared with no incentive or educational programme. Compared with no incentive or education, drug misusers who were provided with a brief educational programme only, were not statistically more likely to return for their TST results (OR = 1.09; 95% CI 0.35-2.00; p = 0.786). However, when a financial incentive of $5 or $10 was offered, either alone or in addition to the brief educational programme, drug misusers were significantly more likely to return for their TST results ($5 alone: OR = 13.59, 95% CI 7.49 to 24.63; p < 0.001; $5 plus education: OR = 12.88, 95% CI 7.13 to 23.24, p < 0.001; $10 alone: OR = 30.94, 95% CI 15.25 to 62.77; p < 0.001; $10 plus education: OR = 25.96, 95% CI 13.17 to 51.17; p < 0.001) No serious limitations were identified for this study.

The results of this RCT were validated by a larger RCT involving 51,078 drug misusers, also carried out by Malotte et al. (1999 [++]), which compared the effectiveness of providing different incentives ($10 in cash, a fast-food voucher worth $10, or a grocery or bus voucher worth $10) or a brief educational programme on the proportion of drug misusers in the USA who returned for their TST reading. The study found that, compared with providing no incentive or education programme, drug misusers were most likely to return for TST reading when $10 cash was offered (OR = 19.9, 95% CI 10.2 to 38.7; p < 0.001). Drug misuers were also significantly more likely to return for TST reading when fast-food or bus vouchers (OR = 5.1, 95% CI 3.3 to 8.0; p = <0.001) or grocery store vouchers (OR = 6.4, 95% CI 4.0 to 10.2; p<0.001) were added to the screening programme compared with no incentive or education. However, a brief educational programme with no other incentive did not significantly increase the likelihood of returning for their TST reading (OR = 0.9, 95% CI 0.6 to 1.3; p = 0.547). The study had no serious limitations.

Fitzgerald et al. (1999 [+]) used a before-and-after study design to compare the introduction of offering a $5 (Canadian dollars) incentive for IDUs in a needle exchange programme to return for their TST results within 72 hours, compared with no incentive. When incentives were provided, 78% (418/549) returned for the TST reading compared with 43% (240/558) in the period before the incentive was provided; this difference was statistically significant (p <0.001). However, it was not known whether some people in the comparison group also received incentives. If this occurred, it would have reduced the differences between the groups. The use of historical controls means that there may have been other differences between the groups that may have affected the results.

The RCT by Pilote et al. (1996 [++]), also described in Section 5.3.2, explored the effectiveness of providing monetary incentives to the homeless to increase the completion of screening at a TB clinic compared with usual care. The study found that

among the 82 participants who were randomised to receive incentives worth $5.00, 69 (84%) adhered to their appointment at the TB clinic and completed screening within three weeks of referral. This was significantly higher than participants who were randomised to usual care, of whom 42 out of 79 (53%) adhered to their appointment at the TB clinic($p<0.001$). The odds for completing treatment was 4.7 (95% CI 2.2-9.8) among those in the monetary incentive arm compared with those in usual care.

Citron et al. (1995 [+]) used a before-and-after study design to compare different screening procedures on the uptake of screening among the homeless. In Phase I (during Christmas of 1992 and 1993) chest X-rays were used to identify people with active TB in a homeless shelter, and in 1993 all those who complained of a cough were also tested by taking sputum specimens. In Phase II (March 1994) monetary food vouchers worth £1.50 were added to chest X-ray screening and the X-rays were taken and read during the initial visit. In Phase III (August and September 1994), the most vulnerable homeless services were targeted (those services most likely to be used by middle-aged and elderly men sleeping rough or in hostels, who had been identified as the subgroup most likely to have TB). In addition, monetary food vouchers worth £3.00 were given.

The study found that in 1992 during Phase I, 342 homeless people out of a possible1,600 (21.4%) who were eligible for testing were X-rayed. In 1993, 253 out of a possible 2,000 homeless people eligible for testing (12.6%) were X-rayed. Of the 595 homeless people who were screened in total, 30 (5%) had suspected active TB (19 in 1992 and 11 in 1993), 9 of these were confirmed cases of active TB: 5 in 1992 (1.5% of those screened; 95% CI 0.5% to 3.4%) and 4 in 1993 (1.6% of those screened; 95% CI 0.4% to 4.0%). However, 13 of the 30 patients referred for hospital investigation failed to attend or refused treatment (43%).

In Phase II when monetary incentives were added to active case finding and test results were read on the spot, uptake of screening was higher but case detection rates were lower: 187 out of a possible 303 (62%) homeless residents volunteered to be screened, of whom 3 (1.6%) had suspected active TB but none were confirmed to have active TB. In Phase III, when shelters housing the highest-risk groups were targeted, 352 out of a possible 779 (45%) homeless people volunteered to be screened with uptake varying between 37% and 63% across the different hostels. A further 259 homeless people from day centres volunteered to be screened in Phase III, however, it is not known how many people were eligible for testing. Active TB was suspected in 48 out of the 611 people screened (7.9%; 95% CI 7.0% to 13.6%) and active TB was confirmed in 12 cases (2%, 95% CI 1.0% to 3.4%). In Phase III, four people (8% of the 48 suspected cases) did not attend for further investigation.

The study is difficult to interpret since the different phases had different durations and several intervention variables changed between the different phases. For example, Phase III tested the effectiveness of targeting services housing the most vulnerable subpopulation, but also increased the monetary incentive from £1.50 to £3.00. Also,

although Phase II was testing adding incentives to their active case finding compared with Phase I, it was the only phase to read the results of CXR testing on the spot, thereby reducing attrition. Lastly, baseline demographics and differences in outcomes were not statistically compared.

Studies reporting effectiveness and economic data

Perlman et al. (2003 [++]) evaluated the effectiveness and cost-effectiveness of introducing a $25 (US dollar) monetary incentive to turn up for a chest X-ray compared with no monetary incentive on injecting drug users (IDUs) in a needle exchange programme in the USA, in a before-and-after study. The study found that IDUs were more likely to attend the chest X-ray appointment, within seven days of referral (OR = 23, 95% CI = 9.5 to 57.0; p < 0.0001) or within any time point (OR = 9.1, 95% CI = 3.9 to 22.0; P < 0.0001) compared with no incentive. The median time to having the chest X-ray was significantly shorter among those given an incentive to attend (two days) compared with no incentive (11 days; p < 0.0001). Receiving an incentive was also independently associated with attending for chest X-ray within seven days (OR =22.9, 95% CI=10.1 to 52.0; p < 0.0001); within 30 days (OR=15.3, 95% CI=6.9 to 33.6; p < 0.0001); and within any time point (OR = 9.7, 95% CI = 4.3 to 21.9; p < 0.0001). Attending for X-ray at any time point was also associated with having unstable housing provision (OR = 2.2, 95% CI1.05 to 4.6, p = 0.04) and having health insurance (OR = 2.8, 95% CI 1.2 to 6.2, p = 0.01).

The study estimated that at three-year follow-up, and estimating that isoniazid treatment was 65% effective and that 31% of people referred for X-ray would attend, not providing any incentives would have prevented three cases of TB and was estimated to have net savings of $46,226. Providing a $25 cash incentive and assuming that 50% of people referred for X-ray would attend, the study estimated that four cases of TB would be prevented, with net savings of $54,770. If attendance for X-ray was100% when providing £25 incentives, the study estimated that seven cases of TB would be prevented with net savings of $93,416. The cost per case of TB prevented was lower and the net savings increased if a five-year follow-up was carried out (compared with three-year follow-up) and if the effectiveness of isoniazid was 90% (compared with 65%) for the groups where incentives were provided.

The before-and-after study design limits the conclusions that can be drawn from this study, as do the baseline differences between the two groups, such as those in the incentive group being significantly older than those in the control group.

Evidence statement 15: Effectiveness of interventions to improve coverage and uptake of screening or active case-finding using monetary incentives

Six comparative studies were identified that provided effectiveness data exclusively on the use of incentives to improve the coverage/uptake of screening. There was a further one study that provided both effectiveness and cost-effectiveness data. Five studies were on drug misusers (Chaisson et al., 1996 [+]; Fitzgerald et al., 1999 [+]; Malotte et

al., 1998 [++]; Malotte et al., 1999 [++]; Perlman et al., 2003 [++]) and two on the homeless (Citron et al., 1995 [+]; Pilote et al., 1996 [++]). The effectiveness data from these five studies have been used to inform the following evidence statements.

ES15.1 **Strong evidence** from five studies, two RCTs (Malotte et al., 1998 [++]; Malotte et al., 1999 [++]) and three before-and-after studies (Chaisson et al., 1996 [+]; Fitzgerald et al., 1999 [+]; Perlman et al., 2003 [++]) shows that drug misusers who are provided with small monetary incentives are statistically more likely to complete screening compared with no incentives ($p = 0.004$, Chaisson et al., 1996 [+]; $p < 0.001$, Fitzgerald et al., 1999 [+]; Malotte et al., 1998 [++]; Malotte et al., 1999 [++]; Perlman et al., 2003 [++]).

ES15.2 **Strong evidence** from two RCTs found that providing drug misusers with a brief educational programme alone is unlikely to increase the proportion who complete screening compared with no incentives or education ($p = 0.786$, Malotte et al., 1998 [++]; $p = 0.547$, Malotte et al., 1999 [++]).

ES15.3 **Moderate evidence** from two studies, one RCT (Malotte et al., 1998 [++]) and one before-and-after study (Chaisson et al., 1996 [+]) suggests that drug misusers who were provided with monetary incentives and a brief educational programme were statistically more likely to complete screening compared with providing no monetary incentives or education ($p = 0.001$, Chaisson et al., 1996 [+]; $p < 0.001$, Malotte et al., 1998 [++]).

ES15.4 **Moderate evidence** from two studies, one RCT (Pilote et al.,1996 [++]) and one before-and-after study, suggests that providing monetary incentives increases the uptake of screening (from 23% with no incentive to 62% with a £1.50 incentive and 45% with a £3.00 incentives, Citron et al., 1995 [+]; and from 53% with no incentive to 84% for $5.00 incentives, p<.001, Pilote et al., 1996 [++]).Although the quality of the studies varied, both studies supported the same findings.

Applicability
One of the seven studies in this section was from the UK, the rest being from the USA and Canada. The UK study found similar benefits from incentives offered to the homeless as seen in the North American studies on the homeless and with drug users. The applicability of these studies to the UK for all hard-to-reach groups is limited, but we have no evidence to suggest that drug users in the UK would not also respond to monetary incentives. There is no evidence on whether incentives make a difference to response rates in new entrant groups in the UK or elsewhere.

Evidence statement 16: Economic evidence for interventions to improve coverage and uptake of screening or active case-finding using monetary incentives

ES16.1 **Weak evidence** from one cost-benefit study suggests that, under the most

conservative assumptions, providing IDUs identified at a needle exchange programme with a $25 cash incentive to return for TST readings might result in greater net savings of $54,770 compared with a net saving of $46,226 from offering screening with no cash incentives (Perlman et al., 2001 [++]). However, this was not directly compared in a cost-effectiveness analysis.

Applicability
The study identified was on drug users in the USA. The applicability of this study to the UK for all hard-to-reach groups is limited, but we have no evidence to suggest that drug users in the UK would not also respond to monetary incentives.

5.4.4 Increasing detection of hard-to-reach populations prior to screening

We identified two studies that both compared the use of port of arrival forms and a register of new patients added to GP practices in order to identify immigrants who might be eligible for screening:

- Lavender et al. (1997 [-]), UK; and
- Ormerod (1998 [-]), UK.

We found no other studies comparing interventions to increase identification of members of other hard-to-reach groups, and no economic studies on this topic.

Effectiveness
Lavender et al. (1997 [-]), in a retrospective cohort study, compared two strategies to identify immigrants with TB from the Indian subcontinent into the UK: using forms completed after assessment at the port of arrival, and/or using a register of all immigrants allocated to a GP by the health authority. POA forms indentified 100 immigrants into the UK, of whom 54% had been screened for TB including 22 of the 36 (61%) who had not registered with a GP. The health service register identified 278 immigrants into the UK, of whom 214 did not have a POA form. However, of those identified by the health service register without a POA form, only 6 (3%) had been screened for TB. Sixty four immigrants into the UK were identified by both POA forms and the health service register. Of these, 32 (50%) had been screened. One person with active TB and two with LTBI were identified in the POA group, but no cases were identified from people listed on the health service register.

The conclusions that can be drawn from this study are limited as it did not compare the effectiveness of the different screening processes on clinical outcomes. The study reported that those identified by the POA forms represented only one-third of immigrants into the UK from the Indian subcontinent. In addition, no baseline demographics were given, and there was no analysis performed to determine if there were any differences between those who had a POA form and those who did not; so any differences in outcomes may have been due to differences between the groups other than the type of screening received.

Ormerod (1998 [-]) also compared the number of immigrants into the UK identified by POA forms compared with the health service register, in a prospective cohort study. During the study period, 2,242 immigrants were screened, of whom 898 (40%) were identified by POA forms and 1,344 (60%) only via the health service register. Overall, 10 people with TB were identified, of whom 5 had active TB. The POA form identified seven of these cases and the health service register identified three of these cases; the difference was significant ($p < 0.05$). The study did not report the baseline characteristics of those identified by the POA system compared with those identified by the health service register, making it difficult to determine whether there were differences between the groups at baseline which may have affected the results.

Economic

We identified no studies that carried out an economic analysis of strategies to identify more members of hard-to-reach groups for subsequent screening.

Evidence statement 17: Effectiveness of interventions to improve coverage and uptake of screening or active case-finding by identifying more members of hard-to-reach groups

Two studies were identified on the effectiveness of increasing the detection of immigrants to improve the coverage/uptake of screening (Lavender et al., 1997 [-]; Ormerod, 1998 [-]).

ES17.1 Weak evidence from two studies, one prospective (Ormerod, 1998 [-]) and one retrospective cohort (Lavender et al., 1997 [-]) suggests that using a health service register of patients could identify a further group of individuals who were not identified on entry to the country by the POA scheme; however, the benefit of these different identification systems on the coverage and yield of screening is inconclusive. Only 6% of immigrants identified via the health service register who were not identified by the POA form were screened for TB (Lavender et al., 1997 [-]) and the yield of active TB was significantly greater among those identified via the POA process compared with those identified via the health service register (Ormerod, 1998 [-]). Both studies had limitations as they did not assess for baseline differences between the two groups.

Applicability

Both studies identified were from the UK and therefore relevant to UK practice today, although they both used registers from the now obsolete FHSAs. There is no evidence on any intervention to increase detection of members of other hard-to-reach groups, in the UK or elsewhere.

5.5 Effectiveness of interventions to improve passive case-finding

Two studies were identified that incorporated an education component to raise awareness about TB among the hard-to-reach population themselves (Citron et al.,

1995 [+]) and/or among staff at a homeless centre (Citron et al., 1995 [+]; Miller et al., 2006 [+]). However, the intervention were not used to improve passive case-finding but was part of an active case-finding strategy. In addition, the interventions incorporated other components (for example, providing monetary incentives, Citron et al., 1995 [+]), therefore the effectiveness relating to the raising awareness of TB cannot be determined. There were no economic studies on this topic.

6.0 Discussion and summary

The primary research question for this review was:

Which interventions are effective and cost-effective at identifying TB and/or raising awareness about screening for TB among hard-to-reach groups?

Most of the studies we identified sought to answer the first part of this question, and have been discussed in detail in the preceding sections. We identified few studies for this review that directly sought to identify strategies to raise awareness about screening for TB in hard-to-reach groups or the staff caring for them.

The secondary research questions were:

What factors impact on the effectiveness of the interventions:

- *Does the efficacy vary by the theories or conceptual models underpinning the interventions?*
    - We identified no studies that set out to evaluate this.

- *Does the efficacy vary by the diversity of the population (in terms of hard-to-reach group, age, or gender)?*

  There was relatively little overlap in the studies we found in terms of type of hard-to-reach group included for different interventions. As such, it is difficult to be certain whether different groups are likely to respond in different ways to any one intervention or strategy. However, we found no evidence to suggest that the effectiveness of different interventions differed among hard-to-reach groups.

  The review found similar effectiveness and cost-effectiveness results across hard-to-reach groups for:
    - beneficial effects of active screening compared with passive case detection for immigrants and new entrants (Laifer et al., 2007 [+]; Monney and Zellweger, 2005 [+]; Verver et al., 2001 [+]) and a combined group of the homeless, IDUs and prisoners (Watson et al., 2007 [++]);
    - screening with a chest X-rays being less costly than TST among immigrants (Dasgupta and Menzies (2005 [-]; Schwartzman et al., 2005 [++];Schwartzman and Menzies (2000 [++]) and prisoners (Jones and Schaffner, 2001 [+]); and
    - benefits from providing incentives to increase screening uptake for drug misusers (Malotte et al., 1998 [++]; Malotte et al., 1999 [++]; Chaisson et al., 1996 [+]; Fitzgerald et al., 1999 [+]; Perlman et al., 2003 [++]) and the homeless (Citron et al., 1995 [+]).

- *Does the efficacy vary by the persons/organisations commissioning/delivering the interventions?*

- We found one study that assessed this question, which found that using former members of the hard-to-reach group as case-managers increased contact identification rates among drug users (Ricks, 2008 [++]).

- *Does the efficacy vary by the way in which the intervention is delivered (for example, one-to-one or group-based)?*
  - We identified no studies that set out to evaluate this.

- *Does the efficacy vary by the involvement of the target population in the planning, design, or delivery of the intervention?*
  - We found one study that assessed this question, which found that using former members of the hard-to-reach group as case-managers increased contact identification rates among drug users (Ricks, 2008 [++]).

- *Does the efficacy vary by the content of different interventions?*
  - This question was addressed by most of the studies we identified and described in more detail below.

- *Does the efficacy vary by the frequency, intensity, and duration of the intervention?*
  - We found one study where undocumented immigrants to Italy were more likely to complete screening if they attended a specialist TB clinic where screening required two visits, compared with attending a general clinic, where screening required three visits. However, it is difficult to be certain how much of the difference was caused by the need for fewer visits (El-Hamad, et al., 2001 [+]).

- *Does the efficacy vary by the time and place that the intervention is delivered?*
  - The review found one study, which suggests that conducting screening of undocumented immigrants in a specialised TB clinic increased screening uptake compared with a general clinic. However, the study did not adjust for known baseline differences between the groups (El-Hamad, et al., 2001 [+]).

- *How transferable are the findings regarding effectiveness to other hard-to-reach populations, other settings, or other times?*
  - Although some of the studies are less likely to be applicable across populations, settings or times, in particular economic studies, and studies of immigrants and new entrants whose destination and country of origin might differ greatly, we found no clear evidence to suggest that the results differed by hard-to-reach population, setting or time. There is therefore no reason to suggest that most of the results are not transferable to other hard-to-reach populations or to the UK setting since 2010.

- *What are the adverse or unintended effects (e.g., increased stigma) of interventions to identify those with TB from hard to reach groups, if any?*
    - We addressed this question in the first of these reviews, a qualitative review on barriers and facilitators to uptake of TB screening. We found no additional data on such adverse effects in the studies identified for this review.

6.1 Key findings

6.1.1 Approaches to screening for latent infection and active TB in different hard-to-reach populations.

The review found several approaches were used to identify latent and/or active TB in different hard-to-reach populations, including:

- TST (for example, Schwartzman et al., 2005 [++]),
- chest X-ray (for example, Dasgupta et al., 2000 [+]),
- *in* vitro tests (Dasgupta and Menzies, 2005 [-]) including IGRA [Quantiferon-Gold] (for example, Verver et al., 2001 [+]),
- serology (Dasgupta and Menzies, 2005 [-]), and
- symptom questionnaires (for example, Jones and Shaffner, 2001).

More screening approaches were identified for immigrants and new entrants; however this reflects that the review found more studies that included these populations.

6.1.2 Approaches to improve passive case-finding and screening uptake aimed at awareness-raising in high-risk groups and those working with high-risk groups, and maximising service accessibility

The review found two studies that included an educational component (among other factors), on the hard-to-reach population themselves (Citron et al., 1995 [+]) and/or in workers at homeless shelters to increase identification of TB (Citron et al., 1995 [+]; Miller et al., 2006 [+]) to increase the identification of TB. However, these studies were concerned with active case-finding and not passive case-detection.

6.1.3 Coverage uptake and yield from screening / active case-finding in different population groups

Hard-to-reach groups are the focus of this series of reviews as they are both at higher risk of having TB and also likely to face barriers to seeking and complying with medical investigation and treatment.

The first stage in identifying TB in hard-to-reach groups is therefore to identify the individuals within those groups. Although we searched broadly for a number of specific hard-to-reach groups, and would have included any additional group who would find it difficult to access medical care, the literature we identified was focused on just those groups detailed in this report, namely immigrants, new entrants and foreign-born residents, the homeless, drug users, prisoners and contacts of active cases who were from these groups.

Members of these groups were targeted in various ways, largely by screening immigrants as they entered the country or registered with a GP, or by taking services to shelters for the homeless or to prisons. Prisoners are a group that has disproportionately high representation from high-risk groups, in particular drug users and the homeless, and therefore targeting prisoners is an effective way of accessing these other hard-to-reach people. However, in general, we found few studies that assessed methods of increasing identification of members of hard-to-reach groups other than immigrants, such as rough-sleepers who do not attend shelters, or injecting drug users who do not use needle exchange services or other drug services. These particularly hard-to-reach individuals may have even higher risks of TB, and may respond differently to screening and management services and options.

Active screening was found to be an effective and cost-effective strategy in several hard-to-reach groups. We found evidence from three retrospective cohort studies that active screening is more effective than passive case-detection in terms of uptake and yield from screening among immigrants and new entrants (Laifer et al., 2007 [+]; Monney and Zellweger, 2005 [+]; Verver et al., 2001 [+]). This was also found among a group comprising the homeless, IDUs and prisoners, where one case-control study found that active screening using mobile X-ray units was more effective than passive case-detection (Watson et al., 2007 [++]).

There was inconsistent evidence from two economic studies that the active screening of immigrants is cost-saving compared with passive case-detection, with the results being dependent on the assumptions used in the economic model (Brassard et al., 2006 [+]; Dasgupta et al., 2000 [+]). This was also found in one case-control study on the homeless, IDUs and prisoners, where active screening was cost-saving in some but not all scenarios. However, the likely benefits were reported to depend on the cost of TB treatment, rather than on the subgroup being screened (Watson et al., 2007 [++]).

Chest X-rays have also been shown to be more cost-effective than TST in immigrants and in prisoners. Three economic studies suggest that screening with chest X-rays among immigrants is less costly compared with TST, and cost-saving when secondary transmission of TB disease is taken into account (Dasgupta and Menzies (2005 [-]; Schwartzman et al., 2005 [++]; Schwartzman and Menzies (2000 [++]). Adding TST to screening with a chest X-ray did not result in cost-savings for immigrants (Schwartzman et al., 2005 [++]). Similar evidence was found in one cost-comparison

study that suggests screening using chest X-rays in prisoners is less costly compared with TST (Jones and Schaffner, 2001 [+]).

6.1.4 Effectiveness of interventions to improve coverage/uptake of screening and active case-finding

The strongest evidence found on the effectiveness of interventions to improve the coverage/uptake of screening and active case-finding came from five studies, two RCTS (Malotte et al., 1998 [++]; Malotte et al., 1999 [++]) and three before-and-after studies (Chaisson et al., 1996 [+]; Fitzgerald et al., 1999 [+]; Perlman et al., 2003 [++]) that found providing a range of monetary incentives to complete screening was more effective than not providing any incentives among drug misusers. Although the strength of the evidence was moderate, one before-and-after study (Citron et al., 1995 [+]) and one RCT (Pilote et al., 1996 [++]) found similar positive results in the homeless.

Two studies were identified, one RCT (Malotte et al., 1998 [++]) and one before-and-after study (Chaisson et al., 1996 [+]) that demonstrated that providing incentives and a brief education programme to complete screening was more effective than not providing such interventions for drug misusers. However, Malotte et al. (1998[++]) and another RCT (Malotte et al., 1999 [++]) demonstrated that providing just a brief educational programme does not improve the completeness of screening among drug misusers. This suggests that monetary incentives to complete screening are more effective than educational interventions for drug misusers.

One economic study found that providing drug misusers with cash incentives resulted in greater net savings to the healthcare providers compared with no cash incentives (Perlman et al., 2001 [++]).

There was some suggestion from two RCTs that using peers from the same hard-to-reach group as part of the screening programme can improve screening outcomes for drug users (Ricks, 2008 [++]) and the homeless (Pilote et al., 1996 [++]) in terms of identifying more contacts (Ricks, 2008 [++]) and ensuring greater adherence to completing screening (Pilote et al., 1996 [++]). However, in addition to using staff from the same hard-to-reach group, the treatment group in Ricks's (2008 [++]) study also received intensive case management.

There is inconclusive evidence from two cohort studies, one prospective (Ormerod, 1998 [-]) and one retrospective cohort (Lavender et al., 1997 [-]) that using a health service register to identify immigrants can improve the coverage and yield of screening compared with just using POA forms.

6.1.5 Effectiveness of interventions to improve passive case-finding

There were no comparative studies identified on the effectiveness of interventions to improve passive case finding among hard-to-reach groups.

6.2 Strengths and weaknesses of the review

This review was conducted according to full systematic review standards and 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.

Insufficient high-quality effectiveness evidence was located to support quantitative meta-analysis. Hence, only a narrative synthesis of the studies was possible.

For the effectiveness review, our criteria regarding study methodology were relatively inclusive. Any study that used either a comparison or control group (randomised or non-randomised), or presented data from before and after the intervention, was included. Only 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 on the effectiveness of screening and active case-finding among hard-to-reach groups. However, a limitation of the review is some of the effectiveness results between the comparative groups were not statistically compared, which limited the conclusions which could be drawn from the findings. This was also the case for some of the economic papers, where cost-effectiveness analyses were not conducted; this also limited the findings particularly when only the costs of screening were presented from studies conducted outside the UK.

6.3 Gaps in the evidence

The aims of this review were to identify the evidence on effective and cost-effective interventions to identify people with TB and to increase awareness about TB among hard-to-reach groups. Despite a comprehensive and exhaustive search, which identified over 15,000 unique studies, we found only 31 studies that provided comparative data of the topic.

Most of these studies focused on immigrants, new entrants and foreign-born residents as the hard-to-reach group; and most sought to identify people with TB rather than to increase awareness of the disease in high-risk groups. As such, this review presents data on strategies to identify people with latent or active TB infection, but has little to report on strategies to increase awareness about TB in at-risk people, in the healthcare staff who are instrumental in screening and testing at-risk people, or in other personnel who could be influential in encouraging at-risk individuals for seeking help or attending for screening.

Although passive case-detection was a common comparator in the studies on active interventions, we identified no studies that focused on how to improve passive case-detection in hard-to-reach groups.

A number of other evidence gaps were identified. We found few studies that evaluated the benefits from contact tracing in hard-to-reach populations. As two thirds of the studies were focused on new entrants, there was a relative lack of evidence on other hard-to-reach groups. About one quarter of the studies were from the UK, and many of the others are likely to be applicable to the UK context, but we found no UK studies for some types of interventions or groups, in particular:

- the effects of offering screening at different or more convenient locations;
- the use of peer workers from the same group;
- the use of incentives; and
- specific data on homeless groups, drug users, and hard-to-reach contacts of people with TB.

Other specific gaps in the evidence in general include high-quality studies on the coverage and yield of screening and active case-finding of TB among:

- the homeless, in particular, those who do not use or attend shelters such as those who are rough sleepers;
- hard-to-reach contacts of people with TB; and
- prisoners.

We identified a number of studies of interventions aimed at improving identification of people with TB, but very few of these interventions had been tested in more than one hard-to-reach group and across a number of different countries. The range of evidence was particularly limited for:

- conducting screening in a convenient location;
- using peers or staff from similar hard-to-reach groups;
- increasing detection of hard-to-reach populations prior to screening, in particular among non-migrant groups; and
- providing incentives to hard-to-reach populations other than problem drug users.

The review found no evidence of the effectiveness of interventions to improve passive case finding.

In addition, many of the secondary research questions pertaining to the factors that may impact on the effectiveness of the interventions could not be addressed as they were not explored in the studies found in the review.

We found 15 economic studies, of which four were from the UK. These reported economic outcomes for immigrants and new entrants, the homeless, prisoners and drug users, although only data on immigrants was reported separately. Economic studies are more challenging to interpret in other countries compared with

effectiveness studies, and high-quality economic studies from the UK are needed to fully inform public health policy in times of increasingly-limited resources.

6.4 Conclusions

A few general conclusions can be drawn from the evidence in this review.

- Active screening seems to increase identification of latent and active TB infection across hard-to-reach groups who are at high risk of infection, compared with passive case-detection, and leads to earlier diagnosis and reduced infective periods in those with active TB.
- The cost-effectiveness of active screening compared with passive case-detection is less certain, and more research is needed to confirm the economic benefits of such strategies in the UK.
- Screening with chest X-rays seems to be more effective than TST in immigrants and prisoners, but there is no clear evidence about whether this is also true for other hard-to-reach groups.
- Tracing household contacts of foreign-born cases appears to be cost effective.
- Offering small monetary incentives or vouchers is an effective and cost-effective strategy to increase the proportion of people who attend for TST test reading or for further investigation or management, in drug users, and seems to be effective in the homeless.
- Educational interventions about TB have not been shown to increase return rates for screening results without an additional monetary incentive, in drug users.
- Using peers from similar hard-to-reach groups as part of the screening programme can help towards identifying more contacts among drug users and improve adherence to completing screening among the homeless.

Other strong conclusions could not be drawn from the literature due to the limited number of studies and/or due to the quality of the evidence provided. More high quality comparative studies are needed on screening amongst hard-to-reach groups, in particular those that address any baseline differences between the intervention groups where RCT studies cannot be done.

6.5 Implications identified by the review team

The first, qualitative, review in this series concluded that members of hard-to-reach groups frequently reported incomplete or inaccurate knowledge about the cause and transmission of TB. Smoking and heredity were commonly thought to be causes of TB by these groups. Because of this, participants did not always understand or appreciate their susceptibility to TB. Their knowledge about the severity of TB was also often incomplete or inaccurate. Although many knew that TB could be fatal, many were unsure whether TB could be treated and cured.

We found very few studies on the effects of educational interventions that seek to

address this lack of knowledge. The two studies we did identify found that giving drug users educational information about TB did not increase their uptake or return rates for screening. The benefit of such education and information therefore remains unproven, and studies are needed to evaluate its impact and how best to format such information to meet the needs of people with language and literacy barriers.

The qualitative review also identified various potential barriers to testing and treatment. The most important barriers were concerns about stigmatisation and a fear of death that prevented many people from getting tested. Many respondents also raised concerns about the ability of GPs to diagnose TB. This point was also reflected in the views of service providers themselves, who raised concerns about the lack of specialist TB healthcare professionals. A few facilitators were mentioned in the literature, including family support and religion—although evidence on facilitators was sparse and inconclusive.

We found no studies that addressed the impact of stigma in hard-to-reach groups, or interventions to reduce such stigma. One study found that more contacts were identified by drug users when they had a case-manager who was a former drug user, which may reflect reduced stigmatisation from such indigenous staff support.

We found only one study that compared the outcomes of screening at a specialist TB clinic with a general healthcare service offered to undocumented immigrants in Italy, which found higher attendance rates for screening at the specialist clinic. Many of the studies we identified used passive case-detection, usually in primary care, as the main comparator for more active interventions. Given the previously identified concerns among hard-to-reach populations about the competence of GPs in dealing with TB, it is difficult to be sure how much of the apparent benefit from specialist active screening are due to the active screening and how much is from the specialist input.

In the hard-to-reach and high-risk populations we have studied, an active approach to identifying people with TB is merited. Where possible, it seems sensible to offer interventions that minimise the number of appointments or visits before a definitive diagnosis is made, such as chest X-rays that can be read during the visit. Where this cannot be offered, the use of a small monetary incentive is likely to be cost-effective in increasing the proportion of infected people who complete screening and start treatment. For hard-to-reach groups where there may be a societal or political barrier to offering such incentives, such as problem drug users, the use of food or travel vouchers seems to be as effective as cash or equally comparable.

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8.0 Appendix A. Search strategies and results

8.1 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.

8.1.1 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

8.1.2 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

8.2 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

8.3 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).

8.4 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 JP. (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 and 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

8.5 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 4 new included studies. Forward citation-chasing was conducted for all included studies using ISI Web of Knowledge. This yielded 491 references, of which 361 were duplicates of records already located through our searches. The remaining 130 unique hits were screened, and one reference was included in this review.

9.0 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 US) 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, multi-disciplinary 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.

10.0 Appendix C. Evidence tables

Abbreviations used in the evidence tables:
95% CI = 95% confidence interval
CXR = chest X-ray
IDU = injection drug users
LTBI = latent TB infection
MDR = multi-drug resistant
NA = not applicable
NR = not reported
POA = port of arrival
QFT-G = QuantiFERON-TB Gold
TB = tuberculosis
TST = tuberculin skin test

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Bothamley et al. **Year:** 2001 **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	**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.	**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	**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	**Primary results:** <u>Number screened with questionnaire:</u> Hospital = 199/1262. Homeless = 262/267. GP = 45/unknown. <u>Number screened with questionnaire who were eligible for TST:</u> Hospital = 181/199. Homeless = 262/262. GP = 39/45. <u>Number of active TB cases:</u> Hospital = 3. Homeless = 0. GP = 0. <u>Total costs:</u> Hospital = £22,646.	**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

general practice and the homeless. *Thorax*, *57*(1), 45-49. **Aim of study:** To compare 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**	**Excluded population:** Individuals who had no symptoms, were not new 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	scheme, in which new entrants are offered Tuberculin (Heaf) testing in a clinic/hospital. Note: all patients across groups were 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	described by Morris and Gardner. **Modelling method and assumptions:** 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, based on 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	Homeless = £3,452. GP = £938. <u>Savings (number of cases prevented):</u> Hospital = £25,621 for 9.5 cases prevented. Homeless = £1,618 for 0.6 cases prevented. GP = £594 for 0.2 cases prevented. <u>Cost per person screened</u>*:* Hospital = £12.70 (savings). Homeless = £0.50. GP = £7.00. <u>Cost per person screened for each case prevented:</u> 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.	

effectiveness studies: Internal validity: NA **External validity:** NA **Quality appraisal economic studies: Quality score:** - **Applicability:** ++	screened for TB. No socio-demographic characteristics are provided for the sample as a whole. **Economic analysis data sources:** Published literature.		prevented assumes that each case of TB gives rise to three others. **Time horizon:** NR	**Attrition details:** NR	

Study Details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Brassard et al. **Year:** 2006 **Citation:**. Brassard, Paul, Steensma, C., Cadieux, L., & Lands, L. C. (2006). Evaluation of a School-Based Tuberculosis-	**Source population/s:** immigrant children in Canada. **Eligible population:** newly-arrived immigrant children (aged 4–18 years) in primary and secondary schools with high numbers of pupils from highly endemic TB	**Method of allocation:** NA **Intervention/s description:** School screening programme: TB screening (TST, Mantoux method) was provided by nurses at school to newly arrived immigrant children. Positive TST was	**Primary outcomes:** Number of children tested. Number of cases (latent and active) identified. Number of active TB cases prevented. Hospitalisation rate of active paediatric TB cases.	**Primary results:** School screening programme: Number of patients tested = 2524/3710 (68%); 542/2524 (41%) had a ≥10mm TST result; 484/542 (89%) presented at the paediatric hospital; 375/484 started LTBI treatment; 2/484 active TB cases identified; 99/2524 had TST result	**Limitations identified by author:** Inconsistent data available for all schoolchildren and child associates who were not available for TST testing, and for those who were non-TST reactors. High rates of attrition: significant decline in the proportion of referred children who presented at the TB clinic for treatment.

Screening Program and Associate Investigation Targeting Recently Immigrated Children in a Low-Burden Country. *Pediatrics*, *117*(2), e148-156. **Aim of study:** To evaluate the cost-effectiveness of a school-based screening programme targeting children at high risk of TB infection in Montreal, Canada compared with passive case finding. To compare the net cost/benefit of the school-based screening alone and that of school-based screening plus investigation	countries. **Selected population:** eligible children whose parents consented to the test. **Excluded population:** schools included in the screening program to investigate a single active TB case within that school were excluded from the study. Children who could provide results of prior testing were also excluded. **Setting:** urban primary and secondary schools. **Economic analysis data source:** primary research and published studies. **Sample characteristics:** 3,710 immigrant children were identified for the	defined as an induration of ≥10 mm in diameter at the site of injection 48 to 72 hours after administration. Children with positive results were referred to the paediatric hospital for a medical consultation with the TB clinic physician, including CXR, plus gastric lavage, sputum smear and cultures when active TB was suspected. Those with 5-9mm diameter induration were also referred to hospital if they presented characteristic symptoms of TB. Children started on isoniazid (INH) therapy for LTBI were followed-up after 2, 4 and 8 months and adherence to treatment assessed. Adherence defined as 80% or more of total prescribed doses taken within 43 weeks of initiating therapy.	Net savings generated by the school-based intervention per year and over 5 years. Net savings generated by the associate investigation per year and over 5 years. **Secondary outcomes:** Adherence to LTBI regimen (not reported in this review). **Time horizon:** Benefits: 5 years Costs: 5 years (20 years for the sensitivity analysis). **Modelling method and assumptions:** All costs are in Canadian $. Cost-benefit comparisons and sensitivity analysis. Cost-benefit comparisons which compared a) and b) (see below): a) Total material and	between 5 and 9 mm; 9/99 (9%) started LTBI treatment. <u>Associates investigation:</u> 599 associates of the 484 TST-positive schoolchildren were seen at the TB clinic. 555 had TST results; 211/555 (38%) were TST-positive; 136/211 were children (<18 years of age); 131/136 presented at the TB clinic; 108/136 started drug treatment; One active case of TB was found. <u>Number of active TB cases prevented</u>: An estimated 36.1 active TB cases were prevented (25.6 through school screening, 10.5 through associate investigation). <u>Costs</u>: The school screening programme cost $126,871 and associate investigation cost $66,590; $193,461 in total. Treating 36.1 active cases would have cost $557,384.	**Limitations identified by review team:** In addition to the above, the study did not state its economic perspective. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** "Drs Brassard and Lands are supported by the Canadian Institutes of Health Research and the Fonds de Recherche en Sante du Quebec, respectively."

of associates of children with LTBI. **Study design:** NA **Type of economic analysis:** Cost-benefit analysis. **Economic perspective:** NR **Quality appraisal non-economic studies:** **Internal validity:** NA **External validity:** NA **Quality appraisal economic studies: +** **Quality score Applicability +**	intervention. Associates were children who were family members or others who had close, sustained contact with an immigrant child. Region of origins of TST-positive children and their associates presenting at the TB clinic: East/Southeast Asia 121/484 (25.0%) cases, 19/131 (14.6%) associates; Eastern Europe 102/484 (21.1%) cases, 24/131 (18.5%) associates; Central Asia 67/484 (13.8%) cases, 21/131 (16.2%) associates; South Asia 67/484 (13.8%) cases, 32/131 (24.6%) associates; South/Central America 39/484 (8.1%) cases, 11/131 (8.5%) associates; North Africa/Middle East 28/484 (5.8%)	Children with active TB were seen every month by a respiratory physician. <u>Associates investigation</u>: people in recent close and sustained contact with the child were offered TB screening. **Comparator/control/s description:** passive case finding (no description in this study). **Sample size:** **a) TB screening at school: N=** 2,524 **b) paediatric medical consultation: N=** 484 **c) associate investigation: N=** 599 **Control:** NA	labour costs associated with the school-screening program and the associate investigations (all associates were included). b) Cost of managing 1 case of active TB through passive case finding, multiplied by the estimated number of prevented active TB cases. The estimate of prevented active TB cases was based on the number of TST-positive children and adults who were screened and treated through the intervention. Estimates of cost of interventions and of number of contacts per child with TB were based on prior primary studies. Estimated number of prevented active TB cases among children and adults who were	The combined school and associate investigation intervention gave a net saving of approximately $363,923 over 5 years ($72,785 per year). $268,393 net savings were generated by the school screening programme alone, and the associate investigation contributed $95,530 of savings ($19,106 per year). Assuming hospitalisation rate of active paediatric TB cases was reduced from 76% to 50%, the combined school screening and associate investigation to generate annual net savings of $23,068 at an annual net cost of $8,224. **Secondary outcomes:** Not reported in this review.	

	cases, 7/131 (5.3%) associates; Caribbean 22/484 (4.5%) cases, 8/131 (6.1%) associates; Sub-Saharan Africa 20/484 (4.1%) cases, 4/131 (3.0%) associates; North America/Western Europe 18/484 (3.7%) cases, 4/131 (3.0%)associates. **Baseline comparisons:** NA **Study sufficiently powered?** NA		screened and treated was based on the rates of successful adherence to therapy and on the estimate that 10% of LTBIs will become active cases. Assumptions on test sensitivity and specificity (90%) and effectiveness of adherence to INH therapy in preventing TB (90%), and adherence rates to LTBI treatment for adult associates were based on prior relevant studies. Relevant sensitivity analyses were performed. Notably, different cost assumptions were used by varying the rate of hospitalisation for treatment of active TB in children. 3% annual discounts were made for cases prevented over a 20 year period for both original and reduced-rate-of-hospitalisation scenarios.		

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Chaisson et al. **Year:** 1996 **Citation:** Chaisson, R. E., Keruly, J. C., McAvinue, S., Gallant, J. E., & Moore, R. D. (1996). Effects of an incentive and education program on return rates for PPD test reading in patients with HIV infection. *JAIDS Journal of Acquired Immune Deficiency Syndromes*, *11*(5), 455-459. **Aim of study:** To determine the impact of a	**Source population/s:** HIV-infected adults in the US. **Eligible population:** HIV clinic users. **Selected population:** 659 patients. **Excluded population:** NA **Setting:** The Johns Hopkins Hospital HIV Clinic, Baltimore, US (between September 1992 and April 1994). **Sample characteristics:** Mean age = 36; 75% African American; 69% male; 50% acquired HIV from IDU; 71% lived in Baltimore. **Economic analysis data sources:** NA	**Method of allocation:** Retrospective based on type of treatment received. **Intervention/s description:** 1) Between March and August 1994 patients were given a food voucher (approx. $4) as an incentive to promote return visits for purified protein derivative (PPD) TST interpretation. 2) From September 1993 to April 1994, a brief (about 3 min) educational message by a nurse was added to the testing protocol, and several posters emphasising the importance of TB testing were conspicuously placed in the clinic. **Comparator/control/s description:** Between September 1992 and February 1993 patients were tested with no	**Primary outcomes:** Proportion of patients returning for skin test reading. **Secondary outcomes:** NR **Method of analysis:** chi-square test, student *t* test, multiple logistic regression. **Modelling method and assumptions:** NA **Time horizon:** NA	**Primary results:** <u>Proportion of patients returning:</u> Control group = 96/ 272 (35%); Voucher only = 111/229 (48%; p=.004 compared with controls, adjusted odds 1.69, 95% CI 1.18-2.45); Voucher and education = 96/158 (61%;p=.0001 compared with controls, adjusted odds 2.98, 95% CI 1.97-4.15). NOTE: being a city resident and male sex were also significantly and independently associated with returning for a PPD reading (city resident: adjusted odds, 1.89, 95% CI 1.32-2.72; male gender: adjusted odds 1.54, 95% CI, 1.09-2.19). **Secondary results:** <u>Positive TST:</u> 14 patients (2%) had skin test reactions >5mm induration; no significant differences between	**Limitations identified by author:** NR **Limitations identified by review team:** NR **Evidence gaps and/or recommendations for future research:** Additional research is needed to explain the influence of gender on returning for results. Additional studies of interventions to improve screening adherence are also needed. **Source of funding:** Agency for Health Care Policy and Research.

food voucher incentive and patient education program in return rates for TST. **Study design:** Before and after (retrospective). **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal effectiveness studies: + Internal validity:** ++ **External validity:** + **Quality appraisal economic studies: Quality score:** NA **Applicability:** NA		further instructions. **Sample sizes: Total:** N = 659. **Intervention: Intervention 1:** N = 229 Intervention 2: N = 158 . **Control:** N = 272. **Baseline comparisons:** No significant differences in demographic characteristics. **Study sufficiently powered?** NR		groups: Controls: 5/ 272; Voucher only: 6/229; Voucher plus education: 3/ 158. **Attrition details:** NR	

Study Details [5600 & 31195]	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Citron et al. [supplemented by evidence reported in Kumar et al.] **Year:** 1995 **Citation:** Citron, K. M., Southern, A., & Dixon, M. (1995). *Out of the shadow Detecting and treating tuberculosis amongst single homeless people*. London: Crisis. **Aim of study:** To assess the prevalence of TB among the	**Source population/s:** Homeless in the UK. **Eligible population:** <u>Phase I</u> Homeless persons residing in a temporary shelter in London during Christmas of 1992 and 1993. <u>Phase II</u> Homeless persons residing in seven cold weather shelters in London in March 1994. <u>Phase III</u> Homeless persons in five hostels, one night shelter, three day centres and a soup kitchen in London in August and September 1994.	**Method of allocation:** NA **Intervention/s description:** <u>Phase I</u> A chest X-ray facility was installed in the shelter and TB screening was advertised through posters, leaflets and regular public announcements. In addition, in 1993 sputum specimens were requested from those who complained of productive cough. In 1992 the x-rays were read by either a consultant radiologist or a consultant chest physician. In 1993 the CXRs were read by consultant chest physicians who also carried out clinical	**Primary outcomes:** TB screening uptake. Cases found. Treatment outcome was also recorded, but is not reported here. **Secondary outcomes:** NA **Method of analysis:** NR **Modelling method and assumptions:** NA **Time horizon:** NA	**Primary results:** <u>Phase I</u> Screening uptake: in 1992, 372/1600 (23%) persons initially volunteered and 342 were x-rayed; in 1993, 270/2000 (14%) initially volunteered and 253 were x-rayed (595 people x-rayed in total). Cases found: Suspected: 30/595 overall (5%); 19 in 1992 and 11 in 1993. Confirmed: 9 cases overall: 5 In 1992 (1.5% of those screened; 95% CI 0.5%-3.4%) and 4 in 1993 (1.6% of those screened; 95% CI 0.4%-4.0%). <u>Phase II</u> Screening uptake: 187/303 (62%) of residents. Cases found: 3 TB cases were	**Limitations identified by author:** NR **Limitations identified by review team:** The design of Phase II was based on results from Phase I, and Phase III based on Phase II. Although this offers a rough comparison across the groups, a direct comparison of the effectiveness of the different strategies cannot be made. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** Department of Health and Glaxo plc (Phase I); London Housing Foundation (Phases II and III).

homeless and the feasibility and effect of incentives and education, and targeting higher risk subpopulations on uptake of screening. **Study design:** Before and after study. **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal effectiveness studies: +** **Quality score:** + **External validity: +** **Quality appraisal economic studies:**	**Selected population:** <u>Phase I</u> In 1992, volunteers who complained of any one of the following: feeling of being unwell for more than two consecutive weeks in the last three months; history of cough for more than two weeks in the last three months; recent weight loss; history of haemoptysis; history of contact with a case of TB. In 1993, anyone who volunteered. <u>Phase II</u> All volunteers. <u>Phase III</u> All volunteers; services most likely to be used by middle-aged and elderly men sleeping rough or in hostels were targeted. **Excluded population:** NA	examinations on subjects who had CXR features suggestive of TB. In 1992 all suspected cases were escorted by a volunteer to a hospital of their choice, where a subsequent outpatient appointment could be arranged. In 1993 cases were referred to consultant chest physicians at one of four major London hospitals. Either immediate hospital admission or subsequent outpatient appointments were set up, as appropriate. <u>Phase II</u> Tested the use of incentives to increase screening uptake compared with Phase I. CXRs were offered to residents at seven cold weather shelters in March 1994. Informative fact sheets and posters were distributed at each shelter. Volunteers were offered a food voucher (value £1.50).		suspected but none was confirmed as active. <u>Phase III</u> Screening uptake: 352/779 hostel residents volunteered for X-ray (45%); . Uptake varied between 37-63% across the hostels. 259 people from the day centres were x-rayed (total of 611 x-rayed) (Note: The uptake rate cannot be calculated as the number of possible users is uncertain). Cases found during phase III across hostels and day centres: active TB was suspected in 48/611 cases overall (7.9%, 95% CI 7.0-13.6) and confirmed in 12 (2%, 95% CI 1.0-3.4). There was no significant difference between hostels and day centres: Hostels: 35/352 suspected (9.9%, 95% CI 7.0-13.6) and 9 confirmed (2.6%, 95% CI 1.2-4.8); Day centres: 13/259 suspected (5.0%, 95% CI 2.7-8.4) and 3 confirmed (1.2%, 95% CI 0.2-3.4). **Secondary results:** NA	

Quality score: NA **Applicability:** NA	**Setting:** temporary shelters, set up in London by Crisis, and other hostels and services for the homeless in London. **Sample characteristics:** <u>Phase I</u> Mean age = 41; 52% born in England; 23% of Irish and 14% of Scottish origin; 46% had "no fixed abode" (sleeping rough, squatters, occasional night shelter users); 27% residents of long or short tem hostels; 88% smoked regularly; 25% had a history of previous lung disease, 4-5% of TB; 15-16% gave a history of contact with a case of TB; 71% consumed alcohol regularly. <u>Phase II</u> "Volunteers [...] were younger (a higher proportion were aged under 30 and there were only nine aged	X-rays were read on the spot by a doctor who examined anyone showing an abnormality. People requiring further investigation were sent to a hospital where prior arrangements had been made to receive them. <u>Phase III</u> Tested the effects of targeting the most vulnerable subpopulation for screening to increase case detection compared with Phase II. CXRs were offered in five hostels, one night shelter, three day centres and a soup kitchen in the central London boroughs of Camden and Westminster. Posters were used to advertise screening. Food vouchers were given to all those volunteering for X-ray, as in phase II (value £3). TB awareness among the homeless people and staff in the hostels and		**Attrition details:** <u>Phase I</u> Overall, 13 of the 30 patients referred for hospital investigation failed to attend or refused treatment (43%). In 1992, 7/19 cases failed to keep their appointments; in 1993, 2 cases refused treatment and 4/9 failed to attend their outpatient appointment. <u>Phase III</u> Four people (8% of the 48 suspected cases) did not attend for investigation.	

	60 or more) and there was a higher proportion of women." Phase III 97% male; average age = 45; 70% between 30-59 years old. **Economic analysis data sources:** NA	day centres was assessed. Arrangements were made with consultant chest physicians and TB nurses at the Middlesex Hospital and St Mary's Hospital for those requiring further investigation and treatment. **Comparator/control/s description:** NA **Sample sizes:** Phase I Total=1600 (1992) + 2000 (1993) Intervention=372 (1992) + 270 (1993) Phase II Total=303 Intervention=187 Phase III Total=NA Intervention=611 **Baseline comparisons:** Phase I "The study populations had very similar socio-demographic characteristics" (p.			

		630). No significance tests were conducted. **Study sufficiently powered?** NR			

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Dasgupta et al. **Year:** 2000 **Citation:** Dasgupta, K., Schwartzman, K., Marchand, R., Tennenbaum, T. N., Brassard, P., & Menzies, D. (2000). Comparison of cost-effectiveness of tuberculosis screening of close contacts and foreign-born populations. *American Journal of Respiratory &*	**Source population/s:** Immigrants to Canada **Eligible population:** all immigration applicants undergoing radiographic screening, and newly arrived immigrants with inactive TB requiring surveillance. These were compared with a third cohort of patients (all close contacts of patients with active contagious TB) who were not necessarily from hard-to-reach populations. **Selected population:** those	**Method of allocation:** NA **Intervention/s description:** <u>Applicant screening</u>: a medical evaluation including a CXR to primarily screen for active TB for all immigrants who applied for permanent residence, or individuals coming to Canada on a work or study visa for longer than 6 months. If radiographic abnormalities were detected, the affected individual was referred, usually to a chest specialist, for further evaluation. Tuberculin screening and close contact	**Primary outcomes:** Active TB disease detected and completely treated. LTBI detected and completed treatment. Costs per active cases detected: included administrative, screening and evaluation costs (but did not include costs for treatment of LTBI). Costs per active cases treated: included the same costs as above plus cost of treatment of LTBI. The total costs of cases prevented: all programme costs estimated for preventing active TB	**Primary results:** <u>Effectiveness outcomes:</u> Active TB detected: 17 cases among applicant screening and 4 cases among medical surveillance groups. Active TB cases who completed treatment: 16 among applicant screening and 4 among medical surveillance group. Estimated future cases of active TB prevented: 7.85 among applicant screening and 1.58 among medical surveillance group. Latent TB detected: 353 cases among applicant screening and 191 cases among medical surveillance group. Latent TB cases who	**Limitations identified by author:** The cost-effectiveness of the active screening programmes may have been underestimated resulting in a lower cost per case found, for various reasons. The cost of outpatient treatment for passive cases was lower than those estimated in other studies ($1,006 compared with $2,305). In addition, the model did not take into account possible rehospitalisation. The risk of active TB disease did not take into account associated risk factors such as HIV infection. The model also assumed treatment for less than 6 months would not have resulted in any benefit. **Limitations identified by review team:** The interventions could have been described in greater detail in order to compare the programmes to policy in the UK

Critical Care Medicine, *162*(6), 2079-2086. **Aim of study:** The study aimed to evaluate the impact and cost-effectiveness of two screening programmes relevant for immigrants in Canada compared with passive case detection. **Study design:** NA **Type of economic analysis:** cost-effectiveness. **Economic perspective:** NR **Quality appraisal non-economic**	who were referred to the Montreal Chest Institute that carries out applicant screening and surveillance between June 1, 1996 and May 30, 1997. **Excluded population:** not reported. **Setting:** TB clinic, hospital **Sample characteristics:** NR **Economic analysis data source:** Medical records were used to obtain sample characteristics and outcome data. Hospital costs were based on the actual costs of the hospital in 1996 (and took into account reimbursement paid by the Canadian government for refugees' health service).	identification were performed by staff members at the Montreal Chest Institute (MCI) for cases diagnosed there, and by staff members of the Montreal Public Health Department for those diagnosed at other Montreal hospitals. <u>Medical surveillance</u>: once arrived in Canada, surveillance of inactive TB for those who underwent applicant screening and for whom inactive TB was detected. Close contact identification was conducted for active case findings of TB. **Comparator/control/s description:** Passive case detection: no further information (used as a hypothetical comparison as practice as usual). **Sample sizes:** **Total:** 13,726.	over the next 20 years. Incremental costs compared the active screening programmes with passive case detection and treatment without screening. Costs of treatment of LTBI: additional costs related to therapy of LTBI. **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method and assumptions:** Markov model. 3% discounting. Canadian dollars. Sensitivity analyses performed to take into account secondary infection, varying risk of active TB, and carrying the cost per passively diagnosed case from $5,000 to $20,000.	completed treatment: 145 among applicant screening, 49 among medical surveillance group. <u>Costs:</u> Active TB disease detected and treated (does not include cost for LTBI): $31,418 for applicant screening and $55,728 for medical surveillance. Total cost for TB infection treated (without detection): $3,958 for applicant screening and $4,739 for medical surveillance. It is not clear whether this includes only LTBI. Total cost for TB disease prevented: $73,125 for applicant screening and $155,729 for medical surveillance. Costs for LTBI treatment only: for TB infections treated: $491 for applicant screening and $452 for medical surveillance. Costs for LTBI treatment only: for TB disease prevented: $9,123 for TB disease prevented for those who underwent	setting. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** Fonds de Recherche en Santé du Québec and MCI Research Centre.

studies: Internal validity: NA **External validity:** NA **Quality appraisal economic studies: Quality score:** + **Applicability:** +	Costs for pharmacology, pharmacists and physician fees were generated from the fee schedule of the Quebec government. Costs for administrative activities were generated via interview of all personnel involved to identify salaries, tasks and time spent on the screening programmes including overhead costs such as office space, rental, heating, insurance and security costs. Costs for outpatient treatment taken from the observed costs in the study. Costs for diagnosis and treatment of a passively diagnosed case were estimated from outcomes in this study; other outcomes were taken from other published research.	**Intervention:** Applicant screening: N = 12,898. Medical surveillance: N = 828. **Control:** hypothetical cohort. **Baseline comparisons:** not reported. **Study sufficiently powered?** NA	Subgroup analyses performed for different populations. **Time horizon:** 20 years.	applicant screening and $14,860 for those in medical surveillance. <u>Incremental costs to diagnose and treat each passively diagnosed case</u>: Costs for prevalent active TB disease treated: the active screening interventions compared with passive case detection and treatment (without screening) had an incremental cost of $20,328 for prevalent active TB disease treated for those who received applicant screening and $24,225 for those who underwent medical surveillance. Total cost for TB disease prevented: the active screening interventions compared with passive case detection and treatment (without screening) had an incremental cost of $39,409 for applicant screening and $65,126 for medical surveillance. Total marginal cost (for TB disease prevented (including only costs for	

				LTBI treatment): had a net savings of $1,967 for TB disease prevented when compared with passive case detection and treatment (without screening). However, medical surveillance had an incremental cost of $3,770 compared with passive case detection and treatment (without screening). **Secondary results:** Sensitivity analyses: Medical surveillance would only have been cost-effective if the cost of passive screening and treatment would have exceeded $40,000. Both active screening programmes would have been considerably more cost-effective if the future risk of TB were to be higher than the baseline estimate of 0.05%. Sub-group analyses: Restricting screening to applicants from countries with a high incidence of TB did not significantly change the results.	

				Attrition details: NA	

Study Details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Dasgupta and Menzies **Year:** 2005 **Citation:** Dasgupta, K., & Menzies, D. (2005). Cost-effectiveness of tuberculosis control strategies among immigrants and refugees. *European Respiratory Journal*, *25*(6), 1107-1116. **Aim of study:** To examine the impact of migration from high TB-incidence countries to low TB-	**Source population/s:** Immigrants to Canada from high TB-prevalence countries. **Eligible population:** NA **Selected population:** Hypothetical cohort of 1,000 immigrants. **Excluded population:** NA **Setting:** Results from literature review applied to Canada. **Sample characteristics:** 1% prevalence of active TB (hypothetical). **Economic analysis data sources:** Published sources and estimates	**Method of allocation:** NA **Intervention/s description:** Alternative testing strategies for immigrants entering Canada: TST; Sputum TB culture; Sputum TB PCR; Serology; *In vitro* tests of CMI. **Comparator/control/s description:** Usual testing strategy: CXR. **Sample sizes:** **Total:** NA **Intervention** NA **Control** NA (compares costs using one hypothetical sample). **Baseline comparisons:** NA **Study sufficiently powered?** NA	**Primary outcomes:** Cost to screen 1,000 persons. Cases detected. False-positive tests. Costs of work-up after positive test. Total cost for screening. Total cost per active case detected. **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method and assumptions:** Average **c**ost of work-up after positive test was $193 for the evaluation of persons with positive screening test in a specialist chest clinic. Costs do not include overhead, administration or patient costs.	**Primary results:** CXR: Cost to screen 1,000 persons = $22,000. Cases of active TB detected n=7. False-positive tests n=238. Costs of work-up after positive test = $47,285. Total cost for screening = $69,285. Total cost per active case detected = $9,898. TST: Cost to screen 1,000 persons = $7,000. Cases of active TB detected n=8. False-positive tests n=470 (assumes that the prevalence of positive TST would be 50%). Costs of work-up after positive test = $92,254. Total cost for screening = $99,254. Total cost per active case detected = $12,407. Sputum TB culture (one specimen):	**Limitations identified by author:** NR **Limitations identified by review team:** Combines a SR-inspired literature review with a brief cost-effectiveness analysis, and that may explain the lack of detail. Not enough information is provided regarding the C-E analysis and the use of different sources is not appropriately explained. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** NR

incidence countries and to compare the cost-effectiveness of different TB control strategies. **Type of economic analysis:** Cost-effectiveness. **Economic perspective:** NR **Quality appraisal non-economic studies:** **Internal validity:** NA **External validity:** NA **Quality appraisal economic studies:** **Quality score:** - **Applicability:** +	provided by the laboratories of the McGill University Health Centre.		All costs in Canadian dollars. **Time horizon:** NR	Cost to screen 1,000 persons = $50,000. Cases of active TB detected n=8.2. False-positive tests n=19.8. Costs of work-up after positive test = $5,404. Total cost for screening = $55,404. Total cost per active case detected = $6,757. <u>Sputum TB culture (three specimens)</u> (includes cost of sputum induction, but does not include acid-fast bacilli smear): Cost to screen 1,000 persons = $150,000. Cases of active TB detected n=9. False-positive tests n=19.8. Costs of work-up after positive test = $5,558. Total cost for screening = $155,558. Total cost per active case detected = $17,284. <u>Sputum TB PCR (one sample)</u> (includes cost of sputum induction, but does not include acid-fast bacilli smear): Cost to screen 1,000 persons = $75,000. Cases of active TB detected n=7.3.	

				False-positive tests n=19.8. Costs of work-up after positive test = $5,230. Total cost for screening = $80,230. Total cost per active case detected = $10,990. <u>Serology</u>*:* Cost to screen 1,000 persons = $19,000 (includes the cost of drawing blood samples, $10). Cases of active TB detected n=5.5. False-positive tests n=99. Costs of work-up after positive test = $20,169. Total cost for screening = $39,169. Total cost per active case detected = $7,122. <u>In vitro tests of CMI</u>: Cost to screen 1,000 persons = $45,000 (includes the cost of drawing blood samples, $10). Cases of active TB detected n=6.5. False-positive tests n=178. Costs of work-up after positive test = $35,609. Total cost for screening = $80,609.	

				Total cost per active case detected = $12,401. **Secondary results:** NA **Attrition details:** NA	

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 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	**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) 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	**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 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	**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 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	**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. <u>Active TB cases</u>: The TBU clinic and 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	**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 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:**

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 **Economic perspective:** NA **Quality appraisal non-economic studies: + Internal validity:** + **External validity:** + **Quality appraisal economic studies: Quality score:** NA **Applicability:**	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 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:**	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 statistically more males, 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	**Time horizon:** NA	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 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	Italian Tuberculosis Projects I (1995) and II (1997) of the Istituto Superiore di Sanità.

NA	<u>MHCU:</u>
	Male = 362 (75%);
	<35 years = 393 (82%);
	Married = 192 (40%);
	Stable work =131 (27%).
	
	Living in: own apartment = 121 (25%);
	with friends = 318 (66%);
	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%).
	
	<u>TBU:</u>
	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: FitzGerald et al. **Year:** 1999 **Citation:** FitzGerald, J. M., Patrick, D. M., Strathdee, S., Rekart, M., Elwood, R. K., Schecter, M. T., Montaner, J., et al., Vancouver Injection Drug Use Study Group (1999). Use of incentives to increase compliance for TB screening in a population of intravenous drug users. *International Journal of Tuberculosis and Lung Disease*, *3*(2), 153-155. **Aim of study:**	**Source population/s:** IDUs, Canada **Eligible population:** Users of the Vancouver Needle Exchange Programme. **Selected population:** 1st cohort (pre-intervention): 558 IDUs. 2nd cohort (intervention): 549 IDUs from the same population. **Excluded population:** NA **Setting:** Vancouver Needle Exchange Programme, a community-based programme used by about 5,000 IDUs. **Economic analysis data source:** NA **Sample characteristics:**	**Method of allocation:** Before and after study design. **Intervention/s description:** May 1996 to October 1996 (2nd period). PPD skin tests. Subjects with symptoms were offered a CXR, and sputum was collected for acid-fast smear and culture. IDUs were asked to return for skin test result reading between 48 and 72 hours after having been planted. $5 (Canadian dollars) were used as incentives to those who returned to have their skin tests read. **Comparator/control/s description:** January to April 1996. (1st period). Same as intervention, but no incentives were given. **Sample sizes:** **Total** NR **Intervention: N =** 549. **Control: N =** 558.	**Primary outcomes:** proportion returning for skin test reading. **Secondary outcomes:** Cases of TB identified. **Method of analysis:** Baseline characteristics and proportion of participants returning for test reading analysed using chi-squared test.	**Primary results:** In the pre-intervention group, 240/558 (43%) made a follow-up visits for PPD test reading. In the intervention group, 418/549 (78%) returned ($p<0.001$). **Secondary results:** 3 cases of suspected active TB were diagnosed from the intervention group (no report of any cases being identified in the pre-intervention period). **Attrition details:** NA	**Limitations identified by author:** Contamination not measured between groups. No record of proportion of IDUs who declined screening. Before and after methodology limits conclusions that can be drawn. **Limitations identified by review team:** Some potential confounders not accounted for (HIV status and homelessness). External validity is questionable: there are not enough details to tell whether findings are generalisable to the source population. The study does not cover those IDUs who did not attend the needle exchange programme. **Evidence gaps and/or recommendations for future research:** Research into innovative modes of surveillance of HIV-associated TB for IDUs. **Source of funding:** British Columbia Ministry of Health and the British Columbia Lung Association.

To evaluate the role of giving a small financial incentive to IDUs to ensure compliance with TB (PPD) screening. **Study design:** Before and after **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal non-economic studies: + Internal validity:** + **External validity:** + **Quality appraisal economic studies:** NA **Quality score:** NA	No information on ethnicity, HIV status and homelessness for pre-intervention cohort (the authors believe they are comparable as they come from the same Needle Exchange programme). No data on the proportion of eligible people who came to the programme during both periods.	**Baseline comparisons:** Similar age and gender characteristics in both groups (p-value not reported). 1st group: 68.1% male Mean age 34.5 (SD 9.97) 2nd group: 63.2% male Mean age 36.5 (SD 9.96) **Study sufficiently powered?** No sample size calculation but $p < 0.001$ for primary outcome.			

Applicability: NA					

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Hardy et al. **Year:** 2010 **Citation:** Hardy, A. B., Varma, R., Collyns, T., Moffitt, S. J., Mullarkey, C., & Watson, J. P. (2010). Cost-effectiveness of the NICE guidelines for screening for latent tuberculosis infection: the QuantiFERON-TB Gold IGRA alone is more cost-effective for immigrants from high burden countries. *Thorax*, *65*(2),	**Source population/s:** immigrants in the UK from countries with high incidence of TB. **Eligible population:** immigrants attending the Leeds TB Screening Service. **Selected population:** Those attending Leeds TB Screening Service in 2007 who were initially from a country with a TB incidence > 340/10,000; this was later changed to 200-339/10,000. **Excluded population:** NR **Setting:** NR **Sample characteristics:**	**Method of allocation:** NA **Intervention/s description:** using QFT for first-line screening of all immigrants from countries with a high incidence of TB, with CXR if QFT was positive. **Comparator/control/s description:** screening all immigrants with CXR; conducting TST for immigrants from countries with a high incidence of TB; conducting a QFT on those who have a positive TST (as per NICE recommendations). **Sample sizes:** **Total:** N= 560 **Intervention:** N= 280 **Control:** N=280	**Primary outcomes:** LTBI identified. **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method and assumptions:** QFT costed at £25.67 per screen. Costs took into account that 6 patients in the intervention group had a second QFT due to indeterminate results. Outcome assumptions were based on the results of 42 cases in the study who received both a QFT and TST screening. These costs include providing all immigrants over the age of 11 and who were not pregnant (n=275) with a CXR at	<u>LTBI identified</u> In the intervention group: 170 (60.7%) QFT negative; 104 (37.1%) QFT positive; 5 (1.8%) indeterminate; 1 (0.3%) laboratory processing error. 104 QFT-positive invited for medical evaluation (CXR): 94/104 (90.3%) attended; All (N = 94) diagnosed with LTBI; none (N = 0) diagnosed with active TB; 64/94 received chemoprophylaxis. The control group was a hypothetical cohort; outcomes discussed in costs. <u>Costs</u> Total costs of using QFT as first-line screening was £9,781.82 (£34.94 per immigrant) and identified 105 cases of LTBI, at a cost of £93.16 per case of	**Limitations identified by author:** The authors note that they changed the screening policy during the study so that initially the service only screened immigrants with a QFT if they were from a country with a TB incidence > 340/10,000; this was later changed to 200-339/10,000. The author states that the TB incidence rate for screening immigrants from countries with a higher incidence rate is 43%, compared with 34% for immigrants from countries with a lower incidence rate. Although the author does not think this affected their results, this could have impacted on the costs as the more cases identified, the lower the cost per case of LTBI identified. **Limitations identified by review team:** The study only considers the cost of the screening tool and not, for example, the different resources

178-180. **Aim of study:** To assess the cost-effectiveness of using QuantiFERON-TB Gold (QFT) for screening immigrants from high risk countries. **Study design:** NA **Type of economic analysis:** **Economic perspective:** Not reported; only considers cost of screening tool. **Quality appraisal non-economic studies: Internal validity:** NA **External validity:** NA	Intervention group (N=280): 139 men (49.6%), mean age of 30.8 years. Control group was a hypothetical cohort, no demographics reported. **Economic analysis data source:** cost data from NICE (2006) guidelines; outcome data from primary research.	(hypothetical sample). **Baseline comparisons:** NA **Study sufficiently powered?** NA	£23.24 each, a TST for those from high TB-incidence countries (N=221) at £13.69 and a QTF for those with a positive TST (N=153) at £25.67 each. **Time horizon:** NR	LTBI identified. Total of cost of screening as per NICE recommendations was £13,346.75 (£47.67 per immigrant) and was estimated to have identified 83 cases of LTBI at a cost of £160.81 per case of LTBI identified. **Secondary results:** NR **Attrition details:** NA	needed to carry out the different screening measures. This provides a very limited view on the cost perspectives for the different screening interventions. Likewise, the study only considered the outcome of LTBI identified and did not consider other benefits and harms of treating LTBI.. **Evidence gaps and/or recommendations for future research:** none reported. **Source of funding:** none.

Quality appraisal economic studies: **Quality score:** - **Applicability:** +					

Study Details	Population and setting	Intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Jones and Schaffner **Year:** 2001 **Citation:** Jones, T. F., & Schaffner, W. (2001). Miniature chest radiograph screening for tuberculosis in jails: a cost-effectiveness analysis. *American Journal of Respiratory &*	**Source population/s:** Prisoners, US (hypothetical cohort). **Eligible population:** NA **Selected population:** NA **Excluded population:** NA **Setting:** Jail **Sample characteristics:** In the hypothetical cohort, the baseline	**Method of allocation:** NA **Intervention/s description:** high speed, low dose miniature chest radiograph screening. **Comparator/control/s description:** TST or symptom screening. **Sample sizes:** **Total:** NA **Intervention:** NA **Control** NA	**Primary outcomes:** Cost per case of active TB identified. **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method and assumptions:** Decision analytic model. Costs were adjusted to 1998 US dollars. 3% discount rate. Took into account baseline incidence of	**Primary results:** <u>Cost of screening per case of active TB identified</u>: Radiographic screening = $9,600; TST = $32,100; symptom questionnaire = $54,100. In a high risk and high-volume setting the cost would increase: Radiographic screening = $37,400; TST = $60,300; symptom questionnaire = $84,100. <u>Cases of active TB identified</u>: Radiographic screening = 0.68 cases per 1,000;	**Limitations identified by author:** NR **Limitations identified by review team:** The start-up costs of implementing the miniature chest radiograph screening were not taken into account. Considering the technology and training necessary to implement such a tool in a prison setting, this information could have had an effect on the costs. The study only compared costs and did not calculate comparative cost-effectiveness such as with an ICER. **Evidence gaps and/or**

Critical Care Medicine, *164*(1), 77-81. **Aim of study:** This study aimed to evaluate the cost-effectiveness of using miniature chest radiography to screen new inmates to jail for TB compared with symptom-based and TST screening. **Study design:** NA **Type of economic analysis:** cost-comparison. **Economic perspective:** NR **Quality appraisal**	incidence of active TB in a jail population was estimated to be 68 per 100,000. 1.1% were estimated to be infected with a multidrug-resistant (MDR) strain. Prevalence of HIV was estimated at 0.5%. 25% of inmates were estimated to have a positive TST. **Economic analysis data source:** Rates of TB, prevalence of HIV infection, and values of other variables associated with screening were based on estimates in the published literature. Sensitivity analyses were derived from studies conducted under a variety of conditions.		active TB, the prevention of contact infection through treatment of index cases, the prevalence of MDR cases, HIV infection, the prevalence of disease identified through screening, and the sensitivity and specificity of various screening methods. Cost assumptions were that a case of active TB would cost an average of $16,640 to treat (including both inpatient and outpatient therapy), treatment of MDR TB would cost $230,000 and that infected contacts without active disease would receive preventive therapy at a cost of $229. Miniature chest radiograph screening was estimated to cost $6.60 per person screened (based on equipment costs, 24-h technician staffing and radiologist services).	TST = 0.25 per 1,000; symptom questionnaire = 0.09 cases per 1,000. <u>Sensitivity analyses:</u> screening with routine miniature chest radiography remained cost effective as estimated TB prevalence fell, test specificity decreased or cost per inmate increased compared with other screening procedures: <u>Costs per case of active TB identified</u>: TB incidence of 40 cases/100,000 = $15,700; TB incidence of 20 cases/100,000 = $28, 500; TB incidence of 10 cases/100,000 =$48, 500; TB incidence of 6.8 cases/ 100,000 (similar to that of the US population) = $62,500. CXR specificity decreased to 0.58 = $46,600. Cost of CXR increased to $25 per inmate = $36, 500. **Secondary results:**	**recommendations for future research:** NR **Source of funding:** NR

non-economic studies: Internal validity: NA **External validity:** NA **Quality appraisal economic studies: Quality score:** + **Applicability: +**			TST was estimated to cost $8.00 per person screened. Screening by symptom questionnaire was estimated to cost $4.80 per person screened (including full-time staff costs). The cost of evaluating a patient for active TB after a positive screening test was estimated to be $180 (including initial and follow-up medical evaluations). **Time horizon:** NR	NR	

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Laifer et al. **Year:** 2007 **Citation:** Laifer, G., Widmer, A. F., Simcock, M.,	**Source population/s:** Immigrants suspected of having TB , Switzerland. **Eligible population:** all patients admitted in a hospital	**Method of allocation:** assignment to groups was naturalistic based on screening policy in Switzerland. **Intervention/s description:** active screening of new	**Primary outcomes:** In-hospital mortality. Number of positive acid-fast smears. Number of positive PCR tests. Number of positive cultures. Number of MDR cases.	**Primary results:** In-hospital mortality: 0/43 (0%) in the immigrant/active screening group compared with 1/59 (1.7%) in the foreign-born/passive screening group. Proportion of patients with	**Limitations identified by author:** NR **Limitations identified by review team:** there are limitations to using this study to look at the differences between active and passive screening as the two groups are categorised

Bassetti, S., Trampuz, A., Frei, R., Tamm, M., et al. (2007). TB in a low-incidence country: differences between new immigrants, foreign-born residents and native residents. *American Journal of Medicine*, *120*(4), 350-356. **Aim of study:** To determine whether active screening should be reinforced for immigrants. **Study design:** retrospective cohort study. **Type of economic analysis:** NA	respiratory isolation unit for suspected TB. **Selected population:** those patients admitted to the isolation unit between January 1997 and July 2004 who had active TB. In this time period, 397 patients had suspected TB, of these 385 were evaluated. 12 (3%) patients were excluded due to incomplete data. **Excluded population:** NR **Sample characteristics:** Active screening group of immigrants: mean age 30.6 years (range 16 – 49); 90.7% male; 0% HIV positive; 14% history of TB; 62.8% from Eastern Europe, 18.6% from Africa, 9.3% from Asia and 9.3% from central Europe.	immigrants at point of entry with CXR, people with abnormalities referred to the clinic. **Control/comparison/s description:** passive screening of foreign-born residents (i.e. those with work permits or student visas) at the GP's discretion when symptoms suspected. **Sample sizes:** **Total:** N = 102. **Intervention:** N = 43. **Control:** N = 59. Note: there was also a third group (N=54) of native residents of Switzerland who were not hard-to-reach. **Baseline comparisons:** significant differences on some demographic characteristics (for the number of TB risk factors; those who were HIV positive; and those who had a history of TB). **Study sufficiently powered?** NR	**Secondary outcomes:** NR **Method of analysis:** *t* test between continuous variables; chi-squared tests between categorical variables; Fisher's exact test; cell counts below 5 in 20% of the cells. **Modelling method and assumptions:** NA **Time horizon:** NA	active disease and at least one positive acid-fast smear test: 15/43 (34.9%) in the immigrant/active screening group compared with 45/59 (76.2%) in the foreign-born/passive screening group ($p<0.05$). Proportion of patients with active disease and at least one positive polymerase chain reaction tests: 24/43 (55.8%) in the immigrant/active screening group compared with 52/59 (89.1%) in the foreign-born/passive screening group ($p<0.05$). Proportion of patients with active disease and at least one positive culture: 33/43 (76.7%) in the immigrant/active screening group compared with 59/59 (100%) in the foreign-born/passive screening group ($p<0.05$). Proportion of patients who were isoniazid resistant: 21.9% in the immigrant/active screening group compared with 10.2% in the foreign-born/passive screening group ($p<0.05$).	differentially depending on whether they participants were new immigrants or foreign-born residents. Therefore any differences in outcomes may not be due to the differences in screening but due to demographic characteristics. This is further confounded by the baseline demographics differences between the two groups. These results also reflect the fact that foreign-born residents were referred by their GP when they presented with a problem, while screening of new entrants occurred whether or not they had symptoms. The study also does not have a clear research question therefore it is difficult to assess whether the study was appropriately designed. In addition it did not have clear outcomes stated *a priori* therefore it was difficult to know whether all the relevant outcomes were reported or whether only notable differences between the groups were reported. **Evidence gaps and/or recommendations for future research:** NR

Economic perspective: NA **Quality appraisal non-economic studies: + Internal validity: - External validity:** + **Quality appraisal economic studies:** **Quality score:** NA **Applicability:** NA	Passive screening of foreign-born group: mean age 35.1 years (range 16 - 86); 61.0% male; 12.5% HIV positive; 1.7% history of TB; 32.2% from Eastern Europe, 25.4% from Southern Europe,16.9% from Asia, 15.3% from Africa and 10.2% from Latin America. **Setting:** hospital. **Economic analysis data source:** NA			Proportion of patients who had multi-drug resistant TB: 6.3% in the immigrant/active screening group compared with 1.7% in the foreign-born/passive screening group ($p<0.05$). **Secondary results:** NR **Attrition details:** NR	**Source of funding:** NR

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Lavender **Year:** 1997 **Citation:** Lavender, M. (1997). Screening immigrants for	**Source population/s:** immigrants, UK. **Eligible population:** immigrants from the Indian subcontinent. **Selected population:**	**Method of allocation:** retrospective based on method used to identify immigrants for screening. **Intervention/s description:** POA forms: active screening of	**Primary outcomes:** Number of immigrants screened. Number of cases detected through screening. **Secondary outcomes:** NR	**Primary results:** <u>Number of immigrants screened</u> POA forms: 100 immigrants from Indian subcontinent were identified through POA forms; of these, 54% had been screened, including 22 of the 36 (61%) of those	**Limitations identified by author:** The author states a limitation was the length of follow-up (1 year) as it was not sufficient to allow for the disease to develop and for screening to be completed. **Limitations identified by review team:** The study did not report

tuberculosis in Newcastle upon Tyne. *Journal of Public Health*, *19*(3), 320. **Aim of study:** To investigate assess the completeness of the identification of new entrants for screening using the POA system alone; to determine the proportion of immigrants that had been screened; and to determine the number of new cases detected by screening. **Study design:** Retrospective cohort. **Type of economic analysis:** NA **Economic**	immigrants identified either via Port of Arrival (POA) forms or by the Family Health Services Authority (FHSA) patient register between January 1, 1993 and March 31, 1994, who gave their country of birth as from the Indian subcontinent. **Excluded population:** NR **Setting:** Port Health Control (port of arrival) and general practice (FHSA). **Sample characteristics:** NR **Economic analysis data source:** NA	immigrants. In this study, usual practice consisted of a two-stage screening process. Stage 1 was a medical evaluation by a medical officer at the Port Health Control only for those immigrants referred at the discretion of the immigration officer. Initial screening was based on clinical history, presence of BCG scar, and CXR if available, and only detected active TB. Results of the screen and the address of the immigrant were noted on POA forms. Stage 2 required a Heaf test and a CXR if not done earlier in order to complete screening. Family Health Services Authority (FHSA) register: used to assess passive screening of new immigrants by their allocated GP. FHSA register was used to identify new immigrants from the Indian subcontinent. GPs'	**Method of analysis:** Completers only. **Modelling method and assumptions:** NA **Time horizon:** 1 year.	who had not registered with a GP. FHSA register: 278 immigrants were identified from the FHSA register, of whom 214 did not have POA form. Of those without a POA form, 6/214 (3%) had been screened. FHSA register + POA forms: 64 duplicate cases identified by both POA forms and FHSA register. Of these 32/64 (50%) had been screened. <u>Number of cases detected through screening</u>: POA forms: 1 active TB case; 2 LTBI cases; FHSA register: none; FHSA register + POA forms: none. **Secondary results:** NA **Attrition details:** NR	any baseline demographic characteristics, therefore it is difficult to determine whether the selected population was representative of the source population. As no baseline demographics were given there was no analysis performed to determine if there were any differences between those who had a POA form and those who did not; any differences in outcomes may have been due to differences between the groups in factors other than the type of screening received. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** NR

perspective: NA **Quality appraisal non-economic studies: - Internal validity:** - **External validity:** + **Quality appraisal economic studies: Internal validity:** NA **Applicability:** NA		notes for these patients were examined to determine whether the patient had been tested and/or treated for TB. FHSA and POA: evaluated both active screening (POA) and passive screening (FHSA). **Comparator/control/s description:** NA **Sample sizes: Total:** N = 314. **Intervention** POA forms: N = 36; FHSA register: N = 214; FHSA register + POA forms: N = 64. **Control:** NA **Baseline comparisons:** NR **Study sufficiently powered?** NR			

Study Details 7760	Population and setting	Method of allocation to intervention/control	Outcomes and methods of analysis:	Results	Notes
Authors:	**Source**	**Method of allocation:**	**Primary outcomes:**	**Primary outcomes:**	**Limitations identified by**

Malotte et al. **Year:** 1998 **Citation:** Malotte, C. K., Rhodes, F., & Mais, K. E. (1998). Tuberculosis screening and compliance with return for skin test reading among active drug users. *American Journal of Public Health*, *88*(5), 792-796. **Aim of study:** The purpose of this study was to assess the independent and combined effects of different levels of monetary incentives and a theory-based educational intervention on return for TB skin test reading in a sample of active injection drug and	**population/s:** Drug misusers, US. **Eligible population:** Active drug users, either injection drugs, crack cocaine or both. **Selected population:** Individuals who showed evidence of recent drug use and were not in a drug treatment programme. Participants were recruited after participating in a street outreach project aimed at HIV prevention for drug users; or by direct street outreach. **Excluded population:** Individuals who had a history of a positive TB skin test. **Setting:** not reported. **Sample characteristics:**	Participants were randomly assigned to 1 of 6 experimental treatment conditions stratified by recruitment source. They were assigned to the experimental conditions in a ratio of 2:2:1:1:2:2. **Intervention/s description:** Condition1: 5- to 10-minute motivational education session plus $10 to return for their skin test reading. Condition 2: 5- to 10-minute motivational education session plus $5 to return for skin test reading. Condition 3: 5- to 10-minute motivational education session and no monetary incentive. Condition 4: No education or incentive was provided but importance of returning for skin test was stressed. Condition 5: $5 monetary incentive for on-time return but no motivational intervention. Condition 6: $10 monetary incentive for on-time return	Return for skin test reading. **Secondary outcomes:** Prevalence of TB/ positive skin test results. **Modelling method and assumptions:** NA **Time horizon:** NA	Condition 1 (($10 and motivational education) = 92.1% returned (odds ratio: 25.96; 95% CI 13.17-51.17; p < 0.001). Condition 2 ($5 and motivational education) = 84.3% returned (odds ratio compared with no intervention 12.88; 95% CI 7.13-23.24; p < 0.001) Condition 3 (Motivational education only) = 34.3% returned (Odds ratio compared with no intervention: 1.09; 95% CI 0.35-2.00; p = 0.786) Condition 4 (no education or incentive) = 33% returned (reference group). Condition 5 ($5 only) = 85.8% returned (odds ratio compared with no intervention 13.59; 95% CI 7.49-24.63; p < 0.001) Condition 6 ($10 only) = 93.0% returned (odds ratio compared with no intervention 30.94; 95% CI 15.25-62.77; p <	**author:** NR **Limitations identified by review team:** None. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** National Institute on Drug Abuse.

crack cocaine users. **Study design:** RCT **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal non-economic studies: ++** **Internal validity:** ++ **External validity:** + **Quality appraisal economic studies:** **Quality score:** NA **Applicability:** NA	Age in years: 18-30: 13.3%; 31-40: 47.3%; 41-50: 32.5%; 51-69: 6.9%. Sex: Male: 68.1%; Female: 31.9%. Urine drug screen results: Negative: 16.6%; Opiates only: 4.2%; Cocaine only: 46.7%; Both: 32.6%. Binge drinking: in previous month: None: 54.6%; Some: 45.4%. Living arrangement: Own home: 43.5% Other's home: 37.7% Motel: 5.0% Shelter: 1.9% Street: 10.5% Other: 1.4% Prior study participation: Past participant: 70.4% New street outreach: 29.6%	but no motivational intervention. Note: The motivational education session focused on behavioural beliefs and subjective norms relevant to behavioural intention, using individual counselling and was delivered by the study nurse. All participants received a TST (Mantoux test) administered by a study nurse. **Control/comparison/s description:** NA **Sample sizes:** **Total:** N = 1,004. **Intervention:** Condition 1: N = 203; Condition 2: N = 198; Condition 3: N = 99; Condition 4: N = 100; Condition 5: N = 204; Condition 6: N = 200. **Baseline comparisons:** NR **Study sufficiently powered?** NR		0.001). **Secondary outcomes:** Overall, 153/835 of skin tests that were read were positive: 139/782 (17.8%) of people returning on time had a positive test; 14/53 (26.4%) of people who did not return on time had a positive test. Positive skin tests were significantly associated with older age, non-white ethnicity, and male gender. Non-injecting crack users were as likely as IDUs to have positive test results, with no significant difference in number of positive tests for different types of drug use. **Attrition details:** NR	

	Economic analysis data source: NA				

Study Details	**Population and setting**	**Method of allocation to intervention/control**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: Malotte et al. **Year:** 1999 **Citation:** Malotte, C. K., Hollingshead, J. R., & Rhodes, F. (1999). Monetary versus nonmonetary incentives for TB skin test reading among drug users. *American Journal of Preventive Medicine*, *16*(3), 182-188. **Aim of study:** The purpose of this study was to compare the effects of monetary versus	**Source population/s:** drug users from Long Beach, California, USA. All study activities were conducted at a storefront research facility. **Eligible population:** active drug users, either injection drugs, crack cocaine, or both. **Selected population:** eligible population recruited following street outreach activities. **Excluded population:** participants in any of the authors' prior studies were	**Method of allocation:** Participants were randomly assigned to 1 of 5 experimental treatment conditions: $10 cash, grocery store coupons, bus tokens/fast-food coupons, motivational education, or usual encouragement to return. **Intervention/s description:** All participants in all groups received a TST (Mantoux test) performed by 1 of 4 study nurses. Participants were scheduled to return for their skin test reading after 48 hours. <u>Cash:</u> In condition 1, participants were offered $10 to return for skin test reading.	**Primary outcomes:** return for skin test reading. **Secondary outcomes:** prevalence/skin test results. **Follow up periods:** September, 1995, and September, 1997 **Methods of analysis:** Baseline differences were assessed using chi-square test for categorical variables and analysis of variance (ANOVA) for continuous variables. Univariate and multivariate analyses were conducted.	**Primary outcomes:** <u>Type of incentive:</u> No incentive = 49.3% returned. Motivational education only = 46.9% returned (Odds ratio compared with no incentive = 0.9; 95% CI 0.6 to 1.3; p = 0.547). Fast-food coupons/bus passes= 82.6 returned (odds ratio compared with no incentive = 5.1; 95% CI 3.3 to 8.0; p = <0.001). Grocery store coupons= 85.7% returned (odds ratio compared with no incentive = 6.4; 95% CI 4.0-10.2; P=<0.001). Cash= 94.9% returned (odds ratio compared with no incentive = 19.9; 95% CI 10.2-38.7;	**Limitations identified by author:** NR **Limitations identified by review team:** None. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** National Institute on Drug Abuse

nonmonetary incentives and a theory-based educational intervention on return for TB skin test reading in a sample of active injection and crack cocaine users. **Study design:** RCT. **Quality score:++** **Internal validity:** ++ **External validity:** +	ineligible for participation. **Sample characteristics:** all participants were active drug users, either injection drugs, crack cocaine, or both. Participants were predominantly male, African-American, and between 31 and 50 years of age. Few worked and many were unstably housed. Crack cocaine was the most commonly used drug, with 77% reporting crack use, 11% reporting injection drug use, and 12% reporting both injection drug and crack use within the past 90 days (most within the past week). **Setting :** NR	<u>Grocery store coupon:</u> In condition 2, participants received grocery store coupons worth $10. <u>Bus passes or fast-food coupon:</u> In condition 3, participants chose between two coupons that were each worth $10. <u>Education session:</u> In condition 4, participants received a 5- to 10-minute motivational education session. This was based on the theory of reasoned action, with counselling to focus participants on subjective norms and behavioural beliefs most likely to encourage their return. **Control/comparison/s description:** In condition 5, participants were informed of the importance of having their skin tests read, but they did not receive either incentives or education. **Sample sizes:**		P=<0.001). <u>Age:</u> 18-30 years= 65.5% returned; 12.1% positive. 31-40 years= 70.7% returned (odds ratio compared with 18-30 years = 1.4; 95% CI 0.9 to 2.1; p = 0.115); 18.4% positive, adjusted OR compared with 18-30 years = 1.55, 95% CI 0.8 to 2.9; p = 0.168. 41-50 years= 75.9 (odds ratio compared with 18-30 years = 2.0; 95% CI 1.2 to 3.1; p = 0.005); 26.4% positive, adjusted OR compared with 18-30 years = 2.20, 95% CI 1.2 to 4.1; p = 0.016. 51-67 years= 80.9% returned (odds ratio compared with 18-30 years = 2.6; 95% CI 1.2 to 5.5; p = 0.014); 33.3% positive, adjusted OR compared with 18-30 years = 3.03, 95% CI 1.3 to 6.8; p = 0.008. <u>Ever *injected* drugs</u>: No = 70.2% returned Yes = 74.6% returned	

		Total : N = 51,078 **Intervention =** Cash: N = 5,217; Grocery store coupon: N = 5,217; Buss pass/fast-food coupon: N = 5,218; Education session: N = 5,211. **Control** No intervention: N = 5,215. **Baseline comparisons:** Following randomisation there were no statistically significant differences among treatment conditions for any demographic, drug use, or cognitive variables. **Study sufficiently powered?** NR		(odds ratio compared with non-injectors =1.3; 95% CI 1.0 to 1.8; p = 0.069). **Secondary outcomes:** NA **Attrition details:** NR	

Study Details	**Population and setting**	**Method of allocation to intervention/ comparator**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: Marra et al.	**Source population/s:** Canada (sub-group	**Method of allocation:** NA	**Primary outcomes:** cost; incremental cost;	**Primary outcomes:** Cost of TST = $25.41 Cost of QFT-G = $43.32	**Limitations identified by author:** Regarding the rate and timing of

Year: 2008 **Citation:** Marra, F., Marra, C. A., Sadatsafavi, M., Morán-Mendoza, O., Cook, V., Elwood, R. K., Morshed, M., et al. (2008). Cost-effectiveness of a new interferon-based blood assay, QuantiFERON-TB Gold, in screening tuberculosis contacts. *The International Journal of Tuberculosis and Lung Disease: The Official Journal of the International Union Against Tuberculosis and Lung Disease*, *12*(12), 1414-1424.	of foreign-born immigrants). **Eligible population:** TB contacts. **Selected population:** hypothetical, modelled after published and provincial data. **Excluded population:** NR **Setting:** NR **Sample characteristics:** (hypothetical sample) 20% foreign-born; 63% Canadian-born (non-aboriginal); 17% aboriginal; 32% 20-30 years old, 36% 30-40 years old, 32% 40-50 years old; 17% BCG positive, 53% BCG negative, 30% BCG unknown. **Economic analysis data source:** Demographic data, prevalence of TST positivity and adherence to and	**Intervention/s description:** 1) QFT-G alone: QFT-G replaced TST while all other parts of the usual treatment (see below) remained unchanged; 2) sequential screening: first TST, then QFT-G. Those who are TST-positive undergo further testing with QFT-G and begin treatment for LTBI if the TST is confirmed. For those with negative results on the first TST, a second TST 8–12 weeks later is utilised. If TST is positive and QFT-G is negative, a second test is conducted with QFT-G 8–12 weeks later. **Comparator/control/s description:** current practice: TST is administered to contacts of a confirmed or suspected case. Those with a positive TST are referred for further follow up and test are offered isoniazid (INH) treatment. Contacts	QALY; ICER; INMB (incremental net monetary benefit, = gain in health outcome X willingness to pay). [data only extracted for foreign-born] **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method and assumptions:** costs included only direct medical costs (staff time, equipment, consumables, commercial kits, physician visits, LTBI treatment, hospitalisation stays, contact investigations and management of LTBI or active TB disease). The model takes into account the efficacy of BCG vaccine; reduction in TB incidence due to LTBI treatment; secondary transmission;	<u>Costs per contact for foreign-born:</u> BCG positive: TST = $406.97; QFT-G = $399.95 ; TST/QFT-G = $387.72. BCG negative: TST = $437.6; QFT-G = $464.09 ; TST/QFT-G = $447.37. BCG unknown: TST = $431.13; QFT-G = $450.46 ; TST/QFT-G = $434.77. <u>QALYs</u> BCG positive: TST = 15.1203; QFT-G = 15.1206 ; TST/QFT-G = 15.1203 BCG negative: TST = 15.1141; QFT-G = 15.1145; TST/QFT-G = 15.1139. BCG unknown: TST = 15.1154; QFT-G = 15.1158 ; TST/QFT-G = 15.1153. <u>Cost-effectiveness of various alternative screening strategies compared with TST alone:</u>	conversion of QFT-G after a contact, a second test was modelled, but a long conversion time for QFT-G may result in higher loss to follow-up rates and less favourable results. Little is known about the rate of TB reactivation after a positive or negative QFT-G. A relatively low rate of initiation (61%) and completion (50%) of treatment was assumed, but a higher adherence rate would result in QFT-G being cost-effective in aboriginal and foreign-born contacts as well. The type of contact (close vs. casual) was not explicitly modelled in the study, although their effects were considered in calculating transition rates and probabilities. HIV-infected contacts were not modelled. **Limitations identified by review team:** no indirect costs considered in the model. The study does not evaluate the cost-effectiveness of different screening strategies in foreign-born residents alone, making it difficult to determine the best strategy for hard-to-reach populations. **Evidence gaps and/or recommendations for future research:** NR.

Aim of study: To assess the cost-effectiveness of QuantiFERON-TB Gold (QFT-G) compared with TST to diagnose LTBI in contacts of active TB cases. **Study design:** NA **Type of economic analysis:** Cost-effectiveness. **Economic perspective:** Third party payer (only medical costs). **Quality appraisal non-economic studies:** **Internal validity:** NA **External validity:** NA	completion of treatment were obtained from a provincial population-based database; efficacy of LTBI treatment and performance of TST and QFT-G were derived from published literature: mortality was derived from the year 2000 Canadian life tables.	with symptoms suggestive of active TB or those with radiographic abnormalities are further evaluated. **Sample sizes:** NA **Baseline comparisons:** NA **Study sufficiently powered?** NA	treatment; incomplete treatment; hospitalisation; mortality; probability of not returning for test results; indeterminate results; TB reactivation. Future costs and effectiveness outcomes were discounted at an annual rate of 3%. All costs in 2005 Canadian Dollars. **Time horizon:** 20 years	QFT-G in foreign born, aboriginal, and BCG-positive contacts, TST in others: Incremental cost= $5.00; Incremental QALY= 0.0002; ICER ($/QALY) = $31,930; INMB (based on the willingness to pay of $50,000 per QALY) = $2.83; ICER ($/active case averted) = $137,320. QFT-G in foreign-born and aboriginal, TST for Canadian-born contacts: Incremental cost = $5.58; Incremental QALY = 0.0001; ICER ($/QALY) = $40,433; INMB = $1.32; ICER ($/active case averted) = $167,447 TST/QFT-G in foreign-born, aboriginal, and BCG-positive contacts, TST in others: Incremental cost = - $1.67; Incremental QALY = 0.0000; ICER ($/QALY) = $135,672; INMB = $1.05; ICER ($/active case averted) = dominant (lower	**Source of funding:** University of British Columbia Centre for Disease Control and the National Sanitorium Association.

Quality appraisal economic studies: **Quality score:** ++ **Applicability:** +				costs and higher effectiveness). TST/QFT-G in foreign-born and aboriginal, TST for Canadian-born contacts: Incremental cost = $-0.67; Incremental QALY = 0.0000; ICER ($/QALY) = dominates (higher costs and lower or equal effectiveness); INMB=- $0.12; ICER ($/active case averted) = dominant. “In conclusion, QFT-G is an economically attractive strategy for LTBI detection in BCG-vaccinated contacts. The uncertainty around the performance characteristics and conversion pattern of QFT-G casts some doubts about its cost-effectiveness as a complete replacement for TST for all contact tracing and investigation programmes.” **Secondary results:** NR **Attrition details:** NA	

Study Details 5837	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 States. *Annals of Epidemiology*, *16*(4), 305-312. **Aim of study:** To evaluate and compare the efficiency of a non state-law-mandated	**Source population/s:** Homeless and prison populations in the US. **Eligible population:** NA **Selected population:** NA **Excluded population:** NA **Setting:** Prison and homeless centre, Texas, US. **Sample characteristics:** 22,920 jailed inmates; 822 homeless persons. **Economic analysis data sources:** Collected by researchers (homeless programme); monthly reports compiled by	**Method of allocation:** NA **Intervention/s description:** <u>Jail programme</u>: 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 offered as appropriate. Medically licensed staff directly observed all TB therapy. <u>Homeless programme</u>: outreach effort which includes on-site TB symptom check, CXR, TST and medical evaluation. Tarrant County Public Health Department staff (who	**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 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	**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 LTBI may have been prescribed for reasons other 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).	**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 **Source of funding:** Center for Disease Control and Prevention.

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:** **Internal validity:** NA **External validity:** NA **Quality appraisal economic studies:** **Quality score:** + **Applicability:** +	the Tarrant County Public Health Department (jail programme); available statistics (additional cost data).	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:** **Total:** N = 23,740. **Intervention:** N = 22,920 (inmates) and 822 (homeless). **Control**: NA **Baseline comparisons:** NR **Study sufficiently powered?** N/R	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	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 programme; 2,142 prison programme. <u>Homeless programme</u> 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. <u>Jail programme</u>*:* 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: Monney and Zellweger **Year:** 2005	**Source population/s:** Foreign-born residents and new entrants to Switzerland.	**Method of allocation:** TB screening policy in Switzerland naturally guided the allocation of groups. **Intervention/s**	**Primary outcomes:** Bacteriological and clinical presentation of TB. Outcomes relating to treatment were also	**Primary results:** *Bacteriological and clinical presentation* 197 patients were notified as having TB. Of these, 71 were asylum seekers	**Limitations identified by author:** The study is a retrospective and therefore relies on the medical records from hospitals and medical offices, where the accuracy of reporting is not

Citation: Monney, M., & Zellweger, J. P. (2005). Active and passive screening for tuberculosis in Vaud Canton, Switzerland. *Swiss Medical Weekly*, (135), 469–474.
 	
Aim of study: This study compared the bacteriological and clinical presentation of TB and the outcome of treatment in immigrants notified for TB after active screening at the border, with other patients diagnosed by passive screening.
 	
Study design: Retrospective cohort study
	Eligible population: People diagnosed with TB who were either individuals coming in at port of entry at Vaud Canton, Switzerland, foreign-born workers, or other foreign-born residents.
	
	Selected population: all foreign-born individuals who were notified as having TB after active or passive screening.
	
	Excluded population: children younger than 15 years and pregnant women were not screened.
	
	Setting: Port of arrival
	
	Sample characteristics:
	<u>Active screening (CXR plus TST):</u>
	21% female; median age = 26 years.
	
	<u>CXR only:</u>
		description:
		<u>Active screening:</u>
		Adult asylum seekers and other immigrants coming from countries other than the European Community, USA, Canada, Australia and New Zealand are actively screened at the port of entry with a TST and a CXR.
		
		Foreign workers from the same countries are screened with CXR only.
		
		It was unclear which professionals were conducting screening.
		
		Comparator/control/s description:
		<u>Passive screening:</u>
		Other immigrants such as foreign students, tourists and illegal immigrants, or Swiss nationals: TB is identified by passive screening only, when they seek medical treatment.
		
		Sample sizes:
		Total = N = 179.
			reported, but are not extracted here.
			
			Secondary outcomes: NR
			
			Method of analysis:
			
			Data were analysed with the non-parametric Wilcoxon-Mann-Whitney test for the duration of symptoms between actively and passively screened populations and with descriptive statistics for the proportion of symptom-free patients in both groups.
			
			Modelling method and assumptions: NA
			
			Time horizon: NA
				actively screened at the border; 35 were foreign workers identified by CXR alone, 34 were other immigrants detected by passive screening, and 39 were Swiss nationals.
				
				<u>Symptom-free at diagnosis:</u>
				Actively screened (asylum-seekers) = 49.3% asymptomatic; 95% CI 37.4% to 61.2%);
				Passively screened: 17.6% asymptomatic; 95% CI 10.3 to 24.9%.
				
				<u>Symptomatic at diagnosis:</u>
				Actively screened (asylum-seekers) = 51% symptomatic;
				foreign workers = 91% symptomatic;
				other immigrants = 71% of symptomatic;
				Swiss = 85% symptomatic.
				
				<u>Pulmonary TB cases who were smear or culture-positive:</u>
				actively screened (asylum-seekers) = 63.4% had positive smear or culture: 42.2% [CI 27.2–57.2] were asymptomatic overall; 22.2% [CI 9.6–34.8] of smear-positive were
					certain. The data depends on information reported by patients, which may be unreliable because of language barriers and cultural interpretations of health and disease.
					
					Recently infected immigrants arriving in Vaud Canton may have negative skin test results and a normal CXR and develop symptomatic TB at a later time. The authors assumed that this was an infrequent event as more new immigrants are detected on active screening than present in the years after entry.
					
					Some immigrants applying for asylum in Switzerland were already in the country before registering. The duration of stay in Switzerland is probably underestimated.
					
					Limitations identified by review team:
					The study reports on clinical and microbiological presentations of people already diagnosed with TB. As such, it does not allow a comparison of different strategies for the initial identification of people with TB.
					
					The way in which the groups were sampled resulted in

Type of economic analysis: NA **Economic perspective:** NA **Quality appraisal non-economic studies: + Internal validity: - External validity: +** **Quality appraisal economic studies: Internal validity:** NA **Applicability:** NA	Foreign workers: 37% female; median age = 34 years. Other immigrants: 56% female; median age = 31 years. **Economic analysis data source:** NA	**Intervention =** N = 71 (all were asylum seekers). **Control -** N = 108 (35 foreign workers; 34 other foreigners; 39 Swiss). **Baseline comparisons:** NR **Study sufficiently powered?** NR		asymptomatic. foreign workers = 74% had positive smear or culture; other immigrants = 65% had a positive smear or culture; Swiss nationals: 72% had a positive smear or culture. **Secondary results:** NR **Attrition details:** NR	differences in sample characteristics, for example the intervention group were asylum seekers while the control groups were a variety of foreign-born workers and other foreigners. **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: Mor et al. **Year:** 2008 **Citation:** Mor, Z., Lerman, Y., & Leventhal, A. (2008). Pre-immigration screening process and pulmonary tuberculosis among 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	**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 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.	**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 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 showed 10 mm induration or more. **Comparator/control/s description:** post-	**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 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.	**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 pre-immigration group compared with post-immigration; rate ratio for TB: 0.82 (p<0.01). Detection period: the difference between the mean number of days between immigration and TB diagnosis for the pre-immigration group was 193 days (S.D. 260) and for the post-immigration group was 487 days (S.D. 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;	**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 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

point of entry among Ethiopian immigrants in Israel. **Study design:** NA **Type of economic analysis:** cost-savings. **Economic perspective:** NR **Quality appraisal non-economic studies:** NA **Internal validity:** NA **External validity:** NA **Quality appraisal economic studies:** **Quality score:** - **Applicability:** +	**Sample characteristics:** Intervention group: mean age at immigration was 27.4 years (S.D. 20.1 years), mean age at diagnosis was 28.7 years (S.D. 20.3 years), sex ratio M:F was 1.04 and 13.8% were HIV positive. Control group: mean age at immigration was 28.8 years (S.D. 22.4 years), mean age at diagnosis was 29.4 years (S.D. 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	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 statistically significant differences. **Study sufficiently powered?** NR		p=0.002). Net direct savings in cost for pre-immigration screening was $449,817 for 5 years assuming that 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	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 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

	Ministry of Health Tariff figures in 2008.				

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Ormerod **Year:** 1998 **Citation:** Ormerod, L. P. (1998). Is new immigrant screening for tuberculosis still worthwhile? *Journal of Infection*, *37*(1), 39-40. **Aim of study:** To compare data on TB screening for immigrants entering the Blackburn, Hyndburn and Ribble Valley local government areas (UK), in	**Source population/s:** Immigrants to UK. **Eligible population:** NR **Selected population:** All immigrants entering Blackburn, Hyndburn and Ribble Valley local government areas (United Kingdom) in 1990-1994. **Excluded population:** NR **Setting:** NR **Sample characteristics:** 1990-1994 cohort**:** Pakistan = 1333; India = 604;	**Method of allocation:** Retrospective based on time period immigrants arrived. **Intervention/s description:** Port of Arrival (POA) system (1983-1988): forms completed to notify consultant in communicable disease control of new immigrants. FHSA system(1990-1994): list of new immigrants registered with Family Health Services Authority (FHSA) in addition to POA system. **Comparator/control/s description:** NA **Sample sizes:** **Total:** N = 3993. **Intervention**	**Primary outcomes:** Number screened and cases identified. Chemoprophylaxis and BCG vaccination rates. Chest clinic follow up. **Secondary outcomes:** NR **Method of analysis:** NR **Modelling method and assumptions:** NA **Time horizon:** NA	**Primary results:** <u>FHSA vs. POA system, 1990-1994:</u> 2,242 new immigrants were screened. Of these: POA system: identified (found) 898/2,242 individuals (40%); FHSA system: identified (found) 1,344/2,242 individuals (60%). <u>Case detection rate</u>: Overall, 10/2242 cases found (0.45%), five with active pulmonary disease: POA system identified 7/898 (0.78%); FHSA system identified 3/1,344 (0.22%) $p < 0.05$. <u>POA system, 1983-1988 (previous study)</u>: 55% of new immigrants were identified through POA forms.	**Limitations identified by author:** NR **Limitations identified by review team:** The author does not adequately report the descriptions of the interventions (POA and FHSA), making it difficult to replicate the study. The author does not report the setting in which the intervention takes place. The authors report a previous study on case detection rates from the POA system in 1983-1988. This was used to assess the comparative effectiveness of the POA and FHSA systems in 1990-1994, but no further details of the 1983-1988 cohort are reported, making such comparison difficult. **Evidence gaps and/or recommendations for future research:** NR

1983-1988 when the POA system was used and the program in 1990-1994 when the POA and FHSA programme was used. **Study design:** Prospective cohort study. **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal non-economic studies: - Internal validity:** - **External validity:** + **Quality appraisal**	other = 305. 1983-1988 cohort: most participants were from Indian subcontinent. **Economic analysis data source:** NA	POA system (1990-1994): N = 2242; FHSA system (1983-1988) N = 1691; **Control:** NA. **Baseline comparisons:** NR **Study sufficiently powered?** NR		<u>Case detection rate</u> = 0.65% of all immigrants. **Secondary results:** NR **Attrition details:** NR	**Source of funding:** NR

economic studies: **Quality score:** NA **Applicability:** NA					

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Pareek et al. **Year:** 2009 **Citation:** Pareek, M., White, P. J., Lalvani, A., & Garnett, G. P. (2009). Modelling the health impact and cost-effectiveness of screening new entrants to the UK for latent tuberculosis infection. *Journal of Infection*, *59*(6), S442.	**Source population/s:** New entrants to the UK. **Eligible population:** NA **Selected population:** NR (presumably hypothetical cohort). **Excluded population:** NA **Setting:** UK **Sample characteristics:** NR **Economic analysis data sources:** NR	**Method of allocation:** NA **Intervention/s description:** TST **Comparator/control/s description:** T-cell interferon gamma release assays (IGRA) with or without TST, done annually or every 3 years **Sample sizes:** NA **Total** **Intervention** **Control** **Baseline comparisons:** NA **Study sufficiently powered?** NA	**Primary outcomes:** monetary savings, cases averted. **Secondary outcomes:** NA **Method of analysis:** NA **Modelling method and assumptions:** compartmental/deterministic model of TB transmission. **Time horizon:** 20 years.	**Primary results:** Introducing screening (TST or T-cell interferon gamma release assays, IGRAs) for LTBI would reduce annual TB incidence by 9.45%. Implementing a 3-yearly TST + IGRA strategy would results in savings of £8,345,291 and 25,538 averted cases in the first 20 years. Implementing annual TST + IGRA would produce incremental cost-effectiveness ratio of £1,298 per case averted. The comparator was not clear. Implementing annual	**Limitations identified by author:** NR **Limitations identified by review team:** Very little detail about population and model. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** NR

Aim of study: To assess the health impact, and cost-effectiveness, of introducing screening for LTBI in new entrants to the UK. **Study design:** Economic evaluation. **Type of economic analysis:** cost-effectiveness. **Economic perspective:** NS **Quality appraisal effectiveness studies:** **Quality score:** N/A **External validity:** N/A **Quality appraisal**				IGRA would produce incremental cost-effectiveness ratio of £25,072 per case averted. The comparator was not clear. **Secondary results:** NA **Attrition details:** NA	

economic studies: **Quality score:** - **Applicability:** **+**					

Study Details	**Population and setting**	**Method of allocation to intervention/ comparator**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: Perlman et al. **Year:** 2001 **Citation:** Perlman, D. C., Gourevitch, M. N., Trinh, C., Salomon, N., Horn, L., & Des Jarlais, D. C. (2001). Cost-effectiveness of tuberculosis screening and observed preventive therapy for active drug	**Source population/s:** IDUs, US **Eligible population:** NA **Selected population:** NA **Excluded population:** NA **Setting:** A hypothetical cohort has been used to measure cost-effectiveness, modelled on data from a screening	**Method of allocation:** NA **Intervention/s description:** TB screening was offered to all participants during syringe-exchange sessions. They were offered tuberculin and anergy skin testing, underwent a staff-administered interview, and were offered HIV counselling and testing. Participants were asked to return 48–72 hours later, when they would receive $15 ($10	**Primary outcomes:** Costs associated with TB screening. Costs estimated for HIV-positive and HIV-negative patients, and for different levels of effectiveness of isoniazid. Note: other outcomes reported in the study that are not related to this review have not been extracted here. **Secondary outcomes:** Overall cost-effectiveness of providing a $25 monetary	**Primary results:** Costs (total and per activeTB case prevented): *3 year follow up, isoniazid 65% effective:* CXR adherence rate 31% (baseline model) with no incentive = 3 cases prevented; $103,078 TB costs prevented; $18,951 per case prevented; $46,226 net savings. CXR adherence rate of 50% with $25 cash = 4 cases prevented; $141,506 TB costs prevented;	**Limitations identified by author:** NR . **Limitations identified by review team:** None. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** National Institute on Drug Abuse.

injectors at a syringe-exchange program. *Journal of Urban Health*, *78*(3), 550-567. **Aim of study:** The authors aim to test whether the costs incurred by a program of TB screening (and Directly observed preventative therapy, DOPT) at a syringe exchange programme are lower than costs of identifying or treating cases of active TB that would have occurred in the absence of the intervention. The authors also examined	intervention conducted in the Lower East Side Needle Exchange Program (LESNEP) in New York City. **Sample characteristics:** NA **Economic analysis data source:** Published data.	cash and $5 transportation tokens). A monetary incentive of $25 aimed to increase adherence to referral for CXR screening was also provided. Screening was performed by specifically trained health educators. **Comparator/control/s description:** No intervention. **Sample sizes:** **Total:** NA **Intervention =** 1,000 hypothetical sample. **Control =** 1, 000 hypothetical sample. **Baseline comparisons:** NA **Study sufficiently powered?** NA	incentive for adherence to referral for screening CXRs. **Method of analysis:** NA **Modelling method and assumptions:** Cumulative costs were calculated from actual rates of adherence to each of the steps of TB screening. Costs include those for supplies, staff time and effort, incentives, screening CXRs, transportation to the off-site radiology facility, physician time to review of the CXRs, disposal of infectious waste and rental of the syringe-exchange storefront space. **Time horizon:** 3-year follow-up for data measuring costs associated with TB screening (primary outcome); and 5-year follow-up times for data relating to provision of monetary incentives	$21,684 per case prevented; $54,770 net savings. CXR adherence rate of 100% with $25 cash = 7 cases prevented; $256,789 TB costs prevented; $23,339 per case prevented; $93,416 net savings. *5 year follow up, isoniazid 65% effective:* CXR adherence rate 31% (baseline model) with no incentive = 3 cases prevented; $103,078 TB costs prevented; $18,951 per case prevented; $46,226 net savings. CXR adherence rate of 50% with $25 cash = 5 cases prevented; $179,934 TB costs prevented; $17,347 per case prevented; $93,199 net savings. CXR adherence rate of 100% with $25 cash =12 cases prevented;	

the potential impact of the addition of a monetary incentive on adherence to referral for screening CXRs for TST-positive individuals. **Study design:** NA **Type of economic analysis:** Cost-effectiveness. **Economic perspective:** Societal perspective. **Quality appraisal non-economic studies: Internal validity:** NA **External validity:** NA **Quality appraisal**			(secondary outcome).	$436,723 TB costs prevented; $13,614 per case prevented; $273,350 net savings. *3 year follow up, isoniazid 90% effective:* <u>CXR adherence rate 31% (baseline model) with no incentive</u> = 3 cases prevented; $141,506 TB costs prevented; $14,213 per case prevented; $84,654 net savings. <u>CXR adherence rate of 50% with $25 cash</u> = 5 cases prevented; $179,934 TB costs prevented; $17,347 per case prevented; $93,199 net savings. <u>CXR adherence rate of 100% with $25 cash</u> =11 cases prevented; $398,295 TB costs prevented; $14,852 per case prevented; $234,922 net savings. *5 year follow up, isoniazid*	

economic studies: **Quality score:** ++ **Applicability:** +				*90% effective:* <u>CXR adherence rate 31% (baseline model) with no incentive</u> = 4 cases prevented; $179,934 TB costs prevented; $14,213 per case prevented; $123,081 net savings. <u>CXR adherence rate of 50% with $25 cash</u> = 7 cases prevented; $256,789 TB costs prevented; $12,391 per case prevented; $170,054 net savings. <u>CXR adherence rate of 100% with $25 cash</u> = 16 cases prevented; $578,229 TB costs prevented; $10,211 per case prevented; $414,856 net savings. **Secondary results:** NA **Attrition details:** NA	

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Perlman et al. **Year:** 2003 **Citation:** Perlman, D. C., Friedmann, P., Horn, L., Nugent, A., Schoeb, V., Carey, J., Salomon, N., et al. (2003). Impact of monetary incentives on adherence to referral for screening chest X-rays after syringe exchange-based tuberculin skin testing. *Journal of Urban Health*, *80*(3), 428-437. **Aim of study:** To compare adherence to referral for CXRs among	**Source population/s:** IDUs in the US. **Eligible population:** IDUs who visited the Lower East Side Needle Exchange Programme, New York. **Selected population:** Patients with a positive tuberculin purified protein derivative (PPD) test, who had not previously completed a course of TB preventive therapy, and who did not have medical contraindications to isoniazid treatment of latent TB. **Excluded population:** NR **Setting:** Needle exchange programme, New York.	**Method of allocation:** Before and after study. **Intervention/s description:** From 1999 to 2001 a $25 incentive based on adherence to CXR referral was introduced in the needle exchange. **Comparator/control/s description:** From 1995 to 1998 IDUs were referred for CXR with no incentive. **Sample sizes:** **Total:** N = 177. **Intervention:** N = 58. **Control:** N = 119. **Baseline comparisons:** The cohorts were comparable in most demographic and clinical characteristics. Statistical differences were found in average age (38 in the no incentive group vs. 43 in the incentive group, p=.002)	**Primary outcomes:** Adherence to CXR referral. Time from referral to screening. **Secondary outcomes:** Factors associated with CXR adherence (within 7 days, 30 days, ever). **Method of analysis:** Univariate analysis: chi-square test for categorical data and *t* test for continuous data. Stepwise logistic regression analyses: to assess the independence of potential predictors of adherence to referral for screening CXRs. All baseline characteristics that showed a univariate P value less than 0.1 were selected for inclusion in the model. Pearson correlation coefficients were used to assess interactions among the variables.	**Primary results:** Adherence to CXR referral within 7 days: 46/58 (79%) in the incentive group compared with 17/119 (14%) in the no incentive group (P<0.0001; OR = 23; 95% CI = 9.5–57.0). Adherence to CXR referral ever was 48/58 (83%) in the intervention group compared with 41/119 (34%) in the control group (P < 0.0001; OR = 9.1; 95% CI = 3.9–22.0). Median time to obtaining a CXR was significantly shorter among the intervention group (2 days vs. 11 days in the control group, P < 0.0001). **Secondary results:** Factors associated with CXR adherence within 7 days: received incentive (P<0.0001; OR=22.9; 95% CI=10.1–52.0). Factors associated with CXR adherence within 30 days: received incentive (P<.0001; OR=15.3; 95%	**Limitations identified by author:** NR **Limitations identified by review team:** NR **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** National Institute of Drug Abuse.

IDUs before and after the implementation of monetary incentives. **Study design:** Before and after. **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal effectiveness studies: ++** **Internal validity:** ++ **External validity:** + **Quality appraisal economic studies:** **Quality score:** NA **Applicability:** NA	**Sample characteristics:** <u>No incentive group</u>:119 IDUs, average age 38; 70% male; ethnically mixed; 55% unstable housing; 83% unemployed; 67% health insured; 61% education 12th grade or higher; 82% not known HIV infected; 2/3 used heroin and cocaine in the last 6 months; 43% used alcohol to intoxication in the last 6 months; 57% not in drug treatment. <u>Incentive group</u>: 58 IDUs, average age 43; 59% male; ethnically mixed; 67% unstable housing; 93% unemployed; 64% health insured; 62% education 12th grade or higher; 86% not known HIV infected; 2/3 used heroin and cocaine in the last 6 months; 45% used alcohol to intoxication in the last 6 months; 59%	**Study sufficiently powered?** NR	**Modelling method and assumptions:** NA **Time horizon:** NA	CI=6.9–33.6). Factors associated with CXR adherence ever: received incentive (P<.0001; OR=9.7; 95% CI=4.3–21.9); unstable housing (P=.04; OR=2.2, 95% CI=1.05-4.6); having health insurance (P=.01; OR=2.8, 95% CI=1.2-6.2). **Attrition details:** NA	

	not in drug treatment. **Economic analysis data sources:** NA				

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Pilote et al. **Year:** 1996 **Citation:** **Aim of study:** To investigate the effectiveness of two interventions compared with usual care to improve the adherence of the homeless to screening appointments at a TB clinic. **Study design:** RCT **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal**	**Source population/s:** Homeless, US. **Eligible population:** Men and women who took part in a population-based survey of HIV and TB infections among the homeless population in San Francisco between June 1992 and April 1994. **Selected population:** Homeless men and woman with positive PPD results. **Excluded population:** NR **Setting:**.TB clinic, hospital setting. **Sample characteristics:** Across groups: Age, median: 39 to 40 years old; Male: 66% to 71%; Homeless > 1 year:44% to 53%;	**Method of allocation:** **Intervention/s description:** Monetary incentives: in addition to the bus token given in usual care, participants also received $5 if they came to the TB clinic. Participants were required to attend the appointment within three weeks of randomisation. Peer health adviser: in addition to the bus token given in usual care, participants were assigned to a peer who was a homeless person or living in unstable conditions. The peer adviser was responsible for accompanying the participant to the clinic. **Comparator/control/s description:** Usual care: appointments for chest X-ray and sputum culture at a TB clinic.	**Primary outcomes:** Adherence to a first follow-up appointment: appointments had to be kept within three weeks. Adherence was verified using medical records across groups but was verified by the peer health adviser or research assistant who provided the monetary incentives for those in the respective treatment groups. **Secondary outcomes:** Predictors of adherence. Note: cases of TB were reported but these were not reported by group and therefore not extracted here. **Method of analysis:** x^2 to measure differences in adherence between groups. Step-wise logistic regression model was used for those	**Primary results:** Adherence to a first follow-up appointment: Monetary incentive: 69/82 (84%); Peer health adviser: 62/83 (75%) Usual care: 42/79 (53%). Monetary incentive ($p < 0.001$) and peer health adviser ($p = 0.004$) were statistically superior compared with usual care. **Secondary results:** Predictors of adherence: Univariate analysis: Monetary incentive compared with usual care: OR = 4.7 (95% CI 2.2 to 9.8; $p < 0.001$); Peer health adviser compared with usual care: OR = 2.6 (95% CI 1.3 to 5.1; $p = 0.001$); Never injected drugs: adjusted OR = 2.5 (95% CI 1.3 to 5.0; p=0.007); Age ≥ 50: adjusted OR = 3.3 (95% CI 1.2 to 8.8; $p = 0.01$); Education was not statistically significant. Logistic regression	**Limitations identified by author:** The study may not be generalisable to the source population as the selected population had already agreed to be screened for the population survey and then to participate in the RCT. **Limitations identified by review team:** Adherence was measured by reviewing medical charts for all the groups but was further verified in the intervention arms by the peer health adviser or the individual providing the monetary incentive. This meant that adherence was more reliably measured in the treatment arms compared with usual care. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** From grants from the Kaiser Family Foundation, Palo, Alto, Calif; Acquired Immunodeficiency Syndrome Research Program, University of California; and from the National Institute on Drug Abuse.

effectiveness studies: ++ **Internal validity: +** **External validity: ++** **Quality appraisal economic studies:** **Quality score:** NA **Applicability:** NA	Ever in jail: 55% to 58%; Crack cocaine use ever: 50 to 56%; IDU ever: 32 to 37%. **Economic analysis data sources:** NA	Participants received the usual bus tokens for transportation. **Sample sizes:** **Total:** N = 244 **Intervention:** Monetary incentive: N = 82; Peer health adviser: N = 83. **Control:** N = 79. **Baseline comparisons:** Authors report that groups were comparable at baseline. **Study sufficiently powered?** NR	variables that had p≤0.10 associated with completing treatment (identified by first doing a, x^2 analysis). **Modelling method and assumptions:** NA **Time horizon:** NA	analysis: Statistically significant predictors of adherence were monetary incentives, peer health adviser, not injecting drugs and age 50 years or older. **Attrition details:** NR	

Study Details	**Population and setting**	**Method of allocation to intervention/ comparator**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: Puisis et al. **Year:** 1996 **Citation:** Puisis, M., Feinglass, J., Lidow, E., & Mansour, M. (1996). Radiographic screening for	**Source population/s:** Prison inmates in the US. **Eligible population:** Inmates at Cook County Jail, Chicago. **Selected population:** 46,711 inmates screened from March 1991 to	**Method of allocation:** before and after comparison. **Intervention/s description:** High speed chest X-ray screening. **Comparator/control/s description:** Mantoux TST with chest X-ray (not high-speed) for	**Primary outcomes:** Cases identified. False positives. Mean time from intake into jail to respiratory isolation. **Secondary outcomes:** Cost per case identified. Cost per new case identified (only for CXR).	**Primary results:** Class 3 active TB cases identified: TST = 26 positive from 46,711 tests (0.056%). CXR = 67 positive from 126,608 tests (0.053%); a further 19 by diagnostic work-up (86 cases of active TB). False positives: TST = 5,412 out of 46,711	**Limitations identified by author:** NR **Limitations identified by review team:** No baseline comparisons conducted; claim that "there is no evidence to suggest that [the increase in cases found] reflects an increase in disease prevalence" is not substantiated. No statistical tests conducted, therefore unable to compare the differences in outcomes between

tuberculosis in a large urban county jail. *Public health reports*, *111*(4), 330-334. **Aim of study:** To evaluate a programme of high speed radiographic screening for pulmonary TB at a large urban correctional institution. **Study design:** Before and after. **Type of economic analysis:** NA **Economic perspective:** NA **Quality appraisal effectiveness studies: - Internal validity: -**	February 1992; 126,608 inmates tested from March 1992 to February 1994. **Excluded population:** NA **Setting:** Jail, Chicago, US. **Sample characteristics:** NR **Economic analysis data sources:** NA	those with a positive TST reading and medical examination for those with active TB. Chest X-ray screening was conducted by a radiologist and medical examination by TB medical staff and physician. **Sample sizes:** **Total:** N = 173,319. **Intervention:** N = 126,608. **Control:** N = 46,711. **Baseline comparisons:** NR **Study sufficiently powered?** NR	**Method of analysis:** Simple comparison. **Modelling method and assumptions:** NR **Time horizon:** NR	tests (11.59%). CXR = 321 out of 126,608 tests (0.25%). Mean time from intake into jail to respiratory isolation: TST = 17.6 days ("often many weeks"). CXR = 2.3 days. **Secondary results:** CXR: Cost per case identified = $5,700. Cost per new case identified = $10,800. **Attrition details:** NR	the two screening groups. Different time periods used in the comparison groups; 12 months for radiographic screening and 24 months for TST. This would have allowed for greater TB detection in the latter group. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** NR

External validity: - **Quality appraisal economic studies:** **Quality score:** NA **Applicability:** NA					

Study Details [30791]	**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*	**Source population/s:** Substance users in the US. **Eligible population:** Substance users undergoing TB treatment in Chicago. **Selected population:** Inclusion criteria: 1) assigned to West Garfield TB nursing station, which was where the primary	**Method of allocation:** Random number sequence assigned to intervention/control, then allocation concealment via sequentially numbered envelopes. **Intervention/s description:** Enhanced model: two person mixed-gender team of indigenous case managers who provided DOT. Indigenous case	**Primary outcomes:** Contact tracing: proportion becoming "extensively interviewed contacts" (EICs). Other primary outcomes of TB treatment completion and treatment compliance not reported here. **Secondary outcomes:** Changing HIV and TB risk behaviours.	**Primary results:** Contact tracing: 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	**Limitations identified by author:** Small sample size and high dropout rate limited the ability to detect changes that may have been small but significant. **Limitations identified by review team:** It is unclear how much of the difference in contact identification was because of the use of indigenous staff, and how much was due to the use of case management itself. **Evidence gaps and/or recommendations for future**

(PhD Thesis). University of Illinois at Chicago, Chicago, Illinois. **Aim of study:** To compare the effectiveness of the Indigenous Leader Outreach Model (ILOM) with standard TB control among substance users in treatment outcomes and contact tracing. **Study design:** RCT **Type of economic analysis:** NA **Economic perspective:** NA	Standard Chicago Department of Public Health (CDPH) nurse case management was located, 2) at least 18 years of age, 3) had used an illicit drug in the 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 the criteria above. **Setting:** Chicago, US (October 1996 to July 2000). **Sample characteristics:** 61% African	managers were recruited from former members of the target population, with the aim of increasing access to drug and alcohol users, increase awareness in this group about TB, assist clients to assess their risk, reinforce behaviour change and encourage preventive behaviour among group members. Outreach members worked in the community to offer education and medical care. **Comparator/control/s description:** Standard Chicago Department of Public Health (CDPH) approach: one public health worker who performed DOT, with limited case management provided by a nurse case manager. **Sample sizes:** **Total:** N = 102. **Intervention:** N = 53. **Control:** N = 49.	TB knowledge. Sense of TB stigma among adult substance users with TB in Chicago [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	standard arm (23% vs. 12%, p=.001). Overall, there were 99 EICs in the intervention group, of whom 47completed follow-up interviews, and 27 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 blood drawn for HTV-testing, and 6) did not have active TB. **Secondary results:** NA	**research:** **Source of funding:** NR

Quality appraisal effectiveness studies: ++ **Internal validity:** ++ **External validity:** + **Quality appraisal economic studies:** **Quality score:** NA **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 six months at their own or partner's house or apartment; leading source of income (20%) was benefits from the VA, disability, and SSI; mean monthly income from all sources was $746 (median $511); 56% had a CXR at time of diagnosis that was consistent with active TB; injecting drug use was low (5%), freebasing cocaine or crack, smoking marijuana, 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.	**Baseline comparisons:** No significant differences in gender, race, education, risk behaviours, TB knowledge, or TB stigma. **Study sufficiently powered?** The study had 76% power to detect a 20% difference in completion rates between the two arms.		**Attrition details:** 100 cases were eligible and consented to participate. Of these, 6 were found after randomisation to not have active TB and 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%).	

	Economic analysis data sources: NA				

Study Details	Population and setting	Method of allocation to intervention/ comparator	Outcomes and methods of analysis:	Results	Notes
Authors: Schwartzman et al. **Year:** 2005 **Citation:** Schwartzman, Kevin, Oxlade, O., Barr, R. G., Grimard, F., Acosta, I., Baez, J., Ferreira, E., et al. (2005). Domestic Returns from Investment in the Control of Tuberculosis in Other Countries. *New England Journal of Medicine*, *353*(10), 1008-1020. **Aim of study:**	**Source population/s:** legal immigrants, undocumented migrants and temporary visitors from Mexico in the US. Secondary analyses looking at legal immigrants, undocumented migrants and temporary visitors from Haiti and Dominican Republic to the US. **Eligible population:** NA **Selected population:** NA **Excluded population:** NA **Setting:** NR **Sample characteristics:**	**Method of allocation:** NA **Intervention/s description:** DOTS expansion: an expanded DOTS programme in Mexico plus radiographic screening before entering the US. TST screening: TST in Mexico plus radiographic screening before entering the US. **Comparator/control/s description:** Radiographic screening: current practice of radiographic screening and TB control in Mexico. **Sample sizes:** **Total:** estimated that over the 20 year period 35.4 million migrants would enter the US	**Primary outcomes:** Cases of active TB detected. Cases of TB averted. TB-related death. Costs (direct and indirect). **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method and assumptions:** Decision-analysis model using multiple Markov processes. 3% discount rate. 2003 US dollars. Modelling cost of radiographic screening: cost of screening per person, $16.73; cost of medical evaluation per person if result	**Primary results:** <u>Radiographic screening</u> Cases of active TB detected: 47,610. TB-related death: 5,245. Total direct costs: $1,985 million. Total indirect costs: $632 million. Total indirect and direct costs: $2,617 million. <u>TST screening</u> Cases of active TB averted (compared with radiographic screening alone): 401. Deaths prevented: 30. Total direct costs: $2,245 million. Added direct cost (compared with radiographic screening	**Limitations identified by author:** The authors state that there was some uncertainty surrounding some parameters used in the model. These included the assumption that the incidence of TB would decrease by 6% annually. This figure was taken from the rate of decline found in Peru after expansion of a DOT programme. However, the expansion of the DOT programme would have remained cost-saving unless the decline was less than 1.2% annually. Another uncertainty noted by the authors was that the patterns of migration would remain constant over 20 years. However, a sensitivity analysis demonstrated that the prevalence of migrants could have dropped to one-third of the estimated values and the expansion of the DOT programme would have remained cost-saving. The model did not consider the secondary spread of TB,

To investigate the health-related outcomes and costs of adding a directly observed treatment, short-course (DOTS) programme in Mexico or a TST to the standard radiographic screening to immigrants in the United States. **Study design:** NA **Type of economic analysis:** cost-saving. **Economic perspective:** societal. **Quality appraisal non-economic studies: Internal**	Modelling assumptions for the sample from Mexico: mean age of 27 years for legal immigrants, 29 years for undocumented migrants and 35 years for temporary visitors; prevalence of LTBI was 6.3% for legal immigrants, 6.3% for undocumented migrants and 6.9% for temporary visitors; prevalence of HIV infection was 0% in legal immigrants and 0.3% for undocumented migrants and temporary visitors; prevalence of underlying MDR infection was 2.4% for all the groups; and average income in the 5th year after entry was \$18,054 for legal immigrants, \$14,443 for undocumented migrants and \$0 for temporary visitors. **Economic analysis data source:**	from Mexico. **Intervention:** N/R **Control:** N/R **Baseline comparisons:** NA **Study sufficiently powered?** NA	abnormal, \$144.36 Modelling cost of TST: cost of screening per person, \$16.51; cost of medical evaluation per person if test is positive, \$100.44. Modelling cost of treatment per person, \$281.69. Modelling costs of initial DOTS expansion: \$34.9 million; costs of antituberculosis drugs in Mexico for 20 years, \$2.8 million. Modelling costs of active TB: direct costs per person \$36,045; and indirect costs \$2,262. Sensitivity analyses varied all the modelling assumptions. Subgroup analyses on the migrants from Haiti and Dominican Republic. **Time horizon:** 20 years.	alone): \$260 million Total indirect costs: \$701 million. Added indirect costs (compared with radiographic screening alone): \$69 million. Added indirect and direct costs (compared with radiographic screening alone): \$329 million. <u>DOTS expansion</u> Cases of TB averted (compared with radiographic screening alone): 2,591. Deaths prevented: 349. Total direct costs: \$1,901 million. Net savings on direct costs (compared with radiographic screening alone): \$84 million. Total indirect costs: \$608 million. Net savings on indirect costs (compared with radiographic screening alone): \$24 million.	however by excluding this, it would have underestimated the cost-savings of the DOTS programme. Lastly, the costs of the DOT programme were uncertain but were taken from the costs of a similar programme in Ecuador, and the effects of varying these costs were calculated in a sensitivity analysis. **Limitations identified by review team:** none in addition to the above. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** grant from the Rockefeller Foundation.

validity: NA **External validity:** NA **Quality appraisal economic studies:** **Quality score:** ++ **Applicability:** +	Various published resources for characteristics of the sample. Costs for the DOT expansion came from those derived from an equivalent expansion project in Ecuador; drugs expenditure from WHO incidence estimates and drug prices in the Global Drug Facility.			Net savings on indirect and direct costs: $108 million. Sensitivity analyses demonstrated that net savings would have occurred even if the US government doubled its initial investment for the DOT programme, or paid for antituberculosis drugs for all new and retreated cases in Mexico for all 20 years, or if the number of migrants was only 33% of the current levels. Likewise, if the number of migrants entering the US or the prevalence of HIV infection, LTBI or drug resistance was higher than estimated, net savings would have been greater. **Secondary results:** <u>Radiographic screening</u> Cases of active TB detected: 7,349 from Haiti and 4,460 from Dominican Republic. Total direct costs: $278 million for migrants from Haiti and $171 million for migrants from Dominican Republic.	

				Total indirect costs:$106 million for migrants from Haiti and $61 million for migrants from Dominican Republic. Total indirect and direct costs: $384 million for migrants from Haiti and $232 million for migrants from Dominican Republic. <u>TST screening</u> Cases of TB prevented (compared with radiographic screening alone): 213 from Haiti and 102 from Dominican Republic. Added direct cost (compared with radiographic screening alone): $64 million for migrants from Haiti and $45 million for migrants from Dominican Republic. Added indirect costs (compared with radiographic screening alone): $10 million for migrants from Haiti and $9 million for migrants from Dominican Republic. Added indirect and direct costs (compared with	

				radiographic screening alone): $74 million for migrants from Haiti and $54 million for migrants from Dominican Republic. <u>DOTS expansion</u> Cases of TB prevented (compared with radiographic screening alone): 342 from Haiti and 248 from Dominican Republic. Net savings on direct cost (compared with radiographic screening alone): $9 million for migrants from Haiti and $5 million for migrants from Dominican Republic. Net savings on indirect costs (compared with radiographic screening alone): $4 million for migrants from Haiti and $2 million for migrants from Dominican Republic. Net savings on indirect and direct costs (compared with radiographic screening alone): $13 million for migrants from Haiti and $7 million for migrants from Dominican Republic.	

				Attrition details: NA	

Study Details	**Population and setting**	**Method of allocation to intervention/ comparator**	**Outcomes and methods of analysis:**	**Results**	**Notes**

Authors: Schwartzman and Menzies
 	
Year: 2000
 	
Citation: Schwartzman, K., & Menzies, D. (2000). Tuberculosis screening of immigrants to low-prevalence countries. A cost-effectiveness analysis. *American Journal of Respiratory & Critical Care Medicine*, *161*(3), 780-789.
 	
Aim of study: To model the cost-
	Source population/s: Immigrants to Canada.
	
	Eligible population: NA
	
	Selected population: 3 simulated cohorts of 20-year-old immigrant applicants to Canada.
	
	Excluded population: NA
	
	Setting: Canada.
	
	Sample characteristics:
	<u>Population 1</u>: 50% TB infection; 10% HIV infection; sub-Saharan Africa.
	
	<u>Population 2</u>: 50% TB infection; 1% HIV infection; South-East
		Method of allocation: NA
		
		Intervention/s description: 1) Mass X-ray screening; 2) mass tuberculin skin test screening.
		
		Comparator/control/s description: no screening/ passive case detection.
		
		Sample sizes: NA
		Total
		Intervention
		Control
		
		Baseline comparisons: see sample section.
		
		Study sufficiently powered? NA
			Primary outcomes: Active TB cases per 1,000 population. Total cost per 1,000 population. Incremental cost per case prevented. Expected years lived.
			
			Secondary outcomes: NR
			
			Method of analysis: cost-effectiveness modelling; one-way sensitivity analysis.
			
			Modelling method and assumptions: Markov models, with projection over 20 years. 3% discount rate for all future expenditures and outcomes. For all Markov processes, a half-cycle correction was used.
			
			<u>Population</u>
				Primary results:
				<u>No screening</u>:
				Pop1:
				active TB cases per 1,000 = 37.4;
				total cost per 1,000 = $332,020.
				
				Pop2:
				active TB cases per 1,000 = 24.6;
				total cost per 1,000 = $218,250.
				
				Pop3:
				active TB cases per 1,000 = 2.5;
				total cost per 1,000 = $21,820.
				
				<u>CXR screening</u>
				(incremental costs relative to no screening):
				Pop1:
				active TB cases per 1,000 = 35.8;
				total cost per 1,000 = $338,310;
				incremental cost per case prevented = $3,943.
					Limitations identified by author: NR
					
					Limitations identified by review team: hypothetical cohorts, lack of varied baseline conditions.
					
					Evidence gaps and/or recommendations for future research: NR
					
					Source of funding: NS

effectiveness of chest radiography and TST for TB prevention among immigrants.
 	
Study design: Economic evaluation.
 	
Type of economic analysis: Cost-effectiveness.
 	
Economic perspective: Third-party payers (federal and provincial governments).
 	
Quality appraisal effectiveness studies: Internal validity: NA **External validity:** NA
 	
Quality appraisal economic studies:
	Asia.
	
	<u>Population 3</u>: 5% TB infection; 1% HIV infection; Western Europe.
	
	Economic analysis data sources: Base assumptions were based on pre-existing epidemiological and effectiveness research, epidemiological approximation methods, or on arbitrary choices when no data was available.
	
	Costs were based on annual reports of the Montreal Chest Institute and Royal Victoria Hospital, and physician fees set by the Quebec health insurance board.
			<u>assumptions:</u>
			For population 1 and 2, prevalence of TB infection was assumed to be 50%, and 5% for population 3. Prevalence of HIV infection was assumed to be 10% for population 1, and 1% for populations 2 and 3.
			
			<u>Intervention assumptions:</u>
			In intervention 2, it is assumed that anergic individuals with active TB or with tuberculous infection are always missed, and that prophylaxis may given to subjects with false-positive tuberculin test results.
			
			<u>Base assumptions:</u>
			Base assumptions were based on pre-existing epidemiological and effectiveness research, epidemiological approximation methods, or on arbitrary choices when no data was available. Assumptions were
				Pop2:
				active TB cases per 1,000 = 23.4;
				total cost per 1,000 = $231,430;
				incremental cost per case prevented = $10,627.
				
				Pop3:
				active TB cases per 1,000 = 2.3;
				total cost per 1,000 = $51,170;
				incremental cost per case prevented = $236,496.
				
				<u>TST screening</u>
				(incremental costs relative to X-ray screening):
				Pop1:
				active TB cases per 1,000 = 32.8;
				total cost per 1,000 = $436,390;
				incremental cost per case prevented = $32,601.
				
				Pop2:
				active TB cases per 1,000 = 21.7;
				total cost per 1,000 = $342,730;
				incremental cost per case prevented = $66,759.
				
				Pop3:
				active TB cases per 1,000	

Quality score
++
Applicability
+
			made about HIV-related mortality at early and later stage, prevalent cases of active TB, TB-associated mortality, risks of reactivation of TB infection based on HIV status, secondary transmission of TB, proportion of further investigation following CXRs, sensitivity and specificity of screening tests, medication use and side effects.
			
			<u>Cost and probabilities of hospitalisation:</u>
			All cost estimates were expressed in 1997 Canadian dollars. Costs were based on annual reports of the Montreal Chest Institute and Royal Victoria Hospital, and physician fees set by the Quebec health insurance board. Physician and personnel costs, equipment and supplies, medications, hospital bed costs, and overheads were included.
				= 2.2;
				total cost per 1,000 = $62,640;
				incremental cost per case prevented = $68,799 (extended dominance over radiographic screening strategy. The incremental cost of TST compared with no screening is $140,352 per active case prevented).
				
				Outcomes and costs with modelling of secondary active cases.
				
				<u>No screening</u>:
				Pop1:
				active TB cases per 1,000 = 60.6;
				total cost per 1,000 = $418,370.
				
				Pop2:
				active TB cases per 1,000 = 39.9;
				total cost per 1,000 = $275,840.
				
				Pop3:
				active TB cases per 1,000 = 4.0;
				total cost per 1,000 = $27,580.
				
				<u>CXR screening</u>:
				Pop1:
				active TB cases per 1,000	

			Hospital admission rates were estimated based on data from six Montreal-area hospitals.
			
			<u>The following cost estimates were made</u>: contact investigation was $694 per index case, with an additional $365 per infected contact placed on prophylaxis. The combined cost of contact investigation and follow-up was assumed to be $1,970 for each passively diagnosed and $1,241 for each actively diagnosed TB case. Secondary cases of active TB were included and were assumed to be identified passively.
			
			<u>Sensitivity analyses:</u> One-way sensitivity analyses were run. HIV infection prevalence was assumed to be 10% and TB infection prevalence was estimated at 50%.
				= 53.5;
				total cost per 1,000 = $398,870;
				incremental cost per case prevented = cost saving.
				
				Pop2:
				active TB cases per 1,000 = 34.0;
				total cost per 1,000 = $266,940;
				incremental cost per case prevented = cost saving.
				
				Pop3:
				active TB cases per 1,000 = 3.4;
				total cost per 1,000 = $54,910;
				incremental cost per case prevented = $46,099 (relative to no screening).
				
				<u>TST screening</u> (incremental costs relative to X-ray screening):
				Pop1:
				active TB cases per 1,000 = 49.2;
				total cost per 1,000 = $492,840;
				incremental cost per case prevented = $21,580.
				
				Pop2:
				active TB cases per 1,000 = 31.5;
				total cost per 1,000 =	

			Time horizon: 20 years.	$375,420;
				incremental cost per case prevented = $43,069.
				
				Pop3:
				active TB cases per 1,000 = 3.2;
				total cost per 1,000 = $65,930;
				incremental cost per case prevented = $43,769 (extended dominance over radiographic screening strategy. The incremental cost of TST compared with no screening is $45,404 per active case prevented).
				
				Note: all estimates in 1997 Canadian dollars.
				
				Secondary results:
				NR
				Attrition details: NA	

Study Details	**Population and setting**	**Method of allocation to intervention/control**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: S. Sciortino et al. **Year:** 1999 **Citation:** Sciortino, S.,	**Source population/s:** foreign-born immigrants (from developed and non-developed countries) to US.	**Method of allocation:** Retrospective, based on type of notification participants received. **Intervention/s description:**	**Primary outcomes:** Period prevalence of TB. Degree of infectiousness.	**Primary outcomes:** 3.5% (95% CI 3.3% to 3.8%) of all persons with a B notification were reported to have active TB within one year of arrival.	**Limitations identified by author:** retrospective design, lack of complete evaluation and follow-up information for B notification group, possibility that the B notification database failed to identify all patients. Some

Mohle-Boetani, J., Royce, S. E., Will, D., & Chin, D. P. (1999). B notifications and the detection of tuberculosis among foreign-born recent arrivals in California. *International Journal of Tuberculosis & Lung Disease*, *3*(9), 778-785. **Aim of study:** To assess the effectiveness of the B notification program for detecting TB among recent foreign-born arrivals in California. **Study design:** Retrospective cohort study. **Type of economic**	**Eligible population:** all foreign-born visa holders with a B notification . B notification is for prospective immigrants from high-risk countries, screened before departure. Adults with CXR signs of active TB but negative sputum culture are given B1 notification; those with X-ray signs of inactive infection are given B2 notification. Children under 15 are tested if they are close contacts of a case or have symptoms of TB. **Selected population:** Those who arrived in California from Jan 1992 to Sept 1995, including foreign-born persons, with or without a B notification, who were in the US for one year or less, with verified cases of TB, either pre-existing or	Immigrants from high-risk countries arriving in California between January 1992 and September 1995 were screened with chest radiography at their home country before departure to the US. If radiography was abnormal, sputum samples were collected for AFB. Those with negative smears were permitted entry. Upon entering the US, those under the B notification program were required to report to a local health department for evaluation of TB. **Control/comparison/s description:** Cases of TB detected in immigrants between January 1992 and September 1996 (B notification cases were tracked from this database) **Sample sizes:** 27,412 with a B notification, of whom 970 were reported with active TB.	Time to reporting of TB. **Method of analysis:** Chi-squared; t-test; multivariate logistic regression. **Modelling method and assumptions:** NA **Time horizon:** NA	Of all 2,547 foreign-born cases of active TB reported within one year of arrival, 38.1% had a B notification. Of all recent arrivals with TB, 80% came from four countries (the Philippines, Vietnam, China and Mexico.) The prevalence of B notification holders among recent arrivals with TB from the Philippines, Vietnam or China was more than fifty times greater than the prevalence among those from Mexico. Among the 2,210 recent arrivals with TB who were adults (>15 years), those with a B notification were more likely to have pulmonary TB (prevalence ratio [PR] = 1.12, 95% CI 1.10 to 1.15), less likely to have smear-positive pulmonary disease (PR=0.32, 95% CI 0.26 to 0.39) and were reported to have TB sooner after their arrival in the US compared with those with no B notification (mean of 3.2 months, compared with 4.7 months without B	patients may have moved out of California before being diagnosed with TB. Some other possible gaps in the data collected. **Limitations identified by review team:** Limited description of intervention. Does not report proportion of people with B notification who received treatment for LTBI soon after arrival. Unclear how many immigrants with TB who did not have B notification were actually screened before migration and had normal results, or how many were not screened. As such, difficult to determine effectiveness of B notification programme. **Evidence gaps and/or recommendations for future research:** Other methods of screening for TB among recent foreign-born arrivals are needed. Studies which aim to determine if overseas screening has occurred but failed to detect disease are also needed. **Source of funding:** California Department of Health

analysis: NA **Economic perspective:** NA **Quality appraisal non-economic studies: + Internal validity:** ++ **External validity:** + **Quality appraisal economic studies: Quality score:** NA **Applicability:** NA	acquired in the US. Two databases were matched to identify all persons with a B notification who were reported to have active TB within one year of their arrival in the US from January 1992 to September 1996. 1st database: 27,412 persons with a B notification who had California as their destination and who arrived in the US from January 1992 to September 1995. After 1 October 1994, the class of B notification (whether B1 or B2) was included in the database. 2nd database: 2,547 foreign-born persons who arrived in the US from January 1992 to September 1995 and who were reported to have active TB in California	2,547 recent arrivals reported with active TB, of whom 970 had B notification. **Baseline comparisons:** Some important differences in region and country of origin. Persons from Latin America comprised 28.3% of all recent arrivals with TB, though only 1.7% entered the US with a B notification. **Study sufficiently powered?** NA		notification, p = 0.001). 60% of the TB cases among recent foreign-born arrivals were not identified by B notification. The B notification programme was unable to identify 87% of the smear-positive pulmonary TB cases in adults, and it failed to identify 99% of highly infectious cases among Latin Americans. **Attrition details:** NA	Services, Tuberculosis Control Branch, Berkeley, California, USA.

	within one year of arrival (reporting from January 1992 to the end of September 1996). **Excluded population:** illegal immigrants, temporary visitors to US, non-immigrant workers. **Sample characteristics:** **B notification**: 27,412 with a B notification, 2,547 recent arrivals with TB (970 of whom had B notification). Visa type: Refugee : 4,971; Immigrant : 20,760; Other: 1,681. Class of B notification: B2: 3,107; B1: 2,663. Sex: Female: 12,791; Male: 14,621.				

	Age group (years): <15: 789; 15–24: 1,889; 25–44: 6,411; 45–64: 11, 758; 65+: 6,565. Region of origin: Latin America: 1,182; Asia/Pacific Islands: 24,834; Other: 1,396. Country of origin: Mexico: 967; Philippines: 9,975; Vietnam: 9,365; China: 3,662; Other: 3,443. **2,547 recent arrivals with TB:** Sex: Female: 1,019; Male: 1,528. Age group (years): <15: 337; 15–24: 435; 25–44: 649; 45–64: 627; 65+: 499. Region of origin: Latin America: 722; Asia/Pacific Islands: 1,714; Other: 111.				

	Country of origin: Mexico: 598; Philippines: 727; Vietnam: 586; China: 149; Other: 487. **Setting:** US, California.				

Study Details	**Population and setting**	**Method of allocation to intervention/ comparator**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: Tan et al. **Year:** 2008 **Citation:** Tan, M. C., Marra, C. A., Sadatsafavi, M., Marra, F., Moran-Mendoza, O., Moadebi, S., Elwood, R. K., et al. (2008). Cost-effectiveness of LTBI treatment for TB contacts in British Columbia.	**Source population/s:** TB contacts (those recently exposed to patients with infectious TB disease) in Canada from various subgroups including those who were born outside of Canada. **Eligible population:** NA **Selected population:** NA **Excluded population:** NA **Setting:** NR	**Method of allocation:** NA **Intervention/s description:** Test and treat: testing TB contacts with TST and treating those with a positive test. Treat all: not testing TB contacts but providing all contacts with preventative therapy. **Comparator/control/s description:** No screening: no screening of contacts; or offering preventative therapy to all contacts.	**Primary outcomes:** QALYs; Active TB cases prevented. **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method and assumptions:** Decision-analytic model. 3% discount rate. Took into account the risk of TB development, harms from LTBI treatment,	**Primary results:** The optimal policy was to test and treat all contacts, except non-aboriginal, non-household contacts aged over 10, for whom no screening was required; and to treat all household contacts younger than 10 years without screening. This would result in a cost of $463, for 4.6176 QALYs and 0.040 risk of TB reactivation per contact over 6 years. No Screening No Screening was the most cost-effective intervention for: 1. Foreign-born TB	**Limitations identified by author:** The study excluded some covariates such as previous TB disease and HIV infection, due to these being associated with a significantly different risk of TB compared with the other covariates used in the study. This therefore reduced the generalisability of the results. The study used a TST cut-off of 5 mm to determine positive cases of LTBI which has a high sensitivity but poor specificity. This means that there would have been false positives which would have impacted on the results, particularly on the risk of developing TB if LTBI was falsely diagnosed.

Value in Health, *11*(5), 842-852. . **Aim of study:** To examine the cost-effectiveness of LTBI screening and treatment for various subgroups, given known risk factors for active TB, using a hypothetical cohort. **Study design:** NA **Type of economic analysis:** cost-effectiveness **Economic perspective:** societal perspective and third party payer's governmental perspective were used in a	**Sample characteristics:** NR **Economic analysis data source:** risk of TB development for each subgroup was estimated from the Centre for Disease Control (a population-based registry in British Columbia). Mortality rates were taken from Canada Life Tables from the Statistics Canada Health Statistics Division. Utilities were taken from a previous study conducted by British Columbia Centre for Disease Control using the Short Form 6D and Health Utilities Index-3 for patients with active TB. Cost data was obtained from the British Columbia Centre for Disease Control, the British	**Sample sizes:** **Total:** NR **Intervention:** NR **Control:** NR **Baseline comparisons:** NA **Study sufficiently powered?** NA	and secondary transmission of the disease. **Time horizon:** 6 years.	contacts with no prior BCG vaccination and with non-household contacts, at a cost of $39 (Canadian Dollars) for 4.6208 QALYs and 0.0037active TB cases prevented. 2. Foreign-born TB contacts with a prior BCG vaccination and with non-household contacts, at a cost of $32 for 4.6210 QALYs and 0.0030 TB cases prevented. No Screening was not cost-effective for all other combinations: 3. Foreign-born TB contacts without prior BCG vaccination and with a household contact, at a cost of $654 for 4.6101 QALYs and 0.0613 TB cases prevented. 4. Foreign-born TB contacts with prior BCG vaccination and with a household contact, at a cost of $240 for 4.6173 QALYs and 0.0225 TB cases prevented. <u>Test and Treat</u> Test and Treat was the	The time horizon may have been too short as the risk of developing TB among those with LTBI remains for more than 19 years whilst the study only investigated a time horizon of 6 years. However a sensitivity analysis demonstrated that a longer time horizon did not impact greatly on the results. **Limitations identified by review team:** the authors reported results for foreign-born subgroups separately, but did not separate out those from countries with high prevalence of TB. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** NR

sensitivity analysis **Quality appraisal non-economic studies: Internal validity:** NA **External validity:** NA **Quality appraisal economic studies: Quality score:** ++ **Applicability:** +	Columbia Medical Association 2004 Medical Services Plan, and hospital costs from a large tertiary referral hospital in Vancouver. Other published studies were consulted.			most cost-effective intervention for: 1. Foreign-born TB contacts without prior BCG vaccination and with a household contact, at a cost of $495 for 4.6136 QALYs and 0.0403 TB cases prevented. The ICER per QALY and per TB cases prevented was dominant for both outcomes using this approach when compared with no screening. 2. Foreign-born TB contacts with prior BCG vaccination and with a household contact, at a cost of $247 for 4.6184 QALYs and 0.0147 TB cases prevented. The ICER per QALY ($6583) and per TB case prevented ($926) was neither dominant nor dominated when compared with no screening. Test and Treat was not cost-effective for all other combinations: 3. Foreign-born TB contacts with no prior BCG vaccination and with a non-	

				household contact, at a cost of $63 for 4.6210 QALYs and 0.0024 active TB cases prevented. The ICER per QALY ($161,059) and per case of TB prevented ($18,899) was neither dominant nor dominated when compared with no screening. 4. Foreign-born TB contacts with a prior BCG vaccination and with a non-household contact, at a cost of $108 for 4.6209 QALYs and 0.0019 TB cases prevented. The ICER per QALY dominated when compared with no screening. However the ICER per case of TB prevented ($73,211) was neither dominant nor dominated when compared with no screening. <u>Treat All</u> Treat All was not cost-effective in any of the four combinations: 1. Foreign-born TB contacts with no prior BCG vaccination and with non-household contacts, at a cost of $142 for 4.6207 QALYs and 0.0024 active	

				TB cases prevented. The ICER per QALY dominated when compared with Test and Treat. The ICER per case of TB prevented ($1,946,064) was neither dominant nor dominated when compared with Test and Treat. 2. Foreign-born TB contacts without prior BCG vaccination and with a household contact, at a cost of $544 for 4.6134 QALYs and 0.0401 TB cases prevented. The ICER per QALY dominated when compared with Test and Treat. The ICER per TB case prevented ($237,372) was neither dominant nor dominated when compared with Test and Treat. 3. Foreign-born TB contacts with a prior BCG vaccination and with non-household contacts, at a cost of $137 for 4.6208 QALYs and 0.0019 TB cases prevented. The ICER per QALY dominated when compared with test and treat. However the ICER per case of TB prevented ($6,610,521)	

				was neither dominant nor dominated when compared with Test and Treat. 4. Foreign-born TB contacts with prior BCG vaccination and with a household contact, at a cost of $273 for 4.6183 QALYs and 0.0147 TB cases prevented. The ICER per QALY dominated when compared with Test and Treat. The ICER per TB case prevented ($862,314) was neither dominant nor dominated when compared with Test and Treat. **Secondary results:** NR **Attrition details:** NA	

Study Details	**Population and setting**	**Method of allocation to intervention/control**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: Verver et al. **Year:** 2001 **Citation:** Verver, S.,	**Source population/s:** immigrants to the Netherlands from highly endemic countries.	**Method of allocation:** Retrospective, based on TB cases who were detected through different screening methods.	**Primary outcomes:** Severity of disease: proportion of cases with smear-positive disease. Duration of symptoms	**Primary outcomes:** Patients found through active screening were less often sputum smear-positive than patients detected passively, (OR=0.5, 95%CI 0.3–0.8).	**Limitations identified by author:** Recall bias was likely for estimation of duration of symptoms. The assumption that the reported period of symptoms represents the infectious period is not necessarily accurate,

Bwire, R., & Borgdorff, M. W. (2001). Screening for pulmonary tuberculosis among immigrants: estimated effect on severity of disease and duration of infectiousness. *International Journal of Tuberculosis & Lung Disease*, *5*(5), 419-425. **Aim of study:** To evaluate the impact of TB screening among recent immigrants on the severity of the disease at diagnosis and on the length of the infectious period. **Study design:** Retrospective cohort study	**Eligible population:** immigrants on the Netherlands TB Register (NTR). **Selected population:** immigrants from countries for which entry screening was mandatory, who had culture-positive pulmonary TB diagnosed within 30 months after arrival in the Netherlands, between 1993 and 1998. **Excluded population:** those with unknown duration of stay. **Sample characteristics:** 822 patients who were detected through passive case-finding (n=368/822; 45%) or screening (n= 454/822; 55%). **Screening group (N=454):** Gender: Male: 289 (64%)	**Intervention/s description:** Mandatory entry screening: All entrants from at-risk countries who intended to stay for longer than 3 months were referred for mandatory screening at a TB clinic (CXR followed by sputum smear and culture if the CXR shows any abnormality. Initial TST may have replaced X-ray in some cases). Immigrants were advised to present for voluntary screening every 6 months after entry for a further 2 years. **Control/comparison/s description:** Passive case finding: immigrants who had sought medical consultation because of symptoms, irrespective of prior screening history. **Sample sizes:** **Total:** N = 822; **Intervention:** N = 454; **Control:** N = 368;	and total infectious period prior to diagnosis. Hospitalisation rates; case fatality rates were measured, but are not reported in this review. **Method of analysis:** Comparisons between groups are summarised using odds ratios. Differences were tested using the chi-squared test and Wilcoxon non-parametric test. No adjustment made for important possible confounders at baseline other than legal/illegal status. **Modelling method and assumptions:** **Time horizon:** NA	Detection of cases through screening was less likely with increasing duration of stay. 302/454 (66%) of the screened group had been in the Netherlands for less than 6 months, compared with 114/368 (31%) of passively-detected cases. In contrast, 26% of passively detected cases had been resident for 24-30 months, compared with 6% of screened patients. Among the 708 (86%) of patients for whom there was information, those who participated in the screening were detected earlier and had a shorter duration of symptoms (p= 0.001) than those detected passively; mean duration of symptoms = 10.5 weeks (median = 7.5 weeks) for passive case detection compared with a mean of 4.2 (median = 0) weeks for screened patients, only 37% of whom had symptoms. Overall, it was estimated that 6-monthly screening would have reduced the infectious period prior to	however the authors assume this may have little influence on the results. **Limitations identified by review team:** Although the groups were similar at baseline, they were not identical, and there was no adjustment for such baseline differences, as well as no discussion of whether and how other confounding factors could have been minimised. Actual illegal immigrant population is difficult to evaluate. **Evidence gaps and/or recommendations for future research:** A cost-effectiveness analysis is needed to identify optimal duration and frequency of follow-up screening in the Netherlands. Follow-up screening for active TB may be compared with possible alternatives such as screening for and treatment of latent TB. **Source of funding:** Dutch Health Research and Development Council (ZON), Prevention Programme.

Type of economic analysis: NA **Economic perspective:** NA **Quality appraisal non-economic studies: + Internal validity:** + **External validity:** + **Quality appraisal economic studies:** **Quality score:** NA **Applicability:** NA	Female: 165 (36%) Age (years): <15: 20 (4%); 15–24: 154 (34%); 25–34: 183 (40%); 35–44: 67 (15%); 45–54: 14 (3%); 55+:16 (4%). Nationality: Somalia: 84 (19%); Morocco: 48 (11%); Other Africa: 73 (16%); Central and Eastern Europe & former USSR: 89 (20%); Turkey: 32 (7%); Latin America: 9 (2%) Legal status: legal: 439 (97%); illegal: 15 (3%). **Passive case detection group (N=368):** Gender: Male: 231 (63%) Female: 137 (37%) Age (years): <15: 11 (3%); 15–24: 130 (35%); 25–34: 144 (39%); 35–44: 44 (12%);	**Baseline comparisons:** Compared with people from Asia, patients from Eastern Europe and the former USSR were more likely to be detected through screening (OR= 2.70, 95% CI 1.58–4.62). However, patients from Somalia (OR=0.57, 95% CI 0.38–0.86) or Latin America (OR=0.23, 95% CI 0.10-0.52) were less likely to be detected by screening than people from Asia. Compared with legal immigrants, illlegal immigrants were less likely to be detected through screening (OR= 0.18 95% CI 0.10–0.32). **Study sufficiently powered?** NA		diagnosis from 3379 to 2355 weeks for the 322 patients identified by passive case detection, a reduction of 30% in the total infectious period, and a reduction of 34% for those who were smear-positive. **Attrition details:** NR	

	45–54: 18 (5%); 55+: 21 (6%). <u>Nationality:</u> Asia: 83 (22%); Somalia: 102 (27%); Morocco: 36 (10%); Other Africa: 68 (18%); Central and Eastern Europe & former USSR: 23 (6%); Turkey: 29 (8%); Latin America: 27 (7%). <u>Legal status:</u> legal: 309 (84%); illegal: 59 (16%). **Setting:** TB clinics, Municipal Health Services (MHS). **Economic analysis data source:** NA				

Study Details	**Population and setting**	**Method of allocation to intervention/ comparator**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: Watson et al. **Year:** 2007	**Source population/s:** Hard-to-reach groups in London.	**Method of allocation:** NA **Intervention/s description:** screening	**Primary outcomes:** prevalence of TB; diagnostic delay and infectivity; cases averted;	**Primary results:** <u>Prevalence of TB (estimated):</u> Overall: 267/100,000 (95% CI 190	**Limitations identified by author:** Recall bias is a potential limitation, but likely non-differential.

Citation: Watson, J. M., Abubaker, I., Story, A., Welfare, R., White, P., Garnett, G., Mugford, M., et al., others. (2007). *Mobile targeted digital chest radiography in the control of tuberculosis among hard to reach groups.* London: Health Protection Agency Centre for Infections; Department of Health. **Aim of study:** To evaluate the digital mobile X-ray unit (MXU) clinical and cost-effectiveness compared with passive case identification. **Study design:** Epidemiological	**Eligible population:** Homeless people, prisoners, IDUs, refugee and asylum seekers, and individuals in ethnic minority community settings. **Selected population:** 20,357 individuals in the groups above. **Excluded population:** NA **Setting:** London, UK. **Sample characteristics:** 5,024 homeless people; 9,020 prisoners; 558 IDUs; 2,861 refugees and asylum seekers; 2,894 ethnic community individuals. **Economic analysis data source:** mobile X-ray unit (MXU) unit costs were obtained from project accounts; unit costs for care from	of homeless, IDU, prisoners or refugees/asylum-seekers via mobile targeted digital chest radiography (MXU)between April 2005 and January 2007. It is not clear who performed the screening tests on participants. **Comparator/control/s description:** passive case detection (homeless, IDU or prisoners presenting with symptoms of TB) between 2004- January 2007, identified retrospectively from the 2003-04 TB profiling study, or prospectively from the same clinics as those used by screened cases. **Sample sizes:** **Total:** N = 288 **Intervention:** N = 43 **Control:** N = 245 **Baseline comparisons:** NA	cost of MXU programme; value of averted cases; NET cost to NHS ICER; cost per QALY. **Secondary outcomes:** NR **Method of analysis:** NA **Modelling method and assumptions:** cost-effectiveness was measured using ICERs and estimated costs per QALY. All costs were discounted at 3.5%. A case of active TB was assumed to cost £5,000 (standard NHS tariff cost) or £10,000 (assuming that cases in hard-to-reach groups are twice as expensive to treat as an average patient –previous research showed that homeless people with TB are four times more likely to be admitted to hospital	to 365/100,000); IDUs: 717 to 1,238/100,000; homeless: 338 to 536/100,000; prisoners: 200 to 273/100,000; refugees and asylum-seekers: 140 to 194/100,000; ethnic minority groups in the community: no cases detected. Diagnostic delay: MXU screening reduced diagnostic delay compared with passive detection (adjusted hazard ratio for delay =0.35, 95% CI 0.21 to 0.59, $p < 0.0001$). Delay in starting treatment: results presented graphically. All MXU-screened cases started treatment within 100 days of onset of symptoms, compared with fewer than 75% of passively-detected controls, significance not reported. Infectivity: MXU reduced infectivity compared with passive detection: 44% of cases smear-positive compared with 66% of passive	**Limitations identified by review team:** none. **Evidence gaps and/or recommendations for future research:** NR **Source of funding:** NR

and economic assessment; case-control study. **Type of economic analysis:** cost effectiveness. **Economic perspective:** NHS in London. **Quality appraisal non-economic studies: Internal validity:** NA **External validity:** NA **Quality appraisal economic studies: ++** **Quality score:** ++ **Applicability:** ++	national data sources and hospital finance departments; MXU resource use was taken from project data.	**Study sufficiently powered?** NA	compared with other patients). **Time horizon:** 10 years	detected controls (adjusted OR 0.35, 95% CI 0.15 to 0.81, p < 0.001). <u>Scenario 1</u>: current activity and follow-up (follow-up of homeless = 63% and prisoners = 73%); and MXU sensitivity = 80%: Over 10 years (2004-2013): Cases averted = 553.73; Cost of MXU Programme = £3,473,275; Value of averted cases (£5,000) = £2,266,090; Value of averted cases (£10,000)= £4,532,180; Net cost to NHS (£5K) = £1,207,184; Net cost to NHS (£10K) = -£1,058,906. Assuming TB treatment costs are £5,000 per case, the ICER is £2,180.11 the cost per QALY is £3,206.05 (£1,397.51 to £15,572.24). Assuming TB treatment costs are £10,000 per case the ICER is -£1,912.33 (so cost per QALY is negligible because the costs are negative and QALYS are positive).	

				[Alternative, hypothetical scenarios not extracted] **Secondary results:** NR **Attrition details:** NA	

Study Details	**Population and setting**	**Method of allocation to intervention/ comparator**	**Outcomes and methods of analysis:**	**Results**	**Notes**
Authors: Yates et al. **Year:** 2009 **Citation:** Yates, S., Story, A., & Hayward, A. C. (2009). Screening prisoners for Tuberculosis: What should the UK do? [Poster]. *Thorax*, 64(Suppl 4), A105-105. [supplemented with data provided by author]	**Source population/s:** prisoners, UK. **Eligible population:** prisoners in London. **Selected population:** those prisoners who volunteered/accepted offer for screening at prison. **Excluded population:** NR **Setting:** Mobile X-ray screening service in London prisons. **Sample**	**Method of allocation:** NA **Intervention/s description:** Symptom screening: Prisoners were screened for TB and data on five key symptoms compatible with active pulmonary TB were collected. It is not clear who performed the symptom screening on prisoners. **Comparator/control/s description:** Untargeted screening: Voluntary CXR.	**Primary outcomes:** Proportion of active pulmonary TB cases who would be missed if screening were restricted to symptomatic prisoners; the prevalence of active pulmonary TB in different symptom groups; and the number needed to screen (NNS). **Secondary outcomes:** NA **Method of analysis:** Data from the screened population (symptoms, active cases identified) was taken to estimate	**Primary results:** <u>Symptom: Cough (>3 weeks)</u> Number of prisoners with symptom: yes = 1,256; no = 4,360. Number of prison TB cases with symptoms: yes = 18; no = 12. Estimated prevalence of active pulmonary TB (per 100,000) = 594. Number needed to screen to identify one active case = 168. Proportion of prisoners needed to be screened = 22.36%. Proportion TB cases missed (if screened based on this symptom) = 40%. <u>Symptom: Night sweat</u> Number of prisoners with	**Limitations identified by author:** NR **Limitations identified by review team:** The study was limited as it was a retrospective study design exploring how many cases would have been identified if screening with a MXU was conducted on patients with symptoms present at the time of screening. However, the study assumes that professionals would have screened with a MXU if these symptoms were present, but in practice this may not occur. **Evidence gaps and/or recommendations for future research:** NR

Aim of study: This study aimed to assess the impact on case detection of limiting chest radiography to only those prisoners who had symptoms of TB. **Study design:** Comparative study. **Type of economic analysis:** **Economic perspective:** **Quality appraisal non-economic studies: - Internal validity:** + **External validity:** - **Quality appraisal economic studies:**	**characteristics:** Almost one-third (30%) of prisoners reported having slept rough in the last two years, 21% had spent time living in hostels for homeless people and 16% knew someone who previously had TB. 38% of prisoners originated from outside the United Kingdom. 71% reported accessing primary care services. Symptoms most frequently reported were cough (22%), night sweats (18%), weight loss (12%), fever (8%) and haemoptysis (4%). Thirteen per cent of prisoners reported cough plus at least one other symptom. **Economic analysis data source:** NA	**Sample sizes: Total =** 13,546 prisoners (only one cohort evaluated; looked at those who had a symptoms present at screening compared with those who did not have symptoms present at screening). **Intervention =** subset of 5,616 prisoners for whom data on symptoms were gathered between 2005-2007. **Control =** N/A **Baseline comparisons:** NR **Study sufficiently powered?** NR	screening outcomes if prisoners were screened by CXR based on symptoms alone. **Modelling method and assumptions:** NA **Time horizon:** NA	symptom: yes = 985; no = 4,628. Number of prison TB cases with symptoms: yes = 10; no = 20. Estimated prevalence of active pulmonary TB (per 100,000): 421. Number needed to screen to identify one active case = 238. Proportion of prisoners needed to be screened = 17.55% Proportion of TB cases missed (if screened by this symptom) = 66.67%. <u>Symptom: Fever</u> Number of prisoners with symptom: yes = 453; no = 5,159. Number of prison TB cases with symptoms: yes = 3; no = 27. Estimated prevalence of active pulmonary TB (per 100,000) = 274. Number needed to screen to identify one active case = 364. Proportion of prisoners needed to be screened = 8.07%. Proportion of TB cases missed (if screened by this	**Source of funding:** NR

Quality score: NA **Applicability:** NA				symptom) = 90.0%. <u>Symptom: Cough + 1 symptom:</u> Number of prisoners with symptom: yes = 703; no = 4,897. Number of prison TB cases with symptoms: yes = 13; no =17. Estimated prevalence of active pulmonary TB (per 100,000) = 765. Number needed to screen to identify one active case = 131. Proportion of prisoners needed to be screened = 12.55%. Proportion of TB cases missed (if screened by this symptom) = 56.67%. <u>Symptom: Weight loss</u> Number of prisoners with symptom: yes = 656; no = 4,960. Number of prison TB cases with symptoms: yes = 7; no = 23 Estimated prevalence of active pulmonary TB (per 100,000) = 442. Number needed to screen to identify one active case = 226. Proportion of prisoners needed to be screened =	

				11.68%. Proportion of TB cases missed (if screened by this symptom) = 76.67%. <u>Symptom: Haemoptysis</u> Number of prisoners with symptom: yes = 219; no = 5,389. Number of prison TB cases with symptoms: yes = 2; no = 28. Estimated prevalence of active pulmonary TB (per 100,000) = 378. Number needed to screen to identify one active case = 265. Proportion of prisoners needed to be screened = 3.91%. Proportion of TB cases missed (if screened by this symptom) = 93.33%. <u>Symptom: Any symptom</u> Number of prisoners with symptom: yes = 2004; no = 3,596. Number of prison TB cases with symptoms: yes =19; no =11. Estimated prevalence of active pulmonary TB (per 100,000) = 392. Number needed to screen to identify one active case = 255. Proportion of prisoners needed to be screened =	

				35.79%. Proportion of TB cases missed (if screened by this symptom) = 36.67%. <u>Summary</u> According to this data, restricting CXRs to prisoners with one or more of the symptoms listed here is likely to lead to many missed cases. **Secondary results:** NA **Attrition details:** NA	

11.0 Appendix D. Studies excluded at full text stage

Table D1. Studies excluded after full text screening.

Reference details	Abstract
Andre, M. et al., 2007. Transmission network analysis to complement routine tuberculosis contact investigations. *American Journal of Public Health*, 97(3), pp.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.
Badiaga, S., Raoult, D. & Brouqui, P., 2008. Preventing and controlling emerging and reemerging transmissible diseases in the homeless. *Emerging Infectious Diseases*, 14(9), pp.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.
Bandyopadhyay, T., Murray, H. & Metersky, M.L., 2002. Cost-effectiveness of tuberculosis prophylaxis after release from short-term correctional facilities. *Chest*, 121(6), pp.1771-1775.	BACKGROUND: There is poor adherence with tuberculosis preventive therapy among patients released from short-term correctional facilities, leading to recommendations against screening for latent tuberculosis infection (LTBI) in this setting. OBJECTIVES: To assess adherence to isoniazid preventive therapy (IPT) following release from short-term correctional facilities, and to estimate the cost-effectiveness of this practice. METHODS: Records of individuals referred for IPT from the Connecticut Department of Corrections to the City of Hartford Chest Clinic between January 1993 and June 1997 were reviewed. The data abstracted included demographics, adherence to IPT, and the duration of IPT completed before release from prison. An analysis was performed to determine the cost-effectiveness of this program. RESULTS: A total of 168 records were reviewed. The mean duration of IPT completed before release from prison was 8 weeks. Eighty-six subjects (57%) never came to clinic after release. Of the 64 subjects (43%) who attended clinic at least once, 35 subjects (55%) completed IPT and 29 subjects (45%) were unavailable for

	follow-up before completing therapy. Thirty-three of the 64 subjects (52%) who attended the clinic had to be restarted on IPT due to a prolonged lapse in therapy prior to the first visit. We estimate that $32,866 was spent on this program, but $42,093 in future costs associated with reactivation tuberculosis was prevented. CONCLUSIONS: Adherence with IPT is poor in patients released from short-term correctional facilities. Nonetheless, this program was cost-effective. An alternative strategy may be to screen for LTBI among inmates of short-term correctional facilities but withhold IPT in inmates expected to be released before therapy would be completed. Instead, these inmates could be referred to an appropriate clinic after release. Prophylaxis may be started in subjects who keep an initial clinic appointment after release.
Barnes, P.F. & Barrows, S.A., 1993. Tuberculosis in the 1990s. *Annals of Internal Medicine*, 119(5), pp.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 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]
Batki, S.L. et al., 2002. A controlled trial of methadone treatment combined with directly observed isoniazid for tuberculosis prevention in injection drug users. *Drug & Alcohol Dependence*, 66(3), pp.283-293.	Substance abuse is associated with high risk for tuberculosis (TB) and poor adherence to medication regimens. This study compared completion rates for isoniazid (INH) preventive therapy for injection drug users (IDUs) randomly assigned to methadone treatment combined with directly observed preventive treatment (DOPT) versus those assigned to routine TB clinic referral without methadone treatment. One hundred and eleven opioid-dependent patients with latent TB were assigned to one of three 6-month treatment conditions: standard methadone treatment including substance abuse counseling combined with daily INH DOPT (n=37); minimal methadone treatment without counseling, also combined with daily INH DOPT (n=35); or routine care referral to TB clinic for monthly INH supplies without DOPT and without methadone treatment (n=39). INH completion rates were 77.1% for minimal methadone and 59.5% for standard methadone, as compared with only 13.5% for routine care (P<0.0001). Mean duration of INH treatment retention was 5.7, 5.0 and 1.6 months, respectively (P<0.0001). TB incidence at 4-year follow-up was 0 of 54 subjects who completed preventive therapy versus 2 of 57 who failed to complete. One of these two had been assigned to routine care, and the other to minimal methadone. In conclusion, INH retention time and completion rates were significantly improved by methadone treatment combined with observed INH, whether or not substance abuse counseling was provided. The results of this study indicate that methadone treatment offers clear public health benefits when it is used to deliver preventive medical services.
Brassard, P. et al., 2006. Evaluation of a school-based tuberculosis-screening	CONTEXT. In countries with a low incidence of tuberculosis (TB), screening programs targeting recent immigrants from TB-endemic countries have been shown to be effective in further reducing TB incidence; however, evaluative data on some aspects of these programs remain sparse.

program and associate investigation targeting recently immigrated children in a low-burden country. *Pediatrics*, 117(2), p.e148.	OBJECTIVE. We sought to retrospectively evaluate a school-based screening program targeting children at high risk for TB infection in Montreal, Canada, as well as subsequently investigate family and household associates of the schoolchildren with latent TB infection (LTBI), based on adherence to LTBI therapy and cost-benefit analysis. DESIGN, SETTING, AND PARTICIPANTS. Newly arrived immigrant children (aged 4–18 years) in selected schools were screened for LTBI by using the tuberculin skin test (TST). The TST was defined as positive at an induration of 10 mm. Each child who tested positive on the TST was referred for medical evaluation. Family and household associates of the TST-positive child also were screened for LTBI. Classroom attendance sheets and medical charts were reviewed for 16 elementary and secondary schools that comprised the school-screening program of the Montreal Children's Hospital from 1998 to 2003. Medical charts of the child associates (<18 years old) who were screened were reviewed also. MAIN OUTCOME MEASURES. The main outcome measures were TST-positivity rate, rate of adherence to LTBI therapy, estimation of factors associated with adherence, and net cost/benefit of the school-screening and associate-investigation programs, both respectively and as a combined program, compared with the cost of passive treatment of TB disease. RESULTS. Of 2524 immigrant children screened, 542 (21%) were TST-positive. Of 342 children started on therapy, 316 (92%) demonstrated adequate adherence. The only predictor of adherence among the schoolchildren was having 2 family members brought in for TB screening (adjusted odds ratio: 2.0; 95% confidence interval: 1.3–3.3). There were 599 associates investigated from the 484 TST-positive schoolchildren seen at the TB clinic. Of 555 associates with TST results, 211 (38%) were found to be TST-positive. Of 136 TST-positive child associates, 131 were seen at the Montreal Children's Hospital TB clinic and had their chart reviewed. Of these, 108 (82%) were started on LTBI therapy, and 78 (79%) of 99 of those children with information complied adequately with their therapy. We found net benefits from both school-based screening and associate investigation, both as stand-alone programs and as 1 coordinated, targeted TB-screening program. CONCLUSION. We demonstrated the effectiveness, including cost-effectiveness, of a targeted, school-based screening program in a low-burden country and the extra benefit given by adding associates to such a program.
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), pp.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.

Burgos, M. et al., 2005. Treatment of multidrug-resistant tuberculosis in San Francisco: an outpatient-based approach. *Clinical Infectious Diseases*, 40(7), pp.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 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), pp.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.
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*	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);

Nursing, 1(3), p.78.	(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) 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), pp.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.
Chaisson, R.E. et al., 2001. A randomized, controlled trial of interventions to improve adherence to isoniazid therapy to prevent tuberculosis in injection drug users. *American Journal of Medicine*, 110(8), pp.610-615.	PURPOSE: To determine the effect of several interventions on adherence to tuberculosis preventive therapy. METHODS: We conducted a randomized trial with a factorial design comparing strategies for improving adherence to isoniazid preventive therapy in 300 injection drug users with reactive tuberculin tests and no evidence of active tuberculosis. Patients were assigned to receive directly observed isoniazid preventive therapy twice weekly (Supervised group, n = 99), daily self-administered isoniazid with peer counseling and education (Peer group, n = 101), or routine care (Routine group, n = 100). Patients within each arm were also randomly assigned to receive an immediate or deferred monthly $10 stipend for maintaining adherence. The endpoints of the trial were completing 6 months of treatment, pill-taking as measured by self-report or observation, isoniazid metabolites present in urine, and bottle opening as determined by electronic monitors in a subset of patients. RESULTS: Completion of therapy was 80% for patients in the Supervised group, 78% in the Peer group, and 79% in the Routine group (P = 0.70). Completion was 83% (125 of 150) among patients receiving immediate incentives versus 75% (112 of 150) among patients with deferred incentives (P = 0.09). The proportion of patients who were observed or reported taking at least 80% of their doses was 82% for the Supervised arm of the study, compared with 71% for the Peer arm and 90% for the Routine arm. The proportion of patients who took 100% of doses was 77% for the Supervised arm (by observation), 6% for the Peer arm (by report), and 10% for the Routine arm (by report; P <0.001). Direct observation showed the median proportion of doses taken by the Supervised group was 100%, while electronic monitoring in a subset of patients showed the

	Peer group (n = 27) took 57% of prescribed doses and the Routine group (n = 32) took 49% (P <0.001). Patients in the Routine arm overreported adherence by twofold when data from electronic monitoring were used as a gold standard. There were no significant differences in electronically monitored adherence by type of incentive. CONCLUSION: Adherence to isoniazid preventive therapy by injection drug users is best with supervised care. Peer counseling improves adherence over routine care, as measured by electronic monitoring of pill caps, and patients receiving peer counseling more accurately reported their adherence. More widespread use of supervised care could contribute to reductions in tuberculosis rates among drug users and possibly other high-risk groups.
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
Chaulk, C.P. et al., 1995. Eleven years of community-based directly observed therapy for tuberculosis. *JAMA*, 274(12), pp.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. 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	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

economics of directly observed therapy in Baltimore. *International Journal of Tuberculosis & Lung Disease*, 4(3), pp.201-207.	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.
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), pp.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 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., 2007. Estimating infectious disease in UK asylum seekers and refugees: a systematic review of prevalence studies. *Journal of Public Health*, 29(4), pp.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]
Codecasa, L.R. & Besozzi, G., 1998. Acceptance of	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

isoniazid preventive treatment by close contacts of tuberculosis cases: a 692-subject Italian study. *International Journal of Tuberculosis & Lung Disease*, 2(3), pp.208-212.	(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.
Coker, R.J., 2003. Public health impact of detention of individuals with tuberculosis: systematic literature review. *Public Health*, 117(4), pp.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.
Davidson, B.L., 1998. A controlled comparison of directly observed therapy vs self-administered therapy for active tuberculosis in the urban United States. *Chest*, (5), pp.1239-43.	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 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), pp.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.
Diez, E. et al., 1996. Evaluation of a social health intervention among homeless tuberculosis patients. *Tubercle and Lung Disease*, 77(5), pp.420-424.	Setting: Homeless and other fringe groups are a priority in the global strategies of tuberculosis prevention and control in big cities, as a consequence of their generally poor adherence to treatment and concurrent multiple social and health problems. Objective: To evaluate a social care and health follow-up programme targeting homeless tuberculosis patients in Ciutat Vella District, Barcelona, which covered 210 patients; from 1987 to 1992. During directly observed treatment, primary health care and, if necessary, accommodation was provided. Design: The differential tuberculosis incidence rate between Ciutat Vella and the other districts of Barcelona, the percentage of successfully completed treatments and the days of hospitalization saved by the programme were measured. Results: There was a significant decrease in the tuberculosis incidence rate among homeless patients in Ciutat Vella (from 32.4 per 105 inhabitants in 1987, to 19.8 per 105 in 1992, P = 0.03), compared to an unchanged rate elsewhere (1.6 per 105 inhabitants in 1987, compared to 1.7 per 105 in 1992, P = 0.34). A smaller than expected proportion, 19.6%, of patients failed to complete their treatment, and a decrease in the mean period of hospitalization for tuberculosis in the district hospital was recorded, falling from a mean 27.1 days in 1986 to a mean 15.7 days in 1992. Conclusion: The programme appears to be both effective and efficient, as it has enabled a large number of homeless patients to complete their treatment successfully, at the same time saving twice the amount of funds invested.
Elk, R. et al., 1993. Compliance with tuberculosis treatment in methadone-maintained patients: Behavioral interventions* 1. *Journal of Substance Abuse Treatment*, 10(4), p.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.
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), pp.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.
Faustini, A., Hall, A.J. & Perucci, C.A., 2005. Tuberculosis treatment	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

outcomes in Europe: a systematic review. *European Respiratory Journal*, 26(3), pp.503-510.	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]
Floyd, K., 2003. Costs and effectiveness: the impact of economic studies on TB control (Brief record). *Tuberculosis*, (1-3), pp.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. 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), pp.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.
Furin, J., 2007. The clinical management of drug-resistant	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

tuberculosis. *Current Opinion in Pulmonary Medicine*, 13(3), pp.212-217.	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]
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 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), p.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.
Gourevitch, M.N. et al., 1998. Cost-effectiveness of directly observed chemoprophylaxis of tuberculosis among drug users at high risk for tuberculosis. *International Journal of Tuberculosis & Lung Disease*, 2(7), pp.531-540.	SETTING: A methadone treatment program with on-site medical care in the Bronx, New York. OBJECTIVE: To define whether costs associated with directly observed preventive therapy (DOPT) of tuberculosis are justified by cases and costs of tuberculosis prevented among persons at high risk for active disease. DESIGN: Detailed data were collected on drug users in treatment regarding human immunodeficiency virus (HIV) and tuberculosis infection and disease, and costs of screening, chemoprophylaxis, direct observation and treatment of active disease. The cost-effectiveness of providing DOPT to this population was modeled. RESULTS: We assessed the impact of providing DOPT to 151 eligible persons. Assuming 65% isoniazid effectiveness, and incorporating costs of screening, observed chemoprophylaxis and clinical monitoring, a net savings in tuberculosis-related hospital costs of $285,284 ($563 per person screened) was associated with DOPT ($10,274 per case prevented). Direct observation of chemoprophylaxis proved cost-effective if associated with even a 10%

	increment in overall isoniazid effectiveness compared with self-administered chemoprophylaxis. DOPT costs per tuberculosis case averted remained below the in-patient costs of a single case of drug-sensitive disease across a range of parameter values. CONCLUSIONS: Providing DOPT is a highly cost-effective intervention for drug users in treatment. Commitment of additional resources required for DOPT should be given priority in this and other populations at high risk for tuberculosis.
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), pp.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.
Guzman-Montes, G.Y., Ovalles, R.H. & Laniado-Laborin, R., 2009. Indirect patient expenses for antituberculosis treatment in Tijuana, Mexico: is treatment really free?. *Journal of Infection in Developing Countries*, 3(10), pp.778-782.	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, 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*	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

Database of Systematic Reviews, (2), p.CD000011.	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 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.
Hirsch-Moverman, Y. et al., 2008. Adherence to treatment for latent tuberculosis infection: systematic review of studies in the US and Canada. *International Journal of Tuberculosis & Lung Disease*, 12(11), pp.1235-1254.	BACKGROUND: There is renewed attention to the critical role of successfully treating latent tuberculosis infection (LTBI) in reducing the overall impact of tuberculosis (TB). However, levels of treatment adherence are consistently low in industrialized countries such as the United States and Canada. OBJECTIVE: A systematic review of studies in the US and Canada was undertaken to analyze measurement of adherence to treatment of LTBI (TLTBI), TLTBI completion rates, predictors of TLTBI adherence and TLTBI adherence interventions. METHODS: PUBMED, MEDLINE and PsycINFO electronic databases were searched for quantitative studies published between 1997 and 2007. Full texts of articles were reviewed for data abstraction and studies were critically examined for their methodology and rigor. The present review presents outcomes from 78 studies. RESULTS: Adherence and completion rates of TLTBI are suboptimal across high-risk groups, regardless of regimen. Associations between adherence and patient factors, clinic facilities or treatment characteristics were found to be inconsistent across studies. Several adherence interventions have been developed to improve TLTBI adherence in the US and Canada; however, no single intervention has shown consistent

	effectiveness. CONCLUSION: LTBI must be effectively treated if the goal of TB elimination is to be realized. Consistently employing tools for measuring and improving adherence is fundamental. Identifying barriers to adherence and treatment completion will facilitate the development of effective, appropriate interventions. A 'one-size-fits-all' approach to treatment for TLTBI adherence is not likely to succeed across all settings. Innovative approaches can inspire future interventions and suggest solutions for the current problems facing LTBI programs and their patients. [References: 105]
Horsburgh, C.R. et al., 2010. Latent TB infection treatment acceptance and completion in the United States and Canada. *Chest*, 137(2), pp.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.
Hwang, S.W. et al., 2005. Interventions to improve the health of the homeless: a systematic review. *American Journal of Preventive Medicine*, 29(4), pp.311-319.	BACKGROUND: Homelessness is a widespread problem in the United States. The primary goal of this systematic review is to provide guidance in the development and organization of programs to improve the health of homeless people. METHODS: MEDLINE, CINAHL, HealthStar, PsycINFO, Sociological Abstracts, and Social Services Abstracts databases were searched from their inception through July 2004 using the following terms: homeless, homeless persons, and homelessness. References of key articles were also searched. 4564 abstracts were screened, and 258 articles underwent full review. Seventy-three studies conducted from 1988 to 2004 met inclusion criteria (use of an intervention, use of a comparison group, and the reporting of health-related outcomes). Two authors independently abstracted data from studies and assigned quality ratings using explicit criteria. RESULTS: Forty-five studies were rated good or fair quality. For homeless people with mental illness, case management linked to other services was effective in improving psychiatric symptoms, and assertive case management was effective in decreasing psychiatric hospitalizations and increasing outpatient contacts. For homeless people with substance abuse problems, case management resulted in greater decreases in substance use than did usual care. For homeless people with latent tuberculosis, monetary incentives improved adherence rates. Although a number of studies comparing an intervention to usual care were positive, studies comparing two interventions frequently found no significant difference in outcomes. CONCLUSIONS: Coordinated treatment programs for homeless adults with mental illness or substance abuse usually result in better health outcomes than usual care. Health care for homeless people should be provided through such programs whenever possible. Research is lacking on interventions for youths, families, and conditions other than mental illness or substance abuse. [References: 84]
Jasmer, R.M. et al., 2000. Twelve months	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

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), pp.1648-1652.	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 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), pp.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.
Juan, G. et al., 2006. Directly observed treatment for tuberculosis in pharmacies compared with self-administered therapy in Spain. *International Journal of Tuberculosis & Lung Disease*, 10(2), pp.215-221.	OBJECTIVES: To compare directly observed treatment (DOT) of tuberculosis through pharmacy offices with self-administered treatment (SAT) in patients at risk for non-adherence. METHODS: Prospective study for DOT (1999-2002) and retrospective study for SAT (1996-1998) in patients at risk for non-adherence (human immunodeficiency virus [HIV] infection, alcoholism, illicit drug use, immigrant or homeless status and/or previous failure to complete). Patients in the DOT programme received medication as out-patients twice a week in pharmacies that supervised adherence and provided socio-sanitary support to patients. RESULTS: There were 101 and 112 patients in the DOT and SAT groups, respectively. Demographic and clinical characteristics were similar in both groups. Differences were observed in risk factors for non-adherence (more immigrants and fewer intravenous drug users in the DOT vs. the SAT groups; $P < 0.05$). In the DOT group, 76 patients (75.2%) completed treatment and were cured compared to only 30 patients (26.7%) in the SAT group ($P < 0.001$). Implementation of DOT increased the cost of treatment by 400 Euro per patient compared to SAT. CONCLUSION: In patients at risk for non-adherence, DOT implemented through pharmacy offices was better than SAT; however, completion rates were still low.
Khan, K. et al., 2002. Global drug-resistance patterns and the management of latent tuberculosis infection	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

in immigrants to the United States. *New England Journal of Medicine*, 347(23), pp.1850-1859.	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
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), p.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.
Kominski, G.F. et al., 2007. Costs and cost-effectiveness of adolescent compliance with treatment for latent tuberculosis infection: results from a randomized trial (Structured abstract). *Journal of Adolescent Health*, (1), pp.61-68.	PURPOSE: Assess the costs and cost-effectiveness of an incentive-based tuberculosis (TB) program designed to promote adolescents' compliance with treatment for latent TB infection (LTBI). METHODS: Randomized controlled trial. Adolescents between the ages of 11 and 19 years who were referred to one of two participating clinics after being screened for TB and receiving a positive diagnosis indicating LTBI (n = 794) were assigned to one of four groups: usual care, peer counseling, contingency contracting, and combined peer counseling/contingency contracting. Primary outcome variables were completion of isoniazid preventive therapy (IPT), total treatment costs, and lifetime TB-related costs per quality-adjusted life year (QALY) in each of the four study groups (three treatment, one control). Cost effectiveness was evaluated using a five-stage Markov model and a Monte Carlo simulation with 10,000 trials. RESULTS: Average costs were 199 dollars for usual care (UC), 277 dollars for peer counseling (PC), 326 dollars for contingency contracting (CC), and 341

	dollars for PC + CC combined. The differences among these groups were all significant at the p = .001 level. Only the PC + CC group improved the rate of IPT completion (83.8%) relative to usual care (75.9%) (p = .051), with an overall incremental CE ratio of 209 dollars per QALY relative to usual care. CONCLUSION: Incentives combined with peer counseling are a cost-effective strategy for helping adolescents to complete care when combined with peer counseling.
Kong, P.M. et al., 2002. Skin-test screening and tuberculosis transmission among the homeless. *Emerging Infectious Diseases*, 8(11), pp.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.
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), pp.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]
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), pp.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.

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), pp.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.
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), p.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, 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), pp.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.
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), pp.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 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), pp.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.
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	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

effectiveness. *Preventive Medicine*, 30(5), pp.425-432.	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.
MacIntyre, C.R. et al., 2003. A randomised controlled clinical trial of the efficacy of family-based direct observation of anti-tuberculosis treatment in an urban, developed-country setting. *International Journal of Tuberculosis & Lung Disease*, 7(9), pp.848-854.	SETTING: A randomised, controlled clinical trial of the effectiveness of a family-based programme of directly observed treatment (DOT) for tuberculosis. METHODS: TB patients seen in Victoria, Australia, were randomly allocated to DOT observed by a family member (FDOT), or to standard supervised but non-observed therapy (ST). The outcome measure was compliance, measured by blinded testing of isoniazid levels in urine. An intention-to-treat analysis was used. RESULTS: Of 173 patients, 87 were allocated to FDOT and 86 to ST. Only 58% in the FDOT group were able to receive FDOT, the major reason being living alone and not having a family member to observe treatment. The rate of non-compliance was 24% (41/173), with no significant difference between FDOT (22/87) and ST (19/86). No clinical or socio-demographic variable predicted compliance. CONCLUSIONS: We were unable to demonstrate a benefit of FDOT in an urban, industrialised country setting. FDOT may be more appropriate in developing countries, where extended family support is often available and the burden of TB is much higher. Poor compliance and the difficulty in predicting non-compliance shown in this study highlights the need for DOT for all TB patients.
MacNeil, J.R., Lobato, M.N. & Moore, M., 2005. An unanswered health disparity: tuberculosis among correctional inmates, 1993 through 2003. *American Journal of Public Health*, 95(10), pp.1800-1805.	OBJECTIVES: We sought to describe disparities and trends in tuberculosis (TB) risk factors and treatment outcomes between 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), pp.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]
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), pp.103-107.	BACKGROUND: Drug users are at increased risk for latent tuberculosis infection (LTBI) and also at increased risk for noncompletion of medication regimens for treatment of LTBI or tuberculosis disease. Directly observed therapy (DOT) provided by outreach workers, the use of incentives, or both have been suggested as a means to increase adherence. OBJECTIVE: 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. METHODS: The research design was a randomized controlled trial in a community outreach program setting. Participants consisted of a volunteer sample of 163 active injection drug and crack cocaine users placed on twice weekly DOT. Condition 1 of the interventions consisted of provision of DOT by an outreach worker at a location chosen by the participant (active outreach) and a $5 per visit incentive. Condition 2 was comprised of active outreach with no monetary incentive, and Condition 3, provision of DOT at the study community site and a $5 per visit incentive. The main outcome measures were percentage of medication taken as prescribed and completion of medication regimen. RESULTS: The percentage of prescribed medication taken was higher for those who received incentives, either with (71%) or without (68%) active outreach, compared to those who received active outreach alone (13%). Only 4% of participants assigned to Condition 2 completed treatment, compared to 53% of Condition 1 participants, and 60% of Condition 3 participants. CONCLUSIONS: Monetary incentives were clearly superior to active outreach. Active outreach in combination with monetary incentives did not increase adherence over incentives alone.
Malotte, C.K., Hollingshead, J.R. & Rhodes, F., 1999. Monetary versus nonmonetary incentives for TB skin test reading among drug users. *American Journal of Preventive Medicine*, 16(3), p.182–188.	BACKGROUND: In a prior study, we reported that monetary incentives were effective in increasing return for tuberculosis (TB) skin test reading. The purpose of this study was to compare the effects of monetary versus nonmonetary incentives and a theory-based educational intervention on return for TB skin test reading in a sample of newly recruited active injection and crack cocaine users, and to determine the prevalence of TB infection in this sample. METHODS: Active injection drug and/or crack cocaine users (n = 1,078), recruited using street outreach techniques, were skin tested for TB. They were randomly assigned to 1 of 5 experimental treatment conditions: $10 cash, grocery store coupons, bus tokens/fast-food coupons, motivational education, or usual encouragement to return. Nonmonetary incentives had a $10 value, and all incentives were provided at return for skin test reading. RESULTS: Ninety-five percent of those who received $10 returned for skin test reading compared to 86% of those who received grocery store coupons and 83% of those who received either bus tokens or fast-food coupons. In contrast, only 47% of those who received the educational session and only 49% of those who received usual encouragement returned for skin test reading. The prevalence of a positive tuberculin test was 21%, and was similar for crack cocaine and injection drug users. CONCLUSIONS: Nonmonetary and monetary incentives dramatically increased the return rate for TB skin test reading among drug users who are at high risk of TB infection. Nonmonetary incentives were somewhat less effective than monetary incentives.
Matteelli, A. et al., 2000. Supervised preventive therapy for latent tuberculosis infection in illegal immigrants in Italy. *American Journal of Respiratory & Critical*	In a multicenter, prospective, randomized, open-label study of isoniazid-preventive therapy (IPT) for latent tuberculosis infection, illegal immigrants from countries where tuberculosis is highly endemic were enrolled at two clinical sites in Northern Italy. Of 208 eligible subjects, 82 received supervised IPT at a dose of 900 mg twice weekly for 6 mo (Regimen A), 73 received unsupervised IPT 900 mg twice weekly for 6 mo (Regimen B), and 53 received unsupervised IPT 300 mg daily for 6 mo (Regimen C). Supervised IPT was delivered at either one tuberculosis clinic or one migrant clinic. The probability of completing a 26-

Care Medicine, 162(5), pp.1653-1655.	wk regimen was 7, 26, and 41% in Regimens A, B, and C, respectively ($p < 0.005$, Log- rank test calculated using Kaplan-Meier plots). The mean time to dropout was 3. 8, 6, and 6.2 wk in Regimens A, B, and C, respectively ($p = 0.003$ for regimen A versus either Regimens B or C). Treatment was stopped in five subjects (2.4%) because of adverse events. The rate of completion of preventive therapy for latent tuberculosis infection among illegal immigrants was low. Supervised, clinic-based administration of IPT significantly reduced adherence. Alternative strategies to implement preventive therapy in illegal immigrants are clearly required.
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), pp.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 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), pp.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.
Mohle-Boetani, J.C. et al., 2002. Tuberculosis outbreak in a housing unit for human immunodeficiency	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

virus-infected patients in a correctional facility: transmission risk factors and effective outbreak control. *Clinical Infectious Diseases*, 34(5), pp.668-676.	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.
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), p.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-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), p.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)
Noyes, 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), pp.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]
Nyamathi, A. et al., 2007. Latent variable assessment of outcomes in a nurse-managed intervention to increase latent tuberculosis treatment completion in homeless adults. *Health Psychology*, 26(1), pp.68-76.	OBJECTIVE: To assess predictors of latent tuberculosis infection (LTBI) completion by using structural equation modeling (SEM) among homeless adults, a group at great risk for LTBI and active tuberculosis (TB). LTBI therapy is effective in stemming the progression to active TB, yet treatment adherence among homeless persons is difficult to attain. DESIGN: By using SEM, the authors assessed predictors of LTBI completion among a sample of 494 homeless adults in Los Angeles, CA, who received either a nurse case-managed program (NCM) or a usual care program. MAIN OUTCOME MEASURES: Latent variables were created with the baseline variables of site type, age, intervention status, dissatisfaction with health care, depression, TB risk assessment, alcohol use, heroin or cocaine use, and TB knowledge. Outcome variables included many of the same baseline variables as well as treatment completion. RESULTS: LTBI treatment completion (100% adherence) was significantly and positively associated with participation in NCM, older age, and less heroin or cocaine use. NCM also predicted greater TB knowledge, greater ease of treatment, and more satisfaction with treatment (NCM completion rate = 64%, control rate = 42%). CONCLUSION: The culturally competent NCM program, combined with active tracking and incentives, was successful in a difficult-to-treat and highly transient population.
Nyamathi, A. et al., 2008. Efficacy of nurse case-managed intervention for latent tuberculosis among homeless subsamples. *Nursing Research*, 57(1), pp.33-39.	BACKGROUND: The efficacy of a nurse case-managed intervention was evaluated in subsamples of participants with one of the following characteristics: female gender, African American ethnicity, recruited from a homeless shelter, a history of military service, lifetime injection drug use, daily alcohol and drug use, poor physical health, and a history of poor mental health. OBJECTIVE: To determine whether a validated nurse case-managed intervention with incentives and tracking would improve adherence to latent tuberculosis infection treatment in subsamples of homeless persons with characteristics previously identified in the literature as predictive of nonadherence. METHODS: A prospective 2-group site-randomized design was conducted with 520 homeless adults residing in 12 homeless shelters and residential recovery sites in the Skid Row region of Los Angeles from 1998 to 2003. RESULTS: Daily drug users, participants with a history of injection drug use, daily alcohol users, and persons who were not of African American race or ethnicity had particularly poor completion rates, even in the nurse case-managed intervention program (48%, 55%, 54%, and 50%, respectively). However, the intervention achieved a 91% completion rate for homeless shelter residents and significantly improved latent tuberculosis infection treatment adherence in 9 of 12 subgroups tested (odds ratios = 2.51-10.41), including daily alcohol and drug users, when potential confounders were controlled using logistic regression analysis. DISCUSSION: Nurse case management with incentives appears to be a good foundation for increasing adherence to 6-month isoniazid treatment in a variety of homeless subgroups and, in particular, for sheltered homeless populations. However, additional social-structural and environmental strategies are needed to address those at greatest risk of nonadherence.
Nyamathi, A.M. et al., 2006. A randomized controlled trial of two treatment programs for homeless adults with latent tuberculosis infection. *International Journal of Tuberculosis & Lung Disease*, 10(7), pp.775-782.	SETTING: Few studies have examined strategies for optimizing adherence to latent tuberculosis infection (LTBI) treatment programs in homeless populations. OBJECTIVES: 1) To compare the effectiveness of an intervention program employing nurse case management and incentives (NCMI) vs. a control program with standard care and incentives on completion of LTBI treatment; and 2) to compare the impact of the two programs on tuberculosis (TB) knowledge among participants. DESIGN: A prospective, two-group site-randomized design conducted among 520 homeless adults residing in the Skid Row region of Los Angeles from 1998 to 2003, assessing completion rates of a 6-month isoniazid (INH) treatment program and change in TB knowledge. RESULTS: Using intent-to-treat analysis, 62% of participants in the intervention program, compared with 39% of controls, completed the full 6-month course of

	LTBI treatment with INH. Logistic regression modeling revealed that intervention participants had three times greater odds of completing INH treatment than controls. TB knowledge improved in both programs, but the increase was greater among the intervention participants (P < 0.001). CONCLUSIONS: Nurse case management combined with education, incentives, and tracking dramatically improves both adherence to LTBI treatment and TB knowledge in homeless persons compared to a standard approach of outreach and incentives.
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), pp.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 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), p.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.
Pillaye, J. & Clarke, A., 2003. An evaluation of completeness of tuberculosis notification in the United Kingdom. *BMC Public Health*, 3, p.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. 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.
Rendleman, N.J., 1999. Mandated tuberculosis screening in a community of homeless people. *American Journal of Preventive Medicine*, 17(2), p.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 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), pp.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.
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), pp.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 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), pp.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.
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), pp.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 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), p.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]
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), pp.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.
Solsona, J. et al., others, 2001. Screening for tuberculosis upon admission to shelters and free-meal services. *European journal of epidemiology*, 17(2), p.123–128.	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 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), pp.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.
Sreeramareddy, C.T. et al., 2009. Time delays in diagnosis of pulmonary tuberculosis: a systematic review of literature. *BMC Infectious Diseases*, 9, p.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 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), p.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.
Storla, D.G., Yimer, S. & Bjune, G.A., 2008. A systematic review of	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

delay in the diagnosis and treatment of tuberculosis. *BMC Public Health*, 8, p.15.	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]
Tanke, E.D. & Leirer, V.O., 1994. Automated telephone reminders in tuberculosis care. *Med Care*, (4), pp.380-389.	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 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), pp.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.
Thomas, R.E., 1997. Mantoux (tuberculosis) testing. Evaluation of guidelines for testing in Canadian institutions. *Canadian Family Physician*, 43, pp.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]
Tulsky, J.P. et al., 2000. Adherence to isoniazid prophylaxis in the homeless: a randomized controlled trial. *Archives of Internal Medicine*, 160(5), pp.697-702.	OBJECTIVES: To test 2 interventions to improve adherence to isoniazid preventive therapy for tuberculosis in homeless adults. We compared (1) biweekly directly observed preventive therapy using a $5 monetary incentive and (2) biweekly directly observed preventive therapy using a peer health adviser, with (3) usual care at the tuberculosis clinic. METHODS: Randomized controlled trial in tuberculosis-infected homeless adults. Outcomes were completion of 6 months of isoniazid treatment and number of months of isoniazid dispensed. RESULTS: A total of 118 subjects were randomized to the 3 arms of the study. Completion in the monetary incentive arm was significantly better than in the peer health adviser arm (P = .01) and the usual care arm (P = .04), by log-rank test. Overall, 19 subjects (44%) in the monetary incentive arm completed preventive therapy compared with 7 (19%) in the peer health adviser arm (P = .02) and 10 (26%) in the usual care arm (P = .11). The median number of months of isoniazid dispensed was 5 in the monetary incentive arm vs 2 months in the peer health adviser arm (P = .005) and 2 months in the usual care arm (P = .04). In multivariate analysis, independent predictors of completion were being in the monetary incentive arm (odds ratio, 2.57; 95% CI, 1.11-5.94) and residence in a hotel or other stable housing at entry into the study vs residence on the street or in a shelter at entry (odds ratio, 2.33; 95% CI, 1.00-5.47). CONCLUSIONS: A $5 biweekly cash incentive improved adherence to tuberculosis preventive therapy compared with a peer intervention or usual care. Living in a hotel or apartment at the start of treatment also predicted the completion of therapy.
Tulsky, J.P. et al., 2004. Can the poor adhere? Incentives for adherence to TB prevention in homeless adults. *International Journal of Tuberculosis & Lung Disease*, 8(1), pp.83-91.	SETTING: Community-based population of homeless adults living in San Francisco, California. OBJECTIVE: To compare the effect of cash and non-cash incentives on 1) adherence to treatment for latent tuberculosis infection, and 2) length of time needed to look for participants who missed their dose of medications. DESIGN: Prospective, randomized clinical trial comparing a 5 dollar cash or a 5 dollar non-cash incentive. All participants received directly observed preventive therapy and standardized follow-up per a predetermined protocol. Completion rates and amount of time needed to follow up participants was measured. RESULTS: Of the 119 participants, 102 (86%) completed therapy. There was no difference between the cash and non-cash arms. Completion was significantly higher among males (OR 5.65, 95%CI 1.36-23.40, P = 0.02) and persons in stable housing at study entry (OR 4.86, 95%CI 1.32-17.94, P = 0.02). No substance use or mental health measures were associated with completion. Participants in the cash arm needed significantly less follow-up to complete therapy compared to the non-cash arm (P = 0.03). In multivariate analysis, non-cash incentive, use of crack cocaine, and no prior preventive therapy were associated with more follow-up time. CONCLUSION: Simple, low cost incentives can be used to improve adherence to TB preventive therapy in indigent adults.
Umbricht-Schneiter, A. et al., 1994. Providing medical care to methadone clinic patients: referral vs on-site care. *American Journal of Public*	OBJECTIVES: Intravenous drug users are at high risk for medical illness, yet many are medically underserved. Most methadone treatment programs have insufficient resources to provide medical care. The purpose of this study was to test the efficacy of providing medical care at a methadone clinic site vs referral to another site. METHODS: Patients with any of four target medical conditions were randomized into an on-site group offered medical care at the methadone treatment clinic and a referred group offered medical care at a nearby clinic.

Health, 84(2), pp.207-210.	Entry to treatment and use of medical services were analyzed. RESULTS: Of 161 intravenous drug users evaluated, 75 (47%) had one or more of the target medical conditions. Fifty-one were randomized. In the on-site group (n = 25), 92% received medical treatment; in the referred group (n = 26), only 35% received treatment. CONCLUSIONS: Providing medical care at a methadone treatment program site is more effective than the usual referral procedure and is a valuable public health intervention.
Underwood, B.R. et al., 2003. Contact tracing and population screening for tuberculosis--who should be assessed?. *Journal of Public Health Medicine*, 25(1), pp.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 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.
Volmink, J. & Garner, P., 1997. Systematic review of randomised controlled trials of strategies to promote adherence to tuberculosis treatment. *British Medical Journal*, 315(7120), pp.1403-1406.	Reliable evidence is available to show some specific strategies improve adherence to tuberculosis treatment, and these should be adopted depending on their appropriateness to practice circumstances. Further innovations require testing to help find specific approaches that will be useful in low income countries. Randomised controlled trials evaluating the independent effects of directly observed treatment are awaited.
Volmink, J. & Garner, P., 2000. Interventions for promoting adherence to tuberculosis management. *Cochrane Database of Systematic Reviews*, (4), p.000010.	BACKGROUND: Up to half the people with tuberculosis do not complete their treatment. Strategies to improve adherence to diagnostic and treatment regimens are therefore important. OBJECTIVES: To assess the effects of various interventions aimed at promoting adherence to anti-tuberculosis treatment and completion of TB diagnostic protocols. SEARCH STRATEGY: We searched the Cochrane Controlled Trials Register, the Cochrane Infectious Diseases Group trials register, Medline, Embase, Lilacs and reference lists of articles. We contacted experts in the field. SELECTION CRITERIA: Randomised and quasi-randomised trials of interventions to promote adherence with curative or preventive chemotherapy and diagnostic protocols for tuberculosis. DATA COLLECTION AND ANALYSIS: Two reviewers independently assessed trial quality and extracted data. MAIN RESULTS: Fourteen trials were included. Reminder cards sent to defaulters, a combination package of a monetary incentive and health education and more supervision of clinic staff increased the number of people completing their tuberculosis treatment. Intensive counselling/education did not help in one study. Direct observation showed better clinical outcomes in one study, and no difference in

	another. Return to the clinic for reading of a tuberculin skin test was enhanced by monetary incentives, assistance by lay health workers, contracts and telephone prompts but not by health education. AUTHORS' CONCLUSIONS: We have found evidence of benefit for a number of specific interventions to improve adherence to anti-tuberculous therapy and completion of diagnostic protocols. These should be implemented by health care providers where appropriate to local circumstances. Future studies in low income countries are a priority and should measure adherence and clinical outcomes. This review summarises trials up to 2000. It is being replaced by a series of reviews on particular intervention strategies. The details are in the 'Published notes' section. [References: 50]
Volmink, J. & Garner, P., 2007. Directly observed therapy for treating tuberculosis. *Cochrane Database of Systematic Reviews*, (4), p.003343.	BACKGROUND: For tuberculosis treatment, policies have been introduced to encourage adherence to treatment regimens. One such policy is directly observed therapy (DOT), which involves people directly observing patients taking their antituberculous drugs. OBJECTIVES: To compare DOT with self administration of treatment or different DOT options for people requiring treatment for clinically active tuberculosis or prevention of active disease. SEARCH STRATEGY: In May 2007, we searched the Cochrane Infectious Diseases Group Specialized Register, CENTRAL (The Cochrane Library 2007, Issue 2), MEDLINE, EMBASE, LILACS, and mRCT. We also checked article reference lists and contacted relevant researchers and organizations. SELECTION CRITERIA: Randomized and quasi-randomized controlled trials comparing a health worker, family member, or community volunteer routinely observing people taking antituberculous drugs compared with routine self administration of treatment at home. We include people requiring treatment for clinically active tuberculosis or medication for preventing active disease. DATA COLLECTION AND ANALYSIS: Both authors independently assessed trial methodological quality and extracted data. Data were analysed using relative risks (RR) with 95% confidence intervals (CI) and the fixed-effect model when there was no statistically significant heterogeneity (chi square P > 0.1). Trials of drug users were analysed separately. MAIN RESULTS: Eleven trials with 5609 participants met the inclusion criteria. No statistically significant difference was detected between DOT and self administration in terms of cure (RR 1.02, 95% CI 0.86 to 1.21, random-effects model; 1603 participants, 4 trials), with similar results for cure plus completion of treatment. When stratified by location, DOT provided at home compared with DOT provided at clinic suggests a possible small advantage with home-based DOT for cure (RR 1.10, 95% CI 1.02 to 1.18; 1365 participants, 3 trials). There was no significant difference detected in clinical outcomes between DOT at a clinic versus by a family member or community health worker (2 trials), or for DOT provided by a family member versus a community health worker (1326 participants, 1 trial). Two small trials of tuberculosis prophylaxis in intravenous drugs users found no statistically significant difference between DOT and self administration (199 participants, 1 trial) or a choice of location for DOT for completion of treatment (108 participants, 1 trial). AUTHORS' CONCLUSIONS: The results of randomized controlled trials conducted in low-, middle-, and high-income countries provide no assurance that DOT compared with self administration of treatment has any quantitatively important effect on cure or treatment completion in people receiving treatment for tuberculosis. [References: 58]
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*	This record was compiled by CRD commissioned reviewers according to a set of guidelines developed in collaboration with a group of leading health economists.

Disease, 4(3), pp.246-251.	
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), pp.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.
White, M.C. et al., 1998. A clinical trial of a financial incentive to go to the tuberculosis clinic for isoniazid after release from jail. *International Journal of Tuberculosis & Lung Disease*, 2(6), pp.506-512.	SETTING: Screening for active tuberculosis (TB) and providing isoniazid (INH) preventive therapy in jails are important control measures. In San Francisco, however, historical data showed that 62% of inmates were released before completing preventive therapy, and of those only 3% attended the TB Clinic for follow-up. OBJECTIVE AND DESIGN: A randomized clinical trial to compare a $5 cash incentive plus standardized TB education with standardized TB education alone in encouraging released inmates to make a first visit to the clinic. RESULTS: Of 79 persons enrolled in the trial, 77.2% were released before INH completion. Rates of first visit were not significantly different for those receiving +5 plus standardized education (25.8%) versus standardized education alone (23.3%), but were higher than rates seen in historical data for inmates not receiving standardized education. Age was an important predictor of completion of a first visit (odds ratio 1.09, 95% confidence interval 1.02-1.16, $P = 0.017$). Other variables predicting adherence included intent to adhere, more previous time in jail, stable housing, and being partnered versus alone, although these were not statistically significant. CONCLUSION: Standardized education may be important in improving follow-up after release. Further work on the role of a financial incentive in this population is needed.
White, M.C. et al., 2002. Randomized controlled trial of interventions to improve follow-up for latent tuberculosis infection after release from jail. *Archives of Internal Medicine*, 162(9), pp.1044-1050.	BACKGROUND: Adherence to treatment of persons with latent tuberculosis infection after release from jail has been poor. METHODS: A randomized controlled trial was conducted at the San Francisco City and County Jail, San Francisco, Calif. Subjects undergoing therapy for latent tuberculosis infection who spoke either English or Spanish were randomly allocated to receive education every 2 weeks while in jail; an incentive if they went to the San Francisco County Tuberculosis Clinic within 1 month of release; or usual care. The main outcome measures were completion of a visit to the tuberculosis clinic within 1 month of release and completion of therapy. RESULTS: Of 558 inmates enrolled, 325 were released before completion of therapy. Subjects in either intervention group were significantly more likely to complete a first visit than were control subjects (education group, 37%; incentive group, 37%; and controls, 24%) (adjusted odds ratio based on pooled results for the education and incentive groups, 1.85; 95% confidence interval, 1.04-3.28; P =0.02). Those

	in the education group were twice as likely to complete therapy compared with controls (adjusted odds ratio, 2.2; 95% confidence interval, 1.04-4.72; P =0.04). Of those who went to the tuberculosis clinic after release, subjects in the education group were more likely to complete therapy (education group, 65% [24/37]; incentive group, 33% [14/42]; and control group, 48% [12/25]; P =0.02). CONCLUSIONS: Education or the promise of an incentive improved initial follow-up. Education was superior to an incentive for the completion of therapy. Fairly modest strategies provided in jail can improve adherence. Further links between jail health services and community care should be explored.
White, M.C. et al., 2003. Strategies for effective education in a jail setting: the Tuberculosis Prevention Project. *Health Promotion Practice*, 4(4), pp.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.
White, M.C. et al., 2005. Improving tuberculosis therapy completion after jail: translation of research to practice. *Health Education Research*, 20(2), pp.163-174.	Inmates have high rates of latent tuberculosis infection (LTBI), but inmates are often released early and do not complete therapy in the community. This study evaluated the translation of results from a randomized trial to improve therapy completion to usual care in a county jail using Rogers' Diffusion of Innovation theory. Inmates who received a single education in the randomized trial in 1998-1999 (study group) were compared to inmates educated by Jail Discharge Planners in 2002-2003 (usual care group). Outcomes were rates of completion of a visit to the TB clinic and completion of therapy. Subjects in the usual care group were significantly less likely to go to clinic in the 30-day period after release (relative risk 0.84, 95% confidence interval 0.75-0.95). The transfer of an educational protocol did not achieve results seen under study conditions, mostly because of implementation fidelity. The educational session in the usual care period for 81.0% of inmates took 5 min, as compared to 10-15 min during the randomized trial. Differences in personnel administering the protocol, training, high turnover and time available may also account for lower rates seen. Practical clinical trials should focus on the context of care as well as the intervention and should have participation by those who will be implementing results.
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), pp.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.
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), pp.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)
Winje, B.A. et al., 2008. Screening for tuberculosis infection among newly arrived asylum seekers: comparison of QuantiFERONTB Gold with tuberculin skin test. *BMC Infectious Diseases*, 8, p.65.	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 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.

12.0 Appendix E. Example quality assessment forms

12.1 Quantitative study

El-Hamad et al. 2001	
1. Is the source population or source area well described?	**Comments**
++	Demographics of participants were evaluated by survey and are thoroughly reported (table 1); country is indicated; study sites (health clinics) are described.
2. Is the eligible population or area representative of the source population or area?	**Comments**
+	The place of recruitment (health clinic site) was identified; however, it is not clear how participants were recruited from each site (e.g., by flyer, referral etc). 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.
3. Do the selected participants or areas represent the eligible population?	**Comments**
++	Method of selection of participants from eligible sample is clearly stated (country of origin, length of stay in Italy). Inclusion/exclusion criteria were explicitly stated.
4. How was confounding minimised?	**Comments**
+	Study authors did not allocate individuals to intervention group. They were recruited directly from the clinic where they would be receiving treatment (screening) so confounding factors (characteristic differences at baseline) remain. However, they statistically account for the baseline differences between groups, therefore reducing bias.
5. Were interventions (and comparisons) well described and appropriate?	**Comments**

++	Described in detail/replicable.
6. Was the allocation concealed?	**Comments**
NA	
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 (to health care site) does not impact on outcomes. The exposure (going through the screening process) 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**
++	Drop-out rates (or completion rates) was the outcome being measured. Therefore, the number of drop-outs was hypothesised to be a reflection of the intervention itself.
12. Did the setting reflect usual UK practice?	**Comments**
+	Undocumented migrants in the UK have similar coverage/access to screening procedures from clinics. The study population in Italy had limited access to public medical care (emergency interventions only) but some groups of undocumented migrants to the UK have greater access to NHS services.
13. Did the intervention or control comparison reflect usual UK practice?	**Comments**

+	Screening was done by specialists at specific TB and unspecialised migrant healthcare clinics, although not by GPs. The study is relevant for UK because screening of immigrants in the UK continues to happen after arrival and at specialist clinic settings as well as by GPs. The study also compares screening by GPs compared with specialists, and is therefore a valuable comparison to the UK setting.
14. Were the outcome measures reliable?	**Comments**
++	The primary outcome measure was the number who completed screening, and it was objectively verified by observation (arrival or non-arrival of individuals to clinics).
15. Were all outcome measurements complete?	**Comments**
++	All were accounted for.
16. Were all important outcomes assessed?	**Comments**
+	Some outcomes were not assessed, for example, reasons for default. This is an important outcome in order to inform the intervention/other outcomes.
17. Were outcomes relevant?	**Comments**
++	The outcome that was assessed (completion of treatment) is a relevant outcome to identify the impact of a two-step compared with three-step screening process. It is consistent with the aims of the paper.
18. Were there similar follow-up times in exposure and comparison groups?	**Comments**
++	Equal time.
19. Was follow-up time meaningful?	**Comments**
++	Study was conducted over 1 year. Follow-up time was sufficient in this case because authors could assess exactly when the screening procedure started and ended - which is the purpose of this study.
20. Were exposure and comparison groups similar at baseline? If not, were these adjusted?	**Comments**

++	Exposure was not similar at baseline, but stratification and multivariate analyses were used to assess the probability of the confounding factor/characteristic biasing the outcome.
21. Was intention to treat (ITT) analysis conducted?	**Comments**
NA	The study's aim was only to measure the completion of treatment, so no further analysis is necessary for those who did not complete treatment other than identifying them.
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**
+	Confounders were adjusted for (stratified) -but not sufficiently between groups.
25. Was the precision of intervention effects given or calculable? Were they meaningful?	**Comments**
++	P value, and CI and OR are all reported.
26. Are the study results internally valid? (i.e., unbiased)	**Comments**
+	The baseline characteristics were different between groups. This is because there was no randomisation of individual participants by the study team. The authors attempted to minimise the these biases by conducting stratification and multivariate analysis. However, the differences between groups were too great for such adjustment to be reliable – a different study design such as an RCT would have been preferable.
27. Are the study results generalisable to the source population? (i.e. externally valid)	**Comments**

+	Not statistically.

12.2 Economic evaluation

Hardy et al. 2010	
1. Is the study population appropriate for the topic being evaluated?	**Comments**
Partly	It is a relevant population for the review but it doesn't explore sub-groups.
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**
Yes	UK study.
4. Were the perspectives clearly stated?	**Comments**
No	Doesn't state the perspective used, only describes where costs came from.
5. Are all direct health effects on individuals included, and are all other effects included where they are material?	**Comments**
No	Only assessed TST or QFT-G test results, with clinic review plus CXR for people testing positive. No clinical outcomes assessed for groups attending or not attending screening. No assessment of effect of different screening strategies on attendance rates.
6. Are all future costs and outcomes discounted appropriately?	**Comments**
No	No discount rate given. Time frame of study is all new immigrants arriving in study area in 1 year (2007).
7. Is the value of health effects expressed in terms of quality adjusted life years (QALYs)?	**Comments**
No	Only reports unit cost and total cost of screening.
8. Are costs and outcomes from other sectors fully and appropriately measured and valued?	**Comments**

No	Only considers cost of the screening tool.
9. Overall judgement (no need to continue if not applicable)	**Comments**
Partly applicable	Although relevant to NHS context & NICE guidelines, the study misses important costs and does not clearly report their perspective and other elements.
10. Does the model structure adequately reflect the nature of the topic under evaluation?	**Comments**
Partly	Focus of the study is to assess costs of the screening strategy recommended by NICE, compared with usual practice.
11. Is the time horizon sufficiently long to reflect all important differences in costs and outcomes?	**Comments**
Partly	The time horizon is appropriate given the limited costs and outcomes that the study is looking for; however these do not take into account all relevant costs & outcomes.
12. Are all important and relevant outcomes included?	**Comments**
No	Does not consider, for example, the benefits and harms of treatment once LTBI is identified; or the impact of different screening strategies on uptake rates.
13. Are the estimates of baseline outcomes from the best available source?	**Comments**
Unclear	Based on data from the Leeds TB screening service.
14. Are the estimates of relative 'treatment' effects from the best available source?	**Comments**
Partly	Based on outcomes for a small cohort of people in their trial, with 32% uptake rate from eligible population.
15. Are all important and relevant costs included?	**Comments**
No	Resource costs not included, neither are costs of treating people who failed to attend for screening.

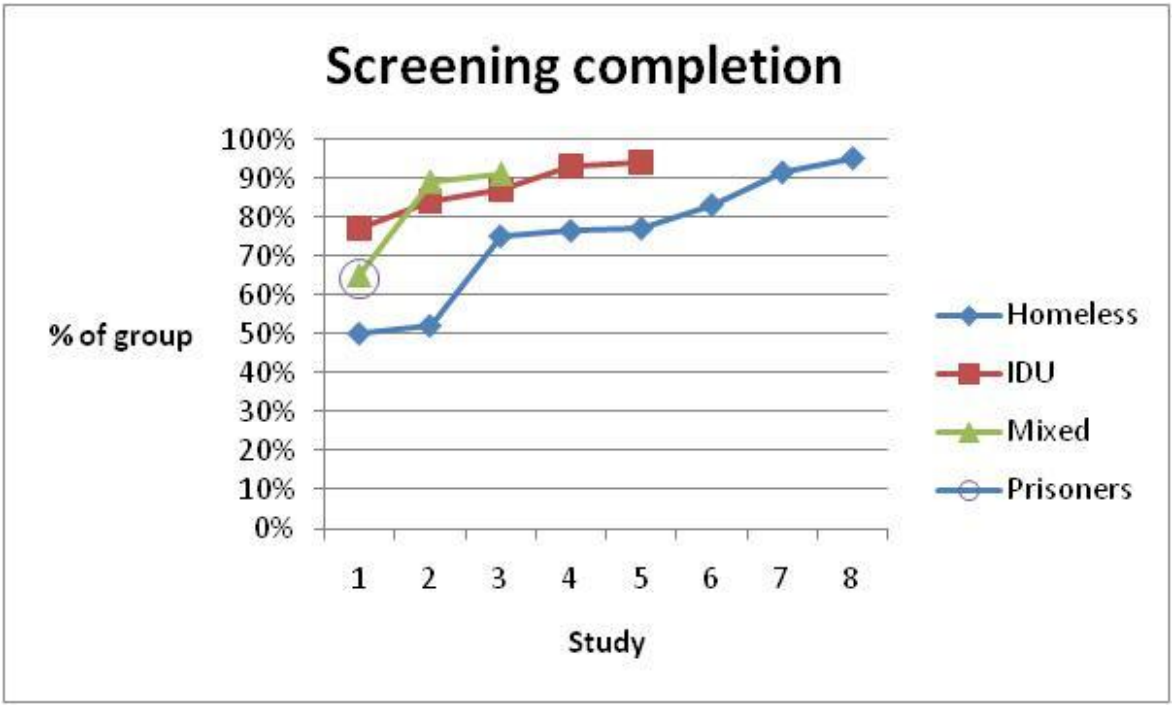
16. Are the estimates of resource use from the best available source?	**Comments**
Unclear	Study does not consider resource use, just costs of tests.
17. Are the unit costs of resources from the best available source?	**Comments**
Yes	NICE guidelines.
18. Is an appropriate incremental analysis presented or can it be calculated from the data?	**Comments**
No	Not performed, and limited data presented.
19. Are all important parameters whose values are uncertain subjected to appropriate sensitivity analysis?	**Comments**
No	Did not conduct a sensitivity analysis
20. Is there any potential conflict of interest?	**Comments**
No	None reported, but funding of study is unclear.
21. Overall assessment	**Comments**
Very serious limitations	

13.0 Appendix F. Non-comparative studies

We identified 39 studies that did not report comparative data on different methods of identifying TB in hard-to-reach groups, but met all the other inclusion criteria for the review. These non-comparative studies reported incidence data on latent or active TB or screening completion rates in selected hard-to-reach populations. They were not included in the main review as they do not offer any information on how effective the identification process might have been at identifying people with TB, but have been included in this section as reference data to support guidance development.

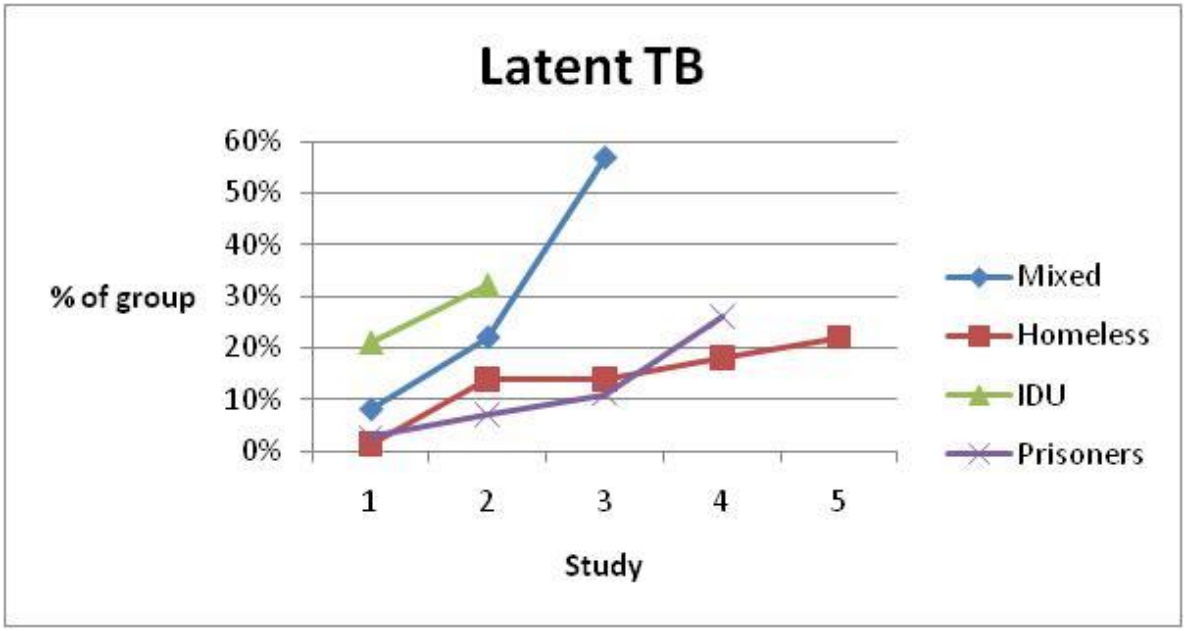
13.1 Screening completion rates

Study	Country	Population	Intervention	Screening completion rate
Bock 1999	USA	Mixed (homeless, IDU, prisoners)	TST	65%
Johnsen 1995	USA	Mixed (homeless, IDU, prisoners)	2-step TST: second test	89%
Johnsen 1995	USA	Mixed (homeless, IDU, prisoners)	2-step TST: first test	91%
Lau 1997	Australia	Homeless	CXR	50%
Falchook 2000	USA	Homeless	'Screening'	52%
Griffin 1999	USA	Homeless	TST	76%
Forman 2003	USA	Homeless	TST	77%
Layton 1995	USA	Homeless	TST, CXR	91%
Kimerling 1999	USA	Homeless	Sputum	95%
Lofy 2006	USA	Homeless; contacts	TST, CXR, sputum	75%
Yun 2003	USA	Homeless; contacts	TST	83%
Riley 2002	USA	IDU	TST	84%
Golub 2008	USA	IDU	TST	87%
Salomon 2000	USA	IDU	$15 incentive	93%
Brassard 2004	Canada	IDU	Financial incentive	94%
Munckhof 2003	Australia	IDU; contacts	TST	77%
Bur 2003	USA	Prisoners; contacts	TST	64%



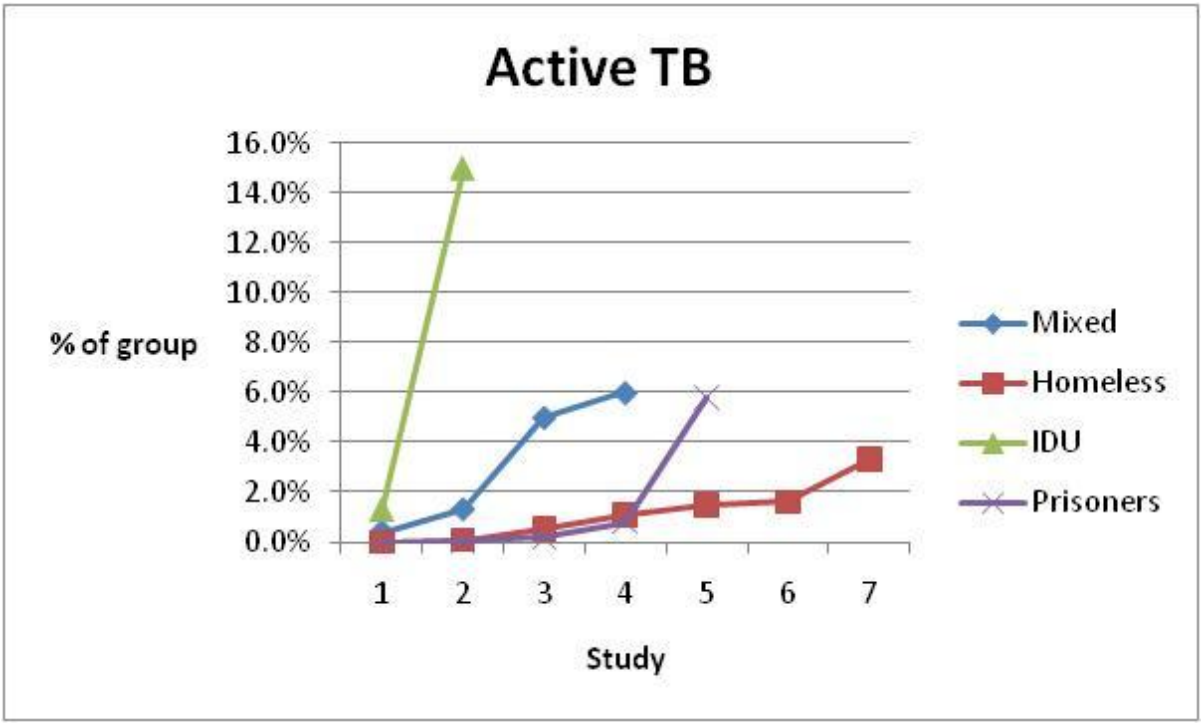
13.2 Latent TB rates

Study	Country	Population	Intervention	LTBI rate
de Vries 2007	Netherlands	Mixed (homeless, IDU)	MXRU	8%
Garfein 2010	Mexico	Mixed (homeless, IDU)	screening	57%
de Vries 2006	Netherlands	Mixed (homeless, IDU): contacts	TST	22%
Kumar 1995	UK	Homeless	CXR	1%
Solsona 2001	Spain	Homeless	TST, CXR	14%
Lashley 2007	USA	Homeless	TST	14%
Falchook 2000	USA	Homeless	screening	22%
Lofy 2006	USA	Homeless; contacts	TST, CXR, sputum	18%
Brassard 2004	Canada	IDU	Financial incentive	21%
Swaminathan 2007	USA	IDU	TST	32%
Rodrigo 2002b	Greece	Prisoner	Sputum	11%
MacIntyre 1999	Australia	Prisoner;	TST	26%
Bur 2003	USA	Prisoner; contacts	TST	3%
Ahmed 2007	UK	Prisoner; contacts	TST, QFT-G, CXR	7%



13.3 Active TB rate

Study	Country	Population	Intervention	Active TB rate
de Vries 2007	Netherlands	Mixed (Homeless, IDU)	Mobile CXR	6.0%
de Vries 2006	Netherlands	Mixed (Homeless, IDU); contacts	CXR	1.3%
de Vries 2006	Netherlands	Mixed (Homeless, IDU); contacts	TST	5.0%
Layton 1995	USA	Homeless	TST, CXR	0.0%
Lau 1997	Australia	Homeless	CXR	0.1%
Garfein 2010	Mexico	Homeless	'Screening'	0.4%
Southern 1999	UK	Homeless	TST, CXR	0.5%
Solsona 2001	Spain	Homeless	TST, CXR	1.1%
Kumar 1995	UK	Homeless	CXR	1.5%
Yun 2003	USA	Homeless	TST	1.6%
Kimerling 1999	USA	Homeless	Sputum	3.3%
Golub 2008	USA	IDU	TST	1.3%
Leonhardt 1994	USA	IDU; contacts	'Screening'	15.0%
Thompson 2009	UK	Prisoner	Symptom questionnaire	0.0%
Pelletier 1993	USA	Prisoner	TST, CXR	0.1%
Rodrigo 2002a	Spain	Prisoner	Sputum	0.2%
Layton 1997	USA	Prisoner	TST, CXR	0.8%
Rodrigo 2002b	Greece	Prisoner	Sputum	5.8%



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14.0 Appendix G. 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 US where new entrants are tested for TB prior to entry into the US. 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.

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.

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.

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.

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

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.

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.

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.

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.