National Institute for Health and Clinical Excellence (NICE)

Economic analysis of identifying and managing tuberculosis in hard to reach groups: homeless and prison populations

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The National Institute for Health and Clinical Excellence (NICE) has been asked to produce a guideline on the Identifying and treating tuberculosis in hard-to-reach populations. What follows is the cost effectiveness analysis developed to support the programme development group (PDG) in coming to recommendations. This analysis has been conducted according to NICE methods outlined in the Guide to the methods of technology appraisals (2008) and the Methods for the development of NICE public health guidance (2009). Thus it follows the NICE reference case (the framework NICE requests all cost effectiveness analysis to follow) in the methodology utilised.

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Declaration of authors' other relevant interests

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Executive summary

This report considers two interventions (mobile X-ray unit (MXU) screening and enhanced case-management (ECM) to improve treatment completion rates) in two hard-to-reach groups (homeless persons and prisoners). The comparator is current practice, i.e. passive case-finding and current case-management.

The key effectiveness evidence comes from a Department of Health-commissioned analysis of the London TB Find & Treat service, which provides mobile X-ray unit case-finding and case-management support; and expert opinion from the NICE Programme Development Group (PDG). Analysis of observational data from the London TB Find & Treat service found that it appears to improve case-finding and successful treatment completion in a hard-to-reach population (Jit et al. in press).

The economic evaluation was a cost-utility analysis, as specified by the NICE reference case (NICE 2009), using an integrated transmission-dynamic and health-economic model. The interventions considered always improved health in the scenarios examined. There is a large amount of uncertainty regarding the effectiveness and cost of both MXU and ECM interventions. Depending upon the setting, the burden of TB in that setting, the cost of treating a case of TB in that setting, and the effectiveness and costs of the intervention options (MXU and ECM), the interventions considered may be cost-saving, cost-effective, or not cost-effective. The burden of TB in the population determines the size of the potential health gains that could be achieved by intervention: a higher burden makes intervention more cost-effective or cost-saving. As successful intervention averts transmission of TB, as well as improving health it reduces treatment costs before fewer cases occur; the magnitude of cost savings depends upon the cost of treating a case.

The cost-effectiveness of mobile X-ray unit case-finding and enhanced case-management interventions is context-specific: the interventions may be cost-saving, cost-effective, or not cost-effective, depending upon the population (homeless or prison) burden of TB in the particular population (the proportion of the population being treated for TB prior to the intervention), the cost(s) of the intervention(s), the effectiveness of the intervention(s), and the cost of treatment of a TB case in the particular population group. Combined case-finding and enhanced case-management interventions produce greater QALY gains than either intervention alone, but it should be noted that the combined effects are not additive, due to the complexities of transmission patterns. The cost-effectiveness of MXU case-finding alone, ECM alone and combined MXU case-finding and ECM depend upon the setting and TB burden as well as the cost of providing ECM, and whether the cost of ECM is lower in a combined intervention.

The PDG highlighted that for homeless patients the out-of-pocket expenses involved in obtaining care could be significant even though to most people the costs may be much more readily affordable. Whilst this may be important from an equity viewpoint, NICE's reference case for economic analysis does not take account of non-public sector expenses or the fact that a particular sum of money may be worth much more to some people than to others.

Summary economic analysis

Base-case analysis for homeless

The base-case analysis for the homeless is summarised in Table S.1. For this base-case analysis for a population of 10,000 homeless people, where under current practice (i.e. prior to intervention) the proportion of the population being treated for TB is 788 per 100,000 (Story at al. 2007) and the treatment completion rate is 55%, combined mobile X-ray screening (with a case-finding rate of 0.78 per case per year) and enhanced case management (ECM, increasing treatment completion to 75%) is the most cost-effective option if ECM costs less than about £38M (if a QALY is valued at £20,000) or less than about £43M (if a QALY is valued at £30,000), over a 20-year time horizon. (This is the "ECM cost threshold" (see Table S.1), and is the increase in incremental net benefit, excluding the cost of ECM, of adding ECM to MXU screening: if the cost of adding ECM is less than the incremental net benefit of doing so then adding ECM is cost-effective.) This equates to approximately £21,000 per case treated in the population of 10,000 over the 20-year time-horizon, if a QALY is valued at £20,000, or about £24,000 per case treated if a QALY is valued at £30,000.

Otherwise, mobile X-ray screening is the most cost-effective option – and is cost-saving as well as improving health. Mobile X-ray screening dominates current practice regardless of the cost of ECM (it provides more QALYs at lower cost). Similarly, combined mobile X-ray screening and ECM always dominates ECM alone (assuming that the additional cost of ECM is the same when it is provided on its own or in combination with mobile X-ray screening).

It is important to note that the cost-effectiveness of interventions is affected by the proportion of the population being treated for TB under current practice prior to intervention: if this proportion is 500 per 100,000 instead of 788 per 100,000 then MXU screening alone is still cost-saving and more cost-effective than current practice, but the price that is worth paying for ECM is reduced. If the proportion of the population being treated for TB under current practice prior to intervention is 100 per

100,000 then MXU screening is not cost-effective and ECM alone is only cost effective if it can be provided for less than about £9M to £10M over 20 years. Sensitivity analysis also shows that the cost-effectiveness of interventions depends upon their costs and effectiveness (in terms of active case-finding rate for MXU and treatment completion rate achieved by ECM), and the cost per case of treating TB in the hard-to-reach population.

Table S.1 Base-case analysis of interventions against TB in the homeless

Prior to intervention the proportion of the population being treated for TB is 788 per 100,000 (Story at al. 2007) and the treatment completion rate is 55%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: current practice	66.0	127,607	-	-	-	-
Mobile X-ray screening	56.9	128,435	-9.2	828.5	25.7	34.0
Enhanced case-management (ECM)	31.3	128,533	-34.7	926.6	53.2	62.5
Combined Mobile X-ray screening and ECM	30.2	128,988	-35.8	1381.7	63.5	77.3
				ECM cost threshold:	37.8	43.3

QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

Base-case analysis for prisoners

The base-case analysis for the prisoners is summarised in Table S.2. For this base-case analysis for a population of 10,000 prisoners, where under current practice (i.e. prior to intervention) the proportion of the population being treated for TB is 208 per 100,000 (Story at al. 2007) and the treatment completion rate is 48%, enhanced case management (ECM, increasing the treatment completion rate to 75%) alone is the most cost-effective option if the cost of providing it is less than £16.5M (if a QALY is valued at £20,000) or £17M (if a QALY is valued at £30,000), over 20 years. This equates to approximately £35,000 per case treated in the population of 10,000 over the 20-year time-horizon, if a QALY is valued at £20,000, or about £40,000 per case treated if a QALY is valued at £30,000. If providing ECM alone costs more than this then combined MXU screening (an active case-finding rate of 0.78 per case per year) and ECM will not be cost-effective (unless combining the interventions allows the cost of ECM over 20 years to be reduced to about £7M to £9M, depending upon whether a QALY is valued at £20,000 or £30,000) because combined MXU screening and ECM has an INB that is lower than ECM alone.

If a QALY is valued at £20,000 and ECM cannot be provided for less than £16.5M then the most cost-effective option is current practice because the incremental net benefit of MXU screening compared with current practice is negative.

If a QALY is valued at £30,000 and ECM cannot be provided for less than £17M then the most cost-effective option is mobile X-ray screening, which is just cost-effective (a small positive INB). The reason is that if a QALY is valued at £30,000 then MXU screening alone has an incremental net benefit (INB) of £1M, which includes the costs of MXU screening, and ECM alone has an INB of £18M, which excludes the cost of ECM – therefore if ECM costs £17M then it has the same overall INB as MXU screening and if ECM costs more than £17M then it has a lower overall INB then MXU screening.

It is important to note that the cost-effectiveness of interventions is affected by the proportion of the population being treated for TB under current practice prior to intervention: if this proportion is 300 per 100,000 instead of 208 per 100,000 then enhanced case management is cost-effective at higher costs: £19M over 20 years (if a QALY is valued at £20,000) or about £20M over 20 years (if a QALY is valued at £30,000), and MXU screening alone is slightly cost-saving as well as beneficial to health. Conversely, the proportion of the population being treated for TB under current practice prior to intervention is 100 per 100,000 then MXU screening alone or combined with ECM are not cost-effective, and ECM alone is only more cost-effective than current practice if it costs less than about £8M (if a QALY is valued at £20,000) or about £9M (if a QALY is valued at £30,000), over 20 years. Sensitivity analysis also shows that the cost-effectiveness of interventions depends upon their costs and effectiveness (in terms of active case-finding rate for MXU and treatment completion rate achieved by ECM), and the cost per case of treating TB in the hard-to-reach population.

Table S.2 Base-case analysis of interventions against TB in prisoners

Prior to intervention the proportion of the population being treated for TB is 208 per 100,000 (Story at al. 2007) and the treatment completion rate is 48%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	18.3	127,877	-	-	-	-
Mobile X-ray screening	21.0	128,004	2.8	126.6	-0.2	1.0
Enhanced case-management (ECM)	4.9	128,030	-13.4	152.4	16.5	18.0
Combined Mobile X-ray screening and ECM	14.9	128,057	-3.3	180.1	6.9	8.7
ECM cost threshold:					16.5	17.0

QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

Main strengths and weaknesses of the evaluation

It is essential that analyses of interventions against infectious diseases such as TB take account of infections averted by rapid diagnosis and successful treatment of infectious cases, as well as the benefit to the individual patient. This important benefit of protecting the population increases the cost-effectiveness of interventions and can even make them cost-saving due to averting future treatment costs depending upon the setting.

We have used a well-established transmission-dynamic modelling method that has been applied successfully to TB as well as many other infectious diseases. We have integrated the transmission-dynamic modelling with the economic analysis to quantify the benefits of interventions in averting transmission as well as in treating identified cases. A large number of model runs have been performed to explore a wide range of parameter space, encompassing the range of values for the proportion of the population being treated for TB prior to the intervention, effectiveness and cost of intervention likely to be found.

The model considers pulmonary TB, both sputum smear-negative and sputum smear-positive. Non-pulmonary TB has not been considered, as it is not transmissible. However, averting transmission from cases of pulmonary TB would avert cases of disease due to non-pulmonary TB. Therefore, our analysis underestimates the health benefits and the cost-savings of interventions.

The main limitations of the work are due to gaps in scientific understanding of TB epidemiology in general, and lack of data from the populations considered in particular, including lack of information on the costs of treatment and case-management in hard-to-reach groups. The TB prevalence estimates (Story et al. 2007) are based on data from one year in one setting: London in 2003. The MXU effectiveness data (Abubakar et al. May 2011) are from only one setting and from a different time. Costing data are sparse, as are quality of life data. Information on costs and effectiveness of case-management interventions are lacking.

It should also be noted that changing social circumstances and penal policy in the future may change the size or composition of the homeless and/or prison populations which may impact the epidemiology of TB. Further empirical study is required to improve cost-effectiveness calculations.

Finally, the PDG highlighted that for homeless patients the out-of-pocket expenses involved in obtaining care could be significant even though to most people the costs may be much more readily affordable. Whilst this may be important from an equity viewpoint, NICE's reference case for economic analysis does not take account of non-public sector expenses or the fact that a particular sum of money may be worth much more to some people than to others.

1. Description of decision problem(s)

1.1 Brief overview of TB

The incidence of tuberculosis (TB) in the UK has increased consistently over the last two decades (Crofts et al, 2008; Health Protection Agency, 2010). This increase has been associated with a change in the epidemiology of the disease: TB used to broadly affect the general population, whereas most cases now occur in particular high risk groups, particularly the non-UK born population. Cases are increasingly concentrated in large urban areas, particularly London (38% of cases in 2009) and the West Midlands (11% of cases in 2009), amongst the non-UK born population, in minority ethnic groups (Health Protection Agency, 2010) and in harder to reach socially excluded groups (Story et al, 2007). In a recent study the estimated prevalence of TB in homeless persons, problem drug users and prisoners ("hard to reach groups") was 788, 354 and 208 per 100,000, respectively (Story et al, 2007). By comparison, the overall prevalence of TB was 27 per 100,000. Although only 17% of TB cases in London are hard to reach, they account for nearly 38% of non-treatment adherent cases, 44% of cases lost to follow up and nearly a third of all highly infectious cases (Story et al, 2007).

TB can affect any part of the body but only respiratory forms of the disease are transmissible. Approximately 10% of patients infected with *Mycobacterium tuberculosis* develop TB disease in their lifetime (Contact Study Sub-Committee of The Research Committee of the British Thoracic Association, 1978; Raviglione et al, 1995).

1.2 Population

"Hard to reach" groups include homeless individuals, alcohol dependents, problem drug users and those with a history of imprisonment, who have been shown to more readily transmit infection (Maguire et al, 2002; Love et al, 2009). They are "hard to reach" because they do not engage well with traditional forms of state services, which are usually hospital-based and have chaotic lifestyle factors that complicate management such as insecure housing tenure, addiction issues and frequent contact with the criminal justice system.

Two “hard to reach” populations were considered as subgroups during analysis: the homeless and prisoners. Substance misusing groups were not considered as separate populations during analysis as parameters were not available to support the modelling work. Immigrants from high-TB-burden countries were not considered due to a lack of data on the effectiveness of interventions and on the dynamics of TB transmission from these groups.

1.3 Intervention

TB control is based on early diagnosis and treatment to minimise the period of infectivity. BCG vaccination can reduce the risk of progression to disease but has only a small impact on transmission by offering limited protection against acquisition (Abubakar et al, Aug 2011; Soysal et al, 2005; Watson, 2006). Traditionally, programmes to tackle TB are founded on the assumptions that symptomatic patients will seek prompt medical help and then complete at least six months of drug therapy, which is required for treatment to be effective. For hard to reach patients these assumptions are flawed. Delayed presentation, not taking treatment regularly and loss to follow-up care result in avoidable transmission of infection and deaths, as well as development of drug resistance.

In many countries Directly Observed Therapy (DOT), where each treatment dose is observed by a responsible adult, is the accepted standard of care (Dye et al, 2005). However, this is not the case in the UK: patients, including those in hard to reach groups, are typically only placed on DOT if they are found to be non-adherent but not lost to follow-up. In London, relatively few homeless, prisoners or drug-using patients started their treatment using DOT, but a much larger proportion ended up being treated in this manner after demonstrating poor adherence (Story et al, 2007).

Mobile X-ray unit screening offers a potential means to rapidly identify pulmonary TB in hard-to-reach groups; enhanced case-management may increase the proportion of patients successfully completing treatment. Both interventions may benefit both the individual patient receiving them, and the wider community through averting onward transmission.

The interventions considered are (i) mobile X-ray screening to identify cases earlier than they would have been found through passive case-finding and (ii) enhanced case-management to increase the proportion of cases who successfully complete treatment.

1.4 Comparator(s)

The comparator is current practice, as this is the current context in which the interventions would be applied. It is also the context from which the evidence on costs, and effectiveness of the MXU intervention, comes.

The standard care pathway is passive case-finding: i.e. patients who present to care services with symptoms compatible with TB (which are non-specific: many diseases cause similar symptoms) may be referred to specialist TB services for diagnostic testing and, if appropriate, treatment. There is often a considerable delay in patients presenting to care and being diagnosed and many patients who initiate treatment do not complete it successfully but are lost to follow-up.

1.5 Outcome(s)

What is the cost-effectiveness of introducing, in addition to current practice, either or both of (i) X-ray screening of homeless or prison populations to identify active or preclinical pulmonary TB; (ii) enhanced case-management to increase the proportion of patients who successfully complete treatment, taking account of the effects on individual recipients of the intervention(s) and the effects on transmission of infection?

In line with the NICE reference case a cost utility analysis was used to analyse cost effectiveness of enhanced case management and/or mobile X-ray screening.

1.6 Main resource use to the NHS

Mobile X-ray screening requires the purchase of a mobile X-ray unit, staff to operate it, a van to transport it, and parking and maintenance facilities for the van. The infrastructure required for case-management support depends upon the details of the intervention to be applied, the specifics of which are not explored here, although threshold analysis was completed. We are not able to calculate what costs may be to commissioners rather than providers.

1.7 Limitations of analysis

There is a lack of evidence regarding the effectiveness of case-management interventions, so in our analysis we have calculated what health gain would be achieved by a specified increase in treatment completion in order to inform decisions regarding how much it would be worth paying to achieve such an increase. Substance misusing groups were not considered separately as parameters were not available to support the modelling work.

2. Summary of effectiveness evidence

Matrix were commissioned to undertake four systematic reviews by NICE in order to inform the recommendations.

The first review examined factors that help or hinder the uptake of TB diagnosis and treatment services by people from hard-to-reach groups. The primary research question was:

- “What factors help or hinder the uptake of TB diagnosis and treatment services by people from hard-to-reach groups, for example, the stigma associated with diagnosis, and how can the barriers be overcome?”

The second review examined effectiveness and cost-effectiveness of strategies to identify TB in the hard to reach. The primary research question 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 third review examined effectiveness and cost-effectiveness of strategies to manage TB in these populations. The primary research questions were:

- “Which interventions are effective and cost-effective at managing TB in people from hard-to-reach groups?”
- “What are effective case management approaches to identify those who may need support to complete treatment?”

The fourth and final review examined effectiveness and cost-effectiveness of service structures aimed at identifying and/or managing TB in hard-to-reach groups.

2.1 Review of barriers and facilitators (Matrix 2011)

During their initial review Matrix found 25 studies which met their inclusion criteria. The gaps identified in the evidence were as follows: cues for action with hard-to-reach people, benefits and implications of using TB services and the range of opinion in different hard-to-reach groups.

In the studies undertaken, knowledge of the cause and transmission of tuberculosis amongst hard-to-reach groups was frequently reported to be incomplete or inaccurate, with smoking and heredity factors being frequently cited as a cause. This led to individuals being unappreciative of their personal risk. Many studies indicated that individuals were unaware that tuberculosis could be treated or cured.

The greatest barriers to testing were highlighted as concerns about stigmatisation and a fear of death. Both members of hard to reach groups and service providers had concerns about the dearth of tuberculosis specialists and the infrequency with which GPs come across tuberculosis cases outside of London and Birmingham. Evidence on facilitators was thin on the ground, but included family support and religion.

2.2 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 (Matrix 2011)

During their second review Matrix found 31 studies which met their inclusion criteria. Most of the studies focussed on the identification of disease rather than increasing awareness. The following evidence gaps were identified, amongst others: studies outside of new entrants and the foreign-born, any seeking to improve passive case detection, UK-based studies in specific groups.

General conclusions were hampered by the quality and quantity of the literature, but are summarised here. Active screening promotes increased and earlier detection of both latent and active tuberculosis amongst new entrants and contacts of foreign-born populations. The cost effectiveness of this strategy is less firm. Peer workers from the same hard-to-reach group may improve outcomes in the homeless/drug users. Vouchers and small monetary incentives are effective and cost-effective at increasing the proportion of individuals who come for follow up appointments in drug users, as well as being effective for the homeless. In drug users, educational incentives have not been shown to be effective without additional monetary incentives.

2.3 Evidence review on the effectiveness and cost-effectiveness of interventions aimed at managing tuberculosis in hard-to-reach groups.

For their third review Matrix found 28 studies which met their inclusion criteria. Their report includes comparative effectiveness or economic data in the management of latent or active TB. A summary of their results is presented below.

Latent TB infection (LTBI): there was weak evidence that education of prisoners increases treatment completion after discharge. Weak evidence suggested that intravenous drug users (IDUs) benefit from peer support, with inconsistent evidence for the foreign born. Weak evidence suggested that illegal immigrants had lower completion rates with supervised treatment. Evidence for the effectiveness of directly observed preventive therapy (DOPT) was shown to be inconsistent with IDUs and weak, but possibly negative, with prisoners. Moderate evidence is available that incentives do not impact on attendance at appointments or treatment completion with prisoners and weak evidence for treatment completion in the foreign born. There was weak evidence that treatment completion or adherence in IDUs or mixed hard to reach groups benefitted from a service model approach/social care support. Combinations of interventions had a mixed range of effects. There was weak evidence for self-administered therapy proving cost saving in managing LTBI in prisoners, moderate for DOPT for drug users and immigrants.

Active TB: there was weak and inconsistent evidence for DOPT improving treatment adherence in IDUs and prisoners, with weak (no statistical difference) and inconsistent evidence on the effect on treatment outcomes in the foreign born and mixed hard to reach groups. There was weak evidence that legal detention reduced treatment completion in drug or alcohol users. There was moderate evidence that adding incentives to DOT improved treatment completion in drug users and mixed hard to reach groups.

Moderate evidence suggested that enhanced case management improved treatment completion amongst drug users. There was weak evidence that a service model/social care support approach decreased the incidence rate of TB amongst the homeless.

Overall, very large gaps in the literature were found regarding the use of different interventions in different hard to reach groups, for both active and LTBI. None of the evidence identified was from the UK; most of the papers came from the USA. No cost-effectiveness studies were found on the management of active TB and little evidence for cost-effectiveness in the management of LTBI.

2.4 Evidence review on the effectiveness and cost-effectiveness of service models or structures to manage tuberculosis in hard-to-reach groups (Matrix 2011)

For their fourth and final review Matrix identified 8 studies for this review. Some key evidence gaps were noted, including comparative studies examining the effectiveness and cost-effectiveness of different service structures. Only one study was undertaken in the UK. Studies were not identified which identified the category of individual responsible for commissioning or on the model of service underpinning the design. The heterogeneous nature of studies meant that evidence could not be synthesised. Generally, quality was poor, so strong conclusions could not be drawn.

The analyses in this report use effectiveness evidence for mobile X-ray screening from analysis of the London TB Find & Treat service, applied to scenarios considering variation in the prevalence of TB in the screened population. Due to the lack of evidence of effectiveness of case-management interventions, the PDG requested that we perform threshold analysis of the cost of enhanced case-management interventions that would be considered cost-effective for different levels of effectiveness.

2.5 Summary of cost effectiveness reviews

As previously stated, three of the four Matrix reviews (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; Evidence review on the effectiveness and cost-effectiveness of interventions aimed at managing tuberculosis in hard-to-reach groups; Evidence review on the effectiveness and cost-effectiveness of service models or structures to manage tuberculosis in hard-to-reach groups (Matrix 2011)) found that relevant cost-effectiveness parameters for this work were lacking.

3. Modelling

3.1 Overview

An integrated transmission-dynamic and economic model was used to evaluate the cost-effectiveness of enhanced TB case-finding and case-management in homeless and prison populations, taking account of cases averted as well as cases found and treated. Active case-finding and enhanced case-management have interacting effects on transmission – finding cases only reduces transmission (and benefits the individual patient) if it results in successful treatment – and so need to be modelled together.

3.2 Population

The evaluation considers homeless persons and prisoners, which are the groups to which the interventions considered would be applied.

3.3 Model structure & assumptions

The model is a compartmental (state transition) model of the type described by Anderson & May (1991), which is a well-established modelling method that has been applied successfully to TB as well as many other infectious diseases. This approach divides the population up according to infection status (i.e. naive, latent infection, active disease, on treatment, recovered, etc), each contained in a separate compartment. There are flows between compartments as individuals become infected, progress to disease, are diagnosed and placed on treatment, etc. The rates of flow depend upon per-capita rates and the number of individuals in the relevant compartment at the particular point in time.

The compartmental structure is based on that of Salomon et al. (2006), which was built on the work of Vynnycky and Fine (1997), and Dye et al. (1998), with the modification of inserting a pre-clinical disease stage between latent infection and active disease: radiological abnormalities often precede clinical signs and symptoms so these individuals' disease is detectable by X-ray but is not yet clinically-detectable (or infectious). The model structure was presented on several occasions to the PDG for approval.

Those who acquire TB infection develop latent infection which is either slow- or fast-progressing. Slow-progressors are at risk of exogenous reinfection, which causes fast-progressing latent infection. Progression from latent infection leads to pre-clinical disease (detectable by X-ray but without clinically-detectable signs or symptoms), followed by active disease. Active disease may be smear-negative or smear-positive, with the latter being much more infectious. Self-cure returns some individuals with active disease to the latent state. Those with active disease who access health care are diagnosed and placed on treatment by passive case-finding, with a proportion destined to complete treatment successfully and the remainder destined to fail treatment. In the model, those undergoing successful treatment are non-infectious and upon completion they enter the recovered compartment, and have reduced susceptibility to subsequent infection. Those who are destined to fail treatment are partially infectious due to poor adherence whilst on treatment and after failure are returned to the compartment from which they commenced treatment. Those with untreated and treated active disease are subject to additional TB-associated mortality.

For the homeless and prison populations, rates of entry and exit were estimated from data on the duration of homelessness or being in prison and the size of the population. The data sources are cited in the parameter table.

We assume that the entire relevant population group (homeless or prisoners) mixes homogeneously and can potentially benefit from the intervention and that within the population group there is equal access to services. The model populations are assumed to remain constant in size over time, except for a small increase in size due to reduced TB mortality when interventions are applied, and prior to intervention the incidence and prevalence of infection and disease are assumed to be constant. Rates of population turnover (i.e. average duration homeless or in prison) are assumed to be constant over time. The rate of passive case-finding is assumed not to change over time.

We assume that treatment options remain unchanged, and that current practice with regard to case-finding and case-management remain unchanged through time, and remain unchanged with the addition of the specific interventions considered.

Homeless persons born overseas are not considered separately from homeless persons born in England or the UK because there are insufficient data to determine whether rates of TB acquisition and transmission in homeless populations involving foreign-born individuals are different from rates of TB acquisition and transmission in homeless populations involving UK-born individuals. Prisoners born overseas are not considered separately from prisoners born in England or the UK because there are insufficient data to determine whether rates of TB acquisition and transmission in foreign-born prisoners are different from rates of TB acquisition and transmission in UK-born prisoners.

3.4 Model flow diagram

For clarity, mortality, entry into and exit from the homeless population are omitted from the flow diagram. Infectious compartments are in red. There are multiple compartments for people who are on treatment so that if people fail treatment they can be returned to the compartment from where they started treatment. People who will fail treatment are placed in separate compartments from those who will complete treatment because the time to failure is usually quite short, whilst the time to successful completion is much longer.

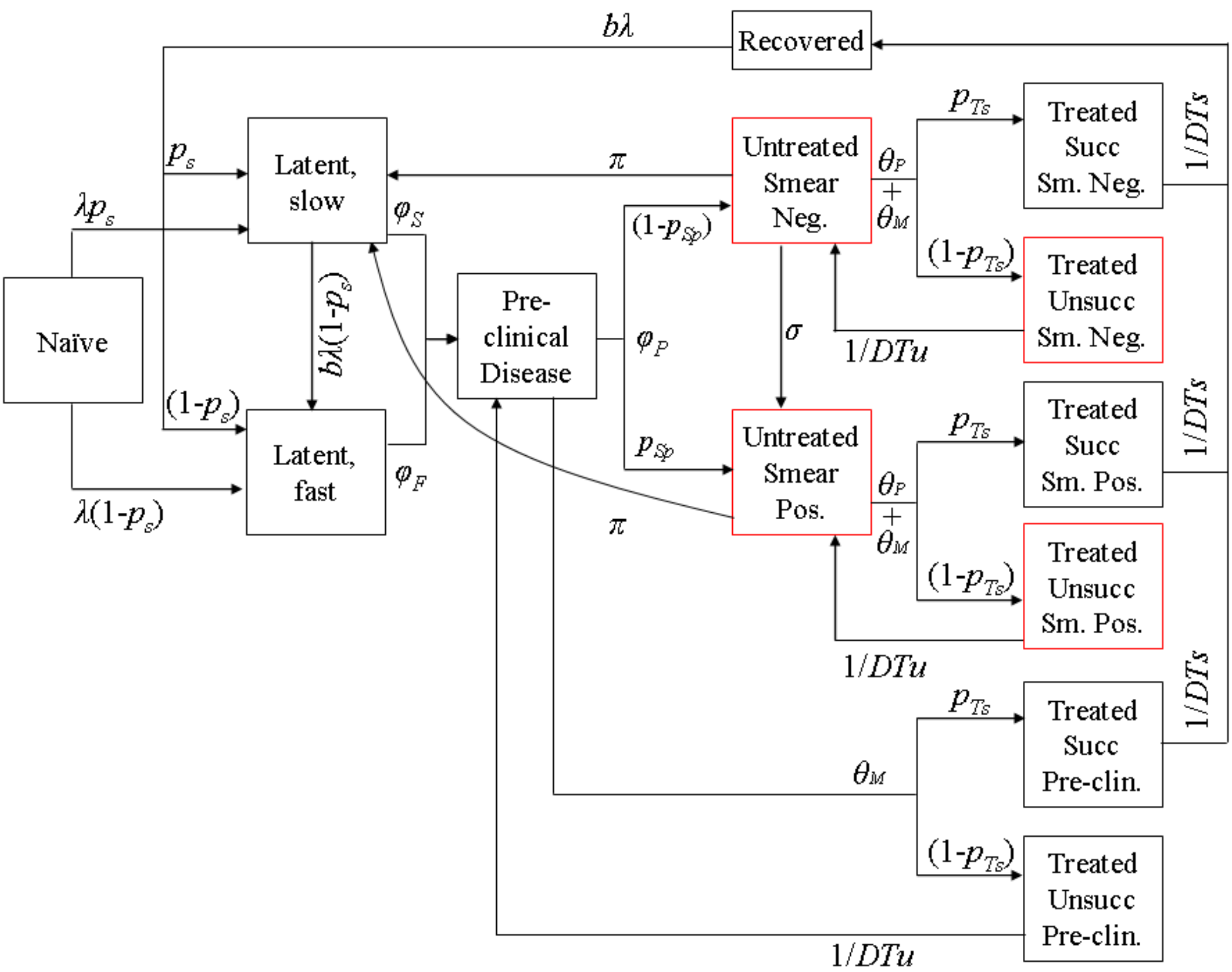


Figure 3.4 Model flow diagram

Movement between health states is shown. Arrow labels are defined in Table 3.5. Abbreviations: Neg. negative; Pre-clin: preclinical; Pos. positive; Sm. smear.

3.5 Data sources

Parameter estimates and data sources are summarised in Table 3.5. Where UK-specific data were not available, parameter estimates from the literature were used. The estimate of the effectiveness for mobile X-ray unit screening – i.e. the per-capita rate of case-finding – was obtained from mean times from symptom onset to diagnosis and proportions of cases found by MXU and passively, from our analysis of the London TB Find & Treat service (Jit et al. in press). The population eligible to be screened by this service was estimated to be 10,000. Our calculations are based on this being the number of persons (homeless or prisoners) who could be reached by such a mobile X-ray service. This could be scaled up at increased cost to increase coverage.

Table 3.5 Transmission model parameters and data sources

Parameter	Description	Value	Source / Reference
Population characteristics			
N_0	Size of population	Homeless: 10000 Prison: 10000	Homeless (London): Office for National Statistics, census 2001 Prison: We assumed that a Mobile X-ray Unit service like London TB Find & Treat could cover the same number of prisoners as homeless persons.
μ	Rate of exit from the population	Homeless: 0.144 p.a. Prison: 0.769 p.a.	Homeless: Social Exclusion Unit report 1998 Prison: Home Office 2001.
TB natural history			
p_S	Proportion of incident infections that are slow-progressing	0.86	Salomon et al. 2006
φ_S	Per-capita rate of slow progression to Pre-clinical disease	1.13×10^{-4} p.a.	Salomon et al. 2006
φ_F	Per-capita rate of fast progression to Pre-clinical disease	0.995 p.a.	Based on Salomon et al. 2006 (0.88 p.a.) but adjusted for insertion of pre-clinical disease state into natural history
φ_P	Per-capita rate of progression from Pre-clinical disease to active disease	7.6 p.a.	Abubakar et al. May 2011
p_{Sp}	Proportion of new disease that is smear positive	0.45	Salomon et al. 2006
μ_{USn}, μ_{USp}	Per-capita mortality rate of untreated active disease	0.23 p.a.	[Indian] National Tuberculosis Institute 1974
σ	Per-capita rate of conversion from smear-negative to positive	0.015 p.a.	Salomon et al. 2006
π	Per-capita rate of self-cure: natural reversion from active disease to latent infection	0.21 p.a.	[Indian] National Tuberculosis Institute 1974
Screening & treatment			
θ_P	Per-capita rate of passive case-finding	3.02 p.a.	Abubakar et al. May 2011
θ_M	Per-capita rate of active case-finding by mobile X-ray	Varied in scenarios	Abubakar et al. May 2011

	unit		
p_{Ts}	Proportion treated successfully	Varied in scenarios	This study
DTs	Mean duration of successful treatment	0.34 years (125 days)	Abubakar et al. May 2011
DTu	Mean duration of unsuccessful treatment	0.16 years (2 months)	Abubakar et al. May 2011
μ_{TuSn}, μ_{TuSp}	Per-capita mortality rate of unsuccessfully treated disease	0.077 p.a.	Salomon et al. 2006
Transmission			
β_P	Transmission parameter for smear-positives	Fitted – varies according to scenario	This study
b_N	Relative infectivity of smear-negatives (vs smear-positives)	0.25	Abu-Raddad et al. 2009
b	Relative susceptibility of Latent (slow) and Recovered individuals (vs Susceptibles)	0.35	Salomon et al. 2006; Abu-Raddad et al. 2009
b_{Tu}	Relative infectivity of unsuccessfully treated (vs untreated)	0.25	Salomon et al. 2006

3.6 Scenarios considered

The scenarios examined were:

3.6.1 Current practice – i.e. no interventions

Only passive case-finding occurs. That is, TB treatment care is provided to individuals with symptomatic TB who seek care, are referred to TB services and diagnosed. Current standard approaches to case-management are used, resulting in 55% of homeless persons and 48% of prisoners successfully completing treatment.

3.6.2 Mobile X-ray unit (MXU) screening

The MXU increases the case-finding rate of those with active TB, and also detects those with pre-clinical disease who are not yet symptomatic. The lifetime of the MXU is 10 years and so the calculations include a replacement cost occurring after 10 years. In the scenario where only case-finding is enhanced, treatment completion rates remain unchanged. In analysis, we used the observed case-finding rate of 0.78 per case per year. The annual number of diagnoses depends upon the rate at which individual cases are found and the average number of cases that are there to be found during that year. The rate at which individual cases are found is the inverse of the average duration from the onset of illness to the time of diagnosis. Our data come from a homeless population where active case-finding by the London TB Find & Treat service MXU and passive case-finding occurred together, in which the rate of case-finding was 3.8 p.a. (corresponding to a mean time from symptom onset to diagnosis of 96 days) and 18 of 58 cases were found by the MXU; therefore rate of case-finding by MXU is 0.78 p.a. and the rate of passive case-finding is 3.02 p.a. (Abubakar et al. May 2011). For this homeless population there was only one year (2009) for which we have data when the London TB Find & Treat service screened the homeless and Enhanced TB Surveillance recorded whether cases were in homeless, prisoners, general population, etc. For prisoners there is no such year: the limited period for which the London TB Find & Treat service screened prisoners did not overlap with the time when Enhanced TB Surveillance recorded whether cases were in prisoners, homeless, the general population, etc. Therefore we do not have comparable data and have had to assume that the case-finding rates in prisoners would be the same as in the homeless. In order to cover a prison population of 10,000 the MXU moves around prisons.

In sensitivity analysis we halved and doubled the active case-finding rate, with costs halved and doubled, respectively.

3.6.3 Enhanced case-management

Several scenarios with increased treatment completion rates were examined, whilst rates of case-finding remain unchanged. As the cost of achieving these increases is not known, we did not incorporate any cost in the analysis. Rather, the purpose of the analysis is to determine the quality of life gain (and potential cost savings, due to averted transmission events) in order to calculate what expenditure on enhanced case management would be likely to be considered cost-effective.

3.6.4 Combined MXU case-finding and enhanced case-management

Scenarios considering both enhanced case-finding and case-management were considered, to account for interactions between them. The costs considered relate to the MXU, including the replacement cost after 10 years. Again, costs of enhanced case-management were not included in order to calculate what expenditure would be likely to be considered cost-effective in light of the quality of life gain and potential cost savings.

3.6.5 Comparison of interventions

Mobile X-ray screening and enhanced case management cannot be compared with each other in terms of dominance/extended dominance because the cost of enhanced case management is unknown. Hence results are given in terms of threshold costs for cost-effectiveness rather than incremental cost-effectiveness ratios.

4. Resource identification, measurement and valuation

4.1 NHS costs

There are no NHS reference costs for “tuberculosis treatment”. The cost of 6 months of TB treatment has been previously estimated at 5,100 in 2006 prices (National Collaborating Centre for Chronic Conditions, CG117, 2011). However, the PDG was aware that this may not capture the costs of dealing with the complex issues involved in managing hard-to-reach populations, such as time required in hospital for treatment, dealing with co-morbidities, housing problems, and more intensive follow-up required to maintain adherence to treatment. Articles identified during the review of evidence on the cost-effectiveness evidence conducted by Matrix were reviewed to see if they contained information about the costs or quality of life effects associated with tuberculosis. Only information that was deemed relevant to the UK situation and the NICE reference case was extracted (based on the selection criteria of costs being from UK-based studies, and quality of life information being measured in QALYs using the EQ-5D instrument). Parameter estimates were discussed with members of the PDG attending the meeting held on 7 June 2011. The PDG suggested that based upon their experience an appropriate estimate of treatment costs of TB among hard-to-reach patients is £15,000 per case.

4.2 Intervention costs

Active case finding (for example, using a mobile X-ray unit) was assumed to incur start-up costs of £1 million for the purchase of screening equipment and associated transportation. This one-off cost was assumed to reoccur after 10 years due to the need to replace this equipment. In addition, it was assumed to incur annual costs of £500,000 for staff salaries, accommodation and other incidental expenses. These costs based on the cost of the mobile X-ray unit used by the London TB Find & Treat service was estimated to be £600,000, while annual costs of the entire service (which includes both active case finding and enhanced case management) was estimated to be £1 million.

The cost of the initial screen (chest X-ray) was assumed to be included in the annual active case finding costs. Cases referred for diagnostic testing (whether or not they were subsequently found to have active TB) were assumed to incur the cost of a laboratory culture test (£7.12), estimated from NHS reference costs (2008/9) for microbiological pathology services. Cases placed on treatment as a result of active or passive case finding were assumed to incur this cost. In addition, false positives were assumed to be referred for diagnostic testing, then detected at the testing stage before being put on treatment. Test specificity of 67% was assumed (Van Cleeff et al, 2005).

Economic parameters are summarised in the Table 4.2.

Table 4.2 Economic parameters

Parameter	Value	Source
X-ray specificity	67%	Van Cleeff et al, 2005
Cost discount rate	3.5% p.a.	NICE 2009
Benefits discount rate	3.5% p.a.	NICE, 2009
Treatment cost	£15,000	PDG consensus (details below)
Diagnostic test cost	£7.12	NHS reference costs 2008/9
Active screening cost (mobile X-ray)	£16	National Collaborating Centre for Chronic Conditions, CG117, 2011
Annual mobile X-ray unit intervention cost	£500,000	Assumed, based on London TB Find & Treat service budget
Mobile X-ray unit capital cost (incurred every 10 years)	£1,000,000	Assumed, based on London TB Find & Treat service budget

4.3 Advice provided by the PDG regarding the cost of TB treatment in hard-to-reach groups

The following advice was provided by the PDG.

In 2003/4 there were 7011 TB cases notified in England. HES data shows 3892 admissions where TB was the primary diagnosis accounting for 64192 bed days (Hospital Episode Statistics 2003-4). This gives an average of 9.15 bed days per TB notification.

The London TB nurses patient profile – 2003-2004 retrospectively collected information on hospitalisations from clinic TB nurses from a cohort of all patients known to service. Because the data collection was retrospective and clinic nurses do not necessarily always know patients' admission history we expect this to underestimate hospitalisations.

In 2003 the profile data showed an average hospital duration of 5.4 bed days per TB patient. Comparing this to the figure derived from national HES and TB notification data this suggests that the TB profile bed day data need to multiplied by a factor of 1.7 to correct for under-ascertainment.

Table 4.3 shows the durations of admission corrected for under-reporting in the groups targeted by the MXU (homeless people and drug users).

Table 4.3 Durations of admission corrected for under-reporting in the groups targeted by the MXU (homeless people and drug users)

	Average hospital duration	Corrected admission duration	Corrected admission costs	Out patient cost	DOT cost	Total
Not hard to reach	5.4	9.2	3386	921	300	4606
Homeless and drug users	11.7	19.9	7320	921	2964	11205

The costs of tuberculosis admissions are calculated from the National Schedule of Reference Costs 2007-08 for NHS Trusts and PCTs. (Department of Health, 2009).

These show an average cost for elective admissions for tuberculosis cases of £1935 with an average of 5.3 days per admission (£368 per bed day). This is a conservative cost because it does not allow for any bed days in critical care or isolation which carry higher costs. Table 4.3 shows the estimated admission costs based on these figures.

Outpatients' costs are also derived from the National Schedule of Reference costs allowing 1 first appointment with a respiratory clinician (£186) and 5 further sessions of TB nurse support (£146 each) for all patients, totalling £921.

It is assumed that all hard to reach patients and 10% of non-hard-to-reach patients should be on 3 weekly DOT for 6 months. This is costed at the minimum listed respiratory outpatient cost of £38 per session (the cost of a non consultant respiratory medicine outpatient appointment that does not include face to face contact). The total DOT cost is estimated at £2964 per DOT case.

Using this methodology the average total cost per case is £4606 (close to the NHS tariff cost for an average TB case) and the cost per case in homeless and drug using populations (the populations targeted by the MXU) is £11205.

This represents the cost of £11205 for an average hard to reach case (using 2008 NHS costs). We note that the proportion of cases who are MDRTB has increased (now 10% of hard to reach cases known to Find and Treat so this a conservative estimate of the average cost per case.

This estimate does not include NHS inflation since 2008 or the increase in the proportion of cases that have MDR TB, which is now 3-4 times the proportion in 2003-4, and assumes that all admission days are ordinary admissions rather than more expensive critical care or isolation room admissions. Thus a £15,000 cost per hard to reach case would seem appropriate.

5. Quality of life

Health-related quality of life weights of 0.675, 0.813 and 0.87 respectively were assumed for cases with active TB not on treatment, cases with active TB on treatment and cases without active TB (Table 5.1). Weights for cases without active TB were based on UK population norms for 20-49 year olds (Kind et al, 1998) as agreed by the PDG. Health-related quality of life weights for cases with TB were amalgamated from data presented in two studies (National Collaborating Centre for Chronic Conditions, CG117, 2011; Kruijshaar et al, 2010).

Table 5.1 Health-related quality of life weights

Health state	QoL weight	QALY loss	Reference
Active TB		0.676	National Collaborating Centre for Chronic Conditions. CG117, 2011
Active TB, start of treatment	0.675		Kruijshaar *et al*,2010
Active TB, 2 months into treatment	0.813		Kruijshaar *et al*,2010
Population norm, 20-39 years old	0.87		Kind et al, 1998
Population norm, 40-49 years old	0.85		Kind et al, 1998

6. Analysis

6.1 Validation

The model is based upon extensive previous modelling TB work performed by ourselves and many others (reviewed by White & Garnett 2010), and is consistent with available data. It has been discussed at several meetings with the PDG, who provided advice on parameterisation. It is not possible to formally validate the model against a suitable independent data-set because no such data exist.

6.2 Sensitivity analysis

6.2.1 Structural uncertainty

Structural uncertainty was not evaluated due to limitations of time and resources. However, the model structure was presented on several occasions to the PDG for approval.

6.2.2 Deterministic sensitivity analysis

Variables subject to deterministic sensitivity analysis were the prevalence of TB in different homeless populations and in prisoners, and in the effectiveness of case-management interventions. These were subject to two-way sensitivity analyses (i.e. combinations of two parameters were varied at the same time). The cost of treatment of hard-to-reach cases was varied in sensitivity analysis.

Since data on the costs of enhanced case management are lacking, instead of assuming a particular value for this we conducted a threshold analysis to determine the cost at which this intervention (alone or in combination with X-ray screening) would be cost-effective. The value used for the cost of X-ray screening was specified by the PDG.

Time and resource constraints meant that not all possible sensitivity analyses could be performed. The PDG's view was that it was most useful to have extensive two-way sensitivity analyses across all scenarios that are presented in this report.

6.2.3 Scenarios considered

The greatest uncertainties are in the prevalence of TB in different homeless populations and in prisoners, and in the effectiveness of case-management interventions. Therefore these were examined in sensitivity analysis.

In the baseline scenarios for homeless and prisoners we use the prevalence of treated TB reported by Story et al. (2007): i.e. 788 per 100,000 for homeless and 208 per 100,000 for prisoners, with cases found passively and given standard care, with a treatment completion rate of 55% in the homeless and 48% in prisoners, as advised by the PDG.

A number of scenarios considering case-finding and case-management interventions in homeless and prisoners were examined, with a 20-year time horizon, as specified by the PDG, taking a public sector perspective. As there are few data on the costs or effectiveness of case-management interventions, and they will vary widely depending on the setting and exact nature of the intervention, we modelled the effect of improved case management on health outcomes and other costs, to guide decisions regarding what it would be worth paying to achieve a particular improvement in treatment outcome.

6.2.4 Probabilistic sensitivity analysis

Probabilistic sensitivity analysis (PSA) was not undertaken, due to time and resource constraints. Instead, we have estimated threshold values at which an intervention may be cost-effective.

7. Results

7.1 Overview of results section

The first part of the Results section provides an overview of intervention outcomes, discussing general principles that are applicable to both homeless and prison populations.

This is followed by analysis of homeless populations, presented in the order previously described in the description of the model. The base case is presented, first showing annual numbers of new infections and annual numbers of new cases of active disease occurring with current practice – i.e. with no intervention. Then the effect of case-finding by mobile X-ray unit (MXU) in the homeless on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred is presented. This is followed by examination of the effect of enhanced case-management in the homeless on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred. Finally, the effect of combined case-finding and enhanced case-management in the homeless on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred is presented.

This is followed by sensitivity analysis of homeless populations, presented in the same order. The effect of varying the proportion of the population being treated for TB under current practice – i.e. with no intervention – on annual numbers of new infections and annual numbers of new cases of active disease occurring is presented.

Then the effect of varying the proportion of the population being treated for TB prior to the intervention on the effect of case-finding by mobile X-ray unit (MXU) in the homeless on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred is presented. The effect of varying the amount of MXU case-finding and varying the proportion of the population being treated for TB prior to the intervention is examined to determine under what circumstances MXU case-finding is cost-effective if a QALY is valued at £20,000 or £30,000. Also examined is how variation in the cost of MXU case-finding and the variation in the cost of treating a case of TB in the homeless affect the cost-effectiveness of MXU case-finding if a QALY is valued at £20,000 or £30,000.

This is followed by examination of the effect of varying the proportion of the population being treated for TB prior to the intervention on the effect of enhanced case-management in the homeless on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred. The effect of varying the treatment completion rate achieved by enhanced case-management and varying the proportion of the population being treated for TB prior to the intervention is examined to determine under what circumstances enhanced case-management is cost-effective if a QALY is valued at £20,000 or £30,000. Also examined is how variation in the treatment completion rate achieved by enhanced case-management and variation in the cost of treating a case of TB in the homeless affect the cost-effectiveness of enhanced case-management if a QALY is valued at £20,000.

Finally, the effect of varying the proportion of the population being treated for TB prior to the intervention on the effect of combined MXU case-finding and enhanced case-management in the homeless on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred is presented. The combined effects of varying the proportion of the population being treated for TB prior to the intervention, the treatment completion rate achieved by enhanced case-management and the amount of MXU case-finding on whether the combined intervention is cost-effective if a QALY is valued at £20,000 or £30,000 is examined.

This is followed by analysis of prison populations, presented in the order previously described in the description of the model. The base case is presented, first showing annual numbers of new infections and annual numbers of new cases of active disease occurring with current practice – i.e. with no intervention. Then the effect of case-finding by mobile X-ray unit (MXU) in prisoners on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred is presented. This is followed by examination of the effect of enhanced case-management in prisoners on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred. Finally, the effect of combined case-finding and enhanced case-management in prisoners on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred is presented.

This is followed by sensitivity analysis of prison populations, presented in the same order. The effect of varying the proportion of the population being treated for TB under current practice – i.e. with no intervention – on annual numbers of new infections and annual numbers of new cases of active disease occurring is presented.

Then the effect of varying the proportion of the population being treated for TB prior to the intervention on the effect of case-finding by mobile X-ray unit (MXU) in prisoners on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred is presented. The effect of varying the amount of MXU case-finding and varying the proportion of the population being treated for TB prior to the intervention is examined to determine under what circumstances MXU case-finding is cost-effective if a QALY is valued at £20,000 or £30,000. Also examined is how variation in the cost of MXU case-finding and the variation in the cost of treating a case of TB in prisoners affect the cost-effectiveness of MXU case-finding if a QALY is valued at £20,000 or £30,000.

This is followed by examination of the effect of varying the proportion of the population being treated for TB prior to the intervention on the effect of enhanced case-management in prisoners on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred. The effect of varying the treatment completion rate achieved by enhanced case-management and varying the proportion of the population being treated for TB prior to the intervention is examined to determine under what circumstances enhanced case-management is cost-effective if a QALY is valued at £20,000 or £30,000. Also examined is how variation in the treatment completion rate achieved by enhanced case-management and variation in the cost of treating a case of TB in prisoners affect the cost-effectiveness of enhanced case-management if a QALY is valued at £20,000.

Finally, the effect of varying the proportion of the population being treated for TB prior to the intervention on the effect of combined MXU case-finding and enhanced case-management in prisoners on annual numbers of new infections averted, annual numbers of new cases of active disease averted, discounted annual numbers of QALYs gained, and discounted annual net costs incurred is presented. The combined effects of varying the proportion of the population being treated for TB prior to the intervention, the treatment completion rate achieved by enhanced case-management and the amount of MXU case-finding on whether the combined intervention is cost-effective if a QALY is valued at £20,000 or £30,000 is examined.

7.2 Overview of intervention outcomes

Enhanced case-finding and case-management reduce the prevalence of untreated active TB, for several reasons. Firstly, people are unwell for a shorter period on average before they are diagnosed and treated. Secondly, the proportion diagnosed who successfully complete treatment increases, so that a smaller proportion of those diagnosed return to the untreated active disease states after diagnosis, due to loss to follow-up. Thirdly, the reduction in prevalence due to faster case-finding and improved case management leads to a reduction in transmission of TB, causing a decrease in incidence of infection (and exogenous reinfection) which leads to a reduced incidence of active disease. In all cases interventions were beneficial to health.

Net costs are highest in the early years of the intervention, due to capital start-up costs being incurred then, and because cost savings due to infections averted accrue in later years. This is because it takes time for the prevalence of untreated active disease to fall – and thus to avert transmission events – and the time taken for disease progression means that a fall in the incidence of new *disease* lags behind a fall in the incidence of new *infection*.

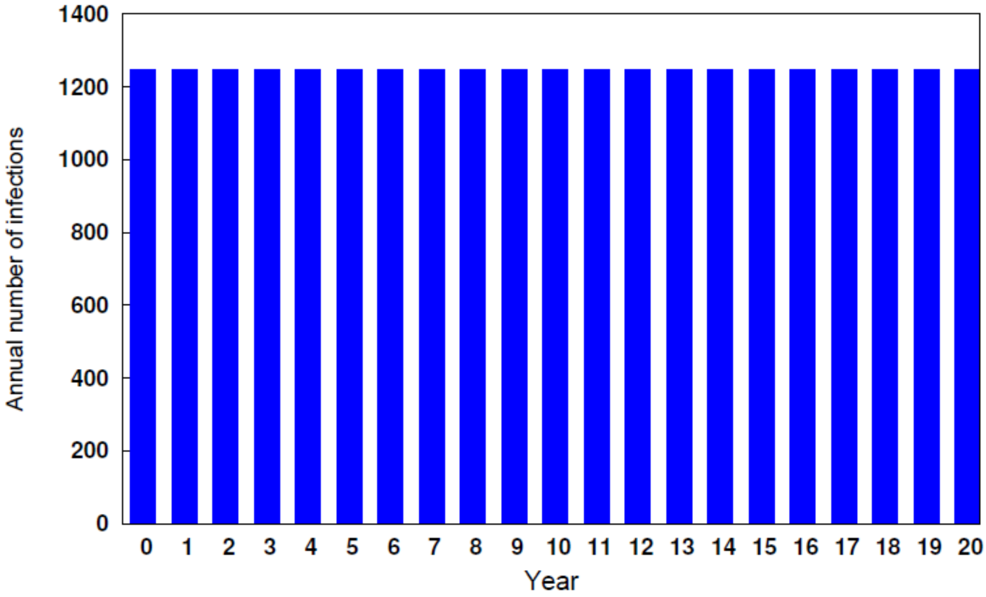
In all cases, QALYs gained and costs incurred are with reference to the baseline scenario.

7.3 Homeless: Base case

7.3.1 Current practice – i.e. no interventions

The base case assumes that the population size is constant, rates of entry and exit are constant, and that current practice for case-finding and treatment remain unchanged. Therefore, the same number of infections and cases of active disease occur in each year. Figure 7.3.1 shows the base case for the homeless, where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000.

(a)



(b)

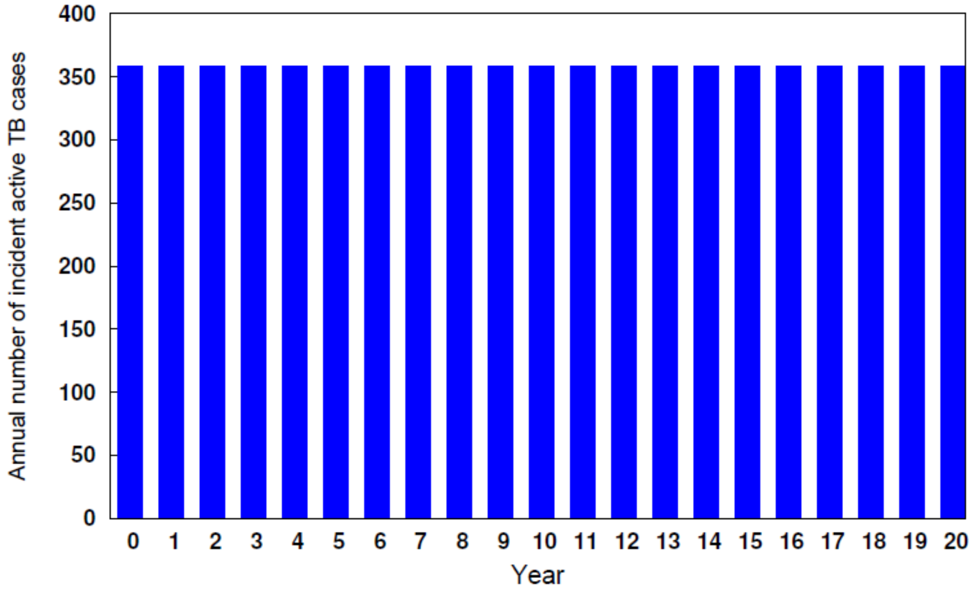


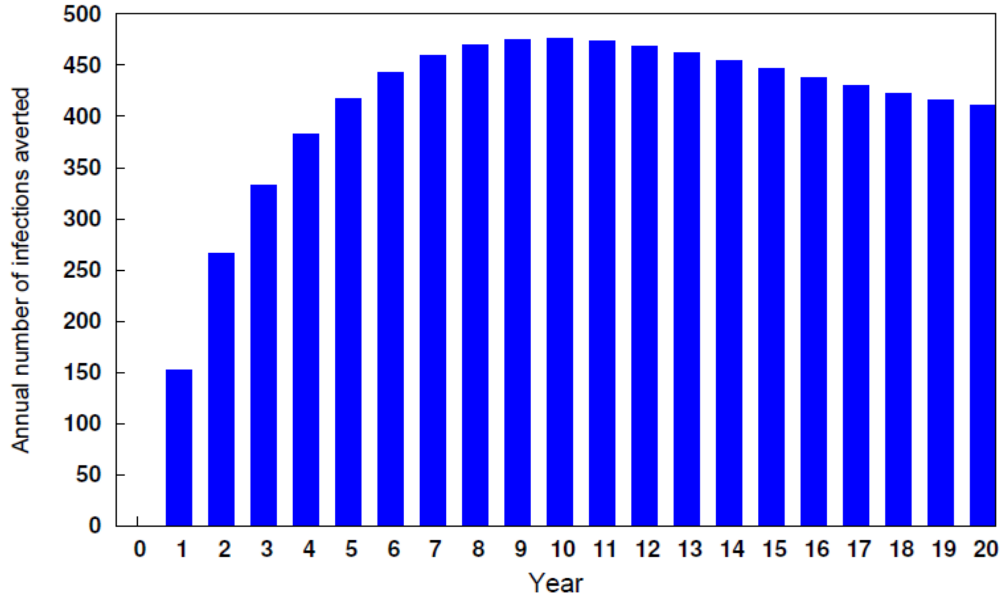
Figure 7.3.1 Annual numbers (undiscounted) of new infections and new cases of active disease in the homeless

(a) Annual numbers (undiscounted) of new infections in a homeless population of 10,000 with the proportion of the population being treated for TB prior to the intervention being 788 per 100,000 and the treatment completion rate being 55%.
(b) Annual numbers (undiscounted) of new cases of active disease in a homeless population of 10,000 with the proportion of the population being treated for TB prior to the intervention being 788 per 100,000 and the treatment completion rate being 55%.

7.3.2 Case-finding by mobile X-ray unit (MXU) in the homeless

The time-courses of annual numbers of infections averted and cases of active disease averted are shown in Figure 7.3.2a. Note that the number of infections averted is greater than the number of active disease cases averted because the majority of infections do not progress to active disease. As time progresses since the introduction of the intervention the annual number of infections averted and cases of active disease averted increases. This is because over time the prevalence of infectious untreated active disease declines, so rates of transmission in the population decline.

(a)



(b)

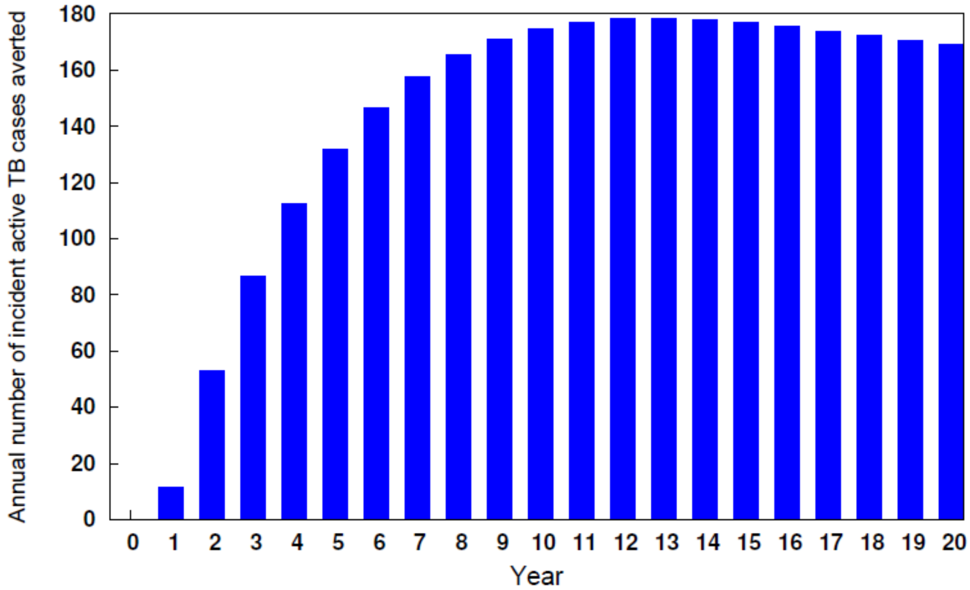


Figure 7.3.2a Annual numbers (undiscounted) of new infections and new cases of active disease averted by mobile X-ray unit case finding in the homeless

(a) Annual numbers (undiscounted) of new infections averted over a 20-year time-horizon by MXU case-finding in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000. The MXU case-finding rate is 0.78 per case per year. The intervention begins in year 1. The treatment completion rate is 55%.
(b) Annual numbers (undiscounted) of new cases of active disease averted over a 20-year time-horizon by MXU case-finding in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000. The MXU case-finding rate is 0.78 per case per year. The intervention begins in year 1. The treatment completion rate is 55%.

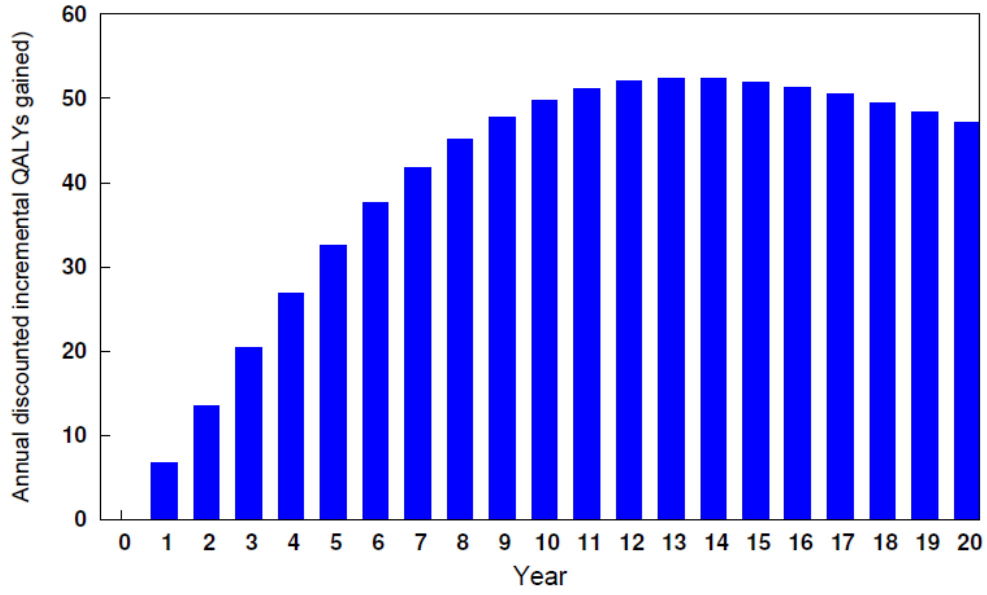
The time-courses of QALYs gained and costs incurred are shown in Figure 7.3.2b. Capital costs (i.e. MXU purchases) are incurred at the start of the intervention and after 10 years. The total discounted QALYs gained and net costs incurred shown in Table 7.3.2c.

Annual QALY gains mirror the annual numbers of active disease cases averted, because active disease is what causes health loss. Discounting means that gains further in the future are valued less than gains that occur earlier.

There are net costs at the beginning of the intervention, due to capital costs, the costs of running the intervention, and increased treatment costs incurred because more cases of active disease are found than would have been found without active MXU case-finding.

Subsequently, there are net savings, as the savings on treatment costs due to the reduction in numbers of active disease cases occurring outweigh the costs of running the intervention. Capital costs (MXU purchase) are incurred at the start of the intervention and 10 years later (MXU replacement). In the year when the MXU has to be replaced the net saving is smaller.

(a)



(b)

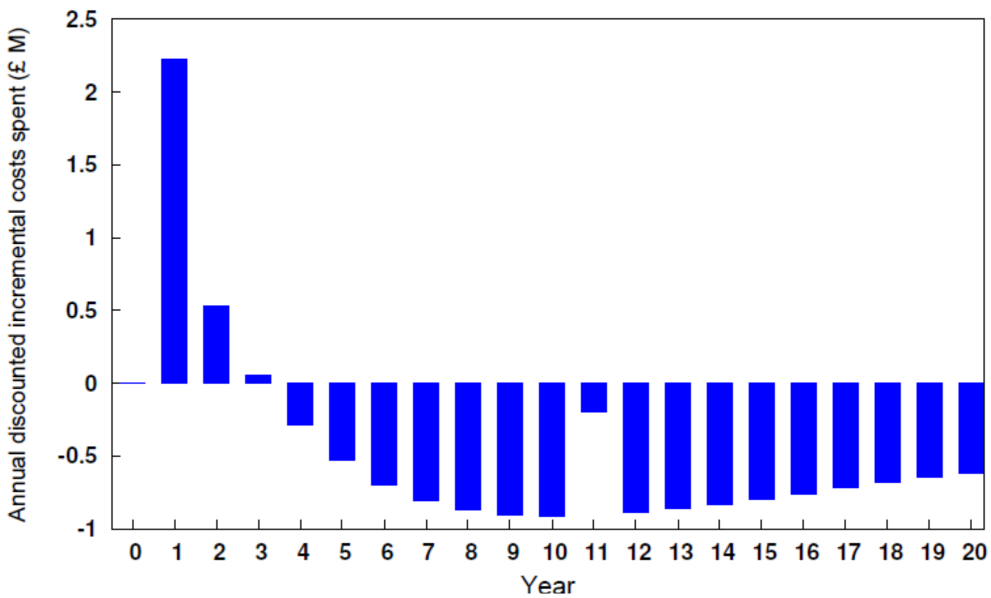


Figure 7.3.2b Discounted annual number of QALYs gained and net costs incurred by mobile X-ray unit case-finding in the homeless

(a) Discounted annual number of QALYs gained over a 20-year time-horizon by MXU case-finding in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the MXU active case-finding rate is 0.78 per case per year. The intervention begins in year 1. The treatment completion rate is 55%.

(b) Discounted annual net costs incurred over a 20-year time-horizon by MXU case-finding in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the MXU active case-finding rate is 0.78 per case per year. Negative net costs incurred indicate net savings. The intervention begins in year 1. The MXU is replaced in year 11. The treatment completion rate is 55%.

Total discounted QALYs gained and net costs incurred) are shown in Table 7.3.2c. The intervention is cost-saving because the savings on treatment costs due to disease cases averted outweigh the intervention costs.

Table 7.3.2c Case-finding by mobile X-ray unit in the homeless

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, compared with current practice, where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the active case-finding rate is 0.78 per case per year. The treatment completion rate is 55%. Negative incremental net costs are net cost savings.

QALYs gained compared with current practice	Incremental costs (£M) compared with current practice	Incremental Net Benefit (£M) compared with current practice	
		If a QALY is valued at £20,000	If a QALY is valued at £30,000
828.5	-9.2	25.7	34.0

7.3.3 Enhanced case-management in the homeless

Increasing rates of treatment completion through enhanced case-management averts transmission events and therefore averts cases of active disease, as shown in Figure 7.3.3a. This is due to (i) infections being averted, thus averting cases of disease requiring treatment, and (ii) a reduction in the number of individuals requiring re-treatment.

The intervention resulted in health benefits (QALYs gained) and reduced treatment costs.

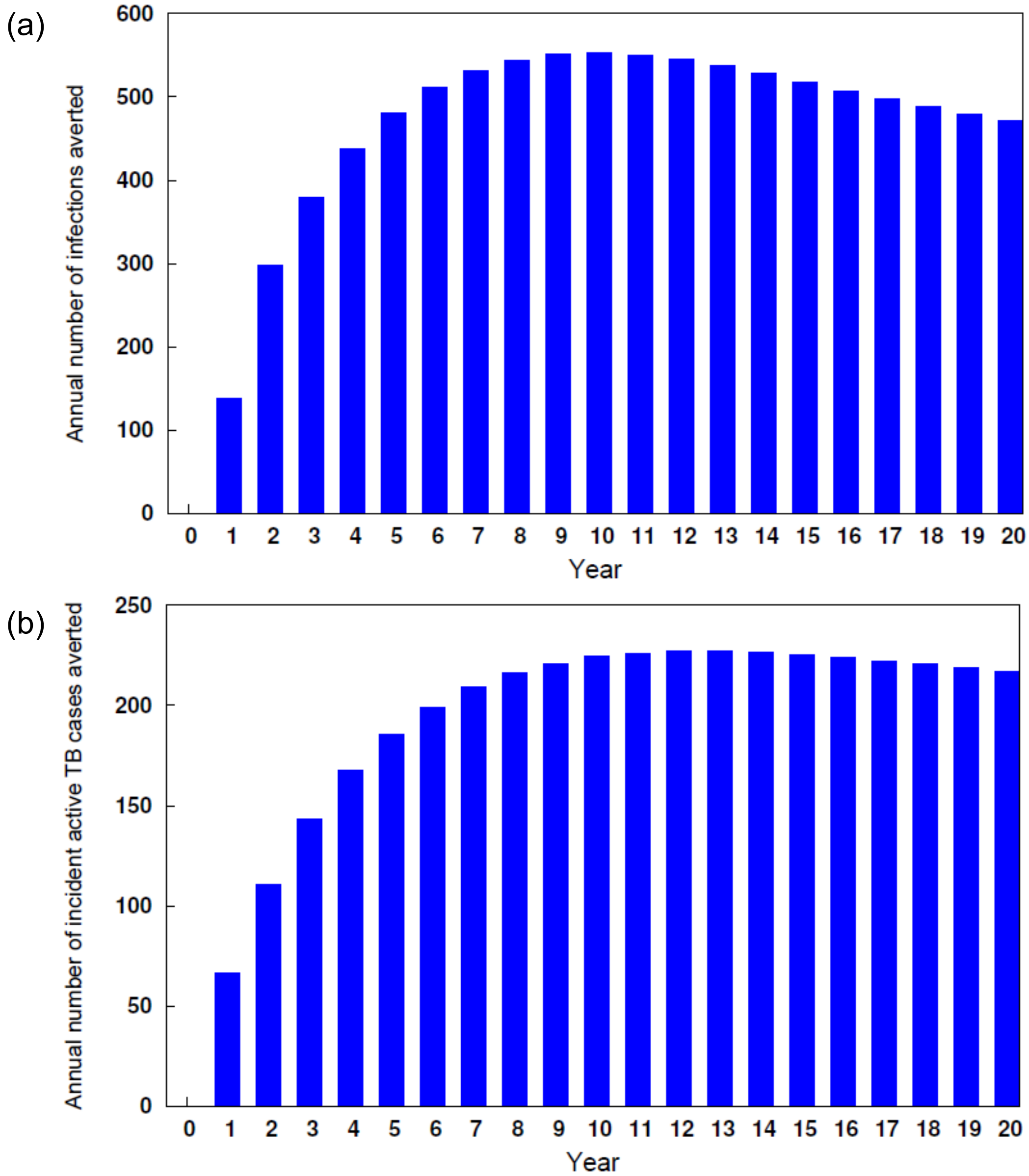


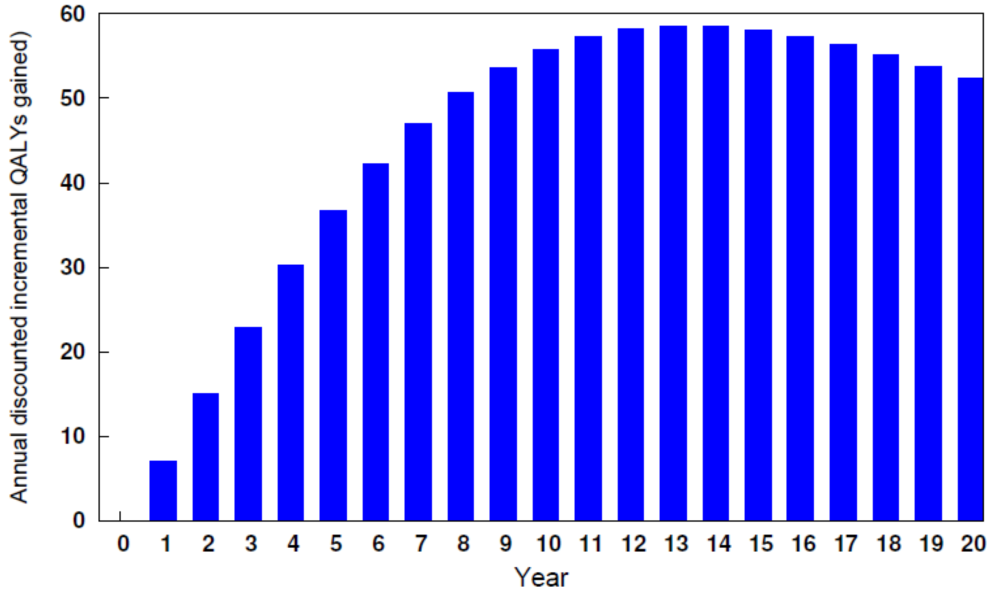
Figure 7.3.3a Annual numbers (undiscounted) of new infections and new cases of active disease averted by enhanced case-management in the homeless

(a) Annual numbers (undiscounted) of new infections averted over a 20-year time-horizon by enhanced case-management in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000, the treatment completion rate prior to the intervention is 55%, and the treatment completion rate with the intervention is 75%. The intervention begins in year 1.
(b) Annual numbers (undiscounted) of new cases of active disease averted over a 20-year time-horizon by enhanced case-management in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%, and the treatment completion rate with the intervention is 75%. The intervention begins in year 1.

The time-courses of QALYs gained and costs incurred are shown in Figure 7.3.3.b and the total discounted QALYs gained and net costs incurred over the 20-year time-horizon are shown in Table 7.3.3c.

As before, annual QALY gains mirror the annual numbers of active disease cases averted, because active disease is what causes health loss. Discounting means that gains further in the future are valued less than gains that occur earlier.

(a)



(b)

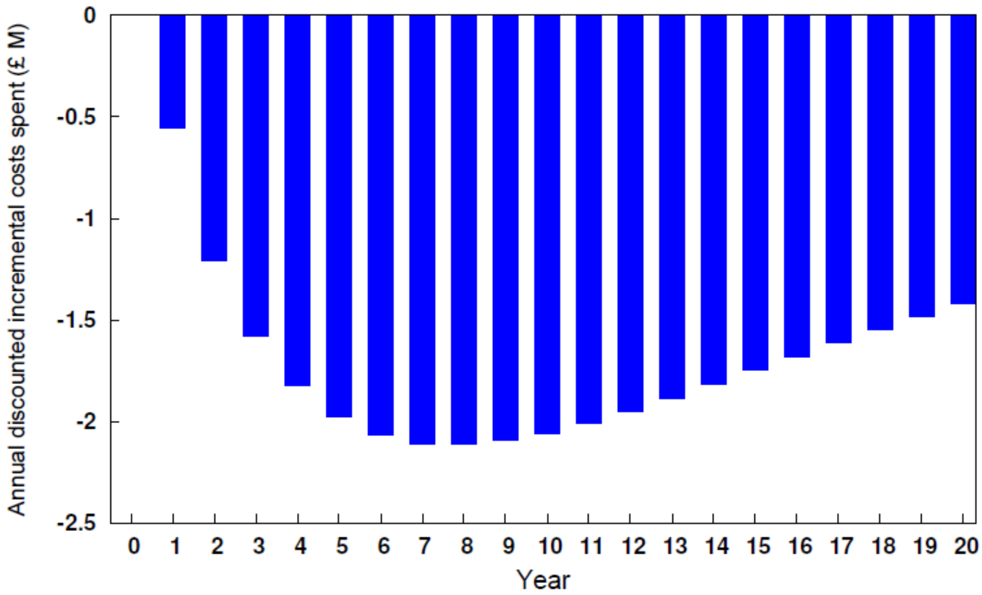


Figure 7.3.3b Discounted annual number of QALYs gained and net costs incurred by enhanced case-management in the homeless

(a) Discounted annual number of QALYs gained over a 20-year time-horizon by enhanced case-management in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%; the treatment completion rate with the intervention is 75%. The intervention begins in year 1.

(b) Discounted annual net costs incurred over a 20-year time-horizon by enhanced case-management in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%; the treatment completion rate with the intervention is 75%. Negative net costs incurred indicate net savings. The intervention begins in year 1.

In Table 7.3.3c we present the incremental net benefit (i.e. the threshold cost at which the intervention would be just cost-effective) of enhanced case management for the population of 10,000 over 20 years if a QALY is valued at £20,000 and £30,000.

Table 7.3.3c Enhanced case-management in the homeless

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, compared with current practice, where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000, the treatment completion rate prior to the intervention is 55%, and the treatment completion rate with the intervention is 75%. Negative incremental net costs are net cost savings.

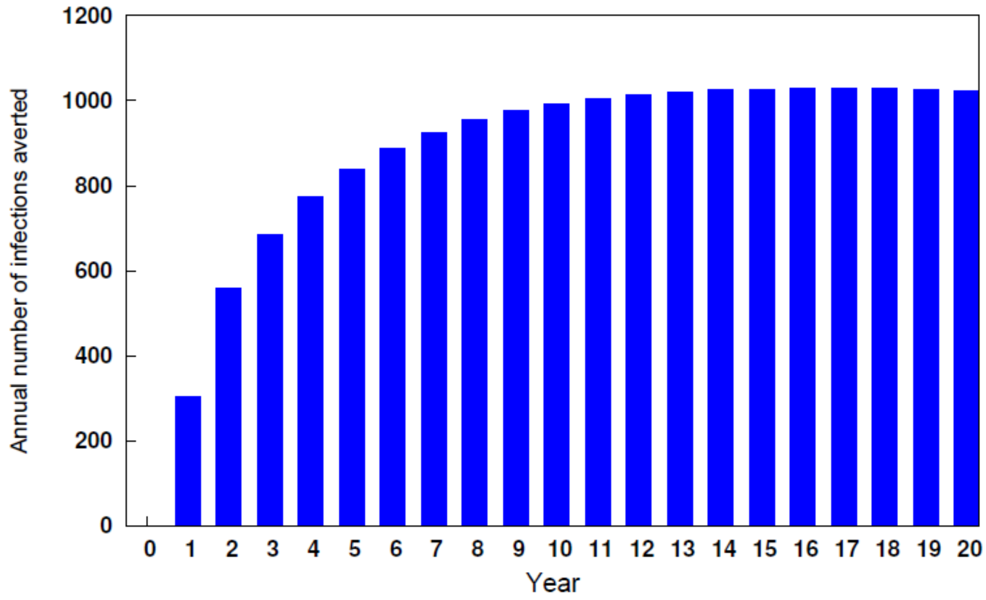
QALYs gained compared with current practice	Incremental costs compared with current practice (omitting intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
		If a QALY is valued at £20,000	If a QALY is valued at £30,000
926.6	-34.7	53.2	62.5

7.3.4 Combined case-finding and enhanced case-management in the homeless

In this analysis we calculate the cost of enhanced case-management for the population of 10,000 over 20 years that would be considered cost-effective when combined with active case-finding by mobile X-ray unit if a QALY is valued at £20,000 and £30,000.

The time-courses of infections averted and cases of active disease averted are shown in Figure 7.3.4a, and of QALYs gained and costs incurred are shown in Figure 7.3.4b. Annual QALY gains reflect annual numbers of cases of active disease averted, but QALY gains are discounted so that those occurring further in the future are valued less. The total discounted QALYs gained and net costs incurred over the 20-year time horizon are shown in Table 7.3.4c.

(a)



(b)

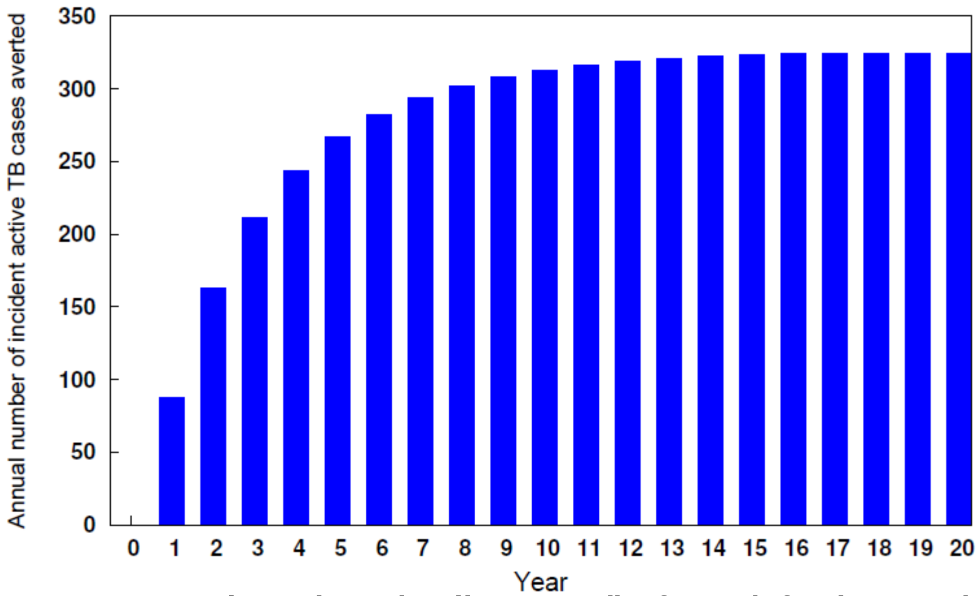


Figure 7.3.4a Annual numbers (undiscounted) of new infections and new cases of active disease averted by combined interventions in the homeless

(a) Annual numbers (undiscounted) of new infections averted, compared with current practice, by combined MXU case-finding and enhanced case-management in a homeless population, where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and treatment completion rate of 55% prior to the intervention. The combined intervention is MXU case-finding at 0.78 p.a. and enhanced case-management increasing the treatment completion rate to 75%. The intervention begins in year 1.

(b) Annual numbers (undiscounted) of new cases of active disease averted, compared with current practice, by combined MXU case-finding and enhanced case-management in a homeless population where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and treatment completion rate of 55% prior to the intervention. The combined intervention is MXU case-finding at 0.78 p.a. and enhanced case-management increasing the treatment completion rate to 75%. The intervention begins in year 1.

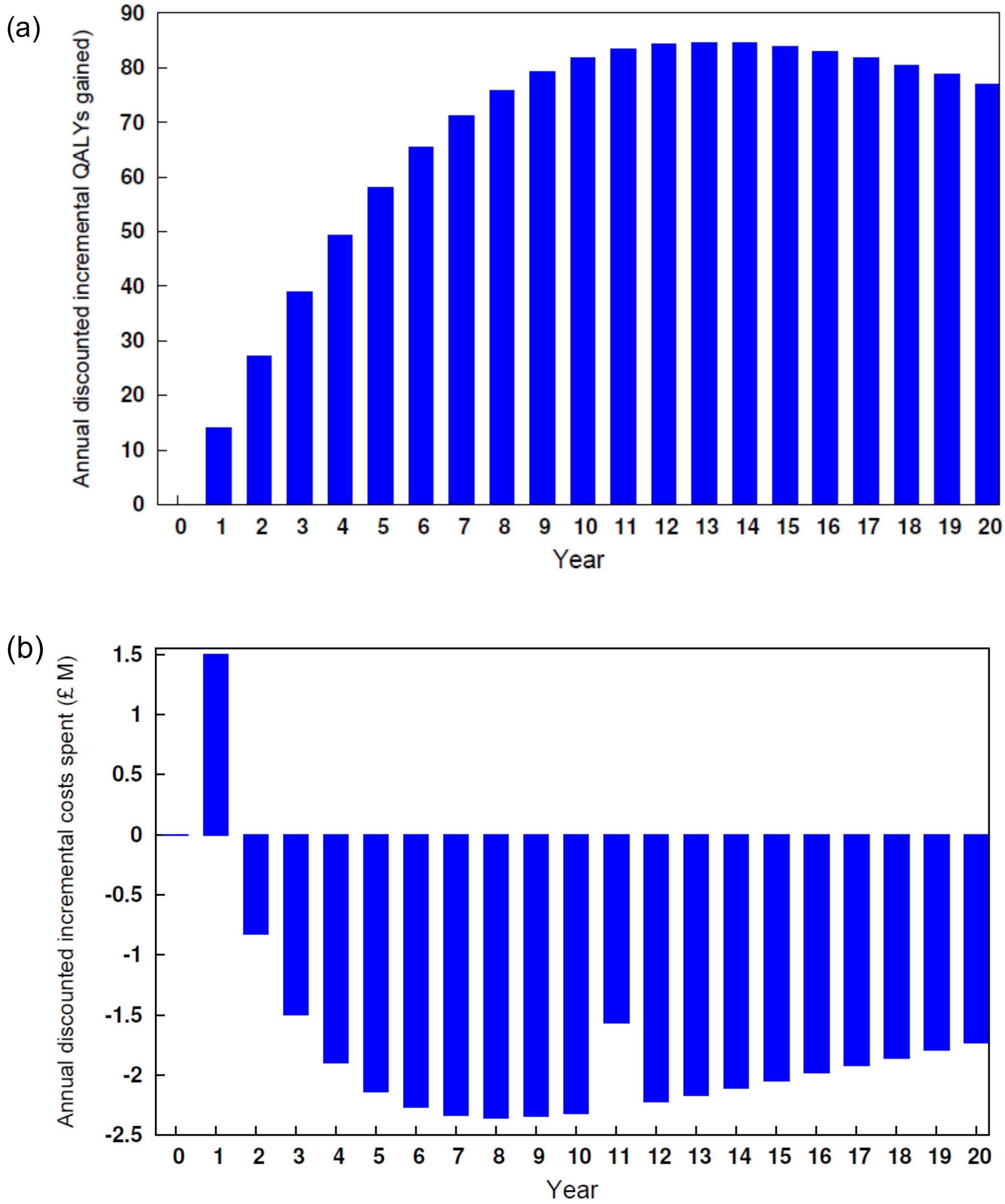


Figure 7.3.4b Discounted annual number of QALYs gained and net costs incurred by combined interventions in the homeless

(a) Discounted annual number of QALYs gained, compared with current practice, by combined MXU case-finding and enhanced case-management in a homeless population where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and treatment completion rate of 55% prior to the intervention. The combined intervention is MXU case-finding at 0.78 p.a. and enhanced case-management increasing the treatment completion rate to 75%. The intervention begins in year 1.
(b) Discounted annual number of net costs incurred compared with current practice, by combined MXU case-finding and enhanced case-management in a homeless population where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and treatment completion rate of 55% prior to the intervention. The combined intervention is MXU case-finding at 0.78 p.a. and enhanced case-management increasing the treatment completion rate to 75%. Negative net costs incurred indicate net savings. The intervention begins in year 1. The MXU is replaced in year 11.

Table 7.3.4c Combined case-finding and enhanced case-management in the homeless

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, compared with current practice, where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000, the treatment completion rate prior to the intervention is 55%, the MXU case-finding rate is 0.78 per case per year and the treatment completion rate with the intervention is 75%. Negative incremental net costs are net cost savings.

QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
		If a QALY is valued at £20,000	If a QALY is valued at £30,000
1381.7	-35.8	63.5	77.3

7.3.5 Summary of base case analysis in homeless

The base-case analysis for the homeless is summarised in Table 7.3.5. Combined mobile X-ray screening (with a case-finding rate of 0.78 per case per year) and enhanced case management (ECM, increasing treatment completion to 75%) is the most cost-effective option if ECM costs less than about £38M (if a QALY is valued at £20,000) or less than about £43M (if a QALY is valued at £30,000), over 20 years. (This is the “ECM cost threshold” (see Table S.1), and is the increase in incremental net benefit, excluding the cost of ECM, of adding ECM to MXU screening: if the cost of adding ECM is less than the incremental net benefit of doing so then adding ECM is cost-effective.) This equates to approximately £21,000 per case treated in the population of 10,000 over the 20-year time-horizon, if a QALY is valued at £20,000, or about £24,000 per case treated if a QALY is valued at £30,000.

Otherwise, mobile X-ray screening is the most cost-effective option. Mobile X-ray screening dominates current practice regardless of the cost of ECM (it provides more QALYs at lower cost). Similarly, combined mobile X-ray screening and ECM always dominates ECM alone (assuming that the additional cost of ECM is the same when it is provided on its own or in combination with mobile X-ray screening).

Table 7.3.5 Base-case analysis of interventions against TB in the homeless

Prior to intervention the proportion of the population being treated for TB is 788 per 100,000 (Story at al. 2007) and the treatment completion rate is 55%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	66.0	127,607	-	-	-	-
Mobile X-ray screening	56.9	128,435	-9.2	828.5	25.7	34.0
Enhanced case-management (ECM)	31.3	128,533	-34.7	926.6	53.2	62.5
Combined Mobile X-ray screening and ECM	30.2	128,988	-35.8	1381.7	63.5	77.3
ECM cost threshold:					37.8	43.3

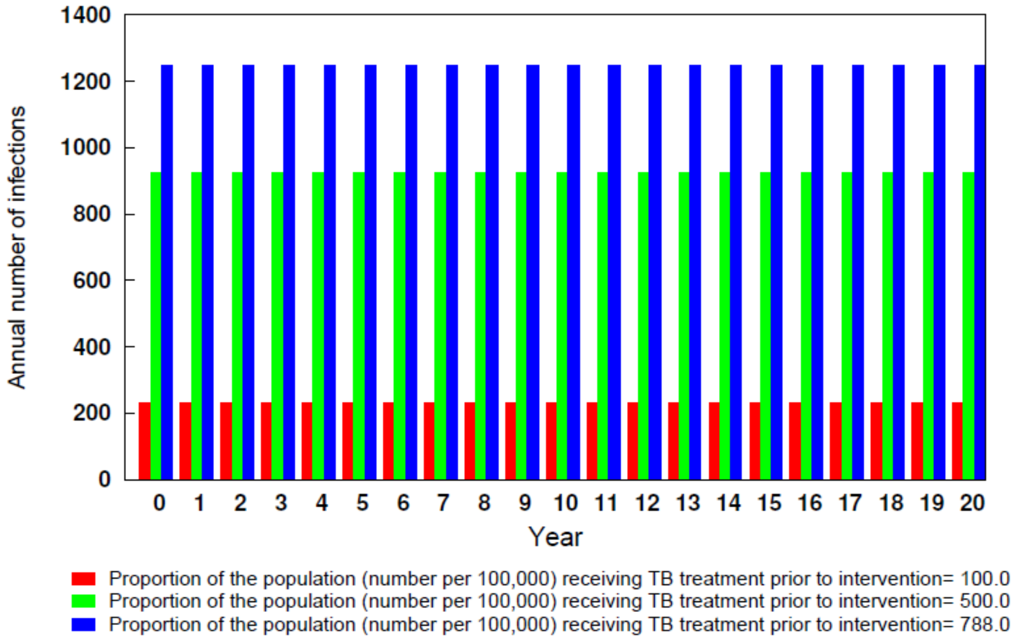
QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

7.4 Homeless: Sensitivity analysis

7.4.1 Current practice – i.e. no interventions

We vary the proportion of the population being treated for TB prior to the intervention. We assume that the population size is constant, rates of entry and exit are constant, and that current practice for passive case-finding and treatment remain unchanged when the intervention is applied – i.e. the intervention is in addition to current practice. Therefore, the same number of infections and cases of active disease occur in each year. Figure 7.4.1 shows the base case for the homeless, where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000, plus lower burden settings of 100 and 500 per 100,000).

(a)



(b)

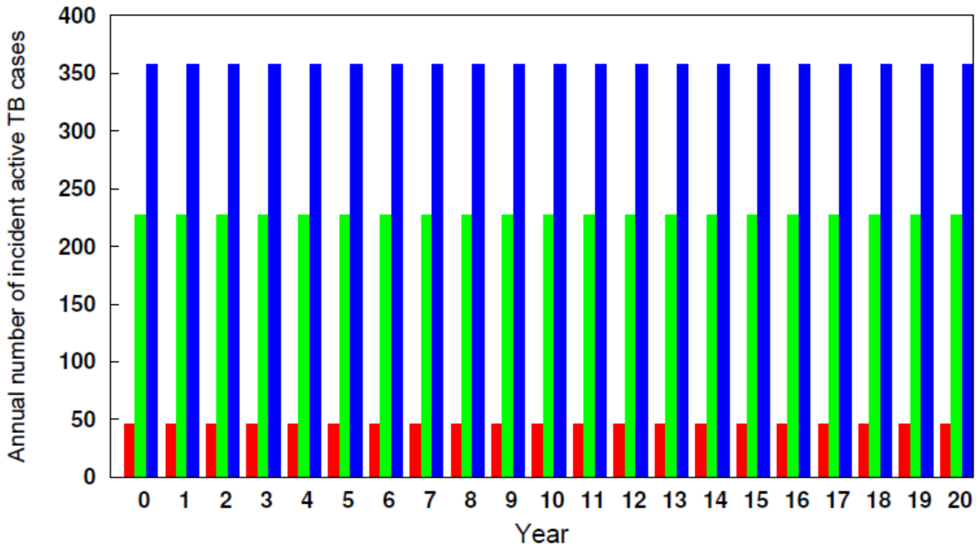


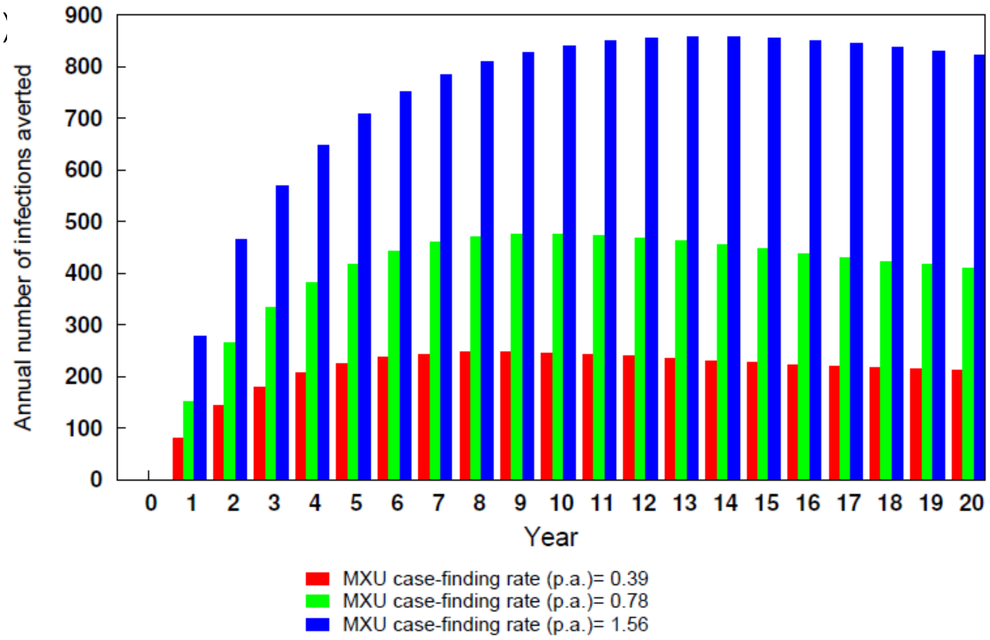
Figure 7.4.1 Annual numbers (undiscounted) of infections and new cases of active disease in the homeless: sensitivity analysis

(a) Annual numbers (undiscounted) of new infections in a homeless population of 10,000 with the proportion of the population being treated for TB prior to the intervention being 100 per 100,000 (red bars), 500 per 100,000 (green bars), and 788 per 100,000 (blue bars). The treatment completion rate is 55%.
(b) Annual numbers (undiscounted) of new cases of active disease in a homeless population of 10,000 with the proportion of the population being treated for TB prior to the intervention being 100 per 100,000 (red bars), 500 per 100,000 (green bars), and 788 per 100,000 (blue bars). The treatment completion rate is 55%.

7.4.2 Case-finding by mobile X-ray unit (MXU) in the homeless

The time-courses of annual numbers of infections averted and cases of active disease averted are shown in Figure 7.4.2a. Note that the number of infections averted is greater than the number of active disease cases averted, because the majority of infections do not progress to active disease. As time progresses since the introduction of the intervention the annual number of infections averted and cases of active disease averted increases. This is because over time the prevalence of infectious untreated active disease declines so rates of transmission in the population decline. The greater the MXU case-finding rate the greater the annual numbers of infections and cases of active disease averted.

(a)



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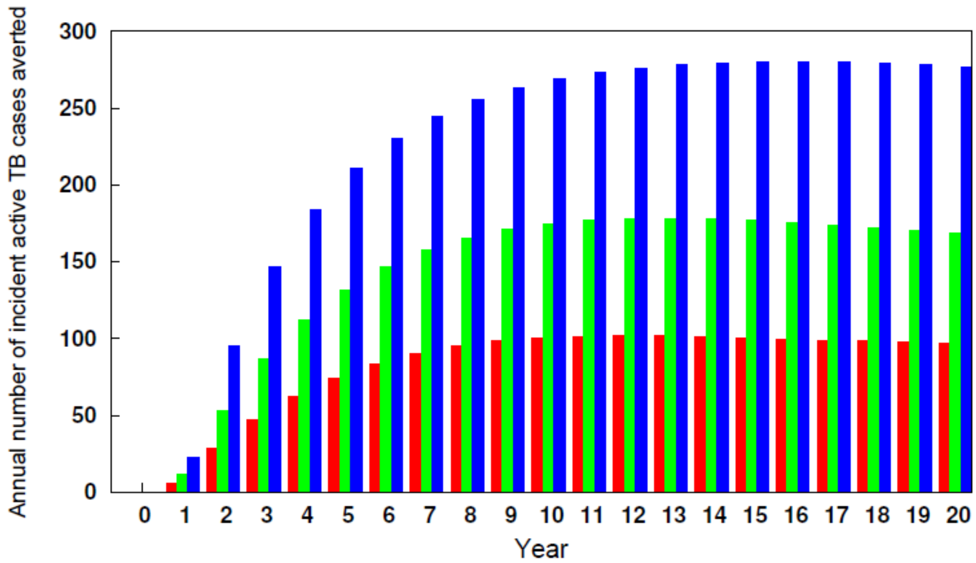


Figure 7.4.2a Annual numbers (undiscounted) of new infections and new cases of active disease averted by mobile X-ray unit case finding in the homeless: sensitivity analysis

(a) Annual numbers (undiscounted) of new infections averted over a 20-year time-horizon by MXU case-finding in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000. The effect of varying the MXU case-finding rate is examined: red bars indicate a rate of 0.39 per case per year; green bars indicate a rate of 0.78 per case per year; blue bars indicate a rate of 1.56 per case per year. The intervention starts in year 1. The treatment completion rate is 55%.

(b) Annual numbers (undiscounted) of new cases of active disease averted over a 20-year time-horizon by MXU case-finding in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000. The effect of varying the MXU case-finding rate is examined: red bars indicate a rate of 0.39 per case per year; green bars indicate a rate of 0.78 per case per year; blue bars indicate a rate of 1.56 per case per year. The intervention starts in year 1. The treatment completion rate is 55%.

The time-courses of QALYs gained and costs incurred are shown in Figure 7.4.2b. Capital costs (i.e. MXU purchases) are incurred at the start of the intervention and after 10 years. The total discounted QALYs gained and net costs incurred shown in Table 7.4.2d.

Annual QALY gains mirror the annual numbers of active disease cases averted, because active disease is what causes health loss. Discounting means that gains further in the future are valued less than gains that occur earlier.

There are net costs at the beginning of the intervention, due to capital costs, the costs of running the intervention, and increased treatment costs incurred because more cases of active disease are found than would have been found without active MXU case-finding. Higher rates of MXU case-finding have higher net costs initially, due to higher intervention costs, and due to more additional cases being treated in the early years, because more cases are found more quickly.

Subsequently there are net savings, as the savings on treatment costs due to the reduction in numbers of active disease cases occurring outweigh the costs of running the intervention. In the year when the MXU has to be replaced the net saving is smaller.

Higher rates of MXU case-finding have higher net costs initially, due to higher intervention costs, and due to more additional cases being treated in the early years, because more cases are found more quickly. Subsequently, there are greater savings on treatment costs, due to more infections being averted. Overall, in the range examined, the higher rate of MXU case-finding was more cost-saving over the 20-year time-horizon.

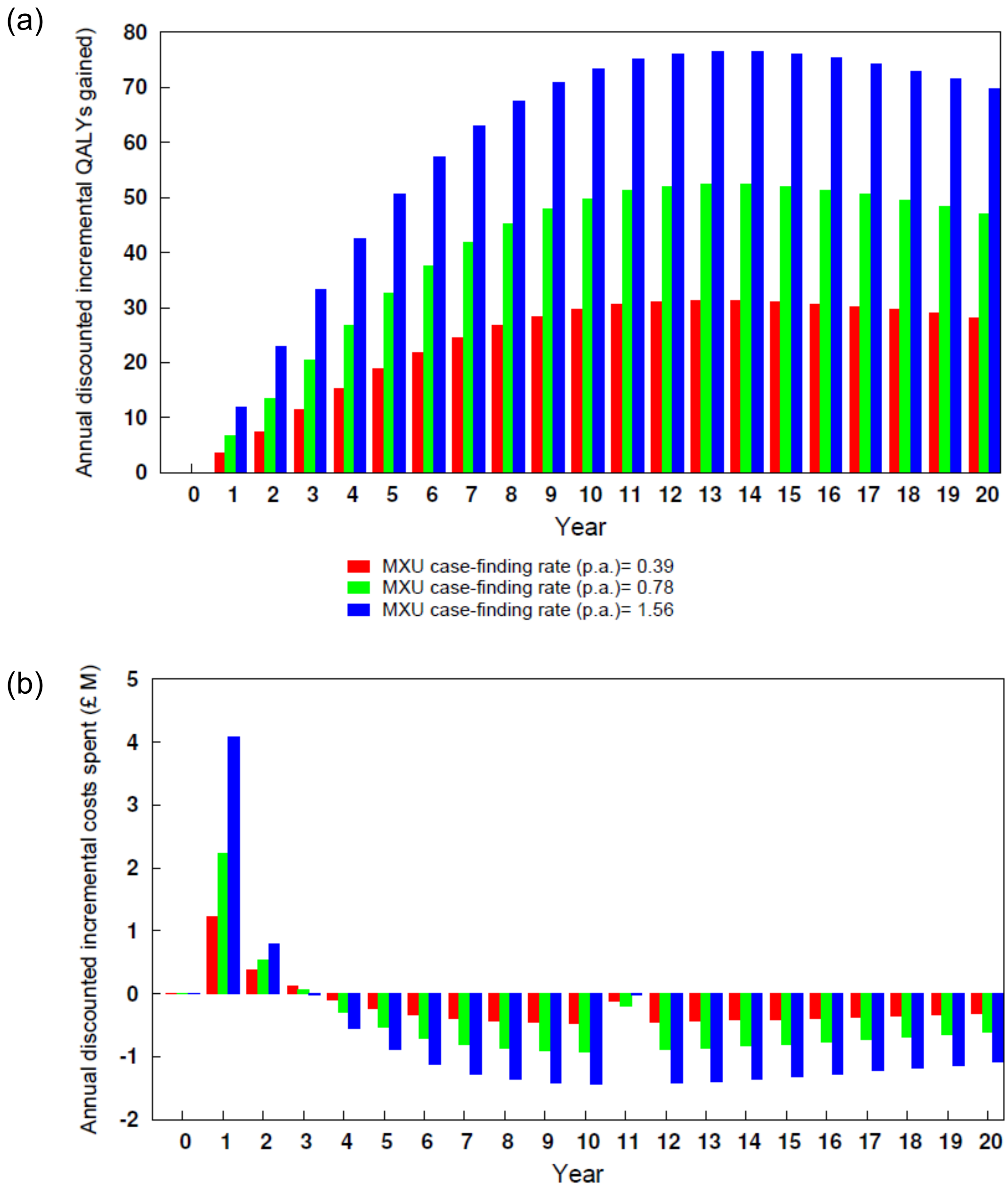


Figure 7.4.2b Discounted annual number of QALYs gained and net costs incurred by mobile X-ray unit case-finding in the homeless: sensitivity analysis

(a) Discounted annual number of QALYs gained over a 20-year time-horizon by MXU case-finding in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000. The effect of varying the MXU case-finding rate is examined: red bars indicate a rate of 0.39 per case per year; green bars indicate a rate of 0.78 per case per year; blue bars indicate a rate of 1.56 per case per year. The intervention starts in year 1. The treatment completion rate is 55%.

(b) Discounted annual net costs incurred over a 20-year time-horizon by MXU case-finding in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000. The effect of varying the MXU case-finding rate is examined: red bars indicate a rate of 0.39 per case per year; green bars indicate a rate of 0.78 per case per year; blue bars indicate a rate of 1.56 per case per year. Negative net costs incurred indicate net savings. The intervention starts in year 1. The MXU is replaced in year 11. The treatment completion rate is 55%.

Figure 7.4.2c summarises the sensitivity analysis of the cost-effectiveness of the mobile X-ray unit (MXU) active case-finding intervention, applied in populations with different proportions of the population being treated for TB prior to the intervention (Story et al (2007). estimated this to be 788 per 100,000 for the homeless), and with differing intensity of intervention. Where the intervention is cost-saving we do not calculate incremental cost-effectiveness ratios (ICERs) but instead consider QALYs gained and costs saved. For other scenarios we calculate ICERs.

The greater the proportion of the population being treated for TB prior to the intervention, the more cost-effective or cost-saving the intervention is likely to be.

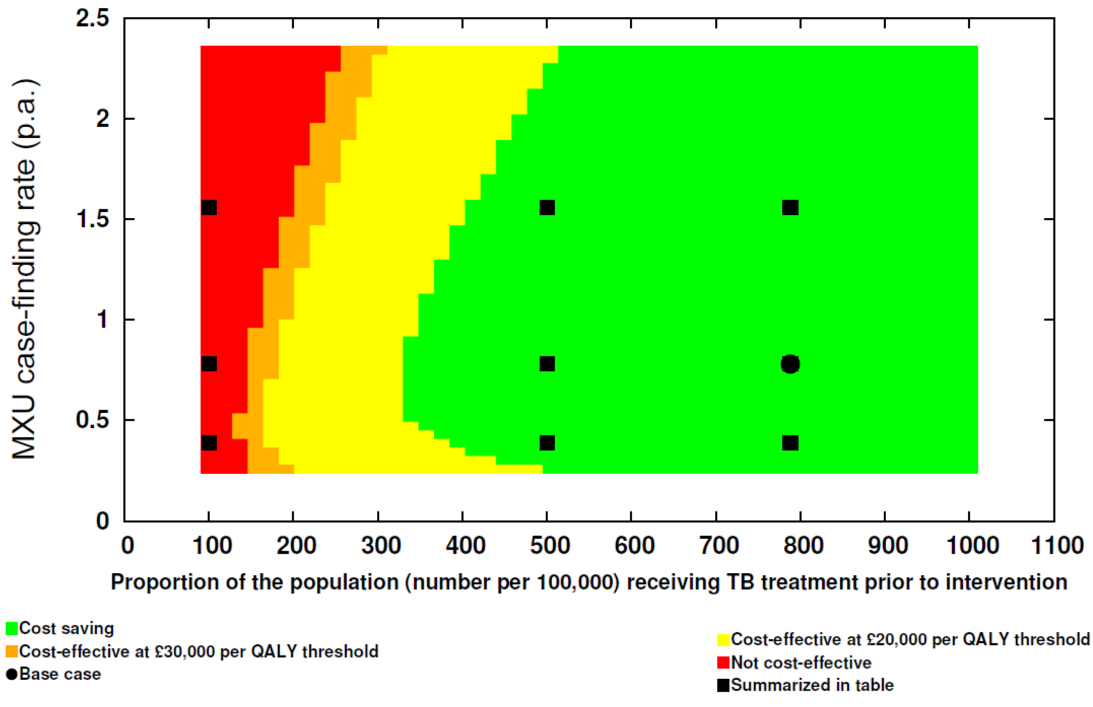


Figure 7.4.2c Cost-effectiveness of case-finding by mobile X-ray unit in the homeless compared with current practice

This figure shows the effects of varying the MXU case-finding rate (vertical axis), in homeless populations with different proportions of the population being treated for TB prior to the intervention (horizontal axis), on whether the intervention is cost-saving, or has an incremental cost-effectiveness ratio (ICER) of less than £20,000 per QALY, an ICER between £20,000 and £30,000 per QALY, or an ICER greater than £30,000 per QALY, over the 20-year time-horizon. The cost of MXU screening is proportional to its case-finding rate. The treatment completion rate is 55%. Black dots indicate the scenarios represented in Table 7.4.2d; the base case is indicated by the circular dot.

For selected scenarios, numerical results (total discounted QALYs gained and net costs incurred) are shown in Table 7.4.2d. In the scenarios examined, the greater the proportion of the population being treated for TB prior to the intervention and the higher the screening rate the more QALYs gained. In the scenarios where the proportion of the population being treated for TB prior to the intervention is 500 or 788 per 100,000, the intervention is cost-saving and the higher MXU case-finding rate the more cost-saving it is (in the range examined) because higher case-finding rates avert more cases of disease over the 20-year period considered, and the savings on treatment costs due to disease cases averted outweigh the increased intervention costs.

In the scenarios where the proportion of the population being treated for TB prior to the intervention is 100 per 100,000, the intervention is not cost-saving, and in fact is not cost-effective. Higher MXU case-finding rates have higher net costs because more-intensive screening is more expensive and savings on treatment costs due to disease cases averted do not outweigh the increased intervention costs.

Table 7.4.2d Case-finding by mobile X-ray unit in the homeless

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, for different rates of MXU case-finding in homeless populations with different proportions of the population being treated for TB prior to the intervention, compared with current practice. The treatment completion rate is 55%. Negative incremental net costs are net cost savings.

Proportion of whole homeless population receiving TB treatment (per 100,000) prior to intervention	MXU case-finding rate (rate per case p.a.)	QALYs gained compared with current practice	Incremental costs (£M) compared with current practice	Incremental Net Benefit (£M) compared with current practice	
				If a QALY is valued at £20,000	If a QALY is valued at £30,000
100	½× (0.39)	88.5	4.4	-2.7	-1.8
	1× (0.78)	133.6	7.5	-4.8	-3.5
	2x (1.56)	173.4	15.2	-11.8	-10.0
500	½× (0.39)	337.4	-1.3	8.0	11.4
	1× (0.78)	566.3	-3.8	15.1	20.8
	2x (1.56)	818.8	-4.0	20.3	28.5
788	½× (0.39)	489.8	-4.2	14.0	18.9
	1× (0.78)	828.5	-9.2	25.7	34.0
	2x (1.56)	1236.6	-14.5	39.2	51.6

The effect of varying the cost of the case-finding intervention and the cost of treatment cost is presented in Figure 7.4.2e. The higher the cost of treatment, the greater the cost saving per infection averted, so the more likely the intervention is to be cost-effective or cost-saving. The higher the cost of the intervention the less likely it is to be cost-effective or cost-saving, especially if the treatment costs per case are low.

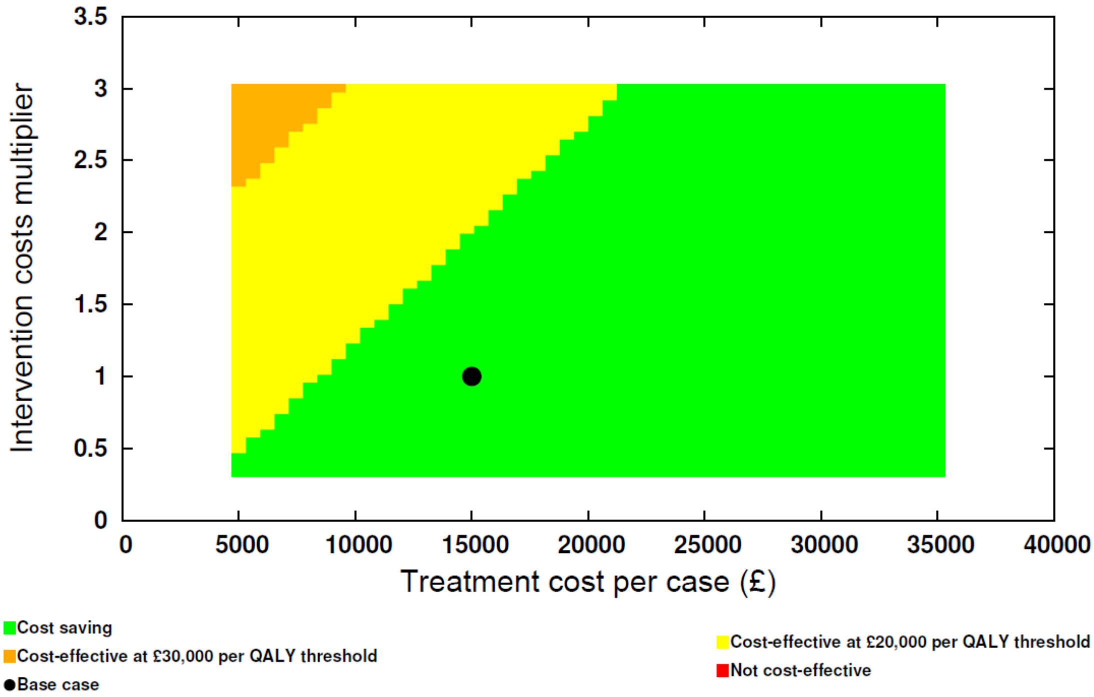


Figure 7.4.2e Cost-effectiveness of case-finding by mobile X-ray unit in the homeless: sensitivity analysis

This figure shows the effects of varying the cost of MXU case-finding intervention (vertical axis) and the cost of treating the average case of TB in this population (horizontal axis) on whether the intervention is cost-saving, or has an incremental cost-effectiveness ratio (ICER) of less than £20,000 per QALY, an ICER between £20,000 and £30,000 per QALY, or an ICER greater than £30,000 per QALY, over the 20-year time-horizon. On the vertical axis, 1 indicates that the intervention costs as much as in the base case, 0.5 indicates that it costs half as much, 2 indicates that it costs twice as much. The proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the active case-finding rate is 0.78 per case per year. The treatment completion rate is 55%.The base case is indicated by the black dot.

7.4.3 Enhanced case-management in the homeless

Increasing rates of treatment completion through enhanced case-management averts transmission events and therefore averts cases of active disease, as shown in Figure 7.4.3a. This is due to (i) infections being averted, thus averting cases of disease requiring treatment, and (ii) a reduction in the number of individuals requiring re-treatment.

In all scenarios, the intervention resulted in health benefits (QALYs gained) and reduced treatment costs.

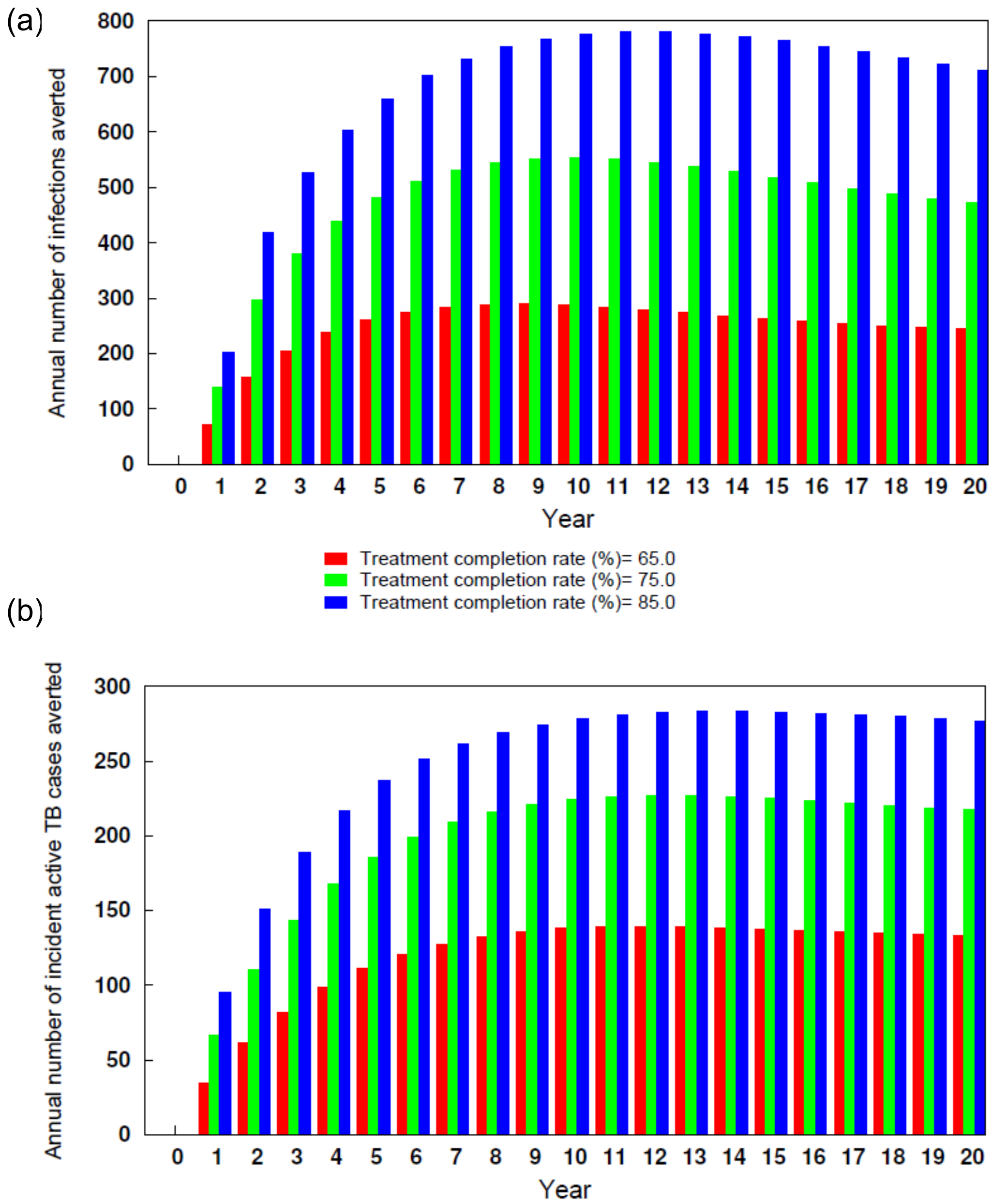


Figure 7.4.3a Annual numbers (undiscounted) of new infections and new cases of active disease averted by enhanced case-management in the homeless: sensitivity analysis

(a) Annual numbers (undiscounted) of new infections averted over a 20-year time-horizon by enhanced case-management in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%. The effect of varying the treatment completion rate achieved by the intervention is examined: red bars indicate 65%; green bars 75%; blue bars 85%. The intervention starts in year 1.

(b) Annual numbers (undiscounted) of new cases of active disease averted over a 20-year time-horizon by enhanced case-management in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%. The effect of varying the treatment completion rate achieved by the intervention is examined: red bars indicate 65%; green bars 75%; blue bars 85%. The intervention starts in year 1.

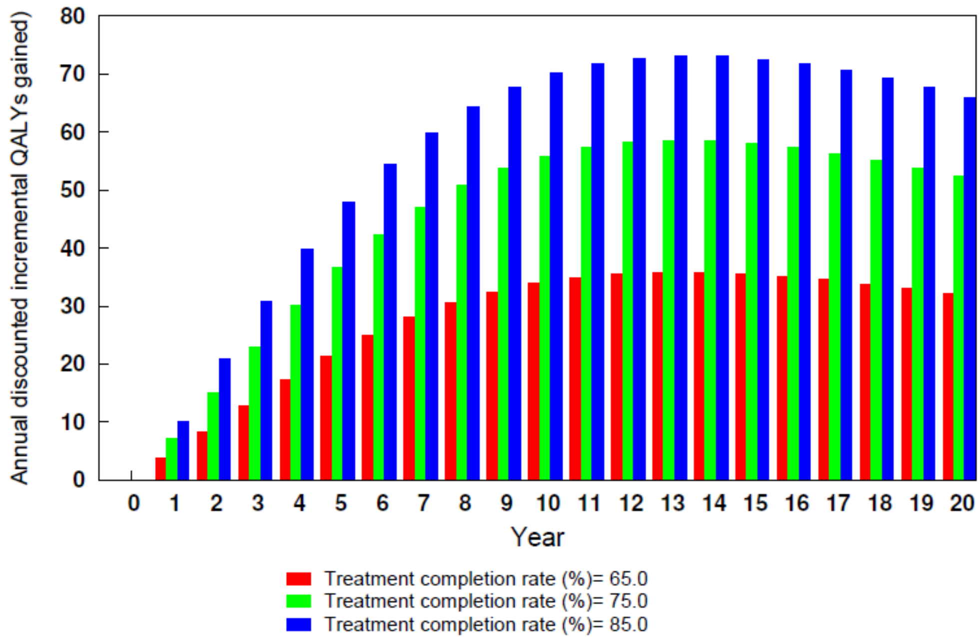
The time-courses of QALYs gained and costs incurred are shown in Figure 7.4.3b and the total discounted QALYs gained and net costs incurred over the 20-year time-horizon are shown in Table 7.4.3d.

As before, annual QALY gains mirror the annual numbers of active disease cases averted, because active disease is what causes health loss. Discounting means that gains further in the future are valued less than gains that occur earlier.

If the cost of the intervention is greater than the estimated incremental net benefit (excluding intervention costs) then enhanced case management may considered cost-effective compared with current practice. Figure 7.4.3c summarises the sensitivity analysis of the threshold costs over 20 years for the population of 10,000 at which the intervention would be just cost-effective if a QALY is valued at £20,000. Note that the cost would not scale up or down for a different population due to non-linearities in the indirect benefits (infections averted), so could not just be multiplied by the number of cases in a particular population to get a new figure. Higher proportions of the population being treated for TB prior to the intervention and a higher treatment success rate achieved by the intervention result in one being willing to pay more for the intervention for a particular value of a QALY.

A smaller proportion of the population being treated for TB prior to the intervention and a lower treatment success rate achieved by the intervention result in one being willing to pay less for the intervention.

(a)



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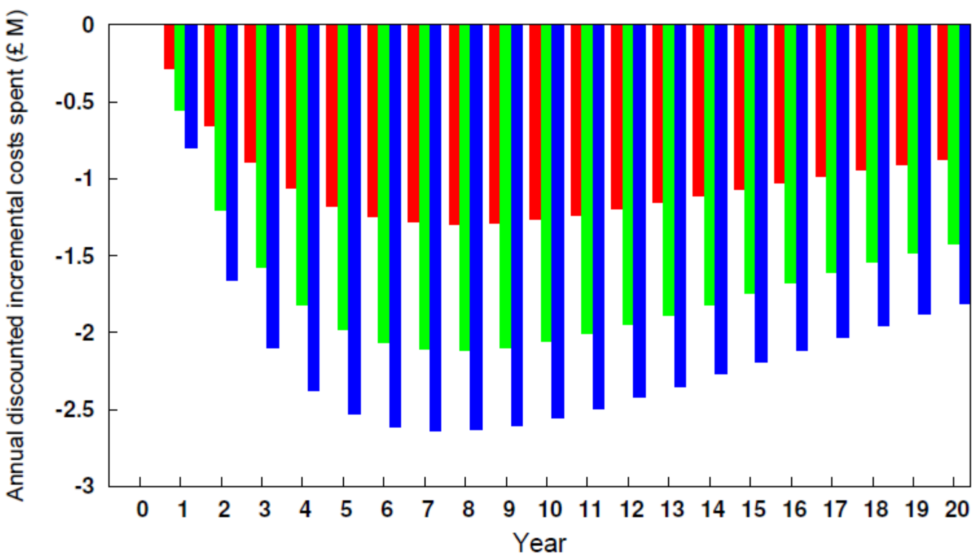


Figure 7.4.3b Discounted annual number of QALYs gained and net costs incurred by enhanced case-management in the homeless: sensitivity analysis

(a) Discounted annual number of QALYs gained over a 20-year time-horizon by enhanced case-management in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%. The effect of varying the treatment completion rate achieved by the intervention is examined: red bars indicate 65%; green bars 75%; blue bars 85%. The intervention starts in year 1.

(b) Discounted annual net costs incurred over a 20-year time-horizon by enhanced case-management in a homeless population in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%. The effect of varying the treatment completion rate achieved by the intervention is examined: red bars indicate 65%; green bars 75%; blue bars 85%. Negative net costs incurred indicate net savings. The intervention starts in year 1.

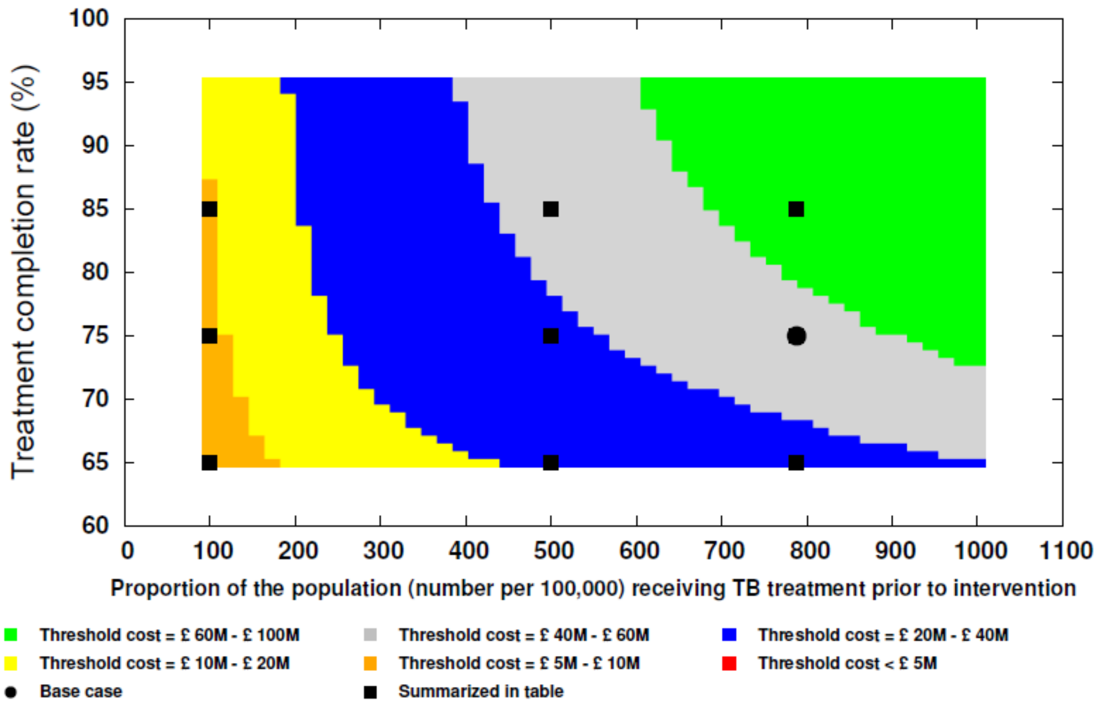


Figure 7.4.3c Cost-effectiveness of enhanced case-management in the homeless compared with current practice

This figure shows the effects of varying the treatment completion rate achieved by the enhanced case-management intervention (vertical axis) and the proportion of the population being treated for TB prior to the intervention (horizontal axis) on the amount that one would be willing to pay for the enhanced case-management intervention in the population of 10,000 over the 20-year time horizon considered if a QALY is valued at £20,000. The treatment completion rate prior to the intervention is 55%. Black dots indicate the scenarios represented in Table 7.4.3d; the base case is indicated by the circular dot.

In Table 7.4.3.d we present the incremental net benefit (i.e. the threshold cost at which the intervention would be just cost-effective) of enhanced case management for the population of 10,000 over 20 years if a QALY is valued at £20,000 and £30,000

Table 7.4.3d Enhanced case-management in the homeless

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, for different treatment completion rates achieved by enhanced case-management in homeless populations with different proportions of the population being treated for TB prior to the intervention, compared with the current practice. Negative incremental net costs are net cost savings.

Proportion of whole homeless population receiving TB treatment (per 100,000) prior to intervention	Treatment completion rate increased from 55% to	QALYs gained compared with current practice	Incremental costs compared with current practice (omitting intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
				If a QALY is valued at £20,000	If a QALY is valued at £30,000
100	65%	98.7	-3.9	5.9	6.9
	75%	145.0	-5.6	8.5	10.0
	85%	168.6	-6.4	9.8	11.5
500	65%	385.0	-14.6	22.3	26.1
	75%	631.2	-23.9	36.5	42.8
	85%	784.4	-29.7	45.4	53.2
788	65%	559.2	-21.0	32.1	37.7
	75%	926.6	-34.7	53.2	62.5
	85%	1173.8	-44.0	67.5	79.2

The effect of varying the cost of the treatment success rate due to enhanced case management and the cost of treatment cost is presented in Figure 7.4.3e. The higher the cost of treatment, the greater the cost saving per infection averted, so the more likely the intervention is to be cost-effective or cost-saving. For almost all of the range of parameter values considered the threshold cost exceeds £40M over 20 years, but when the treatment completion rate is around 65% and the cost per case of treatment is around £5000 then the threshold cost falls, to lie between £10M – £20M over 20 years.

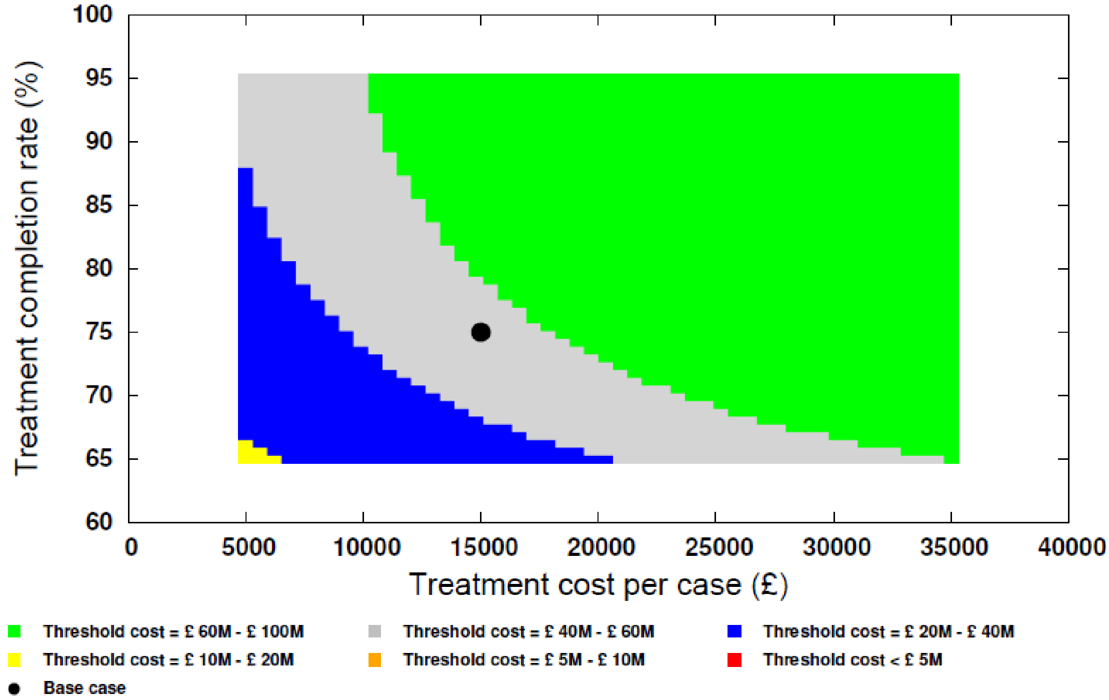


Figure 7.4.3e Cost-effectiveness of enhanced case-management in the homeless: sensitivity analysis

This figure shows the effects of varying the treatment completion rate achieved by the enhanced case-management intervention (vertical axis) and the cost of treating the average case of TB in this population (horizontal axis) on the amount that one would be willing to pay for the enhanced case-management intervention in the population of 10,000 over the 20-year time horizon considered if a QALY is valued at £20,000. The proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%. The base case is indicated by the black dot.

7.4.4 Combined case-finding and enhanced case-management in the homeless

In this analysis we calculate the cost of enhanced case-management for the population of 10,000 over 20 years that would be considered cost-effective when combined with active case-finding by mobile X-ray unit if a QALY is valued at £20,000 and £30,000.

The time-courses of infections averted and cases of active disease averted are shown in Figure 7.4.4a, and of QALYs gained and costs incurred are shown in Figure 7.4.4b. For a given rate of MXU case-finding higher treatment completion rates lead to more infections averted and more cases of active disease averted. Annual QALY gains reflect annual numbers of cases of active disease averted, but QALY gains are discounted so that those occurring further in the future are valued less. Higher treatment completion rates avert more treatment costs due to more infections and cases of active disease being averted by successful treatment preventing transmission.

The total discounted QALYs gained and net costs incurred over the 20-year time horizon are shown in Table 7.4.4d-f. For all proportions of the population being treated for TB prior to the intervention examined higher rates of MXU case-finding and higher treatment completion rates avert more treatment costs.

(a)

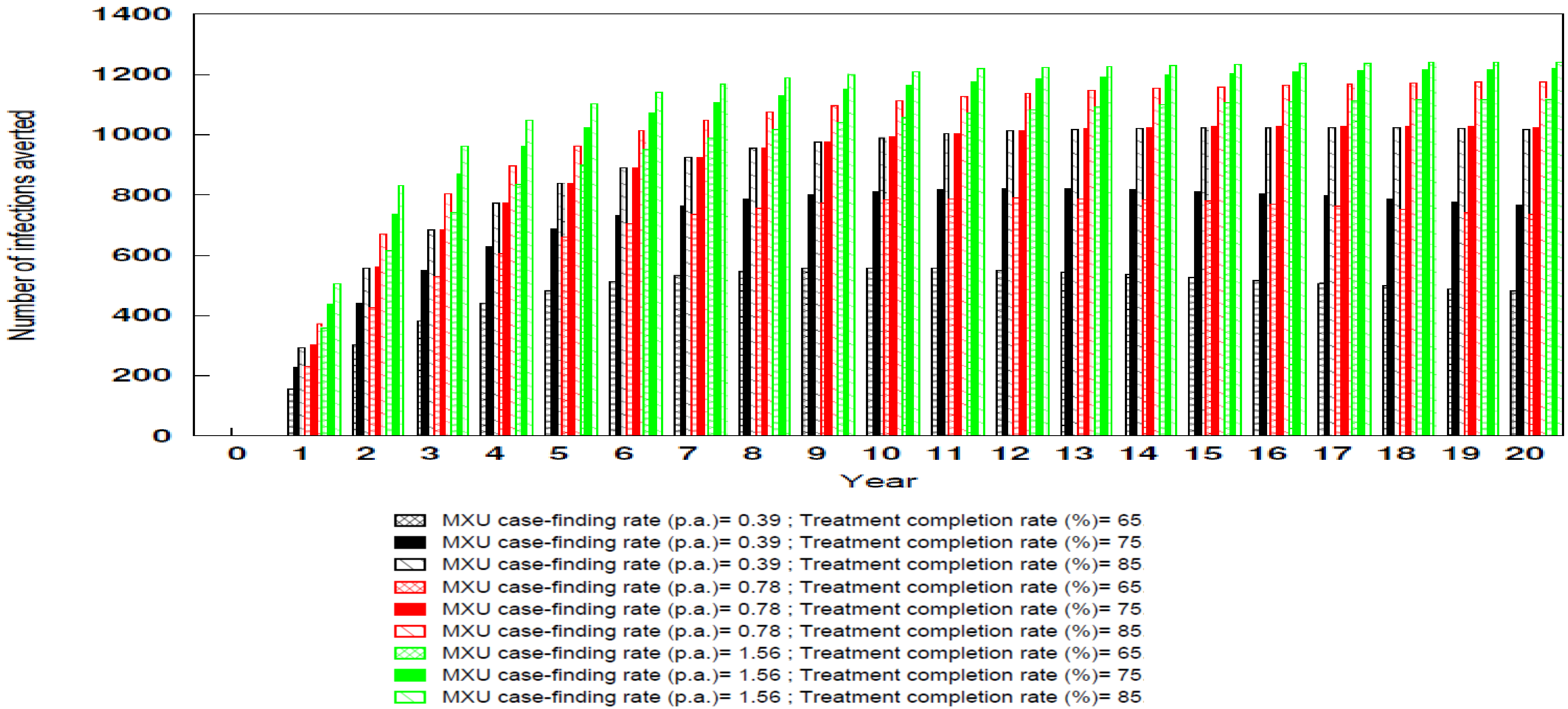


Figure 7.4.4a Annual numbers (undiscounted) of new infections and new cases of active disease averted by combined interventions in the homeless: sensitivity analysis

(a) Annual numbers (undiscounted) of infections averted, compared with current practice, by combined MXU case-finding and enhanced case-management in a homeless population where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and treatment completion rate of 55% prior to the intervention. Scenarios examined are MXU case-finding at 0.78 p.a. (red bars), half that rate (0.39 p.a., black bars), and double that rate (1.56 p.a., green bars). Within each colour grouping, left to right, treatment completion rates are increased to 65%, 75% and 85%.

(b)

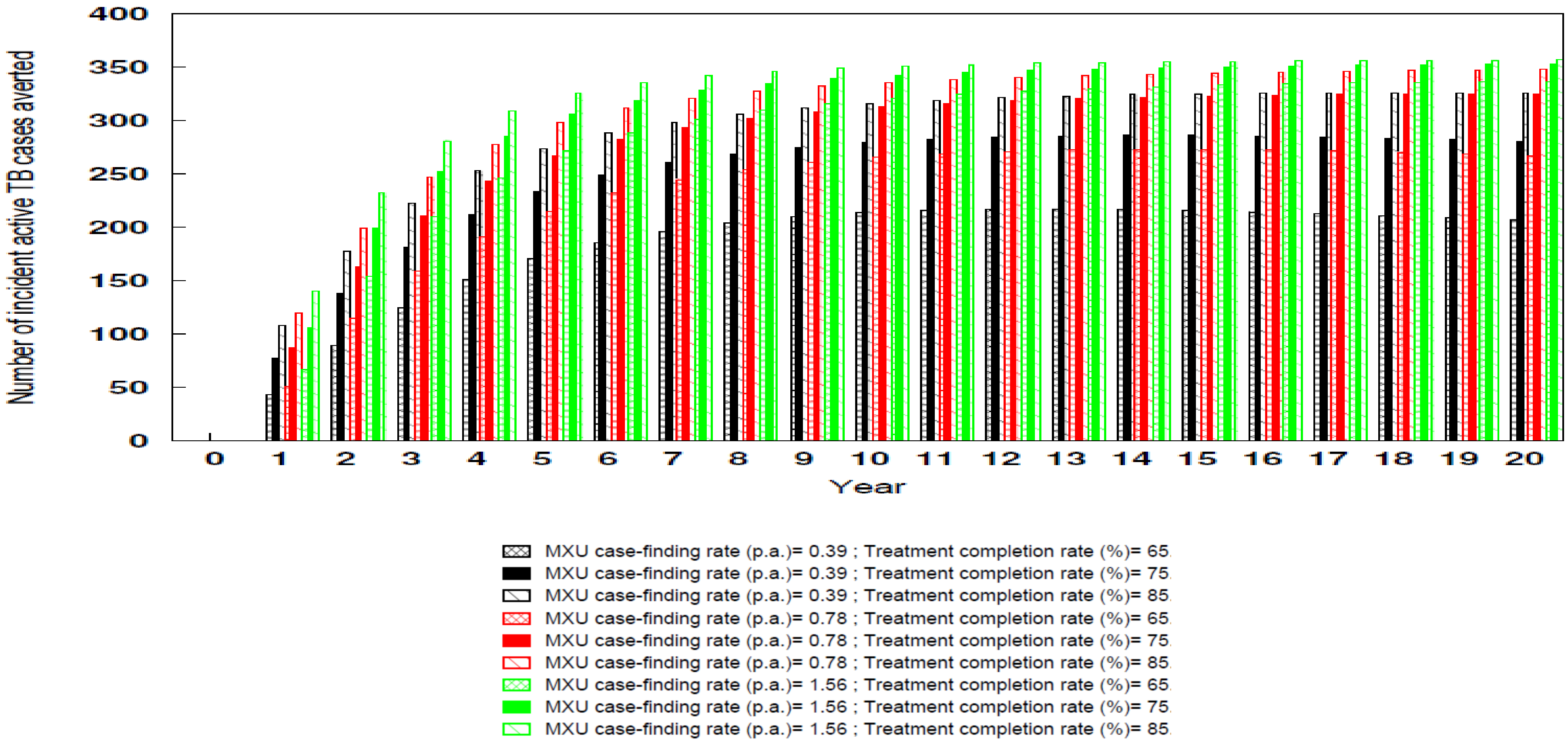


Figure 7.4.4a cont *(b) Annual numbers (undiscounted) of new cases of active disease averted, compared with current practice, by combined MXU case-finding and enhanced case-management in a homeless population where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and treatment completion rate of 55% prior to the intervention. Scenarios examined are MXU case-finding at 0.78 p.a. (red bars), half that rate (0.39 p.a., black bars), and double that rate (1.56 p.a., green bars). Within each colour grouping, left to right, treatment completion rates are increased to 65%, 75% and 85%.*

(a)

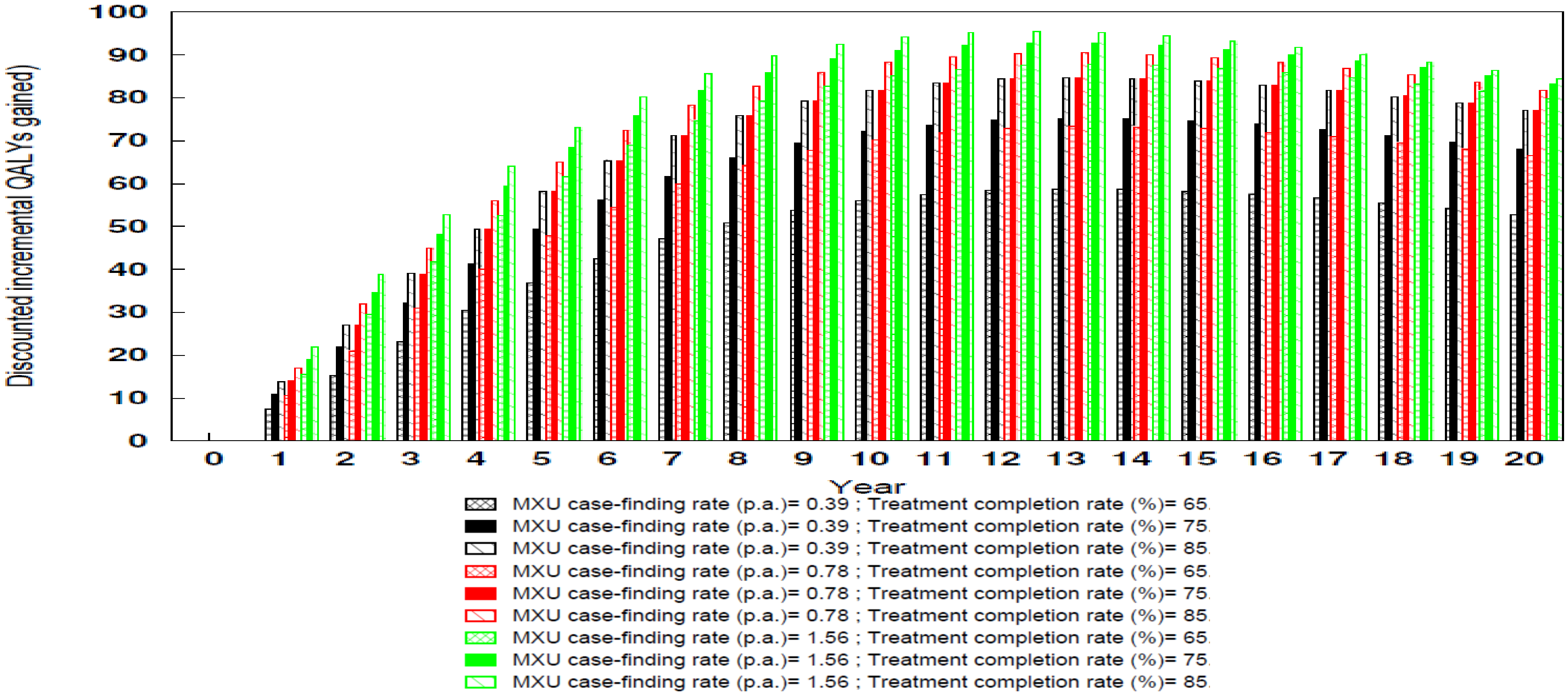


Figure 7.4.4b Discounted annual number of QALYs gained and net costs incurred by combined interventions in the homeless: sensitivity analysis

(a) Discounted annual number of QALYs gained, compared with current practice, by combined MXU case-finding and enhanced case-management in a homeless population where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and treatment completion rate of 55% prior to the intervention. Scenarios examined are MXU case-finding at 0.78 p.a. (red bars), half that rate (0.39 p.a., black bars), and double that rate (1.56 p.a., green bars). Within each colour grouping, left to right, treatment completion rates are increased to 65%, 75% and 85%.

(b)

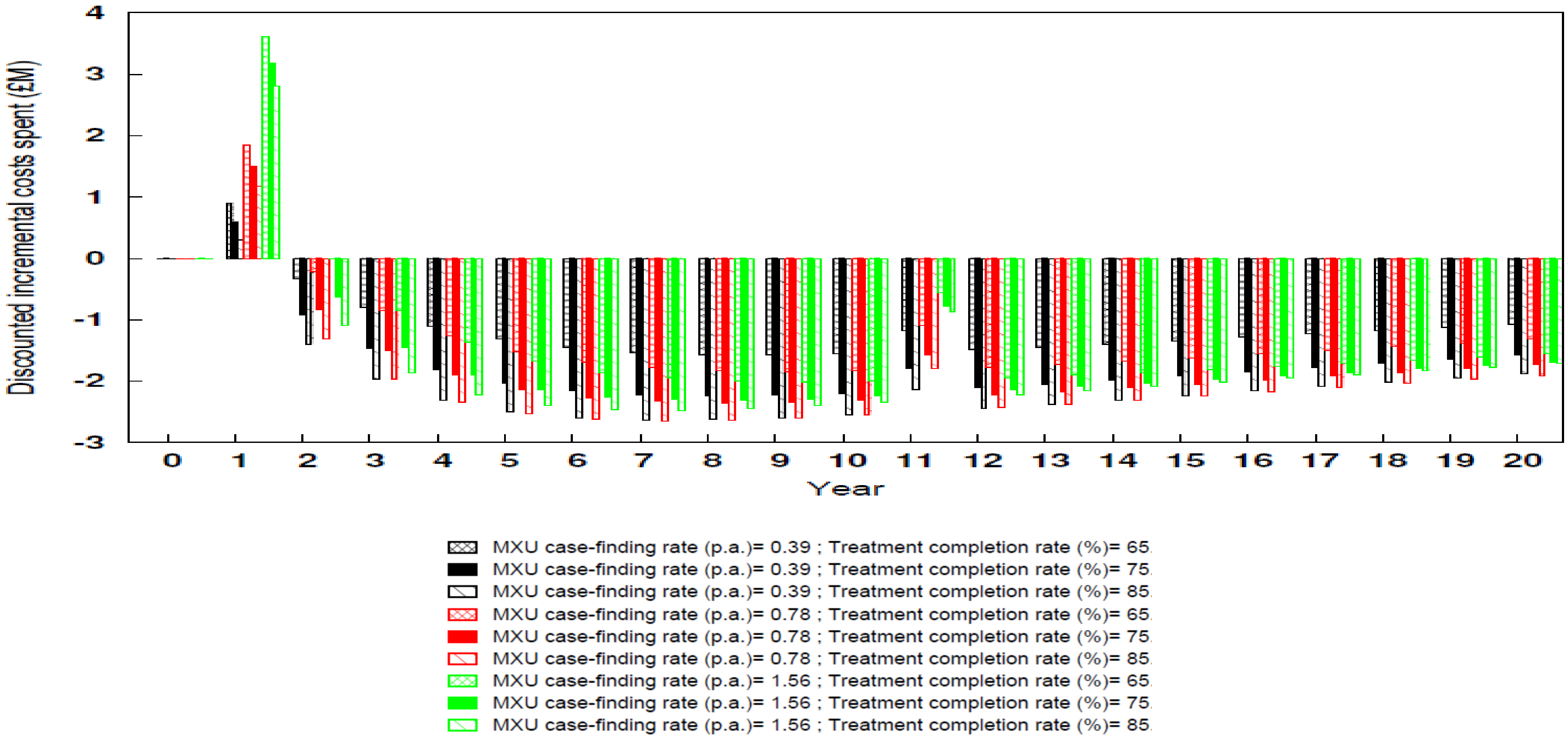


Figure 7.4.4b cont *(b) Discounted annual number of net costs incurred compared with current practice, by combined MXU case-finding and enhanced case-management in a homeless population where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and treatment completion rate of 55% prior to the intervention. Scenarios examined are MXU case-finding at 0.78 p.a. (red bars), half that rate (0.39 p.a., black bars), and double that rate (1.56 p.a., green bars). Within each colour grouping, left to right, treatment completion rates are increased to 65%, 75% and 85%. Negative net costs incurred indicate net savings. The MXU is replaced in year 11.*

Figure 7.4.4c presents a sensitivity analysis of the effect of varying (i) the treatment completion rate achieved by enhanced case-management and (ii) the MXU active case-finding rate on the amount that one would be willing to pay for the enhanced case-management intervention in the population of 10,000 over the 20-year time horizon considered if a QALY is valued at £20,000. For all of the parameter space examined the threshold cost is between £20M and £100M and for most of the parameter space it is between £60M and £100M.

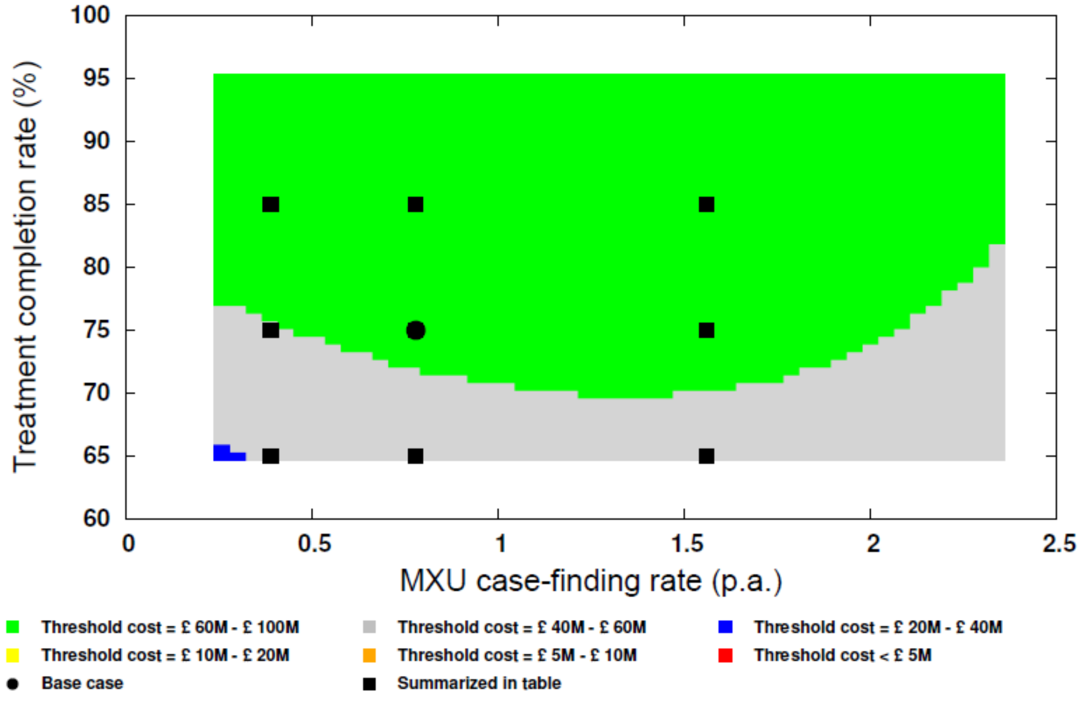


Figure 7.4.4c Cost-effectiveness of combined interventions in the homeless

This figure shows the effects of varying the treatment completion rate achieved by the enhanced case-management intervention (vertical axis) and the rate of MXU case-finding (horizontal axis) on the amount that one would be willing to pay for the enhanced case-management intervention in the population of 10,000 over the 20-year time horizon considered if a QALY is valued at £20,000. The proportion of the population being treated for TB prior to the intervention is 788 per 100,000 and the treatment completion rate prior to the intervention is 55%. The cost of MXU screening is proportional to its case-finding rate. Black dots indicate the scenarios represented in Table 7.4.4f; the base case is indicated by the circular dot.

Table 7.4.4d Combined case-finding and enhanced case-management in the homeless: Scenario with 100 per 100,000 of the homeless population receiving TB treatment prior to intervention

This table shows, for homeless populations in which the proportion of the population being treated for TB prior to the intervention is 100 per 100,000 the total discounted QALYs gained and net discounted incremental costs incurred compared with current practice, and incremental net benefit if a QALY is valued at £20,000 or £30,000.

Scenario		QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
MXU case-finding rate (rate per case p.a.)	Treatment completion rate increased from 55% to			If a QALY is valued at £20,000	If a QALY is valued at £30,000
½× (0.39)	65%	145.2	2.0	0.9	2.3
½× (0.39)	75%	171.6	1.0	2.5	4.2
½× (0.39)	85%	185.9	0.4	3.3	5.2
1× (0.78)	65%	168.7	5.9	-2.5	-0.8
1× (0.78)	75%	185.8	5.2	-1.4	0.4
1× (0.78)	85%	195.5	4.7	-0.8	1.1
2x (1.56)	65%	190.7	14.3	-10.5	-8.6
2x (1.56)	75%	200.0	13.9	-9.9	-7.9
2x (1.56)	85%	205.8	13.6	-9.5	-7.4

Table 7.4.4e Combined case-finding and enhanced case-management in the homeless: Scenario with 500 per 100,000 of the homeless population receiving TB treatment prior to intervention

This table shows, for homeless populations in which the proportion of the population being treated for TB prior to the intervention is 500 per 100,000 the total discounted QALYs gained and net discounted incremental costs incurred compared with current practice, and incremental net benefit if a QALY is valued at £20,000 or £30,000.

Scenario		QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
MXU case-finding rate (rate per case p.a.)	Treatment completion rate increased from 55% to			If a QALY is valued at £20,000	If a QALY is valued at £30,000
½× (0.39)	65%	633.7	-14.1	26.8	33.1
½× (0.39)	75%	804.6	-21.5	37.6	45.6
½× (0.39)	85%	901.2	-25.5	43.5	52.5
1× (0.78)	65%	785.5	-14.4	30.1	38.0
1× (0.78)	75%	900.4	-19.8	37.8	46.8
1× (0.78)	85%	963.2	-22.6	41.9	51.5
2x (1.56)	65%	933.1	-10.3	29.0	38.3
2x (1.56)	75%	990.5	-13.4	33.2	43.1
2x (1.56)	85%	1023.9	-15.1	35.6	45.8

Table 7.4.4f Combined case-finding and enhanced case-management in the homeless: Scenario with 788 per 100,000 of the homeless population receiving TB treatment prior to intervention

This table shows, for homeless populations in which the proportion of the population being treated for TB prior to the intervention is 788 per 100,000 the total discounted QALYs gained and net discounted incremental costs incurred compared with current practice, and incremental net benefit if a QALY is valued at £20,000 or £30,000.

Scenario		QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
MXU case-finding rate (rate per case p.a.)	Treatment completion rate increased from 55% to			If a QALY is valued at £20,000	If a QALY is valued at £30,000
½× (0.39)	65%	931.3	-23.0	41.7	51.0
½× (0.39)	75%	1209.6	-35.0	59.2	71.3
½× (0.39)	85%	1382.3	-42.5	70.1	83.9
1× (0.78)	65%	1177.7	-26.0	49.6	61.3
1× (0.78)	75%	1381.7	-35.8	63.5	77.3
1× (0.78)	85%	1498.2	-41.3	71.3	86.3
2x (1.56)	65%	1443.2	-26.4	55.3	69.7
2x (1.56)	75%	1548.6	-32.3	63.2	78.7
2x (1.56)	85%	1607.5	-35.4	67.5	83.6

7.4.5 Summary of sensitivity analysis in the homeless

The effect of varying the proportion of the population being treated for TB prior to the intervention on the cost-effectiveness of different intervention options is examined in Tables 7.4.5a, b, and c.

If the proportion of the population being treated for TB prior to the intervention is 500 per 100,000 or 788 per 100,000 then combined mobile X-ray screening (with a case-finding rate of 0.78 per case per year) and enhanced case management (ECM, increasing treatment completion to 75%) is the most cost-effective option if ECM costs less than the "ECM cost threshold" (the cost at which the incremental net benefit of adding ECM to MXU screening is completely offset by the cost of ECM – see tables) about £38M over 20 years (if a QALY is valued at £20,000) or less than about £43M over 20 years (if a QALY is valued at £30,000) in the population where the proportion of the population being treated for TB prior to the intervention is 788 per 100,000; or if ECM costs less than about £23M over 20 years (if a QALY is valued at £20,000) or less than about £26M over 20 years (if a QALY is valued at £30,000) in the population where the proportion of the population being treated for TB prior to the intervention is 500 per 100,000. Otherwise, mobile X-ray screening is the most cost-effective option – and is cost-saving as well as improving health. MXU screening dominates current practice regardless of the cost of ECM (it provides more QALYs at lower cost). Similarly, combined mobile X-ray screening and ECM always dominates ECM alone (assuming that the additional cost of ECM is the same when it is provided on its own or in combination with mobile X-ray screening).

In contrast, if the proportion of the population being treated for TB prior to the intervention is 100 per 100,000 then mobile X-ray screening (with a case-finding rate of 0.78 per case per year) alone is not cost-effective, indicated by the negative incremental net benefit. Enhanced case management alone is cost-effective if it costs about £8.5M (if a QALY is valued at £20,000) or about £10M (if a QALY is valued at £30,000), over 20 years. Combined MXU screening and ECM is not cost-effective if a QALY is valued at £20,000 (it has a negative incremental net benefit), and is only cost-effective if a QALY is valued at £30,000 if the ECM component can be provided at a cost of no more than £400,000 over the 20 year time-horizon considered.

Table 7.4.5a Analysis of interventions against TB in the homeless.

Prior to intervention the proportion of the population being treated for TB is 100 per 100,000 (Story at al. 2007) and the treatment completion rate is 55%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	8.4	127,929	-	-	-	-
Mobile X-ray screening	15.9	128,062	7.5	133.6	-4.8	-3.5
Enhanced case-management (ECM)	2.8	128,074	-5.6	145.0	8.5	10.0
Combined Mobile X-ray screening and ECM	13.5	128,115	5.2	185.8	-1.4	0.4
				ECM cost threshold:	8.5	10.0

QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

Table 7.4.5b Analysis of interventions against TB in the homeless

Prior to intervention the proportion of the population being treated for TB is 500 per 100,000 (Story at al. 2007) and the treatment completion rate is 55%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	41.9	127,741	-	-	-	-
Mobile X-ray screening	38.1	128,308	-3.8	566.3	15.1	20.8
Enhanced case-management (ECM)	18.0	128,373	-23.9	631.2	36.5	42.8
Combined Mobile X-ray screening and ECM	22.1	128,642	-19.8	900.4	37.8	46.8
ECM cost threshold:					22.7	26

QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

Table 7.4.5c Analysis of interventions against TB in the homeless

Prior to intervention the proportion of the population being treated for TB is 788 per 100,000 (Story at al. 2007) and the treatment completion rate is 55%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	66.0	127,607	-	-	-	-
Mobile X-ray screening	56.9	128,435	-9.2	828.5	25.7	34.0
Enhanced case-management (ECM)	31.3	128,533	-34.7	926.6	53.2	62.5
Combined Mobile X-ray screening and ECM	30.2	128,988	-35.8	1381.7	63.5	77.3
ECM cost threshold:					37.8	43.3

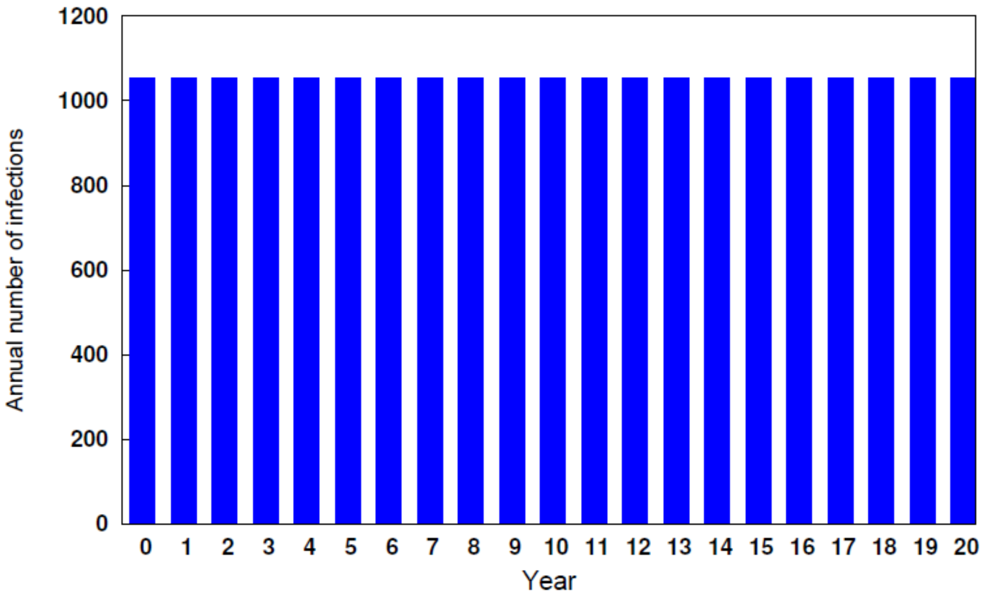
QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

7.5 Prisoners: base case

7.5.1 Current practice – i.e. no interventions

The base case assumes that the population size is constant, rates of entry and exit are constant, and that current practice for case-finding and treatment remain unchanged. Therefore, the same number of infections and cases of active disease occur in each year. Figure 7.5.1 shows the base case for prisoners, where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000.

(a)



(b)

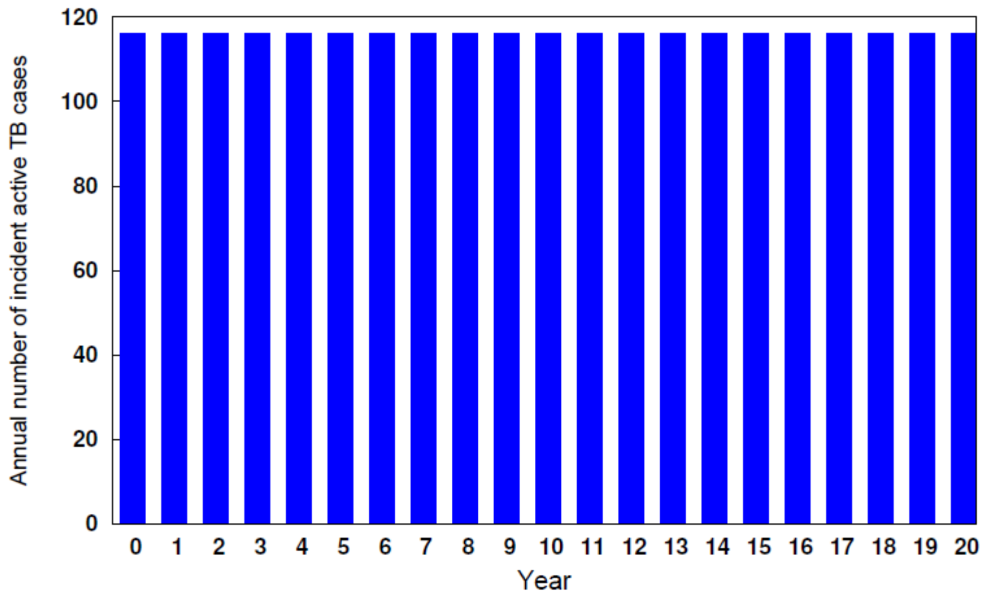


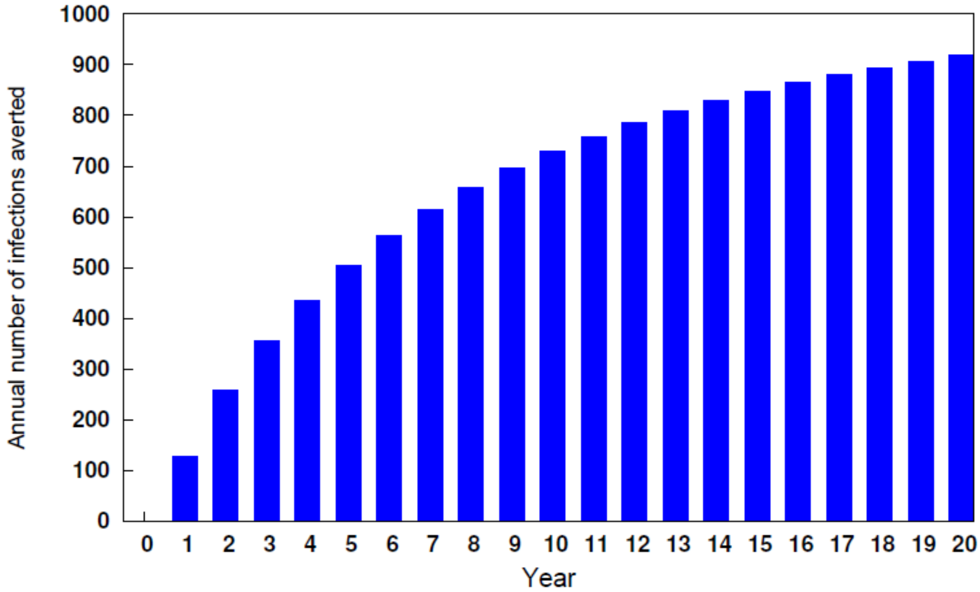
Figure 7.5.1 Annual numbers (undiscounted) of new infections and new cases of active disease in prisoners

(a) Annual numbers (undiscounted) of new infections in a prison population of 10,000 with the proportion of the population being treated for TB prior to the intervention being 208 per 100,000 and the treatment completion rate being 48%.
(b) Annual numbers (undiscounted) of new cases of active disease in a prison population of 10,000 with the proportion of the population being treated for TB prior to the intervention being 208 per 100,000 and the treatment completion rate being 48%.

7.5.2 Case-finding by mobile X-ray unit (MXU) in prisoners

The time-courses of annual numbers of infections averted and cases of active disease averted are shown in Figure 7.5.2a. Note that the number of infections averted is much greater than the number of active disease cases averted because the majority of infections do not progress to active disease. As time progresses since the introduction of the intervention the annual number of infections averted and cases of active disease averted increases. This is because over time the prevalence of infectious untreated active disease declines, so rates of transmission in the population decline.

(a)



(b)

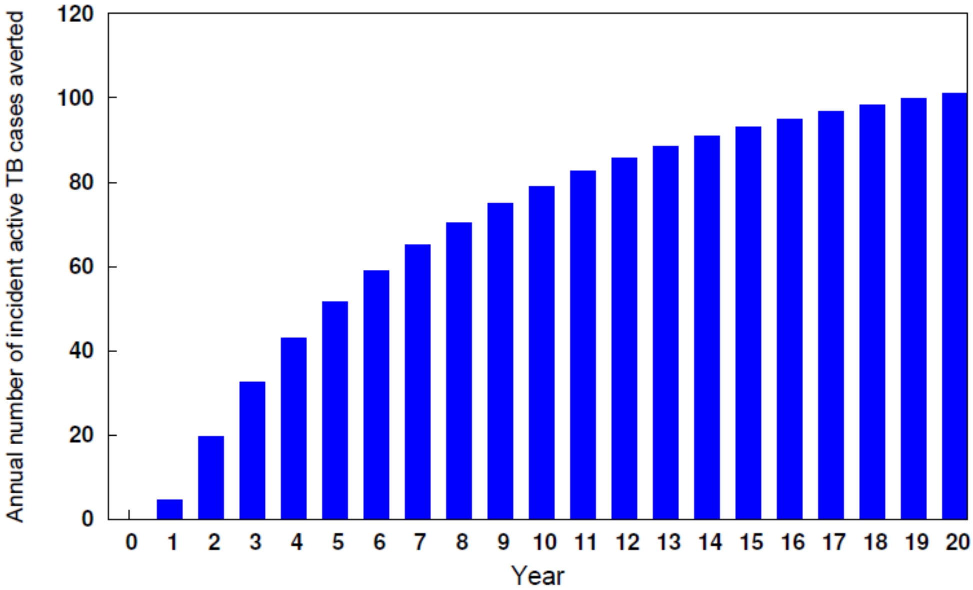


Figure 7.5.2a Annual numbers (undiscounted) of new infections and new cases of active disease averted by mobile X-ray unit case finding in prisoners

(a) Annual numbers (undiscounted) of new infections averted over a 20-year time-horizon by MXU case-finding in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000. The MXU case-finding rate is 0.78 per case per year. The intervention starts in year 1. The treatment completion rate is 48%.
(b) Annual numbers (undiscounted) of new cases of active disease averted over a 20-year time-horizon by MXU case-finding in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000. The MXU case-finding rate is 0.78 per case per year. The intervention starts in year 1. The treatment completion rate is 48%.

The time-courses of QALYs gained and costs incurred are shown in Figure 7.5.2b. Capital costs (i.e. MXU purchases) are incurred at the start of the intervention and after 10 years. The total discounted QALYs gained and net costs incurred shown in Table 7.5.2c.

Annual QALY gains mirror the annual numbers of active disease cases averted, because active disease is what causes health loss. Discounting means that gains further in the future are valued less than gains that occur earlier.

There are net costs at the beginning of the intervention, due to capital costs, the costs of running the intervention, and increased treatment costs incurred because more cases of active disease are found than would have been found without active MXU case-finding.

Subsequently, there are greater savings on treatment costs, due to more infections being averted, off-setting the net costs of running the MXU. MXU case-finding becomes marginally cost-saving in the later years. Capital costs (MXU purchase) are incurred at the start of the intervention and 10 years later (MXU replacement).

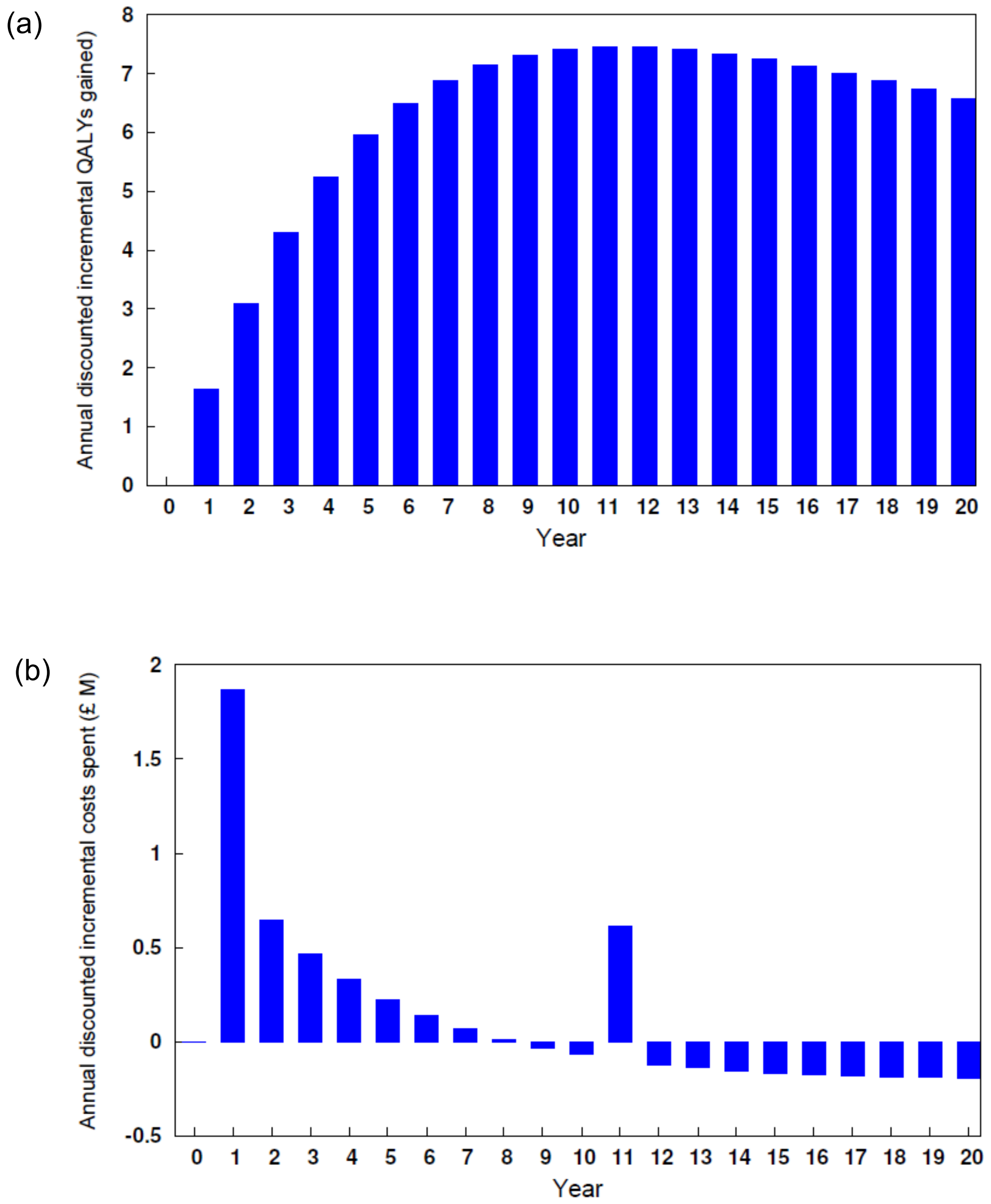


Figure 7.5.2b Discounted annual number of QALYs gained and net costs incurred by mobile X-ray unit case-finding in prisoners

(a) Discounted annual number of QALYs gained over a 20-year time-horizon by MXU case-finding in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000. The MXU active case-finding rate is 0.78 per case per year. The intervention starts in year 1. The treatment completion rate is 48%.
(b) Discounted annual net costs incurred over a 20-year time-horizon by MXU case-finding in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000. The MXU active case-finding rate is 0.78 per case per year. Negative net costs incurred indicate net savings. The intervention starts in year 1. The MXU is replaced in year 11. The treatment completion rate is 48%.

Total discounted QALYs gained and net costs incurred) are shown in Table 7.5.2c. The intervention is not cost-saving in any of the scenarios examined.

Table 7.5.2c Case-finding by mobile X-ray unit in prisoners

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, compared with current practice, where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the MXU active case-finding rate is 0.78 per case per year. The treatment completion rate is 48%.

QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
		If a QALY is valued at £20,000	If a QALY is valued at £30,000
126.6	2.8	-0.2	1.0

7.5.3 Enhanced case-management in prisoners

Increasing rates of treatment completion through enhanced case-management averts transmission events and therefore averts cases of active disease, as shown in Figure 7.5.3a. This is due to (i) infections being averted, thus averting cases of disease requiring treatment, and (ii) a reduction in the number of individuals requiring re-treatment.

In all scenarios, the intervention resulted in health benefits (QALYs gained) and reduced treatment costs.

(a)

(b)

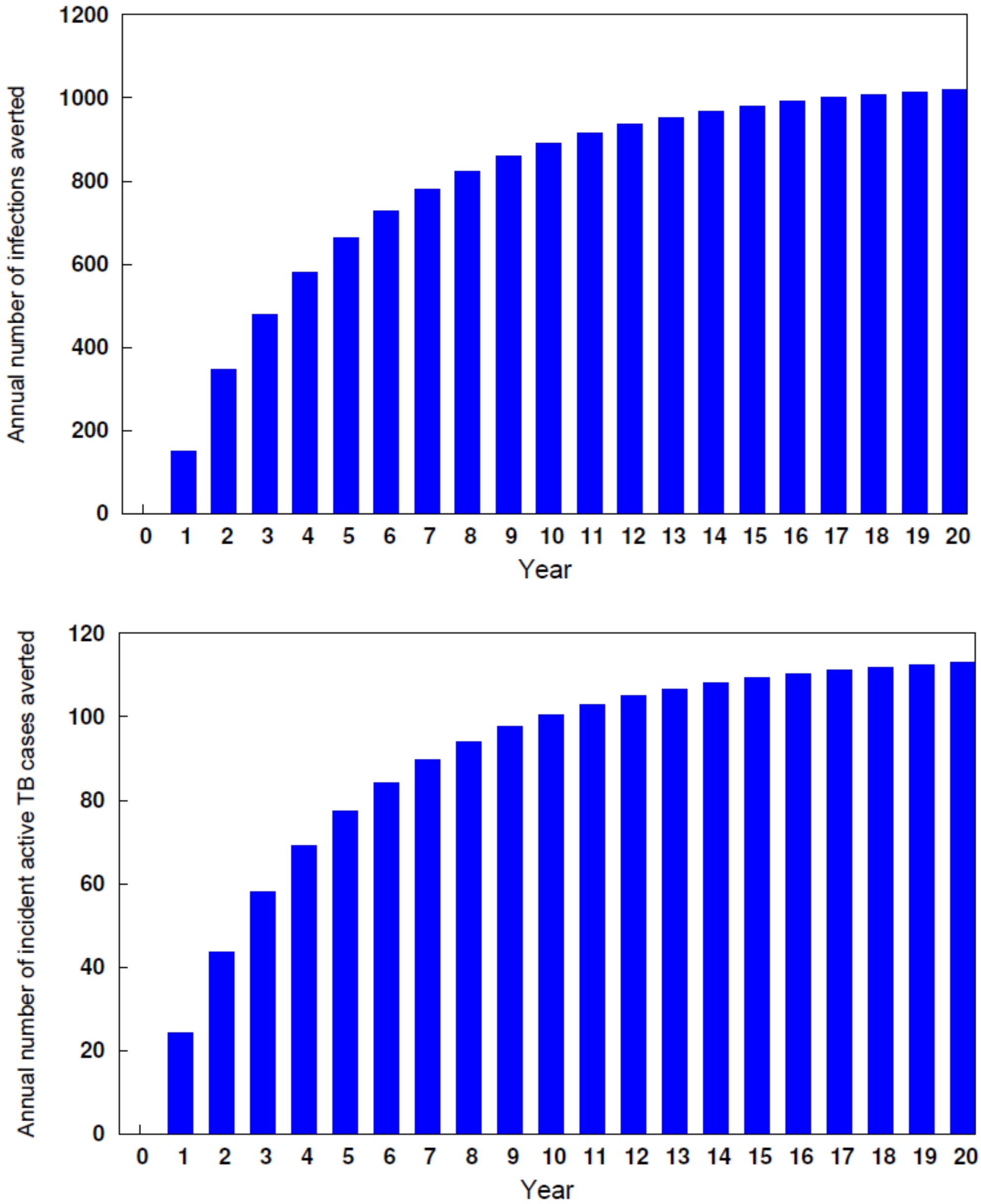


Figure 7.5.3a Annual numbers (undiscounted) of new infections and new cases of active disease averted by enhanced case-management in prisoners

(a) Annual numbers (undiscounted) of new infections averted over a 20-year time-horizon by enhanced case-management in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000, the treatment completion rate prior to the intervention is 48%, and the treatment completion rate with the intervention is 75%. The intervention starts in year 1.

(b) Annual numbers (undiscounted) of new cases of active disease averted over a 20-year time-horizon by enhanced case-management in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000, the treatment completion rate prior to the intervention is 48%, and the treatment completion rate with the intervention is 75%. The intervention starts in year 1.

The time-courses of QALYs gained and costs incurred are shown in Figure 7.5.3b and the total discounted QALYs gained and net costs incurred shown in Table 7.5.3c.

As before, annual QALY gains mirror the annual numbers of active disease cases averted, because active disease is what causes health loss. Discounting means that gains further in the future are valued less than gains that occur earlier.

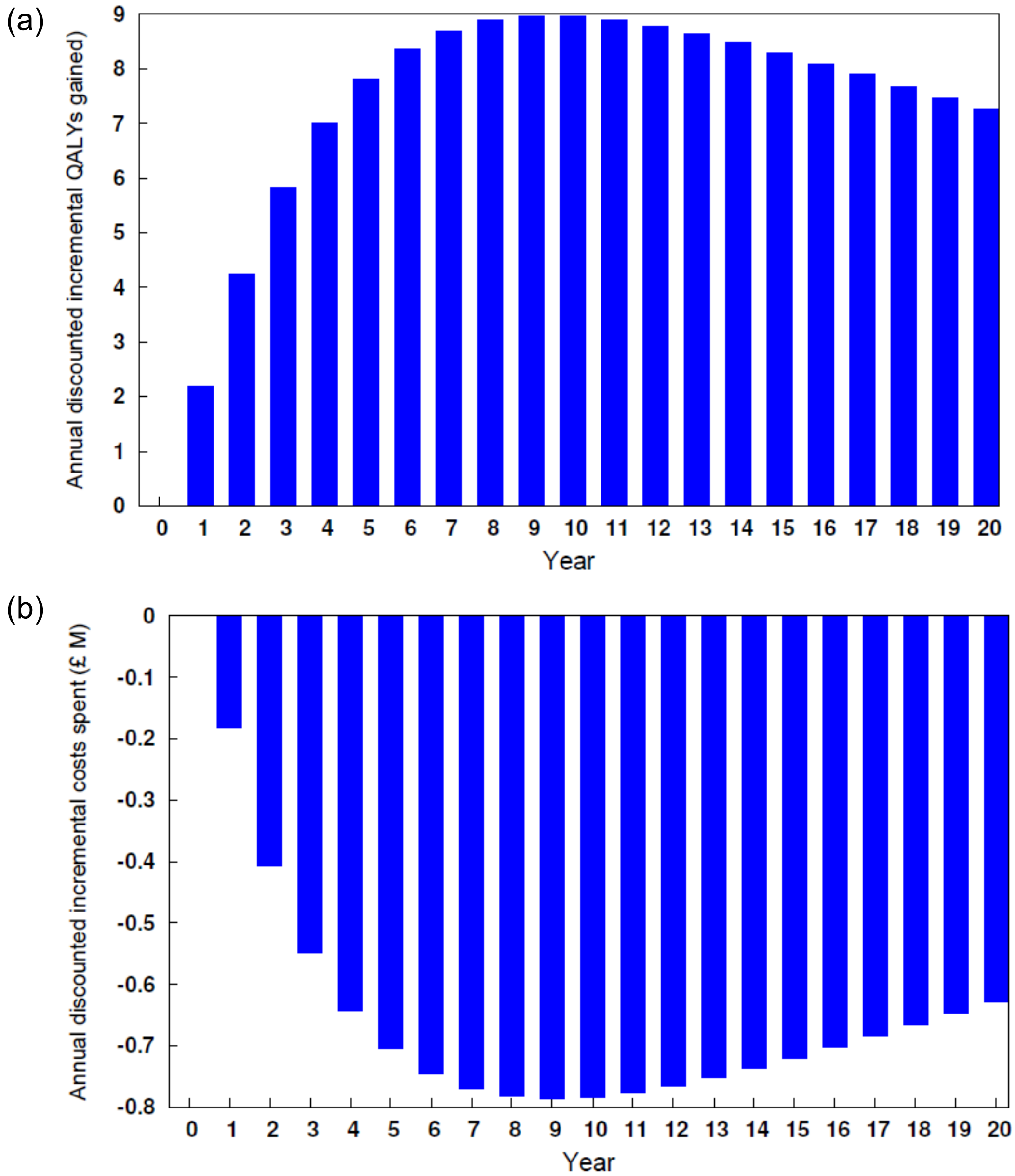


Figure 7.5.3b Discounted annual number of QALYs gained and net costs incurred by enhanced case-management in prisoners

(a) Discounted annual number of QALYs gained over a 20-year time-horizon by enhanced case-management in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the treatment completion rate prior to the intervention is 48%. The treatment completion rate with the intervention is 75%. The intervention begins in year 1.

(b) Discounted annual net costs incurred over a 20-year time-horizon by enhanced case-management in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the treatment completion rate prior to the intervention is 48%. The treatment completion rate with the intervention is 75%. The intervention begins in year 1.

In Table 7.5.3c we present the incremental net benefit (i.e. the threshold cost at which the intervention would be just cost-effective) of enhanced case management for the population of 10,000 over 20 years if a QALY is valued at £20,000 and £30,000.

Table 7.5.3c Enhanced case-management in prisoners

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, compared with current practice, where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000, the treatment completion rate prior to the intervention is 48%, and the treatment completion rate with the intervention is 75%. Negative incremental net costs are net cost savings.

QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
		If a QALY is valued at £20,000	If a QALY is valued at £30,000
152.4	-13.4	16.5	18.0

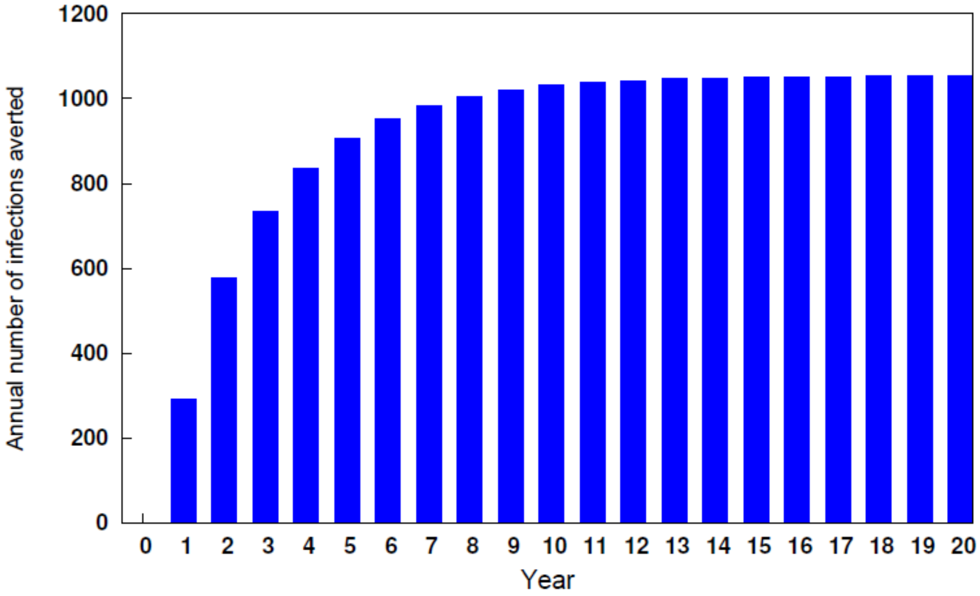
7.5.4 Combined case-finding and enhanced case-management in prisoners

In this analysis we calculate the cost of enhanced case-management for the population of 10,000 over 20 years that would be considered cost-effective when combined with active case-finding by mobile X-ray unit if a QALY is valued at £20,000 and £30,000.

The time-courses of infections averted and cases of active disease averted are shown in Figure 7.5.4a, and of QALYs gained and costs incurred are shown in Figure 7.5.4b. Annual QALY gains reflect annual numbers of cases of active disease averted, but QALY gains are discounted so that those occurring further in the future are valued less.

The total discounted QALYs gained and net costs incurred over the 20-year time horizon are shown in Table 7.5.4c.

(a)



(b)

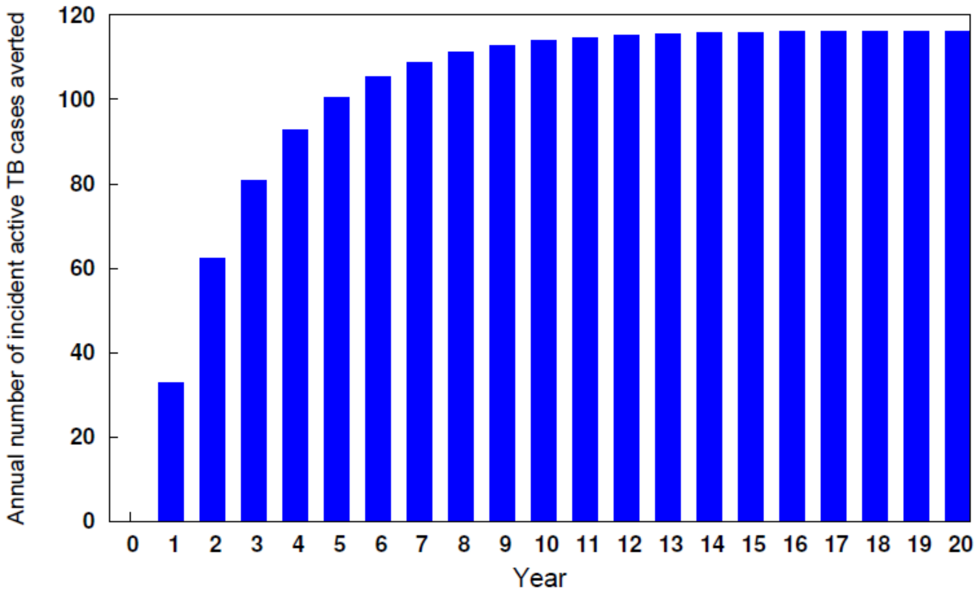


Figure 7.5.4a Annual numbers (undiscounted) of new infections and new cases of active disease averted by combined interventions in prisoners

(a) Annual numbers (undiscounted) of new infections averted, compared with current practice, by combined MXU case-finding and enhanced case-management in a prison population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and treatment completion rate of 48% prior to the intervention. The combined intervention is MXU case-finding at 0.78 p.a. and enhanced case-management increasing the treatment completion rate to 75%. The intervention starts in year 1.

(b) Annual numbers (undiscounted) of new cases of active disease averted, compared with current practice, by combined MXU case-finding and enhanced case-management in a prison population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and treatment completion rate of 48% prior to the intervention. The combined intervention is MXU case-finding at 0.78 p.a. and enhanced case-management increasing the treatment completion rate to 75%. The intervention starts in year 1.

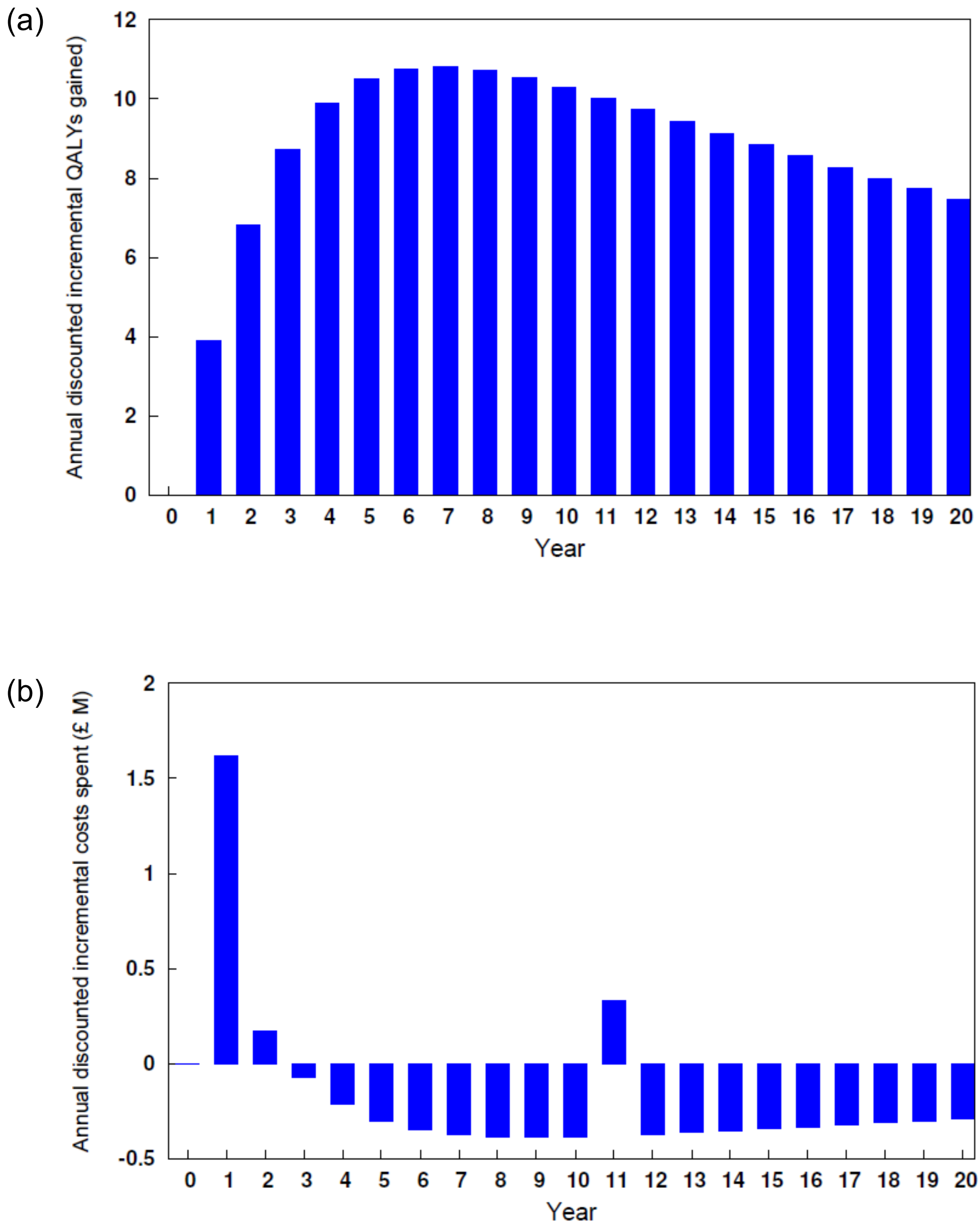


Figure 7.5.4b Discounted annual number of QALYs gained and net costs incurred by combined interventions in prisoners

(a) Discounted annual number of QALYs gained, compared with current practice, by combined MXU case-finding and enhanced case-management in a prison population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and treatment completion rate of 48% prior to the intervention. The combined intervention is MXU case-finding at 0.78 p.a. and enhanced case-management increasing the treatment completion rate to 75%. The intervention starts in year 1.

(b) Discounted annual number of net costs incurred compared with current practice, by combined MXU case-finding and enhanced case-management in a prison population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and treatment completion rate of 48% prior to the intervention. The combined intervention is MXU case-finding at 0.78 p.a. and enhanced case-management increasing the treatment completion rate to 75%. Negative net costs incurred indicate net savings. The intervention starts in year 1. The MXU is replaced in year 11.

Table 7.5.4c Combined case-finding and enhanced case-management in prisoners

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, compared with current practice, where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000, the treatment completion rate prior to the intervention is 48%, the MXU case-finding rate is 0.78 per case per year and the treatment completion rate with the intervention is 75%. Negative incremental net costs are net cost savings.

QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
		If a QALY is valued at £20,000	If a QALY is valued at £30,000
180.1	-3.3	6.9	8.7

7.5.5 Summary of base case analysis in prisoners

The base-case analysis for prisoners is summarised in Table 7.5.5. Enhanced case management (ECM, increasing the treatment completion rate to 75%) alone is the most cost-effective option if the cost of providing it over 20 years is less than £16.5M (if a QALY is valued at £20,000) or £17M (if a QALY is valued at £30,000). This equates to approximately £35,000 per case treated in the population of 10,000 over the 20-year time-horizon, if a QALY is valued at £20,000, or about £40,000 per case treated if a QALY is valued at £30,000. If providing ECM alone costs more than this then combined MXU screening (an active case-finding rate of 0.78 per case per year) and ECM will not be cost-effective (unless combining the interventions allows the cost of ECM to be reduced to about £7M to £9M, depending upon whether a QALY is valued at £20,000 or £30,000) over 20 years because combined MXU screening and ECM has an INB that is lower than ECM alone.

If a QALY is valued at £20,000 and ECM cannot be provided for less than £16.5M then the most cost-effective option is current practice because the incremental net benefit of MXU screening compared with current practice is negative.

If a QALY is valued at £30,000 and ECM cannot be provided for less than £17M then the most cost-effective option is mobile X-ray screening, which is just cost-effective (a small positive INB). The reason is that if a QALY is valued at £30,000 then MXU screening alone has an incremental net benefit (INB) of £1M, which includes the costs of MXU screening, and ECM alone has an INB of £18M, which excludes the cost of ECM – therefore if ECM costs £17M then it has the same overall INB as MXU screening and if ECM costs more than £17M then it has a lower overall INB then MXU screening.

Table 7.5.5 Base-case analysis of interventions against TB in prisoners

Prior to intervention the proportion of the population being treated for TB is 208 per 100,000 (Story at al. 2007) and the treatment completion rate is 48%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	18.3	127,877	-	-	-	-
Mobile X-ray screening	21.0	128,004	2.8	126.6	-0.2	1.0
Enhanced case-management (ECM)	4.9	128,030	-13.4	152.4	16.5	18.0
Combined Mobile X-ray screening and ECM	14.9	128,057	-3.3	180.1	6.9	8.7
				ECM cost threshold	16.5	17.0

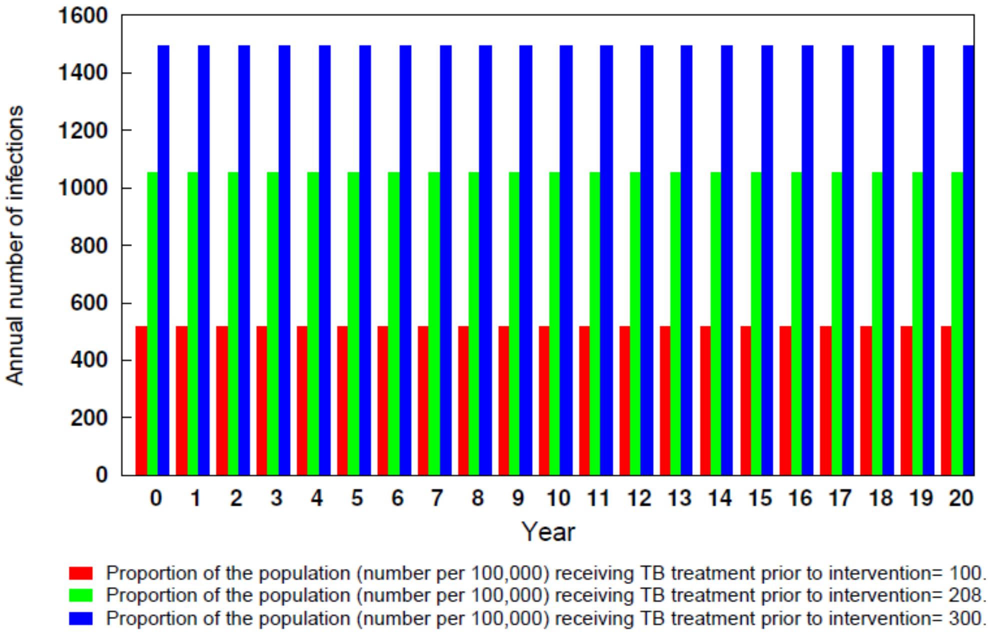
QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

7.6 Prisoners: Sensitivity analysis

7.6.1 Current practice – i.e. no interventions

We vary the proportion of the population being treated for TB prior to the intervention. We assume that the population size is constant, rates of entry and exit are constant, and that current practice for passive case-finding and treatment remain unchanged when the intervention is applied – i.e. the intervention is in addition to current practice. Therefore, the same number of infections and cases of active disease occur in each year. Figure 7.6.1 shows the base case for prisoners, where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000, plus a lower burden setting (100 per 100,000) and a higher burden setting (300 per 100,000).

(a)



(b)

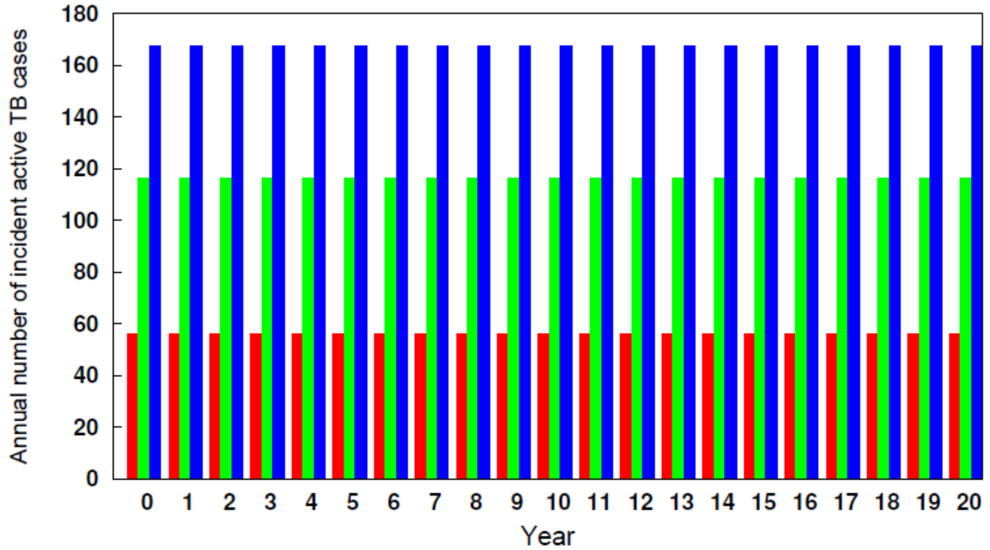


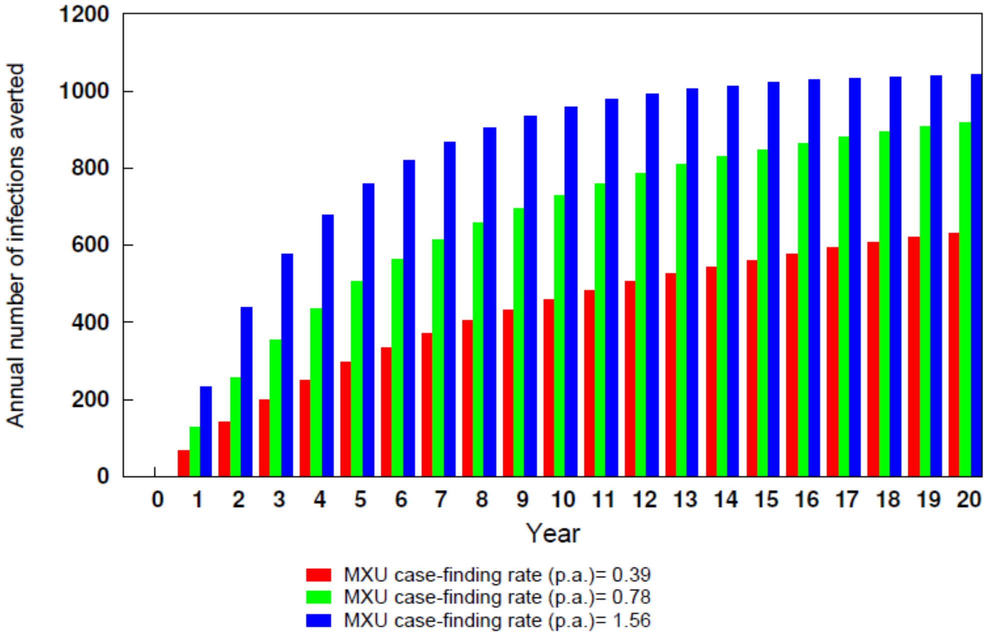
Figure 7.6.1 Annual numbers (undiscounted) of new infections and new cases of active disease in prisoners: sensitivity analysis

(a) Annual numbers (undiscounted) of new infections in a prison population of 10,000 with the proportion of the population being treated for TB prior to the intervention being 100 per 100,000 (red bars), 208 per 100,000 (green bars), and 300 per 100,000 (blue bars). The treatment completion rate is 48%.
(b) Annual numbers (undiscounted) of new cases of active disease in a prison population of 10,000 with the proportion of the population being treated for TB prior to the intervention being 100 per 100,000 (red bars), 208 per 100,000 (green bars), and 300 per 100,000 (blue bars). The treatment completion rate is 48%.

7.6.2 Case-finding by mobile X-ray unit (MXU) in prisoners

The time-courses annual numbers of infections averted and cases of active disease averted are shown in Figure 7.6.2a. Note that the number of infections averted is much greater than the number of active disease cases averted because the majority of infections do not progress to active disease. As time progresses since the introduction of the intervention the annual number of infections averted and cases of active disease averted increases. This is because over time the prevalence of infectious untreated active disease declines so rates of transmission in the population decline. The greater the MXU case-finding rate the greater the annual numbers of infections and cases of active disease averted.

(a)



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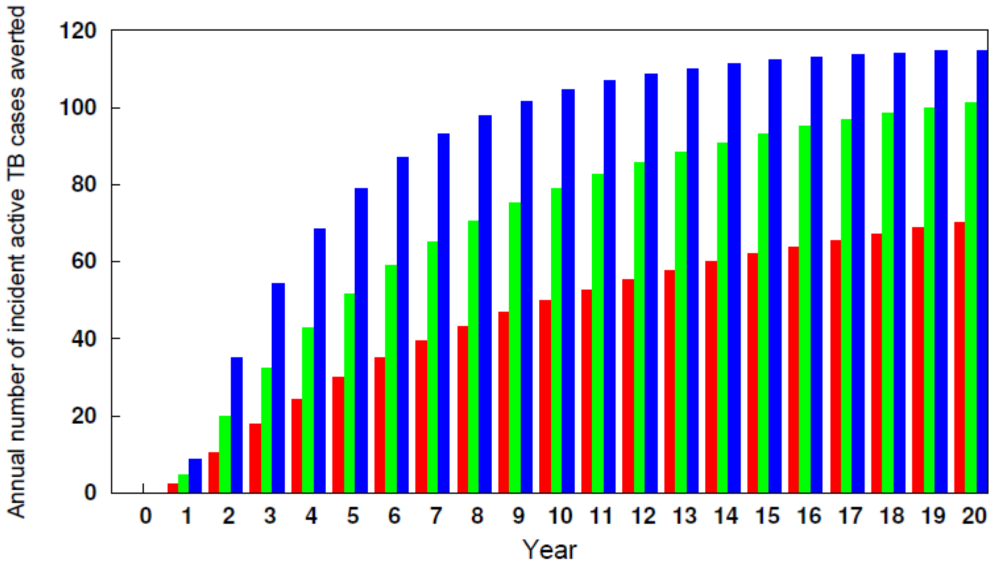


Figure 7.6.2a Annual numbers (undiscounted) of infections and cases averted by mobile X-ray unit case finding in prisoners: sensitivity analysis

(a) Annual numbers (undiscounted) of new infections averted over a 20-year time-horizon by MXU case-finding in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000. The effect of varying the MXU case-finding rate is examined: red bars indicate a rate of 0.39 per case per year; green bars indicate a rate of 0.78 per case per year; blue bars indicate a rate of 1.56 per case per year. The intervention starts in year 1. The treatment completion rate is 48%.

(b) Annual numbers (undiscounted) of new cases of active disease averted over a 20-year time-horizon by MXU case-finding in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000. The effect of varying the MXU case-finding rate is examined: red bars indicate a rate of 0.39 per case per year; green bars indicate a rate of 0.78 per case per year; blue bars indicate a rate of 1.56 per case per year. The intervention starts in year 1. The treatment completion rate is 48%.

The time-courses of QALYs gained and costs incurred are shown in Figure 7.6.2b. Capital costs (i.e. MXU purchases) are incurred at the start of the intervention and after 10 years. The total discounted QALYs gained and net costs incurred over the 20-year time-horizon are shown in Table 7.6.2d.

Annual QALY gains mirror the annual numbers of active disease cases averted, because active disease is what causes health loss. Discounting means that gains further in the future are valued less than gains that occur earlier.

There are net costs at the beginning of the intervention, due to capital costs, the costs of running the intervention, and increased treatment costs incurred because more cases of active disease are found than would have been found without active MXU case-finding.

Higher rates of MXU case-finding have higher net costs initially, due to higher intervention costs, and due to more additional cases being treated in the early years, because more cases are found more quickly.

Subsequently, there are greater savings on treatment costs, due to more infections being averted, off-setting the net costs of running the MXU. MXU case-finding becomes marginally cost-saving in the later years. Capital costs (MXU purchase) are incurred at the start of the intervention and 10 years later (MXU replacement).

(a)

(b)

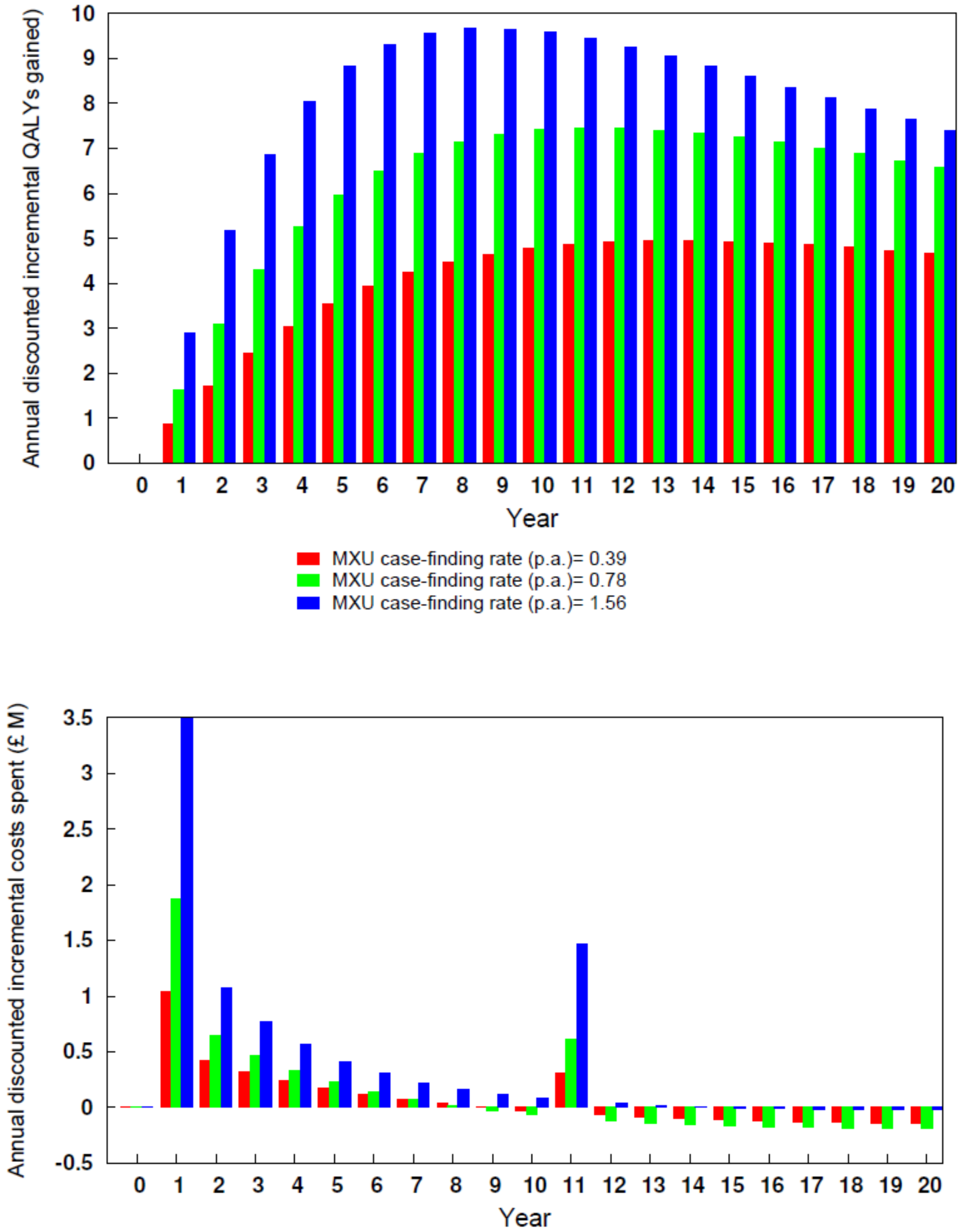


Figure 7.6.2b Discounted annual number of QALYs gained and net costs incurred by mobile X-ray unit case-finding in prisoners: sensitivity analysis

(a) Discounted annual number of QALYs gained over a 20-year time-horizon by MXU case-finding in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000. The effect of varying the MXU case-finding rate is examined: red bars indicate a rate of 0.39 per case per year; green bars indicate a rate of 0.78 per case per year; blue bars indicate a rate of 1.56 per case per year. The intervention starts in year 1. The treatment completion rate is 48%.

(b) Discounted annual net costs incurred over a 20-year time-horizon by MXU case-finding in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000. The effect of varying the MXU case-finding rate is examined: red bars indicate a rate of 0.39 per case per year; green bars indicate a rate of 0.78 per case per year; blue bars indicate a rate of 1.56 per case per year. Negative net costs incurred indicate net savings. The intervention starts in year 1. The MXU is replaced in year 11. The treatment completion rate is 48%.

Figure 7.6.2c summarises the sensitivity analysis of the cost-effectiveness of the mobile X-ray unit (MXU) active case-finding intervention, applied in populations with different proportions of the population being treated for TB prior to the intervention (Story et al. (2007) estimated this to be 208 per 100,000 for prisoners), and with differing intensity of intervention. Where the intervention is cost-saving we do not calculate incremental cost-effectiveness ratios (ICERs) but instead consider QALYs gained and costs saved. For other scenarios we calculate ICERs.

The greater the proportion of the population being treated for TB prior to the intervention, the more cost-effective or cost-saving the intervention will be. For part of parameter space with a relatively high proportion of the population being treated for TB prior to the intervention is cost-saving but there is a large region in which it may not be considered cost-effective. If the population being treated for TB prior to the intervention is 208 per 100,000, as found by Story et al. 2007, then cost-effectiveness is likely to be in the range £20,000 – £30,000 per QALY gained for MXU active case-finding rates of 0.39 p.a. and 0.78 p.a., and to be greater than £30,000 per QALY for an active case-finding rates of 1.56 p.a.

For selected scenarios, numerical results are shown in Table 7.6.2d. In the scenarios examined, the greater the proportion of the population being treated for TB prior to the intervention and the higher the screening rate the more QALYs gained. The intervention is not cost-saving in any of the scenarios examined, but the greater the proportion of the population being treated for TB prior to the intervention the greater the treatment cost savings accrued from averting infections and averting cases of active disease, resulting in lower the net costs.

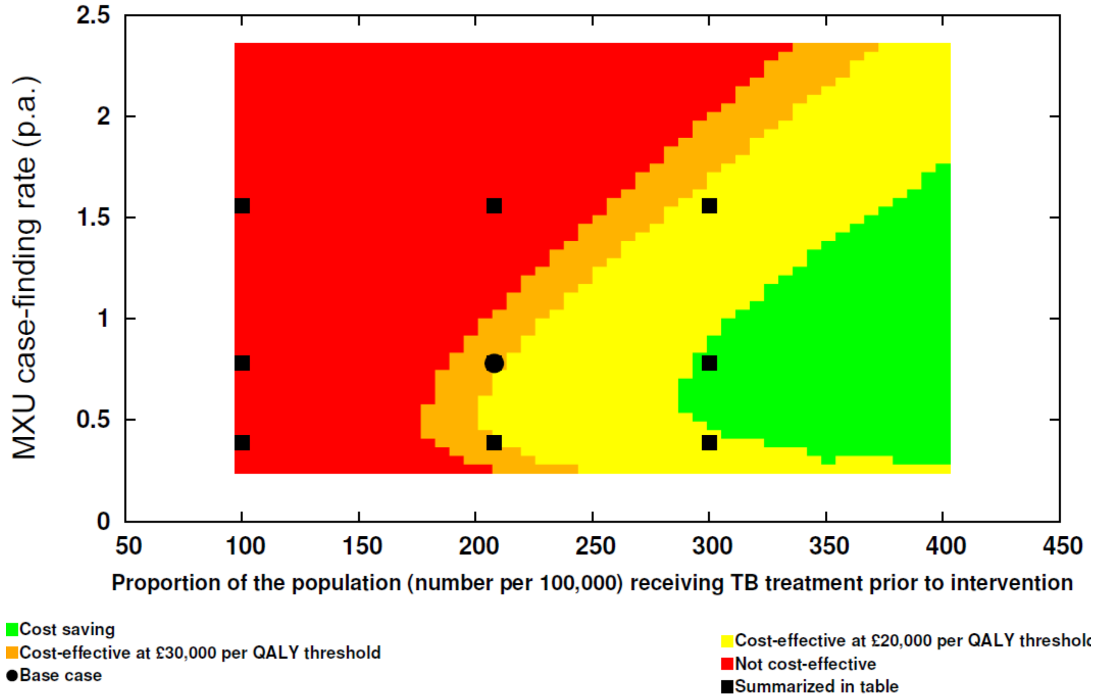


Figure 7.6.2c Cost-effectiveness of case-finding by mobile X-ray unit in prisoners compared with current practice

This figure shows the effects of varying the MXU case-finding rate (vertical axis), in prison populations with different proportions of the population being treated for TB prior to the intervention (horizontal axis), on whether the intervention is cost-saving, or has an incremental cost-effectiveness ratio (ICER) of less than £20,000 per QALY, an ICER between £20,000 and £30,000 per QALY, or an ICER greater than £30,000 per QALY, over the 20-year time-horizon. The cost of MXU screening is proportional to its case-finding rate. The treatment completion rate is 48%. Black dots indicate the scenarios represented Table 7.6.2d; the base case is indicated by the circular dot.

Table 7.6.2d Case-finding by mobile X-ray unit in prisoners

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, for different rates of MXU case-finding in prison populations with different proportions of the population being treated for TB prior to the intervention, compared with current practice. The treatment completion rate is 48%. Negative incremental net costs are net cost savings.

Proportion of whole prison population receiving TB treatment (per 100,000) prior to intervention	MXU case-finding rate (rate per case p.a.)	QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
				If a QALY is valued at £20,000	If a QALY is valued at £30,000
100	½× (0.39)	43.4	4.2	-3.3	-2.9
	1× (0.78)	63.7	7.1	-5.8	-5.2
	2x (1.56)	79.9	14.8	-13.2	-12.4
208	½× (0.39)	82.2	1.7	0.0	0.8
	1× (0.78)	126.6	2.8	-0.2	1.0
	2x (1.56)	164.1	8.6	-5.3	-3.7
300	½× (0.39)	109.1	0.2	2.0	3.1
	1× (0.78)	174.6	-0.3	3.8	5.5
	2x (1.56)	233.5	3.7	1.0	3.3

The effect of varying the cost of the case-finding intervention and the cost of treatment cost is presented in Figure 7.6.2e. The higher the cost of treatment, the greater the cost saving per infection averted, so the more likely the intervention is to be cost-effective or cost-saving. The higher the cost of the intervention the less likely it is to be cost-effective or cost-saving, especially if the treatment costs per case are low. If the proportion of the population being treated for TB prior to the intervention is 208 per 100,000, as found by Story et al. 2007, then MXU case-finding at 0.78 p.a. may or may not be considered cost-effective.

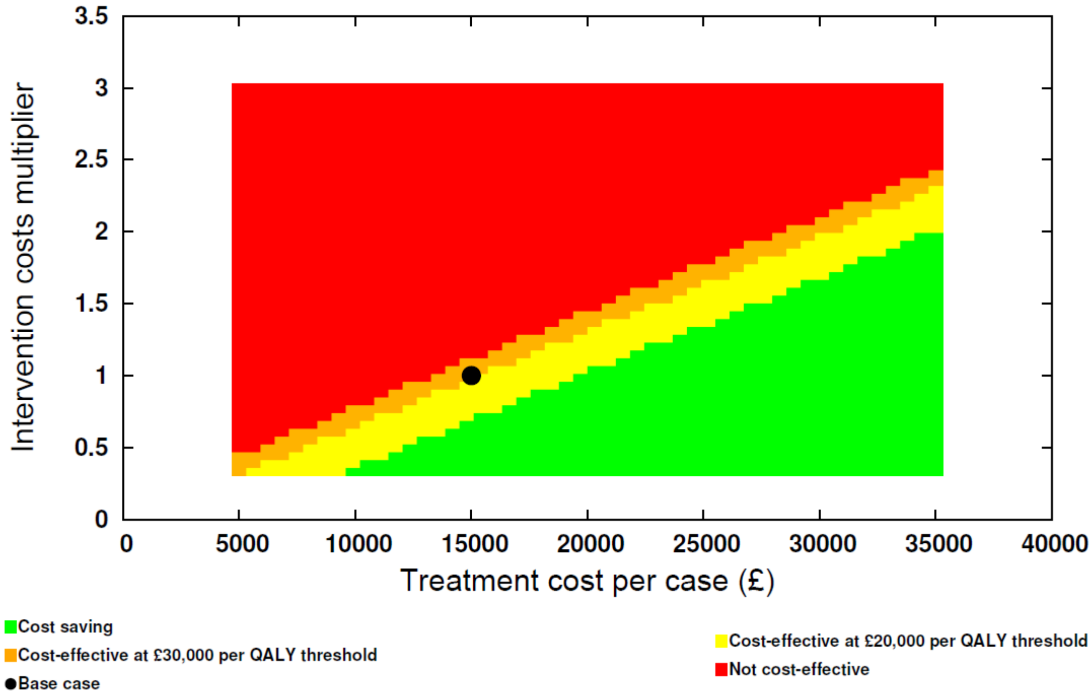


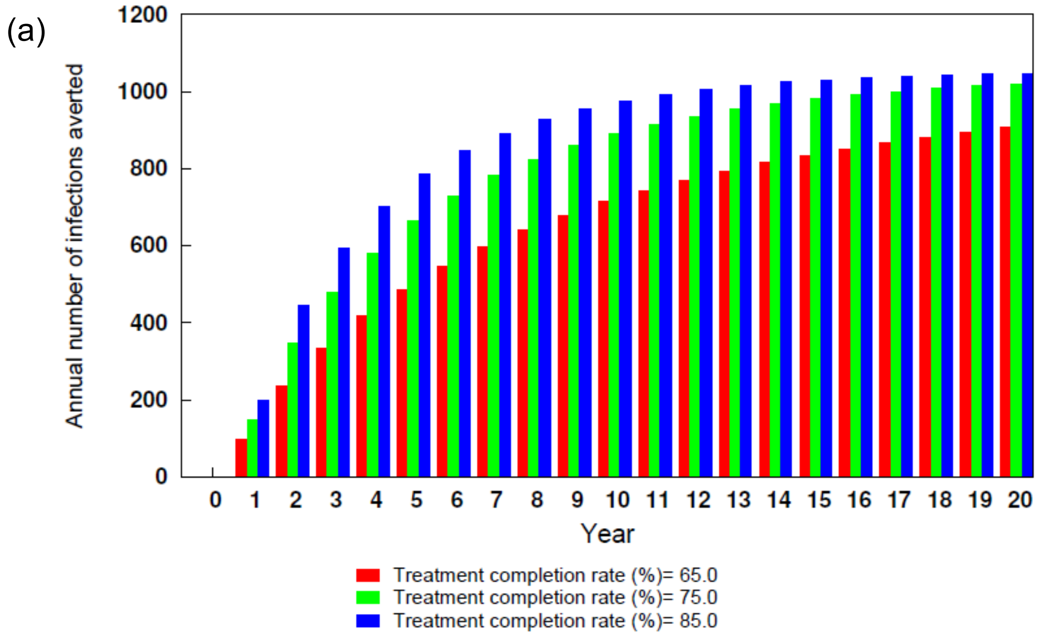
Figure 7.6.2e Cost-effectiveness of case-finding by mobile X-ray unit in prisoners: sensitivity analysis

This figure shows the effects of varying the cost of MXU case-finding intervention (vertical axis) and the cost of treating the average case of TB in this population (horizontal axis) on whether the intervention is cost-saving, or has an incremental cost-effectiveness ratio (ICER) of less than £20,000 per QALY, an ICER between £20,000 and £30,000 per QALY, or an ICER greater than £30,000 per QALY, over the 20-year time-horizon. On the vertical axis, 1 indicates that the intervention costs as much as in the base case, 0.5 indicates that it costs half as much, 2 indicates that it costs twice as much. The proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the active case-finding rate is 0.78 per case per year. The treatment completion rate is 48%. The base case is indicated by the black dot.

7.6.3 Enhanced case-management in prisoners

Increasing rates of treatment completion through enhanced case-management averts transmission events and therefore averts cases of active disease, as shown in Figure 7.6.3a. This is due to (i) infections being averted, thus averting cases of disease requiring treatment, and (ii) a reduction in the number of individuals requiring re-treatment.

In all scenarios, the intervention resulted in health benefits (QALYs gained) and reduced treatment costs.



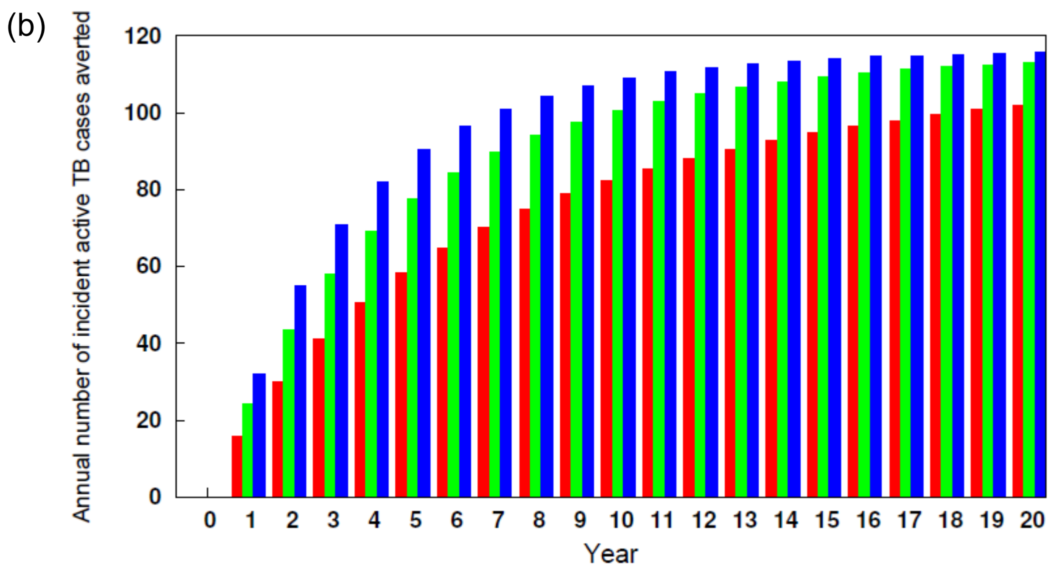


Figure 7.6.3a Annual numbers (undiscounted) of infections and cases averted by enhanced case-management in prisoners: sensitivity analysis

(a) Annual numbers (undiscounted) of new infections averted over a 20-year time-horizon by enhanced case-management in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the treatment completion rate prior to the intervention is 48%. The effect of varying the treatment completion rate achieved by the intervention is examined: red bars indicate 65%; green bars 75%; blue bars 85%. The intervention starts in year 1.

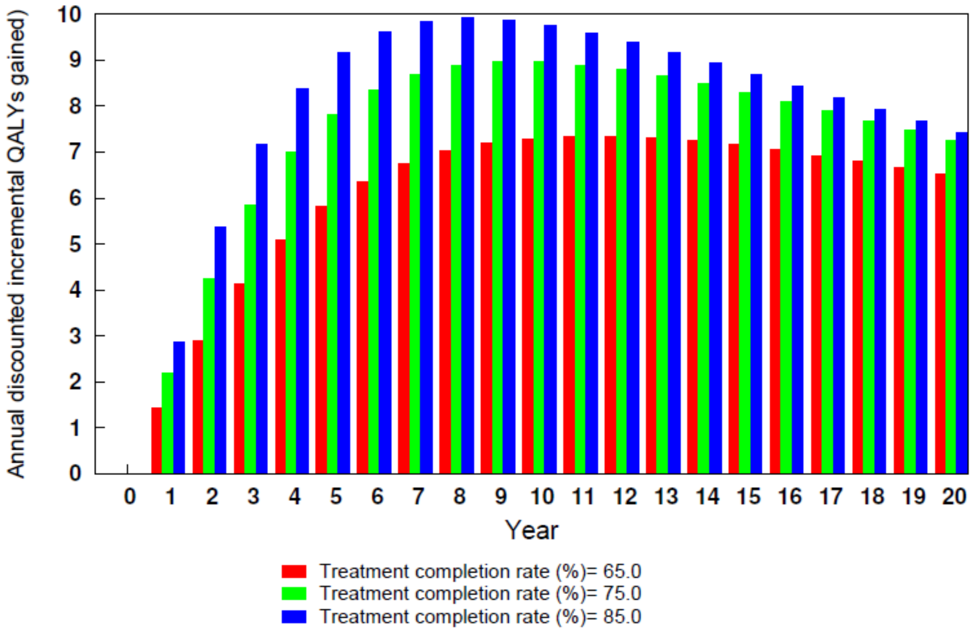
(b) Annual numbers (undiscounted) of new cases of active disease averted over a 20-year time-horizon by enhanced case-management in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the treatment completion rate prior to the intervention is 48%. The effect of varying the treatment completion rate achieved by the intervention is examined: red bars indicate 65%; green bars 75%; blue bars 85%. The intervention starts in year 1.

The time-courses of QALYs gained and costs incurred are shown in Figure 7.6.3b and the total discounted QALYs gained and net costs incurred shown in Table 7.6.3d.

If the cost of the intervention is greater than the estimated incremental net benefit (excluding intervention costs), then enhanced case management may considered cost-effective compared with current practice. Figure 7.6.3c summarises the sensitivity analysis of the threshold costs over 20 years for the population of 10,000 at which the intervention would be just cost-effective if a QALY is valued at £20,000. Note that the cost would not scale up or down for a different population due to non-linearities in the indirect benefits (infections averted), so could not just be multiplied by the number of cases in a particular population to get a new figure. Higher proportions of the population being treated for TB prior to the intervention and a higher treatment success rate achieved by the intervention result in one being willing to pay more for the intervention for a particular value of a QALY.

The greater the proportion of the population being treated for TB prior to the intervention and the greater treatment success rate achieved by the intervention the more one would be willing to pay for the intervention, for a given value of a QALY.

(a)



(b)

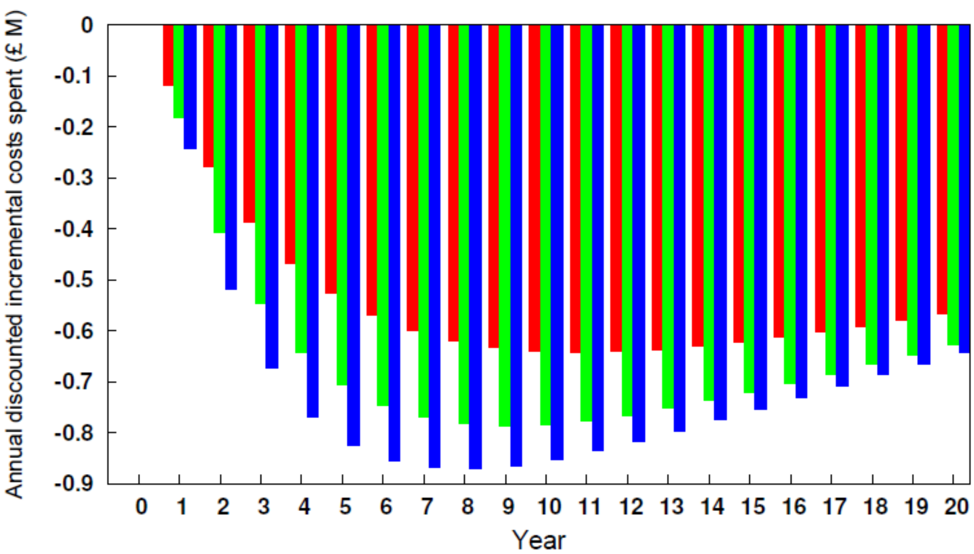


Figure 7.6.3b Discounted annual number of QALYs gained and net costs incurred by enhanced case-management in prisoners: sensitivity analysis

(a) Discounted annual number of QALYs gained over a 20-year time-horizon by enhanced case-management in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the treatment completion rate prior to the intervention is 48%. The effect of varying the treatment completion rate achieved by the intervention is examined: red bars indicate 65%; green bars 75%; blue bars 85%. The intervention starts in year 1.

(b) Discounted annual net costs incurred over a 20-year time-horizon by enhanced case-management in a prison population in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the treatment completion rate prior to the intervention is 48%. The effect of varying the treatment completion rate achieved by the intervention is examined: red bars indicate 65%; green bars 75%; blue bars 85%. Negative net costs incurred indicate net savings. The intervention starts in year 1.

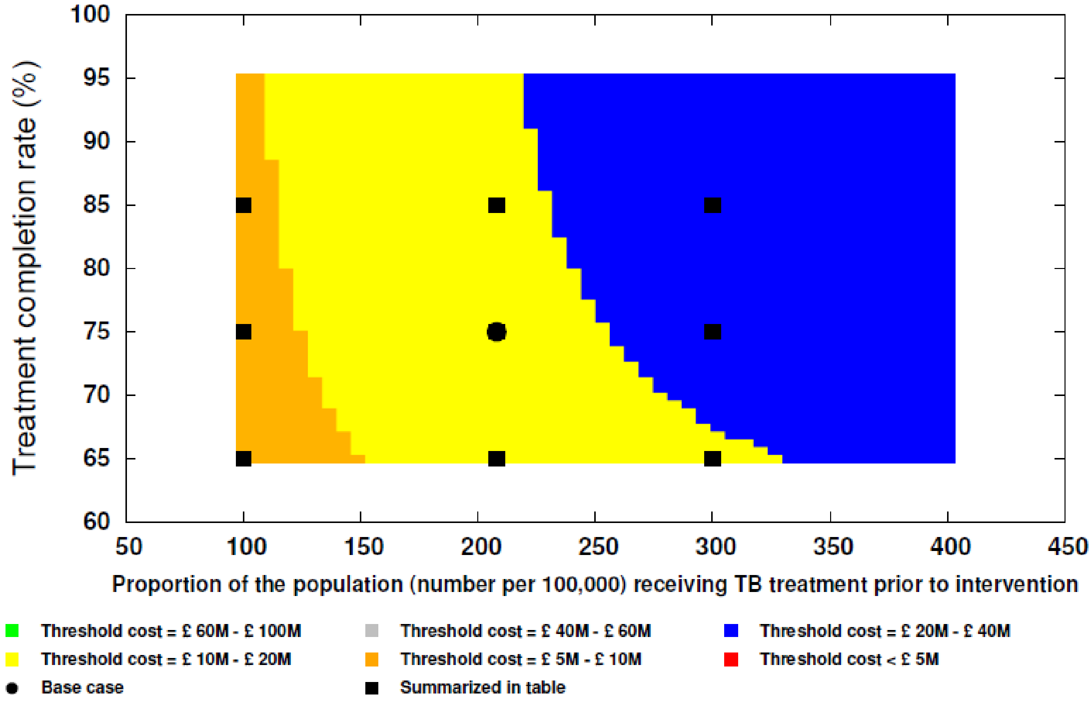


Figure 7.6.3c Cost-effectiveness of enhanced case-management in prisoners compared with current practice

This figure shows the effects of varying the treatment completion rate achieved by the enhanced case-management intervention (vertical axis) and the proportion of the population being treated for TB prior to the intervention (horizontal axis) on the amount that one would be willing to pay for the enhanced case-management intervention in the population of 10,000 over the 20-year time horizon considered if a QALY is valued at £20,000. The treatment completion rate prior to the intervention is 48%. Black dots indicate the scenarios represented in Table 7.6.3d; the base case is indicated by the circular dot.

In Table 7.6.3d we present the incremental net benefit (i.e. the threshold cost at which the intervention would be just cost-effective) of enhanced case management for the population of 10,000 over 20 years if a QALY is valued at £20,000 and £30,000.

Table 7.6.3d Enhanced case-management in prisoners

This table shows the totals over the 20-year time-horizon of discounted number of QALYs gained, discounted incremental costs incurred, and incremental net benefit if a QALY is valued at £20,000 or £30,000, for different treatment completion rates achieved by enhanced case-management in prison populations with different proportions of the population being treated for TB prior to the intervention, compared with the current practice. Negative incremental net costs are net cost savings.

Proportion of whole prison population receiving TB treatment (per 100,000) prior to intervention	Treatment completion rate increased from 48% to	QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
				If a QALY is valued at £20,000	If a QALY is valued at £30,000
100	65%	62.7	-5.5	6.8	7.4
	75%	74.9	-6.6	8.1	8.8
	85%	80.4	-7.2	8.8	9.6
208	65%	124.3	-11.0	13.4	14.7
	75%	152.4	-13.4	16.5	18.0
	85%	167.4	-14.7	18.1	19.8
300	65%	170.9	-15.1	18.5	20.2
	75%	214.8	-18.9	23.2	25.4
	85%	238.6	-21.0	25.8	28.2

The effect of varying the cost of the treatment success rate due to enhanced case management and the cost of treatment cost is presented in Figure 7.6.3e. The higher the cost of treatment, the greater the cost saving per infection averted, so the more likely the intervention is to be cost-effective or cost-saving. The higher the treatment completion rate achieved, the greater the number of infections and active disease cases averted, so the greater the reduction in treatment costs, and the more likely the intervention is to be cost-effective or cost-saving.

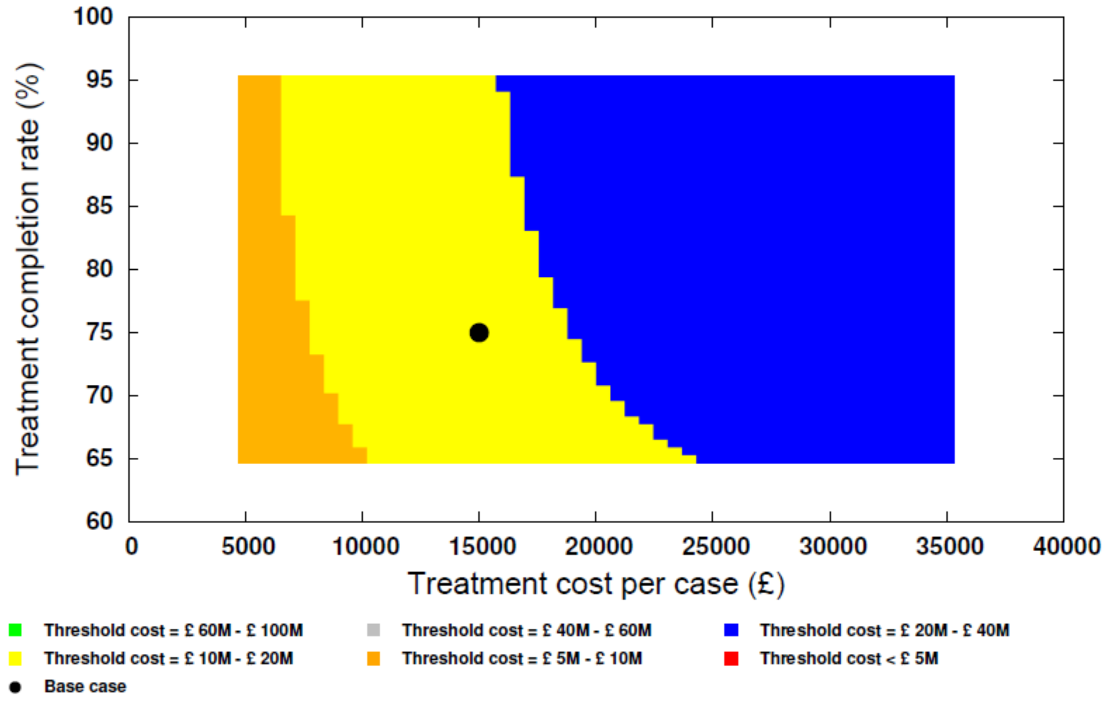


Figure 7.6.3e Cost-effectiveness of enhanced case-management in prisoners: sensitivity analysis

This figure shows the effects of varying the treatment completion rate achieved by the enhanced case-management intervention (vertical axis) and the cost of treating the average case of TB in this population (horizontal axis) on the amount that one would be willing to pay for the enhanced case-management intervention in the population of 10,000 over the 20-year time horizon considered if a QALY is valued at £20,000. The proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the treatment completion rate prior to the intervention is 48%. The base case is indicated by the black dot.

7.6.4 Combined case-finding and enhanced case-management in prisoners

In this analysis we calculate the cost of enhanced case-management for the population of 10,000 over 20 years that would be considered cost-effective when combined with active case-finding by mobile X-ray unit if a QALY is valued at £20,000 and £30,000.

The time-courses of infections averted and cases of active disease averted are shown in Figure 7.6.4a, and of QALYs gained and costs incurred are shown in Figure 7.6.4b. The total discounted QALYs gained and net costs incurred over the 20-year time horizon are shown in Table 7.6.4d-f.

(a)

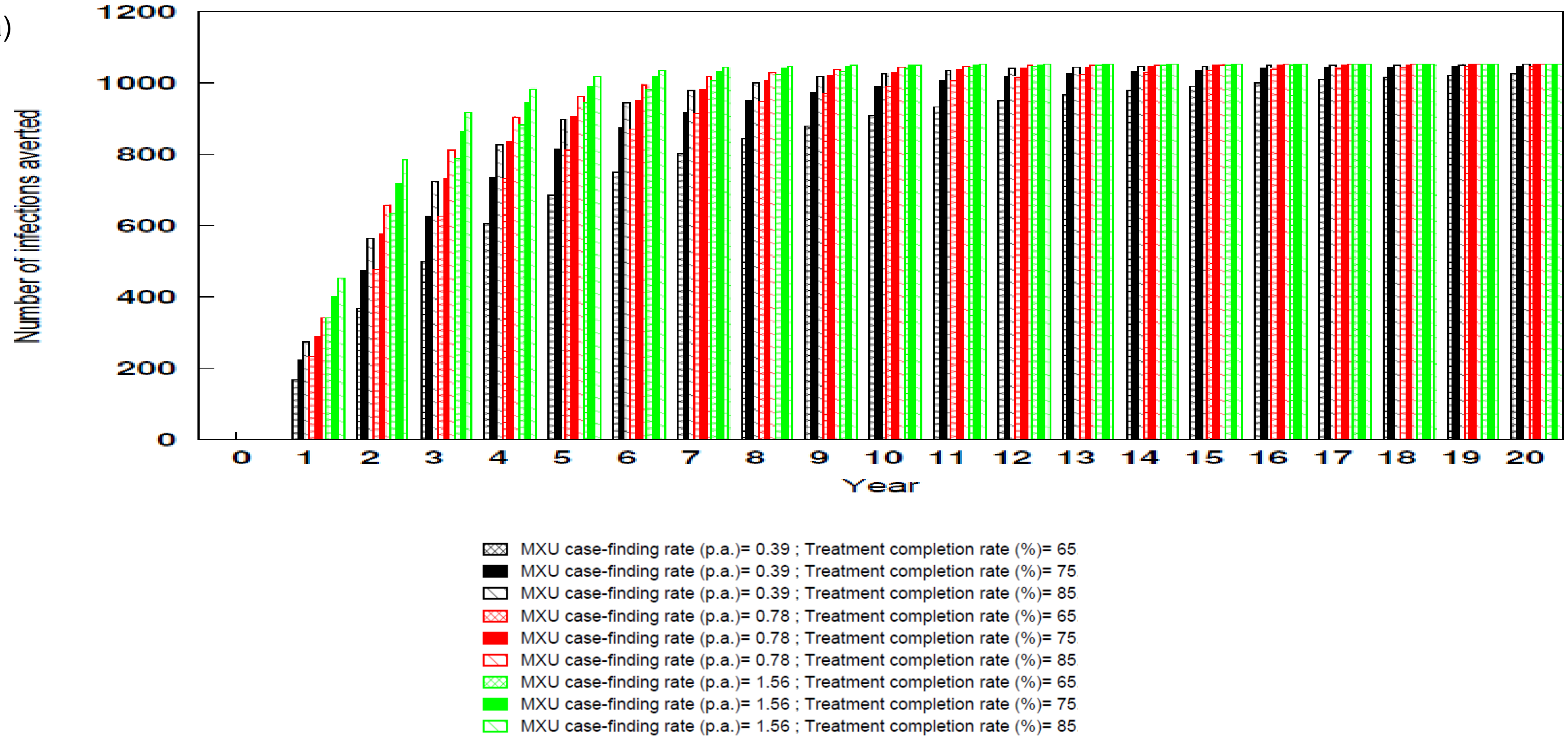


Figure 7.6.4a Annual numbers (undiscounted) of infections and cases averted by combined interventions in prisoners: sensitivity analysis

(a) Annual numbers (undiscounted) of infections averted, compared with current practice, by combined MXU case-finding and enhanced case-management in a prison population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and treatment completion rate of 48% prior to the intervention. Scenarios examined are MXU case-finding at 0.78 p.a. (red bars), half that rate (0.39 p.a., black bars), and double that rate (1.56 p.a., green bars). Within each colour grouping, left to right, treatment completion rates are increased to 65%, 75% and 85%. The intervention begins in year 1.

(b)

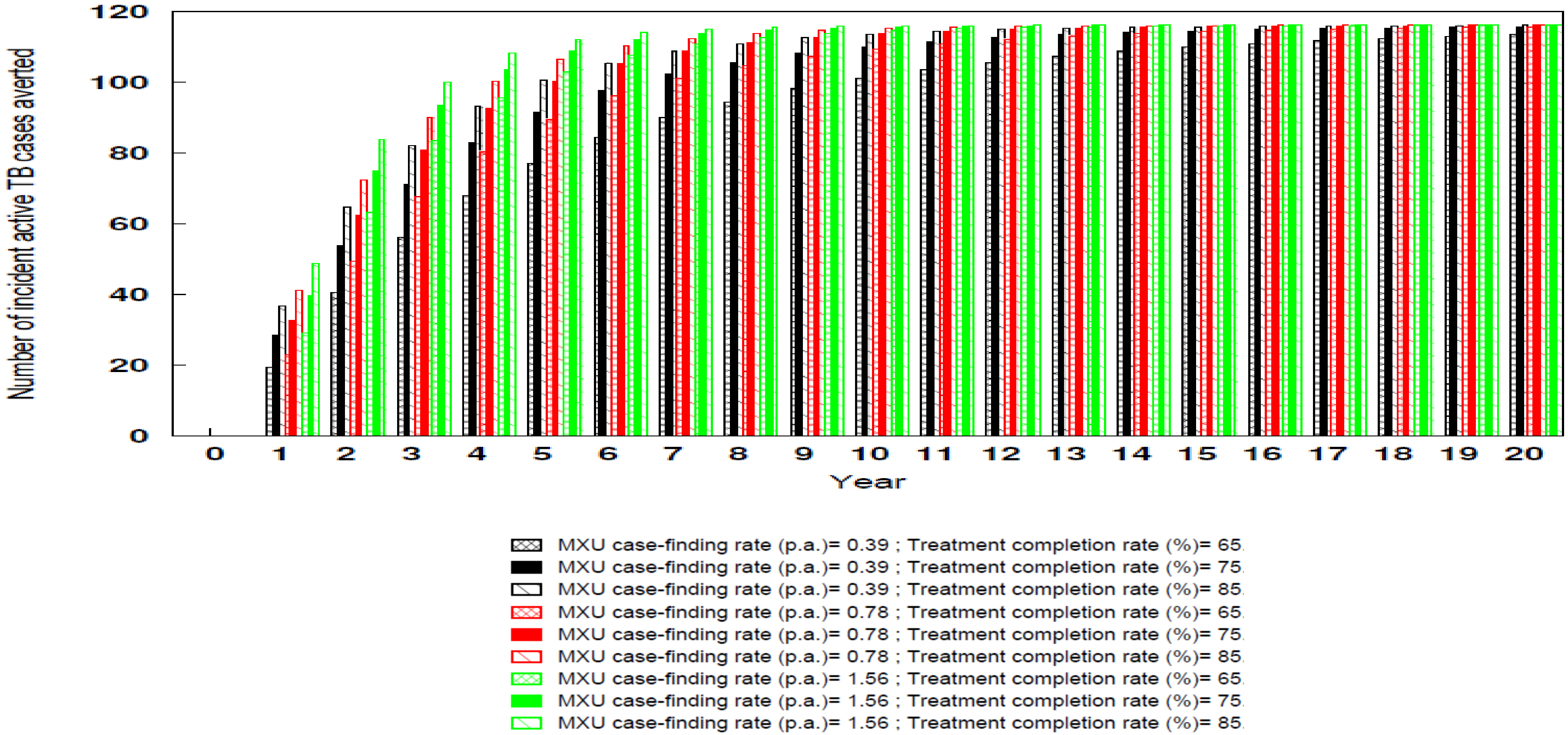


Figure 7.6.4a cont *(b) Annual numbers (undiscounted) of new cases of active disease averted, compared with current practice, by combined MXU case-finding and enhanced case-management in a prison population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and treatment completion rate of 48% prior to the intervention. Scenarios examined are MXU case-finding at 0.78 p.a. (red bars), half that rate (0.39 p.a., black bars), and double that rate (1.56 p.a., green bars). Within each colour grouping, left to right, treatment completion rates are increased to 65%, 75% and 85%. The intervention begins in year 1.*

(a)

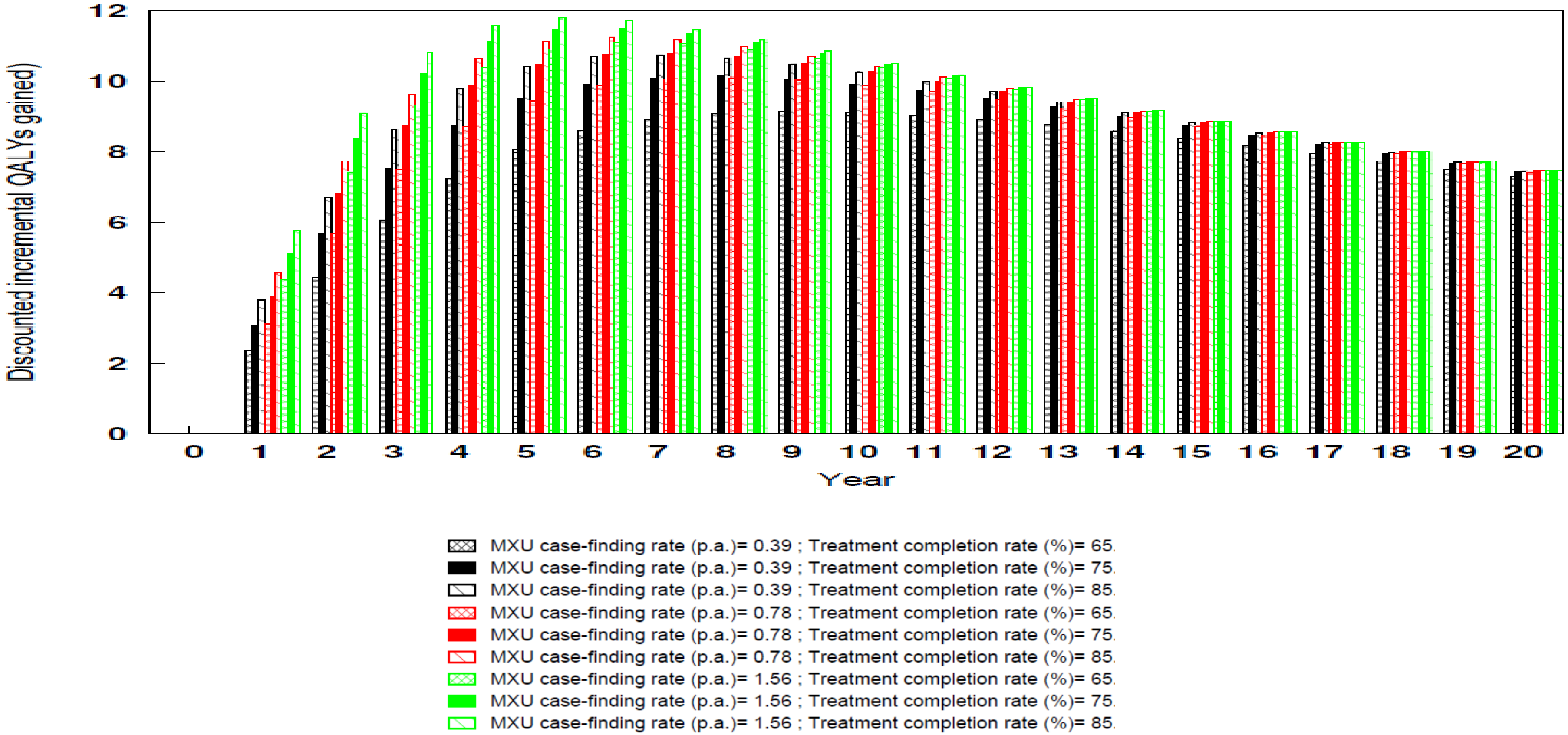


Figure 7.6.4b Discounted annual number of QALYs gained and net costs incurred by combined interventions in prisoners: sensitivity analysis

(a) Discounted annual number of QALYs gained, compared with current practice, by combined MXU case-finding and enhanced case-management in a prison population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and treatment completion rate of 48% prior to the intervention. Scenarios examined are MXU case-finding at 0.78 p.a. (red bars), half that rate (0.39 p.a., black bars), and double that rate (1.56 p.a., green bars). Within each colour grouping, left to right, treatment completion rates are increased to 65%, 75% and 85%. The intervention begins in year 1.

(b)

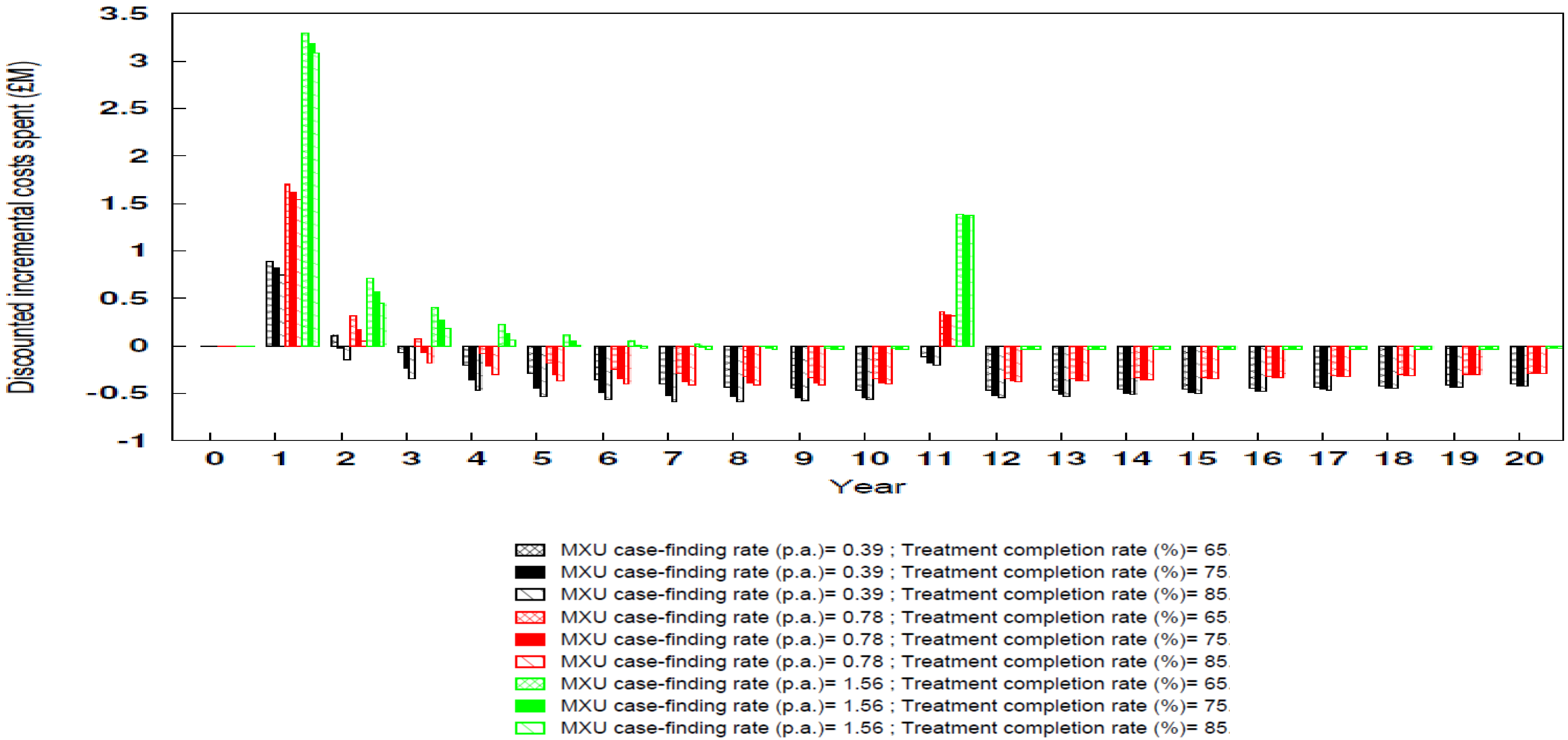


Figure 7.6.4b cont *(b) Discounted annual number of net costs incurred compared with current practice, by combined MXU case-finding and enhanced case-management in a prison population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and treatment completion rate of 48% prior to the intervention. Scenarios examined are MXU case-finding at 0.78 p.a. (red bars), half that rate (0.39 p.a., black bars), and double that rate (1.56 p.a., green bars). Within each colour grouping, left to right, treatment completion rates are increased to 65%, 75% and 85%. Negative net costs incurred indicate net savings. The intervention begins in year 1. The MXU is replaced in year 11.*

Figure 7.6.4c presents a sensitivity analysis of the effect of varying (i) the treatment completion rate achieved by enhanced case-management and (ii) the MXU active case-finding rate on the amount that one would be willing to pay for the enhanced case-management intervention in the population of 10,000 over the 20-year time horizon considered if a QALY is valued at £20,000. If the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 then if MXU case-finding at 0.78 p.a. is combined with enhanced case management then the threshold cost of enhanced case management would be in the range £5M to £10M; at lower rates of MXU case-finding this threshold increases to £10M to £20M for enhanced case management that increases treatment completion rates to 75% or higher.

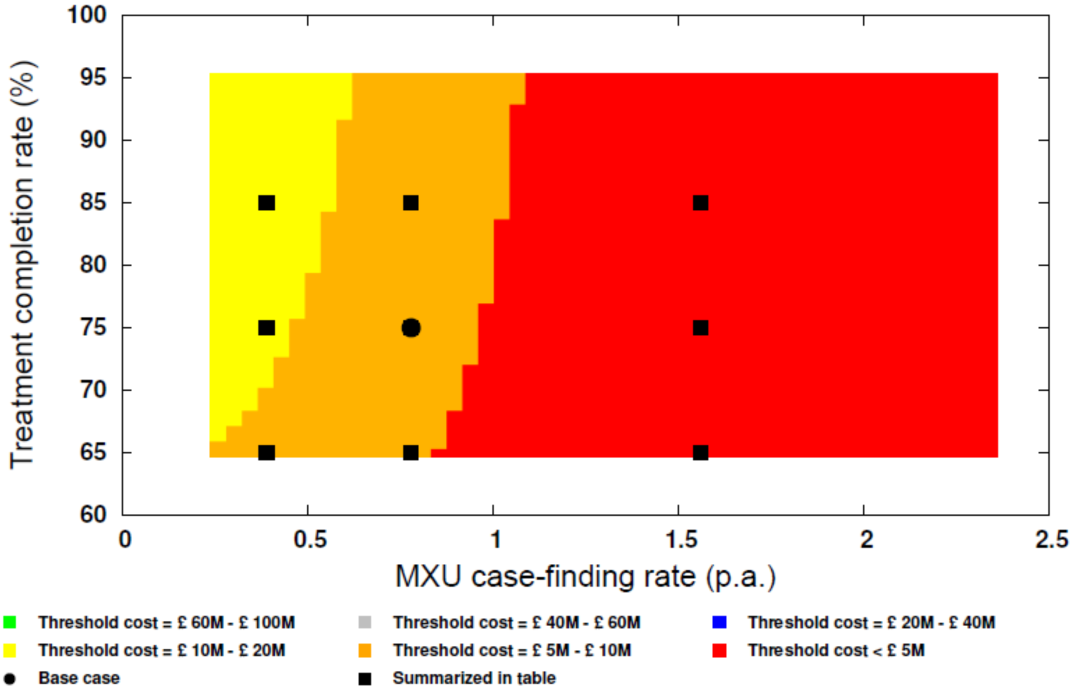


Figure 7.6.4c Cost-effectiveness of combined interventions in prisoners

This figure shows the effects of varying the treatment completion rate achieved by the enhanced case-management intervention (vertical axis) and the rate of MXU case-finding (horizontal axis) on the amount that one would be willing to pay for the enhanced case-management intervention in the population of 10,000 over the 20-year time horizon considered if a QALY is valued at £20,000. The proportion of the population being treated for TB prior to the intervention is 208 per 100,000 and the treatment completion rate prior to the intervention is 48%. The cost of MXU screening is proportional to its case-finding rate. Black dots indicate the scenarios represented in Table 7.6.4e. The base case is indicated by the circular dot.

Table 7.6.4d Combined case-finding and enhanced case-management in prisoners: Scenario with 100 per 100,000 of the prison population receiving TB treatment prior to intervention

This table shows, for prison populations in which the proportion of the population being treated for TB prior to the intervention is 100 per 100,000 the total discounted QALYs gained and net discounted incremental costs incurred compared with current practice, and incremental net benefit if a QALY is valued at £20,000 or £30,000.

Scenario		QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
MXU case-finding rate (rate per case p.a.)	**Treatment completion rate increased from 48% to**			**If a QALY is valued at £20,000**	**If a QALY is valued at £30,000**
½× (0.39)	65%	76.2	0.8	0.7	1.4
½× (0.39)	75%	82.9	0.2	1.5	2.3
½× (0.39)	85%	86.7	-0.2	1.9	2.8
1× (0.78)	65%	82.7	4.9	-3.3	-2.5
1× (0.78)	75%	87.0	4.5	-2.7	-1.8
1× (0.78)	85%	89.6	4.2	-2.4	-1.5
2x (1.56)	65%	88.8	13.6	-11.8	-10.9
2x (1.56)	75%	91.1	13.3	-11.4	-10.5
2x (1.56)	85%	92.7	13.0	-11.2	-10.3

Table 7.6.4e Combined case-finding and enhanced case-management in prisoners: Scenario with 208 per 100,000 of the prison population receiving TB treatment prior to intervention

This table shows, for prison populations in which the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 the total discounted QALYs gained and net discounted incremental costs incurred compared with current practice, and incremental net benefit if a QALY is valued at £20,000 or £30,000.

Scenario		QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
MXU case-finding rate (rate per case p.a.)	Treatment completion rate increased from 48% to			If a QALY is valued at £20,000	If a QALY is valued at £30,000
½× (0.39)	65%	155.5	-5.7	8.9	10.4
½× (0.39)	75%	170.8	-7.3	10.7	12.4
½× (0.39)	85%	179.4	-8.2	11.7	13.5
1× (0.78)	65%	170.5	-2.2	5.6	7.4
1× (0.78)	75%	180.1	-3.3	6.9	8.7
1× (0.78)	85%	185.8	-4.0	7.7	9.6
2x (1.56)	65%	184.0	5.9	-2.2	-0.3
2x (1.56)	75%	189.2	5.1	-1.4	0.5
2x (1.56)	85%	192.5	4.7	-0.8	1.1

Table 7.6.4f Combined case-finding and enhanced case-management in prisoners: Scenario with 300 per 100,000 of the prison population receiving TB treatment prior to intervention

This table shows, for prison populations in which the proportion of the population being treated for TB prior to the intervention is 300 per 100,000 the total discounted QALYs gained and net discounted incremental costs incurred compared with current practice, and incremental net benefit if a QALY is valued at £20,000 or £30,000.

Scenario		QALYs gained compared with current practice	Incremental costs compared with current practice (omitting case-management intervention cost, £M)	Incremental Net Benefit (£M) compared with current practice	
MXU case-finding rate (rate per case p.a.)	Treatment completion rate increased from 48% to			If a QALY is valued at £20,000	If a QALY is valued at £30,000
½× (0.39)	65%	219.7	-11.0	15.4	17.6
½× (0.39)	75%	244.0	-13.5	18.4	20.8
½× (0.39)	85%	257.4	-14.8	20.0	22.6
1× (0.78)	65%	243.5	-8.2	13.0	15.5
1× (0.78)	75%	258.5	-9.9	15.0	17.6
1× (0.78)	85%	267.3	-10.9	16.2	18.9
2x (1.56)	65%	264.6	-0.6	5.9	8.6
2x (1.56)	75%	272.4	-1.7	7.2	9.9
2x (1.56)	85%	277.4	-2.4	8.0	10.8

7.6.5 Summary of sensitivity analysis in prisoners

The effect of varying the proportion of the population being treated for TB prior to the intervention on the cost-effectiveness of different intervention options is examined in Tables 7.6.5a, b, and c.

If the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 or 300 per 100,000 then enhanced case management (ECM, increasing the treatment completion rate to 75%) alone is the most cost-effective option if the cost of providing it is less than £16.5M over 20 years (if a QALY is valued at £20,000) or £17M over 20 years (if a QALY is valued at £30,000) in the population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000; or if ECM costs less than about £19M over 20 years (if a QALY is valued at £20,000) or less than about £20M over 20 years (if a QALY is valued at £30,000) in the population where the proportion of the population being treated for TB prior to the intervention is 300 per 100,000. If providing ECM alone costs more than this then combined MXU screening (an active case-finding rate of 0.78 per case per year) and ECM will not be cost-effective (unless combining the interventions allows the cost of ECM over 20 years to be reduced to about £7M (if a QALY is valued at £20,000) to £8M (if a QALY is valued at £30,000) in the population where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000, or to about £11M (if a QALY is valued at £20,000) to £12M (if a QALY is valued at £30,000) over 20 years in the population where the proportion of the population being treated for TB prior to the intervention is 300 per 100,000) because combined MXU screening and ECM has an INB that is lower than ECM alone. If ECM cannot be provided for a low-enough cost then either current practice or mobile X-ray screening is the most cost-effective option. If the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 then if a QALY is valued at £20,000 then MXU screening is not cost effective compared with current practice (the incremental net benefit (INB) is negative); if a QALY is valued at £30,000, however, then mobile X-ray screening is just cost-effective (a small positive INB). However, if the proportion of the population being treated for TB prior to the intervention is 300 per 100,000 then MXU screening alone is slightly cost-saving as well as beneficial to health.

If the proportion of the population being treated for TB prior to the intervention is 100 per 100,000 then MXU screening alone and MXU screening combined with enhanced case management are not cost effective, as they have negative incremental net benefits. Enhanced case management alone is cost effective if it costs no more than about £8M (if a QALY is valued at £20,000) or about £9M (if a QALY is valued at £30,000), over 20 years.

Table 7.6.5a Analysis of interventions against TB in prisoners

Prior to intervention the proportion of the population being treated for TB is 100 per 100,000 (Story at al. 2007) and the treatment completion rate is 48%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	8.8	127,928	-	-	-	-
Mobile X-ray screening	15.9	127,992	7.1	63.7	-5.8	-5.2
Enhanced case-management (ECM)	2.2	128,003	-6.6	74.9	8.1	8.8
Combined Mobile X-ray screening and ECM	13.2	128,015	4.5	87.0	-2.7	-1.8
ECM cost threshold:					8.1	8.8

QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

Table 7.6.5b Analysis of interventions against TB in prisoners

Prior to intervention the proportion of the population being treated for TB is 208 per 100,000 (Story at al. 2007) and the treatment completion rate is 48%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	18.3	127,877	-	-	-	-
Mobile X-ray screening	21.0	128,004	2.8	126.6	-0.2	1.0
Enhanced case-management (ECM)	4.9	128,030	-13.4	152.4	16.5	18.0
Combined Mobile X-ray screening and ECM	14.9	128,057	-3.3	180.1	6.9	8.7
				ECM cost threshold:	16.5	17.0

QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

Table 7.6.5c Analysis of interventions against TB in prisoners

Prior to intervention the proportion of the population being treated for TB is 300 per 100,000 (Story at al. 2007) and the treatment completion rate is 48%; the MXU has an active case-finding rate of 0.78 per case per year, and enhanced case management increases the treatment completion rate to 75%; time horizon 20 years; population size: 10,000. Costs incurred under current practice are the costs of diagnosing and treating cases of TB found through current practice.

Policy	Cost excluding cost of enhanced case management (£M)	Total QALYs accrued	Compared with baseline		Incremental Net Benefit excluding cost of ECM (£M)	
			Incremental cost (£M)	Incremental QALYs	If a QALY is valued at £20,000	If a QALY is valued at £30,000
Baseline: Current practice	26.4	127,834	-	-	-	-
Mobile X-ray screening	26.1	128,008	-0.3	174.6	3.8	5.5
Enhanced case-management (ECM)	7.4	128,049	-18.9	214.8	23.2	25.4
Combined Mobile X-ray screening and ECM	16.5	128,092	-9.9	258.5	15.0	17.6
				ECM cost threshold:	19.4	19.9

QALYs: Quality Adjusted Life Years; ECM: Enhanced Case Management.

7.7 Interpretation of economic evidence

7.7.1 Summary of findings

The comments in this section apply both to populations of homeless persons and populations of prisoners, unless otherwise stated.

The cost-effectiveness of mobile X-ray unit case-finding and enhanced case-management interventions is context-specific: the interventions may be cost-saving, cost-effective, or not cost-effective, depending upon the population (homeless or prison) burden of TB in the particular population (the proportion of the population being treated for TB prior to the intervention), the cost(s) of the intervention(s), the effectiveness of the intervention(s), and the cost of treatment of a TB case in the particular population group. Combined case-finding and enhanced case-management interventions produce greater QALY gains than either intervention alone, but it should be noted that the combined effects are not additive, due to the complexities of transmission patterns. The cost-effectiveness of MXU case-finding alone, ECM alone and combined MXU case-finding and ECM depend upon the setting and TB burden as well as the cost of providing ECM, and whether the cost of ECM is lower in a combined intervention. This is discussed in more detail below.

Active MXU case-finding and enhanced case-management reduce the prevalence of infectious untreated active TB, for several reasons. Firstly, people are unwell for a shorter period on average before they are diagnosed and treated. Secondly, the proportion diagnosed who successfully complete treatment increases, so that a smaller proportion of those diagnosed return to the untreated active disease states after diagnosis, due to loss to follow-up. Thirdly, the reduction in prevalence of infectious untreated active TB due to faster case-finding and improved case management leads to a reduction in transmission of TB, causing a decrease in incidence of infection (and exogenous reinfection) which leads to a reduced incidence of active disease, which in turn leads to further-reduced prevalence of infectious untreated active TB. In all cases examined for this report interventions were beneficial to health.

Where TB burden (i.e. the proportion of the population being treated for TB under current practice) is relatively low the benefits of MXU case-finding are small because few cases of active disease are identified so few individual patients benefit from being found by the intervention. Also, in lower-burden settings the population-level effects of reducing onward transmission through MXU case-finding and enhanced case management are small; this means that savings on future treatment costs and gains in QALYs due to averting infections and cases of disease are small. Conversely, in high-burden settings MXU case-finding identifies larger numbers of individuals and so individual-level patient benefits are greater. Furthermore, high-burden settings the population-level effects of reducing onward transmission through MXU case-finding and enhanced case management can be large, producing large savings on future treatment costs due to averting infections and cases of disease. QALY gains can also be large, due to large numbers of infections and cases of active disease being averted.

The intensity of MXU screening also affects the cost-effectiveness of the intervention. In high-burden homeless settings, screening at double the rate achieved by the London TB Find & Treat service incurs higher intervention costs but may be more cost-effective because it reduces the prevalence of untreated active disease more rapidly and therefore reduces transmission rates more rapidly and hence averts more infections over the period of the analysis. In our analysis both the net cost savings savings and the QALY gains of screening at a higher rate were greater.

However, in lower-burden settings, screening at a higher rate may be less cost-effective because the treatment cost savings due to additional numbers of infections averted may be relatively small and not off-set the additional costs of MXU screening.

The magnitude of savings on treatment costs as a result of infections and cases of active disease being averted by interventions obviously depends upon the cost of treatment of each individual case as well as the number of cases averted. For this reason, higher treatment costs per case tend to make interventions more cost-effective or cost-saving. It is worth noting that the treatment costs for hard-to-reach cases can be much higher than for other cases, due to their being more likely to have co-morbidities and to be hospitalised – and to require costly critical care or isolation room facilities – as well as requiring more intensive support to maintain adherence to treatment. This is why the estimated cost of treatment per case is £15,000, which is much higher than the estimated cost of TB treatment in the 2006 NICE TB clinical guidelines (NICE, 2006).

Lack of information on the costs and effectiveness of enhanced case-management meant that instead of assessing cost-effectiveness, we assessed the amount that one would be willing to pay for an enhanced case-management intervention if a QALY is valued at £20,000 and £30,000. This was done both for ECM alone and for combined MXU case-finding and ECM. The amount that one would be willing to pay tends to increase with TB prevalence, with the effectiveness of the enhanced case-management intervention, and with the cost of treatment.

The cost-effectiveness of combined MXU case-finding and enhanced case management depends upon the setting (homeless or prison) and the proportion of the population being treated for TB prior to the intervention.

In the homeless, if the proportion of the population being treated for TB prior to the intervention is 500 per 100,000 or 788 per 100,000 then combined MXU case-finding and enhanced case management may be the most cost-effective option, depending upon the cost of providing ECM. Otherwise MXU screening alone is the most cost-effective, and is in fact cost-saving. If the proportion of the homeless population being treated for TB prior to the intervention is 100 per 100,000 then mobile X-ray screening alone is not cost-effective, ECM alone may be cost-effective (depending upon the cost of ECM), and combined mobile X-ray screening and ECM would only be cost-effective if ECM can be provided for less than £400,000 over the 20-year time-horizon.

In prison populations where the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 or 300 per 100,000 ECM may be cost-effective (depending upon the cost of intervention) and combined MXU screening and ECM is likely only to be cost-effective if the cost of providing ECM is much lower in a combined intervention than for ECM alone. If ECM cannot be provided for a low-enough cost then either current practice or mobile X-ray screening is the most cost-effective option, depending upon whether a QALY is valued at £20,000 or £30,000 and whether the proportion of the population being treated for TB prior to the intervention is 208 per 100,000 or 300 per 100,000.

If the proportion of the prison population being treated for TB prior to the intervention is 100 per 100,000 then MXU screening alone and MXU screening combined with enhanced case management are not cost effective, and whether ECM alone is cost-effective depends upon the cost of providing it.

7.7.2 Comparison with published economic literature

As previously stated, the Matrix review found that relevant evidence on cost-effectiveness was lacking. Hence it was not possible to compare the results with other published studies. However, an evaluation of the cost-effectiveness of the TB Find & Treat programme in London suggested that the combination of active case finding and enhanced case management in a homeless setting where the proportion of the population being treated for TB prior to the intervention is high could be cost-effective without considering the effects on TB transmission (Jit et al. in press), and cost saving if effects on transmission are included (Abubakar et al. May 2011).

7.7.3 Relevance to different patient groups

Differences in setting need to be carefully considered, since the parameters used were based on the experience of the London TB Find & Treat service. However, key parameters were varied over a very wide range, so commissioners wishing to evaluate a similar intervention in their own setting should refer to results for parameters most relevant to them.

Successful specialised case-finding and case-management programmes may create opportunities to reduce resources spent on present passive case finding methods. Combining TB case-finding and case-management with case-finding and – management of other conditions affecting the same hard-to-reach population groups (e.g. hepatitis C) may offer cost savings and improvements in the effectiveness in the management of both / all diseases.

7.7.4 Main strengths and weaknesses of the evaluation

It is essential that analyses of interventions against infectious diseases such as TB take account of infections averted by rapid diagnosis and successful treatment of infectious cases, as well as the benefit to the individual patient. This important benefit of protecting the population increases the cost-effectiveness of interventions and can even make them cost-saving due to averting future treatment costs depending upon the setting.

We have used a well-established transmission-dynamic modelling method that has been applied successfully to TB as well as many other infectious diseases. We have integrated the transmission-dynamic modelling with the economic analysis to quantify the benefits of interventions in averting transmission as well as in treating identified cases. A large number of model runs have been performed to explore a wide range of parameter space, encompassing the range of values for the proportion of the population being treated for TB prior to the intervention, effectiveness and cost of intervention likely to be found.

The model considers pulmonary TB, both sputum smear-negative and sputum smear-positive. Non-pulmonary TB has not been considered, as it is not transmissible. However, averting transmission from cases of pulmonary TB would avert cases of disease due to non-pulmonary TB. Therefore, our analysis underestimates the health benefits and the cost-savings of interventions.

The main limitations of the work are due to gaps in scientific understanding of TB epidemiology in general, and lack of data from the populations considered in particular, including lack of information on the costs of treatment and case-management in hard-to-reach groups. The TB prevalence estimates (Story et al. 2007) are based on data from one year in one setting: London in 2003. The MXU effectiveness data (Abubakar et al. May 2011) are from only one setting and from a different time. Costing data are sparse, as are quality of life data. Information on costs and effectiveness of case-management interventions are lacking.

Scientific understanding of TB epidemiology has limitations, particularly in the modern setting (White & Garnett 2010), but we have benefited from the advice of the PDG. In common with all modelling studies of TB, we lack contemporaneous data on the untreated natural history of TB (such as progression rates and mortality rates) because these data cannot be obtained ethically. Therefore we have used parameter estimates from historical data. Additionally, we do not have direct measurements of the incidence or prevalence of *infection* in the population groups considered: most infection does not progress to disease and so is not detected by finding cases of *disease*, but nevertheless *infection* rates affect the dynamics of transmission and of disease. Furthermore, we do not have direct measurements of the incidence or prevalence of *disease*, only of *diagnosed* disease. Cases of disease that are not accessible to case-finding may nevertheless contribute to transmission. Unfortunately we have no data to inform modelling.

There is no time-series of passively-diagnosed TB cases to inform the model. Without a time series we have insufficient data to determine if there is a secular trend in TB diagnoses in homeless and prisoners, much less understand the causes of any such trend (e.g. changes in population sizes; changes in rates of turnover; changes in the composition of the populations such as country of origin, which is associated with variation in TB prevalence). Clearly therefore the further into the future one looks the greater the uncertainty. Nevertheless, even if there is a secular trend that would modulate the model results if we had information about it, it remains the case that faster diagnosis and improved adherence to treatment result in not only improved outcomes for individuals but also transmission events averted, resulting in health benefits to the population and reduced costs of treatment to the health service.

There are insufficient data to stratify the model according to individuals' country or global region of origin. However, we have no evidence to determine whether rates of transmission in the population groups considered (i.e. homeless and prisoners) from cases of active disease are affected by the country of origin of the affected individual. It is possible that screening targeted by country of origin would increase cost-effectiveness by reducing the number of individuals who need to be screened to identify a case of disease but this needs to be investigated empirically to determine the predictive value of country of origin in the particular population groups considered.

It should also be noted that changing social circumstances and penal policy in the future may change the size or composition of the homeless and/or prison populations which may impact the epidemiology of TB.

The PDG highlighted that for homeless patients the out-of-pocket expenses involved in obtaining care could be significant even though to most people the costs may be much more readily affordable. Whilst this may be important from an equity viewpoint, NICE's reference case for economic analysis does not take account of non-public sector expenses or the fact that a particular sum of money may be worth much more to some people than to others.

7.7.5 Further analyses that could be undertaken

There is a need for further empirical work to better-characterise the epidemiology of TB in hard-to-reach groups, including prevalence, incidence, heterogeneity in the distribution of infection and rates of TB transmission, and monitoring trends in the size, composition, and disease burden of hard-to-reach groups. Additionally, there needs to be better characterisation of patients diagnosed with TB, better monitoring of treatment outcomes, and better collection of data on costs. Well-designed studies of the effectiveness of case-management interventions are badly needed, particularly integrated approaches to managing the multiple social and health problems that are common in hard-to-reach groups.

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