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Cost-effectiveness of interferon-gamma release assay for entry tuberculosis screening in prisons

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SUMMARY

The incidence of active tuberculosis (TB) and latent tuberculosis infection (LTBI) in inmates and prison staff is higher than that in the general population. *Mycobacterium tuberculosis*-specific interferon-gamma release assays (IGRAs) provide more accurate diagnosis of *M. tuberculosis* infection with higher specificity than the tuberculin skin test (TST). To assess the cost-effectiveness of QuantiFERON®-TB Gold In-Tube (QFT) compared to TST, TST followed by QFT and chest X-ray, we constructed Markov models using a societal perspective on the lifetime horizon. The main outcome measure of effectiveness was quality-adjusted life-years (QALYs) gained. The incremental cost-effectiveness was compared. The QFT-alone strategy was the most cost-effective for entry TB screening in prisons in developed countries. Cost-effectiveness was not sensitive to the rates of BCG vaccination, LTBI, TB, HIV infection and multidrug-resistant TB. Entry TB screening using an IGRA in prisons should be considered on the basis of its cost-effectiveness by public health intervention.

Key words: Cost-effectiveness study, public health, screening programme, tuberculosis (TB).

INTRODUCTION

The global prison population is gradually increasing on the basis of socioeconomic and political factors [1]. Prisoners often have poor health conditions, such as alcoholism, smoking, malnutrition, drug use and human immunodeficiency virus (HIV) infection, all of which can lead to a depressed immune system. As such, they are at increased risk of developing active tuberculosis (TB) if infected with *Mycobacterium tuberculosis*. Additionally, overcrowding, poor hygiene, and poor ventilation in prisons are adverse factors for developing active TB as well as increased transmission if active TB cases are present [2]. The incidence of TB and latent tuberculosis infection (LTBI) in inmates and prison staff worldwide is much higher (5–70 times) than that in the general population [1, 3–5]. Moreover, the incidence of multidrug-resistant tuberculosis (MDR-TB), a serious global problem, is higher in prisons than in the general population [1, 6, 7], and multidrug resistance is defined as resistance to isoniazid and rifampicin.

By the time a prisoner in the general prison community is diagnosed with TB, their infection is likely to have spread among their fellow inmates and prison staff. Once an active TB case is identified in a prison, a large-scale TB contact investigation is sometimes needed among inmates, their visitors, and prison staff. Moreover, the investigation should be promptly initiated, as delayed detection of secondary TB cases and delayed initiation of active TB treatment increases the opportunity of further spread of TB

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infection in prisons that are connected to the community. The WHO guidelines on TB control in prisons, recommend chest X-ray (CXR) examination for screening of new prisoners [1]. However, CXR cannot detect LTBI, and generally only detects active pulmonary TB present at the time of the CXR. Therefore a negative CXR result does not rule out active TB, due to its moderate sensitivity, and its inability to detect LTBI that may progress to active TB during the period of the prisoner's incarceration [8]. Active TB often occurs in prisoners who had a negative CXR at entry examination. CXR also has poor specificity for detecting active TB and may lead to over-diagnosis and the costs associated with unnecessary follow-up examinations. Effective TB screening in prisons is important not only to control TB in that setting, but also to prevent the spread of TB in the general community. Early and precise diagnosis of LTBI, and chemoprevention for those positive, would limit development of active TB in prison inmates and staff, thereby enhancing TB control.

M. tuberculosis-specific interferon-gamma release assays (IGRAs) – QuantiFERON®-TB Gold In-Tube (QFT; Cellestis Ltd, Australia) and T-SPOT®.TB (Oxford Immunotec, UK) are widely available and provide a more accurate diagnosis of *M. tuberculosis* infection with higher specificity than that of the tuberculosis skin test (TST) especially in bacillus Calmette-Guérin (BCG)-vaccinated individuals, mainly because they are not affected by BCG vaccination. QFT is currently the only available IGRA in Japan.

TB services in prisons, which are usually funded by governments, are under economic constraints and the methods chosen should not only provide good medical care, but also be cost-effective [6, 7]. The reagent costs for TB screening using IGRAs are higher than those for TST and CXR, but numerous studies have demonstrated IGRAs are both more effective and less expensive on a programme basis in different settings [9–14]. In this study, we assessed the cost-effectiveness of QFT compared to TST, TST followed by QFT and CXR in order to evaluate the optimal entry TB screening method in prisons.

METHODS

Target population

Prisoners aged 20 years old were chosen as a hypothetical cohort on a lifetime horizon in developed countries. HIV status and MDR-TB rate were considered in our models. Four cohorts were established; (i) base case; (ii) inclusion of HIV infection; (iii) inclusion of MDR-TB; (iv) inclusion of both HIV infection and MDR-TB.

Markov models

The following four clinical states were included in our model to represent the possible clinical states in the target population: (i) healthy (no LTBI and no TB); (ii) LTBI; (iii) TB; (iv) death [9]. Decision-analytical calculations were performed using Tree Age Pro Healthcare Module 2009 (Tree Age Software Inc., USA). Each cycle length was 1 year.

As this was a modeling study with all inputs and parameters derived from published literature, ethics approval was not required.

Markov models were developed for four strategies: QFT, TST, TST followed by QFT, and CXR. The prisoners were stratified by BCG vaccination for TST strategies (Fig. 1).

QFT strategy

By this strategy the prisoner undergoes QFT testing. If the QFT is positive, active TB is detected by CXR, and the sputum smears and/or cultures are positive, the prisoner is treated according to the standard 6-month protocol for active TB. If the QFT is positive and active TB is not detected by CXR, the prisoner is treated for 9 months with isonicotinyl hydrazide (INH) chemoprophylaxis. We also considered the adherence and complication rates of chemoprophylaxis. If the QFT is negative, a CXR is not required and there is no need for follow-up. We used published estimates of sensitivities and specificities of QFT with and without HIV infection from a meta-analysis of studies of developed countries [15, 16]. Published estimates of sensitivity and specificity of CXR were also used [17, 18].

TST strategy

The prisoner undergoes TST testing. If the TST induration diameter is $\geqslant$5 mm in a non-BCG-vaccinated prisoner and $\geqslant$10 mm in a BCG-vaccinated prisoner, the prisoner undergoes CXR. If active TB is detected by CXR, and the sputum smears and/or cultures are positive, the prisoner is treated according to the standard 6-month protocol for active TB. If active TB is not detected by CXR, the prisoner

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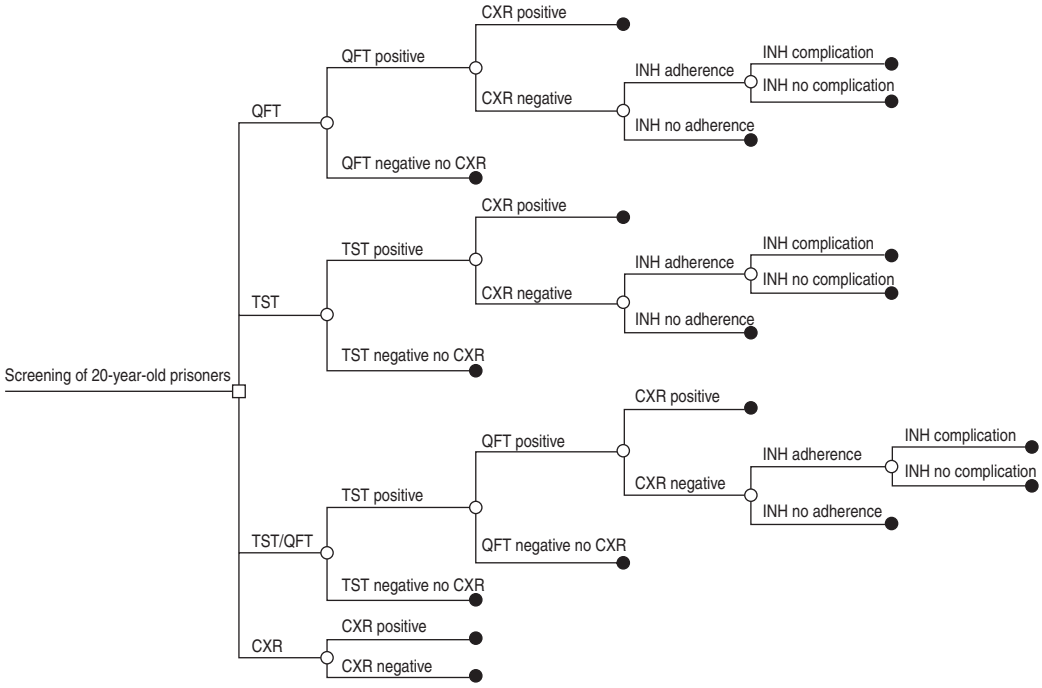

Fig. 1. Simplified illustration of the Markov models for entry tuberculosis screening in prisons. A square node represents the decision node. An open circular node (○) represents a chance node. Branches from a chance node represent possible outcomes. A solid circular node (●) represents a Markov node. CXR, Chest X-ray examination; QFT, QuantiFERON-TB Gold In-Tube; INH, standard 9-month INH chemoprophylaxis protocol for latent tuberculosis infection; TST, tuberculin skin test; TST/QFT, TST followed by QFT strategy.

is treated according to the standard 9-month INH chemoprophylaxis protocol for LTBI. If the TST induration diameter is <5 mm in a non-BCG-vaccinated prisoner and <10 mm in a BCG-vaccinated prisoner, a CXR is not required and there is no need for follow-up. We used published estimates of sensitivity and specificity of the TST with and without HIV infection from a meta-analysis of studies of developed countries [15, 16].

TST followed by QFT strategy

The prisoner undergoes TST testing. If the TST induration diameter is $\geqslant 5$ mm in a non-BCG-vaccinated prisoner and $\geqslant 10$ mm in a BCG-vaccinated prisoner, the prisoner undergoes QFT. If the QFT is positive, active TB is detected by CXR, and the sputum smears and/or cultures are positive, the prisoner is treated according to the standard 6-month protocol for active TB. If the QFT is positive and active TB is not detected by CXR, the prisoner receives 9 months of INH chemoprophylaxis treatment. If the TST induration diameter is <5 mm in a non-BCG-vaccinated prisoner and <10 mm in a BCG-vaccinated prisoner, neither QFT nor CXR are required, and there is no need for follow-up.

CXR strategy

The prisoner undergoes CXR. If active TB is detected by CXR, and the sputum smears and/or cultures are positive, the prisoner is treated according to the standard 6-month protocol for active TB. If active TB is not detected by CXR, there is no need for follow-up.

Data sources, data, outcomes, and assumptions

Using Medline, we undertook a search of the literature published from 1980 to 9 September 2012. Age-specific all-cause mortality rates were obtained from Japanese life tables [19]. The risk of TB-related mortality was assumed to increase with age, based on data from the Japanese Ministry of Health, Labour and Welfare and from other Japanese studies [20]. Cohort studies performed in Japanese individuals were used to obtain the adherence rate (the proportion of patients who accept LTBI treatment) of the standard 9-month INH chemoprophylaxis protocol, the probability of INH-induced hepatitis, and the efficacy (preventing progression from LTBI to TB) of the standard 9-month chemoprophylaxis protocol [21]. We assumed the probability of successful active TB treatment [22] (Table 1). Data from meta-analyses,

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Table 1. *Baseline estimates for selected model variables*

	Baseline value	One-way sensitivity analysis range	Ref.
Annual incidence of LTBI	0·026	0·013–0·084	[27]
Annual incidence of TB	0·0024	0·0016–0·0064	[27]
Probability of having HIV	0·08	0·04–0·40	[1]
Probability of having MDR-TB	0·07	0·03–0·11	[1]
Mortality rate by active TB in TB patients			[20]
Age 20 years	0·000595		
Age 30 years	0·000946		
Age 40 years	0·002349		
Age 50 years	0·008512		
Age 60 years	0·015800		
Age 70 years	0·050108		
Age 80 years	0·195661		
Probability of developing active TB from LTBI			[35]
Age 16–35 years	0·0037		
Age 36–55 years	0·0028		
Age 56–80 years	0·0015		
Increased likelihood of progression from LTBI to active TB in advanced, untreated HIV infection	9·9	8·7–11	[4]
Probability of successful TB treatment	0·392	0·1–0·6	[22]
Probability of recurrence of active TB after treatment	0·035	0·02–0·05	[36]
Efficacy of standard 9-month INH chemoprophylaxis protocol	0·7	0·6–0·8	[21, 37]
Adherence rate of standard 9-month INH chemoprophylaxis protocol	0·8	0·5–0·9	[21, 37]
Probability of INH-induced hepatitis by INH prophylaxis	0·038	0·023–0·061	[38]
BCG vaccination rate	0·977	0–1	[39]
Sensitivity of QFT for LTBI	0·70	0·63–0·78	[16]
Specificity of QFT for LTBI	0·99	0·98–1·00	
Sensitivity of TST for LTBI	0·77	0·71–0·82	
Specificity of TST (BCG-vaccinated) for LTBI	0·59	0·46–0·73	
Specificity of TST (non BCG-vaccinated) for LTBI	0·97	0·95–0·99	
Sensitivity of QFT for LTBI in HIV patients	0·66	0·60–0·71	[15]
Specificity of QFT for LTBI in HIV patients	0·91	0·89–0·98	
Sensitivity of TST for LTBI in HIV patients	0·43	0·37–0·50	
Specificity of TST (BCG-vaccinated) for LTBI in HIV patients	0·59	0·47–0·70	
Specificity of TST (non BCG-vaccinated) for LTBI in HIV patients	0·92	0·91–0·94	
Sensitivity of CXR for active TB in HIV patients	0·70	0·59–0·82	[17, 18]
Specificity of CXR for active TB in HIV patients	0·60	0·52–0·63	
Cost (US$ 2012) (1 US$ = ¥83)			
QFT	75·9	38·0–151·8	[23]
TST	19·3	9·6–38·6	
CXR	45·4	22·7–90·8	
Smear and culture of sputum examination	87·5	43·8–175·0	
Chemoprophylaxis by INH for 9 months	968·4	484·2–1936·9	[21]
Treatment of INH-induced hepatitis by INH chemoprophylaxis	14900·2	7450·1–29800·3	
Treatment of TB for 6 months	18625·8	9312·9–37251·5	
Treatment of MDR-TB	241500	120750–483000	[21, 25]
Average physician income per hour for physicians	65·9	32·9–131·8	[24]
Average income per hour for radiology or laboratory technicians	28·8	14·4–57·6	

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Table 1 (*cont.*)

	Baseline value	One-way sensitivity analysis range	Ref.
Utility			
Healthy	1·00		[26]
LTBI	1·00		
Non MDR-TB taking chemoprophylaxis (9 months) with no complication	1·00		
Non MDR-TB taking chemoprophylaxis with the complication (liver dysfunction)	0·85		
Active non MDR-TB during treatment and before	0·80		
Dead	0·00		
Active MDR-TB during treatment and before	0·58		[25]

BCG, Bacillus Calmette-Guérin; CXR, chest X-ray examination; HIV, human immunodeficiency virus; INH, isonicotinyl hydrazide; LTBI, latent tuberculosis infection; MDR-TB, multidrug-resistant tuberculosis, QFT, QuantiFERON®-TB Gold In-Tube; TB, tuberculosis; TST, tuberculin skin test.
On Monte Carlo stimulation distributions, costs are in lognormal distribution and utilities are in β distribution.

which included studies from numerous countries, were used for determining the sensitivities and specificities of QFT with and without HIV [15, 16], and CXR [17, 18]. The sensitivity and specificity of TST with and without HIV were also assumed [15, 16].

All costs were adjusted to 2012 Japanese yen, using the medical care component of the Japanese consumer price index [23], and were converted to US dollars, using the OECD purchasing power parity rate in 2009. Cost data were collected from various published sources [21, 23–25]. Direct costs, such as inpatient and outpatient costs, and indirect costs arising from loss of productivity, as reported by the Japanese Ministry of Health, Labour and Welfare in 2009, were included. The cost of QFT screening included the screening kits, one physician visit, and the labour cost for laboratory technicians. The cost of TST screening included the labour cost for two physician visits and the TST reagents. The cost of CXR included the material cost of CXR, one physician visit, and the labour cost for radiological technicians. The cost of treating active TB, MDR-TB and INH chemoprophylaxis was determined based on the published literature. [21, 25] The costs of the smear and culture examinations of sputum were also considered when active TB was detected by CXR. The cost of standard 9-month INH chemoprophylaxis, as well as the treatment of adverse effects was considered [21] (Table 1).

The main outcome measure of effectiveness was quality-adjusted life-years (QALYs) gained. The incremental cost-effectiveness of each screening arm was applied and compared. All costs and clinical benefits were discounted at a fixed annual rate of 3%.

Health state utilities were calculated using a utility weight of 0·80 for active non-MDR-TB, 0·58 for active MDR-TB, 0·85 for non-MDR-TB taking chemoprophylaxis (9 months) with complication, and 1·00 for non-MDR-TB taking chemoprophylaxis with no complication [25, 26].

Sensitivity analyses

Using one-way and two-way sensitivity analyses, the range of cost-effectiveness was explored by comparing all strategies simultaneously to determine which strategy yielded the greatest benefits. Each model variable was assigned a distribution based on the values in the literature or assumptions. We also conducted probabilistic sensitivity analysis with Monte Carlo simulation, using the cost-effectiveness acceptability curve. The type of distribution used for each variable, their median and 95% confidence interval (if available) are given in Table 1. On Monte Carlo stimulation distributions, costs are in lognormal distribution and utilities are in β distribution.

RESULTS

Base case

In the base-case analysis, QFT [US$1477·92, 27·91988 quality-adjusted life-years (QALYs)] was more

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Table 2. *Cost-effectiveness of four strategies for TB screening of prisoners* (*BCG vaccination rate = 0·977*)

Strategy	Cost (US$ 2012)	Incremental cost (US$)	Effectiveness (QALYs)	Incremental effectiveness (QALYs)	ICER (US$/QALYs)
Base case					
QFT	1477·92		27·91988		
TST/QFT	1515·38	37·46	27·91999	0·00011	349574·93
TST	1890·20	374·82	27·89481	−0·02518	Dominated
CXR	8911·10	7395·72	26·55811	−1·36188	Dominated
Inclusion of HIV infection					
QFT	1791·31		27·90787		
TST/QFT	1837·21	45·91	27·90785	−0·00002	Dominated
TST	2156·64	365·33	27·88342	−0·02444	Dominated
CXR	9240·92	7449·61	26·53962	−1·36825	Dominated
Inclusion of MDR-TB					
QFT	1552·84		27·91540		
TST/QFT	1590·16	37·31	27·91552	0·00012	318561·73
TST	1971·02	380·86	27·89033	−0·02518	Dominated
CXR	9006·08	7415·92	26·55363	−1·36189	Dominated
Inclusion of both HIV infection and MDR-TB					
QFT	1866·05		27·90339		
TST/QFT	1911·03	44·98	27·90338	0·00001	Dominated
TST	2236·32	370·27	27·87895	−0·02443	Dominated
CXR	9353·27	7487·22	26·53518	−1·36819	Dominated

CXR, Chest X-ray examination; HIV, human immunodeficiency virus; ICER, incremental cost-effectiveness ratio; MDR-TB, multidrug-resistant tuberculosis; QALYs, Quality-adjusted life-years; QFT, QuantiFERON®-TB Gold In-Tube; TB, tuberculosis; TST, tuberculin skin test; TST/QF, TST followed by QFT strategy.

cost-effective than TST (US$1890·20, 27·89481 QALYs), TST followed by QFT (US$1515·38, 27·91999 QALYs), and CXR (US$8911·10, 26·55811 QALYs). When HIV infection was added to the base-case analysis, QFT (US$1791·31, 27·90787 QALYs) remained more cost-effective than TST (US$2156·64, 27·88342 QALYs), TST followed by QFT (US$1837·21, 27·90785 QALYs), and CXR (US$9240·92, 26·53962 QALYs). Similarly, addition of MDR-TB to the base-case analysis found QFT (US$1552·84, 27·91540 QALYs) more cost-effective than TST ($US1971·02, 27·89033 QALYs), TST followed by QFT (US$1590·16, 27·91552 QALYs), and CXR (US$9006·08, 26·55363 QALYs). When both HIV infection and MDR-TB were added to the base-case analysis, QFT (US$1866·05, 27·90339 QALYs) remained more cost-effective than TST (US$2236·32, 27·87895 QALYs), TST followed by QFT (US$1911·03, 27·90338 QALYs), and CXR (US$9353·27, 26·53518 QALYs) (year 2012 values) (Table 2). On the analysis of all prisoners exposed to MDR-TB, QFT (US$2548·27, 27·85583 QALYs) remained more cost-effective than TST (US$3044·75, 27·83089 QALYs), TST followed QFT (US$2583·60, 27·85608 QALYs), and CXR (US$10267·99, 26·49407 QALYs). Incremental cost-effectiveness ratio of QFT-alone strategy resulted in a cost saving of US$141580·09/QALYs gained compared to the TST followed by QFT strategy.

Sensitivity analyses

One-way and two-way sensitivity analyses were performed over the ranges for each variable. The cost-effectiveness was not sensitive to BCG vaccination rate (Table 3), LTBI rate, TB rate, HIV infection rate and MDR-TB rate.

Probabilistic sensitivity analyses

The cost-effectiveness acceptability curve of 20-year-old prisoners by Monte Carlo simulations for 10 000 trials demonstrated that QFT strategy was the most cost-effective, with a value of 100% at all willingness-to-pay levels compared to TST, TST followed by QFT, and CXR strategies (Fig. 2).

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Table 3. *Sensitivity analysis of BCG vaccination rate*

BCG vaccination rate	Strategy	Cost (US$ 2012)	Effectiveness (QALYs)	ICER (US$/QALYs)	Dominance
Base case					
0	QFT	1477·92	27·91988	0	
0	TST	1498·00	27·91846	−14108·68	Dominated
0	TST/QFT	1565·27	27·89084	−3007·55	Dominated
0	CXR	8911·10	26·55811	−5458·46	Dominated
0·2	QFT	1477·92	27·91988	0	
0·2	TST/QFT	1555·06	27·89681	−3342·76	Dominated
0·2	TST	1578·29	27·91362	−16019·30	Dominated
0·2	CXR	8911·10	26·55811	−5458·463	Dominated
0·4	QFT	1477·92	27·91988	0	
0·4	TST/QFT	1544·84	27·90277	−3911·80	Dominated
0·4	TST	1658·58	27·90877	−16264·16	Dominated
0·4	CXR	8911·10	26·55811	−5458·46	Dominated
0·6	QFT	1477·92	27·91988	0	
0·6	TST/QFT	1534·63	27·90874	−5090·42	Dominated
0·6	TST	1738·86	27·90393	−16360·34	Dominated
0·6	CXR	8911·10	26·55811	−5458·46	Dominated
0·8	QFT	1477·92	27·91988	0	
0·8	TST/QFT	1524·42	27·91471	−8987·74	Dominated
0·8	TST	1819·15	27·89909	−16411·73	Dominated
0·8	CXR	8911·10	26·55811	−5458·46	Dominated
1	QFT	1477·92	27·91988	0	
1	TST/QFT	1514·21	27·92068	45739·05	
1	TST	1899·44	27·89425	−14576·84	Dominated
1	CXR	8911·10	26·55811	−5428·65	Dominated
Inclusion of HIV infection					
0	QFT	1791·31	27·90787	0	
0	TST	1812·31	27·90652	−15643·50	Dominated
0	TST/QFT	1882·13	27·88100	−3381·15	Dominated
0	CXR	9240·92	26·53962	−5444·63	Dominated
0·2	QFT	1791·31	27·90787	0	
0·2	TST/QFT	1872·94	27·88650	−3820·44	Dominated
0·2	TST	1882·8	27·90179	−15069·50	Dominated
0·2	CXR	9240·92	26·53962	−5444·63	Dominated
0·4	QFT	1791·31	27·90787	0	
0·4	TST/QFT	1863·74	27·89200	−4563·94	Dominated
0·4	TST	1953·28	27·89707	−14998·10	Dominated
0·4	CXR	9240·92	26·53962	−5444·63	Dominated
0·6	QFT	1791·31	27·90787	0	
0·6	TST/QFT	1854·55	27·89749	−6095·03	Dominated
0·6	TST	2023·77	27·89234	−14970·20	Dominated
0·6	CXR	9240·92	26·53962	−5444·63	Dominated
0·8	QFT	1791·31	27·90787	0	
0·8	TST/QFT	1845·35	27·90299	−11074·50	Dominated
0·8	TST	2094·26	27·88761	−14955·30	Dominated
0·8	CXR	9240·92	26·53962	−5444·63	Dominated
1	QFT	1791·31	27·90787	0	
1	TST/QFT	1836·16	27·90848	72876·29	
1	TST	2164·74	27·88288	−12834·97	Dominated
1	CXR	9240·92	26·53962	−5409·42	Dominated
Inclusion of MDR-TB					
0	QFT	1552·84	27·9154	0	
0	TST	1751·54	27·9144	−198935·84	Dominated

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Table 3 (*cont.*)

BCG vaccination rate	Strategy	Cost (US$ 2012)	Effectiveness (QALYs)	ICER (US$/QALYs)	Dominance
0	TST/QFT	1812·75	27·88678	−9081·79	Dominated
0	CXR	9006·08	26·55363	−5473·20	Dominated
0·2	QFT	1552·84	27·91540	0	
0·2	TST/QFT	1767·18	27·89266	−9427·34	Dominated
0·2	TST	1796·47	27·90947	−41112·97	Dominated
0·2	CXR	9006·08	26·55363	−5473·20	Dominated
0·4	QFT	1552·84	27·91540	0	
0·4	TST/QFT	1721·62	27·89854	−10014·10	Dominated
0·4	TST	1841·4	27·90455	−26588·19	Dominated
0·4	CXR	9006·08	26·55363	−5473·20	Dominated
0·6	QFT	1552·84	27·91540	0	
0·6	TST/QFT	1676·05	27·90443	−11230·07	Dominated
0·6	TST	1886·33	27·89962	−21133·69	Dominated
0·6	CXR	9006·08	26·55363	−5473·20	Dominated
0·8	QFT	1552·84	27·91540	0	
0·8	TST/QFT	1630·48	27·91031	−15257·22	Dominated
0·8	TST	1931·26	27·89469	−18274·88	Dominated
0·8	CXR	9006·08	26·55363	−5473·20	Dominated
1	QFT	1552·84	27·91540	0	
1	TST/QFT	1584·92	27·91619	40415·81	
1	TST	1976·19	27·88976	−14805·43	Dominated
1	CXR	9006·08	26·55363	−5446·47	Dominated
Inclusion of both HIV infection and MDR-TB					
0	QFT	1866·05	27·90339	0	
0	TST	2050·90	27·90244	−194795·00	Dominated
0	TST/QFT	2114·83	27·87692	−9398·97	Dominated
0	CXR	9353·27	26·53518	−5472·29	Dominated
0·2	QFT	1866·05	27·90339	0	
0·2	TST/QFT	2073·11	27·88233	−9835·58	Dominated
0·2	TST	2088·85	27·89763	−38704·60	Dominated
0·2	CXR	9353·27	26·53518	−5472·29	Dominated
0·4	QFT	1866·05	27·90339	0	
0·4	TST/QFT	2031·39	27·88775	−10574·70	Dominated
0·4	TST	2126·81	27·89282	−24683·70	Dominated
0·4	CXR	9353·27	26·53518	−5472·29	Dominated
0·6	QFT	1866·05	27·90339	0	
0·6	TST/QFT	1989·70	27·89317	−12097·40	Dominated
0·6	TST	2164·77	27·88802	−19433·10	Dominated
0·6	CXR	9353·27	26·53518	−5472·29	Dominated
0·8	QFT	1866·05	27·90339	0	
0·8	TST/QFT	1947·95	27·89859	−17055·70	Dominated
0·8	TST	2202·73	27·88321	−16684·30	Dominated
0·8	CXR	9353·27	26·53518	−5472·29	Dominated
1	QFT	1866·05	27·90339	0	
1	TST/QFT	1906·23	27·90400	65330·53	
1	TST	2240·68	27·87840	−13063·80	Dominated
1	CXR	9353·27	26·53518	−5440·48	Dominated

BCG, Bacillus Calmette-Guérin; CXR, chest X-ray examination; HIV, human immunodeficiency virus; ICER, incremental cost-effectiveness ratio; MDR-TB, multidrug-resistant tuberculosis; QALYs, quality-adjusted life-years; QFT, QuantiFERON®-TB Gold In-Tube; TST, tuberculin skin test; TST/QFT, TST followed by QFT strategy.

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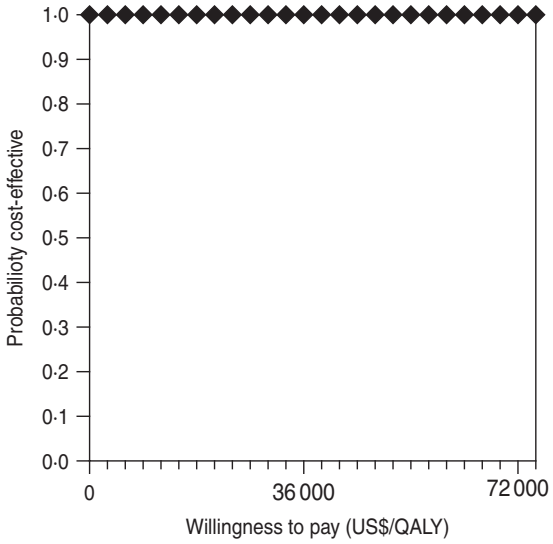

Fig. 2. Cost-effectiveness acceptability curve. The curve uses willingness to pay to chart the changing percentage of interventions for which QFT strategy (◆) is cost-effective relative to TST, TST followed by QFT, and CXR strategies. The cost-effectiveness acceptability curve demonstrates that the QFT strategy was the most cost-effective, with a value of 100% at all willingness-to-pay levels compared to TST, TST followed by QFT, and CXR strategies. QFT, QuantiFERON-TB Gold In-Tube; QALY, quality-adjusted life-year.

DISCUSSION

In this study, we demonstrated that the QFT strategy was the most cost-effective for entry TB screening in prisons in developed countries. We previously reported the cost-effectiveness of IGRA compared to TST and CXR for screening high-risk group such as healthcare workers (HCWs) and rheumatoid arthritis patients prior to initiation of tumour necrosis factor-α antagonist therapy, and also showed that QFT-alone yielded the greatest benefits at the lowest cost [9, 11–13]. de Perio and colleagues demonstrated that use of the QFT leads to superior clinical outcomes and lower costs than the TST. They also concluded that QFT should be considered for screening non-BCG-vaccinated and BCG-vaccinated new HCWs for LTBI [10]. Hardy and colleagues showed that QFT blood testing followed by CXR is feasible for TB screening, cheaper than screening using the NICE guideline and identifies more cases of LTBI in immigrants from high-risk countries [14].

To our knowledge, this study is the first cost-effectiveness analysis of IGRA compared to TST, TST followed by QFT and CXR for TB screening in prisons using Markov models. Our models also considered influences of HIV infection and MDR-TB in prisoners and found that QFT remained the most cost-effective strategy. Our finding that QFT provided superior cost-effectiveness probably results from the higher specificity of QFT compared to TST and CXR. Cost-effectiveness was not sensitive to the BCG vaccination rate. These findings may be applicable to other developed countries regardless of the BCG vaccination rate. Effective TB screening at diagnosis also enabled the modelling to avoid the thorny issue of 'churn' that occurs in many prisons, where prisoners on remand are moved rapidly between a number of prisons within the prison estate. This inevitably can also lead to increased transmission as well as difficulty in follow-up of any infected prisoners.

Baussano and colleagues examined the high incidence of LTBI and TB in prisons compared to the incidence in the corresponding local general population by systematic review [27]. They concluded that improved TB control in prisons could potentially protect prisoners and staff from within-prison spread of TB and also reduce spread to the community, and would significantly reduce the national burden of TB. Reichard and colleagues [28] assessed TB screening and management activities in large US jail systems. They concluded that completion rates and timeliness of TB screening, diagnostic, and treatment measures should be evaluated to identify areas needing improvement for documenting and monitoring inmate healthcare related to TB. They also suggested promoting therapy completion for inmates as a means of preventing TB transmission in the community. Lee and colleagues [29] demonstrated that TB services delivered in prisons have increased in the last decade, but systematic information on funding levels and gaps, services provided, and cost-effective delivery models for delivering TB services in prisons were lacking. Reid and colleagues [30] argued that improved implementation of conventional TB control activities in a broader range of public health interventions and prevention for HIV was needed for TB and HIV control in sub-Saharan African prisons. Several studies have demonstrated that the TB case-finding rate is greatly increased by utilizing mini-CXR screening [31–33]. Cost-effective TB screening in prisons should be reconsidered for control of TB in prisons by public health intervention using tax, not only to significantly reduce TB in prisons, but also to avoid the spread of MDR-TB in the local community throughout the world. Both prison resource and containment strategies vary across countries. Optimal TB

strategies across countries will be needed globally in the near future.

Our study had several limitations. First, only HIV infection and MDR-TB were considered in this model, but prisoners have more complex health problems in their society, such as alcoholism, smoking, and drug abuse. Second, there are few published data on the rates of LTBI and active TB, as well as transmission, in prisons. Third, the high costs of purchasing and maintaining equipment for CXR examination was not calculated in our model. Fourth, the period of imprisonment is not calculated in our model and we could find no data on the median time period of imprisonment. Fifth, each model variable was assigned a distribution based on the values in the literature or assumptions, performing one-way and two-way sensitivity analyses. However, there were only sparse TB and cost data for prisons globally. Different countries have different policies and resources for TB screening of prisoners. Further studies are needed to identify more specific TB policies in each country. Sixth, this analysis was for entry TB screening in prisons. Further cost-effectiveness studies for annual LTBI screening of prisoners using IGRAs are needed. Seventh, the time lag of the wait for sputum culture results of MDR-TB is not included in this Markov model. Finally, only a 9-month daily isoniazid regimen was considered in our model. For example, in a randomized controlled trial Chan and colleagues [34] demonstrated that a 4-month daily rifampicin regimen was safer and had a higher completion rate than the standard 6-month daily isoniazid regimen as a treatment for LTBI in male prisoners.

We conclude that QFT-alone is the most cost-effective strategy for entry TB screening in prisons in developed countries. Entry TB screening of prisoners using an IGRA should be considered on the basis of its cost-effectiveness by public health intervention, not only to significantly reduce TB in prisons, but also to better control the spread of TB infection in the community.

DECLARATION OF INTEREST

None.

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