Cost Effectiveness Analysis Of High-Risk Group Tb Screening In Malaysia

Nor Zam Azihan Mohd Hassan (zamazihan@yahoo.com)
Institute for Health Systems Research https://orcid.org/0000-0002-0683-1249
Asmah Razali
Disease Control Division, Ministry of Health Malaysia
Mohd Ridzwan Shahari
Medical Development Division, Ministry of Health Malaysia
Mohd Shaiful Jefri Mohd Nor Sham Kunusagaran
Institute for Health Systems Research
Juanita Halili
Institute for Health Systems Research
Nur Amalina Zaimi
Institute for Health Systems Research
Mohd Shahri Bahari
Institute for Health Systems Research
Farhana Aminuddin
Institute for Health Systems Research

Research article

Keywords: Cost Effectiveness Analysis, Tuberculosis, High-Risk Group Screening

Posted Date: December 1st, 2020

DOI: https://doi.org/10.21203/rs.3.rs-113831/v1

Abstract

Background: Screening of high-risk groups for TB is considered as the cornerstone for TB elimination but the measure of cost-effectiveness is also crucial in deciding the strategy for TB screening. This study aims to measure the cost-effectiveness of TB screening between the various high-risk groups in Malaysia.

Methods: A decision tree model was developed to assess the cost-effectiveness of TB screening among the high-risk group from provider perspective using a secondary data from year 2016 to 2018. The outcome is presented in term of cost per TB case detected and the ICER. Deterministic and Probabilistic Sensitivity Analysis were also performed to measure the robustness of the model.

Results: The most cost-effective strategy was TB screening among PL HIV, with MYR 2,597.00 per one TB case detected. This is followed by elderly, prisoners and smokers with MYR 2,868.62, MYR 3,065.24 and MYR 4,327.76 per one TB case detected respectively. There was an incremental costs of MYR 2.49 per screening, and 3.4 TB case detection per 1000 screening for TB screening among PL HIV in relation to TB screening among prisoners. The probability of symptomatic cases diagnosed as TB was the key driver for increasing cost effectiveness efficacy among PL HIV.

Conclusions: Results of the study suggest prioritization of high-risk group TB screening programme by focusing on the most cost-effective strategy such as screening among PL HIV, prisoners and elderly, which has lower cost per TB case detected.

1. Background

Tuberculosis (TB) remains as public health challenge and a leading cause of morbidity and mortality. It continues to kill more than a million people annually, despite the availability of effective medication with high cure rates since the 1960s (1). About two-thirds of global TB cases are in Western Pacific region, of which Malaysia is part of. Malaysia is classified as an intermediate TB burden country with a notification rate of less than 100 cases per 100,000 population (1).

Detection of active TB can either be done through mass screening, or targeted screening, wherein, it focusses on selected high-risk groups (2). Based on published reports, various groups were identified as having higher risk for TB and given priority in TB screening program (3). Compared to the general population, TB incidence are generally much higher among individuals with the Human Immunodeficiency Virus (HIV), alcoholics, drug abusers, prisoners, homeless and recent immigrants from TB endemic areas (3, 4). Past study revealed that the total prevalence of TB among high risk groups was around 0.5% (3).

Malaysia have initiated HRG screening since 2016 in line with WHO End TB Strategy recommendation under Pillar 1. For years, Ministry of Health (MOH), Malaysia has been focusing TB screening among those high risk of developing TB. This include a close contacts to TB cases (both household and nonehousehold contacts), immunocompromised patients such as those suffering from Diabetes Mellitus, Rheumatoid Arthritis and Person Living with Human Immunocompromise Virus (PL HIV), substance abusers and cigarette smokers, living in overcrowded conditions such as incarceration and institutionalisation (whether in Cure and Care Rehabilitation Centres (CCRC), residents of old folks home, prisoners and etc) and an elderly (5).

Chest X-Ray (CXR) has been the main screening tool in Malaysia for diagnosing TB among the asymptomatic high-risk population (5). However, it is known to give an unreliable result when used for diagnosing TB among the asymptomatic (6). Whereas, for the symptomatic, both CXR and sputum smear remains the mainstay of TB screening tool. (5). Based on a study done in Malaysia on CXR screening among the asymptomatic, HIV was found to have the highest yield (25%), followed by smokers (20.7%), End Stage Renal Failure (ESRF) (20%), individual with substance abuse (13.3%), diabetic patients (10.6%), institutionalised individual (7.2%), and close contacts of TB cases (4.4%) (7).

Despite that, for an effective TB screening programme, prioritization of key interventions and target groups are necessary (8). Unsystematic and poorly targeted screening may not lead to the desired outcomes. In the contrary, it can be very expensive, and gives minute impact in TB case detection (8, 9). Hence, screening for active tuberculosis should target those with high risk, while taking into account the measures of effectiveness (8).

For the past few years, MOH Malaysia has allocated substantial amount of resources for TB screening among the high-risk groups. However, there has not been any measure of efficiency done for this programme in term of economic efficacy. Ergo, this study aims to measure the cost-effectiveness analysis (CEA) of TB screening between various high-risk groups in the purpose of identifying the low-cost and most effective screening strategy to ensure the optimal use of resources from the perspective of health care provider, i.e. the Ministry of Health.

2. Methods

A decision tree model was developed to estimate the relative cost effectiveness measure of TB screening between different high-risk groups. Subsequently, costing and probability data were calculated and introduced into the model. The effectiveness parameters used were the probability of each screening strategy manage to detect one TB case. These take into the form of probability for the symptomatic or the asymptomatic screening for each high-risk group results in TB case detection (Table 2). Data were obtained from various source as shown in Table 1. The costs per screening, cost per TB case detected and incremental cost-effectiveness ratio (ICER) for each high-risk group were presented as the final outcome of this study. In order to assess the robustness of the model, sensitivity analysis was also conducted. All costs were valued in 2018 and presented in Malaysia Ringgit (MYR). The discounted value of 3% was used where necessary. Willingness-to-pay was capped at MYR 120,000 as of 3 times GDP per capita as suggested by World Health Organisation (WHO) (10, 11). In 2018, Malaysia GDP per capita was valued around MYR 40,000 (~ USD 9,660) (12).

Table 1
Source of Data

Data	Type of Data	Source of Data
Capital Cost	Secondary	Disease Control Section, MOH
Personnel Cost	Secondary	Disease Control Section, MOH
Consumables Cost	Secondary	Disease Control Section, MOH
TB Screening for High Risk Group	Secondary	TBIS 204S for year 2016 to 2018 from Sabah and Sarawak State Health Departments
Tbis Tuberculosis Information System, MOH Ministry of Health		

2.1 Decision Tree Model

A Decision Tree Model was developed using TreeAge Pro version 2019 by TreeAge Software, Inc. (Fig. 1). The model was constructed in concordance to the high-risk group TB screening guideline from MOH Malaysia (5). A total of 11 high risk groups were included in the decision model, which were: 1) CCRC inmates; 2) Old folks home residents; 3) ESRF patients; 4) Prisoners; 5) Diabetes Mellitus patients; 6) Methadone Clinic clients; 7) Rheumatoid Arthritis patient; 8) PL HIV; 9) Chronic Obstructive Airway Disease (COAD) patients; 10) Smokers, and; 11) Elderly (60 years and above). In this model, each high-risk group was branched out as symptomatic or asymptomatic.

Analysis of decision tree model were executed based on few assumptions. Firstly, all screening procedures were assumed to be standardized, wherein, no significant variation in term of number of personnel, machineries, consumables used and times consumed. Thus, no difference of cost incurred despite of different screening done in different setting. Secondly, the TB screening programme is strictly following the guideline from MOH, in which the asymptomatic would only be screened through CXR, while the symptomatic is screened using both CXR and SAFB test.

2.2 Estimation for Probabilities of TB Case Detection

Secondary data on high risk group TB screening was used to estimate probabilities of TB case detected per screening of each high-risk group. This data was based on three years Sabah and Sarawak State Health Department data on TB screening among high-risk groups, from 2016 to 2018 recorded in TBIS 204S for each State Health Departments. Cases of pending for investigation results, referral to specialist for TB diagnosis, TB diagnosis by other modalities than Chest X-Ray (CXR) and sputum AFB (SAFB), and contact screening were excluded from this study. There were total of 65,400 cases included for estimating the probabilities parameters. Probabilities parameters measured is shown in Table 2 consisted of the probabilities for individual in each high-risk group having any symptom (i.e. symptomatic). Whereas, the effectiveness parameters include the number of TB case detected per 1000 screening for symptomatic and asymptomatic cases (Table 3).

Table 2
Clinical Input Data for Probabilities

Probability Parameters	Probability Value	Range[¶]	Distributions[§]
Symptomatic COAD patients	0.2132	0.1599–0.2665	Beta
Symptomatic CCRC inmates	0.0341	0.0256–0.0426	Beta
Symptomatic Diabetes Mellitus patients	0.0749	0.0562–0.0936	Beta
Symptomatic ESRF (Haemodialysis)	0.0449	0.0337–0.0561	Beta
Symptomatic Smokers	0.2198	0.1649–0.2748	Beta
Symptomatic PL HIV	0.2086	0.1565–0.2608	Beta
Symptomatic Methadone Clinic clients	0.0833	0.0625–0.1041	Beta
Symptomatic Prisoners	0.0567	0.0425–0.0709	Beta
Symptomatic Old Folks Home residents	0.0416	0.0312–0.0520	Beta
Symptomatic Rheumatoid Arthritis patients	0.1875	0.1406–0.2344	Beta
Symptomatic Elderly (60 years and above)	0.2796	0.2097–0.3495	Beta

COAD Constrictive Obstructive Airway Disease, CCRC Cure and Care Rehabilitation Centre, ESRF End Stage Renal Failure, PL HIV Person Living with Human Immunodeficiency Virus, TB Tuberculosis, na not available

[¶] The probability parameter values are varied by ± 25%.

[§] Selection of distributions for each parameter are believed to be the best practice. Beta distribution is best used for probability value due to its properties, which ranges from 0 to 1.

Table 3
Clinical Input Data for Effectiveness

Effectiveness Parameters	Value (TB case detected per 1,000 screening)	Range[¶]	Distributions[§]
COAD patients			
Symptomatic	20.4	15.3–25.5	Beta
Asymptomatic	1.8	1.4–2.3	Beta
CCRC inmates			
Symptomatic	0.0	na	
Asymptomatic	3.3	2.5–4.1	Beta
Diabetes Mellitus patients			
Symptomatic	23.4	17.6–29.3	Beta
Asymptomatic	1.5	1.1–1.9	Beta
ESRF (Haemodialysis)			
Symptomatic	75.3	56.5–94.1	Beta
Asymptomatic	1.0	0.8–1.3	Beta
Smokers			
Symptomatic	37.6	28.2–47.0	Beta
Asymptomatic	2.4	1.8–3.0	Beta
PL HIV			
Symptomatic	57.5	43.1–71.9	Beta
Asymptomatic	6.1	4.6–7.6	Beta
Methadone Clinic clients			
Symptomatic	0.0	na	
Asymptomatic	0.0	na	
Prisoners			
Symptomatic	97.3	73.0–121.6	Beta

[¶] The effectiveness parameter values are varied by ± 25%.

[§] Selection of distributions for each parameter are believed to be the best practice. Beta distribution is best used for effectiveness since this value also represents probability.

Effectiveness Parameters	Value (TB case detected per 1,000 screening)	Range¶	Distributions§
Asymptomatic	8.4	6.3–10.5	Beta
Old Folks Home residents			
Symptomatic	0.0	na	
Asymptomatic	0.0	na	
Rheumatoid Arthritis patients			
Symptomatic	0.0	na	
Asymptomatic	0.0	na	
Elderly (60 years and above)			
Symptomatic	46.9	35.2–58.6	Beta
Asymptomatic	3.5	2.6–4.4	Beta

¶ The effectiveness parameter values are varied by ± 25%.

§ Selection of distributions for each parameter are believed to be the best practice. Beta distribution is best used for effectiveness since this value also represents probability.

2.3 Estimation of Costs

This study only includes direct costs from the perspectives of MOH. This consist of capital, personnel and consumables costs (Table 1). The costs were calculated using a mixed of step-down and Activity Based Costing (ABC) methods.

Capital costs comprise of medical equipment and yearly maintenance costs for both Chest X-Ray (CXR) and Sputum for Acid Fast Bacilli (SAFB). Whereas, personnel costs include both staff's salaries and allowance per year based on the pay slip and claim forms received from administrative department. This was apportioned according on the duration it took to complete one whole procedure, which was based on expert panels. Finally, the consumables costs consist of all materials used as part of the procedures.

In measuring the cost for conducting one symptomatic screening and asymptomatic screening, the of cost for running one CXR and SAFB procedure were estimated. Based on the guidelines from MOH, cost for one symptomatic screening is equal to cost of one CXR and SAFB, while the cost for asymptomatic screening only consist of a cost for one CXR procedure (Table 4).

2.4 Cost-Effectiveness Analysis

The cost-effectiveness analysis was performed comparing all the high-risk groups in line with the guideline from MOH. The final outcomes of the study were presented in term of the cost per TB screening, cost effectiveness (CE) measure, which is the cost per one TB case detected, and ICER. The initial reference case strategy for ICER was chosen based on the lowest cost for TB screening among the high-risk groups. Subsequently, the reference case is replaced by the dominant strategy as the analysis process move on. (Table 4).

Table 4
Cost Input Data

Cost Parameters	Unit Cost (MYR)	Range (MYR)[¶]	Distributions[§]
Chest X-Ray			
Capital	5.12		
Personnel	31.56		
Consumables	3.59		
Total Cost for Chest X-Ray	**40.27**		
Sputum AFB			
Capital	3.18		
Personnel	5.07		
Consumables	8.13		
Total Cost for SAFB	**16.38**		
Asymptomatic screening			
Cost for Chest X-Ray	40.27	30.20–50.34	Gamma
Total	**40.27**		
Symptomatic screening			
Cost for Chest X-Ray	40.27	30.20–50.34	Gamma
Cost for SAFB	16.38	12.29–20.48	Gamma
Total	**56.65**		

SAFB Sputum for Acid Fast Bacilli,

[¶] The cost parameters values are varied by ± 25%.

[§] All cost parameters are assigned with gamma distributions, which is the best practice. Gamma distribution is considered with parameters that have skewed distribution. It confined only to positive values and thus, is used in representing uncertainty for cost parameters.

2.5 Deterministic Sensitivity Analysis (DSA)

One-way sensitivity analysis was performed to assess the model robustness toward change in parameters. Parameter values were changed with the corresponding minimum and maximum values, based on the range listed in Table 2, Table 3 and Table 4. The result is demonstrated in the form of Tornado Diagram as shown in Fig. 4. Tornado diagram is useful in identifying the key drivers for ICER values by demonstrating the changes in economic conclusion based on the variation of values of the selected parameters.

2.6. Probabilistic Sensitivity Analysis (PSA)

Bayesian methods such as PSA are often used to measure the uncertainty effect of model parameters (13, 14). In this study, PSA was performed by assigning the model parameters with appropriate distributions model as shown in Table 2, Table 3 and Table 4. The probabilities and costs parameters were allowed to varied and the effect of uncertainties were assessed by running a large number of simulations. PSA results are graphically demonstrated in cost-effectiveness plane scatter diagram and Cost-Effectiveness Acceptability Curve (CEAC).

3. Results

Results of cost-effectiveness analysis as shown in Table 5, consist of cost per TB screening, cost per TB case detected and the ICER. Figure 2 shows the cost-effectiveness plane of the analysis. TB screening among CCRC inmates had the lowest cost per screening with MYR 40.83, while TB screening among elderly was the highest with MYR 44.85 per screening. The results also showed that TB screening among PL HIV as the most cost-effective strategy with MYR 2,597.00 per TB case detected. This was followed by screening of TB among elderly, prisoners and smokers with MYR 2,868.62, MYR 3,065.24 and MYR 4,327.76 per TB case detected respectively.

As the initial reference point, TB screening among CCRC inmates would costs MYR 40.83 per screening, resulted in 3.2 TB case detection per 1000 screening and costs MYR 12,809.08 per one TB case detected. TB screening among old folks' home residents revealed increment of MYR 0.12 cost per screening and less 3.2 TB case detected per 1000 screening. This was a case of dominated strategy, providing worse outcomes but at much higher cost. TB screening among ESRF patient on the other hand, resulted in extended dominated. Both the costs per screening and also TB cases detection increased by for MYR 0.18 and 1.1 per 1000 screening respectively. The subsequent strategy, which is TB screening among prisoners was a dominant case, with much better outcomes, even though the costs is slightly higher than screening the ESRF patients, resulting in positive ICER. Screening TB among prisoners increased the costs as much as MYR 0.19 but resulted in increment of 9.1 TB case detection per 1000 screening. The next dominant strategy was TB screening among PL HIV. This strategy resulted in increment costs of

MYR 2.49 per screening, and 3.4 TB case detection per 1000 screening in relation to TB screening among prisoners. The other strategies resulted in dominated case with worse outcomes but at higher costs.

Table 5
Results of Cost-Effectiveness Analysis of Different High-Risk Group TB Screening

Strategy	Cost Per Screening (MYR)	TB Cases Detected (per 1000 Screening)	Cost per TB Case Detected (MYR)	ICER
CCRC inmates	40.83	3.2	12,809.08	Dominant*
Old Folks Home Residents	40.95	0.0	na	Dominated**
ESRF	41.01	4.3	9,456.83	Ext. Dominated***
Prisoner	41.20	13.4	3,065.24	Dominant*
Diabetes Mellitus	41.50	3.1	13,214.26	Dominated**
Methadone Clinic Client	41.63	0.0	na	Dominated**
Rheumatoid Arthritis	43.34	0.0	na	Dominated**
PL HIV	43.69	16.8	2,597.00	Dominant*
COAD	43.76	5.8	7,590.33	Dominated**
Smoker	43.87	10.1	4,327.76	Dominated**
Elderly (60 years and above)	44.85	15.6	2,868.62	Dominated**
ICER incremental cost effectiveness ratio				
** Better outcomes, lower costs*				
*** Worse outcomes, higher costs*				
**** Better outcomes, lower costs but the subsequent strategy has a positive ICER*				

3.1 Sensitivity Analysis

Figure 2 shows the results of Deterministic Sensitivity Analysis for TB screening among PL HIV against the prisoners as the reference strategy (Fig. 3). Results showed that the ICER never falls below zero after the iterations, indicating TB screening among PL HIV would remain relatively dominant in comparison to the reference strategy. Probability of TB detection among symptomatic PL HIV is shown to be the key driver for the ICER. As the probability of TB detection among symptomatic PL HIV is getting higher, the ICER value would be lower, and vice versa. Nevertheless, cost for CXR did not affect the ICER.

PSA results for TB screening among the high-risk groups is demonstrated in Fig. 4. The cost-effectiveness plane depicted 1,000 simulations of incremental cost and incremental effectiveness, which is the number of TB case detected per 1000 screening. Almost 100% of the time, screening among PL HIV was more expensive compared to screening among prisoners. However, 74.3% of the iterations were in quadrant 1, which showed screening among PL HIV was more effective compared to the prisoners. Whereas, the CEAC demonstrates the probability of screening among PL HIV was more effective compared to the prisoners throughout various willingness to pay threshold values until MYR 240,000. The results showed that screening among PL HIV was cost-effectives around 48.6% of the iterations, almost at full length of the corresponding values for willingness-to-pay.

4. Discussion

This study indicates that TB screening among PL HIV is the most cost-effective strategy. The result consistent with past studies, which revealed TB screening among HIV is cost effective in both community and hospital settings (15, 16). HIV is a well-known risk factor for TB infection in low- and middle-income countries (1). In comparison to the non-HIV, there are 16 to 27 times risks of getting TB infection among PL HIV. This is reflected in the prevalence of TB/HIV co-infection in Malaysia of 6% for 2018 (17). From the results of this study, it was also estimated that the cost to detect one TB case from PL HIV screening would be around MYR 2,597.00. The key driver for cost effectiveness model is the probability of TB case detected among the symptomatic cases. The higher the probability of TB case detected among the symptomatic, the lower the ICER; thus, the lower the cost for detecting one TB case.

In addition, TB screening among elderly and prisoners also showed to be cost-effective. It would cost around MYR 2,868.62 and MYR 3,065.24 to detect one TB case by screening the elderly and prisoners respectively. Studies done in US and Soviet Union also revealed similar results, in which screening of prisoners was more cost effective than those of conventional community screening (2). The high prevalence of TB among the jailed population is well documented in previous reports and studies (1). This is due to the environmental condition such as enclosed space and poor ventilation, which lead to poor air circulation and subsequently precipitate TB infection (18, 19). Apart from that, there was enough evidence to show that TB incidence increases with age. However, TB problem among elderly is likely underestimated due to the difficulty of diagnosing TB among older age group (20). Hence, there was suggestion that TB screening among elderly should focus on active case detection (21).

On the other hand, TB screening among Diabetic patient was shown to have the highest cost per one TB case detected among the high-risk groups, with MYR 13,214.26. This might be due to low TB case detection despite of large amount of screening done compared to the other high-risk groups. The association between TB and DM is well documented. However, there are several well-known micro factors that precipitate TB infection in DM patients (22). For example, patient with uncontrolled glycaemic level and low BMI are known to have a higher risk of contracting TB (23). Thus, past studies recommend focusing on TB screening among low Body Mass Index (BMI), high Fasting Blood Sugar and low Triglycerides rather than the entire DM patients (24). Similarly, cost per one TB case detected was also high for CCRC inmates, with MYR 12,809.08. People Who Use Drugs (PWUD) is also known to be at higher risk for TB infection (25). Plus, living in a closed, packed and condensed environment such as in rehabilitation centre put them at much higher risk for TB infection (18, 19). A study done on TB screening at substance abuse treatment centres in Malaysia revealed that the PWUD is at much higher risk of Latent Tuberculosis Infection (LTBI), which can later progress into active disease (26). Nevertheless, MOH report showed only small percentage actually being diagnosed as TB (27).

The decision to focus TB screening on one strategy or to expand it to other strategies should depend on the ICER value. This study suggests that to implementation of TB screening among PL HIV will incur additional cost per screening even though the benefit outweigh the reference strategy, i.e. TB screening among the prisoners. Hence, it would cost additional MYR 735.82 to switch the strategy from prisoners to PL HIV with an additional one TB case being diagnosed. Considering the number of screening will affect the number of TB case detected, the availability of those specific high-risk group will affect how much it will cost for each TB screening strategy.

This study main strength is the comprehensiveness of analysis method with the inclusion of various high-risk groups. Hence, this study provides better understanding for TB screening among the high-risk groups in term of its' cost-effectiveness. While providing better overview of each high-risk groups cost-effectiveness, this study will be useful for policy makers in strategizing future TB elimination programme. Besides that, this study also received input from MOH and programme owner, who directly involved in managing TB screening programme.

Notwithstanding the above, this study may provide significant input to the policy makers. Screening among high risk groups has been recognized as the cornerstone for TB elimination (28). However, different strategies are required due to the variability in term of resource availability and disease transmission in local setting (29). In re-strategizing national TB programme, prioritisation is necessary to make sure the current available resources are being allocated in the best possible manner. In a limited budget availability, focusing TB screening among the highly cost-effective strategies seems to be the way forward for the policymakers. For example, in Japan and US, older people are given priority for TB screening (30). Hence, in Malaysia, TB screening among PL HIV, elderly and prisoners should be the focus for TB screening programme as suggested by this study. In addition, this study is also useful for budgetary planning. By setting target for TB case detection, the cost for each TB case detection can be used to estimate the required budget for TB programme implementation.

Nevertheless, there are several limitations to this study. The measure of effectiveness used in this study was generic, i.e. cost per TB case detected. Most of the cost effectiveness studies among TB high risk group expressed the effectiveness measure using Quality Adjusted Life Years (QALY), Disability Adjusted Life Years (DALY) averted or death averted, but there are some which expressed the measure of effectiveness in term of TB cases detected (2). The lack of standardisation for outcome measurement makes it difficult to compare the findings with other studies. Besides, the benefit of current study might be overestimated or underestimated due to this outcome measures. For example, the overestimation of benefit in screening among the elderly versus younger age group due to the effect of time horizon analysis, as well as the screening for cases in confined space versus non-confined space. Data used in this study also confined to Sabah and Sarawak state. Thus, probabilities for certain high-risk groups might not represents the exact probabilities for the country. This was particularly noticeable especially on probabilities for old folks' home residents, clients of Methadone Clinic, and Rheumatoid Arthritis patients. By using secondary data, the current study also limits further detail analysis.

5. Conclusions

In conclusion, this study recommends prioritisation on several high risk-groups in TB screening programme based on the most cost-effective strategies, such as among PL HIV, elderly and prisoners. TB screening among other high-risk groups should be implemented based on the available resources. Therefore, to exercise strategic plan for TB screening, the policy makers must also take into account the effect of these factors and how it will benefit in long run. It is suggested that detail analysis to be conducted in future study, for example by looking at the cost effectiveness of TB screening between different sub-groups of DM. Future research should also focus on screening for latent TB in Malaysia. Despite of that, current study suggests that re-strategizing TB screening program among high-risk group should be the way forward. With the scarce resources and new modalities coming in for TB diagnosis, there is a need for prioritizing the TB screening programme. Hence, the limited resources can be used for the most cost-effective measures and to tackle other issues, while moving forward into eliminating TB.

List Of Abbreviations

CCRC Cure and Care Rehabilitation Center

CE Cost Effectiveness

CEAC Cost Effectiveness Acceptability Curve

COAD Chronic Obstructive Airway Disease

CXR Chest X-Ray

DALY Disability Adjusted Life Years

DM Diabetes Mellitus

DSA Deterministic Sensitivity Analysis

ESRF End Stage Renal Failure

GDP Gross Domestic Product

HIV Human Immunodeficiency Virus

ICER Incremental Cost Effectiveness Ratio

LTBI Latent Tuberculosis Infection

MOH Ministry of Health, Malaysia

MYR Malaysian Ringgit

PL HIV Person Living With HIV

PSA Probabilistic Sensitivity Analysis

QALY Quality Adjusted Life Years

SAFB Sputum for Acid Fast Bacilli

TB Tuberculosis

US United States

USD United States Dollar

WHO World Health Organisation

WTP Willingness To Pay

Declarations

Ethics approval and consent to participate

This study has obtained ethics approval from Medical Research and Ethics Committee (MREC), MOH Malaysia and registered under National Medical Research Register, MOH Malaysia (NMRR-19-3443-51729).

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing Interest

The authors declare that they have no competing interests.

Funding

Funding for this research was fully sponsored by Ministry of Health Malaysia.

Author Contributions

Nor Zam Azihan Mohd Hassan performed the economic development model, and was involved in manuscript development and review. Asmah Razali was responsible for data collection and approved the economic model development. Ridzwan Shahari assisted in economic model development, assisted in data collection, giving technical advice and review the final manuscript. Mohd Shaiful Jefri assisted in data collection for costing and review the final manuscript. Juanita Halili assisted in literature review. Nur Amalina Zaimi, Mohd Shahri Bahari and Farhana Aminuddin were all assisted in analysis and review of final manuscript. All authors approved the final manuscript.

Acknowledgements

Firstly, the authors would like to acknowledge Director General of Health Malaysia for giving permission to publish this article. Not to forget, Director of Institute for Health Systems Research for providing support and guidance. Head of Sectors for Disease Control Division (TB/Leprosy) and MOH staff's assistance in data collection were also much appreciated. Authors would also like to acknowledge Sarawak and Sabah State Health Department for providing data for this research.

References

1. Oliver J. WHO - Tuberculosis report. Journal of Chemical Information and Modeling. World Health Organisation (WHO); 2019.
2. Dobler CC. Screening strategies for active tuberculosis: Focus on cost-effectiveness. Vol. 8, ClinicoEconomics and Outcomes Research. Dove Medical Press Ltd; 2016. p. 335–47.
3. Jiménez-Fuentes MA, Milaauge C, Gómez MNA, Peiro JS, de Souza Galvao ML, Maldonado J, et al. Screening for active tuberculosis in high-risk groups. International Journal of Tuberculosis and Lung Disease. 2014 Dec 1;18(12):1459–65.
4. Zenner D, Southern J, van Hest R, DeVries G, Stagg HR, Antoine D, et al. Active case finding for tuberculosis among high-risk groups in low-incidence countries. Vol. 17, International Journal of Tuberculosis and Lung Disease. 2013. p. 573–82.
5. MOH. Surat Pekeliling KPK Bil 1 2016 - Pengukuhan Saringan Golongan Berisoko Tinggi Tuberculosis (Tibi) di bawah Program Kawalan Tibi Kebangsaan KKM -.pdf. 2016.
6. Nishikiori N, van Weezenbeek C. Target prioritization and strategy selection for active case-finding of pulmonary tuberculosis: A tool to support country-level project planning. BMC Public Health. 2013;13(1).

7. Hanis A, Shushami A. Associated Factors for Positive CXR Among TB High Risk Group Screening in Kedah Unmet Health Need Among Elderly With Diabetes in Penang: A Mixed Method Study View project. J of Biomed & Clin Sci Dec [Internet]. 2019;4(1):11–5. Available from: http://apps.amdi.usm.my/journal/
8. Smit GSA, Apers L, de Onate WA, Beutels P, Dorny P, Forier AM, et al. Cost-effectiveness of screening for active cases of tuberculosis in flanders, Belgium. Bulletin of the World Health Organization. 2017 Jan 1;95(1):27–35.
9. Kranzer K, Afnan-Holmes H, Tomlin K, Golub JE, Shapiro AE, Schaap A, et al. The benefits to communities and individuals of screening for active tuberculosis disease: A systematic review. International Journal of Tuberculosis and Lung Disease. 2013 Apr 1;17(4):432–46.
10. World Health Organization. Commission on Macroeconomics and Health., Sachs Jeffrey. Macroeconomics and health : investing in health for economic development : report of the Commission on Macroeconomics and Health. World Health Organization; 2001. 202.
11. Marseille E, Larson B, Kazi DS, Kahn JG, Rosen S. Thresholds for the cost–effectiveness of interventions: Alternative approaches. Bulletin of the World Health Organization. 2015;93(2):118–24.
12. International Monetary Fund. GDP per capita, current prices. World Economic Outlook [Internet]. 2018;(October 2018):2018–20. Available from: https://www.imf.org/external/datamapper/PPPPC@WEO/THA
13. Baio G, Dawid AP. Probabilistic sensitivity analysis in health economics. Statistical Methods in Medical Research. 2015 Dec 1;24(6):615–34.
14. Andronis L, Barton P, Bryan S. Sensitivity analysis in economic evaluation: An audit of NICE current practice and a review of its use and value in decision-making. Health Technology Assessment. 2009;13(29).
15. Zwerling A. Costs of tuberculosis screening among inpatients with HIV. Vol. 7, The Lancet Global Health. Elsevier Ltd; 2019. p. e163–4.
16. Gilbert JA, Shenoi S v., Moll AP, Friedland GH, Paltiel AD, Galvani AP. Cost-effectiveness of community-based TB/HIV screening and linkage to care in rural South Africa. PLoS ONE. 2016 Dec 1;11(12).
17. Ministry of Health. Country Progress Report on HIV / AIDS. Country Progress Report on HIV/AIDS [Internet]. 2018;1–45. Available from: http://www.moh.gov.my/resources/index/Penerbitan/Laporan/Report_GAM_2018_Final_(2).pdf
18. Migliori GB, Ambrosio LD, Centis R, Boom M van den, Ehsani S, Dara M. Guiding Principles to Reduce Tuberculosis Transmission in the WHO European Region. Who [Internet]. 2018;1–51. Available from: http://www.euro.who.int/pubrequest
19. CDC. CDC Infectious Control. :189–226. Available from: https://www.cdc.gov/tb/education/corecurr/pdf/chapter7.pdf
20. Marchand R, Tousignant P, Chang H. Cost-effectiveness of screening compared to case-finding approaches to tuberculosis in long term care facilities for the elderly. International Journal of

Epidemiology. 1999;28(3):563–70.

21. Lee SH. Active Case Finding in the Elderly Tuberculosis in South Korea. Tuberculosis and Respiratory Diseases. 2019;82(3):261.

22. Lee PH, Fu H, Lee MR, Magee M, Lin HH. Tuberculosis and diabetes in low and moderate tuberculosis incidence countries. International Journal of Tuberculosis and Lung Disease. 2018 Jan 1;22(1):7–16.

23. Lee PH, Fu H, Lai TC, Chiang CY, Chan CC, Lin HH. Glycemic Control and the Risk of Tuberculosis: A Cohort Study. PLoS Medicine. 2016 Aug 1;13(8).

24. Ji Y, Cao H, Liu Q, Li Z, Song H, Xu D, et al. Screening for pulmonary tuberculosis in high-risk groups of diabetic patients. International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases [Internet]. 2020 Jan; Available from: https://linkinghub.elsevier.com/retrieve/pii/S1201971220300217

25. Nava-Aguilera E, Andersson N, Harris E, Mitchell S, Hamel C, Shea B, et al. Risk factors associated with recent transmission of tuberculosis: Systematic review and meta-analysis. Vol. 13, International Journal of Tuberculosis and Lung Disease. 2009. p. 17–26.

26. Al-Darraji HAA, Wong KC, Yeow DGE, Fu JJ, Loeliger K, Paiji C, et al. Tuberculosis screening in a novel substance abuse treatment center in Malaysia: Implications for a comprehensive approach for integrated care. Journal of Substance Abuse Treatment. 2014 Feb;46(2):144–9.

27. MoH. National Strategic Plan for Tuberculosis Control in Georgia 2016-2020 [Internet]. 2015. Available from: http://www.moh.gov.mywebsites

28. Jamison DT, Breman JG, Measham AR, Alleyne G, Claeson M, Evans DB, et al. Disease Control Priorities in Developing Countries (2nd Edition). Disease Control Priorities in Developing Countries (2nd Edition). Oxford University Press; 2006.

29. Menzies NA, Gomez GB, Bozzani F, Chatterjee S, Foster N, Baena IG, et al. Cost-effectiveness and resource implications of aggressive action on tuberculosis in China, India, and South Africa: a combined analysis of nine models. The Lancet Global Health. 2016 Nov 1;4(11):e816–26.

30. Chong KC, Leung CC, Yew WW, Zee BCY, Tam GCH, Wang MH, et al. Mathematical modelling of the impact of treating latent tuberculosis infection in the elderly in a city with intermediate tuberculosis burden. Scientific Reports. 2019 Dec 1;9(1).

Figures

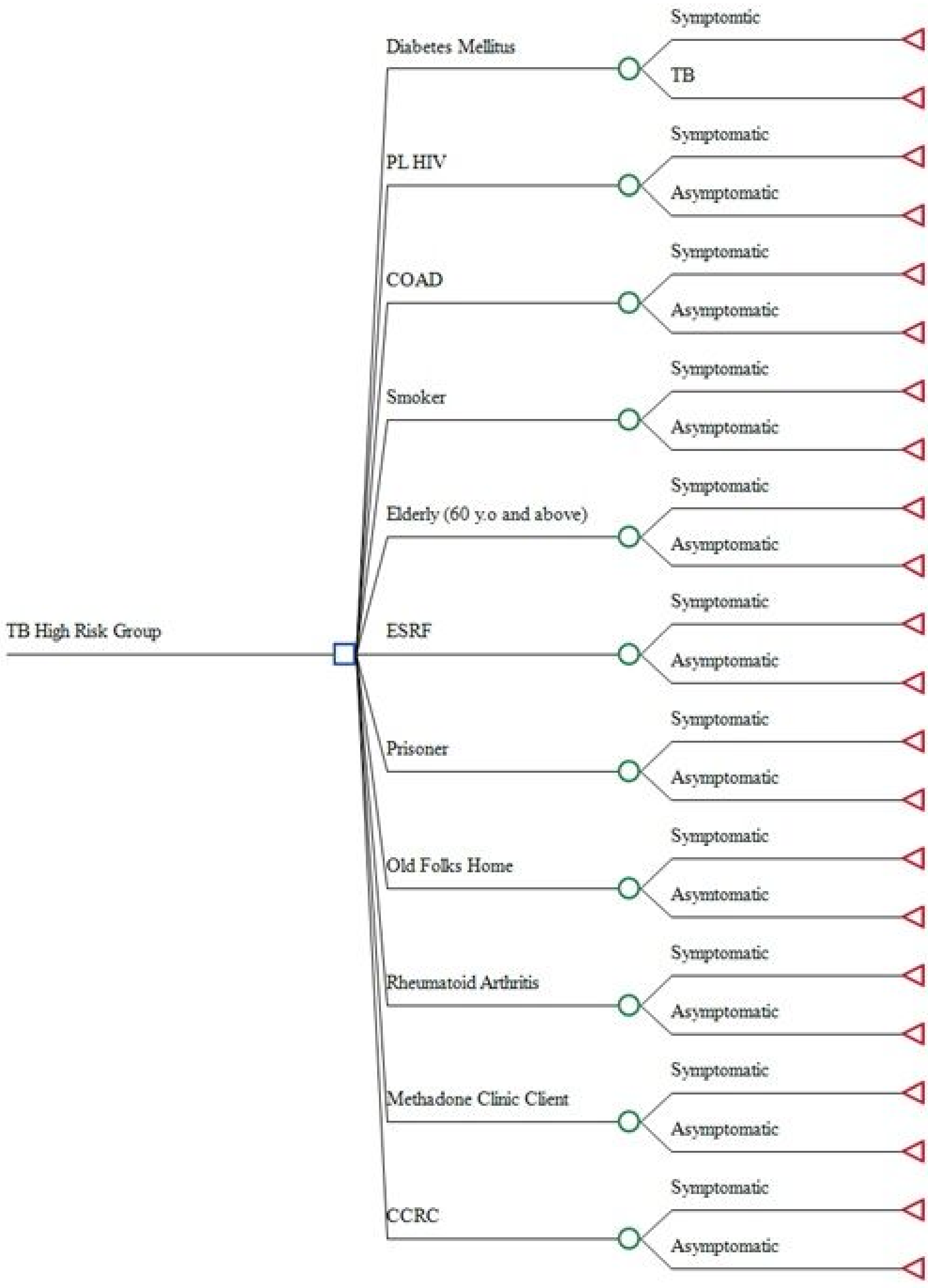


Figure 1

Decision Tree Model

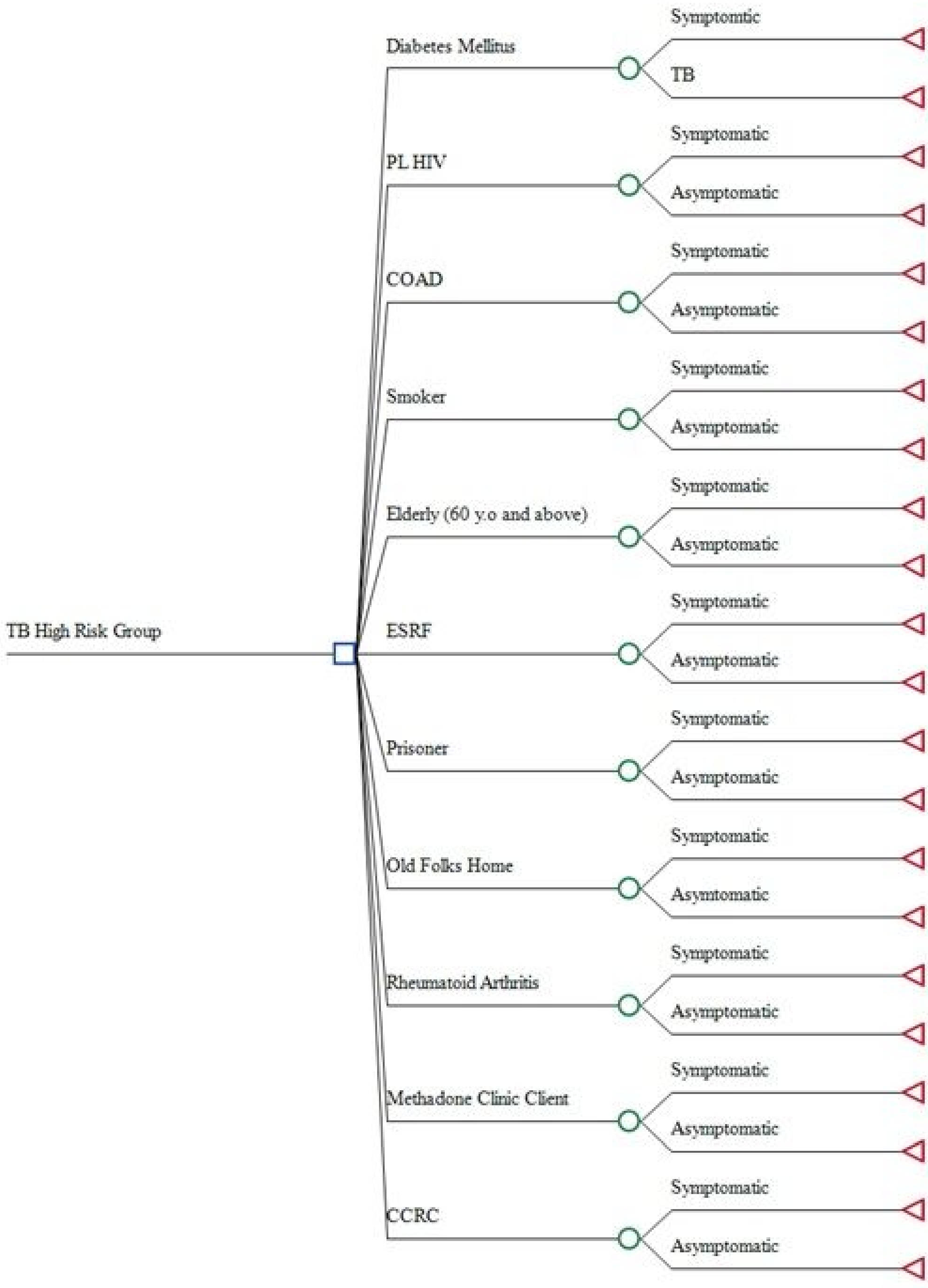


Figure 1

Decision Tree Model

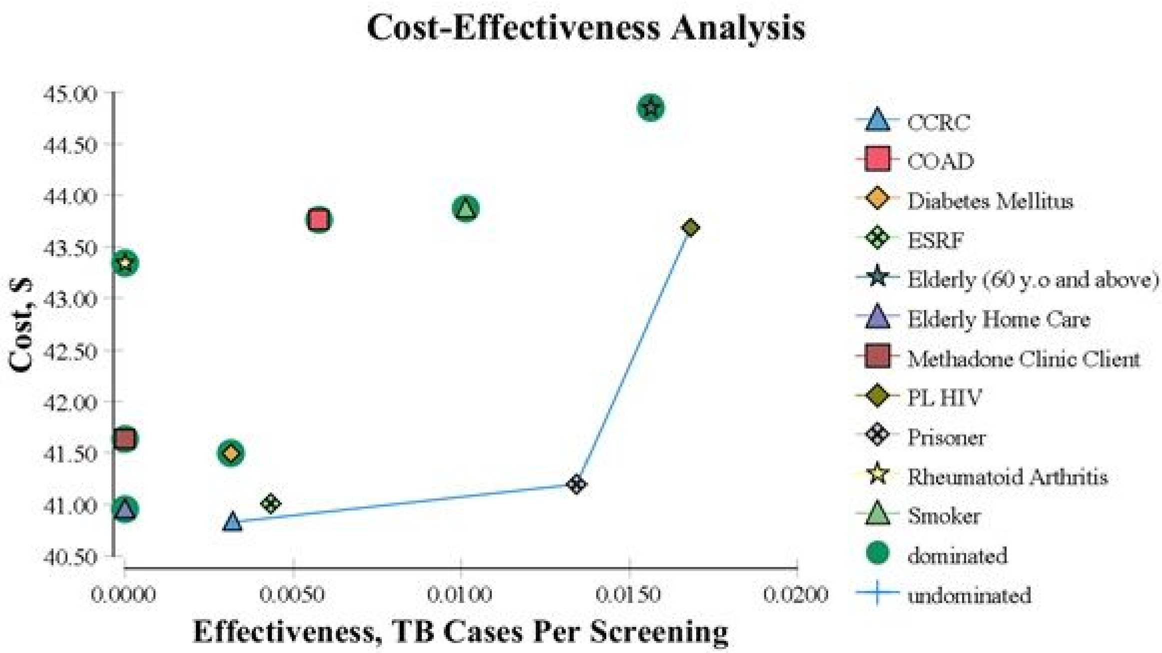


Figure 2

Cost-effectiveness Plane of TB screening among high-risk groups. The frontier is made up of CCRC, prisoners and PL HIV. The cost-effectiveness plane visualises each strategy effectiveness and cost in relation to the others.

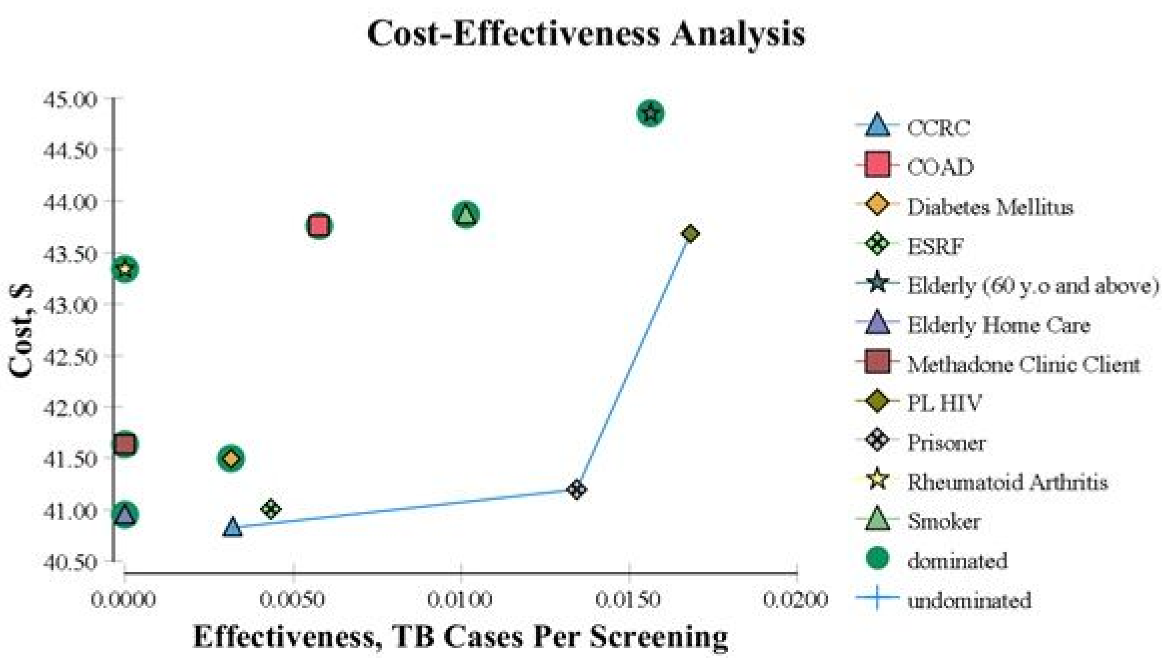


Figure 2

Cost-effectiveness Plane of TB screening among high-risk groups. The frontier is made up of CCRC, prisoners and PL HIV. The cost-effectiveness plane visualises each strategy effectiveness and cost in relation to the others.

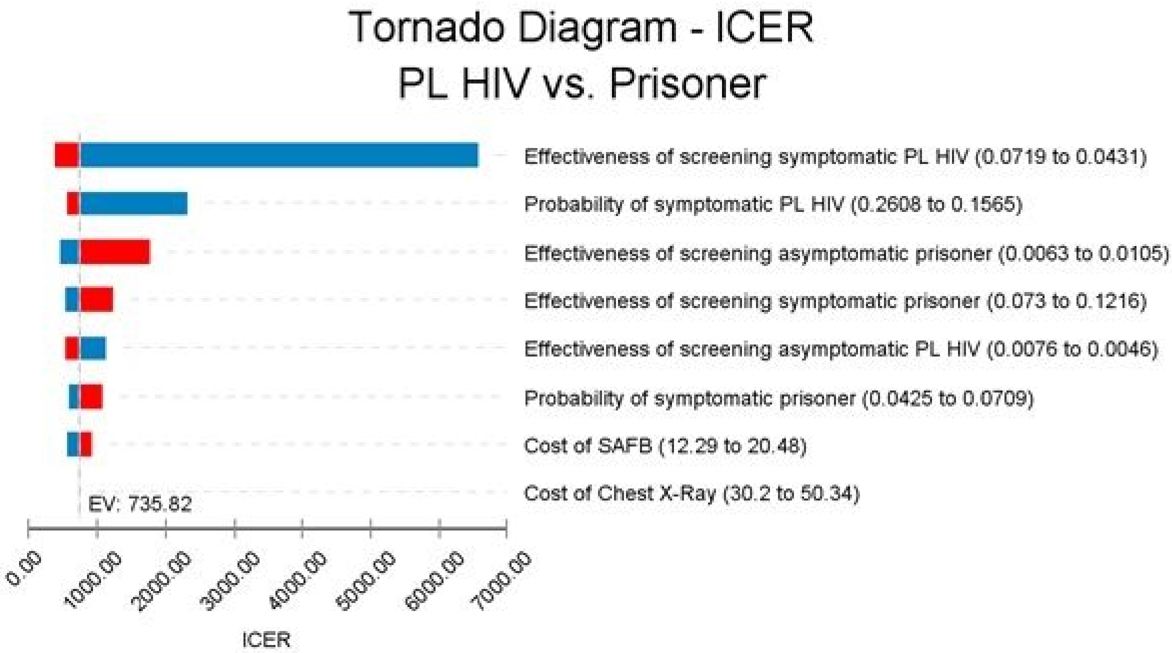


Figure 3

One-Way Sensitivity Analysis for TB screening among PL HIV versus prisoners; Tornado diagram of the significant parameters. This diagram shows the sensitivity of the ICER values upon changes in the model parameters. Value for each parameter is substituted one by one, starting with the lowest plausible value to the highest plausible value. This will make it possible to identify the key driver for the model outcome. Parameters that have the highest impact on the model are shown at the top, while the least impact is displayed at the bottom.

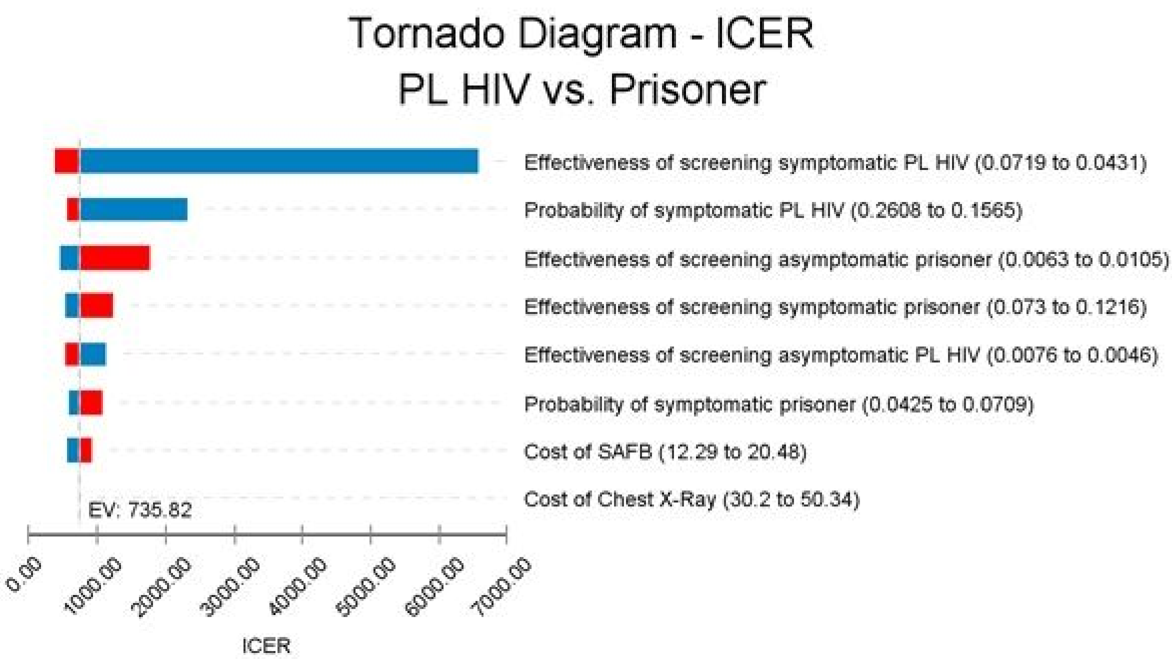
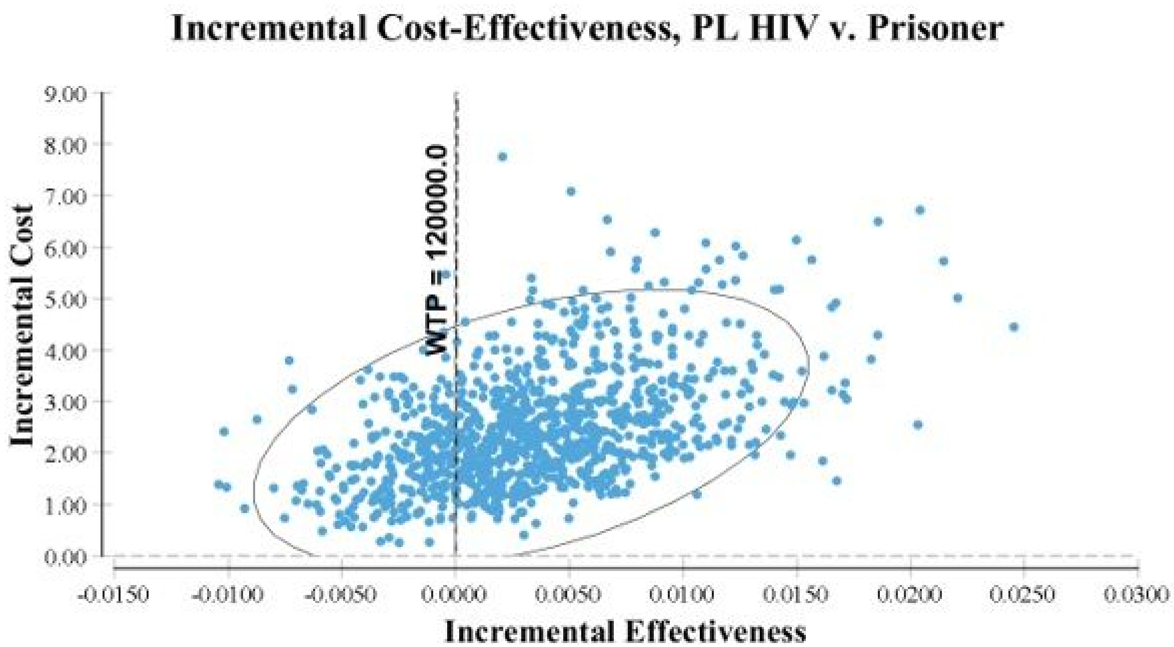


Figure 3

One-Way Sensitivity Analysis for TB screening among PL HIV versus prisoners; Tornado diagram of the significant parameters. This diagram shows the sensitivity of the ICER values upon changes in the model parameters. Value for each parameter is substituted one by one, starting with the lowest plausible value to the highest plausible value. This will make it possible to identify the key driver for the model outcome. Parameters that have the highest impact on the model are shown at the top, while the least impact is displayed at the bottom.



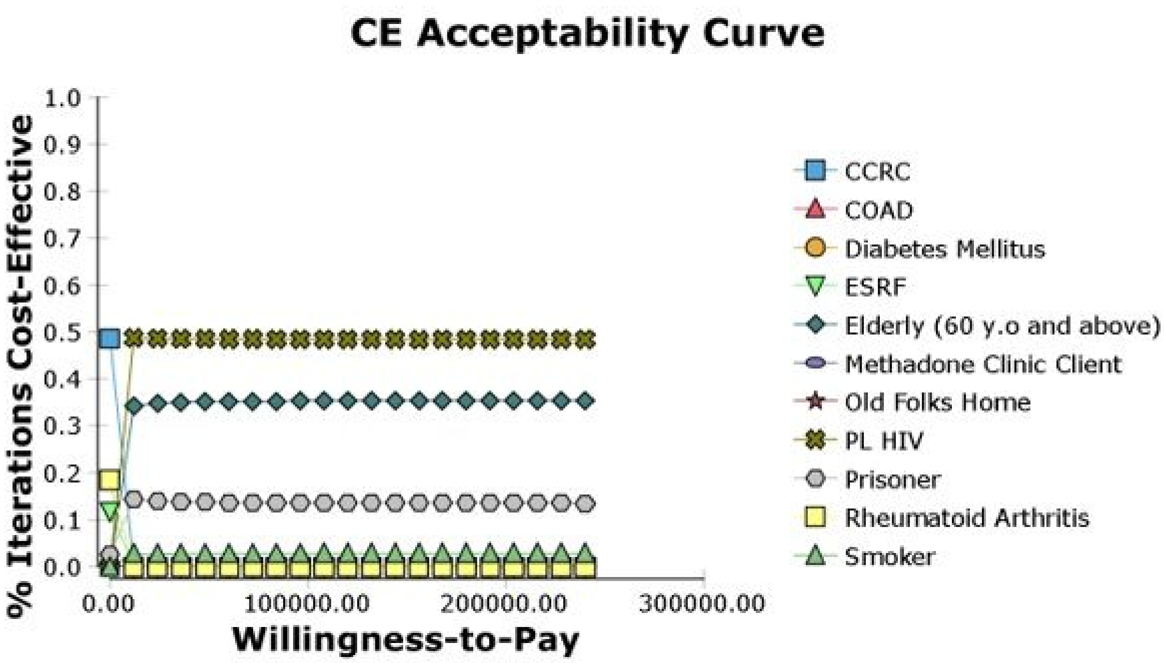
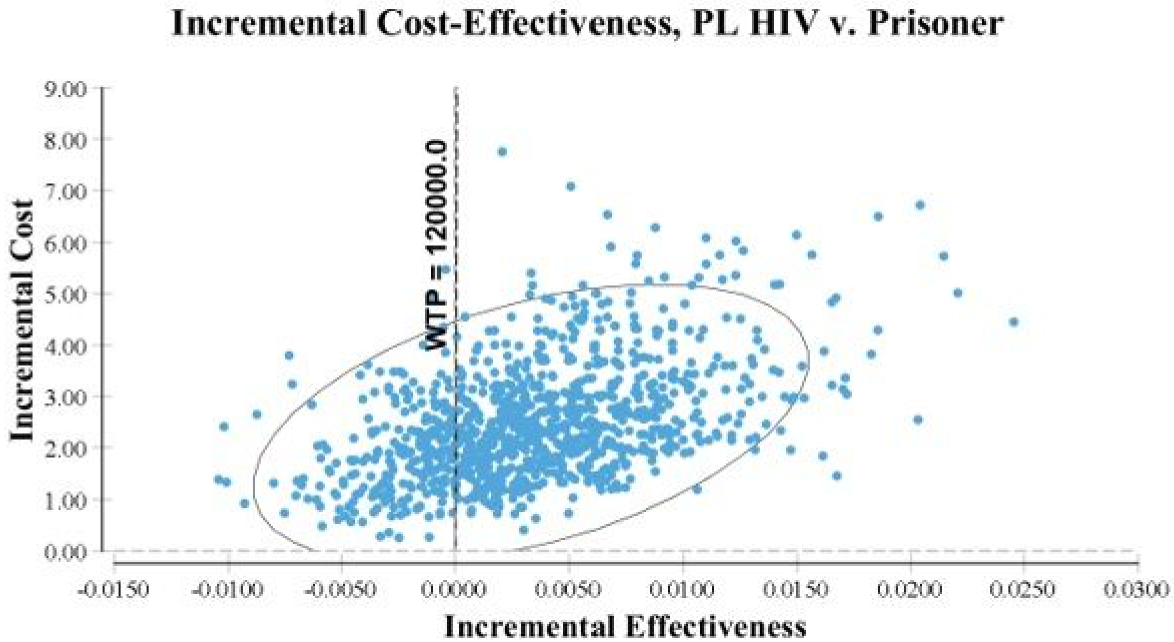


Figure 4

Probabilistic Sensitivity Analysis for TB screening among high-risk groups. Each parameter in the model is assigned with suitable statistical distributions and allowed to diverse based on the corresponding distributions. The results of 1,000 simulations is shown in the cost-effectiveness plane as scatter plot of incremental cost and incremental effectiveness for PL HIV versus prisoners. The Cost-Effectiveness Acceptability Curve (CEAC) shows the cost-effectiveness of screening among high-risk groups at various level of willingness to pay threshold.



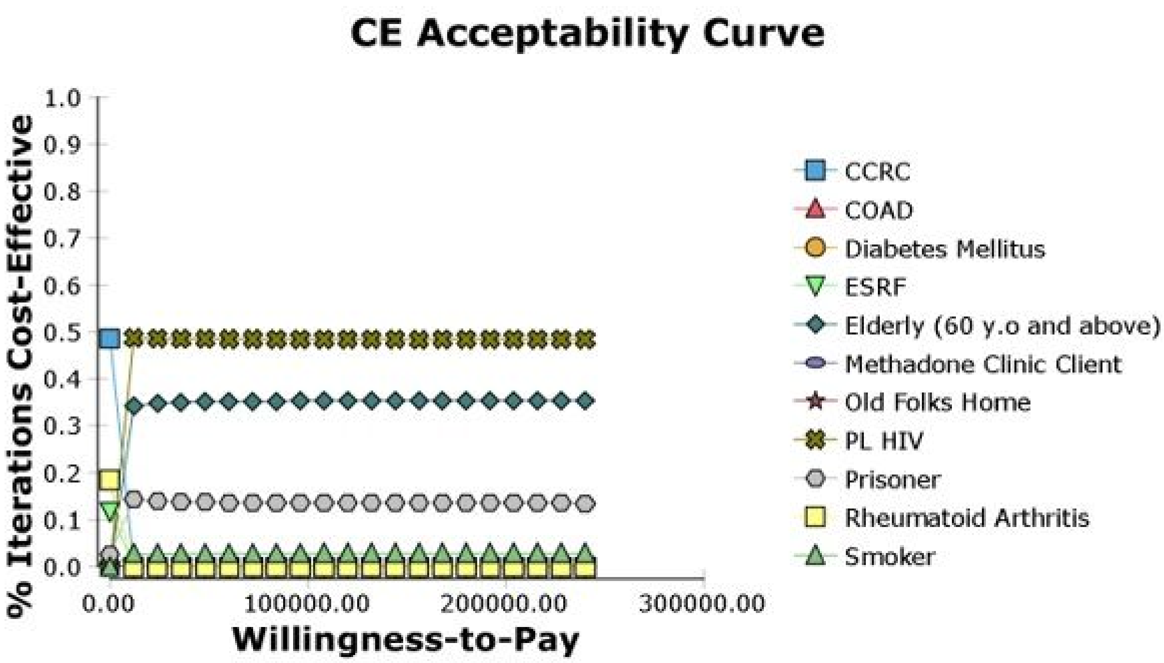


Figure 4

Probabilistic Sensitivity Analysis for TB screening among high-risk groups. Each parameter in the model is assigned with suitable statistical distributions and allowed to diverse based on the corresponding distributions. The results of 1,000 simulations is shown in the cost-effectiveness plane as scatter plot of incremental cost and incremental effectiveness for PL HIV versus prisoners. The Cost-Effectiveness Acceptability Curve (CEAC) shows the cost-effectiveness of screening among high-risk groups at various level of willingness to pay threshold.