Prospective migrants to countries where the incidence of tuberculosis (TB) is low (low-incidence countries) receive TB screening; however, screening for latent TB infection (LTBI) before immigration is rare. We evaluated the cost-effectiveness of mandated and sponsored preimmigration LTBI screening for migrants to low-incidence countries. We used discrete event simulation to model preimmigration LTBI screening coupled with postarrival follow-up and treatment for those who test positive. Preimmigration interferon-gamma release assay screening and postarrival rifampin treatment was preferred in deterministic analysis. We calculated cost per quality-adjusted life-year gained for migrants from countries with different TB incidences. Our analysis provides evidence of the cost-effectiveness of preimmigration LTBI screening for migrants to low-incidence countries. Coupled with research on sustainability, acceptability, and program implementation, these results can inform policy decisions.

The World Health Organization (WHO) has continued working toward tuberculosis (TB) elimination, aiming to reduce the overall TB burden by ≈90% to <1 case/1 million persons in countries where TB incidence is low (low-incidence countries) (1). Meeting this target will require new and innovative strategies. Typically, the TB burden in low-incidence countries is highest among populations born abroad; ≈70% of TB cases occur in these populations in Canada, the United States, and much of Europe (2). For the most part, TB prevention in these populations has focused on identifying persons with active TB before immigration to reduce transmission after arrival. Stagnant rates of TB suggest additional methods are required to accelerate declines in TB incidence (3).

Universal or targeted postarrival screening for latent TB infection (LTBI) has been suggested as a method to accelerate the decline of TB (4); however, domestic LTBI programs exhibit suboptimal performance (5), are resource intensive (6), and may not be cost-effective (7). One major reason for the reduced effectiveness of postarrival LTBI screening programs is the substantial attrition in the LTBI cascade of care. More than half of patients do not reach the point of initiating treatment, which results in fewer than one fifth completing treatment (5).

Currently, most immigrant-receiving, low-incidence countries employ mandatory preimmigration medical exams (8). As part of these medical exams, a chest radiograph and medical evaluation are performed to detect TB disease before arrival or identify those who may be at increased risk for TB disease in the future; these costs are borne by the patient within their country of origin. Only a select few countries employ some form of mandated LTBI screening (8), and data are scarce on the yield of such programs.

A report sponsored by the US Centers for Disease Control and Prevention (Atlanta, GA, USA) suggested mandatory LTBI screening and treatment as part of routine preimmigration medical exams (9); however, this strategy was viewed as inequitable and unjustly coercive (10) and has never been employed. Alternatively, mandating and fully sponsoring only LTBI screening as a formal part of the immigration process would avoid such ethics quandaries and could substantially reduce postarrival TB incidence. Preimmigration screening coupled with postarrival follow-up could improve the yield of LTBI screening programs >2-fold (5), because all case-patients reporting postarrival would already have completed LTBI screening.

We evaluated the cost-effectiveness of mandating and fully sponsoring LTBI screening in prospective migrants as part of routine preimmigration medical exams, coupled with passive postarrival follow-up and treatment. We evaluated 6 strategies among migrants from 4 different TB incidence groups to determine the optimal strategy in each group for this intervention.

Cost-effectiveness of Latent Tuberculosis Infection Screening before Immigration to Low-Incidence Countries

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Methods

Model Overview
We chose discrete event simulation for this model because of its flexibility in varying transition times between health states in a single simulation, ability to simulate simultaneous events, and capability to model several different patient covariates. These advantages make it preferable to traditional Markov models and enable the creation of a highly representative cohort in a single simulation (11). We modeled new migrants, which in this evaluation refers specifically to persons who have been granted permanent resident status but have not yet become citizens of the countries they reside in. Of interest were migrants from countries belonging to 4 distinct TB incidence categories: low, <30 cases/100,000 persons/year; moderate, ≥30 and <100 cases/100,000 persons/year; high, ≥100 and <200 cases/100,000 persons/year; and very high, ≥200 cases/100,000 persons/year.

We further defined the 4 populations of interest by 4 covariates: patient age, bacillus Calmette-Guérin (BCG) vaccination status, chest radiograph results, and LTBI prevalence. Patient age was defined based on an age distribution of a reference cohort of permanent residents to Canada in 2014 (12). BCG vaccination was determined through presence of a universal BCG vaccination policy in each country of origin and adjusted by 36-year average BCG vaccine uptake (13–15). For chest radiograph, a reference cohort of permanent residents who came to Ontario during 2002–2011 was used to identify prevalence of abnormal chest radiograph results (15). LTBI prevalence was calibrated in each population using 2-year TB incidence in permanent resident cohorts to Ontario during 2002–2011 (15) and age-adjusted using the results of a meta-analysis of test-positive rates (16).

We estimated LTBI prevalence using several assumptions. First, we assumed that 85% of incident TB resulted from reactivation of LTBI (17); second, that TB reactivation did not change over time post arrival (18); and last, that LTBI prevalence approximately matched reported rates of interferon-gamma release assay (IGRA) positivity in persons from each of the 4 TB incidence categories (16). In sum, an LTBI reactivation rate of 1.1 cases/1,000 person-years approximated literature values and yielded reasonable estimates of LTBI prevalence (17).

The model evaluates implementation of the intervention: preimmigration LTBI screening coupled with postarrival follow-up and treatment. The base case in this model was considered to be preimmigration TB screening without any evaluation for LTBI before or after arrival but with routine postarrival follow-up for those flagged through TB screening. We calibrated baseline TB incidence estimates and rates of postarrival follow-up to TB incidence data in permanent resident cohorts to Ontario during 2002–2011 (15). We considered 3 preimmigration LTBI screening options and 2 postarrival LTBI treatment options, for a total of 6 unique strategies to compare with the base case (Table 1).

We screened migrants with a tuberculin skin test (TST), IGRA, or sequential screening, in which persons testing positive by TST were given a confirmatory IGRA. We defined a positive TST result as an induration measuring ≥10 mm and a positive IGRA result using manufacturer’s recommendations, with IGRA performance being a composite measure of results from commercially available products (19–21). Although preimmigration testing was mandated, postarrival follow-up and treatment was not mandated and instead assumed to be passive, following published rates of postarrival follow-up in several countries (22). That is, in migrants who tested positive for LTBI, it was recommended that they attend a clinic for treatment postarrival, but no system was in place to enforce this. Those who reported for care postarrival would be treated with 9 months of isoniazid or 4 months of rifampin.

The model took a healthcare system perspective for the fully sponsored and mandated preimmigration LTBI screening: all LTBI screening costs preimmigration, along with typical postarrival costs, were the responsibility of the receiving country’s healthcare system. We used a 3% annual discount rate for costs and outcomes (23) and a 25-year time horizon from arrival. The main outcomes of the model were quality-adjusted life-years (QALYs), number of TB cases, and costs per 1,000 permanent residents from each of the 4 populations analyzed. These data were used to calculate the cost-effectiveness ratio, a measure that indicates the cost per additional QALY gained by an intervention strategy compared with the base case (Appendix, https://wwwnc.cdc.gov/EID/article/25/4/17-1630-App1.pdf).

A simplified model structure is displayed in Figure 1. In the intervention, migrants were given an LTBI diagnostic test along with the rest of their medical exam; those who tested positive were referred for postarrival follow-up. Those who complied with postarrival follow-up were recommended for LTBI therapy. After initiating treatment, they either completed treatment in full, partially completed treatment, or ceased due to an adverse event that may result in death. After treatment, results for all patients were simulated to the 25-year time horizon, with annual risks of TB reactivation and death.

We made the following assumptions in the model. Those with previous TB or an abnormal chest radiograph result identified during the preimmigration medical exam were also referred for postarrival follow-up. With the intervention, all those who began screening completed it,
Table 1. Intervention strategies for screening and treatment of latent TB infection in immigrants*

| Intervention strategy | Premigration | Postarrival if test is positive |
|-----------------------|--------------|-------------------------------|
| **Base case**         | TB screening as part of routine preimmigration medical exams, consisting of a chest radiograph, medical history, and symptom screen. If diagnosed with TB, treatment must be completed before immigrating. | Routine follow-up of those with abnormal chest radiograph results or previous TB. |
| **TST/INH**           | In addition to the base case, a TST is performed at the time of the medical exam. If the result is positive (induration >10 mm) referral is made for follow-up postarrival. If the TST result is negative, no further action is taken. | Recommendation for follow-up; if patient reports for follow-up, 9-month course of INH. |
| **TST/RIF**           | Same as above. | Recommendation for follow-up; at follow-up, 4-month course of RIF. |
| **IGRA/INH**          | In addition to the base case, an IGRA is placed at the time of the medical exam. If the result is positive (as defined by the manufacturer) referral is made for follow-up postarrival. If the IGRA result is negative, no further action is taken. If the IGRA result is indeterminate, a second is performed; a second consecutive indeterminate is treated as a negative. | Recommendation for follow-up; if patient reports for follow-up, 9-month course of INH. |
| **IGRA/RIF**          | Same as above. | Recommendation for follow-up; at follow-up, 4-month course of RIF. |
| **SEQ/INH**           | In addition to the base case, a TST is placed at the time of the medical exam. If the result is positive (as defined by an induration >10 mm) a second test is performed with an IGRA. If the subsequent IGRA result is positive (as defined by the manufacturer) referral is made for follow-up postarrival. If the initial TST is negative or if the subsequent IGRA is negative, no further action is taken. If the IGRA result is indeterminate, a second is performed; a second consecutive indeterminate is treated as a negative. | Recommendation for follow-up; at follow-up, 9-month course of INH. |
| **SEQ/RIF**           | Same as above. | Recommendation for follow-up; at follow-up, 4-month course of RIF. |

*No intervention required for migrants with negative results of base case screening. IGRA, interferon-gamma release assay; INH, isoniazid; RIF, rifampin; SEQ, sequential screening; TB, tuberculosis; TST, tuberculin skin test.

We derived model estimates from the literature or expert opinion (Table 2). A meta-analysis provided evidence for domestic LTBI program performance (5), therapy efficacy was derived from the literature (24,27,28), and adverse events were imputed from several randomized controlled trials reported in previous analysis (24,25). Diagnostic performance of LTBI screening tests was derived from systematic reviews and modeled to be the same in each country (19–21). Adherence with postarrival follow-up was estimated by reanalysis of reported data (22) (Appendix Figure 1). Death from tuberculosis (3), probability of TB therapy extension (30), and relapse rate (31) were derived from Canada sources. Life tables for Canada estimated background mortality (32).

We derived all costs from Canada sources and assumed that the costs of screening abroad were equal to screening costs in Canada. We derived costs for LTBI treatment and screening, including drugs, screening tests, routine monitoring, and clinician time, from the British Columbia Centre for Disease Control. Adverse event costs, including hospitalization rates and time, and the cost of TB disease were as reported in the literature (30,33,34). We inflated all costs to 2016 Canadian dollars using consumer price indices (35) (Table 3).

We derived health utility data from a study (38) in Canada of migrants who reported for postarrival follow-up. We based adjustments due to adverse events or hospitalization on previous studies (30,33).

**Sensitivity Analysis**

We performed a probabilistic sensitivity analysis (PSA) to capture uncertainty of model estimates using an outer sample size of 1,000 and inner sample size of 50,000 (Tables 2, 3). To guide policymakers, we created cost-effectiveness acceptability curves (CEAC) to determine the probability that the most cost-effective intervention strategy in deterministic analysis would fall below various willingness-to-pay (WTP) thresholds. Exploratory sensitivity analysis and additional probabilistic sensitivity analyses are included in the Appendix.
Results

Primary Results
Among migrants from moderate- to very high–incidence countries, IGRA screening coupled with postarrival rifampin treatment was the optimal intervention strategy in deterministic analysis. Sequential screening coupled with postarrival rifampin treatment was the optimal intervention strategy among migrants from low-incidence countries. Intervention strategies involving TST identified the most migrants for postarrival follow-up, whereas strategies involving sequential screening identified the fewest. Intervention strategies involving rifampin resulted in the fewest TB cases (46% reduction compared with the base case) (Table 4).

Low-Incidence Countries
For migrants from low-incidence countries, screening with TST alone resulted in a net loss in population QALYs because of poor specificity of the TST. Sequential screening, the most specific screening method, coupled with postarrival rifampin treatment yielded the lowest cost per QALY gained at $191,889. IGRA screening, the most sensitive screening method, coupled with rifampin treatment resulted in the fewest TB cases (46.2% reduction) but had a higher cost per QALY gained ($373,773) because of its lower specificity compared with that of sequential screening.

Moderate-Incidence Countries
For migrants from moderate-incidence countries, the optimal intervention strategy was IGRA screening coupled with postarrival rifampin treatment for those from moderate-incidence countries with a cost per QALY gained of $43,343. Sequential screening coupled with postarrival rifampin treatment was cheaper overall but had a cost per QALY gained of $47,561.

High-Incidence Countries
Among migrants from high-incidence countries, IGRA screening coupled with postarrival rifampin treatment was the optimal intervention strategy, at a cost per QALY gained of $664.

Figure 1. Flow structure of model used for cost-effectiveness analysis of screening and interventions of migrants for TB and LTBI. LTBI, latent tuberculosis infection; TB, tuberculosis.
gained of $26,350. Sequential screening coupled with rifampin treatment was less expensive, but also less efficient, with a cost per QALY gained of $29,997.

**Very High–Incidence Countries**

Among migrants from very high–incidence countries, IGRA screening coupled with postarrival rifampin treatment had a

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**Table 2. Model parameter estimates and values used for sensitivity analyses of intervention strategies for screening and treatment of latent TB infection in immigrants**

| Parameter | Estimate | Range evaluated in PSA | PSA distribution | References |
|-----------|----------|------------------------|------------------|------------|
| **Screening parameters** | | | | |
| TST sensitivity | 0.782 | 0.69–0.87 | Beta (43,12) | (19) |
| TST specificity, no BCG | 0.974 | 0.963–0.982 | Beta (770,21) | (20,21) |
| TST specificity, BCG | 0.602 | 0.561–0.642 | Beta (239,158) | (20,21) |
| IGRA sensitivity | 0.889 | 0.688–0.993 | Beta (8,1) | (19) |
| IGRA specificity | 0.957 | 0.948–0.968 | Beta (900,40) | (20,21) |
| IGRA indeterminate† | 0.06 | 0.05–0.07 | Beta (83,1286) | (21) |
| Complete TST‡ | 1 | Fixed | Fixed | |
| Complete medical evaluation§ | 1 | Fixed | Fixed | |
| **Population characteristics¶** | | | | |
| LTBI prevalence | | | | |
| Very high incidence | 0.3162 | 0.2686–0.3880 | Varied with reactivation rate | (12,15–17) |
| High incidence | 0.2016 | 0.1706–0.2464 | Varied with reactivation rate | (12,15–17) |
| Moderate incidence | 0.0902 | 0.0763–0.1102 | Varied with reactivation rate | (12,15–17) |
| Low incidence | 0.0159 | 0.0135–0.0195 | Varied with reactivation rate | (12,15–17) |
| Abnormal chest radiograph results or previous TB | | | | |
| Very high incidence | 0.039 | Fixed | Fixed | (15) |
| High incidence | 0.028 | Fixed | Fixed | (15) |
| Moderate incidence | 0.029 | Fixed | Fixed | (15) |
| Low incidence | 0.008 | Fixed | Fixed | (15) |
| Adherence to postarrival follow-up# | 0.684 | 0.646–0.721 | Beta (404,50,186,87) | (22) |
| **Treatment parameters** | | | | |
| Initiate** | 0.938 | 0.907–0.964 | Beta (180,83,11,95) | (5) |
| Complete, INH | 0.616 | 0.561–0.670 | Beta (131,66,82,07) | (5) |
| Complete, RIF | 0.814 | 0.745–0.876 | Beta (76,85,17,56) | (5) |
| Adverse event, INH | 0.049 | 0.044–0.055 | Beta (249,4789) | (24,25) |
| Adverse event, RIF | 0.021 | 0.018–0.025 | Beta (109,4877) | (24,25) |
| Adverse event hospitalization | 0.01 | 0.0005–0.03 | Beta (1,99) | (25) |
| Death, INH | 0.000000988 | 0–0.00002 | Beta (2,022495) | (26) |
| LTBI risk reduction, INH | 0.90 | 0.78–0.95 | Normal (–2,3.0,5)†† | (27) |
| LTBI risk reduction, RIF | 0.90 | 0.63–0.97 | Normal (–2,3.0,8)†† | (28,24) |
| Partial risk reduction, INH | 0.346 | 0.267–0.490 | Combination of normal distributions††, ‡‡ | Expert opinion, (25) |
| Partial risk reduction, RIF | 0.30 | 0.17–0.40 | Normal (–0.35,0.1)†† | Expert opinion, (24,28) |
| Adverse event duration | 7 d | 0–24 | Gamma (0.7,10) | Expert opinion, (25) |
| **TB parameters** | | | | |
| Death from TB | 0.0476 | 0.0391–0.0566 | Beta (76,1523) | (3) |
| Reactivation rate | 0.0011 | 0.0009–0.0013 | Beta (90,92,82545,55) | (15–17) |
| Abnormal CXR risk change | 3.9 | 3.0–4.9 | Normal (1,3.6,0.15)†† | (29) |
| Extended therapy | 0.124 | 0.029–0.264 | Beta (2,366,16,713) | Expert opinion, (30) |
| Relapse rate | 0.0359 | 0.0197–0.0654 | Normal (–3,327,0.365)†† | Expert opinion, (30) |
| Hospitalization duration | 17 d | Fixed | Fixed | Expert opinion, (30) |
| **Model parameters** | | | | |
| BCG vaccination, <30 cases | 0.605 | 0.60–0.61 | Beta (45137,29502) | (12,13) |
| BCG vaccination, ≥30 cases | 0.998 | 0.997–0.999 | Beta (185381,384) | (12,13) |
| BCG vaccination uptake | 0.837 | Fixed | Fixed | (14) |
| Discount rate | 0.03 | Fixed | Fixed | (23) |
| Time horizon | 25 y | Fixed | NA | |

*AE, adverse event; BCG, bacillus Calmette-Guérin; IGRA, interferon-gamma-release assay; INH, isoniazid; LTBI, latent tuberculosis infection; NA, not available; PSA, probabilistic sensitivity analysis; RIF, rifampin; TST, tuberculin skin test; TB, tuberculosis.
†Treated as a negative result if it occurred; was equally likely to occur in those with and without LTBI.
‡Without being mandatory, this value is 78% (imputed from 43.7 of 56 individuals completing medical evaluation) (5).
§Without being mandatory, this value is 78% (imputed from 43.7 of 56 individuals completing medical evaluation) (5).
¶Very high incidence, >200 cases/100,000; high incidence, >100 and <200 cases/100,000; moderate incidence, >30 and <100 cases/100,000; low incidence, <30 cases/100,000.
#From a meta-analysis (22); see also Appendix (https://wwwnc.cdc.gov/EID/article/25/4/17-1630-App1.pdf).
**This model assumes all who report postarrival due to a positive preimmigration LTBI diagnostic test are offered treatment. Exploratory analysis adjusts this assumption so that only the number who would complete TST screening begin treatment.
††Results from this distribution are exponentiated.
‡‡Formula: 0.33 × (Normal(–1.168,0.228)) + 0.374 × (Normal(–0.381,0.169)) + 0.293 × 1.
Sensitivity Analysis
Among migrants from low-incidence countries, sequential screening coupled with postarrival rifampin treatment was the most cost-effective option in deterministic analysis. In PSA, this intervention had a probability of cost-effectiveness of 49.1% at a WTP threshold of $50,000/QALY and 50.7% at a WTP threshold of $100,000/QALY. This probability did not substantially increase past these thresholds, however, resulting in a probability of cost-effectiveness of 52% at a WTP threshold of $200,000/QALY (Figure 2, panel A).

Among migrants from moderate-, high-, and very high-incidence countries, IGRA screening coupled with postarrival rifampin treatment was the most cost-effective option in deterministic analysis. This intervention strategy at WTP thresholds of $50,000/QALY gained had probabilities of cost-effectiveness of 57.5% among migrants from moderate-incidence countries (Figure 2, panel B), 68.2% among migrants from high-incidence countries (Figure 2, panel C), and of 73.2% among migrants from very high-incidence countries (Figure 2, panel D). At a WTP threshold of $100,000/QALY gained probabilities of cost-effectiveness were 59.8% among migrants from moderate-incidence countries, 70.6% among migrants from high-incidence countries, and 75.2% among migrants from very high-incidence countries.

Discussion
The intervention of premigration LTBI screening followed by postarrival treatment among new migrants from countries with a TB incidence ≥30 cases/100,000 persons appears to be an effective method for reducing TB incidence post-arrival. The use of IGRA screening coupled with postarrival rifampin treatment provided the lowest cost-effectiveness ratio in migrants from these countries. This intervention strategy reduced TB incidence by >45% and yielded costs <$50,000/QALY gained.

Table 3. Cost and QALY estimates and values used for sensitivity analysis of intervention strategies for screening and treatment of latent TB infection in immigrants

| Parameter                      | Estimate, $  | Range evaluated in PSA | PSA distribution | References |
|--------------------------------|--------------|------------------------|------------------|------------|
| Costs                          |              |                        |                  |            |
| Full INH treatment             | 992          | 804–1,179              | Triangular, 804–1,179 | BCCDC, (33,36) |
| Drug costs                     | 181          |                        |                  |            |
| Nurse and clinician costs      | 741          |                        |                  |            |
| Follow-up chest radiograph     | 42           |                        |                  |            |
| Routine tests                  | 28           |                        |                  |            |
| Full RIF treatment             | 575          | 464–686                | Triangular, 464–686 | BCCDC, (33,36) |
| Drug costs                     | 98           |                        |                  |            |
| Nurse and clinician costs      | 421          |                        |                  |            |
| Follow-up chest radiograph     | 42           |                        |                  |            |
| Routine tests                  | 14           |                        |                  |            |
| Partial INH                    | 462          | 174–804                | Triangular, 174–804 | BCCDC, (33,36) |
| Partial RIF                    | 319          | 178–464                | Triangular, 178–464 | BCCDC, (33,36) |
| Complete TST                   | 31           | 24–38                  | Triangular, 24–38 | BCCDC, (33,36) |
| TST cost                       | 11           |                        |                  |            |
| Nurse costs (2 visits)         | 20           |                        |                  |            |
| Incomplete TST                 | 21           | 17–25                  | Triangular, 17–25 | BCCDC, (33,36) |
| IGRA                           | 54           | 31–62                  | Triangular, 31–62 | BCCDC, (33,36) |
| Kit and technician cost         | 47           |                        |                  |            |
| Nurse costs                    | 7            |                        |                  |            |
| Chest radiograph               | 42           | 32–52                  | Triangular, 32–52 | BCCDC, (33,36) |
| Cost per radiograph            | 35           |                        |                  |            |
| Nurse costs                    | 7            |                        |                  |            |
| TB                             | 20,532       | 7,141–39,525           | Gamma (4.1064,5,000) | Expert opinion, (33,34) |
| LTBI adverse event             | 732          | 549–916                | Triangular, 549–916 | (33)       |
| Hospitalization                | 6,641        | 5,305–9,985            | Triangular, 5,305–9,985 | (30)       |
| Death                          | 26,933       | 13,079–40,788          | Triangular, 13,079–40,788 | (37)       |

QALYs

| Parameter      | Estimate, $ | Distribution | References |
|----------------|-------------|--------------|------------|
| LTBI           | 0.81        | Assumed      | (38)       |
| Healthy        | 0.81        | 0.58–0.97    | Beta (7.85, 1.84) | (38) |
| Adverse event disutility | 0.2 | 0.15–0.25 | Triangular, ± 25% | (30,33) |
| TB             | 0.69        | 0.08–0.24†   | Beta (9.51) | (38) |
| Hospitalization| 0.5         | 0.28–0.51†   | Beta (19.5,30.5) | (30) |
| Death          | 0           | Fixed        | Standard   |

*All costs are in 2016 Can $. BCCDC, British Columbia Centre for Disease Control; IGRA, interferon-gamma release assay; INH, isoniazid; LTBI, latent tuberculosis infection; PSA, probabilistic sensitivity analysis; RIF, rifampin; TB, tuberculosis; TST, tuberculin skin test.

†Sampled as a percent decrement compared to healthy QALY.
Because prevalence of LTBI was low among migrants from countries with a TB incidence <30 cases/100,000 persons and specificities of LTBI diagnostic tests are imperfect, this intervention may result in a high number of uninfected persons receiving treatment unnecessarily. This finding suggests that with some strategies, the QALYs lost due to treatment side effects among those with false-positive diagnostic results may be greater than the QALYs gained by averted TB in those with true-positive diagnostic results. If screening and treatment must be performed in these low LTBI prevalence populations, more specific screening methods (i.e., sequential screening) are preferred to avoid inappropriate treatment.

Probabilistic sensitivity analysis suggests a certain degree of uncertainty in results. The behavior of CEACs as WTP thresholds increase suggests that the intervention offers small increases in population QALYs or large increases in cost in many replications. It is important to understand how well the model parameters represent the local setting when using the results of this analysis to inform evidence-based policy. These results suggest that intervention offers domestic benefits to the receiving country, but several factors need to be carefully examined. IGRA use in high-resource settings suffers from variability, in part related to several operational issues (39), and TST variability remains an issue (40). For both types of test, variability may be exacerbated in low-resource settings where LTBI prevalence rates are likely to be higher. In this model, we did not consider the costs of program initiation and maintenance; although they are outside the scope of this analysis, these costs merit careful evaluation when seeking to implement policy.

This model considered only the costs of persons who became permanent residents. The data from Canada indicated that ≈50%–60% of those who begin the process of becoming a permanent resident successfully complete it (3,15). For migrants from very high–incidence countries, assuming only half of migrants receiving preimmigration

### Table 4. Results in various TB incidence settings of implementing intervention strategies for screening and treatment of latent TB infection in immigrants

| Intervention          | % Identified for postarrival followup | Cost/1,000 persons, $ | No. QALYs/1,000 persons | No. TB cases/1,000 persons | % Reduction in TB incidence | Cost per QALY gained, $† |
|-----------------------|--------------------------------------|-----------------------|-------------------------|---------------------------|-----------------------------|--------------------------|
| **Low TB incidence countries** |                                     |                       |                         |                           |                             |                          |
| Base case             | 0.82                                 | 9,681                 | 13,761.03               | 0.41                      | NC                          | NC                       |
| SEQ/RIF               | 4.02                                 | 60,996                | 13,761.30               | 0.26                      | 36.87                       | 191,889                  |
| SEQ/INH               | 4.02                                 | 67,309                | 13,761.08               | 0.28                      | 32.00                       | 1,289,335‡               |
| IGRA/RIF              | 6.43                                 | 80,107                | 13,761.22               | 0.22                      | 46.16                       | 373,773‡                 |
| IGRA/INH              | 6.43                                 | 91,056                | 13,761.07               | 0.25                      | 39.07                       | 2,315,425‡               |
| TST/RIF               | 22.99                                | 120,910               | 13,760.85               | 0.24                      | 40.08                       | Dominated                |
| TST/INH               | 22.99                                | 162,233               | 13,760.59               | 0.27                      | 34.12                       | Dominated                |
| **Moderate TB incidence countries** |                                     |                       |                         |                           |                             |                          |
| Base case             | 2.88                                 | 58,301                | 13,735.03               | 2.47                      | NC                          | NC                       |
| SEQ/RIF               | 11.99                                | 121,950               | 13,736.36               | 1.57                      | 36.52                       | 47,561‡                  |
| IGRA/RIF              | 14.52                                | 129,036               | 13,736.66               | 1.33                      | 46.36                       | 43,343                   |
| SEQ/INH               | 11.99                                | 142,739               | 13,735.71               | 1.72                      | 30.55                       | 122,821‡                 |
| IGRA/INH              | 14.52                                | 154,804               | 13,736.69               | 1.50                      | 39.47                       | 58,154‡                  |
| TST/RIF               | 38.96                                | 206,145               | 13,736.84               | 1.46                      | 40.77                       | 81,548‡                  |
| TST/INH               | 38.96                                | 277,998               | 13,735.98               | 1.61                      | 34.88                       | 230,641‡                 |
| **High TB incidence countries** |                                     |                       |                         |                           |                             |                          |
| Base case             | 2.79                                 | 122,928               | 13,702.56               | 5.39                      | NC                          | NC                       |
| SEQ/RIF               | 19.13                                | 194,289               | 13,704.93               | 3.44                      | 36.06                       | 29,997                   |
| IGRA/RIF              | 23.60                                | 199,878               | 13,705.48               | 2.91                      | 45.99                       | 26,350                   |
| SEQ/INH               | 19.13                                | 231,835               | 13,704.38               | 3.73                      | 30.73                       | 59,655‡                  |
| TST/RIF               | 44.24                                | 247,488               | 13,704.35               | 3.28                      | 39.21                       | 69,421‡                  |
| TST/INH               | 44.24                                | 263,572               | 13,704.93               | 3.22                      | 40.18                       | 59,154‡                  |
| **Very high TB incidence countries** |                                     |                       |                         |                           |                             |                          |
| Base case             | 3.87                                 | 184,357               | 13,666.32               | 8.12                      | NC                          | NC                       |
| SEQ/RIF               | 27.45                                | 263,628               | 13,870.25               | 5.18                      | 36.23                       | 20,165                   |
| IGRA/RIF              | 33.86                                | 268,840               | 13,671.50               | 4.41                      | 45.61                       | 16,291                   |
| TST/RIF               | 49.82                                | 318,025               | 13,670.32               | 5.62                      | 30.76                       | 33,403‡                  |
| TST/INH               | 49.82                                | 318,435               | 13,671.23               | 4.86                      | 40.16                       | 27,296‡                  |
| IGRA/INH              | 33.86                                | 337,716               | 13,671.02               | 4.97                      | 38.82                       | 32,657‡                  |
| TST/INH               | 49.82                                | 415,877               | 13,669.91               | 5.33                      | 34.34                       | 64,494‡                  

*Very high incidence: >200 cases per 100,000; high incidence: >100 and <200 cases/100,000; moderate incidence, ≥30 and <100 cases/100,000; low incidence: <30 cases/100,000. IGRA, interferon-gamma release assay; INH, isoniazid; NC, not calculable; QALY, quality-adjusted life year; RIF, rifampin; SEQ, sequential screening; TB, tuberculosis; TST, tuberculin skin test.

†The cost per QALY gained is calculated in comparison to the base case. Dominated indicates that an intervention strategy has higher costs and worse outcomes compared to the base case. Costs are in CAD.

‡This intervention strategy is strictly dominated by another intervention strategy. It is more expensive and has worse outcomes.
screening became permanent residents, the cost-effectiveness ratio increased 60% to \(\approx 26,000\) when the intervention strategy was IGRA coupled with rifampin. Another consideration is the feasibility of the intervention. In a country like Canada, 2%–3% of new permanent residents are requested to follow up postarrival based on preimmigration medical exams (3,15). If the country implemented preimmigration IGRA screening for migrants from moderate- to very high-incidence countries, 17.6% would be requested to follow up postarrival (3,15). However, coupling IGRA with postarrival rifampin treatment could prevent 3.9% of all TB cases in Canada in the first year (3,12,15). Applied to new permanent residents to Canada in 2014, this process would increase the number requested to follow up postarrival from 6,100 to 45,800 but would result in the prevention of 61 TB cases in the first year (1 case prevented/651 additional postarrival referrals). If this process were then consistently implemented in successive cohorts in the future, it could annually prevent \(\approx 400\) TB cases.

Regardless of how preimmigration LTBI screening is implemented, investment in LTBI infrastructure in high TB incidence settings will be essential for global TB elimination. Evidence suggests that introduction of routine preimmigration TB screening in many high-income, low-incidence countries has played a role in improving infrastructure for TB programs in low-resource areas (41). Further introducing LTBI screening as part of these routine medical exams may have similar impact.

The cost-effectiveness of preimmigration LTBI screening and postarrival treatment has not been evaluated since 2003. Previously, Schwartzman and Menzies (42) examined the idea of preimmigration TST screening in addition to

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**Figure 2.** Cost-effectiveness acceptability curves of the base case of no intervention compared with intervention strategies in evaluation of screening and treatment of latent tuberculosis infection in immigrants. The graphs demonstrate the probability that an option is more cost-effective at various willingness-to-pay thresholds per quality-adjusted life year gained. A) Comparison of the base case with the intervention strategy of preimmigration SEQ screening coupled with postarrival RIF treatment among migrants from low-incidence countries. B) Comparison of the base case with the intervention strategy of preimmigration IGRA screening coupled with postarrival rifampin treatment among migrants from moderate-incidence countries. C) Comparison of the base case with the intervention strategy of preimmigration IGRA screening coupled with postarrival RIF treatment among migrants from high-incidence countries. D) Comparison of the base case with the intervention strategy of preimmigration IGRA screening coupled with postarrival RIF treatment among migrants from very high-incidence countries. IGRA, interferon-gamma release assay; RIF, rifampin; SEQ, sequential.
standard preimmigration chest radiograph coupled with post-
arrival isoniazid treatment. They found the cost per TB case
prevented was approximately Can $94,500. In our study, us-
ing this intervention strategy in very high incidence countries
resulted in a cost per TB case prevented of approximately Can
$83,000. Schwartzman et al. (43) later investigated the cost
associated with performing a TST in all new legal immigrants
from Mexico, a low-incidence country, and coupling it with
postarrival isoniazid treatment. This resulted in a cost per TB
case prevented of $1.2 million (2016 Can $). Using this same
intervention strategy in our study resulted in a cost per TB
case prevented of $1.1 million (2016 Can $). By evaluating
new strategies applied to a variety of TB incidence settings,
our study represents a much-needed update to the literature.

Our analysis has several strengths. Use of discrete
event simulation enabled realistic modeling of time spent
in various health states, which is difficult to implement
in Markov models. This type of model also allowed age-
representative modeling of new migrants for application
of age-adjusted LTBI prevalence. The source of most of
the cost data was the British Columbia Center for Disease
Control, which handles most TB cases in the province of
British Columbia. This analysis estimated LTBI prevalence
and abnormal chest radiograph prevalence using several
years of immigration and TB data from Ontario. The data
are likely to be generalizable, because Ontario accepts 40%
of new permanent residents (12) and the data fit well with
reported LTBI prevalence estimates (16), suggesting these
parameters are reflective of long-term TB trends.

In this study, we assumed that all migrants were rec-
ommended postarrival LTBI treatment when they had
a positive LTBI diagnostic test, which is not necessarily
true; for some persons, the risk for serious adverse events
may outweigh the benefit of treatment. Social factors and
concurrent conditions may increase the risk for reactiva-
tion of LTBI. We have shown that the benefits of rifampin
treatment for migrants from moderate- to very high–in-
cidence countries who test positive by IGRA preimmi-
gration outweigh the potential risks of adverse events.
However, in practice, individual adverse-event risk is con-
sidered, and treatment may not be offered to all migrants.
Further research designed to identify the specific popula-
tions who should be offered treatment would help inform
future analyses.

We derived the reactivation rate of LTBI from the lit-
erature, but because many of those studies were based on
TB incidence in those who were positive by TST, it is pos-
sible that the predictive value of the TST caused underesti-
mation of true reactivation rates. Our analysis did not con-
sider 3 months of once-weekly isoniazid and rifapentine as
an LTBI treatment modality because it was not universally
available. Literature data, however, suggest this modality
may yield similar results to rifampin treatment (44).

Our analysis used a healthcare system perspective,
which does not consider costs incurred by persons expe-
riencing the intervention (45). It is possible that consid-
eration of costs and benefits from a societal perspective
would change the results of this analysis; however, it is also
likely that this difference would strengthen the preference
for screening with IGRA, which requires only 1 visit, in-
stead of TST, which requires 2, due to reduced absenteeism
associated with IGRA testing. Costs per QALY gained may
increase for all strategies if the time costs for migrants to
follow up for LTBI treatment were considered. Finally, we
assumed that TB reactivation was constant, which, while
demonstrated previously (18), contradicts the common par-
adigm of decreasing risk over time (46). Where possible,
we performed sensitivity analyses to view the effects our
limitations may have on our results to better inform deci-
dion makers.

In conclusion, preimmigration IGRA screening
coupled with postarrival rifampin treatment among
migrants from countries with moderate to very high
incidence of TB resulted in the lowest cost-effectiveness
ratios. This evidence can be used to support policy
decisions surrounding preimmigration LTBI screening
in high-income, immigrant-receiving countries, when
coupled with evaluations on program implementation,
acceptability, and sustainability. Next steps in research
should be to identify subgroups at highest risk for
progression to TB disease to limit individual risk
associated with LTBI treatment and improve the
likelihood of feasibility and sustainability.

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created the model, performed data analysis and interpretation,
and drafted the manuscript. J.C.J. provided expert input on the
data informing the model, data interpretation, and performed
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provided expert input on the data informing the model and edited
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interpretation and edited the manuscript. F.M. reviewed the
model inputs collected and the data analysis, provided expert
input for data interpretation, and edited the manuscript. All
authors approved the study objective, design, and final manuscript.
About the Author

Dr. Campbell received his PhD from the University of British Columbia in Vancouver and is currently a postdoctoral fellow at McGill University in Montreal, Quebec, Canada. His primary research interests include health economics, evidence-based public health policy, and infectious disease.

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Tuberculosis (TB) remains a major cause of illness and death in the 21st century. There were an estimated 9.6 million incident cases worldwide in 2014. In addition, an estimated 3.3% of new cases and 20% of retreatment cases are multidrug-resistant TB (MDR TB), which is defined as TB resistant to at least rifampin and isoniazid, the 2 most powerful first-line drugs. This resistance threatens global TB control efforts. MDR TB patients need access to treatment, require longer treatment with toxic medications, and have a lower probability of cure.
Cost-effectiveness of Latent Tuberculosis Infection Screening before Immigration to Low-Incidence Countries

Appendix

Cost-effectiveness Ratio Calculation

To calculate the incremental cost-effectiveness ratio (ICER), the difference in costs between an intervention strategy ($Cost_i$) and the base case ($Cost_b$) is divided by the difference in quality-adjusted life years (QALYs) between an intervention strategy ($QALY_i$) and the base case ($QALY_b$). This is calculated through the formula:

$$ ICER = \frac{Cost_i - Cost_b}{QALY_i - QALY_b} $$

This value can then be compared to a policy maker’s willingness-to-pay (WTP) threshold. A value below this threshold is considered cost-effective and can be used as a component supporting new policies.

Efficiency Frontier

The efficiency frontier plots the costs and QALYs of each intervention and connects interventions that provide the next best option in terms of costs and QALYs. Interventions not on the frontier are either dominated by other interventions (i.e., they have higher costs and lower QALYs than other interventions) or are excluded due to extended dominance (i.e., a more expensive intervention provides a lower ICER). The values listed adjacent to lines along the frontier represent the ICER of going from one intervention to the next and can be used to support policy makers decisions on optimal intervention strategies.
Probability of Creating a Secondary Tuberculosis Case Calculation

We assumed that 85% of tuberculosis (TB) cases from our data source were due to reactivation of previously acquired latent TB infection (LTBI). To account for the remaining cases, we modeled the creation of secondary cases when a case of reactivation TB occurred. The formula based on this assumption is:

\[
\text{Probability of Creating a Secondary Case} = \left( \frac{1}{0.85} \right) - 1 = 17.6\%
\]

In this way, all TB cases are accounted for in this model and we minimize underestimation of overall longitudinal TB burden. Further to this, the method of modeling secondary cases will result in reductions in TB transmission as incidence of TB reactivation is reduced – in this way TB transmission was directly tied to incidence of TB reactivation.

Meta-Analysis of Reported Rates of Post-Arrival Reporting for Passive Follow-Up

A meta-analysis was performed using Stata software, version 12.1 (StataCorp, www.stata.com). To complete this, logit-transformed proportions were meta-analyzed using random-effects. The weighted pooled point estimate was back transformed into a proportion for ease of interpretation (Appendix Figure 1). The result of this meta-analysis is that 68.4% (95% CI: 64.6% to 72.1%) of those referred for passive (unenforced) post-arrival follow-up actually attend the clinic post-arrival.

Additional Sensitivity Analysis

Probabilistic Sensitivity Analysis

Probabilistic sensitivity analysis (PSA) was performed to assess the uncertainty in parameters and their impact on decisions. To complete this, probabilistic distributions are created and sampled each replication. When detailed cost data was available and known to fall within well-defined ranges, costs were modeled with a triangular distribution; when cost data was more uncertain, a gamma distribution, which can accommodate skewed cost data, was used. Beta distributions were used for most probabilities. When literature data was available and exact proportions of persons experiencing an event could be calculated, \( \beta \) distributions parameters
were defined as: $\alpha =$ number of persons experiencing event; $\beta =$ number of persons not experiencing event. If this level of detail was not known, a $\beta$ distribution was fit to represent reported 95% CI or means and standard deviations. In the case of treatment effect, lognormal distributions were used based on 2x2 tables of effectiveness or fit to our perceived level of uncertainty. For sampling health state utilities, we first sampled from the distribution of the healthy QALY. We assumed those with LTBI would have the same value. For TB and hospitalization QALYs, we sampled from distributions to decrement these QALYs based on the sampled healthy QALY.

The average results of the PSA are reported in Appendix Table 1. Variability can be seen through plots of the differences in costs and QALYs on a cost-effectiveness plane for the PSA of select strategies (Appendix Figure 2). The results of the PSA support the findings from the deterministic analysis: the intervention strategy of preimmigration interferon-gamma release assay (IGRA) screening coupled with postarrival follow-up and treatment with rifampin was the preferred strategy in migrants from moderate- to very high-incidence countries. Further analysis of the relationship between decisions is provided below in efficiency frontiers.

Efficiency frontiers are displayed in Appendix Figure 3. In each of the plotted frontiers, only one intervention was included on the frontier, with others excluded due to strict or extended dominance. Among migrants from low-incidence countries, only SEQ/RIF fell on the frontier, while among migrants from moderate high and very high-incidence countries, only IGRA/RIF fell on the frontier.

**Exploratory Sensitivity Analysis**

Various exploratory sensitivity analyses were performed. We analyzed the impact of limiting LTBI screening by age on outcomes. We then analyzed the impact certain parameters may have on cost-effectiveness including: modeling low LTBI therapy uptake postarrival, ensuring 100% adherence in postarrival follow-up, ensuring 100% adherence and participation in all steps of the LTBI cascade of care, extending the time horizon, altering TB reactivation rate, and modeling high and low estimates of costs.

Parameter changes evaluated for exploratory sensitivity analysis are listed in Appendix Table 2. In the case of varying the reactivation rate, LTBI prevalence estimates were also adjusted to reflect the expected TB incidence based on data used to calibrate these parameters in
the base analysis. This would result in nearly identical number of overall TB cases over the time horizon, but costs due to increasing or decreasing LTBI prevalence will change.

Results of exploratory analyses are presented in Appendix Tables 3–6. Only screening certain portions of new migrants based on age did not significantly impact cost per QALY gained but did lessen the overall reductions in TB incidence seen. Mandating postarrival follow-up improved the reduction in TB incidence by 40% compared with a passive system. On the contrary, if we modeled initiation of LTBI therapy at an extreme low value of 63.5%, reduction in TB incidence was reduced by $\approx$30%. This further impacted decisions on which intervention strategy was likely to be the most cost-effective. Fully mandating all parts of the LTBI cascade of care (i.e., all those test-positive must follow-up postarrival and complete treatment, except in cases of adverse events) increased overall costs of intervention strategies $\approx$40%, but overall reductions in TB incidence exceeded 80%.

Using a lifetime time horizon significantly improved cost-effectiveness of intervention strategies. Adjusting reactivation rate or costs did not significantly impact cost-effectiveness but did impact the overall cost of intervention strategies. In the case of adjusting reactivation rate, this was due to increasing or decreasing the number of persons with LTBI.

### Appendix Table 1. Average PSA results of implementing intervention strategies in various TB incidence settings

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, $† |
|--------------|--------------|-----------------|--------------------|-----------------------------|---------------------|
| **Low TB incidence** | | | | | |
| Base case | 9,653 | 13,797.86 | 0.40 | NC | NC |
| SEQ/RIF | 60,425 | 13,798.51 | 0.27 | 33.76 | 77,885 |
| SEQ/INH | 76,006 | 13,798.11 | 0.29 | 26.41 | 228,858† |
| IGRA/RIF | 75,449 | 13,798.32 | 0.23 | 43.35 | 143,563‡ |
| IGRA/INH | 86,579 | 13,798.19 | 0.25 | 37.03 | 233,564‡ |
| TST/RIF | 121,260 | 13,798.08 | 0.25 | 38.07 | 498,153‡ |
| TST/INH | 163,467 | 13,798.06 | 0.27 | 33.63 | 751,114‡ |
| **Moderate TB incidence** | | | | | |
| Base case | 59,131 | 13,770.72 | 2.51 | NC | NC |
| SEQ/RIF | 121,736 | 13,771.95 | 1.62 | 35.45 | 50,590§ |
| IGRA/RIF | 125,439 | 13,772.73 | 1.38 | 44.92 | 32,938 |
| SEQ/INH | 142,037 | 13,772.33 | 1.72 | 31.53 | 51,332‡ |
| IGRA/INH | 151,623 | 13,772.54 | 1.53 | 39.12 | 50,769‡ |
| TST/RIF | 207,659 | 13,772.66 | 1.52 | 39.47 | 76,512‡ |
| TST/INH | 281,239 | 13,772.58 | 1.64 | 34.53 | 119,301‡ |
| **High TB incidence** | | | | | |
| Base case | 124,384 | 13,733.54 | 5.43 | NC | NC |
| SEQ/RIF | 195,166 | 13,737.25 | 3.52 | 35.16 | 19,047§ |
| IGRA/RIF | 198,604 | 13,738.15 | 3.04 | 44.01 | 16,093 |
| SEQ/INH | 232,435 | 13,736.49 | 3.76 | 30.82 | 36,612‡ |
| IGRA/INH | 245,804 | 13,737.39 | 3.31 | 38.99 | 31,501‡ |
| TST/RIF | 266,307 | 13,737.79 | 3.31 | 38.99 | 33,343‡ |
| TST/INH | 352,574 | 13,737.35 | 3.58 | 34.05 | 59,891‡ |
| **Very high TB incidence** | | | | | |
| Base case | 184,977 | 13,696.10 | 8.13 | NC | NC |
| SEQ/RIF | 265,405 | 13,701.78 | 5.31 | 34.66 | 14,163§ |
| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, $ |
|--------------|--------------|-----------------|-------------------|-----------------------------|-----------------|
| IGRA/RIF     | 268,953      | 13,702.93       | 4.58              | 43.67                       | 12,299          |
| SEO/INH      | 320,020      | 13,700.59       | 5.68              | 30.12                       | 30,062†         |
| TST/RIF      | 322,422      | 13,702.09       | 5.00              | 38.48                       | 22,941‡         |
| IGRA/INH     | 337,776      | 13,701.61       | 5.03              | 38.12                       | 27,709‡         |
| TST/INH      | 420,458      | 13,701.09       | 5.39              | 33.70                       | 47,149‡         |

*All costs in 2016 CAD. Dominated: This intervention strategy has higher costs and worse outcomes compared to the base case. §All costs in 2016 CAD. Dominated: This intervention strategy has higher costs and worse outcomes compared to the base case. ‡Very high incidence, >200 cases per 100,000; high incidence, 100 and <200 cases/100,000; moderate incidence, 30 and <100 cases/100,000; low incidence, <30 cases/100,000. §This intervention strategy is strictly dominated by another intervention strategy. It is more expensive and has worse outcomes. ‡This intervention strategy is extendedly dominated by another intervention strategy. While it increases QALYs, it has a higher ICER rather than a more expensive intervention strategy.

### Appendix Table 2. Parameter changes for the exploratory sensitivity analysis*

| Parameter                  | Original estimate | Exploratory sensitivity analysis estimate(s), range |
|----------------------------|-------------------|---------------------------------------------------|
| Full INH treatment         | $992              | $804, $1,179                                      |
| Full RIF treatment         | $575              | $464, $686                                       |
| Partial INH treatment      | $462              | $174, $804                                       |
| Partial RIF treatment      | $319              | $178, $464                                       |
| Complete TST               | $31               | $24, $38                                        |
| Incomplete TST             | $21               | $17, $25                                        |
| IGRA                       | $54               | $31, $62                                        |
| Tuberculosis               | $20,532           | $7,141, $39,525                                  |
| LTBI adverse event         | $732              | $549, $916                                       |
| Hospitalization            | $6641             | $5,305, $9,985                                   |
| Death                      | $26,933           | $13,079, $40,788                                 |
| Initiate treatment         | 93.8%             | 100%                                             |
| Complete INH               | 61.6%             | 100%                                             |
| Complete RIF               | 81.4%             | 100%                                             |
| Annual reactivation rate†  | 0.11%             | 0.09%; 0.13%                                    |
| Time horizon               | 25 y              | Lifetime                                         |
| Adherence to post-arrival follow-up | 68.4% | 100% |

*All costs in 2016 CAD. §INH, isoniazid; IGRA, interferon-gamma release assay; LTBI, latent tuberculosis infection; RIF, rifampin; TST, tuberculin skin test.
†Also changes the prevalence of LTBI.

### Appendix Table 3. Results of exploratory sensitivity analyses in TB screening in migrants from low TB incidence countries*

| Intervention       | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, $ |
|--------------------|--------------|-----------------|-------------------|-----------------------------|-----------------|
| Only screen persons ≤60 y of age |                |                 |                   |                             |                 |
| Base case          | 9,681        | 13,761.03       | 0.41              | NC                          | NC              |
| SEO/RIF            | 58,830       | 13,761.33       | 0.26              | 35.00                       | 166,639         |
| SEO/INH            | 65,133       | 13,761.11       | 0.29              | 28.20                       | 767,845†        |
| IGRA/RIF           | 77,220       | 13,761.25       | 0.23              | 44.02                       | 312,764‡        |
| IGRA/INH           | 87,622       | 13,761.10       | 0.26              | 37.10                       | 1,243,726‡      |
| TST/RIF            | 116,550      | 13,760.62       | 0.25              | 38.07                       | Dominated       |
| TST/INH            | 156,102      | 13,760.67       | 0.27              | 33.35                       | Dominated       |

| Only screen persons ≤35 y of age |                |                 |                   |                             |                 |
| Base case          | 9,681        | 13,761.03       | 0.41              | NC                          | NC              |
| SEO/RIF            | 45,484       | 13,761.34       | 0.34              | 16.46                       | 118,623         |
| SEO/INH            | 49,337       | 13,761.11       | 0.35              | 12.80                       | 501,351†        |
| IGRA/RIF           | 59,255       | 13,761.26       | 0.33              | 19.69                       | 222,482‡        |
| IGRA/INH           | 66,138       | 13,761.10       | 0.34              | 15.84                       | 811,778‡        |
| TST/RIF            | 89,077       | 13,760.62       | 0.35              | 14.71                       | Dominated       |
| TST/INH            | 117,358      | 13,760.68       | 0.34              | 16.50                       | Dominated       |

| Only screen persons 10–60 y of age |                |                 |                   |                             |                 |
| Base case          | 9,681        | 13,761.03       | 0.41              | NC                          | NC              |
| SEO/RIF            | 50,922       | 13,761.33       | 0.28              | 31.13                       | 138,216         |
| SEO/INH            | 55,929       | 13,761.11       | 0.29              | 29.15                       | 611,279‡        |
| IGRA/RIF           | 66,222       | 13,761.25       | 0.24              | 39.86                       | 257,727‡        |
| IGRA/INH           | 75,153       | 13,761.10       | 0.27              | 34.48                       | 990,386‡        |
| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, $ |
|--------------|---------------|-----------------|------------------|--------------------------|-------------------|
| TST/RIF      | 99,155        | 13,760.62       | 0.26             | 34.80                    | Dominated         |
| TST/INH      | 132,435       | 13,760.68       | 0.28             | 31.05                    | Dominated         |

Only 63.5% initiate therapy after arrival
- Base case: 9,459, 13,760.96, 0.41, NC, NC
- SEQ/RIF: 58,376, 13,761.30, 0.30, 25.75, 143,147
- SEQ/INH: 62,759, 13,761.20, 0.32, 21.79, 224,620
- IGRA/RIF: 75,049, 13,761.22, 0.28, 32.26, 255,693
- IGRA/INH: 82,340, 13,761.16, 0.29, 27.98, 386,844
- TST/RIF: 96,641, 13,760.75, 0.29, 29.46, Dominated
- TST/INH: 124,688, 13,760.68, 0.31, 23.79, Dominated

100% Adherence to post-arrival follow-up
- Base case: 9,937, 13,761.12, 0.40, NC, NC
- SEQ/RIF: 65,283, 13,761.84, 0.19, 52.25, 77,011
- SEQ/INH: 74,668, 13,761.48, 0.23, 44.11, 178,931
- IGRA/RIF: 68,258, 13,761.73, 0.14, 64.91, 129,787
- IGRA/INH: 104,144, 13,761.66, 0.18, 55.75, 176,541
- TST/RIF: 158,280, 13,761.05, 0.17, 58.17, Dominated
- TST/INH: 218,474, 13,761.03, 0.20, 50.85, Dominated

No losses in the LTBI cascade of care
- Base case: 10,173, 13,761.32, 0.39, NC, NC
- SEQ/RIF: 65,488, 13,762.28, 0.15, 60.59, 57,335
- SEQ/INH: 79,499, 13,762.13, 0.17, 57.04, 85,631
- IGRA/RIF: 89,899, 13,762.27, 0.08, 78.12, 822,940
- IGRA/INH: 112,814, 13,762.16, 0.10, 75.41, 122,324
- TST/RIF: 164,894, 13,762.19, 0.12, 68.64, 176,445
- TST/INH: 258,857, 13,762.15, 0.13, 65.48, 299,189

Reactivation rate is 0.9 cases/1,000 PY
- Base case: 9,709, 13,760.03, 0.41, NC, NC
- SEQ/RIF: 61,978, 13,760.30, 0.25, 38.35, 195,474
- SEQ/INH: 68,898, 13,760.08, 0.28, 31.52, 1,324,840
- IGRA/RIF: 81,411, 13,760.22, 0.22, 45.03, 380,575
- IGRA/INH: 92,642, 13,760.07, 0.24, 40.56, 2,359,934
- TST/RIF: 121,635, 13,759.59, 0.24, 40.74, Dominated
- TST/INH: 163,310, 13,759.64, 0.27, 35.05, Dominated

Reactivation rate is 1.3 cases/1,000 PY
- Base case: 9,533, 13,761.67, 0.40, NC, NC
- SEQ/RIF: 60,332, 13,761.94, 0.26, 35.38, 189,954
- SEQ/INH: 66,632, 13,761.72, 0.29, 27.67, 1,277,446
- IGRA/RIF: 79,335, 13,761.86, 0.22, 45.67, 370,447
- IGRA/INH: 89,844, 13,761.71, 0.25, 37.93, 2,285,044
- TST/RIF: 120,192, 13,761.23, 0.24, 41.31, Dominated
- TST/INH: 161,282, 13,761.28, 0.26, 34.15, Dominated

Lifetime time horizon
- Base case: 13,375, 20,735.49, 0.57, NC, NC
- SEQ/RIF: 63,180, 20,735.79, 0.35, 38.24, 161,566
- SEQ/INH: 69,518, 20,735.76, 0.39, 30.40, 203,916
- IGRA/RIF: 82,257, 20,736.47, 0.32, 44.05, 69,939
- IGRA/INH: 93,122, 20,735.95, 0.35, 37.45, 173,790
- TST/RIF: 123,069, 20,734.57, 0.34, 40.34, Dominated
- TST/INH: 164,387, 20,735.02, 0.37, 33.97, Dominated

Minimum estimated costs
- Base case: 7,709, 13,761.03, 0.41, NC, NC
- SEQ/RIF: 45,709, 13,761.30, 0.26, 36.87, 142,099
- SEQ/INH: 51,306, 13,761.08, 0.28, 32.00, 975,411
- IGRA/RIF: 52,694, 13,761.22, 0.22, 46.16, 238,752
- IGRA/INH: 62,376, 13,761.07, 0.25, 39.07, 1,555,483
- TST/RIF: 99,230, 13,760.59, 0.24, 40.08, Dominated
- TST/INH: 135,984, 13,760.65, 0.27, 34.12, Dominated

Maximum estimated costs
- Base case: 11,653, 13,761.03, 0.41, NC, NC
- SEQ/RIF: 72,938, 13,761.30, 0.26, 36.87, 229,171
- SEQ/INH: 79,963, 13,761.08, 0.28, 32.00, 1,528,335
- IGRA/RIF: 92,536, 13,761.22, 0.22, 46.16, 429,269
- IGRA/INH: 104,750, 13,761.07, 0.25, 39.07, 2,648,963
- TST/RIF: 142,655, 13,760.59, 0.24, 40.08, Dominated
- TST/INH: 188,544, 13,760.65, 0.27, 34.12, Dominated
Appendix Table 4. Results of exploratory sensitivity analyses in migrants from moderate TB incidence countries*

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, $† |
|--------------|---------------|-----------------|-------------------|-----------------------------|---------------------|
| Only screen persons ≤60 y of age | | | | | |
| Base case | 58,301 | 13,735.03 | 2.47 | NC | NC |
| SEQ/RIF | 118,834 | 13,736.66 | 1.64 | 33.66 | 37,076§ |
| IGRA/RIF | 129,679 | 13,736.95 | 1.41 | 42.91 | 34,924§ |
| SEQ/INH | 137,416 | 13,736.01 | 1.74 | 29.41 | 80,574§ |
| IGRA/INH | 149,533 | 13,736.94 | 1.56 | 36.67 | 47,669§ |
| TST/RIF | 199,887 | 13,737.13 | 1.54 | 37.55 | 67,186§ |
| TST/INH | 268,497 | 13,736.27 | 1.67 | 32.52 | 168,567§ |
| Only screen persons ≤35 y of age | | | | | |
| Base case | 58,301 | 13,735.03 | 2.47 | NC | NC |
| SEQ/RIF | 98,543 | 13,736.00 | 2.09 | 15.25 | 31,697‡ |
| IGRA/RIF | 103,655 | 13,736.59 | 2.00 | 18.90 | 29,012 |
| SEQ/INH | 107,793 | 13,735.65 | 2.13 | 13.94 | 79,979§ |
| IGRA/INH | 116,023 | 13,736.58 | 2.07 | 16.28 | 37,222§ |
| TST/RIF | 159,486 | 13,736.77 | 2.04 | 17.56 | 58,010§ |
| TST/INH | 206,294 | 13,735.91 | 2.11 | 14.55 | 167,437§ |
| Only screen persons 10–60 y of age | | | | | |
| Base case | 58,301 | 13,735.03 | 2.47 | NC | NC |
| SEQ/RIF | 108,704 | 13,736.57 | 1.68 | 31.89 | 32,638‡ |
| IGRA/RIF | 114,669 | 13,736.88 | 1.49 | 39.59 | 30,343 |
| SEQ/INH | 125,466 | 13,735.94 | 1.79 | 27.63 | 73,548§ |
| IGRA/INH | 135,916 | 13,736.87 | 1.63 | 34.05 | 42,064§ |
| TST/RIF | 176,404 | 13,737.07 | 1.59 | 35.78 | 57,931§ |
| TST/INH | 235,861 | 13,736.21 | 1.75 | 29.27 | 150,695§ |
| Only 63.5% initiate therapy after arrival | | | | | |
| Base case | 58,301 | 13,734.92 | 2.50 | NC | NC |
| SEQ/RIF | 117,154 | 13,736.00 | 1.84 | 26.33 | 54,608§ |
| IGRA/RIF | 123,323 | 13,736.33 | 1.70 | 32.08 | 46,250 |
| SEQ/INH | 130,963 | 13,735.79 | 1.93 | 22.58 | 83,767§ |
| IGRA/INH | 140,730 | 13,736.09 | 1.81 | 27.61 | 70,514§ |
| TST/RIF | 170,321 | 13,736.57 | 1.78 | 28.69 | 67,777§ |
| TST/INH | 218,771 | 13,736.42 | 1.87 | 25.25 | 107,079§ |
| 100% Adherence to post-arrival follow-up | | | | | |
| Base case | 58,301 | 13,734.93 | 2.45 | NC | NC |
| SEQ/RIF | 130,209 | 13,737.12 | 1.18 | 51.75 | 32,935‡ |
| IGRA/RIF | 139,318 | 13,738.23 | 0.83 | 66.10 | 24,577 |
| SEQ/INH | 159,527 | 13,736.93 | 1.36 | 44.67 | 50,690§ |
| IGRA/INH | 177,134 | 13,737.59 | 1.09 | 55.63 | 44,712§ |
| TST/RIF | 262,181 | 13,737.91 | 1.02 | 58.50 | 68,474§ |
| TST/INH | 367,517 | 13,737.10 | 1.23 | 49.65 | 142,888§ |
| No losses in the LTBI cascade of care | | | | | |
| Base case | 60,621 | 13,735.17 | 2.33 | NC | NC |
| SEQ/RIF | 127,849 | 13,737.68 | 0.92 | 60.38 | 26,863§ |
| IGRA/RIF | 136,690 | 13,738.68 | 0.52 | 77.51 | 21,717 |
| SEQ/INH | 169,175 | 13,737.77 | 0.98 | 57.87 | 41,819§ |
| IGRA/INH | 188,938 | 13,738.41 | 0.60 | 74.47 | 39,639§ |
| TST/RIF | 269,509 | 13,738.19 | 0.76 | 67.35 | 69,219§ |
| TST/INH | 429,117 | 13,737.59 | 0.81 | 65.19 | 152,307§ |
| Reactivation rate is 0.9 cases/1,000 PY | | | | | |
| Base case | 59,005 | 13,729.18 | 2.50 | NC | NC |
| SEQ/RIF | 127,864 | 13,730.85 | 1.57 | 37.06 | 41,217‡ |
| IGRA/RIF | 135,775 | 13,731.33 | 1.34 | 46.46 | 35,627 |
| SEQ/INH | 150,721 | 13,730.75 | 1.71 | 31.77 | 58,282§ |
| IGRA/INH | 164,567 | 13,731.44 | 1.50 | 40.17 | 46,683§ |

*All costs in 2016 Can $. Dominated: This intervention strategy has higher costs and worse outcomes compared with the base case. IGRA, interferon-gamma release assay; INH, isoniazid; NC, not calculable; QALY, quality-adjusted life year; RIF, rifampin; SEQ, sequential screening; TB, tuberculosis; TST, tuberculin skin test.
†The cost per QALY gained is calculated in comparison to the base case.
‡This intervention strategy is strictly dominated by another intervention strategy. It is more expensive and has worse outcomes.
§This intervention strategy is extendedly dominated by another intervention strategy. While it increases QALYs, it has a higher ICER than a more expensive intervention strategy.

% Reduction in TB incidence calculated with base case.
Table 5. Results of exploratory sensitivity analyses in migrants from high TB incidence countries

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($) |
|--------------|--------------|------------------|--------------------|-----------------------------|----------------------|
| Only screen persons <60 y of age | | | | | |
| Base case | 122,928 | 13,702.56 | 5.39 | NC | NC |
| SEQ/RIF | 189,766 | 13,703.94 | 3.57 | 33.80 | 48,452‡ |
| IGRA/RIF | 195,130 | 13,705.08 | 3.08 | 42.80 | 28,627 |
| SEQ/INH | 223,538 | 13,703.44 | 3.80 | 29.51 | 113,251§ |
| IGRA/INH | 239,543 | 13,704.43 | 3.43 | 36.35 | 62,167§ |
| TST/RIF | 256,075 | 13,705.02 | 3.34 | 38.07 | 54,092† |
| TST/INH | 336,983 | 13,704.39 | 3.66 | 32.05 | 117,017§ |
| Only screen persons <35 y of age | | | | | |
| Base case | 122,928 | 13,702.56 | 5.39 | NC | NC |
| SEQ/RIF | 162,376 | 13,703.32 | 4.56 | 15.42 | 51,575‡ |
| IGRA/RIF | 166,890 | 13,705.57 | 4.36 | 19.13 | 43,327 |
| SEQ/INH | 177,765 | 13,703.19 | 4.64 | 13.78 | 86,006§ |
| IGRA/INH | 186,811 | 13,703.28 | 4.49 | 16.73 | 88,102§ |
| TST/RIF | 213,873 | 13,703.41 | 4.44 | 17.59 | 107,075§ |
| TST/INH | 263,567 | 13,702.20 | 4.60 | 14.65 | 215,255§ |
| Only screen persons 10–60 y of age | | | | | |
| Base case | 122,928 | 13,702.56 | 5.39 | NC | NC |
| SEQ/RIF | 179,377 | 13,704.28 | 3.70 | 31.33 | 32,716‡ |
| IGRA/RIF | 183,730 | 13,705.06 | 3.24 | 39.78 | 24,321 |
| SEQ/INH | 210,766 | 13,703.81 | 3.94 | 26.87 | 70,087§ |
| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| IGRA/INH     | 223,488        | 13,704.55       | 3.56              | 33.89                     | 50,319§                |
| TST/RIF      | 235,007        | 13,704.25       | 3.50              | 34.96                     | 66,195§               |
| TST/INH      | 304,261        | 13,704.11       | 3.77              | 30.10                     | 116,849§              |

Only 63.5% initiate therapy after arrival

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| Base case    | 123,493        | 13,701.90       | 5.46              | NC                        | NC                     |
| TST/INH      | 287,689        | 13,703.11       | 4.12              | 24.65                     | 135,974§               |

100% adherence to post-arrival follow-up

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| Base case    | 123,590        | 13,701.71       | 5.32              | NC                        | NC                     |
| TST/INH      | 441,135        | 13,705.29       | 2.71              | 49.10                     | 88,850§                |

No losses in the LTBI cascade of care

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| Base case    | 123,337        | 13,702.66       | 5.13              | NC                        | NC                     |
| TST/INH      | 501,470        | 13,705.89       | 1.80              | 64.93                     | 116,949§               |

Reactivation rate is 0.9 cases/1,000 PY

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| Base case    | 123,878        | 13,689.10       | 5.42              | NC                        | NC                     |
| TST/INH      | 359,562        | 13,691.89       | 3.51              | 35.11                     | 84,512§                |

Reactivation rate is 1.3 cases/1,000 PY

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| Base case    | 122,758        | 13,710.67       | 5.38              | NC                        | NC                     |
| TST/INH      | 377,756        | 20,404.24       | 4.97              | 33.69                     | 106,493§               |

Lifetime time horizon

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| Base case    | 97,691         | 13,702.56       | 5.39              | NC                        | NC                     |
| TST/INH      | 291,076        | 13,704.15       | 3.54              | 34.36                     | 121,070§               |

Minimum estimated costs

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| Base case    | 148,167        | 13,702.56       | 5.39              | NC                        | NC                     |
| TST/INH      | 406,415        | 13,704.15       | 3.54              | 34.36                     | 161,677§               |

Maximum estimated costs

| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($)† |
|--------------|----------------|-----------------|-------------------|---------------------------|------------------------|
| Base case    | 230,715        | 13,704.35       | 3.44              | 36.06                     | 34,699§                |
| TST/INH      | 287,910        | 13,704.35       | 3.28              | 39.21                     | 77,883§                |
| Intervention | Cost/1,000, $ | No. QALYs/1,000 | No. TB cases/1,000 | % Reduction in TB incidence | Cost/QALY gained, ($) |
|---------------|-------------|-----------------|-------------------|-----------------------------|---------------------|
| Only screen persons ≤60 y of age | | | | | |
| Base case | 184,357 | 13,666.32 | 8.12 | NC | NC |
| SEQ/RIF | 257,138 | 13,670.07 | 5.36 | 33.99 | 19,422‡ |
| IGRA/RIF | 262,010 | 13,671.02 | 4.64 | 42.77 | 16,507‡ |
| SEQ/INH | 307,723 | 13,669.52 | 5.78 | 28.79 | 38,514§ |
| TST/RIF | 310,389 | 13,670.59 | 5.05 | 37.82 | 29,494§ |
| IGRA/INH | 325,585 | 13,669.95 | 5.16 | 36.45 | 38,909§ |
| TST/INH | 402,151 | 13,669.61 | 5.52 | 32.05 | 66,187§ |
| Only screen persons <35 y of age | | | | | |
| Base case | 184,357 | 13,666.32 | 8.12 | NC | NC |
| SEQ/RIF | 223,125 | 13,668.52 | 6.89 | 15.08 | 17,593‡ |
| IGRA/RIF | 226,103 | 13,668.80 | 6.55 | 19.29 | 16,848|
| SEQ/INH | 244,909 | 13,675.52 | 7.03 | 13.44 | 50,260§ |
| IGRA/INH | 255,309 | 13,668.30 | 6.80 | 16.28 | 35,749§ |
| TST/RIF | 265,651 | 13,668.53 | 6.74 | 16.94 | 36,847§ |
| TST/INH | 316,918 | 13,679.99 | 6.92 | 14.77 | 79,512§ |
| Only screen persons 10–60 y of age | | | | | |
| Base case | 184,357 | 13,666.32 | 8.12 | NC | NC |
| SEQ/RIF | 246,752 | 13,670.05 | 5.97 | 31.33 | 16,711‡ |
| IGRA/RIF | 250,991 | 13,671.01 | 4.93 | 39.31 | 14,206|
| TST/RIF | 290,406 | 13,670.58 | 5.28 | 34.94 | 24,898§ |
| SEQ/INH | 292,011 | 13,669.51 | 5.94 | 26.85 | 33,753§ |
| IGRA/INH | 307,714 | 13,669.93 | 5.35 | 34.05 | 34,114§ |
| TST/INH | 370,423 | 13,669.60 | 5.63 | 30.38 | 56,781§ |
| Only 63.5% initiate therapy after arrival | | | | | |
| Base case | 183,165 | 13,667.06 | 8.14 | NC | NC |
| SEQ/RIF | 255,496 | 13,671.71 | 6.08 | 25.22 | 27,222‡ |
| IGRA/RIF | 260,008 | 13,670.45 | 5.61 | 31.07 | 22,661|
| TST/RIF | 268,729 | 13,669.35 | 5.85 | 28.10 | 44,932§ |
| SEQ/INH | 291,805 | 13,669.14 | 6.36 | 21.85 | 52,130§ |
| IGRA/INH | 305,683 | 13,669.01 | 5.94 | 26.93 | 62,670§ |
| TST/INH | 352,634 | 13,669.30 | 6.19 | 23.92 | 75,655§ |
| 100% Adherence to post-arrival follow-up | | | | | |
| Base case | 185,064 | 13,667.21 | 8.01 | NC | NC |
| SEQ/RIF | 277,526 | 13,672.40 | 3.86 | 51.83 | 17,814‡ |
| IGRA/RIF | 266,742 | 13,673.61 | 2.75 | 65.72 | 15,931|
| SEQ/INH | 356,943 | 13,671.03 | 4.50 | 43.88 | 45,057§ |
| IGRA/INH | 305,683 | 13,669.01 | 5.94 | 26.93 | 62,670§ |
| TST/INH | 352,634 | 13,669.30 | 6.19 | 23.92 | 75,655§ |
| No losses in the LTBI cascade of care | | | | | |
| Base case | 184,268 | 13,668.16 | 7.73 | NC | NC |
| SEQ/RIF | 269,103 | 13,674.32 | 3.10 | 59.97 | 13,783‡ |
| IGRA/RIF | 275,614 | 13,675.78 | 1.75 | 77.33 | 11,997|
| TST/RIF | 366,899 | 13,675.63 | 2.52 | 67.46 | 24,447§ |
| SEQ/INH | 376,306 | 13,674.16 | 2.37 | 57.66 | 31,918§ |
| IGRA/INH | 411,237 | 13,675.77 | 1.97 | 74.47 | 30,634§ |
| TST/INH | 512,140 | 13,672.17 | 4.08 | 49.11 | 65,978§ |
| Reactivation rate is 0.9 cases/1,000 PY | | | | | |
| Base case | 185,203 | 13,646.81 | 8.14 | NC | NC |
| SEQ/RIF | 283,301 | 13,651.14 | 5.19 | 36.26 | 22,626‡ |
| IGRA/RIF | 291,963 | 13,651.90 | 4.43 | 45.15 | 20,962|
| TST/RIF | 330,139 | 13,651.84 | 4.85 | 40.39 | 28,775§ |
| SEQ/INH | 346,376 | 13,650.64 | 5.63 | 30.82 | 42,038§ |
| IGRA/INH | 370,889 | 13,651.29 | 4.96 | 39.11 | 41,386§ |
| TST/INH | 433,739 | 13,651.04 | 5.34 | 34.41 | 58,669§ |
| Reactivation rate is 1.3 cases/1,000 PY | | | | | |
| Base case | 181,988 | 13,680.54 | 8.02 | NC | NC |
## Intervention Cost/1,000, $  | No. QALYs/1,000  | No. TB cases/1,000  | % Reduction in TB incidence  | Cost/QALY gained, $† |
|-----------------|----------------|-------------------|---------------------------|-----------------|
| SEQ/RIF         | 250,392        | 13,684.51         | 5.19                       | 35.28           | 17,215‡ |
| IGRA/RIF        | 252,612        | 13,684.78         | 4.39                       | 45.28           | 16,672 |
| SEQ/INH         | 297,483        | 13,682.75         | 5.57                       | 30.53           | 52,289§ |
| TST/RIF         | 309,989        | 13,684.00         | 4.84                       | 39.65           | 36,943§ |
| IGRA/INH        | 313,436        | 13,683.69         | 4.91                       | 38.75           | 41,738§ |
| TST/INH         | 403,690        | 13,683.21         | 5.32                       | 33.63           | 83,081§ |

### Lifetime time horizon

| Intervention  | Cost/1,000, $  | No. QALYs/1,000  | No. TB cases/1,000  | % Reduction in TB incidence  | Cost/QALY gained, $† |
|---------------|----------------|-------------------|-------------------|---------------------------|-----------------|
| Base case     | 257,337        | 20,201.68         | 11.34             | NC                        | NC              |
| SEQ/RIF       | 259,830        | 20,208.76         | 7.29              | 36.09                      | 8,415‡ |
| IGRA/RIF      | 260,977        | 20,212.11         | 6.23              | 46.93                      | 6,946 |
| TST/RIF       | 262,091        | 20,207.77         | 7.30              | 30.34                      | 17,210§ |
| SEQ/INH       | 264,532        | 20,208.76         | 6.64              | 39.71                      | 15,141§ |
| IGRA/INH      | 278,284        | 20,208.92         | 7.00              | 38.33                      | 16,718§ |
| TST/INH       | 349,696        | 20,207.51         | 7.48              | 34.93                      | 34,692§ |

### Minimum estimated costs

| Intervention  | Cost/1,000, $  | No. QALYs/1,000  | No. TB cases/1,000  | % Reduction in TB incidence  | Cost/QALY gained, $† |
|---------------|----------------|-------------------|-------------------|---------------------------|-----------------|
| Base case     | 146,557        | 13,666.32         | 8.12              | NC                        | NC              |
| SEQ/RIF       | 207,111        | 13,670.25         | 5.18              | 36.23                      | 15,404§ |
| SEQ/INH       | 254,658        | 13,670.32         | 5.62              | 30.76                      | 27,013§ |
| TST/RIF       | 260,362        | 13,671.23         | 4.86              | 40.16                      | 23,169§ |
| IGRA/INH      | 267,040        | 13,671.02         | 4.97              | 38.82                      | 25,656§ |
| TST/INH       | 346,126        | 13,669.91         | 5.33              | 34.34                      | 55,593§ |

### Maximum estimated costs

| Intervention  | Cost/1,000, $  | No. QALYs/1,000  | No. TB cases/1,000  | % Reduction in TB incidence  | Cost/QALY gained, $† |
|---------------|----------------|-------------------|-------------------|---------------------------|-----------------|
| Base case     | 222,159        | 13,666.32         | 8.12              | NC                        | NC              |
| SEQ/RIF       | 313,033        | 13,670.25         | 5.18              | 36.23                      | 23,117‡ |
| IGRA/RIF      | 315,886        | 13,671.50         | 4.41              | 45.61                      | 18,073 |
| SEQ/INH       | 374,284        | 13,670.32         | 5.62              | 30.76                      | 38,015§ |
| TST/RIF       | 376,642        | 13,671.23         | 4.86              | 40.16                      | 31,450§ |
| IGRA/INH      | 393,477        | 13,671.02         | 4.97              | 38.82                      | 36,481§ |
| TST/INH       | 485,765        | 13,669.91         | 5.33              | 34.34                      | 73,432§ |

*All costs in 2016 Can $. IGRA, interferon-gamma release assay; INH, isoniazid; NC, not calculable; QALY, quality-adjusted life year; RIF, rifampin; SEQ, sequential screening; TB, tuberculosis; TST, tuberculin skin test.†The cost per QALY gained is calculated in comparison to the base case.‡This intervention strategy is extendedly dominated by another intervention strategy. While it increases QALYs, it has a higher ICER than a more expensive intervention strategy.§This intervention strategy is strictly dominated by another intervention strategy. It is more expensive and has worse outcomes.
Appendix Figure 1. Meta-analysis of adherence with a request for post-arrival follow-up. This was used to inform the proportion who report for LTBI treatment post-arrival.
Appendix Figure 2. Cost-effectiveness planes demonstrating the variability in probabilistic sensitivity analysis replications for select intervention strategies in migrants from low incidence (A), moderate incidence (B), high incidence (C), and very high TB incidence (D) countries.
Appendix Figure 3. Efficiency frontier of population QALYs versus population costs among migrants from low (A), moderate (B), high (C), and very high (D) TB incidence countries. The frontier is read from left to right, with intervention strategies connected if they fall on the frontier. Those subsequent to the initial intervention strategy have an increased cost, but an increased benefit, and represent the next best value at increasing funding thresholds. The slope between 2 connected intervention strategies represents cost-effectiveness: a steeper slope represents poorer cost-effectiveness, while a shallow slope represents better cost-effectiveness. An intervention strategy that is extendedly dominated has a higher cost-per QALY gained and fewer population QALYs than the subsequent intervention on the frontier and is therefore less efficient. IGRA, interferon-gamma release assay; INH, isoniazid; QALY, quality-adjusted life year; RIF, rifampin; SEQ, sequential screening; TST, tuberculin skin test.