

ONLINE DATA SUPPLEMENT

Cost-effectiveness of overseas testing and treatment for tuberculosis infection among United States-bound refugees: a mathematical modelling analysis

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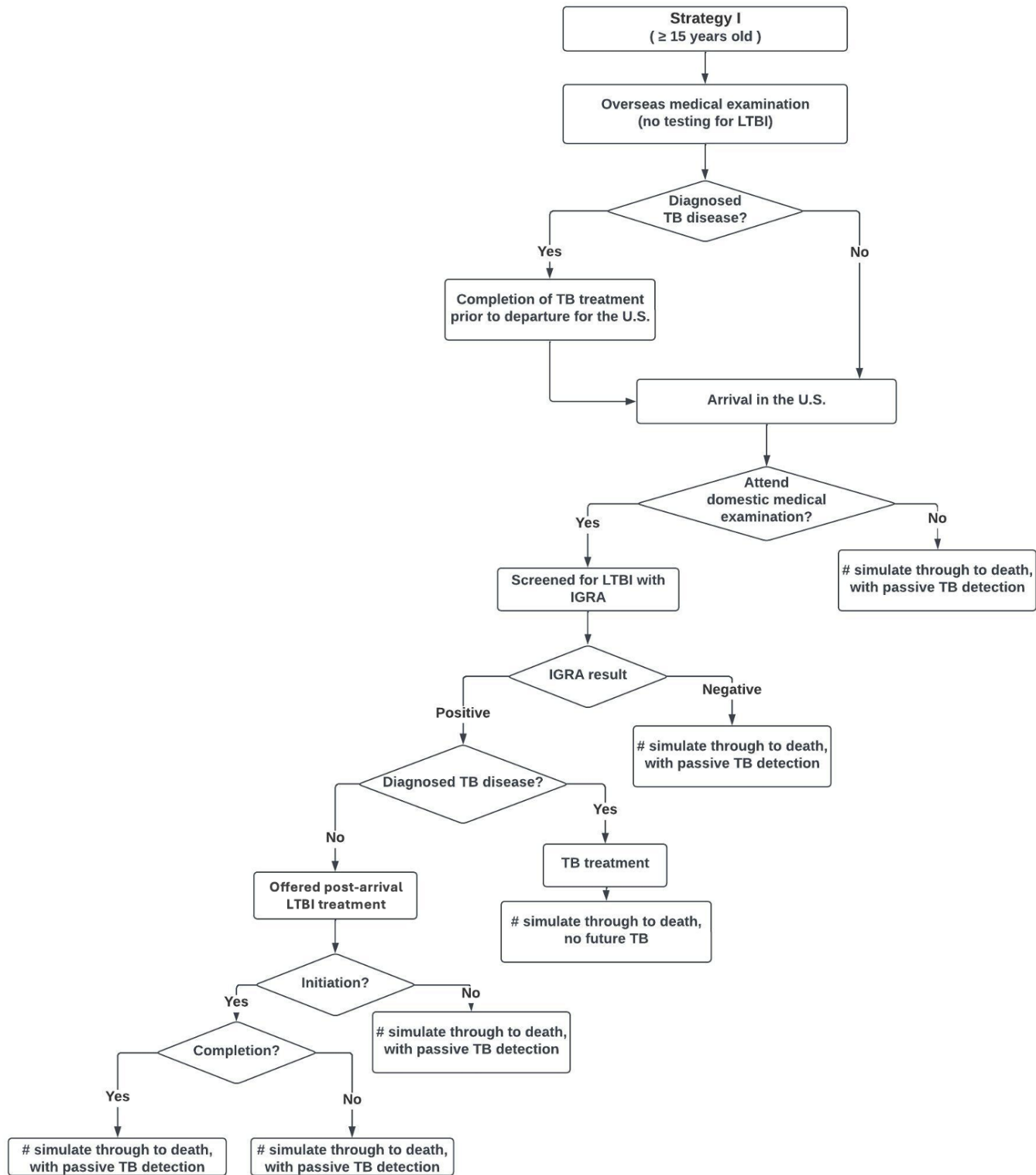
Table S1. Countries included in the analysis

Countries of Birth (ISO 3166 alpha-3¹)
AFG, AGO, ARE, ARM, AZE, BDI, BEL, BEN, BFA, BGD, BGR, BIH, BLR, BRA, BRN, BTN, BWA, CAF, CHN, CIV, CMR, COD, COG, COL, CUB, CYP, CZE, DEU, DJI, DOM, DZA, ECU, EGY, ERI, EST, ETH, FJI, FRA, FSM, GAB, GBR, GEO, GHA, GIN, GMB, GTM, GUM, HND, HTI, IDN, IND, IRN, IRQ, ISL, ISR, ITA, JOR, KAZ, KEN, KGZ, KHM, KOR, KWT, LAO, LBN, LBR, LBY, LKA, LTU, LVA, MAR, MDA, MDG, MEX, MLI, MLT, MMR, MNG, MOZ, MRT, MWI, MYS, NAM, NER, NGA, NIC, NPL, NRU, PAK, PAN, PER, PHL, PNG, POL, PRK, QAT, ROU, RUS, RWA, SAU, SDN, SEN, SLE, SLV, SMR, SOM, SSD, STP, SWE, SYR, TCD, TGO, THA, TJK, TKM, TUN, TUR, TZA, UGA, UKR, URY, UZB, VEN, VNM, YEM, ZAF, ZMB, ZWE (A total of 128 countries)
Countries of Examination (ISO 3166 alpha-3¹)
AFG, AGO, ARG, ARM, AZE, BDI, BEN, BFA, BGD, BIH, BLR, BRA, BRN, BWA, CAF, CHN, CIV, CMR, COD, COG, COL, DJI, DOM, DZA, ECU, ERI, ETH, FJI, GAB, GEO, GHA, GIN, GMB, GTM, GUY, HKG, HND, HTI, IDN, IND, IRQ, KAZ, KEN, KGZ, KHM, KOR, LAO, LBR, LKA, LTU, MAC, MAR, MDA, MDG, MEX, MLI, MMR, MNG, MOZ, MRT, MWI, MYS, NAM, NER, NGA, NIC, NPL, NRU, PAK, PER, PHL, PLW, PNG, QAT, ROU, RUS, RWA, SDN, SEN, SLE, SLV, SOM, SSD, TCD, TGO, THA, TJK, TKM, TLS, TUN, TZA, UGA, UKR, URY, UZB, VEN, VNM, YEM, ZAF, ZMB, ZWE (A total of 101 countries)

Text S1. Countries (ISO 3166 alpha-3¹) where Strategy 3 could not be implemented

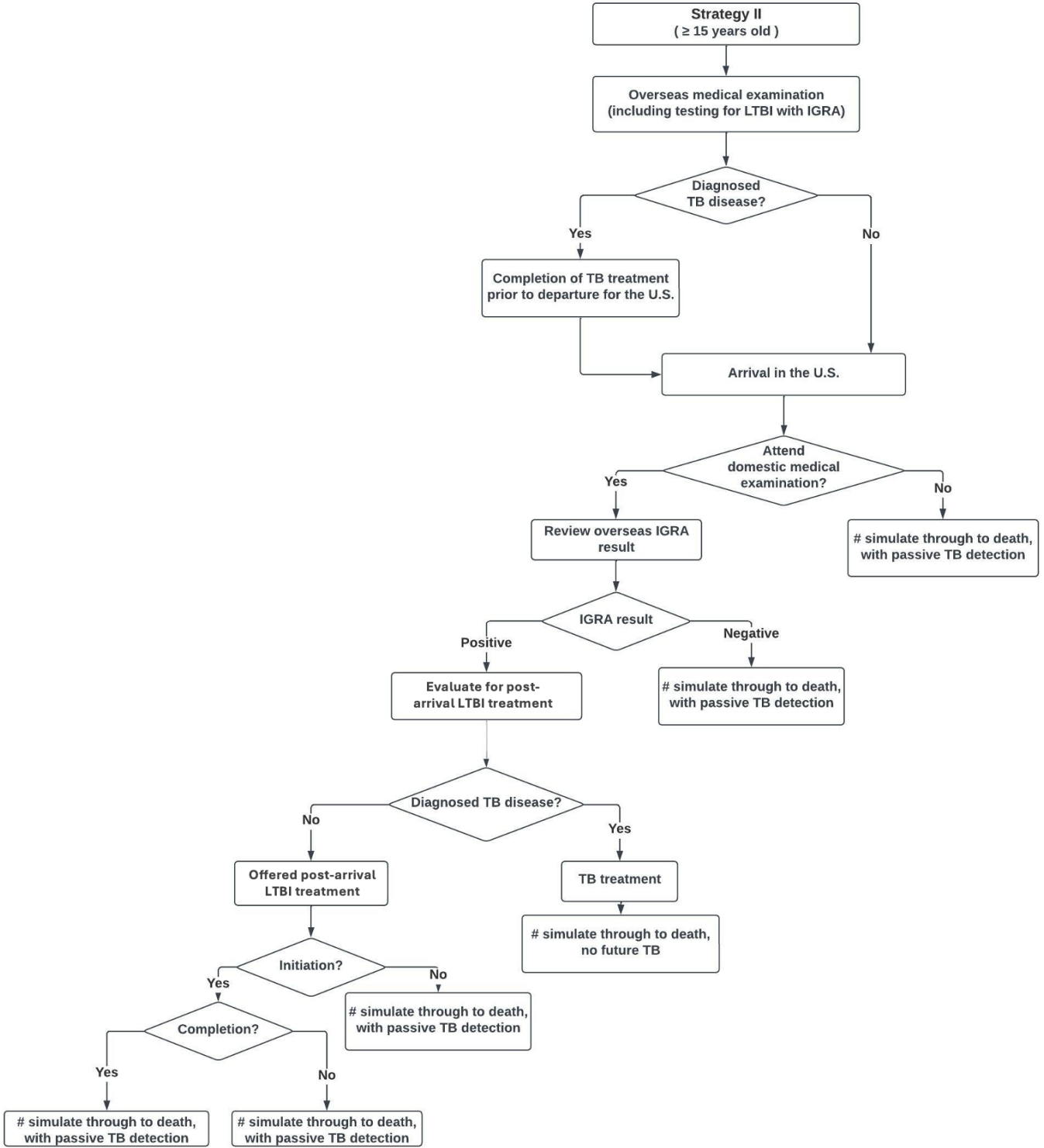
Based on our discussion with experts at the International Organization of Migration, we assumed that no LTBI treatment is able to be offered in the following countries in Strategy 3. That is, in Strategy 3, refugees from these countries shared the same simulated outcome as they would in Strategy 2, where LTBI testing was required prior to U.S. entry but no LTBI treatment was offered overseas: AGO, BEN, BWA, CIV, COD, COG, DJI, ERI, GAB, GMB, LBR, MDG, MLI, MOZ, MRT, NAM, NER, SDN, SEN, SOM, SSD, TCD, TCD, ZAF.

Figure S1A: Flowchart for Strategy 1 (adults)*



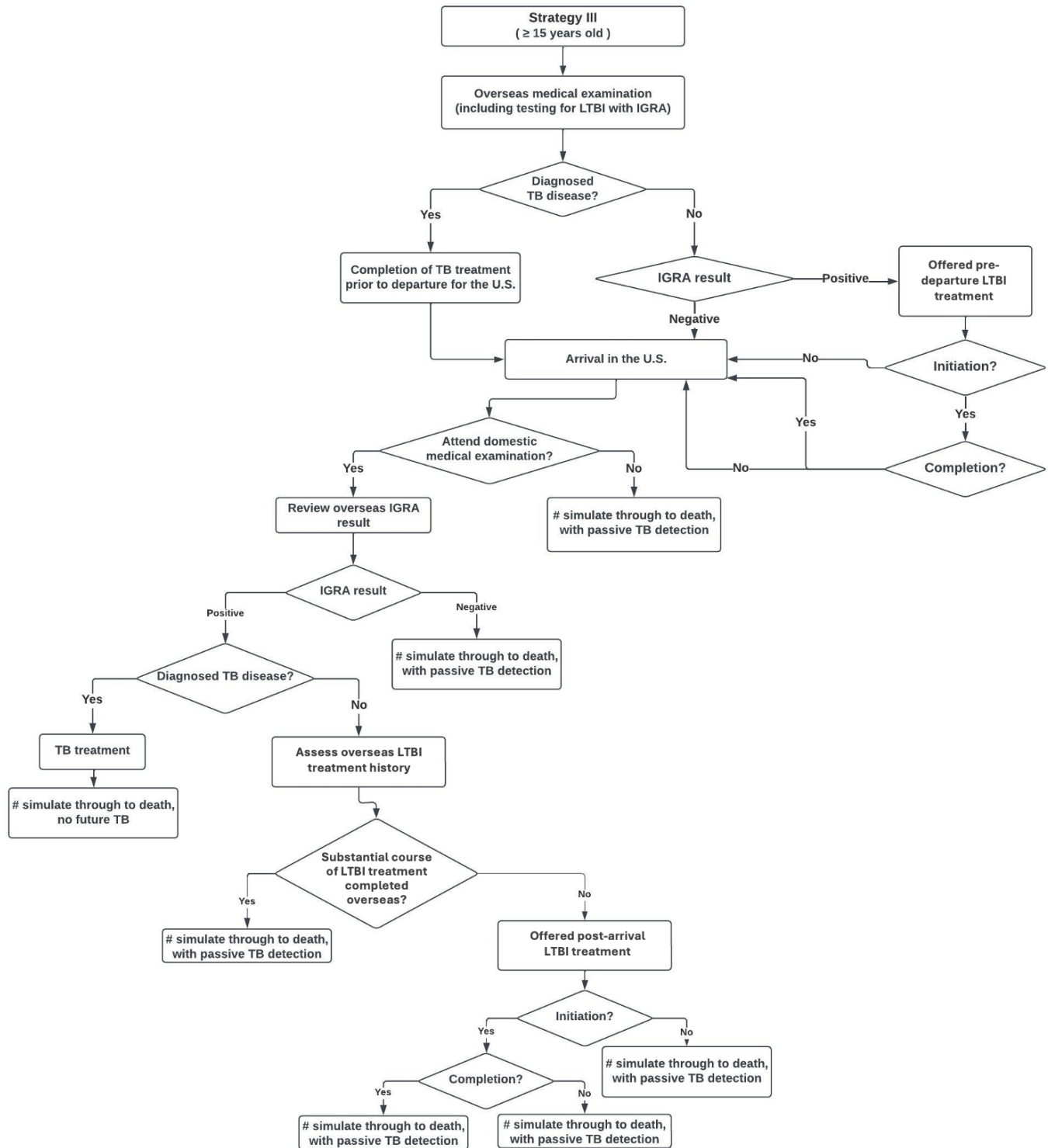
Abbreviations: LTBI, latent TB infection; U.S., United States; IGRA, interferon gamma release assay. * IGRA testing and LTBI treatment are offered after TB disease has been ruled out at the post-arrival medical examination. This strategy represents the pre-2024 screening requirements for U.S.-bound refugees ≥15 years old, tested in high-risk countries.

Figure S1B: Flowchart for Strategy 2 (adults)*



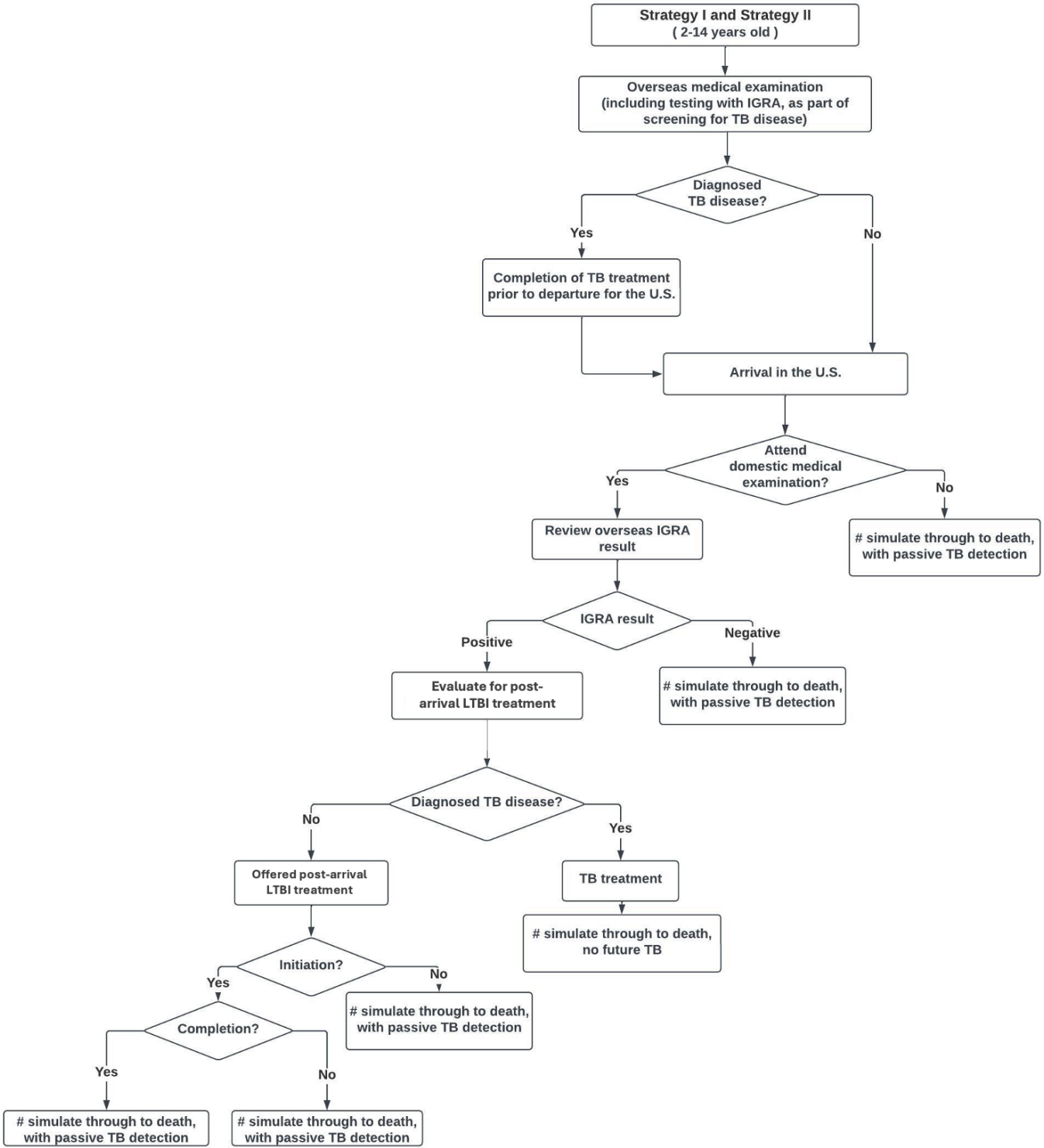
Abbreviations: LTBI, latent TB infection; U.S., United States; IGRA, interferon gamma release assay. * Pre-departure IGRA testing is required. Individuals testing IGRA-positive are offered LTBI treatment after TB disease has been ruled out at the post-arrival medical examination. This strategy represents the current screening requirements for U.S.-bound refugees ≥15 years old tested in high-risk countries, adopted in 2024.

Figure S1C: Flowchart for Strategy 3 (adults)*



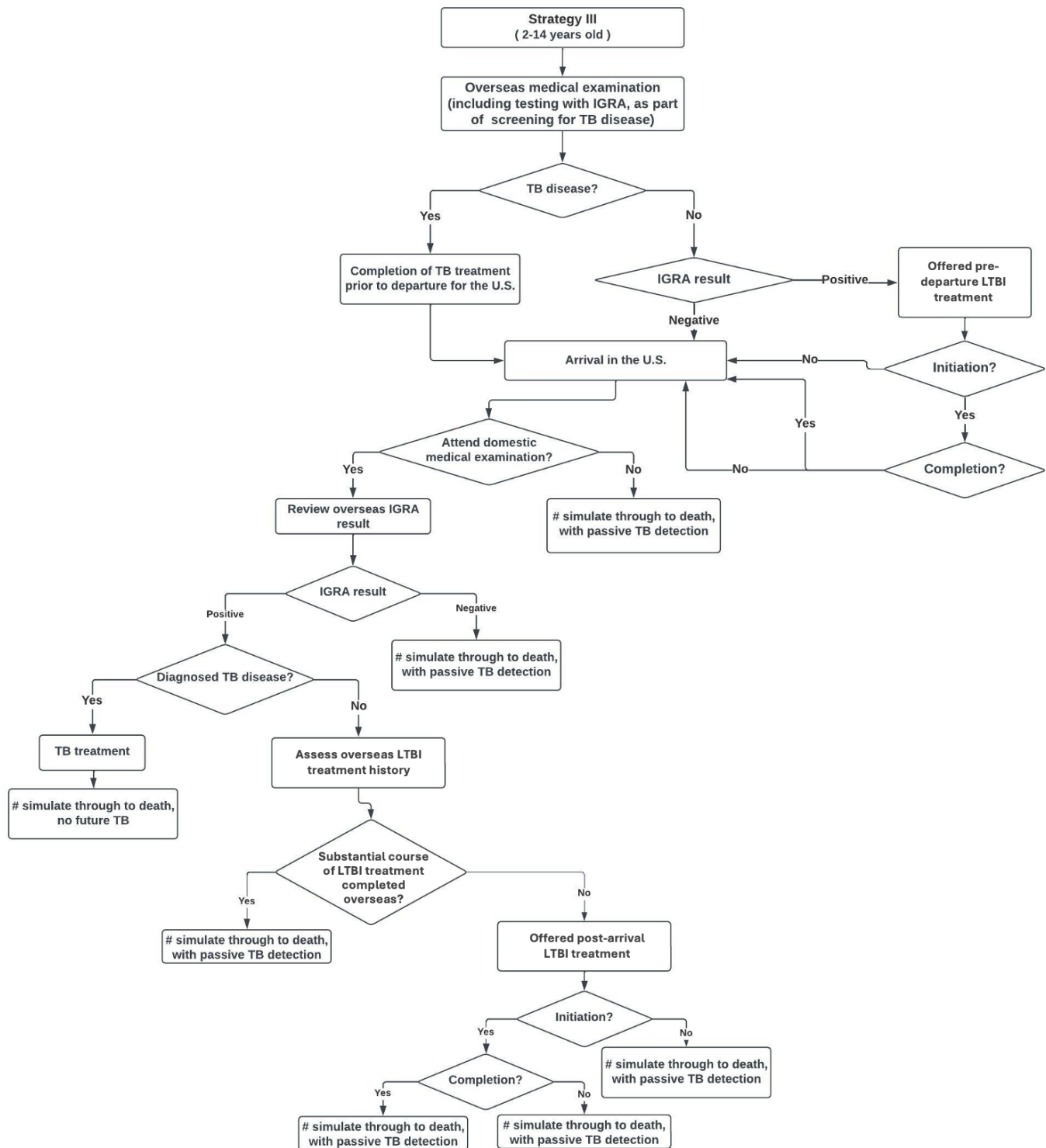
Abbreviations: LTBI, latent TB infection; U.S., United States; IGRA, interferon gamma release assay. * Pre-departure IGRA testing is required, with pre-departure LTBI treatment offered to individuals testing IGRA-positive, after TB disease has been ruled out. After U.S. arrival and domestic medical examination to rule out TB, LTBI treatment is offered again to those who decline LTBI treatment overseas. For those who initiate treatment overseas but do not complete the regimen, a proportion are assumed to re-initiate a full course of LTBI treatment during their post-arrival medical examination.

Figure S1D: Flowchart for Strategies 1 and 2 (children)*



Abbreviations: LTBI, latent TB infection; U.S., United States; IGRA, interferon gamma release assay. * Pre-departure IGRA testing is required. Individuals testing IGRA-positive receive a medical examination after U.S. arrival to identify TB disease, with LTBI treatment offered after TB has been ruled out. This strategy represents the pre-2024 screening requirements for U.S.-bound refugees aged 2-14 years old tested in high-risk countries.

Figure S1E: Flowchart for Strategy 3 (children)*



Abbreviations: LTBI, latent TB infection; U.S., United States; IGRA, interferon gamma release assay. * Pre-departure IGRA testing is required, with pre-departure LTBI treatment offered to individuals testing IGRA-positive, after TB disease has been ruled out. After U.S. arrival and domestic medical examination to rule out TB, LTBI treatment is offered again to those who decline LTBI treatment overseas. For those who initiate treatment overseas but do not complete the regimen, a proportion are assumed to re-initiate a full course of LTBI treatment during their post-arrival medical examination.

Table S2. Parameter Table

Parameter	Point estimate (95% interval, if included in probabilistic sensitivity analysis)	Source and comments
Epidemiological parameters		
Background mortality rate	Varies by age	2017 US Life Tables for foreign born individuals ²
Mortality hazard ratio among those completed TB treatment	1.78	Following Lee Rodriguez 2020 <i>JAMA Netw Open</i> ³ , the hazard ratio was applied for 6 years after completion of TB treatment.
LTBI prevalence	Varies by age group and country-of-birth	Menzies 2024 <i>Lancet Global Health</i> ⁴
Future TB incidence rates for the study cohort	Varies by age, country-of-birth, and time since entry	Hill 2020 <i>Epidemics</i> ⁵
Overseas IGRA testing and LTBI treatment (when implemented, see Figure S1)		
% Screened with IGRA	100	Assumption
% Initiated LTBI treatment,(3HP) conditional on a positive IGRA result	65 (51, 79)	Assumption
% Completed 3HP regimen, or completed a sufficient proportion of regimen prior to U.S. entry such that re-initiation is not required, conditional on having initiated treatment	88 (83, 92)	Assumption
Domestic IGRA testing and LTBI treatment (when implemented, see Figure S1)		
% Attended domestic medical evaluation for refugees	88 (83, 92)	Assumption
% Screened with IGRA, conditional on not tested with IGRA overseas and no signs of TB disease	100	Assumption
% Offered LTBI treatment (3HP) domestically, conditional on a positive IGRA result from overseas or domestic testing, with TB disease ruled out and one of the following: not offered LTBI treatment overseas, offered but did not initiate LTBI treatment overseas, or initiated overseas but did not complete a sufficient proportion of LTBI treatment signaling a need to re-initiate treatment	100	Assumption
% Initiated 3HP, conditional on being offered treatment, regardless of LTBI treatment history	76 (69, 82)	CDC data from the Electronic Disease Notification 2013-2023, provided by Christina Phares, Division of Global Migration Health, 2024-03-20. (variables: DiagnosisBest, USTreatmentInitYesBest) ⁶

Parameter	Point estimate (95% interval, if included in probabilistic sensitivity analysis)	Source and comments
% Completed 3HP regimen, conditional on having initiated treatment, regardless of LTBI treatment history	63 (56, 69)	CDC data from the Electronic Disease Notification 2013-2023, provided by Christina Phares, Division of Global Migration Health, 2024-03-20. (variables: USTreatmentInitYesBest, USTreatmentComp) ⁶
Time from U.S. entry to post-arrival domestic medical evaluation, if attended (months)	1.0	CDC data from the Electronic Disease Notification 2013-2023, provided by Christina Phares, Division of Global Migration Health, 2024-03-20. (variable: US_ArrivalToExam) ⁶
Test characteristics		
Specificity of IGRA for LTBI (%)		
Aged < 15 years (based on proportion IGRA-negative among individuals with no TB disease)	96 (84, 97)	Hirabayashi 2024 JIC ⁷
Aged ≥ 15 years (based on proportion IGRA-negative among individuals with no evidence of TB exposure)	98 (95, 99)	Jonas 2023 JAMA Network ⁸
Sensitivity of IGRA for LTBI (%)		
Aged < 15 years (based on proportion IGRA-positive among individuals with TB disease)	77 (43, 94)	Hirabayashi 2024 JIC ⁷
Aged ≥ 15 years (based on proportion IGRA-positive among individuals with TB disease)	89 (84, 94)	Jonas 2023 JAMA Network ⁸
Specificity of TB diagnosis (%)	100	Assumption
Sensitivity of TB diagnosis (%)	100	Assumption
Treatment characteristics		
LTBI treatment		
Length of LTBI treatment received in the U.S. among those who initiated a new course of LTBI treatment in the U.S. (regardless of LTBI treatment history overseas), and completed the regimen (weeks)	18.2	Feng 2023 J. Clin. Tuberc. Mycobact. Dis. ⁹
Length of LTBI treatment received in the U.S. among those who initiated a new course of LTBI treatment in the U.S. (regardless of LTBI treatment history overseas), and did not complete the regimen (weeks)	3.0	Assumption
% Reduction in risk of future TB disease due to LTBI (efficacy), for individuals not completing LTBI treatment	0	Assumption

Parameter	Point estimate (95% interval, if included in probabilistic sensitivity analysis)	Source and comments
% Reduction in risk of future TB disease due to LTBI (efficacy), for individuals completing LTBI treatment	93	Sterling 2011 NEJM ¹⁰
TB treatment (HRZE)		
% Initiated treatment for TB disease, among those diagnosed with TB disease via active screening or through passive detection	100	Assumption
% Dead at TB diagnosis and therefore not eligible to begin TB treatment, among those diagnosed with TB disease	1.6	Unpublished CDC estimates from surveillance data for non-US-born population, National Tuberculosis Surveillance System, 2010-2019. ¹¹
% Completed treatment for TB, among those who do not die on TB treatment	91.6	
% Died on TB treatment, among those alive at TB diagnosis	5.4	
Length of TB treatment received in the U.S. among those who initiated TB treatment in the U.S. and completed the treatment (weeks)	36.0	Assumption based on 6-months treatment for drug-susceptible or drug-resistant TB
Length of TB treatment received in the U.S. among those who initiated TB treatment in the U.S. and did not complete the treatment (weeks)	3.0	Assumption
Time between symptom onset and diagnosis for TB cases not identified through the post-arrival medical examination (year)	0.5	Assumption
Time between TB diagnosis and treatment initiation (days)	3.0	Assumption
Time before treatment reinitiation, after treatment discontinuation (months)	6.0	Assumption
% Cured of TB, among individuals not completing TB treatment	0	Assumption
% Cured of TB, among individuals completing TB treatment	100	Assumption
Utility weights		
No LTBI	1.0	
LTBI not on treatment	1.0	
On LTBI treatment	No toxicity: 1.0 With toxicity: 0.75	Jo 2021 <i>Clin Infect Dis Off Publ Infect Dis Soc Am</i> ¹²
TB disease, not receiving treatment	0.75 (0.66, 0.83)	Bauer et al, <i>Qual Life Res</i> 2015 ¹³
TB disease, on TB treatment	Untreated TB, 1 st month of treatment: 0.75 (0.66, 0.83) TB treatment after 1 st month: 0.89 (0.76, 0.95)	Bauer et al, <i>Qual Life Res</i> 2015 ¹³

Parameter	Point estimate (95% interval, if included in probabilistic sensitivity analysis)	Source and comments
Individuals surviving TB disease	0.99 (0.981, 0.993)	Menzies 2021 <i>Lancet GH</i> ¹⁴
Cost parameters for overseas TB services (2023 US dollars)		
Cost of IGRA, incl. all costs (per test)	50 (29, 77)	IOM estimates
Cost of LTBI treatment (3HP, DOT) for those who initiated treatment and received the full course of treatment		GDF and IOM estimates, see Tables S4-1, S4-2
Adults	214 (105, 361)	
Children	208 (99, 357)	
Cost of LTBI treatment (3HP, DOT) for those who initiated treatment and discontinued treatment prior to entering U.S.		GDF and IOM estimates, assuming a discontinuation after a mean of 3 visits.
Adults	53 (35, 74)	
Children	52 (34, 74)	
Cost parameters for domestic TB services (2023 US dollars)		
Cost of IGRA, incl. all costs (per test)	61.98 (47, 79)	CMS Clinical Lab Fee Schedule 2023 ¹⁵
Cost of TB screening with chest x-ray 2 views, incl. all costs (per test)	34.23 (25, 45)	CMS Physician Fee Schedule 2023 ¹⁶
Cost of LTBI treatment (3HP, SAT) for those who initiated treatment (same for cases of treatment completion and discontinuation)		CDC estimates for LTBI treatment costs 2021, see Tables S4-1, S4-2
Adults	486 (275, 756)	
Children	528 (314, 799)	
Cost of TB treatment for those who initiated treatment (same for cases of treatment completion and non-completion)	24,846 (16,115, 35, 419)	Winston 2023 <i>EID</i> ¹⁷
Annual discount rate (%)	3.0	Neumann 2016 Cost-Effectiveness in Health and Medicine ¹⁸
Personal Consumption Expenditure Health (PCE-Health) Index	Varies by year	US Bureau of Economic Analysis ¹⁹

Abbreviations: LTBI, latent TB infection; U.S., United States; IGRA, interferon gamma release assay; DOT, directly observed therapy; SAT, self-administered therapy; HRZE, standard TB treatment regimen (isoniazid, rifampicin, pyrazinamide, ethambutol); 3HP, once-weekly isoniazid and rifapentine for 3 months.

Table S3. Distributional characteristics of the uncertain input parameters for probabilistic sensitivity analysis

Parameters	Mean	Median	95% Uncertainty Interval	Parameter Distribution	Source and comments
Overseas TBI testing and treatment					
% Initiated LTBI treatment, conditional on a positive IGRA result	65.0	65.0	50.8 – 79.3	Uniform (0.50, 0.80)	IOM estimates
% Completed the full course of LTBI treatment, or completed a sufficient proportion of LTBI treatment prior to U.S. entry such that a re-initiation is not required, conditional on having initiated LTBI treatment	88.0	88.2	82.7 – 92.5	Beta (147.80, 20.16)	Khan 2022 <i>EID</i> ²⁰
Domestic TBI testing and treatment					
% Attended domestic medical evaluation for refugees	88.0	88.2	82.7 – 92.5	Beta (147.80, 20.16)	Assumption
% Initiated LTBI treatment, conditional on being offered treatment, regardless of LTBI treatment history	76.0	76.1	69.2 – 82.2	Beta (124.00, 39.16)	CDC data from the Electronic Disease Notification 2013-2023, provided by Christina Phares, Division of Global Migration Health, 2024-03-20. ⁶
% Completed LTBI treatment, conditional on having initiated treatment, regardless of LTBI treatment history	63.0	63.0	56.4 – 69.4	Beta (131.54, 77.25)	CDC data from the Electronic Disease Notification 2013-2023, provided by Christina Phares, Division of Global Migration Health, 2024-03-20. ⁶
Test characteristics					
Specificity (%) of IGRA for < 15 years old, based on proportion IGRA-negative among individuals with no TB disease	96.0	96.8	87.6 – 99.7	Beta (274.45, 3.05)	Hirabayashi 2024 <i>J Infect and Chemotherapy</i> ⁷
Specificity (%) of IGRA for ≥ 15 years old, (based on proportion IGRA-negative among individuals with no evidence of TB exposure	98.0	98.2	95.6 – 99.5	Beta (191.10, 3.90)	Jonas 2023 <i>JAMA Network</i> ⁸
Sensitivity (%) of IGRA for < 15 years old, based on proportion IGRA-positive among individuals with TB disease	77.0	78.9	47.8 – 96.0	Beta (7.62, 2.28)	Hirabayashi 2024 <i>J Infect and Chemotherapy</i> ⁷
Sensitivity (%) of IGRA for ≥ 15 years old, based on proportion IGRA-positive among individuals with TB disease	89.0	89.2	83.7 – 93.4	Beta (138.52, 17.12)	Jonas 2023 <i>JAMA Network</i> ⁸

Parameters	Mean	Median	95% Uncertainty Interval	Parameter Distribution	Source and comments
Treatment characteristics					
TB treatment (HRZE)					
Time between symptom onset and diagnosis for TB cases not identified through the post-arrival screening program (year)	0.50	0.50	0.25 – 0.75	Normal (0.5, 0.125)	Assumption of 6 months, with 3-9 month 95% uncertainty interval.
% Completed treatment for TB, among those that do not die on TB treatment	91.6	91.7	89.0 – 93.9	Beta (450.16, 41.28)	Unpublished CDC estimates from surveillance data for non-US-born population, National Tuberculosis Surveillance System, 2010-2019 ¹¹
Utility weights					
TB not on TB or LTBI treatment	0.750	0.752	0.660 – 0.826	1 – Gamma (34.60, 0.007225)*	Bauer 2015 Qual Life Res ¹³
Anyone on TB treatment (1 st month of treatment)	0.750	0.752	0.660 – 0.826	1 – Gamma (34.60, 0.007225)	Bauer 2015 Qual Life Res ¹³
Anyone on TB treatment (after 1 st month of treatment)	0.874	0.880	0.761 – 0.951	1 – Gamma (6.61, 0.01906)	Bauer 2015 Qual Life Res ¹³
Anyone after TB treatment completion if cured	0.988	0.988	0.981 – 0.993	1 – Gamma (16, 0.00075)	Menzies 2021 <i>Lancet GH</i> ¹⁴
Cost parameters for overseas TB services					
LTBI treatment (3HP, DOT) for those who initiated treatment and received the full course of treatment (2023 US dollars) for adults – healthcare costs	214	207	104 – 363	Gamma (10.30, 20.77)	GDF and IOM estimates, see Tables S4-2
LTBI treatment (3HP, DOT) for those who initiated treatment and received the full course of treatment (2023 US dollars) for children – healthcare costs	208	201	99 – 358	Gamma (9.73, 21.37)	GDF and IOM estimates, see Tables S4-1
LTBI treatment (3HP, DOT) for those who initiated treatment and discontinued treatment prior to entering U.S. (2023 US dollars) for adults – healthcare costs	53	52	35 – 74	Gamma (28.09, 1.89)	GDF and IOM estimates, assuming a discontinuation after a mean of 3 visits.
LTBI treatment (3HP, DOT) for those who initiated treatment and discontinued treatment prior to entering U.S. (2023 US dollars) for children – healthcare costs	52	51	34 – 73	Gamma (27.04, 1.92)	GDF and IOM estimates, assuming a discontinuation after a mean of 3 visits.
IGRA, incl. all costs (per test, 2023 US dollars)	50	49	29 – 77	Gamma (16.00, 3.13)	IOM estimates
Cost parameters for domestic TB services					

Parameters	Mean	Median	95% Uncertainty Interval	Parameter Distribution	Source and comments
LTBI treatment (3HP, SAT) for those who initiated treatment (same for cases of treatment completion and discontinuation; 2023 US dollars) for adults – healthcare costs	486	475	275 – 760	Gamma (15.12, 32.15)	CDC LTBI treatment cost estimates, see Table S4-2
LTBI treatment (3HP, SAT) for those who initiated treatment (same for cases of treatment completion and discontinuation; 2023 US dollars) for children – healthcare costs	528	518	312 – 800	Gamma (17.84, 29.59)	CDC LTBI treatment cost estimates, see Table S4-1
TB disease treatment for those who initiated treatment (same for cases of treatment completion and non-completion) (2023 US dollars) – healthcare costs	24,846	24,511	16,031 – 35,561	Gamma (24.69, 1006.20)	Winston 2023 <i>EID</i> ¹⁷
IGRA, incl. all costs (per test, 2023 US dollars)	61.98	61.61	46.73 – 79.35	Gamma (55.32, 1.12)	CMS Clinical Lab Fee Schedule 2023 ¹⁵
TB screening with chest x-ray 2 views, incl. all costs (per test, 2023 US dollars)	34.23	33.99	25.14 – 44.70	Gamma (46.87, 0.73)	CMS Physician Fee Schedule 2023 ¹⁶

Abbreviations: LTBI, latent TB infection; U.S., United States; IGRA, interferon gamma release assay; DOT, directly observed therapy; SAT, self-administered therapy; HRZE, standard TB treatment regimen (isoniazid, rifampicin, pyrazinamide, ethambutol); 3HP, once-weekly isoniazid and rifapentine for 3 months. * Gamma distribution parameters are expressed as shape and scale.

Table S4-1. Cost estimation for complete course of LTBI treatment overseas and in the United States, for children

Categories	Overseas	Domestic
LTBI treatment regimen	12 weeks of once-weekly isoniazid (900 mg) and rifapentine (900 mg), directly observed therapy [3HP, DOT]	12 weeks of once-weekly isoniazid (900 mg) and rifapentine (600 mg), self-administered therapy [3HP, SAT]
Total cost for medication	\$11	\$171
Weekly cost for medication	\$0.94	\$14.28
Total doses	12	12
Total cost for clinic visits	\$180	\$225
Total clinic visits	12	3
Unit cost for the initial clinic visit	\$15	\$156
Unit cost for a follow-up clinic visit	\$15	\$34
Total supplies costs	\$11	\$87
Adverse events costs	\$6	\$21
Estimated total cost	\$208	\$528

Abbreviations: LTBI, latent TB infection. Dosage for isoniazid and rifapentine in children is based on weight.²¹ We used the mean weight of the sampled study population ≤ 14 (31.45 kilograms) to approximate the cost of 3HP. The mean weight was based on the mean age of the sampled children cohort (8 years old).²² Estimates of domestic costs are based on by Veteran Affairs drug cost information, adjusted to 2023 US dollars.²³ Overseas clinic and supply costs are based on expert input from the International Organization of Migration, and overseas medication costs are based on Global Drug Facility catalogue.²⁴

Table S4-2. Cost estimation for complete course of LTBI treatment overseas and in the United States, for adults

Categories	Overseas	Domestic
LTBI treatment regimen	12 weeks of once-weekly isoniazid (900 mg) and rifapentine (900 mg), directly observed therapy [3HP, DOT]	12 weeks of once-weekly isoniazid (900 mg) and rifapentine (900 mg), self-administered therapy [3HP, SAT]
Total cost for medication	\$17	\$130
Weekly cost for medication	\$1.38	\$10.85
Total doses	12	12
Total cost for clinic visits	\$180	\$224
Total clinic visits	12	3
Unit cost for the initial clinic visit	\$15	\$156
Unit cost for a follow-up clinic visit	\$15	\$34
Total supplies costs	\$12	\$87
Adverse events costs	\$6	\$43
<i>Estimated total cost</i>	\$214	\$486

Abbreviations: LTBI, latent TB infection. Estimates of domestic costs are based on by Veteran Affairs drug cost information, adjusted to 2023 US dollars.²³ Overseas clinic and supply costs are based on expert input from the International Organization of Migration, and overseas medication costs are based on Global Drug Facility catalogue.²⁴

Table S5-1. Cost-effectiveness analysis results for the scenario analysis where LTBI prevalence is *double the value assumed in the main analysis*

Strategy	Total QALY per refugee (95% UI)	Total cost per refugee (95% UI)	Incremental QALYs (95% UI)	Incremental Costs (95% UI)	ICER (\$ / QALY gained)
Children					
<i>No intervention scenario</i>	29.8808 (29.8802 – 29.8813)	51 (35 – 70)	--	--	--
<i>Strategy 1, 2</i>	29.8813 (29.8808 – 29.8817)	106 (59 – 169)	--	--	Dominated by Strategy 3
<i>Strategy 3</i>	29.8816 (29.8811 – 29.8819)	74 (33 – 136)	0.0008 (0.0008 – 0.0013)	23 (-2.2 – 54.7)	28,750
Adults					
<i>No intervention scenario</i>	25.5133 (25.5115 – 25.5148)	216 (161 – 282)	--	--	--
<i>Strategy 1</i>	25.5165 (25.5152 – 25.5177)	365 (229 – 531)	--	--	Dominated by Strategy 3
<i>Strategy 2</i>	25.5165 (25.5152 – 25.5176)	378 (235 – 564)	--	--	Dominated by Strategy 3
<i>Strategy 3</i>	25.5187 (25.5175 – 25.5196)	275 (169 – 416)	0.0054 (0.0042 – 0.0068)	59 (-25.7 – 140)	10,925

Abbreviations: LTBI, latent TB infection; QALY, quality-adjusted life year; 3HP once-weekly isoniazid and rifapentine for 3 months; UI, uncertainty interval; --, not applicable. All costs and QALYs are discounted and in 2023 US dollars, analyzed from TB services perspective (overseas TB screening not included) with a lifetime analytic horizon. Costs are rounded to integers.

No intervention scenario: No IGRA testing and LTBI treatment for the refugee cohort, except for IGRA testing as part of mandatory TB screening in children. Strategy 1: pre-departure IGRA testing for children (2-14 years) and post-arrival IGRA testing for adults (>14 years), with 3HP offered in the United States for IGRA-positive individuals after ruling out TB disease. Strategy 2: pre-departure IGRA testing children and adults, and post-arrival 3HP offered for IGRA-positive individuals after ruling out TB disease; Strategy 3: pre-departure IGRA testing for children and adults, and pre-departure 3HP offered for IGRA-positive individuals testing after ruling out TB disease, with 3HP re-offered in the United States for individuals not completing treatment before U.S. arrival.

Table S5-2. Cost-effectiveness analysis results for the scenario analysis where LTBI prevalence is *half the value assumed in the main analysis*

Strategy	Total QALY (per refugee, 95% UI)	Total cost (per refugee, 95% UI)	Incremental QALY	Incremental cost	ICER (\$ / QALY gained)
Children					
<i>No intervention scenario</i>	29.8819 (29.8817 – 29.8821)	12 (6 – 20)	--	--	--
<i>Strategy 1, 2</i>	29.8820 (29.8818 – 29.8822)	36 (15– 77)	--	--	Dominated by Strategy 3
<i>Strategy 3</i>	29.8821 (29.8819 – 29.8822)	28 (9 – 66)	0.0002 (0.0002 – 0.0004)	16 (0.3 – 46)	80,000
Adults					
<i>No intervention scenario</i>	25.5201 (25.5194 – 25.5206)	54 (38 – 73)	--	--	--
<i>Strategy 1</i>	25.5209 (25.5204 – 25.5213)	122 (56 – 198)	--	--	Dominated by Strategy 3
<i>Strategy 2</i>	25.5209 (25.5204 – 25.5213)	135 (80 – 208)	--	--	Dominated by Strategy 3
<i>Strategy 3</i>	25.5214 (25.5210 – 25.5217)	109 (66 – 165)	0.0013 (0.0009 – 0.0018)	55 (23 – 89)	42,308

Abbreviations: LTBI, latent TB infection; QALY, quality-adjusted life year; 3HP once-weekly isoniazid and rifapentine for 3 months; UI, uncertainty interval; --, not applicable. All costs and QALYs are discounted and in 2023 US dollars, analyzed from TB services perspective (overseas TB screening not included) with a lifetime analytic horizon. Costs are rounded to integers.

No intervention scenario: No IGRA testing and LTBI treatment for the refugee cohort, except for IGRA testing as part of mandatory TB screening in children. Strategy 1: pre-departure IGRA testing for children (2-14 years) and post-arrival IGRA testing for adults (>14 years), with 3HP offered in the United States for IGRA-positive individuals after ruling out TB disease Strategy 2: pre-departure IGRA testing children and adults, and post-arrival 3HP offered for IGRA-positive individuals after ruling out TB disease; Strategy 3: pre-departure IGRA testing for children and adults, and pre-departure 3HP offered for IGRA-positive individuals testing after ruling out TB disease, with 3HP re-offered in the United States for individuals not completing treatment before U.S. arrival.

Reference

- 1 ISO - ISO 3166 — Country Codes. ISO. <https://www.iso.org/iso-3166-country-codes.html> (accessed Feb 12, 2025).
- 2 Medina M, Sabo S, and Vespa J. Living Longer: Historical and Projected Life Expectancy in the United States, 1960 to 2060. U.S. Census Bureau, 2020 <https://www.census.gov/content/dam/Census/library/publications/2020/demo/p25-1145.pdf>.
- 3 Lee-Rodriguez C, Wada PY, Hung Y-Y, Skarbinski J. Association of Mortality and Years of Potential Life Lost With Active Tuberculosis in the United States. *JAMA Network Open* 2020; **3**: e2014481.
- 4 Menzies NA, Swartwood NA, Cohen T, *et al*. The long-term effects of domestic and international tuberculosis service improvements on tuberculosis trends within the USA: a mathematical modelling study. *Lancet Public Health* 2024; **9**: e573–82.
- 5 Hill AN, Cohen T, Salomon JA, Menzies NA. High-resolution estimates of tuberculosis incidence among non-U.S.-born persons residing in the United States, 2000–2016. *Epidemics* 2020; **33**: 100419.
- 6 Unpublished CDC data from the Electronic Disease Notification 2013-2023 (only data children 2-14 years, provided by Christina Phares, Division of Global Migration Health, 2024-03-20).
- 7 Hirabayashi R, Nakayama H, Yahaba M, Yamanashi H, Kawasaki T. Utility of interferon-gamma releasing assay for the diagnosis of active tuberculosis in children: A systematic review and meta-analysis. *Journal of Infection and Chemotherapy* 2024; **30**: 516–25.
- 8 Jonas DE, Riley SR, Lee LC, *et al*. Screening for Latent Tuberculosis Infection in Adults: Updated Evidence Report and Systematic Review for the US Preventive Services Task Force. *JAMA* 2023; **329**: 1495–509.
- 9 Feng P-JI, Horne DJ, Wortham JM, Katz DJ. Trends in tuberculosis clinicians' adoption of short-course regimens for latent tuberculosis infection. *J Clin Tuberc Other Mycobact Dis* 2023; **33**: 100382.
- 10 Sterling TR, Villarino ME, Borisov AS, *et al*. Three Months of Rifapentine and Isoniazid for Latent Tuberculosis Infection. *N Engl J Med* 2011; **365**: 2155–66.
- 11 Unpublished 2022 CDC data for non-US born population residing in the United States for less than 10 years (2010-2019), the U.S. CDC Surveillance Team, Division of Tuberculosis Elimination, 2022-10-06.
- 12 Jo Y, Shrestha S, Gomes I, *et al*. Model-based Cost-effectiveness of State-level Latent Tuberculosis Interventions in California, Florida, New York, and Texas. *Clin Infect Dis* 2021; **73**: e3476–82.

- 13 Bauer M, Ahmed S, Benedetti A, *et al.* The impact of tuberculosis on health utility: a longitudinal cohort study. *Qual Life Res* 2015; **24**: 1337–49.
- 14 Menzies NA, Quaife M, Allwood BW, *et al.* Lifetime burden of disease due to incident tuberculosis: a global reappraisal including post-tuberculosis sequelae. *The Lancet Global Health* 2021; **9**: e1679–87.
- 15 Clinical Laboratory Fee Schedule | CMS. <https://www.cms.gov/medicare/medicare-fee-for-service-payment/clinicallabfeesched> (accessed Feb 19, 2023).
- 16 Physician Fee Schedule | CMS. <https://www.cms.gov/medicare/payment/fee-schedules/physician> (accessed June 30, 2025).
- 17 Winston CA, Marks SM, Carr W. Estimated Costs of 4-Month Pulmonary Tuberculosis Treatment Regimen, United States. *Emerg Infect Dis* 2023; **29**: 2102–4.
- 18 Neumann PJ, Ganiats TG, Russell LB, Sanders GD, Siegel JE, editors. Cost-Effectiveness in Health and Medicine. Oxford University Press, 2016
DOI:10.1093/acprof:oso/9780190492939.001.0001.
- 19 BEA Interactive Data Application.
https://apps.bea.gov/iTable/?reqid=19&step=3&isuri=1&select_all_years=0&nipa_table_list=2014&series=m&first_year=2020&last_year=2022&scale=-99&categories=underlying&thetable=&_gl=1*3rlonf*_ga*MTgwMjc2NTUwMC4xNzM2NDU3MTQy*_ga_J4698JNNFT*MTczNjQ1NzE0Mi4xLjEuMTczNjQ1NzYxMy41LjAuMA.#eyJhcHBpZCI6MTksInN0ZXBzIjpbMSwyLDMsM10sImRhdGEiOiI0bmlmNhdGVnb3JpZXMlLCJvbmRlcmx5aW5nIl0sWyJOSVBBX1RhYmxiX0xpc3QiLClyMDE3Il0sWyJGaXJzdF9ZZWFyIiwiaWJyMCJdLFsiTGZzF9ZZWFyIiwiaWJyMyJdLFsiU2NhbmGUlCItNiJdLFsiU2VyaWVzIiwiaWJyTSJdXX0= (accessed Jan 9, 2025).
- 20 Khan A, Phares CR, Phuong HL, *et al.* Overseas Treatment of Latent Tuberculosis Infection in US–Bound Immigrants. *Emerg Infect Dis* 2022; **28**: 582–90.
- 21 Sterling TR. Guidelines for the Treatment of Latent Tuberculosis Infection: Recommendations from the National Tuberculosis Controllers Association and CDC, 2020. *MMWR Recomm Rep* 2020; **69**. DOI:10.15585/mmwr.rr6901a1.
- 22 Vital and Health Statistics, Series 3, Number 46.
- 23 Logistics O of P Acquisition and. VA.gov | Veterans Affairs.
<https://www.va.gov/opal/nac/fss/pharmprices.asp> (accessed June 10, 2025).
- 24 GDF Product Catalog | Stop TB Partnership. <https://www.stoptb.org/what-we-do/facilitate-access-tb-drugs-diagnostics/global-drug-facility-gdf/products-catalog> (accessed June 30, 2025).