Supplementary Materials for "Impact and Efficiency of State-level Tuberculosis (TB) interventions in California, Florida, New York and Texas: A model-based analysis."

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S-1 Model Calibration

We started the model calibration with our baseline model, which is already calibrated to demographic data, including the size and the age-specific distribution of US and non-US born populations, and time-, age-, and nativity-specific TB incidence in each of the four states [1]. Hence, we specifically focused on calibrating additional risk factors, i.e., diabetes, HIV, incarceration and homelessness. We systematically calibrated our model to represent the each of the risk populations in each of the four states.

To incorporate diabetes in our model, we assumed that individuals were subjected to an annual per capita rate of developing diabetes (p_{dm}). The rates were fit to be consistent with prevalence of diabetes in each of the four states averaged between 2010 to 2014 [2]. Diabetes was modeled to potentially increase reactivation risk of LTBI: individuals that were diabetic, were modeled to experience a differential risk of reactivating LTBI compared to a non-diabetic individual, where the ratio of reactivation rates comparing diabetics vs. non-diabetic was taken to be r_{dm}. This ratio was fit such that the proportion of incident TB among diabetics in each of the four states were consistent with the proportions observed in NTSS data.

To incorporate HIV in our model, we assumed that individuals were subject to an annual per capita rate of developing HIV (p_{HIV}). The rates were fit to be consistent with prevalence of HIV in each of the four states averaged between 2010 to 2014 [3]. We assumed that HIV increased the risk of reactivating LTBI. HIV+ individuals were assumed to experience a differential risk of reactivating LTBI compared to a HIV- individual, where the ratio of reactivation rates comparing HIV+ vs. HIV- was taken to be r_{HIV}. This ratio, as previously, was fit such that the proportion of incident TB among HIV+ in each of the four states were consistent with the data.

To incorporate a population of incarcerated, we assumed that individuals also subject to an annual per capital rate of being incarcerated (p_{incar}). The rates were fit such that the incarceration rates in each of the four states were consistent with the Bureau of Justice Statistics' counts of jurisdictional population averaged between 2010 to 2014 [4]. We assumed that being incarcerated increased the risk of acquiring TB disease via transmission: differential risk in transmission among individuals that were incarcerated (ratio of transmission rates comparing incarcerated individual vs. non-incarcerated individual) was taken to be r_{incar}. Again, this ratio was fit such that the proportion of incident TB among incarcerated in each of the four states were consistent with the data.

To incorporate homelessness in our model, we assumed that individual also subject to an annual per capita rate of being homeless (p_{hl}). The rates were fit such that the levels of homelessness in each of the four states were consistent with the data (measured as one year estimate of homelessness averaged between 2013 and 2015) [5]. We assumed that being homeless also increased the risk of acquiring TB disease via transmission: and the differential risk in transmission (ratio of transmission rates comparing homeless individual vs. non-homeless individual) was taken to be r_{hl}. This ratio was also fit such that the proportion of incident TB among homeless in each of the four states were consistent with the data.

Each of the parameters associated with the risk factors were fit separately in each of the four states to the data representing the size of the population in the risk group (various data sources described above), and the amount of TB that occurs in the risk group (data taken from NTSS). In each of the four states, we conducted 10,000 model simulations in which all of the above parameters were simultaneously varied using a Latin Hypercube Sampling. We choose those model parameters in which the model simulated size of the risk group and the amount of TB occurring in the risk group were within +/- 10% of data. We used the distribution of parameters of these data-consistent simulations to calibrate the model: the median was taken as the point estimate, and 95% range as the 95% range of the estimate. Shown in Figs. S-1-S-4, are the estimated parameters for each of the four states. Estimated magnitude of increases in either reactivation rates or acquisition rates for each of the risk factor in each of the four states are also

summarized in Table S-1.

Risk group	**California**	**Florida**	**New York**	**Texas**
Diabetic	1.54 (1.16-1.94)	1.11 (1.01-1.45)	1.12 (1.01-1.43)	1.09 (1.00-1.32)
HIV-positive	16.36 (10.79-28.9)	86.54 (57.60-99.36)	28.37 (16.41-44.84)	65.75 (35.10-95.91)
Homeless	37.42 (19.38-70.91)	46.64 (25.85-83.30)	12.81 (12.81-12.81)	87.27 (61.86-99.81)
Incarcerated	42.39 (20.58-84.56)	17.93 (10.68-37.13)	19.11 (10.03-41.69)	73.56 (45.33-97.95)

Table S-1: Estimated magnitude of increases in reactivation rates (for diabetic, and HIV-positive), and acquisition rate (for homeless and incarcerated) in each of the four states.

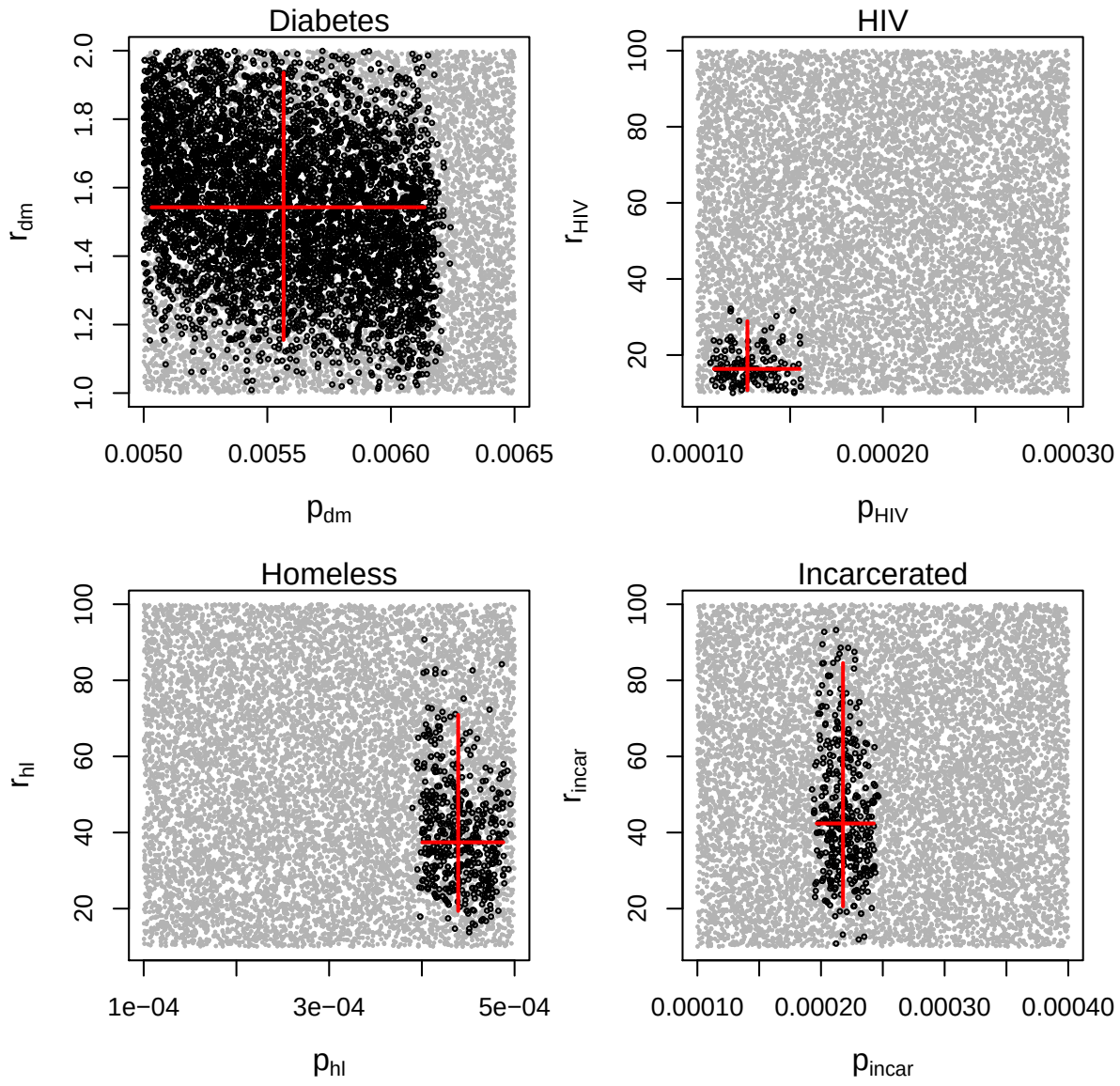

Figure S-1: Calibration of risk factors in California. Shown are calibrations for populations consisting of diabetic [top-left], HIV-positive [top-right], homeless [bottom-left] and incarcerated [bottom-right]. In each panel, shown in grey circles are all simulations, and shown in black are data-consistent simulations. Intersection point of the two red lines represent the point estimates, and the endpoints represent the 95% range.

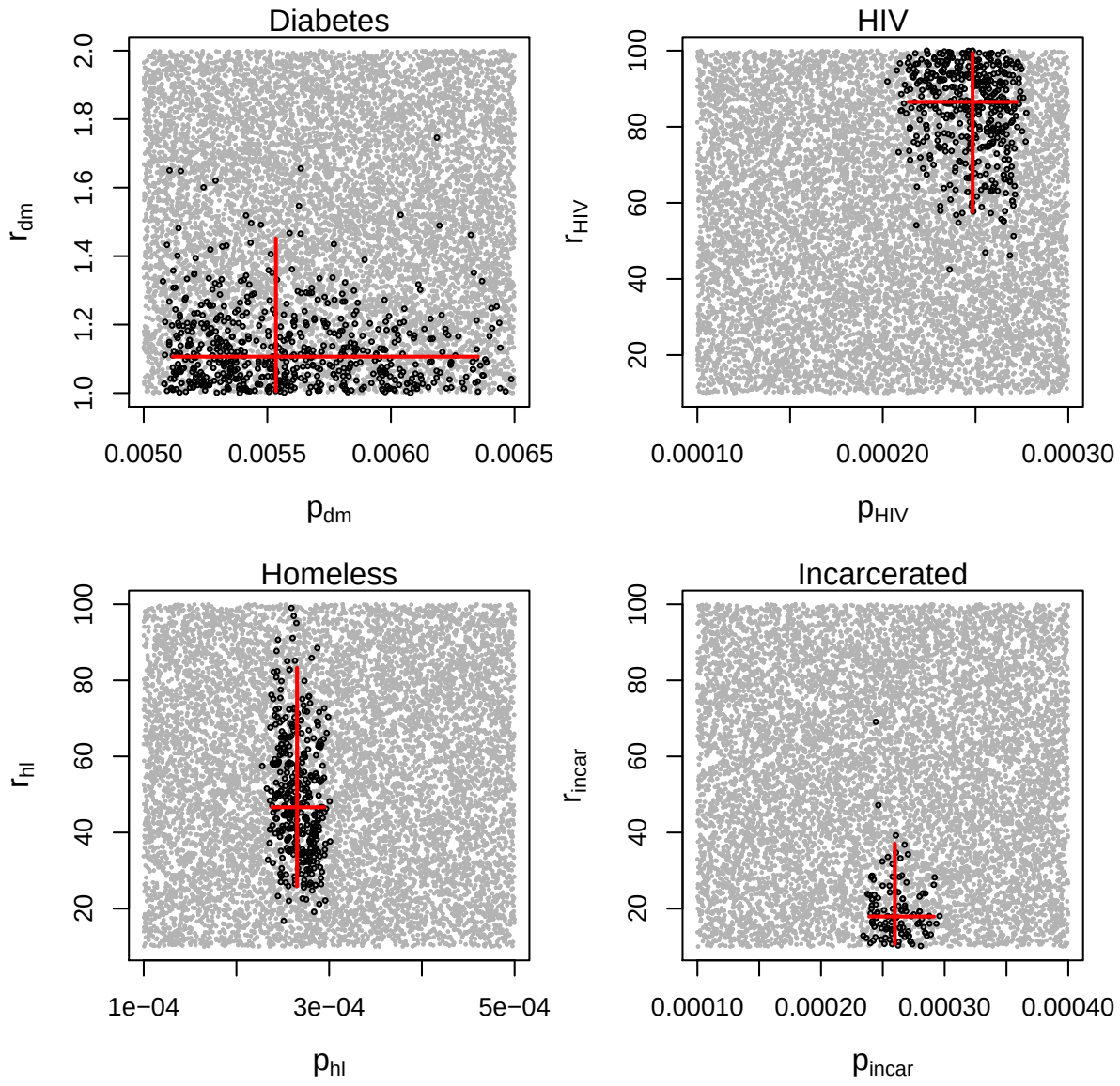

Figure S-2: Calibration of the risk factors in Florida. Shown are calibrations for populations consisting of diabetic [top-left], HIV-positive [top-right], homeless [bottom-left] and incarcerated [bottom-right]. In each panel, shown in grey circles are all simulations, and shown in black are data-consistent simulations. Intersection point of the two red lines represent the point estimates, and the endpoints represent the 95% range.

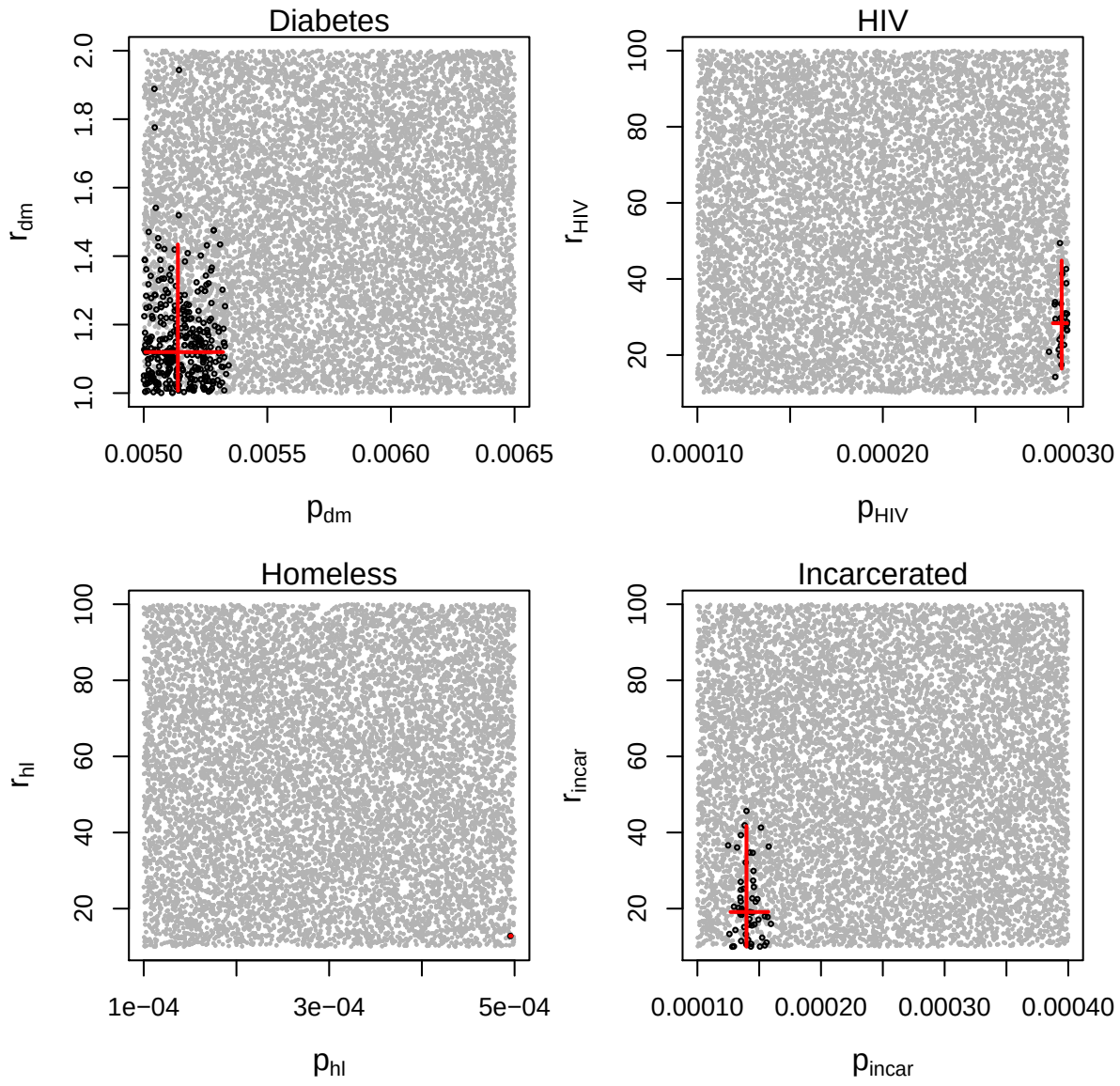

Figure S-3: Calibration of the risk factors in New York. Shown are calibrations for populations consisting of diabetic [top-left], HIV-positive [top-right], homeless [bottom-left] and incarcerated [bottom-right]. In each panel, shown in grey circles are all simulations, and shown in black are data-consistent simulations. Intersection point of the two red lines represent the point estimates, and the endpoints represent the 95% range.

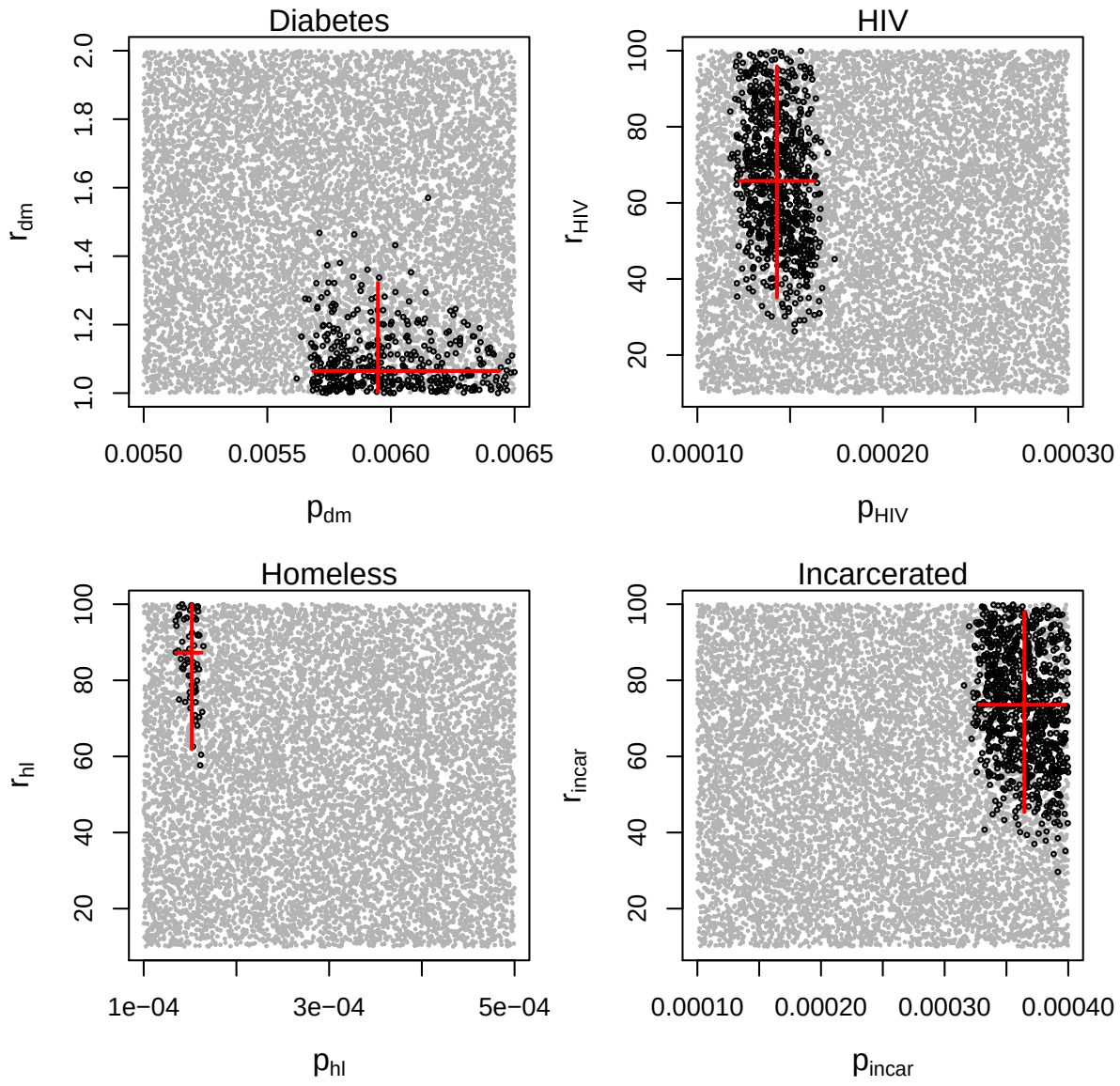

Figure S-4: Calibration of the risk factors in Texas. Shown are calibrations for populations consisting of diabetic [top-left], HIV-positive [top-right], homeless [bottom-left] and incarcerated [bottom-right]. In each panel, shown in grey circles are all simulations, and shown in black are data-consistent simulations. Intersection point of the two red lines represent the point estimates, and the endpoints represent the 95% range.

S-2 Sensitivity analysis: ECI

To explore the sensitivity of ECI, we varied two key parameters that characterized this intervention: (i) the odds of active TB due to recent transmission while comparing contacts to the general population (O_T); and (ii) the odds of LTBI while comparing contacts to the general population (O_L). For each of these parameters, we generated a sampling range spanning 0.75 to 1.25 times the point estimate (i.e., 929 to 1550). We then uniformly sampled the 10,000 parameters from this range, and generated model-based estimates of the impact of ECI (% reduction in TB incidence) for each parameter combination. Shown in Fig. S-5 as box-plots are the impact of ECI in each of the fours states, when the each of the two parameteres are in the bottom decile (in yellow), and the top decile (in blue).

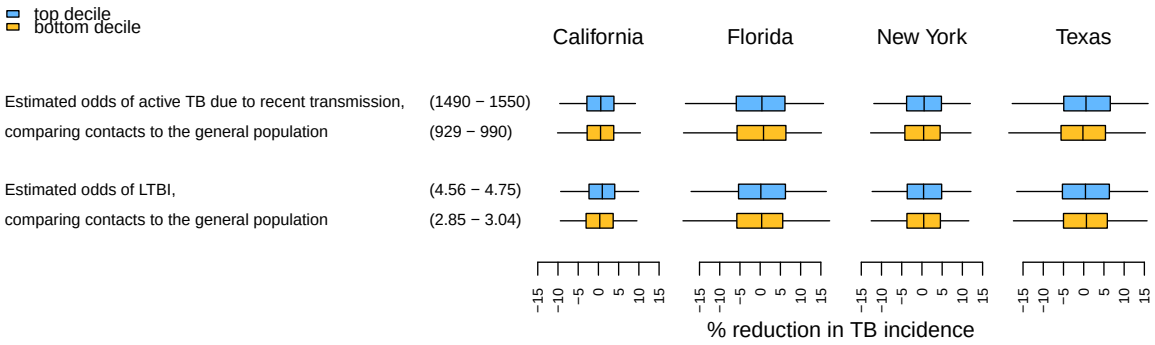

Figure S-5: Sensitivity of ECI Shown in box-plots are the impact of ECI in simulations with parameters in the top decile (in blue), and in the bottom decile (in yellow) for each of the four states. Top column shows the impact when O_T is varied, and bottom row shows the impact when O_L is varied. The numbers in parentheses represent the range for the top and bottom deciles. In each of the box-plot, the edges of the box represent the lower and upper interquartile range, the band in the middle represents the median, and the end of the whiskers represent 2.5^{th} and 97.5^{th} percentiles.

S-3 Sensitivity analyses: TTT

To explore the sensitivity analyses of TTT, we systematically varied parameters that characterize TTT targeting each of the high risk populations, and observed the variability in the impact of % reduction in TB incidence, in each of the four states. For TTT targeting diabetic individuals, we varied the annual per capita rate of developing diabetes, and the differential risk of reactivation (ratio of reactivation rates comparing diabetics vs. non-diabetic). For TTT targeting HIV-positive individuals, we varied the annual per capita rate of developing HIV, and the differential risk of reactivation (ratio of reactivation rates comparing HIV+ vs. HIV-). For TTT targeting incarcerated individuals, we varied the annual per capita rate of being incarcerated, and the differential risk in transmission (ratio of transmission rates comparing incarcerated individual vs. non-incarcerated individual). For TTT targeting homeless individuals, we varied the annual per capita rate of being homeless, and the differential risk in transmission (ratio of transmission rates comparing homeless individual vs. non-homeless individual).

Parameter range for each of the parameter in each instance corresponded to the 95% range estimated from model calibration. We used Latin Hypercube Sampling to sample 10,000 sets of parameters; each parameter uniformly sampled from the specified range. We estimated the impact specific TTT in each of the four states, and observed the variability in the estimates for extreme values of the parameters. Shown in Figs. S-6-S-9 are distributions of TTT impact for top and bottom decile of the parameters.

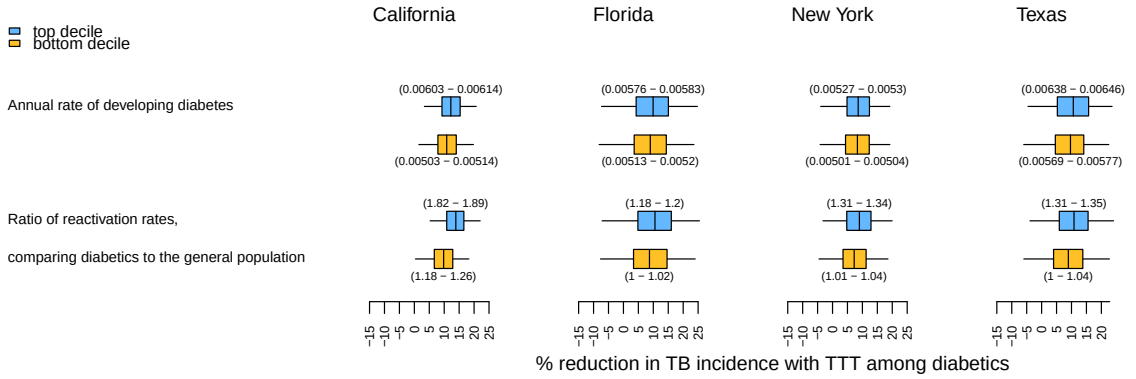

Figure S-6: Sensitivity of TTT targeting diabetic individuals. Shown in box-plots are the impact of TTT targeting diabetics in simulations with parameters in the top decile (in blue), and in the bottom decile (in yellow) for each of the four states. Top column shows the impact when the annual rate of developing diabetes is varied, and bottom row shows the impact when the ratio of reactivation rates (diabetic vs. non-diabetic) is varied. The numbers in parentheses above/below the box represent the range for the top and bottom deciles. In each of the box-plot, the edges of the box represent the lower and upper interquartile range, the band in the middle represents the median, and the end of the whiskers represent 2.5^{th} and 97.5^{th} percentiles.

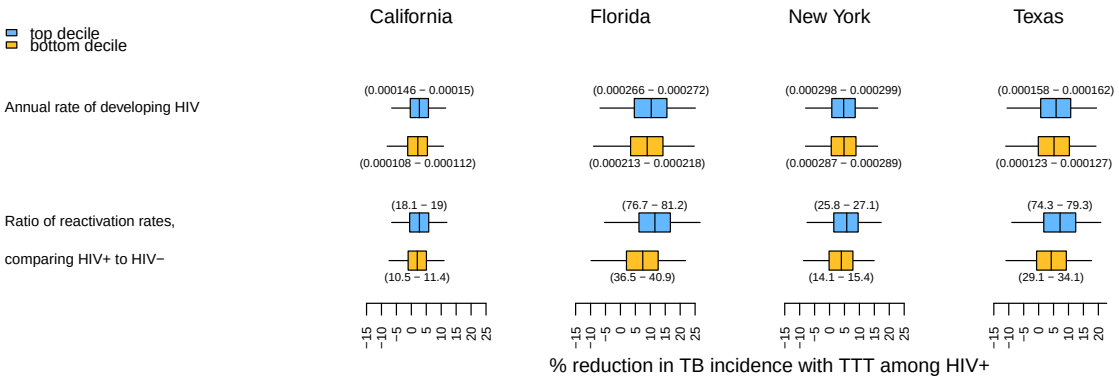

Figure S-7: Sensitivity of TTT targeting HIV-positive individuals. Shown in box-plots are the impact of TTT targeting HIV-positives in simulations with parameters in the top decile (in blue), and in the bottom decile (in yellow) for each of the four states. Top column shows the impact when the annual rate of developing HIV is varied, and bottom row shows the impact when the ratio of reactivation rates (HIV+ vs. HIV-) is varied. The numbers in parentheses above/below the box represent the range for the top and bottom deciles. In each of the box-plot, the edges of the box represent the lower and upper interquartile range, the band in the middle represents the median, and the end of the whiskers represent 2.5^{th} and 97.5^{th} percentiles.

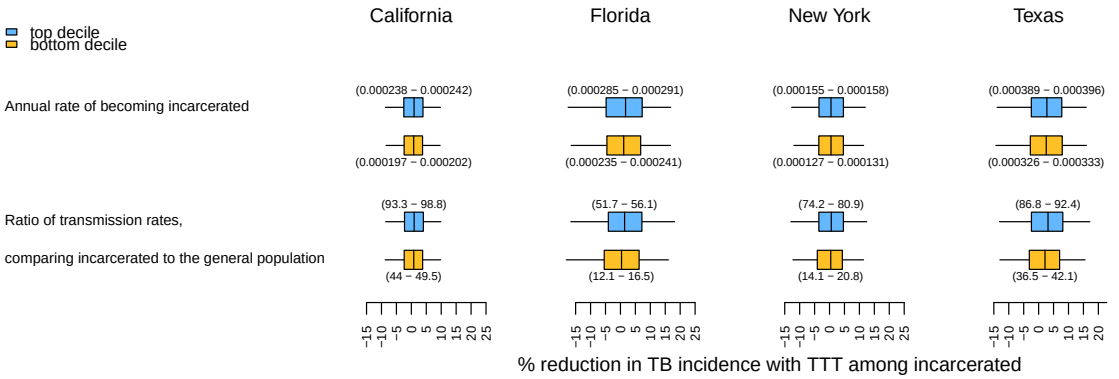

Figure S-8: Sensitivity of TTT targeting individuals that are incarcerated. Shown in box-plots are the impact of TTT targeting incarcerated individuals in simulations with parameters in the top decile (in blue), and in the bottom decile (in yellow) for each of the four states. Top column shows the impact when the annual rate of being incarcerated is varied, and bottom row shows the impact when the ratio of transmission rates (incarcerated vs. unincarcerated) is varied. The numbers in parentheses above/below the box represent the range for the top and bottom deciles. In each of the box-plot, the edges of the box represent the lower and upper interquartile range, the band in the middle represents the median, and the end of the whiskers represent 2.5^{th} and 97.5^{th} percentiles.

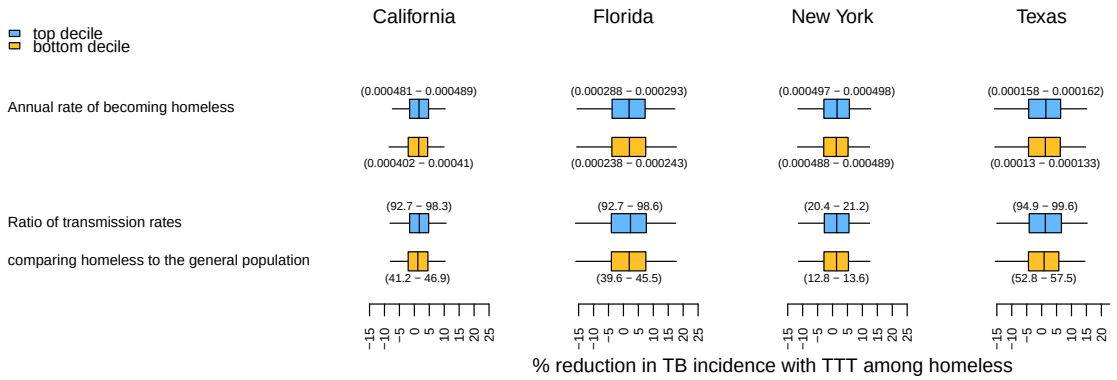

Figure S-9: Sensitivity of TTT targeting homeless individuals. Shown in box-plots are the impact of TTT targeting homeless individuals in simulations with parameters in the top decile (in blue), and in the bottom decile (in yellow) for each of the four states. Top column shows the impact when the annual rate of becoming homeless is varied, and bottom row shows the impact when the ratio of transmission rates (homeless vs. non-homeless) is varied. The numbers in parentheses above/below the box represent the range for the top and bottom deciles. In each of the box-plot, the edges of the box represent the lower and upper interquartile range, the band in the middle represents the median, and the end of the whiskers represent 2.5^{th} and 97.5^{th} percentiles.

S-4 Alternative model of TTT using 3HP

In the alternative model of TTT, we assumed 82% completion of LTBI therapy, and 86% efficacy of treatment for LTBI among those who complete therapy (closer to data from 3HP studies [6]). As in the previous model of TTT, outcomes were measured over 10 years following the interventions. The projected yields are shown in Table S-2 and can be compared to Table 3 in the manuscript; and the ~~the~~ projected impacts are shown in Table S-3 and can be compared to Table 4 in the manuscript. Overall, these results show that there are minimal difference between the impact of the two models.

Number of individuals (per 100,000 population)	California	Florida	New York	Texas
Non US-born[a]				
Individuals screened	13,389 (13,383-13,395)	9,698 (9,689-9,706)	10,951 (10,943-10,960)	7,880 (7,874-7,887)
Diagnoses of active TB	3.2 (3.0-3.4)	1.0 (0.9-1.2)	1.2 (1.1-1.4)	1.1 (1.0-1.2)
LTBI treatment completed	2,563 (2,559-2,567)	1,337 (1,332-1,342)	1,526 (1,521-1,532)	958 (954-962)
Diabetic[b]				
Individuals screened	7,776 (7,769-7,784)	8,359 (8,348-8,369)	7,566 (7,556-7,576)	7,878 (7,869-7,886)
Diagnoses of active TB	1.2 (1.0-1.3)	0.4 (0.3-0.5)	0.3 (0.2-0.4)	0.4 (0.3-0.5)
LTBI treatment completed	802 (799-805)	528 (523-533)	566 (560-572)	346 (344-348)
HIV-positive[c]				
Individuals screened	358 (357-360)	602 (599-605)	690 (687-693)	334 (332-336)
Diagnoses of active TB	0.29 (0.23-0.36)	0.51 (0.42-0.61)	0.23 (0.17-0.29)	0.27 (0.22-0.33)
LTBI treatment completed	41 (40-42)	30 (30-31)	46 (45-47)	13 (13-13)
Homeless[c]				
Individuals screened	760 (757-763)	548 (544-552)	967 (963-970)	270 (268-272)
Diagnoses of active TB	0.24 (0.19-0.28)	0.16 (0.10-0.21)	0.07 (0.04-0.10)	0.11 (0.07-0.14)
LTBI treatment completed	152 (151-153)	104 (103-106)	107 (105-109)	44 (43-44)
Incarcerated[c]				
Individuals screened	381 (379-383)	527 (524-531)	272 (270-274)	642 (639-644)
Diagnoses of active TB	0.11 (0.08-0.14)	0.06 (0.03-0.10)	0.03 (0.01-0.05)	0.26 (0.20-0.32)
LTBI treatment completed	80 (80-81)	64 (62-65)	35 (34-35)	94 (93-95)
All intervention[d]				
Individuals screened	20,580 (20,571-20591)	18,036 (18,024-18,049)	18,644 (18,633-18656)	15,747 (15,734-15,760)
Diagnoses of active TB	4.3 (4.1-4.5)	1.7 (1.6-1.9)	1.6 (1.4-1.8)	1.7 (1.6-1.9)
LTBI treatment completed	3,212 (3,207-3,217)	1,813 (1,805-1,822)	2,022 (2,012-2,030)	1,284 (1,280-1,288)

Table S-2: Projected yields of targeted testing and treatment (TTT) for tuberculosis in California, Florida, New York, and Texas under an alternative model of TTT.

[a] Assuming 50% coverage of TTT among all non US-born adults in each state.

[b] Assuming 80% coverage of TTT among all diabetic population in each state.

[c] Assuming TTT coverage to the entire population of the associated risk factor in each state.

[d] Assuming TTT of the above risk groups, each at the specified coverage.

Targeted risk population	**California**	**Florida**	**New York**	**Texas**
non US-born[a]	26.4% (24.9-27.9)	22.1% (18.5-25.6)	20.0% (16.7-22.8)	21.1% (18.5-23.7)
Diabetic[b]	11.0% (9.2-12.7)	8.4% (4.3-11.8)	7.4% (4.0-10.7)	7.1% (3.9-10.1)
HIV-positive[c]	2.1% (0.1-4.0)	9.1% (4.7-12.9)	4.9% (1.5-8.2)	3.1% (-0.1-6.1)
Homeless[c]	1.9% (0.0-3.7)	0.9% (-3.5-4.9)	1.1% (-2.4-4.5)	0.5% (-2.6-3.8)
Incarcerated[c]	0.7% (-1.1-2.5)	-0.2% (-4.6-4.0)	-0.2% (-3.7-3.1)	2.7% (-0.6-5.4)
All five risk groups[d]	35.1% (34.1-36.9)	35.7% (32.6-38.8)	28.9% (26.0-31.8)	31.7% (29.5-33.9)

Table S-3: Projected 10-year reduction in TB incidence under alternative model of TTT.
[a] Assuming 50% coverage of TTT among all non US-born adults in each state.
[b] Assuming 80% coverage of TTT among all diabetic population in each state.
[c] Assuming TTT coverage to the entire population of the associated risk factor in each state.
[d] Assuming TTT of the above risk groups, each at the specified coverage.

S-5 Alternative model of expanded contact investigation

In the alternative model of expanded TB contact investigation, we modeled ~~as~~ an increase in the number of index patients for whom contact investigations are performed, from the current estimate of about 50% to include all patients diagnosed with active TB, i.e. a 50% scale-up. We assumed that the general characteristics of the individuals detected in expanded contact investigations would remain similar to those currently observed. In particular, we estimated the number of contacts elicited and examined per index case, the odds of TB (active or LTBI) among contacts relative to the general population, and the rates of treatment completion among contacts diagnosed with LTBI from recent national data, and assumed these rates would continue in the expanded contact investigations (see Table 2 in the manuscript). This intervention was also modeled to take place over 10 years starting 2015, and the outcomes were measured over the same duration. The results in Table S-4 show that the impact of expanding contact investigation is small, as in the model explored in the main text.

Number of individuals (per 100,000 population)	**California**	**Florida**	**New York**	**Texas**
TB cases triggering contact investigation	49.6 (48.9-50.2)	24.4 (23.7-25.1)	31.2 (30.4-31.9)	33.2 (32.6-33.9)
Contacts screened	419.0 (413.6-424.5)	206.3 (200.7-212.3)	263.4 (256.7-269.8)	280.8 (275.3-286.3)
Additional Active TB diagnoses made	1.46 (1.21-1.75)	0.66 (0.33-0.69)	0.51 (0.45-0.86)	0.99 (0.75-1.24)
Additional LTBI treatments completed	36.9 (35.6-38.1)	10.8 (9.9-11.8)	15.7 (14.6-16.8)	10.1 (9.4-10.8)
Percentage reduction in TB incidence	1.3 (-0.65-3.19)	0.99 (-3.07-4.89)	0.26 (-3.37-3.78)	1.04 (-1.96-4.03)

Table S-4: Alternative model of expanded contact investigation.

S-6 Model-based estimates of LTBI prevalence

In Fig. S-10, we present model-based estimates of LTBI prevalence in the four states in 2015. Our modeling works shows that there could be substantial heterogeneity in the LTBI prevalence between the states, including among the non-US-born populations. These heterogeneities could be driven by the composition of the non-US-born population (e.g., non-US-born population in Florida and Texas have historically come from lower burden countries such as Cuba and Mexico, whereas in California they have come from higher burden countries such as the Phillipines or Vietnam.), or the historical levels of TB (e.g., TB incidence were substantially higher in New York compared to Texas in 1993, whereas they are at similar levels in both states currently).

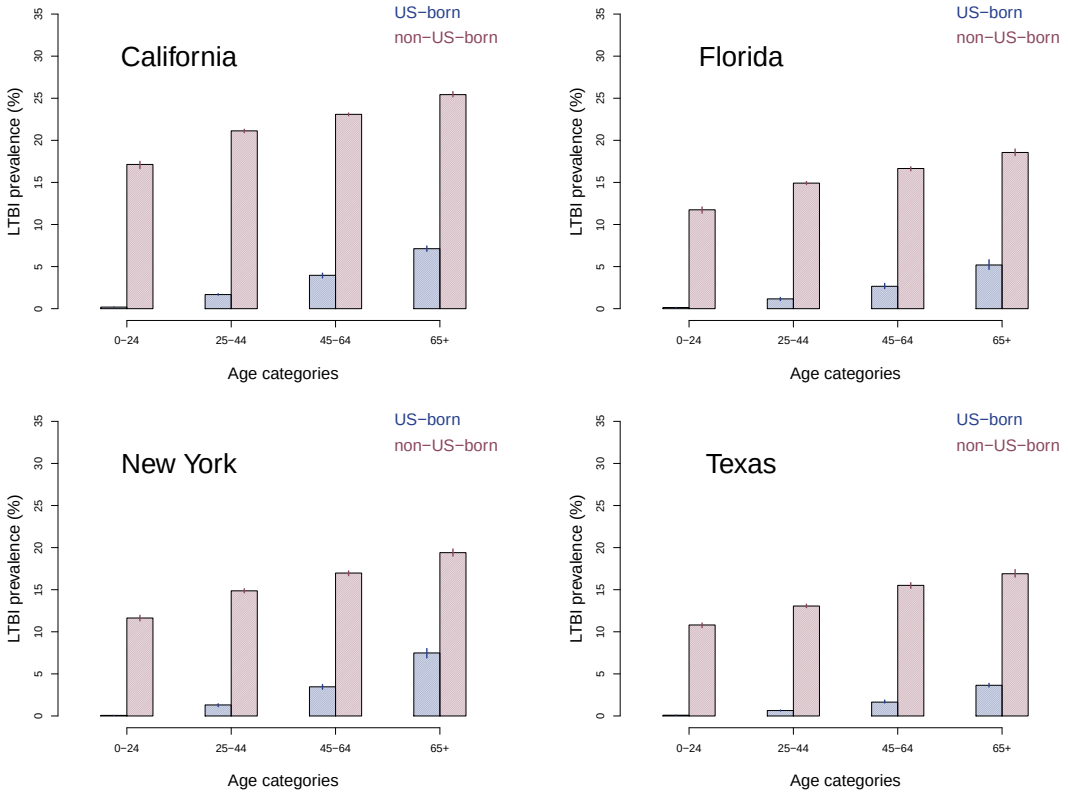

Figure S-10: LTBI prevalence. Shown are model-based estimates for LTBI prevalence in 2015 in the four states; [top-left] California, [top-right] Florida, [bottom-left] New York, and [bottom-right] Texas. Shown in red are estimates for non-US-born individuals, and shown in blue are estimates for US-born individuals.

In Table. S-5, we compare our model-based estimates against estimates from Haddad et al [7].

	California	**Florida**	**New York**	**Texas**
		Overall		
Haddad estimates	5.3%	3.3%	4.0%	4.2%
Model estimates	7.4%	4.4%	5.1%	3.1%
		US-born		
Haddad estimates	1.3%	1.7%	0.9%	1.9%
Model estimates	1.8%	1.5%	1.9%	0.9%
		Non-US-born		
Haddad estimates	16.1%	10.4%	14.9%	16.3%
Model estimates	22.4%	16.0%	16.1%	14.0%

Table S-5: Comparing LTBI estimates.

S-7 Comparing low and high NUSB LTBI prevalence scenarios

To explore sensitivity of model results to variation in LTBI prevalence in the NUSB population, we modeled TTT among NUSB in California under two different scenarios, one with low LTBI prevalence, and another with high LTBI prevalence.

	Scenario Low	**Scenario High**
LTBI prevalence among NUSB	20.5%	25.8%
Individuals screened (per 100,000 population)	13,379 (13,370-13,389)	13,386 (13,380-13,392)
Diagnoses of active TB (per 100,000 population)	2.3 (2.2-2.5)	3.2 (3.0-3.3)
LTBI treatment completed (per 100,000 population)	2,337 (2,333-2,341)	2,937 (2,932-2,941)
Reduction in TB incidence	26.1% (24.8-27.4)	24.8% (23.3-26.2)

Table S-6: Comparing TTT among NUSB in low and high LTBI prevalence scenarios.
Note: Assumes 50% coverage of TTT among all non US-born adults in each state.

S-8 NUSB TB cases by time since arrival

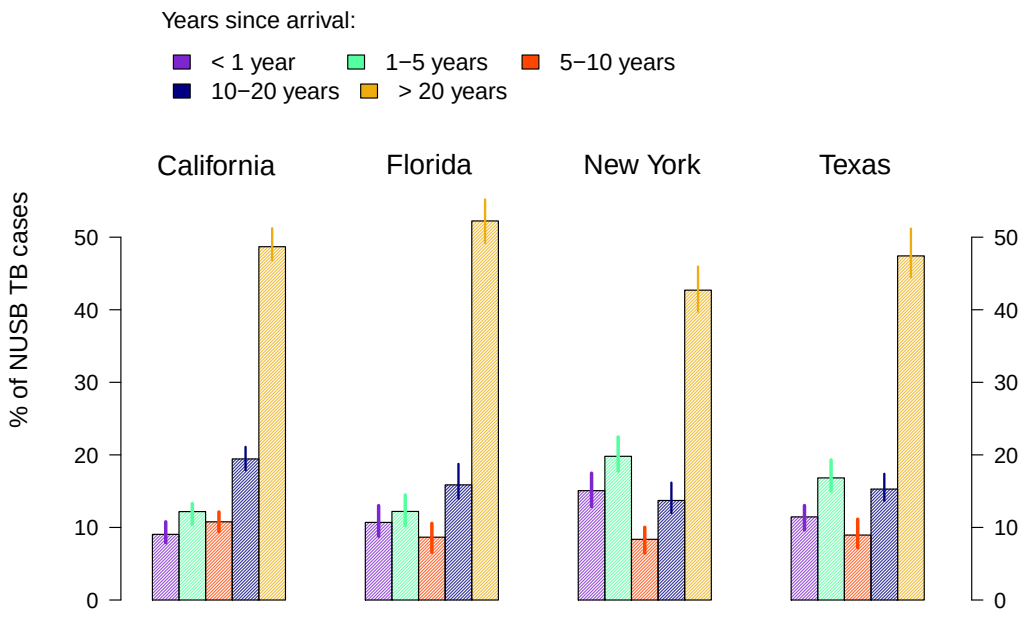

Figure S-11: Distribution of TB cases among NUSB individuals by time of arrival. Shown are model-based estimates for % of TB cases among NUSB, by time of arrival in to the US for California, Florida, New York, and Texas.

S-9 Model-based estimates for projected number of individuals screened for TTT

We estimated the number of individuals screened for TTT among various populations (presented in Table S-7), based on model-based estimates of the rates per 100,000 (Table 3, manuscript), and estimated population sizes for each of the four states. 2015 population estimates were 38,993,940 for California; 20,244,914 for Florida; 19,747,183 for New York and 27,429,639 for Texas.

Targeted risk population	**California**	**Florida**	**New York**	**Texas**
non US-born[a]	5,217,174	1,963,435	2,162,839	2,162,065
Diabetic[b]	3,027,658	1,690,180	1,494,210	2,161,962
HIV-positive[c]	139,634	121,749	136,732	91,090
Homeless[c]	302,454	110,433	190,549	74,139
Incarcerated[c]	147,951	106,514	53,687	177,016
All five risk groups[d]	8,021,624	3,648,742	3,682,537	4,321,179

Table S-7: Model-based estimates for projected number of individuals screed for TTT among various population groups.
[a]Assuming 50% coverage of TTT among all non US-born adults in each state.
[b]Assuming 80% coverage of TTT among all diabetic population in each state.
[c] Assuming TTT coverage to the entire population of the associated risk factor in each state.
[d] Assuming TTT of the above risk groups, each at the specified coverage.

S-10 Model-based projections of TB cases averted

We converted the projected reductions in TB incidence to generate estimates of number of TB cases averted by the two interventions over the 10 year period. The estimates (presented in Table S-8) were based on population projection for each of the states for the year 2020 (midway between 2015 and 2025). The projections were: 40,730,041.98 for California, 21,797,706.61 for Florida, 20,098,190.16 for New York and 29,803,662.74 for Texas.

Targeted risk population	**California**	**Florida**	**New York**	**Texas**
non US-born[a]	6,728 (6,418-7,026)	1,217 (1,084-1,358)	1,782 (1,592-1,965)	2,339 (2,109-2,579)
Diabetic[b]	2,553 (2,224-2,876)	393 (233-554)	526 (337-715)	768 (527-995)
HIV-positive[c]	528 (167-861)	401 (240-541)	356 (169-540)	448 (221-691)
Homeless[c]	359 (20-725)	91 (-61-246)	82 (-102-298)	87 (-158-310)
Incarcerated[c]	161 (-151-474)	70 (-104-227)	43 (-157-242)	211 (-18-471)
All five risk groups[d]	8,690 (8,392-8,968)	1,740 (1,602-1,894)	2,321 (2,155-2,490)	3,259 (3,033-3,463)
ECI	169 (-142-509)	28 (130-178)	55 (-130-247)	38 (-210-263)

Table S-8: Projected numbers of TB cases averted by TTT and ECI over 10 year period.
[a]Assuming 50% coverage of TTT among all non US-born adults in each state.
[b]Assuming 80% coverage of TTT among all diabetic population in each state.
[c] Assuming TTT coverage to the entire population of the associated risk factor in each state.
[d] Assuming TTT of the above risk groups, each at the specified coverage.

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