**Supporting information text on the model**

***Model overview***

The model focused on pulmonary TB and simply assumed all TB are pulmonary TB. The model features the natural history of TB according to the needs of the active case-finding algorithms of interest. Before healthcare, the model divides active TB by asymptomatic/symptomatic stage. The active TB states provide the force of infection to drive the transmission process. A group of latent TB infection states (LTBIs) captures those who do not progress active TB directly after infection and those who recovered from active TB. The LTBIs still have the risk of TB infection but with a lower susceptibility and TB reactivation/relapse among them are possible. We also considered the development of TB as a reversible process. That is, the active TB can be spontaneously cured and the LTBIs has a chance of self-clearance, which reverts the LTBIs to an uninfected state. Governing equations for India and South Africa are given in the next section, with calibration targets shown in Table S1.

In India, the model distinguishes public and private sectors. We modelled the ‘vulnerable’ population as consistent with undernutrition, the TB risk factor with the greatest population attributable risk in India (ref). Consistent with data from the Food and Agriculture Organisation (ref), we assumed that 16% of the population suffers undernutrition, and further that this population has three times the prevalence of TB as the general population. In South Africa, the model takes account of HIV status, stratified into HIV-negative; those with HIV but not on ART; and those on ART. We did not aim to model the transmission dynamics of HIV, instead treating this as an exogenous input. We drew data from UNAIDS for HIV incidence, and ART coverage, over time (ref) and assumed the declining in HIV infection and increasing in ART initiation following the five year trend between 2015-2019.

The simulation starts with at least 300 years warm-up until steady states at 2010. Then, we simulated to 2019 for pre-COVID dynamics, to 2022 for considering care disruption from COVID. The interventional strategies were evaluated from 2023 to the end of 2030

To capture the state of the TB epidemic in the pre-COVID period, we calibrated the model to each of the calibration targets shown in Table S1. To propagate uncertainty systematically from model inputs to model projections, we used a Sequential Monte Carlo for approximate Bayesian computation (ABC-SMC). We used an adaptive ABC-SMC which harmonised the metropolis hastings to effectively exploring sample spaces into SMC and enhanced the stability of sampling process. For calibration targets shown in Table S1 we constructed a distance function capturing the Euclidean distance between data and the simulation, scaling by uncertainty intervals of the calibration targets. Upon the convergence of the sampling, we collected 1,000 effective posterior samples for presentation. We computed all model projections on the basis of these samples, estimating central values as the median estimate, and the 95% Bayesian credible interval as the range between 2.5th and 97.5th percentiles.

Next, to capture the effects of COVID disruptions, we used the same approach to that currently employed by WHO, for estimates of TB burden in the wake of these disruptions: we adjusted the care seeking rate in order to match the quarterly notifications in each country, assuming that any drop in notifications, relative to 2019, were attributable to inaccessibility of TB services. Finally, we simulated all interventions assuming that they are initiated in 2023, scaled up over the subsequent three years, and sustained thereafter. Figure S1 shows the resulting trajectories for incidence and mortality, under each intervention scenario.

***Equations***

Uninfected

, where deaths include all types of causes (all terms with ) and is population size.

Latent TB infection and the recovered TB

, where

Active TB

\*For India

The India model has public and private for TB diagnostics and care provision. Therefore, diagnosis and treatment outcomes will depend on the system as will. Explicitly,

\*For South Africa

The South Africa model has the dimension for HIV dynamics with {x = Non-HIV, y = PLHIV not ART, z = PLHIV on ART}. For example, . Continuing the general equations for demography and TB dynamics, , , and , we have:

, where “ “ means the terms stated previously for each state. Apart from the HIV-mortality, the TB-HIV comorbidity was simply modelled on TB progression with incidence rate ratios for those with/without ART. That is, for all ,

**Table S1. Calibration targets for each country,** used forcalibration to pre-COVID conditions.

|  |  |  |
| --- | --- | --- |
| **Indicator** | **India** | **South Africa** |
| Prevalence of untreated TB, all types and all ages | Asymptomatic: 182 (167-197)  Symptomatic, pre-care seeking: 54.9 (46.8 - 63.3)  Symptomatic, sought care: 60.2 (51.8 - 68.8)  \* per 100k population, 95% CI calculated with binomial distributions  (ref) | Asymptomatic: 351 (289 - 414)  Symptomatic, pre-care seeking: 147 (108 - 187)  Symptomatic, sought care: 85.2 (56.8 - 116.5)  \* per 100k population, 95% CI calculated with binomial distributions  (ref) |
| TB case notification | TB case notification, 2017-2019 (after Nikshay launched) by public and private sectors | WHO TB case notification data, 2014-2019 |
| TB incidence and mortality | WHO TB burden estimates 2014-2019 | WHO TB burden estimates 2014-2019  UNAIDS TB incidence among PLHIV |

**Table S2. Baseline model parameters relevant to modelled interventions (calibrated parameters)**

|  |  |  |
| --- | --- | --- |
| **Parameter** | **India** | **South Africa** |
| Probability of diagnosis and treatment initiation, per patient careseeking visit | 60% for public sector  27% for private sector | 45% |
| Average duration of symptomatic TB before first careseeking | 3.8 (3.3 - 4.4) months | 3.2 (2.5 - 4.0) months |
| Average duration of subclinical TB before symptom onset | 4.5 (3.9 - 5.1) months | 2.6 (1.9 - 3.5) months |

**Table S3. Summary of impacts for each intervention scenario in 2030**

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Intervention scenario** | **India** | **South Africa** |
| **Cumulative TB incidence averted, 2023 - 2030** | Increased diagnostic uptake in healthcare settings | 8.5% (6.4% - 10.3%)  with PPM | 7.7% (5.7% - 9.5%) |
| Proactive case-finding, symptomatic TB | 8.8% (6.6% - 10.8%) | 6.4% (4.8% - 8.0%) |
| ACF, 10% of asymptomatic TB in vulnerable population | 1.3% (1.0% - 1.5%) | 1.3% (0.7% - 1.7%) |
| All measure combined | 13.9% (10.5% - 16.5%) | 14.0% (11.4% - 16.6%) |
| **Cumulative TB mortality averted, 2023 - 2030** | Increased diagnostic uptake in healthcare settings | 16.3% (13.8% - 19.1%) | 14.9% (11.3% - 18.1%) |
| Proactive case-finding, symptomatic TB | 17.0% (14.3% - 19.8%) | 12.1% (9.7% - 15.2%) |
| ACF, 10% of asymptomatic TB in vulnerable population | 1.8% (1.5% - 2.0%) | 1.7% (1.0% - 2.2%) |
| All measure combined | 25.5% (22.2% - 28.8%) | 25.2% (22.1% - 29.8%) |

**Table S4. Model parameters**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Parameter | Symbol | Value | Range | Source/Notes |
|  |  |  |  |  |
| Crude mortality rate |  | Exogenous input |  | Projection 2010 and 2030 population sizes from WPP2022 (ref) |
| TB-caused mortality, untreated TB |  | 0.127 |  | 70\% and 20\% untreated case-fatality for smear+/-ve  with 3 year disease duration (ref) |
| Background mortality rate |  |  |  | Reweighted crude mortality by excluded TB-caused deaths (+ HIV-related deaths for SA) |
| Population growth rate between 1970 and 2030 |  | Exogenous input |  | Calculated with 2010 and 2030 population sizes from WPP2022 |
| HIV incidence (SA only) |  | Exogenous input |  | Smoothed data based on UNAIDS data, and projected linearly at log scale |
| ART initiation (SA only) |  | Exogenous input |  |  |
| HIV mortality (SA only) |  | Exogenous input |  |  |
|  |  |  |  |  |
| **TB natural history** |  |  |  |  |
| Symptom development rate |  | 1 | 0.5, 6 | 2-24 months subclinical stage |
| Proportion of TB progress within two years following infection |  | 0.1 | 0.09, 0.14 | (ref) |
| Spontaneous recovery rate |  | 0.206 |  | (ref) |
| Self-clearance rate |  | 0.03 | 0.02, 0.04 | (ref) |
| Stabilisation rate, after infection |  | 0.5 |  | 2 years with high progression risk |
| Stabilisation rate, after the end of treatment |  | 2/3 |  | 1.5 years with high progression risk |
| Primary TB progression rate |  |  |  |  |
| Reactivation rate |  | 0.001 | 0.0005, 0.0015 | (ref) |
| Relapse rate, after treatment incompletion |  | 0.14 | 0.105,0.175 | (ref) |
| Relapse rate, after treatment completion |  | 0.032 | 0.024, 0.04 |
| Relapse rate, long-term |  | 0.002 | 0.0011, 0.0019 |
|  |  |  |  |  |
| **TB transmission** |  |  |  |  |
| Transmission rate |  | 10 | 1, 20 | Assumed range |
| The immunity to reinfection with the previous infection (reduction in susceptibility) |  | 21% | 14%, 30% | (ref) |
| Incidence rate ratio of PLHIV without ART (SA only) |  |  | 1, 30 | Assumed range |
| Incidence rate ratio of PLHIV with ART (SA only) |  |  | 1, | Assumed range |
|  |  |  |  |  |
| **Routine care, India** |  |  |  |  |
| Rate of initial care-seeking after the symptom onset |  |  | 1, 15 | Assumed range |
| Rate of revisit care-seeking |  |  | 1, 15 | Assumed range |
| Prop. seeking care from private sector |  | 0.5 | 0.4, 0.6 | Assumed range |
| Prop. correctly diagnosed per visit, public sector |  | 0.6 |  | (ref) |
| Prop. correctly diagnosed per visit, private sector |  | 0.27 |  | Assumed range |
| Treatment duration |  | 0.5 |  | A duration of 6 months as the WHO guideline |
| Prop. successful treatment |  | Public: 0.824  Private: 0.691  Overall: 0.779 |  | Matched to 2017-2021 India TB report data by public/private sectors and 2015-2019 WHO TB treatment outcomes |
| Prop. death during treatment period |  | Public: 0.041  Private: 0.025  Overall: 0.036 |  | Matched to 2017-2021 India TB report data by public/private sectors and 2015-2019 WHO TB treatment outcomes |
| Prop. failed and loss to follow-up on treatment |  |  |  |  |
| Rate of successful treatment |  | 1 / dur |  |  |
| Rate of death during treatment period |  |  |  |  |
| Rate of failed and loss to follow-up on treatment |  |  |  |  |
|  |  |  |  |  |
| **Routine care, South Africa** |  |  |  |  |
| Rate of initial care-seeking after the symptom onset |  |  | 1, 15 | Assumed range |
| Rate of revisit care-seeking |  |  | 1, 15 | Assumed range |
| Prop. correctly diagnosed per visit |  |  | 0.3, 0.7 | Assumed range |
| Treatment duration |  | 0.5 |  | A duration of 6 months as the WHO guideline |
| Prop. successful treatment |  | 0.782 |  | Matched to 2015-2019 WHO TB treatment outcomes |
| Prop. death during treatment period |  | 0.064 |  | Matched to 2015-2019 WHO TB treatment outcomes |
| Prop. failed and loss to follow-up on treatment |  |  |  |  |
| Rate of successful treatment |  | 1 / dur |  |  |
| Rate of death during treatment period |  |  |  |  |
| Rate of failed and loss to follow-up on treatment |  |  |  |  |

Chart

Description automatically generated

**Figure S1. Incidence and mortality curves under each intervention scenario.** These projections underlie the results for averted incidence and mortality, shown in Figure 1 in the main text. All interventions are as described in Figure 1.