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Assessing potential targeting strategies for future tuberculosis vaccines in India: a country-led modelling study

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Abstract

Background: Vaccination is a critical tool for achieving prevention at the scale required to meet the End TB targets. With promising TB vaccine candidates nearing licensure, and amid anticipated supply and delivery constraints, country-specific evidence is crucial to define vaccination priorities in high burden countries. Focusing on India, the country with the world's largest TB burden, we developed a country-led mathematical model to address this need. Based on the most recent epidemiological and programmatic data, we evaluate potential impact of different vaccine targeting strategies in India while establishing a model that can flexibly support future policy analyses as evidence evolves.

Design/Methods: Building on prior work and in consultation with India's key government stakeholders and technical experts, we constructed a deterministic compartmental model of TB transmission in India. We incorporated Prevention-of-Relapse (PoR) alongside Prevention-of-Disease (PoD) and Prevention-of-Infection (PoI) vaccine profiles to evaluate both pre- and post-treatment vaccination strategies; and key stratifications by age (<15 and ≥15 years), clinical risk factors focusing on nutritional status (BMI <18.5 vs ≥18.5 kg/m²) and Diabetes mellitus (DM), and urban–rural setting. Assuming 50% efficacy for all three vaccines as per WHO Preferred Product Characteristics (WHO PPC), we evaluated four targeting strategies: (i) untargeted vaccination; (ii) vaccinating individuals with low BMI; (iii) vaccinating individuals with Diabetes Mellitus; and (iv) vaccinating those in urban areas. We compared strategies according to overall impact, and cases averted per person vaccinated between 2027 and 2046.

Results: Across vaccine types, PoD vaccine consistently outperformed PoI and PoR vaccines, averting respectively 1.4 and 8 times more cases per vaccinated person. Model results highlight that optimal targeting strategies depend on vaccine availability. For example, for a PoD vaccine, if fewer than 300 million doses are available between 2030 and 2046, then the greatest

epidemiological impact would be achieved by targeting adults with low BMI, independently of urban/rural setting or Diabetes Mellitus. An 80% coverage scenario would avert 14.1% (95% uncertainty intervals (UI): 11.4–16.7) cases between 2027 and 2046. For higher vaccine availability, epidemiological impact would be maximised by expanding eligibility to all adults: an 80% coverage scenario would avert 44.1% (95% UI: 38.9–49.0) cases between 2027 and 2046.

Conclusion: Optimal tuberculosis vaccine deployment strategies will depend on the amount of vaccine available. Developed collaboratively with national stakeholders and by in-country modellers, this adaptable model can be readily adapted to incorporate new evidence and evolving programme priorities, such as other risk groups or data on emerging vaccines, to help guide vaccine policy decisions at both state- and national-level.

Keywords: Tuberculosis; TB vaccination; Compartmental modelling; Vaccine targeting; Vaccine prioritisation.

Manuscript

Research in context

Evidence before this study

A scoping review of papers published in PubMed from India and other low- and middle-income countries from 2014 to date, identified 11 studies (*Supplementary appendix S5*), estimating the impact of TB vaccination in India. However, only two studies addressed potential targeting strategies: one study focusing on adults with undernutrition, and another focusing on spatially targeted ('hot spot') strategies in the state of Gujarat. No previous study has directly compared different potential targeting strategies within a single model.

Added value of this study

We developed a compartmental deterministic TB transmission model informed by consultations with national policy stakeholders and technical experts. Guided by these consultations, and to our knowledge for the first time, our analysis incorporates several potential targeting strategies (age, clinical risk groups and urban populations) into a single modelling framework, for direct comparison. Secondly, the model used context specific updated epidemiological and programmatic input data. The model was calibrated to detailed data from India's national prevalence survey, including on the country-specific association between these risk factors and TB. Model projections suggest that – under conditions of limited vaccine supply – the greatest epidemiological impact would arise from targeting adults with low BMI, regardless of diabetes status or urban/rural location. However, if there is sufficient vaccine to saturate coverage in this group, then the greatest epidemiological impact would arise from making vaccination available to all adults in the country, regardless of urban/rural location or clinical risk.

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84 ***Implications of all the available evidence***

85 For any future TB vaccine, optimal deployment will depend on the amount of vaccine that will
86 be available, as well as the roles of various risk factors for TB. In India, our findings highlight
87 the importance of undernutrition in adults – compared to other factors such as diabetes or urban
88 location – in targeting the deployment of a future TB vaccine. Our work provides an example
89 of the value of country-led approaches, for country decision-making in future deployment of a
90 TB vaccine.

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Introduction

Vaccination is likely to be an important strategy for TB prevention at the required scale to achieve the End TB goals [1]. The World Health Organisation (WHO)'s full-value assessment (2022) emphasized the health and economic benefits of vaccines, especially in LMICs [2]. The only licenced vaccine currently against TB is BCG, which is routinely administered at birth and protects young children from severe forms of TB but is not effective in preventing adult pulmonary TB [3]. However, with encouraging developments in vaccine candidates such as M72/AS01E, VPM1002, Immuvac, MTBVAC, it is a timely moment to begin assessing the implementation priorities for a future, more effective TB vaccine that could become available within the next 5–10 years [4].

The National TB Elimination Programme (NTEP) in India has identified and is implementing several interventions to achieve TB elimination in India [5]. However, as a country with the world's largest TB burden, an effective TB vaccine would have profound impact on TB burden reduction [6, 7]. In such a diverse country of over 1.4 billion people, it is likely that targeting may be necessary in the initial stages of vaccine rollout, when supply may be limited. However, it is unclear which targeting strategies may be most effective; for example, based on clinical risk factors for TB [8], or high-prevalence geographic areas [9]. Although previous modelling studies in India have examined age-based, risk-based, or spatially targeted approaches ([8–10]) separately, no study has directly compared these strategies with one another in a single model [11]. We addressed this gap by developing a mathematical transmission model that leverages the most recent epidemiological and programmatic data to evaluate the potential impact of different vaccine targeting strategies in India.

Methods

The model was developed collaboratively with national stakeholders, technical experts, and in-country modellers to develop its structure and calibrate it using context specific epidemiological and programmatic features and corresponding data, as summarised below.

Country consultations to inform model development

We convened an Expert Advisory Group including experts from national institutes and organisations of national importance, and decision-makers actively engaged in strategic planning for vaccine deployment. This group included representatives from the National Institute for Research in Tuberculosis (NIRT), project collaborators and partners, and key stakeholders and advisors from Central TB Division (CTD) and the Indian Council of Medical Research (ICMR). Two clinical risk groups emerged as priorities: low body mass index (BMI) (BMI <18.5 kg/m^2) and diabetes, both leading risk factors in terms of their population-attributable fractions associated with TB [11]. For example, the Annual India TB Report 2024 highlights undernutrition and diabetes as key programmatic risk factors for TB, with targeted efforts under NTEP including nutritional support and bidirectional TB-diabetes screening [6]. In addition, stakeholders emphasised the potential value of geographically focused strategies: specifically, targeting urban areas for vaccination. Given the range of vaccine candidates currently under development, stakeholders recommended that the model remain vaccine-agnostic to allow flexible application across potential products. Guided by this feedback, we developed an extended model structure incorporating undernutrition, diabetes and geographic heterogeneity in TB burden in India, in a single model. Other important risk groups, including individuals with a previous history of TB, household contacts, tobacco or alcohol use, and people living with HIV, were not included in the current analysis. Given the complexity of the model structure, we focused on two clinical risk groups in this first application. However, the

model was designed to be adaptable, and future applications can incorporate additional risk groups as relevant evidence and data become available.

Model structure

We built on previous work [8], developed in collaboration with Central TB division (CTD), Ministry of Health & Family Welfare-Government of India (MoHFW-GOI), which employed a deterministic compartmental model of TB transmission and healthcare delivery in India, representing TB transmission, natural history, diagnosis, treatment, and health-service pathways while distinguishing between public and private healthcare sectors.

We adapted the model to incorporate epidemiological and programmatic features identified as priorities through stakeholder consultations as specified above. Specifically, we incorporated key stratifications by age (<15 and ≥15 years); clinical risk factors i.e., nutritional status (BMI <18.5 vs ≥18.5 kg/m²) and Diabetes mellitus (DM) and urban–rural setting. Additionally, we incorporated a Prevention-of-Relapse (PoR) vaccine alongside Prevention-of-Disease (PoD) and Prevention-of-infection (PoI) vaccine profiles. Recurrence encompasses both exogenous reinfection endogenous relapse, although these mechanisms may be affected differently by different vaccines. WHO PPCs envisage a 'prevention of recurrence' vaccine targeting both. However, through its mechanism of protection, a PoI vaccine is likely to target reinfection as well as primary infection. For biological plausibility, therefore, we characterized a 'prevention of relapse' vaccine as one targeting endogenous relapse alone, assuming that a PoI vaccine would target prevention of reinfection. The model structure is illustrated schematically in Figure 1. The model structure is illustrated schematically in Figure 1.

We assumed that undernutrition and DM are associated with increased rates of progression from TB infection to disease, consistent with their known immunosuppressive effects. We modelled the greater burden of TB in urban than rural areas by assuming a higher intensity of transmission in urban areas subject to sensitivity analysis (discussed further below). To account for the fact that not all TB treatment in India is notified to public health authorities, the model distinguishes notifying and non-notifying healthcare providers. Age-specific transmission was represented using an age-structured contact matrix, with the force of infection estimated separately for child and adult/adolescent populations in urban and rural settings to capture differences in contact patterns and transmission intensity.

For the impact of a future vaccine, we modelled three types of vaccine effect: we assumed that a PoI vaccine would reduce susceptibility to infection; that a PoD vaccine would reduce rates of progression from TB infection to disease; and that a PoR vaccine would be implemented to self-cured individuals and individuals following TB treatment by notifying providers, reducing the risk of endogenous, post-treatment relapse. In practice, a future vaccine may be expected to have some combination of these effects: for simplicity, we assumed exclusive effects, e.g. that a PoD vaccine would have no PoI or PoR efficacy. Full governing equations are provided in the supporting information.

Data and calibration

Data was drawn from the National TB Prevalence survey in India (NTBPS 2019–2021) [12], India TB report 2024 [6], and WHO burden estimates [13] (*Table 1*). Clinical risk factors were incorporated by applying relative risks (RRs) of TB disease for low BMI and diabetes, using estimates derived from the reanalysis of unpublished NTBPS data for univariate RRs. Population prevalence estimates for risk groups, including individuals with low BMI and

diabetes, were derived from health surveys [14] and cohort studies [15]. Data for TB notifications were incorporated to reflect the current coverage and performance of routine TB services in India.

For each source of data, we constructed likelihood functions using log-normal distributions for rates and beta distributions for proportions, with uniform priors assigned to all parameters, spanning plausible parameter ranges. The posterior density was obtained as the product of individual likelihoods, with computations performed using log-likelihoods for numerical stability. We sampled from this posterior distribution using adaptive Bayesian Markov Chain Monte Carlo (MCMC) [16], with 50,000 samples retained from the final MCMC run (details of the calibration procedure are provided in the *supplementary appendix*). Following an initial burn-in phase and thinning of the chain to reduce autocorrelation, 200 posterior samples were drawn. Model outputs—including projections of cases averted, deaths averted, and cumulative people vaccinated —were computed for each sample, with median estimates reported as point values, and 95% uncertainty intervals (UIs) defined by the 2.5th and 97.5th percentiles of the posterior distribution.

Intervention scenarios

For PoD, PoI and PoR vaccines separately, we modelled vaccine deployment under three targeting strategies: (i) untargeted (i.e. regardless of risk group); (ii) targeted amongst individuals having clinical risk factors (diabetes or undernutrition); and (iii) urban populations. We also compared vaccination targeting in children vs adults. In all scenarios, we assumed the vaccine to become available in 2027, with efficacy of 50%, in line with the WHO Preferred Product Characteristics (WHO-PPC) [17] for new tuberculosis vaccines.

For comparability across vaccine types and age scenarios, we assumed a constant hazard of vaccine uptake. Coverage assumptions were informed by India's Japanese encephalitis vaccination campaign, which achieved 88.4% coverage among more than 10.5 million children [18], demonstrating the feasibility of high vaccine uptake in large-scale campaigns. In addition, previous India-specific TB vaccine modelling studies assumed routine vaccination coverage of 80% [19]. Therefore, we estimated this limit to be around 80% of the eligible population, representing a feasible implementation target in India. For each targeting strategy, we simulated a range of vaccination coverages up to and including this limit. We interpret vaccination coverage as the prevalence of vaccine-induced immunity in the population once this prevalence reaches a steady state. For the present analysis, we considered coverage levels of 20%, 50%, and 80% to represent low, intermediate, and high vaccination coverage, respectively. For each targeting strategy, we then plotted epidemiological impact (percent cases and deaths averted) against the cumulative number of people vaccinated between 2027 and 2046. These outputs enabled us to compare targeting strategies at different levels of vaccine availability.

As a comparator, we modelled a 'no vaccine' scenario assuming that current epidemiological and programmatic conditions continue indefinitely. Consistent with previous work [8], we assumed that vaccine-induced protection lasts for an average of ten years. Vaccination of children was assumed to be performed in addition to routine BCG immunisation, rather than as a replacement.

Sensitivity Analyses

We performed parametric sensitivity analysis using Partial Rank Correlation (PRCCs) to identify those model parameters most strongly associated with key modelled outputs,

specifically the percent reduction in cumulative incidence. We explored uncertainty in vaccine efficacy by modelling alternative scenarios of 25% and 75% efficacy.

Study tool: This model was coded and implemented in *MATLAB*, version R2024b software (MathWorks Inc. Natick, MA, USA).

Role of the funding source

The study was executed through funding support from both Gates Ventures and Knowledge Integration and Translational Platform (KnIT, a Biotechnology Industry Research Assistance Council (BIRAC) initiative). The funder had no role in the model design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit.

Results

The resulting model comprises 288 compartments capturing TB natural history, age, clinical risk group and urban–rural stratifications, healthcare pathways, and vaccine effects.

Supplementary Figures S4.1–S4.3 present the model calibration results, including MCMC convergence, posterior parameter distributions, and agreement between model outputs and calibration targets.

Results in Figure 2 reveal the relative value of different targeting strategies, with steeper curves corresponding to strategies that can achieve greater epidemiological impact per person vaccinated, and with each curve terminating at points representing 80% coverage in each respective eligible population. Under the PoD strategy targeting all adults (Figure S6A), cumulative vaccination scaled up to approximately 2.38 billion individuals by 2046 at 80% coverage, yielded the greatest projected epidemiological benefit, averting 44.1% (95% uncertainty interval [UI]: 38.9–49.0) of cumulative incidence by 2046 (Table 2). In comparison, PoD strategies targeting low BMI adults (0.28 billion cumulative vaccinations),

urban adults (0.87 billion), and adults with diabetes (0.32 billion) achieved reductions of 14.1% (95% UI: 11.4–16.7), 8.18% (95% UI: 7.26–9.45), and 7.60% (95% UI: 5.89–9.33), respectively. The corresponding reductions in cumulative deaths by 2046 were 39. 8% (95% UI: 35.4–44.1) for all adults, 12.6% (10.3–14.8) for adults with low BMI, 6.69% (5.30–8.16) for adults with diabetes, and 4.08% (3.41–5.26) for urban adults (Table 2).

Overall, and consistent with previous work [9, 20, 21], a PoD vaccine (solid lines) would have more epidemiological impact per person vaccinated than a PoI or PoR vaccine with the same efficacy (respectively, dashed and dotted lines). For a PoD vaccine in particular, limited vaccine supply targeted toward adults with low BMI generated substantial epidemiological benefit (green, solid-line curve) – for example, with a vaccination programme having 50% coverage amongst adults with low BMI per year averting 10.3% (95% UI: 8.38–12.15) of cumulative incidence by 2046 and involving 0.21 billion people being vaccinated during this time. Further, where there is sufficient vaccine supply to saturate coverage in adults with low BMI, our results suggest that the most efficient strategy for a PoD vaccine would be to expand coverage to all adults irrespective of BMI, DM status, or urban/rural location (blue, solid-line curve). For example, a vaccination programme with 50% amongst adults would avert 26.8% (95% UI: 23.0–30.8) of cumulative cases by 2046, with 1.39 billion people being vaccinated during this time.

Figure S6B and S6C in the supporting information shows similar patterns for PoI and PoR vaccines, but at substantially lower levels of impact. For example, a PoR vaccine covering 80% of adults completing treatment in the public sector, as well as those being managed by private providers engaged with the NTEP, would reduce cumulative incidence by 6.4% (95% UI: 5.2–8.3) by 2046.

Figure 3 shows illustrative epidemic curves for TB incidence and mortality, under the two most efficient strategies, i.e. targeting a PoD vaccine towards adults with low BMI, and towards adults in general. The figures highlight how epidemiological impact would increase with vaccine coverage, with burden reductions summarised in Table 3. Increasing vaccination coverage, as defined elsewhere, substantially reduced TB incidence and mortality under both vaccination strategies. By 2046, vaccinating all adults produced the greatest epidemiological impact, reducing TB incidence from 185.9 to 132.2 and 74.4 cases per 100,000 population under the medium- and high-coverage scenarios, respectively, with corresponding mortality declining from 25.4 to 18.5 and 10.5 deaths per 100,000 population.

Sensitivity analyses

PRCC analysis assessed model inputs associated with the relative impact of targeting adults with low BMI versus all adults, measured as the relative gradient in cumulative TB cases averted by 2046. The strongest negative associations were with the proportion of births among individuals with low BMI and the activation rate; the strongest positive associations were with child mortality and the relative risk associated with low BMI. Other inputs had smaller associations (Supplementary Figure S7.1).

At a vaccine efficacy of 25%, PoD vaccination at 80% coverage averted 24.9% (95% UI: 21.1–28.8) of cases and 22.3% (19.1–25.6) of deaths among all adults, compared with 7.0% (5.7–8.3) of cases and 6.2% (5.1–7.3) of deaths among adults with low BMI. For all-adult vaccination, PoI averted 17.5% (11.1–25.0) of cases and PoR 3.2% (2.6–4.2) (Table S7.1; Figure S7.2).

At a vaccine efficacy of 75%, PoD vaccination averted 59.0% (53.8–63.2) of cases among all adults and 21.2% (17.2–25.2) among adults with low BMI. For all-adult vaccination, PoI averted 41.0% (28.3–53.4) of cases and PoR 9.6% (7.8–12.4) (Table S7.3; Figure S7.3). These

sensitivity analyses were consistent with the main results, with PoD vaccination of all adults achieving the greatest overall impact across the vaccine efficacy scenarios.

Discussion

In the initial stages of deployment of a future TB vaccine, when supply may be limited, it will be important to anticipate what targeting strategies may yield the greatest epidemiological impact. Earlier work has addressed targeting those with clinical risk factors [8], or high-prevalence geographic areas [9], both key strategies raised by decision-makers. Here, to our knowledge for the first time, we have used data from India's recent national TB prevalence survey to combine both in a single model, allowing us directly to compare the potential epidemiological impact of these strategies. Consistent with previous work [8], model findings highlight the importance of targeting vaccination appropriately under given levels of vaccine availability (Figure 2). While vaccinating all adults achieved the largest absolute reductions in incidence and mortality by 2046, targeting adults with low BMI generated substantial epidemiological gains with a considerably smaller number of vaccinations, highlighting its potential value when vaccine supply is constrained.

Our findings suggest that a PoD vaccine has the greatest overall impact, averting 44.1% of cumulative TB cases with approximately 2.38 billion vaccinations at 80% coverage, compared with 30.8% for PoI and 6.41% for PoR vaccines at the same efficacy. This pattern likely reflects the ability of PoD vaccines to interrupt progression to disease more directly, thereby generating greater reductions in transmission and downstream burden. Under constrained vaccine supply, targeting adults with low BMI remains an impactful strategy: at 80% coverage, approximately 0.28 billion vaccinations could avert 14.09% of cumulative cases. This finding is particularly relevant in the Indian context, where undernutrition remains a major contributor to TB burden

and targeted strategies may maximise the epidemiological benefit obtained per vaccine delivered. However, once vaccine supply is sufficient to saturate coverage within this group, the most impactful strategy would become vaccinating all adults irrespective of geography or BMI status. This suggests that the optimal targeting strategy may shift towards broader population-level vaccination as supply and delivery capacity increases.

While these findings identify strategies that maximise epidemiological impact, translating these gains into practice will require consideration of broader implementation and health-system factors that influence vaccine introduction and delivery. For example, while a PoR vaccine may have the least impact of the scenarios modelled here, it is also likely to be operationally much more straightforward to implement than a PoD or PoI vaccine, given that it involves TB patients already being managed by the programme. Another key consideration is the potential for variation in vaccine effectiveness across population subgroups, in ways that clinical trials may not be powered to detect, but that are nonetheless consequential for programmatic prioritisation. For example, vaccine effectiveness may be hindered by the immunomodulatory effects of undernutrition, meaning that the actual impact of vaccination in adults with low BMI may be lower than modelled here. This possibility highlights the need for post-introduction monitoring [22], to strengthen the evidence basis for prioritisation. WHO guidance on new vaccine introduction further emphasises considerations such as health system capacity, supply chain readiness, financing, and implementation planning [23], while Indian operational guidelines underscore the importance of microplanning, workforce training, logistics preparedness, and real-time monitoring to support effective rollout [24].

This study's strengths include its grounding in nationally representative NTBPS data, explicit incorporation of country-prioritised risk groups in a single framework, and programmatic context informed through consultation with national stakeholders involved in National TB Elimination Programmes and adult vaccination campaigns. Designed and implemented by in-

country modellers, the model has strong country ownership; it was developed to be adaptable, allowing for future refinement as new vaccine trial results, more granular epidemiological data, or programme delivery strategies become available. The structured inclusion of multiple heterogeneities—clinical, demographic, and geographic—also provides a foundation for integrated planning as India develops plans for phased vaccine introduction.

As with any modelling study, there are limitations to be acknowledged. This analysis focuses on two clinical risk factors for TB, undernutrition and diabetes. While these are leading risk factors for TB in India, with estimated population attributable fractions (PAF) of 24.8% and 15%, respectively [25, 26], the model does not address other risk factors such as past history of TB, tobacco use, alcohol dependence, household contacts, or HIV. Vaccine characteristics were modelled using WHO Preferred Product Characteristics (WHO-PPC), but real-world efficacy, duration of protection, and varied efficacy across risk groups remain uncertain. We did not model dosing schedules, assuming for simplicity that individuals would receive a single dose. For any future vaccine requiring multiple doses, there will be important questions about the degree of protection associated with incomplete uptake of this regimen. Provided data on this partial protection, our model can be adapted to account for any incomplete uptake observed in real world vaccine deployment. This study also does not evaluate costs or cost-effectiveness analyses, which will be crucial for determining whether targeted or broad-based strategies are realistic for implementation. Additionally, although the model incorporates urban–rural variation, India's TB burden varies substantially across states, suggesting that more granular subnational modelling will be important for state-level decision-making.

Despite these limitations, the findings have clear policy implications. Where the rollout of a new TB vaccines faces constraints in supply, delivery capacity, or coverage, PoD vaccination of adults, particularly those with low BMI, offers the highest impact, both in absolute terms and per person vaccinated. As supply expands and delivery capacity strengthens, broader

strategies such as general adult vaccination may become appropriate. As Phase III trial data become available and India prepares for phased introduction of new TB vaccines, the country-owned modelling model developed here can support scenario analysis, equity assessments, and vaccination delivery strategies aligned with national priorities.

This work represents a country-led effort by India-based modellers in collaboration with national decision-makers and stakeholders. In this first application of the model, we evaluated population-wide and risk-targeted vaccination strategies across different modes of vaccine protection to understand how targeted deployment of new vaccines could accelerate TB decline. The model provides an adaptable framework that can be continually refined to incorporate emerging evidence, evolving vaccine characteristics, additional population stratifications, and future policy priorities, thereby supporting ongoing evidence-informed decision-making for TB vaccine introduction in India.

Declarations

Ethics approval and consent to participate

Not applicable. This study used secondary data and mathematical modelling and did not involve the collection of primary data from human participants.

Consent for publication

Not applicable. This study does not contain any individual person's data or identifiable information.

Availability of data and materials

The data used in this study were obtained from publicly available sources and from research institutions. The data supporting the findings of this study are provided in the main manuscript and Supplementary Information.

Competing interests

The authors declare that they have no competing interests.

Author contribution:

RG and SSw conceptualized the study. NA, RR, and SP designed the model structure. RJ implemented the model, coded and conducted the modelling analyses. SSe, AB, RJ, and BP acquired, curated, and prepared the input data for the model. Programmatic and scientific inputs that informed model assumptions and parameterization were provided by ManM, UBS, VD, SR, RR, and SSn. Data interpretation and alignment of the study findings with programmatic priorities were undertaken by MM, UBS, VD, RR, SR, SSn, RG, NA, JJ, SuH, MuM, and RJ. RJ, NA, and JJ prepared the first draft of the manuscript. All authors reviewed and revised

subsequent versions of the manuscript, provided intellectual input, and approved the final version for submission.

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References

1. The Global Plan to End TB 2023-2030. United Nations Office for Project Services, 2023. Stop TB Partnership, 2022. 2023.

2. World Health Organization. (2022, December 8). An investment case for new tuberculosis vaccines (Technical document).

3. Colditz GA, Brewer TF, Berkey CS, Wilson ME, Burdick E, Fineberg HV, et al. Efficacy of BCG vaccine in the prevention of tuberculosis. Meta-analysis of the published literature. JAMA. 1994;271:698–702.

4. An Y, Ni R, Zhuang L, Yang L, Ye Z, Li L, et al. Tuberculosis vaccines and therapeutic drug: challenges and future directions. Mol Biomed. 2025;6:4. https://doi.org/10.1186/s43556-024-00243-6.

5. National Tuberculosis Elimination Programme. https://dghs.mohfw.gov.in/national-tuberculosis-elimination-programme.php. Accessed 22 July 2026.

6. Ministry of Health and Family Welfare. Government of India. India TB Report 2024.

7. Central Tuberculosis Division. National Strategic Plan to End TB in India 2020-25. https://tbcindia.mohfw.gov.in/national-strategic-plan-to-end-tb-in-india-2020-25/. Accessed 17 Sept 2026.

8. Arinaminpathy N, Rade K, Kumar R, Joshi RP, Rao R. The potential impact of vaccination on tuberculosis burden in India: a modelling analysis. Indian J Med Res. 2023;157:119–26. https://doi.org/10.4103/ijmr.ijmr_328_23.

9. Clark RA, Portnoy A, Weerasuriya CK, Sumner T, Bakker R, Harris RC, et al. Estimating the potential health and economic impacts of new tuberculosis vaccines under varying

463 delivery strategies in Delhi and Gujarat, India: a modelling study. Lancet Reg Health -
464 Southeast Asia. 2024;31. https://doi.org/10.1016/j.lansea.2024.100424.

465 10. Shrestha S, Chatterjee S, Rao KD, Dowdy DW. Potential impact of spatially targeted
466 adult tuberculosis vaccine in Gujarat, India. J R Soc Interface. 2016;13:20151016.
467 https://doi.org/10.1098/rsif.2015.1016.

468 11. Selvaraju S, Velayutham B, Rao R, Rade K, Thiruvengadam K, Asthana S, et al.
469 Prevalence and factors associated with tuberculosis infection in India. J Infect Public Health.
470 2023;16:2058–65. https://doi.org/10.1016/j.jiph.2023.10.009.

471 12. Central Tuberculosis Division. National TB Prevalence Survey in India 2019 – 2021.
472 https://tbcindia.mohfw.gov.in/2023/06/06/national-tb-prevalence-survey-in-india-2019-2021/.
473 Accessed 8 Sept 2025.

474 13. World Health Organization (WHO), WHO 2024. Global TB Report 2024.

475 14. International Institute for Population Sciences (IIPS) & ICF. National Family Health
476 Survey (NFHS-5), 2019-21: India Fact Sheet.

477 15. Anjana RM, Unnikrishnan R, Deepa M, Pradeepa R, Tandon N, Das AK, et al. Metabolic
478 non-communicable disease health report of India: the ICMR-INDIAB national cross-
479 sectional study (ICMR-INDIAB-17). Lancet Diabetes Endocrinol. 2023;11:474–89.
480 https://doi.org/10.1016/S2213-8587(23)00119-5.

481 16. van Ravenzwaaij D, Cassey P, Brown SD. A simple introduction to Markov Chain
482 Monte–Carlo sampling. Psychon Bull Rev. 2018;25:143–54. https://doi.org/10.3758/s13423-
483 016-1015-8.

484 17. World Health Organization. WHO preferred product characteristics for new tuberculosis
485 vaccines. Geneva: World Health Organization; 2018.

486 18. Ghosh RS, Haldar P, Jacobson J. Lessons learned from the Japanese encephalitis vaccine
487 introduction in India that supported the introduction of ivermectin–diethylcarbamazine–
488 albendazole for lymphatic filariasis elimination. Am J Trop Med Hyg. 2022;106 5 Suppl:48–
489 55. https://doi.org/10.4269/ajtmh.21-1168.

490 19. Clark RA, Weerasuriya CK, Portnoy A, Mukandavire C, Quaife M, Bakker R, et al. New
491 tuberculosis vaccines in India: modelling the potential health and economic impacts of
492 adolescent/adult vaccination with M72/AS01E and BCG-revaccination. medRxiv.
493 2023;:2023.02.24.23286406. https://doi.org/10.1101/2023.02.24.23286406.

494 20. Arinaminpathy N, Rade K, Kumar R, Joshi RP, Rao R. The potential impact of
495 vaccination on tuberculosis burden in India: A modelling analysis. Indian J Med Res.
496 2023;157:119–26. https://doi.org/10.4103/ijmr.ijmr_328_23.

497 21. Clark RA, Weerasuriya CK, Portnoy A, Mukandavire C, Quaife M, Bakker R, et al. New
498 tuberculosis vaccines in India: Modelling the potential health and economic impacts of
499 adolescent/adult vaccination with M72/AS01E and BCG-revaccination. medRxiv.
500 2023;:2023.02.24.23286406. https://doi.org/10.1101/2023.02.24.23286406.

501 22. WHO Evidence Considerations for Vaccine Policy Development for Tuberculosis
502 Vaccines Intended for Adults and Adolescents.
503 https://www.who.int/publications/i/item/9789240093980. Accessed 6 Oct 2025.

504 23. World Health Organization. Introduction of new vaccines: implementation guidance.
505 Geneva: World Health Organization; https://www.who.int/teams/immunization-vaccines-and-

biologicals/essential-programme-on-immunization/implementation/introduction-of-new-vaccines. Accessed 25 Feb 2026.

24. Ministry of Health and Family Welfare, Government of India. COVID-19 vaccine operational guidelines. New Delhi: MoHFW; 2020.

25. Bhargava A, Bhargava M, Beneditti A, Kurpad A. Attributable is preventable: Corrected and revised estimates of population attributable fraction of TB related to undernutrition in 30 high TB burden countries. J Clin Tuberc Mycobact Dis. 2022;27:100309. https://doi.org/10.1016/j.jctube.2022.100309.

26. Rakesh PS, Balakrishnan S, Mathew ME, Mrithunjayan S, Manu MS. Population Attributable Risk of Tuberculosis Vulnerabilities in Kerala, India. Indian J Community Med Off Publ Indian Assoc Prev Soc Med. 2020;45:367–70. https://doi.org/10.4103/ijcm.IJCM_336_19.

Figures:

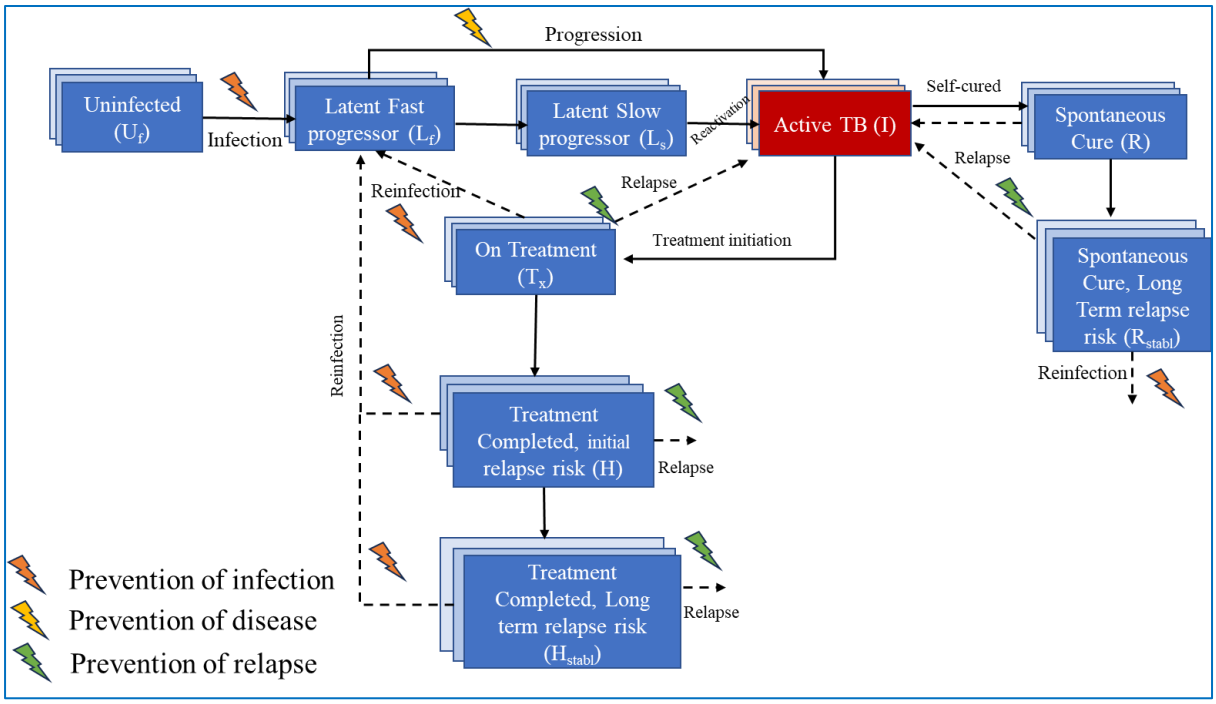

Figure 1: Schematic illustration of the model. *Compartments in red indicate infectious states. Blue-shaded layers denote different levels of vaccination status (unvaccinated, vaccinated). Dashed Arrows represent Relapse (to Active TB i.e. I) and reinfection (to Latent Fast progressor, L_f). Note: Age structure (stratification of all compartments into ≤14 years and ≥15 years), Risk status (i.e. Gen Pop. & with risk) and TB-related mortality are not shown in this representation.*

Figure 2: Projected TB vaccination impact (cases and deaths averted) across scenarios. The x-axis represents the cumulative number of individuals vaccinated over the period of 2027–2046, while the y-axis shows the percentage of cumulative TB cases/deaths averted by 2046. Points represent the 20%, 50%, and 80% target coverage scenarios. Solid, dashed, and dotted lines represent prevention of disease (PoD), prevention of infection (PoI), and prevention of relapse (PoR) vaccines, respectively. Target populations are represented by colour, with blue denoting the all-population strategy, green denoting low-BMI populations, orange denoting populations with diabetes mellitus (DM), and black denoting urban populations. Lighter and darker shades distinguish child and adult vaccination strategies, respectively. Lines have a finite extent, terminating at the point corresponding to a hypothesised maximum plausible vaccination effort, defined as vaccination coverage equivalent to 80% of the eligible population per year.

Different strategies reached their maximum achievable impact at different vaccination levels, reflecting saturation within the targeted populations (Supplementary Figure S6: A-C). Lines corresponding to smaller subgroups terminated earlier on the x-axis.

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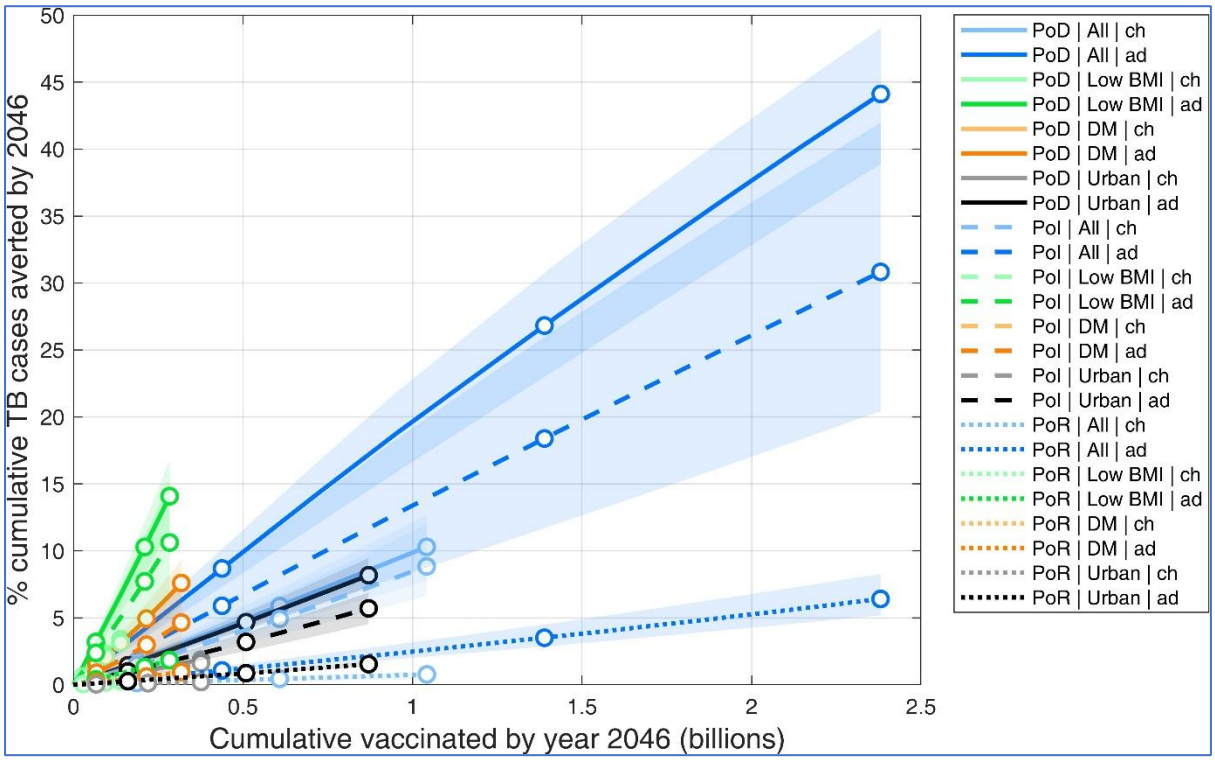

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548 *(2.A) Percentage of cumulative TB cases averted by 2046*

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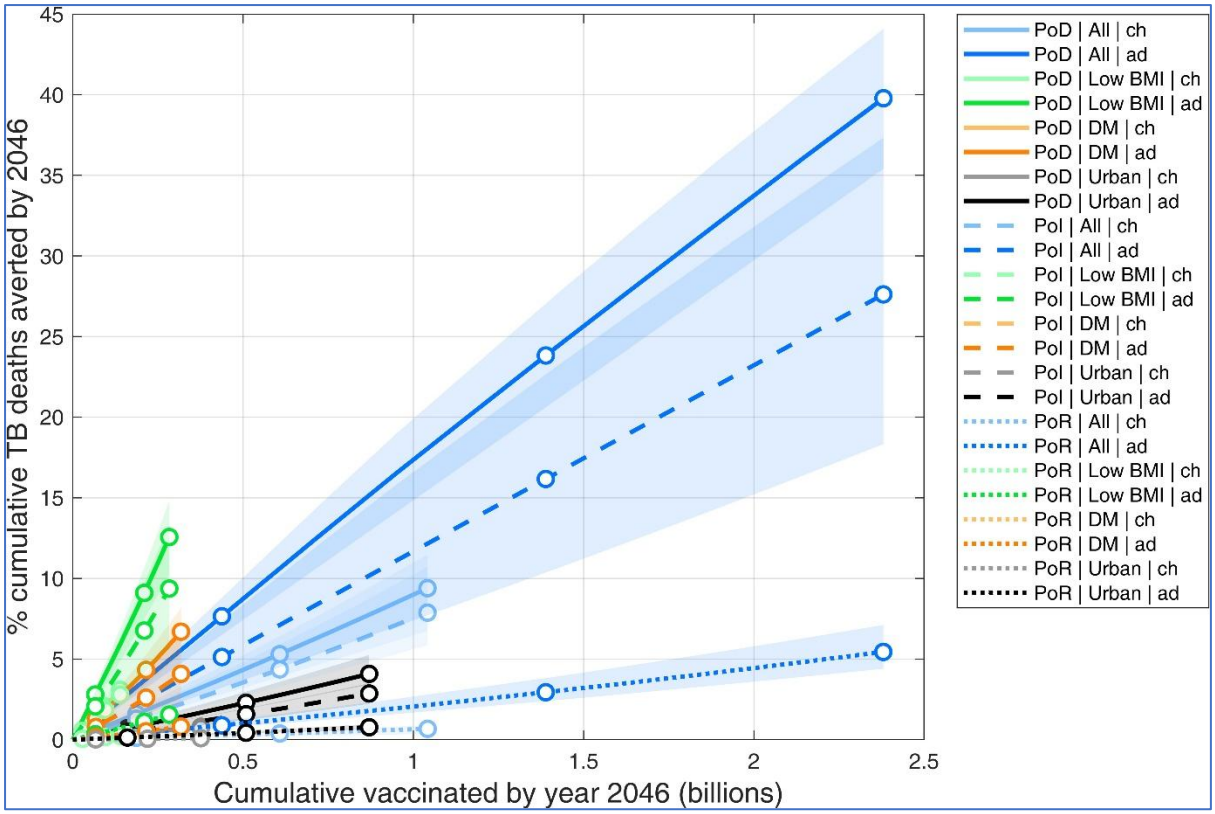
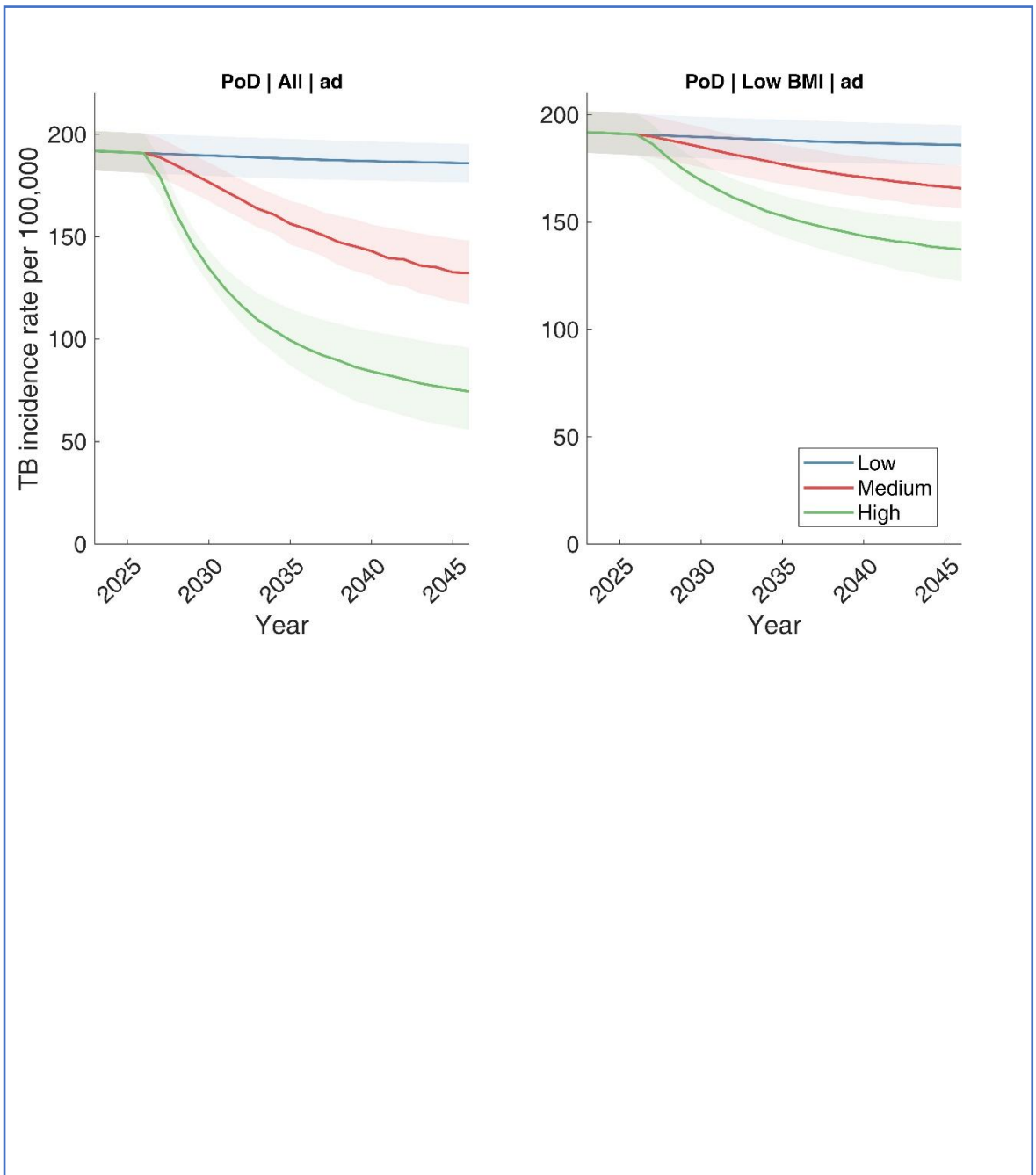
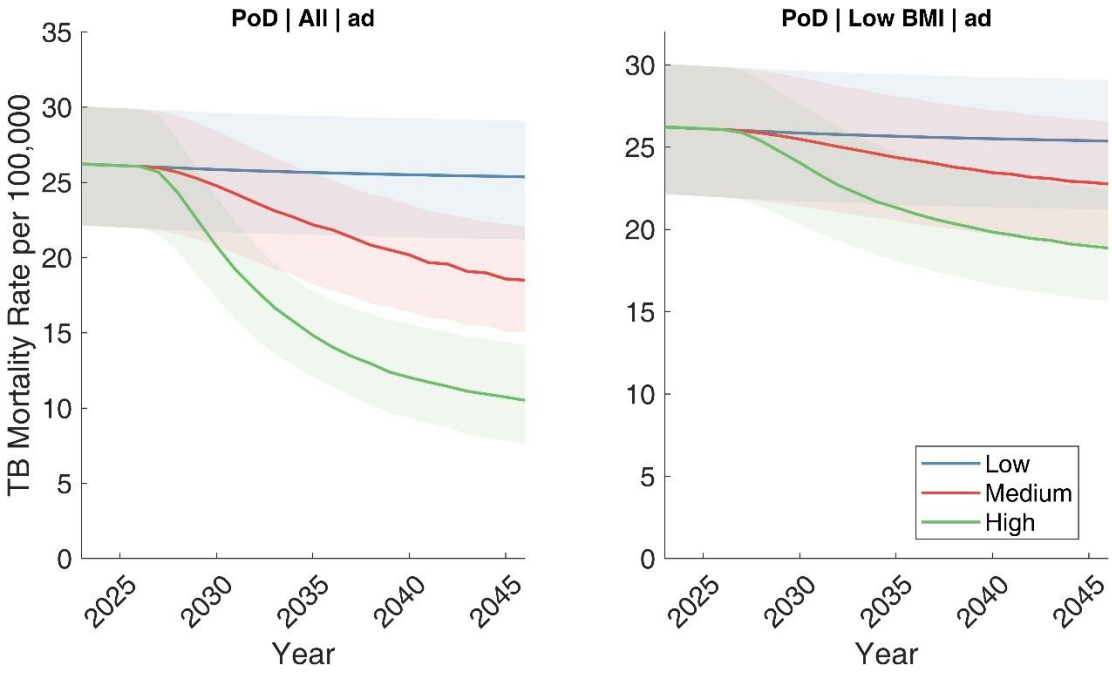


(2.B) Percentage of cumulative TB deaths averted by 2046

Figure 3. Projected TB incidence and mortality trajectories under PoD vaccination strategies targeting all adults and adults with low BMI at different vaccination coverage levels.

Projected annual TB incidence (top panels) and TB mortality (bottom panels) from 2023 to 2046 under prevention of disease (PoD) vaccination strategies targeting all adults (left panels) and adults with low BMI (right panels). Curves are shown for low, medium, and high vaccination coverage scenarios, corresponding to approximately the 20%, 50%, and 80% target coverage levels used in the efficiency analysis. Incidence and mortality rates are expressed per 100,000 population. A




PoD | All | ad
TB Mortality Rate per 100,000
35
30
25
20
15
10
5
0
2025
2030
2035
2040
2045
Year
PoD | Low BMI | ad
30
25
20
15
10
5
0
Low
Medium
High
2025
2030
2035
2040
2045
Year

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567

568

569 Tables:

570 Table 1: Data for model calibration

Indicator	**Value**	**Source**
Incidence in 2023	195[164 - 228]	WHO Global TB report 2024[13]
Prevalence in 2020	312 [286, 337]	National TB prevalence survey[12]
Out of prevalent cases, proportion who hadn't sought care at time of prevalence survey	0.66 [0.56, 0.76]	National TB prevalence survey [12]
Notification (Treatment initiations in public sector)	125[100, 143.75]	Programmatic Data
TB mortality in 2023	22[16, 30]	WHO Global TB report 2024 [13]
Relative risk of TB, Low BMI vs general population	3.86 (3.41, 4.38)	Re-analysed National TB prevalence survey data
Relative risk of TB, Diabetes vs general population	1.68 (1.36, 2.08)	Re-analysed National TB prevalence survey data
Proportion of population Under nourished	15 (10-15)	NFHS-5 (2019-21)[14]
Proportion of population with Diabetes	11·4 (10·2–12·5)	Anjana et al., 2023 (ICMR-INDIAB-17)[15]
Prevalence of LTBI in the overall population	0.25[0.20 0.30]	National TB prevalence survey [12]

Proportion of population that is less than 15years old	29*[0.85 1 1.15]/100	World bank estimates

571

572

573 ***Table 2: Cumulative vaccination, percentage cases and deaths averted by 20246 across***

574 ***scenarios with varied target coverage***

575

Vaccine type	**Target population**	**Age group**	**Target coverage**	**Cumulative vaccinated by 2046 (in billions)**	**% Cases averted by 2046 (95% CI)**	**% Deaths averted by 2046 (95% CI)**
PoD	All	Children	20	0.19	1.78 (1.39-2.16)	1.59 (1.19-1.92)
			50	0.61	5.89 (4.52-7.16)	5.30 (3.91-6.41)
			80	1.04	10.30 (7.74-12.67)	9.39 (6.75-11.47)
		Adult	20	0.44	8.68 (7.32-10.12)	7.65 (6.51-8.80)
			50	1.39	26.83 (23.00-30.76)	23.83 (20.62-27.05)
			80	2.38	44.12 (38.90-49.00)	39.78 (35.41-44.08)
	Low BMI	Children	20	0.03	0.68 (0.54-0.82)	0.61 (0.47-0.73)
			50	0.10	2.28 (1.79-2.80)	2.06 (1.56-2.50)
			80	0.14	3.41 (2.64-4.22)	3.09 (2.30-3.80)
		Adult	20	0.07	3.20 (2.60-3.74)	2.80 (2.31-3.25)
			50	0.21	10.29 (8.38-12.15)	9.09 (7.48-10.63)

			80	0.28	14.09 (11.43-16.74)	12.57 (10.25-14.79)
	DM	Children	20	0.00	0 (0-0)	0 (0-0)
			50	0.00	0 (0-0)	0 (0-0)
			80	0.00	0 (0-0)	0 (0-0)
		Adult	20	0.07	1.51 (1.17-1.86)	1.31 (1.04-1.61)
			50	0.22	4.94 (3.84-6.07)	4.32 (3.43-5.27)
			80	0.32	7.60 (5.89-9.33)	6.69 (5.30-8.16)
	Urban	Children	20	0.07	0.32 (0.24-0.37)	0.14 (0.10-0.18)
			50	0.22	1.06 (0.77-1.22)	0.45 (0.32-0.58)
			80	0.38	1.87 (1.32-2.15)	0.80 (0.55-1.04)
		Adult	20	0.16	1.46 (1.28-1.69)	0.71 (0.59-0.92)
			50	0.51	4.67 (4.13-5.42)	2.29 (1.91-2.97)
			80	0.87	8.18 (7.26-9.45)	4.08 (3.41-5.26)
PoI	All	Children	20	0.19	1.48 (1.13-2.02)	1.30 (0.99-1.76)
			50	0.61	4.92 (3.73-6.71)	4.36 (3.29-5.90)
			80	1.04	8.84 (6.65-11.98)	7.88 (5.86-10.70)
		Adult	20	0.44	5.90 (3.67-8.49)	5.12 (3.23-7.33)
			50	1.39	18.39 (11.70-25.98)	16.17 (10.37-22.65)
			80	2.38	30.83 (20.45-41.97)	27.62 (18.33-37.33)
			20	0.03	0.62 (0.47-0.86)	0.54 (0.41-0.75)

	Low BMI	Childr en	50	0.10	2.09 (1.57-2.92)	1.83 (1.37-2.58)
			80	0.14	3.14 (2.37-4.43)	2.79 (2.06-3.94)
		Adult	20	0.07	2.38 (1.45-3.46)	2.06 (1.26-2.97)
			50	0.21	7.72 (4.70-11.16)	6.76 (4.13-9.73)
			80	0.28	10.62 (6.51-15.24)	9.37 (5.75-13.38)
	DM	Childr en	20	0.00	0 (0-0)	0 (0-0)
			50	0.00	0 (0-0)	0 (0-0)
			80	0.00	0 (0-0)	0 (0-0)
		Adult	20	0.07	0.90 (0.50-1.48)	0.78 (0.44-1.26)
			50	0.22	2.98 (1.65-4.82)	2.60 (1.46-4.14)
			80	0.32	4.65 (2.56-7.46)	4.08 (2.27-6.46)
	Urban	Childr en	20	0.07	0.27 (0.22-0.32)	0.12 (0.09-0.15)
			50	0.22	0.90 (0.71-1.08)	0.39 (0.30-0.50)
			80	0.38	1.62 (1.24-1.94)	0.70 (0.52-0.91)
		Adult	20	0.16	0.99 (0.77-1.21)	0.48 (0.37-0.60)
			50	0.51	3.20 (2.52-3.89)	1.58 (1.22-1.94)
			80	0.87	5.71 (4.55-6.89)	2.86 (2.22-3.50)
PoR	All	Childr en	20	0.19	0.14 (0.08-0.18)	0.12 (0.06-0.15)
			50	0.61	0.44 (0.25-0.58)	0.38 (0.21-0.50)
			80	1.04	0.77 (0.42-1.03)	0.67 (0.35-0.89)
		Adult	20	0.44	1.07 (0.87-1.37)	0.89 (0.72-1.15)
			50	1.39	3.51 (2.86-4.50)	2.94 (2.39-3.81)

		80	2.38	6.41 (5.19-8.27)	5.44 (4.40-7.11)
Low BMI	Children	20	0.03	0.06 (0.03-0.07)	0.05 (0.03-0.06)
		50	0.10	0.18 (0.11-0.24)	0.16 (0.09-0.21)
		80	0.14	0.27 (0.15-0.36)	0.23 (0.13-0.31)
	Adult	20	0.07	0.40 (0.32-0.51)	0.33 (0.27-0.43)
		50	0.21	1.32 (1.05-1.69)	1.11 (0.88-1.43)
		80	0.28	1.84 (1.45-2.36)	1.55 (1.22-2.01)
DM	Children	20	0.00	0 (0-0)	0 (0-0)
		50	0.00	0 (0-0)	0 (0-0)
		80	0.00	0 (0-0)	0 (0-0)
	Adult	20	0.07	0.19 (0.15-0.25)	0.16 (0.12-0.21)
		50	0.22	0.62 (0.48-0.82)	0.52 (0.40-0.69)
		80	0.32	0.96 (0.73-1.28)	0.81 (0.61-1.08)
Urban	Children	20	0.07	0.04 (0.02-0.04)	0.02 (0.01-0.02)
		50	0.22	0.12 (0.07-0.14)	0.05 (0.03-0.07)
		80	0.38	0.20 (0.11-0.24)	0.09 (0.05-0.12)
	Adult	20	0.16	0.27 (0.24-0.30)	0.13 (0.11-0.16)
		50	0.51	0.87 (0.78-0.97)	0.42 (0.36-0.53)
		80	0.87	1.54 (1.39-1.74)	0.77 (0.65-0.96)

576

577 ***Table 3: Projected TB incidence and mortality rate under PoD vaccination strategies targeting all adults and adults with low BMI at different***

578 ***vaccination coverage levels, 2023–2046.***

579

Year	**Incidence rate**						**Mortality rate**					
	General population (All)			Low BMI			General population (All)			Low BMI		
	Low coverage	Medium coverage	High coverage	Low coverage	Medium coverage	High coverage	Low coverage	Medium coverage	High coverage	Low coverage	Medium coverage	High coverage
2023	191.8 (182.2-201.6)	191.9 (182.3-201.6)	191.9 (182.3-201.6)	191.8 (182.2-201.6)	191.9 (182.3-201.6)	191.9 (182.3-201.6)	26.2 (22.1-30.1)	26.2 (22.2-30.1)	26.2 (22.2-30.1)	26.2 (22.1-30.1)	26.2 (22.2-30.1)	26.2 (22.2-30.1)
2024	191.5 (181.8-201.2)	191.6 (181.9-201.3)	191.6 (181.9-201.3)	191.5 (181.8-201.2)	191.6 (181.9-201.3)	191.6 (181.9-201.3)	26.2 (22.1-30.0)	26.2 (22.1-30.0)	26.2 (22.1-30.0)	26.2 (22.1-30.0)	26.2 (22.1-30.0)	26.2 (22.1-30.0)

2025	191.2 (181.5-200.8)	191.2 (181.6-200.9)	191.2 (181.6-200.9)	191.2 (181.5-200.8)	191.2 (181.6-200.9)	191.2 (181.6-200.9)	26.1 (22.0-29.9)	26.1 (22.0-29.9)	26.1 (22.0-29.9)	26.1 (22.0-29.9)	26.1 (22.0-29.9)	26.1 (22.0-29.9)
2026	190.8 (181.2-200.5)	190.9 (181.2-200.5)	190.9 (181.2-200.5)	190.8 (181.2-200.5)	190.9 (181.2-200.5)	190.9 (181.2-200.5)	26.1 (21.9-29.9)	26.1 (22.0-29.9)	26.1 (22.0-29.9)	26.1 (21.9-29.9)	26.1 (22.0-29.9)	26.1 (22.0-29.9)
2027	190.5 (180.8-200.1)	188.7 (179.1-198.2)	179.3 (170.2-188.4)	190.5 (180.8-200.1)	189.8 (180.2-199.4)	186.4 (176.9-195.5)	26.0 (21.9-29.8)	26.0 (21.8-29.7)	25.7 (21.6-29.4)	26.0 (21.9-29.8)	26.0 (21.9-29.8)	25.9 (21.8-29.7)
2028	190.2 (180.4-199.8)	184.8 (175.3-194.2)	161.0 (153.0-169.5)	190.2 (180.4-199.8)	188.2 (178.6-197.6)	179.8 (170.7-188.3)	26.0 (21.8-29.8)	25.7 (21.6-29.4)	24.3 (20.4-27.8)	26.0 (21.8-29.8)	25.9 (21.7-29.6)	25.4 (21.4-29.1)
2029	189.9 (180.1-199.4)	180.8 (171.4-190.0)	146.4 (138.7-154.4)	189.9 (180.1-199.4)	186.6 (177.2-195.9)	174.1 (165.2-182.4)	25.9 (21.8-29.7)	25.3 (21.2-28.9)	22.5 (18.9-25.8)	25.9 (21.8-29.7)	25.7 (21.6-29.5)	24.7 (20.9-28.3)

2030	189.6 (179.7-199.1)	176.7 (167.6-186.2)	134.7 (127.5-143.2)	189.6 (179.7-199.1)	185.0 (175.6-194.2)	169.4 (160.6-177.9)	25.9 (21.7-29.6)	24.8 (20.8-28.4)	20.8 (17.4-24.0)	25.9 (21.7-29.6)	25.5 (21.4-29.2)	24.1 (20.3-27.6)
2031	189.3 (179.4-198.8)	172.3 (163.1-182.0)	124.7 (117.0-134.6)	189.3 (179.4-198.8)	183.1 (173.8-192.3)	165.3 (156.7-173.5)	25.8 (21.7-29.6)	24.2 (20.3-27.8)	19.2 (15.9-22.3)	25.8 (21.7-29.6)	25.3 (21.3-29.0)	23.3 (19.8-26.9)
2032	189.0 (179.1-198.5)	168.1 (159.0-177.9)	116.6 (107.9-127.9)	189.0 (179.1-198.5)	181.5 (172.3-190.8)	161.3 (152.9-170.0)	25.8 (21.6-29.5)	23.7 (19.8-27.2)	17.9 (14.7-20.9)	25.8 (21.6-29.5)	25.0 (21.0-28.7)	22.7 (19.3-26.2)
2033	188.7 (178.9-198.3)	163.7 (154.6-174.1)	109.5 (99.9-122.4)	188.7 (178.9-198.3)	180.0 (170.7-189.2)	158.4 (149.6-167.3)	25.7 (21.6-29.5)	23.1 (19.2-26.6)	16.7 (13.6-19.6)	25.7 (21.6-29.5)	24.8 (20.9-28.5)	22.2 (18.9-25.7)
2034	188.4 (178.6-198.0)	160.9 (151.7-170.8)	104.4 (93.6-118.4)	188.4 (178.6-198.0)	178.5 (169.1-187.3)	155.1 (146.2-164.5)	25.7 (21.5-29.5)	22.7 (18.9-26.1)	15.8 (12.8-18.6)	25.7 (21.5-29.5)	24.6 (20.7-28.3)	21.7 (18.5-25.1)

2035	188.1 (178.4-197.7)	156.3 (146.3-167.5)	99.4 (87.3-114.8)	188.1 (178.4-197.7)	176.9 (167.8-186.0)	152.9 (143.2-162.4)	25.7 (21.5-29.4)	22.2 (18.2-25.5)	14.8 (12.1-17.7)	25.7 (21.5-29.4)	24.4 (20.6-28.1)	21.3 (18.1-24.7)
2036	187.8 (178.2-197.5)	153.8 (143.6-165.3)	95.5 (82.3-111.9)	187.8 (178.2-197.5)	175.5 (166.5-184.8)	150.5 (140.7-160.3)	25.6 (21.5-29.4)	21.9 (17.8-25.2)	14.1 (11.5-17.1)	25.6 (21.5-29.4)	24.2 (20.3-27.9)	21.0 (17.8-24.3)
2037	187.6 (178.0-197.2)	150.9 (140.7-162.0)	92.1 (77.9-109.5)	187.6 (178.0-197.2)	174.2 (165.3-183.8)	148.6 (138.3-158.7)	25.6 (21.4-29.4)	21.4 (17.5-24.6)	13.5 (10.8-16.7)	25.6 (21.4-29.4)	24.0 (20.2-27.7)	20.6 (17.5-24.0)
2038	187.3 (177.8-197.0)	147.3 (136.1-160.1)	89.6 (74.0-107.4)	187.3 (177.8-197.0)	172.9 (164.1-182.2)	146.8 (136.1-157.3)	25.6 (21.4-29.3)	20.8 (17.0-24.2)	13.0 (10.2-16.3)	25.6 (21.4-29.3)	23.8 (20.0-27.5)	20.4 (17.2-23.8)
2039	187.1 (177.6-196.7)	145.3 (133.3-158.6)	86.4 (70.0-105.2)	187.1 (177.6-196.7)	171.8 (162.5-181.1)	145.2 (134.0-156.1)	25.5 (21.4-29.3)	20.5 (16.7-23.9)	12.4 (9.7-15.8)	25.5 (21.4-29.3)	23.6 (19.8-27.4)	20.1 (16.9-23.6)

2040	186.9 (177.4-196.5)	143.0 (131.0-155.9)	84.3 (67.5-103.8)	186.9 (177.4-196.5)	170.9 (162.0-180.5)	143.4 (131.8-154.8)	25.5 (21.4-29.3)	20.2 (16.4-23.5)	12.0 (9.4-15.6)	25.5 (21.4-29.3)	23.5 (19.7-27.2)	19.8 (16.7-23.3)
2041	186.7 (177.2-196.3)	139.6 (127.0-154.4)	82.4 (65.1-102.4)	186.7 (177.2-196.3)	170.0 (160.2-179.5)	142.3 (130.2-154.0)	25.5 (21.3-29.2)	19.7 (16.0-23.1)	11.7 (9.0-15.3)	25.5 (21.3-29.2)	23.4 (19.6-27.1)	19.7 (16.5-23.1)
2042	186.5 (177.1-196.1)	138.9 (125.7-153.0)	80.5 (62.8-100.8)	186.5 (177.1-196.1)	168.8 (159.8-178.9)	141.0 (127.9-152.8)	25.5 (21.3-29.2)	19.6 (15.9-22.9)	11.4 (8.7-15.0)	25.5 (21.3-29.2)	23.2 (19.5-27.0)	19.5 (16.2-22.9)
2043	186.4 (176.9-195.8)	135.9 (122.4-151.6)	78.4 (60.3-99.3)	186.4 (176.9-195.8)	168.1 (158.4-178.0)	140.2 (126.8-152.2)	25.4 (21.3-29.2)	19.1 (15.5-22.6)	11.1 (8.3-14.8)	25.4 (21.3-29.2)	23.1 (19.3-26.9)	19.3 (16.1-22.8)
2044	186.2 (176.8-195.6)	135.1 (120.7-150.2)	77.0 (58.7-98.1)	186.2 (176.8-195.6)	167.1 (157.7-177.5)	138.7 (124.8-151.2)	25.4 (21.3-29.1)	19.0 (15.5-22.4)	10.9 (8.1-14.6)	25.4 (21.3-29.1)	22.9 (19.2-26.7)	19.1 (15.9-22.7)

20 45	186.1 (176.7-195.4)	132.6 (118.4-149.1)	75.7 (57.2-97.0)	186.1 (176.7-195.4)	166.4 (156.9-176.7)	137.9 (123.5-150.3)	25.4 (21.2-29.1)	18.6 (15.1-22.2)	10.7 (7.9-14.4)	25.4 (21.2-29.1)	22.9 (19.1-26.7)	19.0 (15.7-22.6)
20 46	185.9 (176.5-195.2)	132.2 (117.0-148.0)	74.4 (55.8-95.8)	185.9 (176.5-195.2)	165.7 (156.4-176.3)	137.2 (122.5-149.9)	25.4 (21.2-29.1)	18.5 (15.0-22.1)	10.5 (7.7-14.2)	25.4 (21.2-29.1)	22.8 (19.1-26.6)	18.9 (15.7-22.4)

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