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Health and economic impacts of Vaccae vaccination incorporating active case finding in India and South Africa: a modelling study

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ABSTRACT

Introduction Tuberculosis (TB) is a major global health issue, particularly, in India and South Africa. We aim to evaluate the potential of the new TB vaccine, Vaccae, to enhance TB control by integrating with active case finding (ACF) strategies in these regions.

Methods Using age-structured dynamic models, we projected the epidemiological and economic outcomes of combining Vaccae vaccination with ACF over 27 years. In India, four age-targeted strategies were analysed: (1) adolescent (15 years), (2) adolescent and young adult (AYA, 15–34 years), (3) adult (18–55 years) and (4) elderly (60+ years). In South Africa, strategies were based on HIV status: (1) HIV-targeted, (2) non-HIV and (3) general population. The vaccine efficacy of Vaccae was set at 54.7%, priced at US$120 per course. Outcomes measured included reductions in TB incidence and mortality, prioritised based on budget, incremental cost-effectiveness ratios (ICER) and benefit-cost ratios (BCR).

Results In India, the adult strategy could prevent 8.70 (95% UI: 6.86–11.13) million TB cases and 0.61 (0.39–0.91) million deaths, reducing incidence and mortality by 20.1% (18.7%–23.5%) and 19.0% (17.5%–22.5%), respectively. In South Africa, the general population strategy could avert 0.67 (0.45–0.99) million TB cases and 0.21 (0.15–0.28) million deaths, reducing incidence by 28.1% (26.1%–30.3%) and mortality by 27.0% (23.5%–30.0%). The vaccination budgets for the AYA strategy in India and the HIV-targeted strategy in South Africa were US$14.0 (10.14–23.29) billion and US$0.09 (0.06–0.15) billion, respectively. The ICERs were US$1082 (927–1426) and US$70 (53–123) per disability-adjusted life year averted, and the BCRs were 2.0 (1.6–2.4) and 176 (83.4–255.3), respectively. Thus, the AYA strategy in India and the HIV-targeted strategy in South Africa were the most favourable.

Conclusion Integrating Vaccae vaccination with ACF could significantly enhance TB control in high-burden countries. Policymakers should consider these strategies, with further research needed to confirm the findings.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Existing research on potential tuberculosis (TB) vaccines has focused on those in clinical trials or theoretical stages.

⇒ Vaccae is the first clinically approved next-generation TB vaccine. We have modelled its health and economic impacts on vaccinating the elderly in China.

WHAT THIS STUDY ADDS

⇒ This study provides insights into Vaccae's real-world application among populations with latent TB infection (LTBI) in high-burden countries like India and South Africa.

⇒ By integrating active case finding with the vaccination strategy and using a multifaceted economic analysis, this study offers a comprehensive view of the vaccine's impact, aiding policymakers in making informed decisions.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Integrating Vaccae vaccination into India's National Tuberculosis Elimination Programme and South Africa's National Tuberculosis Programme could significantly enhance TB elimination efforts.

⇒ These findings may influence global TB policies, encouraging high-burden countries to adopt similar vaccination strategies tailored to their epidemiological profiles, potentially setting a new benchmark in TB, TB-HIV and LTBI management.

INTRODUCTION

Tuberculosis (TB), an infectious disease caused by *Mycobacterium tuberculosis* (*M. tuberculosis*), remains a major global public health concern. Roughly two billion people are latently infected with *M. tuberculosis*, and around 10% might develop active TB.[1] TB was the leading cause of death attributed to infectious diseases in the general population, as well as the greatest threat to people living with HIV (PLHIV).[2] The COVID-19 pandemic

has posed unprecedented challenges to global efforts in combating TB, as the resources that were once dedicated to TB prevention, diagnosis and treatment were redirected. In 2021, of the estimated 10.6 million cases of tuberculosis worldwide, only 6.4 million were detected and notified.[2] Only through coordinated and innovative tools, for prevention, diagnosis and treatment, can we overcome the setbacks caused by the pandemic. Active case finding (ACF) has been demonstrated to increase detection rate of TB and may be a central component of the WHO 'End TB' programme.[3] Moreover, by targeting different aspects of the *M. tuberculosis*, the next-generation TB vaccine candidates hold the potential to not only prevent TB infection but also offer better protection for individuals already infected.[4] It is imperative that we prioritise and invest in the deployment of these tools to accelerate progress towards the global goal of a TB-free world.

Vaccae was approved in China in June 2021 to treat individuals with latent TB infection (LTBI).[5] A phase 3 trial indicated that six doses of Vaccae (22.5 µg per dose) were 54.7% (95% UI: 29.8%–70.8%) effective in preventing active TB in LTBI carriers (online supplemental tables S1, S2 and figures S1, S2). The LTBI screening identified individuals who tested positive for the tuberculin skin test (TST) and had negative chest X-ray (CXR) results, forming part of the ACF process. Thus, ACF is a crucial prerequisite for implementing a post-infection (PSI) vaccine like Vaccae. We have previously demonstrated that Vaccae vaccination among the elderly may be a reliable and cost-effective option for controlling TB epidemic in China, where the population is ageing.[5] However, the value of Vaccae in controlling TB in various epidemiological settings is still unknown.

India and South Africa serve as prime examples for the study of tuberculosis control strategies. On the one hand, India, ranks first among the TB high-burden countries and accounts for 27% of all estimated incident TB cases worldwide in 2022.[2] TB mainly affected the younger population in India, with 65% of cases occurring within the 15–45 age group.[6] According to the National TB prevalence survey, 2021, the crude prevalence of LTBI among individuals >15 years was 31.3% (95% UI: 30.8%–31.9%).[7] On the other hand, South Africa ranks first among the TB/HIV high-burden list.[2] A national survey showed that PLHIV in South Africa had one of the highest burdens of TB globally, with an estimated prevalence of 1734 cases (1219–2249) per 100 000 population.[8] Considering the high burden of TB in the two countries, it becomes crucial to explore the potential effectiveness of Vaccae in these settings.

In this modelling study, we conducted an economic evaluation of integrating Vaccae vaccination with ACF as a dual strategy for enhancing TB control efforts in India and South Africa. This study employs a sophisticated epidemiological model tailored to each country's specific TB landscape, incorporating demographic, clinical and economic data to simulate disease progression and intervention impact over time. Through this approach, we aim to provide valuable insights for public health decisions, helping to identify the optimal use of limited resources to reduce the TB burden in these high-burden settings.

METHODS

Dynamic transmission modeling

We adapted the dynamic transmission models from our earlier study,[5] using R software V.4.2.1 (R Foundation for Statistical Computing, Vienna, Austria). The model for India characterised the natural TB progression through five distinct states (compartments): susceptible (S), latently infected (L), infectious active TB disease showing bacteriologically positivity (I), noninfectious active disease despite bacteriological negativity (NI) and those recovered from active disease (R). The entry point for newborns within the model was the susceptible (S) compartment. For South Africa, these states were integrated with three additional HIV-related strata: HIV-negative individuals (HIV^- stratum), HIV-positive individuals not undergoing antiretroviral therapy (HIV^+ stratum) and HIV-positive individuals engaged in antiretroviral therapy (ART stratum), with progression visualised in a supplementary flowchart (online supplemental figure S3).

The model tracked several key transmissions, including (1) the acquisition of TB infection (categorised by fast or slow progression); (2) the emergence of active disease (from fast progression or through reactivation, reinfection or relapse); (3) the detection, treatment and recovery; and (4) TB-related mortality (as illustrated in online supplemental figure S3 and table S3). The simulation of TB dynamics encompassed the entire population demographic, ranging from newborns to centenarians, and spanned across 150 years from 1900 to 2050, applying age-adjusted contact patterns based on predictive matrices.[9] In the model, individuals within the HIV^+ and ART strata were predisposed to an increased risk of active TB development and faced higher mortality rates than those in the HIV^- stratum.

Initial population structures, birth rates and death rates (online supplemental tables S4–S7) for both countries drew from the United Nations Population Prospects.[10] Comprehensive literature reviews yielded parameters for TB transmission and disease progression (online supplemental tables S8 and S9), while the trajectory of the South African HIV epidemic was modelled through HIV-specific incidence rates, AIDS-related mortality and ART coverage (outlined in online supplemental tables S10–S12). The model presumed ART to diminish the additional TB risk associated with HIV by 65% in adults and 70% in children.[11 12]

Calibration was conducted with the directed-search Nelder-Mead (NM) method within the 'dfoptim' R package,[13] considering uncertainties through a hundred best-fitting simulations (online supplemental table S13).

The calibration focused on specific demographic and epidemic benchmarks in online supplemental tables S14 and S15, ensuring it aligned with estimated figures for TB prevalence, incidence, mortality and TB-HIV coinfection statistics specific to South Africa. The calibration intrinsically included the impacts of existing TB control interventions, operating under the presumption that related variables would remain consistent.

Vaccination strategies and health outcomes

The following age-specific vaccination strategies were evaluated for implementation in India: (1) the adolescent (aged 15 years) strategy, (2) the adolescent and young adult (AYA, 15–34 years) strategy, (3) the adult (18–55 years) strategy and (4) the elderly (60+ years) strategy. In contrast, the proposed strategies for South Africa were structured with an emphasis on HIV status: (1) the HIV-targeted strategy, (2) the non-HIV strategy and (3) the general population strategy. The assumptions underlying the strategies were displayed in table 1. It was anticipated that the vaccination rollout, complemented with ACF approaches, would commence in 2024. The transmission models were designed to forecast health outcomes spanning from 2024 to 2050—a 27-year evaluation window. We assumed vaccine coverage would increase from 30% to 80% over 5 years. Achieving 80% is ambitious but feasible, given the 91% pneumococcal vaccine coverage in India and 90% human papillomavirus vaccine coverage in South Africa.[14 15]

The vaccine efficacy (VE) was set as 54.7% (95% UI: 29.8%–70.8%) against active TB (see online supplemental table S2 for case definition). The duration of protection was set at 20 years, after which immunity was completely lost. For the South Africa setting, a 20% (5%–30%) reduction in VE was anticipated for HIV^+ individuals relative to their HIV^- counterparts, as referenced in sources.[16–18] TST screening sensitivity was reported as 77.2%.[19] The Centers for Disease Control and Prevention of USA recommends a ≥5 mm cut-off to define a positive TST in PLHIV,[20] with sensitivity of 78.2%.[19] Our study assumed consistent TST sensitivity for individuals with or without HIV, with different cut-offs. The ACF component is modelled using a mechanistic approach simulating sequential screening processes (TST and CXR). We assumed ACF interventions could increase the case detection rate by 25% (0%–30%) compared with the status quo.[21]

The primary outcomes were the numbers of prevented TB cases and deaths relative to a 'no vaccination' strategy (status quo). In addition, secondary outcomes included the incidence rate reduction, mortality rate reduction, as well as the number needed to vaccinate (NNV) to avert a single case or death.

Economic evaluation

A detailed overview of key cost assumptions can be found in table 1. The pricing for Vaccae was established at US$120 in 2021 for a complete course of six doses, which was roughly one-third of the market price observed in China, reflecting efforts to make it more affordable. We discussed these price assumptions with Jiang Pu, senior director at ZhiFei Biological Products Co. Ltd.[5] The cost analysis included considerations from both healthcare sector (direct medical costs) and societal (direct medical costs, direct non-medical costs and indirect costs) perspectives. The costs for LTBI screening (ACF) were tabulated at US$1.12 (95% UI: 0.99–1.25) per TST and US$4.2 (3.3–5.0) per CXR in India.[22 23] In South Africa, these costs were higher, at US$3.90 (3.32–7.27) for the TST and US$14.0 (11.2–16.8) for the CXR.[24 25] TB diagnosis and treatment expenses in India were calculated to be US$14.82 (11.86–17.78) and US$538.6 (447.9–623.7) respectively.[26 27] Comparable costs in South Africa were US$25.90 (20.72–31.08) for diagnosis and US$440.9 (205.7–723.9) for treatment.[27 28] Additionally, the analysis took into account the costs associated with ART in South Africa. We calculated the costs of vaccination programme ($C_{vaccination}$) as the combined total of the vaccine-associated cost ($C_{vaccine}$) and the screening cost ($C_{screening}$).

Disability-adjusted life years (DALYs) were calculated using the standard equation of years of life lost (YLLs)+ years lived with disability (YLDs) derived from simulation outputs. Calculation for YLLs was based on annual TB mortality rates and corresponding life expectancies with specific details available in online supplemental tables S16 and S17. The YLDs were determined annually by multiplying the total number of TB cases by an appropriate disability weight (DW). DW, provided by the Global Burden of Disease, for TB without HIV (0.333) and with HIV (0.408), were incorporated.[29] Both costs and DALYs were discounted annually at a 3% rate.

A systematic evaluation approach was applied to evaluate strategies for Vaccae vaccination programme. The process began with the budget impact analysis to ascertain the costs involved, including those related to the vaccine and screening ($C_{vaccination}$). Subsequently, the cost-effectiveness analysis was conducted. Critical indicators included the average cost-effectiveness ratio (ACER), measuring the cost per TB case or death prevented, and the incremental cost-effectiveness ratio (ICER), focusing on the cost per DALY averted ($\triangle C/\triangle E$). The willingness-to-pay (WTP, λ) threshold was established according to the WHO's criteria, set at the gross domestic product (GDP) per capita for 2021: US$ 2257 for India and US$ 7055 for South Africa, as reported by the World Bank Open Data (https://data.worldbank.org/indicator/NY.GDP.PCAP.CD). The third step entailed the cost-benefit analysis to evaluate the economic benefits of each strategy comprehensively, considering not just healthcare outcomes but broader economic effects. The benefit-cost ratio (BCR) was computed by comparing the total benefits—comprising both reduced direct medical costs ($\triangle C_{treatment}$) and the monetised value of DALYs ($\lambda \triangle E$)—with the cost of the vaccination programme. A BCR exceeding one indicates that benefits surpass costs, signifying monetary savings.

Table 1 Key model parameters and assumptions

Parameters	India	South Africa	Source
Strategy	(1) Adolescent strategy: routine age 15	(1) HIV-targeted strategy: routine age 15, campaign for ages 16–65 for HIV$^+$ individuals	
	(2) Adolescent and young adult strategy: routine age 15, campaign for ages 16–34	(2) Non-HIV strategy: routine age 15, campaign for ages 16–65 for HIV$^-$ individuals	
	(3) Adult strategy： campaign for ages 18–55	(3) General population strategy: routine age 15, campaign for ages 16–65	
	(4) Elderly strategy: routine age 60, campaign for ages 61+	–	
Disability weight			
Tuberculosis, not HIV infected	0.333	0.333	39
Tuberculosis, HIV infected	–	0.408	39
Willingness-to-pay			
One time GDP per capita in 2021	2257	7055	40
	Base-case value (range for sensitivity analysis)		
Vaccination and ACF			
Sensitivity of TST	77.2% (66.4%–85.3%)		19
Vaccine efficacy (VE)	54.7% (29.8%–70.8%)		5
VE reduction in PLHIV	20% (5%–30%)		18
Vaccination coverage	80% (linear scale-up in 5 years)		
Duration of protection	20 years (10 years-lifelong)		
LTBI screening increases CDR	25% (0%–30%)		21 30
Costs (US$)			
Direct medical costs			
TB diagnosis	14.82 (11.86–17.78)	25.90 (20.72–31.08)	26 28
DS-TB treatment, per course*	317 (254–374)	165 (93–287)	27
DR-TB treatment, per course†	3891 (3382–4401)	6163 (2543–9784)	27
Direct non-medical costs‡			
Transportation	25.60 (20.48–30.72)	26.46 (21.17–31.75)	23 41
Food and nutrition	16.93 (13.54–20.32)	48.36 (38.69–58.03)	41–43
Indirect costs (productivity loss)‡			
Patient ≤19 years§	2257 (1806–2708)	7055 (5644–8466)	40
Patient 20–59 years¶	1128 (940.2–1354)	3528 (2822–4234)	40
Caregiver	30.5 (24.4–36.6)	114.1 (91.28–137.28)	23 44
Indl**	2257 (1806–2708)	7055 (5644–8466)	40
ACF costs			
TST††	1.12 (0.99–1.25)	3.90 (3.32–7.27)	22 24
CXR‡‡	4.2 (3.3–5.0)	14.0 (11.2–16.8)	23 25
Vaccination costs			
Vaccine price, per course	120 (30–372)	120 (30–372)	5
Delivery, per course	11.28 (6.78–14.4)§§	13.28 (10.62–15.94)¶¶	26 45
Wastage	5% (4%–6%)	5% (4%–6%)	
ART cost, per person year	–	254 (203–305)	28

Data are presented as median and 95% UI.
*Drug-susceptible tuberculosis.
†Drug-resistant tuberculosis.
‡Applied to the analysis from a societal perspective.
§Patients younger than 20 years would start working 1 year late because of their TB-related long-term sick leave. It would lead to productivity losses based on per capita GDP for 1 year.
¶Patients older than 20 years would return to work from 6 months' TB-related sick leave. It would lead to productivity losses based on per capita GDP for a half year.
**Lifelong productivity loss due to premature death was calculated by per capita GDP×working years.
††Tuberculin skin test.
‡‡Chest X-ray.
§§Including the value of personnel, transport, maintenance, training, cold chain equipment, building and other recurrent costs.
¶¶Including the social mobilisation, transport, transport for outreach services, cold chain equipment, vaccinator cost and per diem for outreach service delivery.
ACF, active case finding; ART, antiretroviral therapy; CDR, case detection rate; CXR, chest X-ray; DR-TB, drug-resistant tuberculosis; DS-TB, drug-susceptible tuberculosis; GDP, gross domestic product; LTBI, latent TB infection; PLHIV, people living with HIV; TB, tuberculosis; TST, tuberculin skin test.

Following the analyses, the strategies were prioritised based on their rankings of vaccination programme budget ($C_{vaccination}$), ICER and BCR. A lower $C_{vaccination}$ or ICER corresponded to a higher priority; whereas, a higher BCR denoted a higher priority rank. After prioritising the above three items, we summed up the total priority. By implementing this methodical approach, policymakers can allocate resources to the optimal strategy that are both economically sustainable and have the highest potential for positive impact.

Uncertainty analyses

The sensitivity analyses included both deterministic (DSA) and probabilistic sensitivity analysis (PSA). The one-way DSA was presented as a tornado diagram, underscoring the 10 variables with the greatest impact. For example, we adopted a conservative assumption that individuals in the pre-symptomatic stage were not detectable by ACF (0%), and an optimistic assumption that ACF could enhance case detection by 30%, based on the findings in the ZAMSTAR study.[30] For the PSA, 100 simulations were conducted, drawing each parameter from its specified probability distribution. The outcomes were illustrated using scatter plots and cost-effectiveness acceptability curves to demonstrate variability.

Furthermore, scenario analyses took into consideration a variety of factors to assess different potential outcomes. These factors included variations in VE (considering both 29.8% and 70.8% rates), the duration of vaccine protection (spanning from 10 years to lifelong protection), the potential introduction year of the programme (envisioned as 2034) and the speed of programme implementation (examining an instant scale-up to 80% coverage).

RESULTS

Health impacts of Vaccae vaccination in India and South Africa

Our examination of the demographic and epidemiological data produced well-fitted models for India and South Africa, as depicted in figure 1A,B and E,F and elaborated on in online supplemental figures S4–S7 respectively. In India, the temporal scope from 2024 to 2050 under a 'no vaccination' strategy forecasted 83.74 (95%

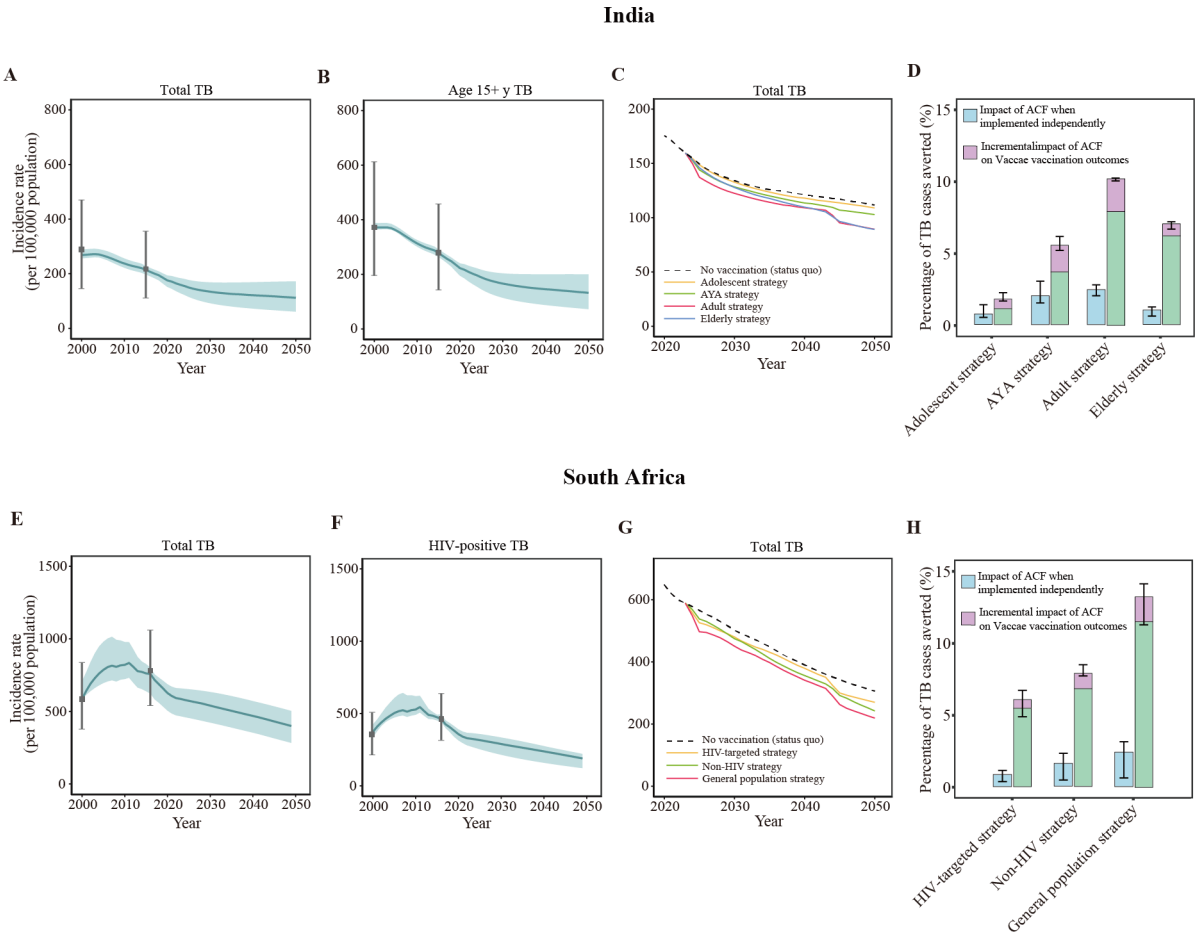

Figure 1 Projection of tuberculosis (TB) incidence under different vaccination strategies in India and South Africa. (A–B) Calibration of the TB incidence rate in India's total TB and aged ≥15 years. (C) Projected TB incidence rates from 2000 to 2050, in response to age-specific vaccination strategies. (D) Percentage of TB cases averted of Vaccae vaccination and active case finding (ACF) in India. (E–F) Calibration of the TB incidence rate in South Africa's total TB and HIV-positive TB. (G) Projected TB incidence rates from 2000 to 2050, in response to HIV-specific vaccination strategies. (H) Percentage of TB cases averted of Vaccae vaccination and ACF in South Africa.

Table 2 Costs, effectiveness and benefits of the Vaccae vaccination strategies in India and South Africa, from healthcare sector perspective

India	Adolescent strategy	AYA strategy	Adult strategy	Elderly strategy
N (number of vaccinee, million)	37.7 (23.0–78.1)	111.2 (71.0–213.0)	278.2 (190.6–439.4)	289.5 (222.8–361.3)
Averted TB cases (million)	1.52 (0.95–3.35)	4.69 (3.32–7.86)	8.70 (6.86–11.13)	5.92 (4.58–6.76)
Averted TB deaths (million)	0.10 (0.06–0.28)	0.31 (0.22–0.67)	0.61 (0.39–0.91)	0.43 (0.23–0.51)
Costs				
Vaccine cost ($C_{vaccine}$, US$ billion)	3.59 (2.20–7.26)	10.90 (7.01–20.14)	25.10 (17.36–38.24)	24.51 (18.89–30.41)
Screening cost ($C_{screening}$, US$ billion)	1.62 (1.61–1.63)	3.12 (3.09–3.14)	3.07 (3.04–3.09)	1.88 (1.87–1.88)
Reduced treatment cost ($^{\triangle}C_{treatment}$, US$ billion)	0.17 (0.09–0.56)	0.54 (0.32–1.31)	1.21 (0.66–2.00)	1.03 (0.46–1.26)
Incremental total cost ($^{\triangle}C=C_{vaccine} + C_{screening} - {}^{\triangle}C_{treatment}$, US$ billion)	5.1 (3.8–8.4)	13.5 (9.8–22.0)	27.0 (19.4–39.9)	25.5 (19.8–31.2)
Effectiveness and benefit				
Averted DALY ($^{\triangle}E$, million)	3.8 (2.4–10.2)	11.1 (8.1–23.1)	18.2 (13.9–26.6)	9.2 (6.2–11.3)
NMB ($^{\triangle}B = \lambda^{*\triangle}E + {}^{\triangle}C_{treatment}$, US$ billion)	8.7 (5.4–23.6)	25.4 (18.7–53.5)	42.3 (32.1–62.1)	21.7 (14.7–26.7)
South Africa	**HIV-targeted strategy**	**Non-HIV strategy**	**General population strategy**	
N (number of vaccinee, million)	0.6 (0.2–1.1)	10.3 (7.6–13.5)	10.8 (7.7–14.4)	
Averted TB cases (million)	0.30 (0.20–0.48)	0.43 (0.24–0.58)	0.67 (0.45–0.99)	
Averted TB deaths (million)	0.09 (0.06–0.13)	0.13 (0.08–0.16)	0.21 (0.15–0.28)	
Costs				
Vaccine cost ($C_{vaccine}$, US$ billion)	0.05 (0.02–0.10)	0.90 (0.65–1.16)	0.94 (0.67–1.25)	
Screening cost ($C_{screening}$, US$ billion)	0.04 (0.03–0.04)	0.62 (0.61–0.64)	0.66 (0.64–0.67)	
Reduced treatment cost ($^{\triangle}C_{treatment}$, US$ billion)	0.06 (0.03–0.1)	0.1 (0.06–0.13)	0.16 (0.10–0.22)	
Increased ART cost ($^{\triangle}C_{ART}$, US$ billion)	0.13 (0.09–0.18)	0.06 (0.03–0.10)	0.19 (0.15–0.23)	
Incremental total cost ($^{\triangle}C=C_{vaccine} + C_{screening} - {}^{\triangle}C_{treatment} + {}^{\triangle}C_{ART}$, US$ billion)	0.2 (0.1–0.2)	1.5 (1.3–1.8)	1.6 (1.4–2.0)	
Effectiveness and benefit				
Averted DALY ($^{\triangle}E$, million)	2.2 (1.4–3.1)	3.2 (1.8–4.1)	5.2 (3.5–7.1)	
NMB ($^{\triangle}B = \lambda^{*\triangle}E + {}^{\triangle}C_{treatment} - {}^{\triangle}C_{ART}$, US$ billion)	15.3 (9.5–22.0)	22.4 (12.6–29.1)	36.4 (24.6–49.8)	

Data are presented as median and 95% UI.
ART, antiretroviral therapy; AYA, adolescent and young adult; DALY, disability-adjusted life year; NMB, net monetary benefit; TB, tuberculosis; λ, willingness-to-pay (WTP); $\lambda^{*\triangle}E$, monetised DALY benefit.

UI: 65.86–99.19) million TB cases and approximately 5.97 (4.19–7.50) million TB-related fatalities. For South Africa, within the same timeframe, we anticipate 5.33 (3.43–7.22) million TB cases and 1.58 (1.22–1.91) million TB-associated deaths (online supplemental figure S8).

For India, data indicated that the adult vaccination strategy could forestall 8.70 (95% UI: 6.86–11.13) million TB cases and prevent 0.61 (0.39–0.91) million related deaths (presented in table 2), slashing the TB incidence and mortality rates by 20.1% (18.7%–23.5%) and 19.0% (17.5%–22.5%), respectively, by the year 2050 (figure 1C and online supplemental table S18). This effect dwarfed that of alternative strategies. The higher number of vaccine doses used in the elderly scenario can be attributed to the fact that the elderly strategy was a combination of routine and campaign vaccination; whereas, the adult strategy was purely a campaign strategy (table 1). The age-specific LTBI carriers and corresponding TB incidence are presented in online supplemental figure S9.

In South Africa, on the other hand, the general population strategy was predicted to avert 0.67 (95% UI: 0.45–0.99) million TB cases and 0.21 (0.15–0.28) million TB-related deaths (table 2). There would be an associated decline in TB incidence and mortality rates by 28.1% (26.1%–30.3%) and 27.0% (23.5%–30.0%), respectively, by the year 2050 (figure 1G and online supplemental table S18). Comparatively, the HIV-targeted strategy was poised to be most efficacious, with the model reflecting the smallest NNV per case

Table 3 Prioritisation of Vaccae vaccination strategies

India	Adolescent strategy	AYA strategy	Adult strategy	Elderly strategy
Vaccination programme budget ($C_{vaccination}$=$C_{vaccine}$+ $C_{screening}$, US$ billion)	5.27 (3.86–9.00)	14.01 (10.14–23.29)	28.17 (20.43–41.86)	26.41 (20.76–32.29)
Budget rank	1/4	2/4	4/4	3/4
ICER ($\triangle C/\triangle E$, US$ per DALY averted)	1259 (823–1608)	1082 (927–1426)	1416 (1091–2094)	2691 (2023–4458)
ICER rank	2/4	1/4	3/4	4/4
BCR ($\triangle B/C_{pro}$)	1.8 (1.4–2.6)	2.0 (1.6–2.4)	1.6 (1.1–2.0)	0.8 (0.5–1.1)
BCR rank	2/4	1/4	3/4	4/4
Total priority rank	2/4	1/4	3/4	4/4
South Africa	**HIV-targeted strategy**	**Non-HIV strategy**	**General population strategy**	
Vaccination programme budget ($C_{vaccination}$=$C_{vaccine}$+ $C_{screening}$, US$ billion)	0.09 (0.06–0.15)	1.53 (1.29–1.81)	1.61 (1.34–1.94)	
Budget rank	1/3	2/3	3/3	
ICER ($\triangle C/\triangle E$, US$ per DALY averted)	70 (53–123)	468 (337–945)	312 (234–515)	
ICER rank	1/3	3/3	2/3	
BCR ($\triangle B/C_{pro}$)	176.0 (83.4–255.3)	14.7 (7.3–20.5)	23.1 (13.8–30.6)	
BCR rank	1/3	3/3	2/3	
Total priority rank	1/3	3/3	2/3	

Data are presented as median and 95% UI.
AYA, adolescent and young adult; BCR, benefit-cost ratio; DALY, disability-adjusted life year; ICER, incremental cost-effectiveness ratio.

or death averted, at 2 (1–5) and 5 (3–16), respectively (online supplemental table S19).

Figure 1D and H showed per cent reductions in TB cases in India and South Africa under different intervention strategies. When ACF was implemented independently, it avoided 0.7% to 2.5% of TB cases in India and 0.6% to 1.7% in South Africa. With the implementation of Vaccae vaccination strategies, the incremental impact of ACF was diminished. This reduction occurred because the Vaccae vaccine itself caused a substantial decrease in TB cases, thereby, lessening the additional impact that ACF could provide. Online supplemental figure S10 presented the estimated TB-associated DALYs with and without Vaccae vaccination and ACF strategies in India and South Africa.

Optimal strategy of Vaccae vaccination in India

The cost of the adolescent vaccination strategy was the lowest, reaching approximately US$5.27 (95% UI: 3.86–9.00) billion (table 3), followed by the AYA strategy, estimated at US$14.01 (10.14–23.29) billion. These immunisation approaches have facilitated a decrease in TB incidence, and consequently, have contributed to reductions in diagnoses and treatment expenses (table 2).

In the cost-effectiveness analysis (CEA) from the healthcare sector perspective, the adolescent, AYA and adult strategies were cost-effective, with the ICERs at US$1259 (95% UI: 823–1608), 1082 (927–1426) and 1416 (1091–2094) per DALY averted (table 3), when compared with status quo. The ACERs stood at US$3230 (2394–4179), US$2778 (2492–3181) and US$3021 (2339–3881) per case averted; and US$47 092 (29 702–63834), US$38 780 (31 883–56307) and US$42 921 (31 306–73221) per death averted for each respective strategy (online supplemental table S20). The AYA strategy stood out as most cost-effective. From the social perspective, the strategies maintain cost-effectiveness, with the adolescent and AYA strategies registering as cost-saving (online supplemental table S20).

The benefit-cost ratios from the healthcare sector perspective were favourable at 1.8 (95% UI: 1.4–2.6), 2.0 (1.6–2.4) and 1.6 (1.1–2.0) for adolescent, AYA and adult strategies, respectively (table 3). A compelling BCR of 3.2 (2.4–3.7) for the AYA strategy is observed from the societal perspective (online supplemental table S20).

In prioritising strategies for optimal epidemic control within India, the AYA strategy ranks as the optimal approach (table 3), balancing both economic benefits and feasibility.

Optimal strategy of Vaccae vaccination in South Africa

The financial allocation for the HIV-targeted Vaccae vaccination programme was the most modest of all strategies, with a budget estimation of merely US$0.09 (95% UI: 0.06–0.15) billion (table 3). Despite achieving reductions in TB management costs, ART expenditures witnessed an uptick. This paradoxical outcome arose

from the vaccine's effectiveness in prolonging the lifespan of HIV-infected individuals already on ART by curtailing TB-related mortalities, which subsequently inflated the demand for ART. Similarly, immunising HIV-positive individuals not already under ART slowed TB progression and deference in mortality, leading to an increment in the cohort that eventually commenced ART (table 2).

From the healthcare sector perspective, the CEA suggested that all three strategies—focusing on HIV^+ population, HIV^- population and the general population—were cost-effective relative to the existing status quo. The ICERs were commendable at US$70 (95% UI: 53–123), US$468 (337–945) and US$312 (234–515) per DALY averted, respectively (table 3). The strategies also boasted ACERs of US$502 (382–923) per case averted and US$1702 (1292–2788) per death deferred for the HIV-targeted strategy (online supplemental table S20). From the societal perspective, each strategy achieved cost-saving milestones (online supplemental table S20).

The CBA revealed that the HIV-targeted strategy prevented 2.2 (95% UI: 1.4–3.1) million DALYs, amassing benefits approximating US$15.3 (9.5–22.0) billion, overwhelmingly surpassing the status quo (table 2). The BCR for this strategy stood at 176.0 (83.4–255.3), markedly surpassing the other two strategies which maintain BCRs of 14.7 (7.3–20.5) and 23.1 (13.8–30.6) (table 3). The societal perspective corroborated the substantial economic benefit that the HIV-targeted strategy provided, yielding a BCR of 264.4 (125.3–392.4) (online supplemental table S20). When considering the hierarchy of these three indicators, the HIV-targeted strategy emerged as the optimal candidate in South Africa.

Online supplemental tables S21 and S22 presented the costs, cost-effectiveness and cost-benefit of the vaccination strategies for the 10-year and lifelong protection scenarios.

Sensitivity and scenario analyses

A bedding of input parameters through one-way sensitivity analyses signified that the potency of the economic model was significantly influenced by factors such as vaccine price and efficacy in both India and South Africa, from the healthcare sector perspective (figure 2A and E). Notably, in South Africa, the factor of VE reduction in PLHIV had some impact on the economic model, located in the fifth place of the one-way sensitivity analysis, from the healthcare sector perspective. The PSA ascertained that, with a one-time GDP per capita threshold in India, the AYA strategy boasted a 92% likelihood of cost-effectiveness (figure 2B,C). The societal perspective authenticated the 100% probability of the AYA strategy's economic viability (online supplemental figure S11). In South Africa, from both healthcare and societal perspectives, the HIV-targeted strategy overwhelmingly showed a 100% probability of being cost-effective compared with current practices (figure 2F,G and online supplemental figure S11).

The scenario analyses were performed to prognosticate the fiscal outcomes under different conditions. In India, scenarios with 70.8% VE, lifelong duration of protection and instant scale-up to 80% coverage prevented more TB cases than the base-case AYA strategy, with figures at 5.49 (95% UI: 3.87–9.31), 4.92 (3.5–8.23) and 7.97 (5.7–12.97) million (figure 2D). Moreover, these scenarios were more cost-effective than the base-case with ICERs of US$912 (776–1213), US$971 (825–1299) and US$1035 (875–1400) per DALY averted, respectively. For South Africa, similar scenarios outperformed the base-case HIV-targeted strategy, averting up to 0.59 (0.4–0.92) million TB cases and proffering lower ICERs across the board, indicating enhanced cost-effectiveness (figure 2H).

DISCUSSION

Primary findings

The examination of demographic and epidemiological data on the health impacts of Vaccae vaccination in India and South Africa revealed significant findings. In both countries, the vaccination strategies are projected to reduce TB incidence and mortality rates substantially by 2050. In India, without vaccination, TB cases and deaths are expected to reach 83.74 million and 5.97 million, respectively. The adult vaccination strategy could prevent 8.70 million cases and 0.61 million deaths, reducing incidence and mortality rates by 20.1% and 19.0%. However, the AYA strategy was notably cost-effective, requiring fewer vaccinations per case or death averted. In South Africa, the general population strategy could avert 0.67 million TB cases and 0.21 million deaths, with incidence and mortality rates dropping by 28.1% and 27.0%. In contrast, the HIV-targeted strategy proved most effective, with the lowest numbers needed to vaccinate per case or death averted. Economically, the AYA strategy in India and the HIV-targeted strategy in South Africa emerged as the optimal, providing significant health and economic benefits. Sensitivity analyses confirmed the robustness of these findings, with high probabilities of cost-effectiveness under various scenarios. The insights gained from the study hold the promise of being exceptionally informative and valuable for researchers and policymakers engaged in the fight against TB.

Comparison with other studies

Our study contributes to the literature on TB vaccination in India and South Africa but is not the first of its kind. For example, an earlier study demonstrated that routine adolescent vaccination would not be cost-effective if the vaccine only provided PSI efficacy. The divergence in findings may be due to the application of a substantially lower WTP threshold (US$264 per DALY averted).[27] Similarly, in South Africa, a prior study suggested that the most cost-effective approach was to target the adult population aged 18–50 years, with secondary priority given to HIV-infected adults.[28] Our study's different conclusions can be attributed to our broader outcome metrics. Unlike the

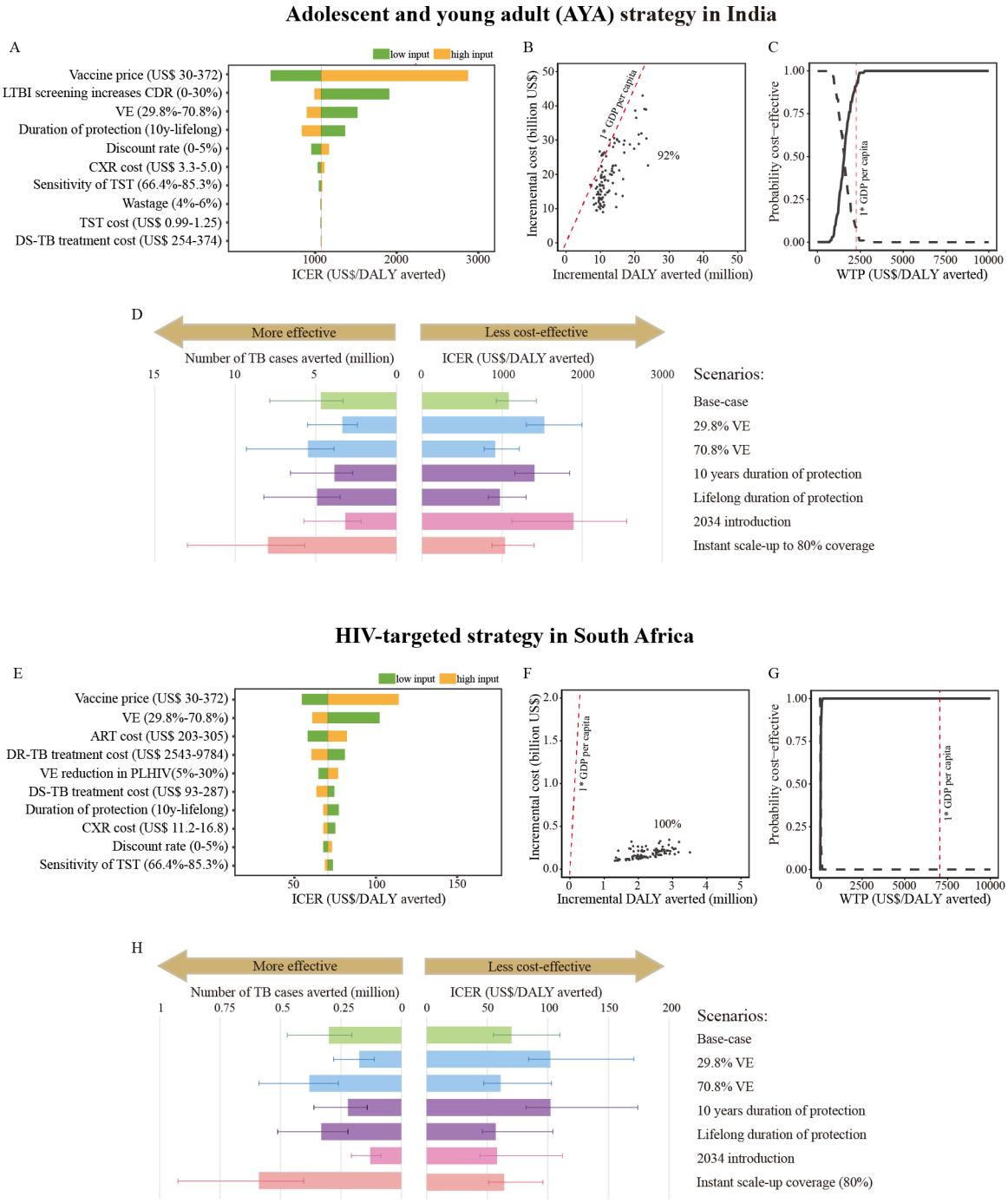

Figure 2 Sensitivity and scenario analyses of the vaccination strategies in India and South Africa. One-way sensitivity analysis (A, E), probability sensitivity analysis (B–C, F–G) and scenario analysis (D, H) of the adolescent and young adult (AYA) strategy in India and the HIV-targeted strategy in South Africa, respectively. Data are presented as median and corresponding 95% UI. ART, antiretroviral therapy; CXR, chest X-ray; DALY, disability-adjusted life year; DR-TB, drug-resistant tuberculosis; DS-TB, drug-susceptible tuberculosis; GDP, gross domestic product per capita; ICER, incremental cost -effectiveness ratio; LTBI, latent TB infection; TST, tuberculin skin test; VE, vaccine efficacy; WTP willingness-to-pay.

previous work, which centred solely around the ICER for gauging cost-effectiveness priority, our analysis employed a multidimensional set of evaluation criteria. Another study by Sumner *et al* demonstrated that the M72/AS01E vaccine in South Africa, targeting individuals aged 15–34, including both HIV-positive and HIV-negative individuals, was cost-effective.[31] However, our study focused exclusively on vaccinating the HIV-positive population, aligning more closely with the higher HIV prevalence in South Africa.

Policy implications

India's National Tuberculosis Elimination Programme (NTEP) has developed a structured approach organised around the four strategic pillars of Detect-Treat-Prevent-Build (DTPB).[32] Introducing the Vaccae vaccination into

this framework could significantly impact the effectiveness of NTEP, potentially sealing various gaps within the existing model. The immunisation could lead to a substantial decline in new TB cases, while ACF initiatives were expected to increase the case detection.[33] Moreover, the findings are not confined to India alone but may resonate across other high-burden TB countries, such as Indonesia, the Philippines and Bangladesh.[2] The lessons learnt regarding age-specific Vaccae vaccination might inform their own national programmes, adapted to reflect distinct epidemiological and socioeconomic circumstances.

In South Africa, the National Tuberculosis Programme's adoption of the Vaccae vaccine may be a major leap forward in realising its aspirational goals to 'End TB' and 'End HIV'. This preventive strategy may notably curtail TB rates among PLHIV, who are particularly susceptible to contracting active TB. HIV and LTBI screening, when combined with the vaccine's deployment, could enhance disease detection within the country. The vaccine's seamless integration with existing protocols would bolster the push for a more encompassing strategy, in harmony with antimicrobial TB treatment and HIV antiretroviral therapy. Moreover, South Africa's approach might serve as an influential model for other regions grappling with high HIV prevalence, such as Gabon, Kenya and Thailand.[2] These nations may also benefit from a tailored TB vaccine strategy aimed at addressing the intertwined HIV-TB challenge and alleviating their substantial healthcare burdens.

Concerning LTBI management, the WHO endorses TB preventive treatment (TPT) as a pivotal tactic in the journey to eliminate TB. The current recommendation highlights three rifamycin-based regimens: 3 months of isoniazid combined with weekly rifapentine (3HP), 4 months of daily rifampin (4R) or 3 months of daily isoniazid plus rifampin (3HR).[34] Japan, which is a TB middle-burden country, has made the notification of LTBI mandatory since 2006, with TPT offered based on risk assessment.[35] Nonetheless, the potential for adverse reactions partly accounts for patient hesitancy, thereby, hindering the widespread adoption of TPT.[36] Integrating Vaccae vaccination as an alternative to TPT could address these concerns by offering a potentially safer and more acceptable option for both patients and healthcare providers. This could lead to improved compliance with preventative measures and bolster the fight against TB in contexts where TPT encounters substantial barriers to implementation.

Vaccine price and payment mechanisms are crucial for scaling up TB vaccination programmes. Biopharmaceutical companies often adjust prices by region based on market demand, economic conditions and healthcare infrastructure, typically lowering prices outside their home countries. For instance, Gilead Sciences priced its hepatitis C drug in China at one-fifth of the US price.[37] Similarly, we assumed that the Vaccae vaccine price in India and South Africa was one-third of its price in China to enhance affordability (personal communication with Dr. Jiang Pu, senior officer of the Vaccae manufacturer). The affordability of the vaccine impacts the ability of healthcare systems, particularly, in low-income and middle-income countries, to procure and distribute the vaccine widely. Sustainable funding models, including government budgets, international aid and public-private partnerships, can help ensure that the vaccine reaches the populations most at risk.[38]

Strength and limitations

Our study is characterised by several notable strengths that set it apart from other studies in the field. First, it is anchored by the employment of the first clinically approved next-generation tuberculosis vaccine, apart from other studies that have relied on hypothetical vaccines or vaccines still under trial. The utilisation of an actionable vaccine in real-world contexts provided more practical insights and direct applicability of our study's findings, compared with those inferred from studies based on vaccines with uncertain futures. Second, our analysis extended to a thorough consideration of ACF as an integral component of the PSI vaccine strategy. In doing so, we avoided underestimation and provide a more accurate assessment of the full potential of the PSI vaccine; whereas, other studies overlooked the costs associated with and the significance of ACF screening. Last but not least, we adopted a comprehensive evaluative stance through the incorporation of budget analysis, cost-effectiveness analysis and cost-benefit analysis. This approach extends beyond merely focusing on the ICER or any other singular metric. Consequently, this broadens our capacity to make well-informed decisions regarding the practicality and the economic ramifications of TB vaccine rollouts, providing a more expansive selection of indicators for policymakers' guidance.

Admittedly, this study has several limitations. The vaccine was assumed to provide 'all-or-nothing' protection, yet the alternative 'degree/leaky' (efficacy was implemented as a reduction in natural history) assumption might reduce effect estimates. Our model omitted the analysis of regional disparities throughout the nation, gender-related variation, the spectrum of immune response, patterns of drug resistance, along with the extent of vaccine receptivity and adherence. These elements present valuable opportunities for prospective research. Delving into these details can enrich future studies, leading to models that more accurately reflect the intricacies associated with the deployment of TB vaccines and their more extensive influence on public health.

CONCLUSIONS

The combined approach of Vaccae vaccination and active case finding appears to be a promising investment for countries like India and South Africa, which carry a high TB burden. It would be advisable for policymakers in these nations to contemplate the incorporation of such

strategies into their TB control programmes. Further research and real-world implementation studies are warranted to validate these findings.

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REFERENCES

1 WHO Guidelines Approved by the Guidelines Review Committee. *Guidelines on the Management of Latent Tuberculosis Infection*, Copyright © World Health Organization 2015. Geneva: World Health Organization, 2015.
2 World Health Organization. Global tuberculosis report. 2023. Available: https://www.who.int/teams/global-tuberculosis-programme/tb-reports [Accessed 07 Dec 2023].
3 Burke RM, Nliwasa M, Dodd PJ, *et al*. Impact of Community-Wide Tuberculosis Active Case Finding and Human Immunodeficiency Virus Testing on Tuberculosis Trends in Malawi. *Clin Infect Dis* 2023;77:94–100.
4 Anderson T. The tuberculosis vaccine challenge. *Bull World Health Org* 2023;101:303–4.
5 Mao J-J, Zang X, Yue W-L, *et al*. Population-level health and economic impacts of introducing Vaccae vaccination in China: a modelling study. *BMJ Glob Health* 2023;8:e012306.
6 Central TB Division MoHaFW, India. India TB report. 2023. Available: https://tbcindia.mohfw.gov.in/wp-content/uploads/2023/05/5646719104TB_AR_2023_04-04-2023_LRP_final.pdf
7 Chauhan A, Parmar M, Dash GC, *et al*. The prevalence of tuberculosis infection in India: A systematic review and meta-analysis. *Indian J Med Res* 2023;157:135–51.
8 Moyo S, Ismail F, Van der Walt M, *et al*. Prevalence of bacteriologically confirmed pulmonary tuberculosis in South Africa, 2017-19: a multistage, cluster-based, cross-sectional survey. *Lancet Infect Dis* 2022;22:1172–80.
9 Prem K, Zandvoort K van, Klepac P, *et al*. Projecting contact matrices in 177 geographical regions: An update and comparison with empirical data for the COVID-19 era. *PLoS Comput Biol* 2021;17:e1009098.
10 United Nations Population Division. World population prospects. 2022. Available: https://population.un.org/wpp/Download/Standard/CSV/ [Accessed 20 May 2023].
11 Suthar AB, Lawn SD, del Amo J, *et al*. Antiretroviral therapy for prevention of tuberculosis in adults with HIV: a systematic review and meta-analysis. *PLoS Med* 2012;9:e1001270.
12 Dodd PJ, Prendergast AJ, Beecroft C, *et al*. The impact of HIV and antiretroviral therapy on TB risk in children: a systematic review and meta-analysis. *Thorax* 2017;72:559–75.
13 Zang X, Krebs E, Min JE, *et al*. Development and Calibration of a Dynamic HIV Transmission Model for 6 US Cities. *Med Decis Making* 2020;40:3–16.
14 Krishnamoorthy Y, Eliyas SK, Nair NP, *et al*. Impact and cost effectiveness of pneumococcal conjugate vaccine in India. *Vaccine (Auckl)* 2019;37:623–30.
15 Tan N, Sharma M, Winer R, *et al*. Model-estimated effectiveness of single dose 9-valent HPV vaccination for HIV-positive and HIV-negative females in South Africa. *Vaccine (Auckl)* 2018;36:4830–6.
16 Crum-Cianflone NF, Wallace MR. Vaccination in HIV-infected adults. *AIDS Patient Care STDS* 2014;28:397–410.
17 Nicolini LA, Giacobbe DR, Di Biagio A, *et al*. Insights on common vaccinations in HIV-infection: efficacy and safety. *J Prev Med Hyg* 2015;56:E28–32.
18 Li X, Stander MP, Van Kriekinge G, *et al*. Cost-effectiveness analysis of human papillomavirus vaccination in South Africa accounting for human immunodeficiency virus prevalence. *BMC Infect Dis* 2015;15:566.
19 Krutikov M, Faust L, Nikolayevskyy V, *et al*. The diagnostic performance of novel skin-based in-vivo tests for tuberculosis infection compared with purified protein derivative tuberculin skin tests and blood-based in vitro interferon-γ release assays: a systematic review and meta-analysis. *Lancet Infect Dis* 2022;22:250–64.
20 Targeted tuberculin testing and treatment of latent tuberculosis infection. American Thoracic Society. *MMWR Recomm Rep* 2000;49:1–51.
21 Azman AS, Golub JE, Dowdy DW. How much is tuberculosis screening worth? Estimating the value of active case finding for tuberculosis in South Africa, China, and India. *BMC Med* 2014;12:216.
22 Maheshwari P, Chauhan K, Kadam R, *et al*. Market assessment of tuberculosis diagnostics in India in 2013. *Int J Tuberc Lung Dis* 2016;20:304–13.
23 Pantoja A, Lönnroth K, Lal SS, *et al*. Economic evaluation of public-private mix for tuberculosis care and control, India. Part II. Cost and cost-effectiveness. *Int J Tuberc Lung Dis* 2009;13:705–12.
24 Kim H-Y, Hanrahan CF, Martinson N, *et al*. Cost-effectiveness of universal isoniazid preventive therapy among HIV-infected pregnant women in South Africa. *Int J Tuberc Lung Dis* 2018;22:1435–42.

25 Meyer-Rath G, Schnippel K, Long L, *et al*. The impact and cost of scaling up GeneXpert MTB/RIF in South Africa. *PLoS One* 2012;7:e36966.
26 Weerasuriya CK, Harris RC, McQuaid CF, *et al*. The epidemiologic impact and cost-effectiveness of new tuberculosis vaccines on multidrug-resistant tuberculosis in India and China. *BMC Med* 2021;19:60.
27 Harris RC, Quaife M, Weerasuriya C, *et al*. Cost-effectiveness of routine adolescent vaccination with an M72/AS01$_E$-like tuberculosis vaccine in South Africa and India. *Nat Commun* 2022;13:602.
28 Jayawardana S, Weerasuriya CK, Pelzer PT, *et al*. Feasibility of novel adult tuberculosis vaccination in South Africa: a cost-effectiveness and budget impact analysis. *NPJ Vaccines* 2022;7:138.
29 Vos T, Lim SS, Abbafati C, *et al*. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. *The Lancet* 2020;396:1204–22.
30 Ayles H, Muyoyeta M, Du Toit E, *et al*. Effect of household and community interventions on the burden of tuberculosis in southern Africa: the ZAMSTAR community-randomised trial. *Lancet* 2013;382:1183–94.
31 Sumner T, Clark RA, Mukandavire C, *et al*. Modelling the health and economic impacts of M72/AS01E vaccination and BCG-revaccination: Estimates for South Africa. *Vaccine (Auckl)* 2024;42:1311–8.
32 Majumdar P. Tuberculosis in India: Overview, Challenges, and Way Forward in the Post-COVID-19 Era. *Soc Dev Issues* 2022;44.
33 Garg T, Chaisson LH, Naufal F, *et al*. A systematic review and meta-analysis of active case finding for tuberculosis in India. *Lancet Reg Health Southeast Asia* 2022;7:100076.
34 Assefa DG, Bedru A, Zeleke ED, *et al*. Efficacy and safety of different regimens in the treatment of patients with latent tuberculosis infection: a systematic review and network meta-analysis of randomized controlled trials. *Arch Public Health* 2023;81:82.
35 Kawatsu L, Uchimura K, Ohkado A. Trend and treatment outcomes of latent tuberculosis infection among migrant persons in Japan: retrospective analysis of Japan tuberculosis surveillance data. *BMC Infect Dis* 2021;21:42.
36 Rajpal S, Arora VK. Latent TB (LTBI) treatment: Challenges in India with an eye on 2025: "To Treat LTBI or not to treat, that is the question." *Ind J Tuberc* 2020;67:S43–7.
37 Chen P, Jin M, Cao Y, *et al*. Cost-Effectiveness Analysis of Oral Direct-Acting Antivirals for Chinese Patients with Chronic Hepatitis C. *Appl Health Econ Health Policy* 2021;19:371–87.
38 Nunes C, McKee M, Howard N. The role of global health partnerships in vaccine equity: A scoping review. *PLOS Glob Public Health* 2024;4:e0002834.
39 Global Burden of Disease Collaborative Network. Global burden of disease study 2019 (GBD 2019) disability weights. Seattle, United States of America Institute for Health Metrics and Evaluation (IHME); 2020. Available: https://ghdx.healthdata.org/record/ihme-data/gbd-2019-disability-weights [accessed 24 Apr 2023]
40 World Bank. World bank country and lending groups. Washington, DC The World Bank; 2021. Available: https://data.worldbank.org/indicator/NY.GDP.PCAP.CD?locations=IN-ZA
41 Foster N, Vassall A, Cleary S, *et al*. The economic burden of TB diagnosis and treatment in South Africa. *Soc Sci Med* 2015;130:42–50.
42 John KR, Daley P, Kincler N, *et al*. Costs incurred by patients with pulmonary tuberculosis in rural India. *Int J Tuberc Lung Dis* 2009;13:1281–7.
43 Chandra A, Kumar R, Kant S, *et al*. Costs of TB care incurred by adult patients with newly diagnosed drug-sensitive TB in Ballabgarh block in northern India. *Trans R Soc Trop Med Hyg* 2022;116:63–9.
44 Mudzengi D, Sweeney S, Hippner P, *et al*. The patient costs of care for those with TB and HIV: a cross-sectional study from South Africa. *Health Policy Plan* 2017;32:iv48–56.
45 Bell E, Brassel S, Oliver E, *et al*. Estimates of the Global Burden of COVID-19 and the Value of Broad and Equitable Access to COVID-19 Vaccines. *Vaccines (Basel)* 2022;10:1320.