The Health and Economic Benefits Possible with Novel Tuberculosis Vaccines – A Modeling Study in India and Indonesia

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Article

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Abstract

Health and economic benefits possible with emerging tuberculosis vaccines are not fully known. We estimated gains possible with novel post-exposure vaccines, in India and Indonesia. We modeled vaccine impact on TB incidence, TB mortality, and on national income growth and the intrinsic value of living longer, known as Full-income. We considered several vaccine efficacies, initiation and scale-up scenarios. We found that if all age groups are vaccinated in 2025, then 2.3 million TB deaths in India and 695,000 TB deaths in Indonesia can be prevented, adding 0.09 years and 0.17 years to individual life expectancy at birth, on average annually. Full-income savings is US$2 trillion in India and US$680 billion in Indonesia. Even if delayed until 2030, 1.6 million deaths in India and 489,000 deaths in Indonesia can be prevented, with full-income savings of US$1.5 trillion and US$490 billion. These benefits suggest that further investment in the vaccines is prudent.

Significance Statement There are no prior economic evaluations of candidate tuberculosis vaccines. Our study addresses this gap to answer two questions: (1) is there value in making the vaccine available given the efficacies demonstrated to date; and (2) is there an optimal time window for making the vaccine available. The conclusions in relation to these two questions are important because: (1) they are based on findings from two countries, which jointly account for 35% of global TB incidence and 38.8% of global TB mortality in 2019; (2) they provide guidance for future investment in the vaccine and roll-out in those countries.

Introduction

Despite nearly a century long search, a vaccine capable of interrupting the transmission of tuberculosis (TB)—the leading killer among infectious diseases, has been beyond reach. The need for a vaccine has been made dire by TB's colossal human and economic losses, mounting at an increasing rate due to the spread of drug resistant strains and the epidemiological synergy with HIV/AIDS. The Bacille Calmette-Guérin (BCG) vaccine, the only licensed TB vaccine to date, which has been in use for more than 90 years, has had a modest effect in containing the spread of TB in high burden developing countries[1]. The protection conferred by BCG is time-limited and not effective in populations exposed to other mycobacterial antigens[2]. To date, the pursuit for a vaccine to replace or to augment BCG, has yielded disappointing results[3].

In September 2018, the phase 2b proof-of-concept efficacy trial of the M72/AS01$_E$ adjuvanted protein candidate vaccine (M72 vaccine), conducted in South Africa, Kenya and Zambia, demonstrated a 54.0% (90% confidence interval [CI]: 13.9–75.4%) protection against pulmonary TB in a per-protocol cohort (57.0% efficacy in the intention-to-treat cohort)[4]. In July 2018, a phase 2 trial examining whether revaccination with BCG can confer partial protection, found that even though revaccination did not prevent initial immunologic sensitization (as measured by an interferon-γ release assay-QFT), it reduced the rate of sustained QFT conversion with an efficacy of 45.4% (P = 0.03). While both trials generated considerable optimism, their target populations were different. In the BCG revaccination trial, efficacy was

demonstrated in individuals who were previously unexposed to Mycobacterium tuberculosis (Mtb) and the human immunodeficiency virus (HIV)[5], and had a negative result on a QFT assay. In the M72 vaccine trial, efficacy was demonstrated in individuals who were previously exposed to Mtb but unexposed to HIV[4]. In October 2019, a phase 2b trial to evaluate the efficacy of BCG revaccination in 1,800 participants in South Africa was launched by the Bill & Melinda Gates Medical Research Institute[6]. A subsequent trial for the M72 vaccine is yet to come to fruition.

A vaccine with efficacy limited to populations latently infected with Mtb and previously unexposed to HIV, may yield sufficient health and economic benefits to justify development and launch. Beyond health and productivity gains, such a vaccine can also contribute to broader economic welfare, as TB affects a wide spectrum of social outcomes[7,8,9]. The impact on income growth measured by national income accounts and the value of additional life years gained by averting deaths, commonly known as Full-income, provides a reasonable assessment of the broader economic welfare losses due to disease, in a manner consistent with standard welfare theory[10]. We previously estimated full-income losses due to premature deaths from TB in 120 countries (forthcoming).

To explore whether there is sufficient health and economic value in making such a vaccine available in India and Indonesia - two populous countries where TB incidence is high and HIV prevalence is low[11], we modeled its epidemiological impact on latently infected populations. Based on reductions in TB incidence and TB deaths, we estimated full-income and life expectancy impacts between 2020 and 2050, under several vaccination scenarios. Our analysis aimed to answer two questions: (1) is there value in making such a vaccine available in India and Indonesia, given the efficacies demonstrated in the limited phase 2b trials; (2) is there an optimal time window for making the vaccine available given that a phase 3 trial is yet to begin. We present what we believe to be the first comprehensive assessment of the health and economic impact of the vaccine in the two countries.

Methods

We modeled the vaccine's impact in preventing the progression of latent to active TB and related deaths, in India and Indonesia from 2020 to 2050. We employed a deterministic, age structured TB transmission dynamic model, fitted to World Health Organization's (WHO's) TB incidence and mortality estimates[12], and World Population Prospects' (WPP's) population size estimates[13]. The model is an adaptation of our previously validated and published TB vaccine model[14,15] (SI Appendix-1 section A).

We assumed that the vaccine was 49.7% effective as a lower bound (90% CI: 12.1%-71.2%) and 54.1% effective as an upper bound (20.3%-73.6%), in preventing latent to active progression. The lower bound was demonstrated for the per-protocol cohort and the upper bound for the total efficacy cohort, for the first case definition of the M72 vaccine trial[16]. We modeled the impact of vaccination initiation in 2020, 2025 and 2030, to individuals of all ages and individuals aged 18-49 years, with the duration of protection lasting 10 years or lifetime. We assumed that 90% coverage will be reached within 10 years of

vaccination initiation. Even though the M72 vaccine was trialed for HIV negative populations, we disregarded the HIV status given the low HIV prevalence in both countries (0.2% and 0.4% in India and Indonesia, respectively, in individuals aged 15-49 years[11]). We also assumed that individuals who are vaccinated but develop TB disease were 50% less infectious than individuals who were not vaccinated. Though not directly parameterized, our model implicitly mirrored the trial scenario where vaccination was administered en masse, with a second dose after one month following the initial dose (with no catch-up vaccination).

We estimated the potential gains in life expectancy at birth and at age 35 due to the reduction in TB deaths from vaccination, using the multiple decrement life-table method[17] to construct the cause-eliminated life tables from 2020 to 2050, using the abridged life tables and population projections from WPP[13] (SI Appendix-1 section B). To calculate the full-income value of the deaths averted ($V(e_i, e_j, y)$), following Jamison et al.[10], we transformed the change in mortality risk at each age interval (due to vaccination) to Standardized Mortality Units (a 1/10,000 change in mortality risk). We then calculated the population value of this risk change for each country and year (p_k), by multiplying the value by the population in each age interval ($n(a)$) and rescaling the risk to age using 35 years as the reference age. To arrive at the monetary value of the risk change, we multiplied the rescaled population value of the risk change by the value of a statistical life year (VSLY) (for the country and year), calculated as a proportion of the income per capita (y), which we modeled over the 30 years (SI Appendix-1 section D).

$$V(e_i, e_j, y) = \frac{GDP}{capita} \cdot \gamma \int_0^{\infty} n(a)\, \Delta smu(e_i, e_j) \frac{e(a)}{e(35)} da$$

To identify empirically estimated country VSLs, we conducted a rapid literature review. Where not available, we calculated VSL values based on benefits transfer by adjusting the VSL in the United States (in purchasing power parity adjusted international $ rates)[18], assuming an income elasticity of 1.0 (1.5 considered in the sensitivity analysis)[19]. We calculated the present value of gainsfrom the perspective of 2020, assuming a discount rate of 3% (rates between 3% and 5% considered in the sensitivity analysis)[20]. All calculations were performed using Stata (Stata/IC version 14.2). We report all costs in 2018 US$ rates using exchange rates and deflator values available from the World Bank[21].

Results

India

We estimated that between 2020 and 2050 there would be 53,789,255 incident cases of active TB (annual mean = 1,735,137; std. dev = 123,864) and 8,763,539 related deaths (annual mean = 282,695; std. dev = 30,772) (SI Appendix-2 Sect. 2). Both incidence and deaths peak in ages 15–20 in 2020 and in ages 25–30 in 2050. If the deaths were averted within the year that they occurred, then 0.514 years would be

added to life expectancy at birth (95% CI: 0.49–0.53) and 0.17 years (0.16–0.18) would be added to life expectancy at age 35, per person on average annually. We valued the economic losses due to deaths to be US$6.63 trillion (present value in 2020 at a 3% discount rate).

If the vaccine was introduced in India in 2025, to individuals aged 18–49 years, who were latently infected with pulmonary TB and who were previously unexposed to HIV (the population in which the reported efficacies were demonstrated [16]), then with upper bound efficacy and lifetime protection, 12,861,850 incident cases and 1,663,179 TB deaths could be averted (a 19% reduction from the counterfactual scenario above). The reduction in deaths adds 0.1 years (0.05–0.15) to life expectancy of the average Indian at birth and 0.03 years (0.01–0.05) to life expectancy at age 35, annually between 2020 and 2050. The economic benefits from the averted deaths is US$1.5 trillion, a 22.5% savings from the counterfactual scenario. If the vaccine conferred the same level of efficacy in individuals of all ages, then 2,259,533 deaths could be averted (a 25.8% reduction), thereby adding 0.13 years (0.08–0.19) to life expectancy at birth and 0.04 years (0.01–0.06) to life expectancy at age 35, on average annually. The economic savings due to the averted deaths is US$2.0 trillion (30.3% savings from the counterfactual scenario) (Fig. 1A-1C; Table 1).

If vaccine introduction was delayed until 2030 and the population aged 18–49 years was vaccinated, then 1,121,412 TB deaths could be averted (a 12.8% reduction from the counterfactual scenario) and 0.07 years (0.03–0.11) would be added to life expectancy at birth and 0.02 years (0.00-0.04) to life expectancy at age 35, annually on average, between 2020 and 2050. The economic benefits due to the averted deaths is US$1.1 trillion (a 16% savings from the counterfactual scenario). If individuals of all ages were vaccinated, then 1,597,500 deaths could be averted (18.2% reduction) and 0.1 years (0.05–0.15) could be added to life expectancy at birth and 0.14 years (0.11–0.17) to life expectancy at age 35, on average annually. The economic savings due to the averted deaths is US$1.5 trillion (a 22.6% savings from the counterfactual scenario) (Fig. 1A-1C; Table 1; SI Appendix-2 Sect. 1).

Figure 1: Impact of M72 vaccine in India between 2020–2050, on (A) TB deaths, (B) life expectancy at birth and at age 35, and (C) economic losses, by year of initiation and age of vaccination. Vaccine efficacy assumed to be 54.1% with lifetime protection. TB deaths are reported in absolute values. Life expectancy at birth and age 35 reported as mean annual losses per person. Economic losses reported in absolute values (in 2018 US$ billions).

Indonesia

In Indonesia, we estimated that 23,327,937 incident TB cases (annual mean = 752,514; std. dev = 46,485), could give rise to 3,229,266 TB deaths (annual mean = 104,170; std. dev = 6.75), between 2020 and 2050 (SI Appendix 2 Sect. 3). Both incidence and deaths peak in the 15–20 year age group in 2020 and in the 30–35 year age group in 2050. If the deaths were averted each year that they occurred, 0.82 years (95% CI: 0.80–0.84) would be added to life expectancy at birth and 0.44 years (0.43–0.46) to life expectancy at age 35, on average annually, per person. The economic losses due to the 3,229,266 TB deaths would be US$2.95 trillion.

If the vaccine was introduced in 2025, with upper bound efficacy and lifetime protection, to the population aged 18–49 years, then 390,531 deaths could be averted (a 12.1% reduction from the counterfactual scenario), which adds 0.1 years (0.05–0.15) to life expectancy at birth and 0.05 years (0.02–0.09) to life expectancy at age 35, on average annually between 2020 and 2050. The averted deaths result in US$380 billion in economic savings (a 12.9% savings compared to the counterfactual scenario). If the vaccine was able to confer the same level of protection to all ages, then 694,762 deaths could be averted, adding 0.17 years (0.10–0.25) to life expectancy at birth and 0.09 years (0.05–0.14) to life expectancy at age 35, on average annually. US$680 billion in economic losses could be avoided as a result (23.1% savings compared to the counterfactual scenario) (Fig. 2A-2C; Table 1).

If introduced in 2030 instead of 2025, to the population aged 18–49, then 257,843 deaths could be averted (8% reduction compared to the counterfactual scenario), thereby adding 0.07 years (0.01–0.11) to life expectancy at birth and 0.03 years (0.00-0.07) to life expectancy at age 35, on average annually. The economic savings would be US$260 billion (8.8% savings compared to the counterfactual scenario). Vaccinating individuals of all ages elevates the gains: instead of 257,843 deaths, 489,216 deaths would be averted (a 15.2% reduction), 0.12 years (0.05–0.19) would be added to life expectancy at birth and 0.38 years (0.33–0.42) to life expectancy at age 35, on average annually - the economic value of which would be US$490 billion (a 16.6% savings compared to the counterfactual scenario) (Fig. 2A-2C; Table 1; SI Appendix-2 Sect. 2).

Figure 2: Impact of M72 vaccine in Indonesia between 2020–2050, on (A) TB deaths, (B) life expectancy at birth and at age 35, and (C) economic losses, by year of initiation and age of vaccination. Vaccine efficacy assumed to be 54.1% with lifetime protection. TB deaths are reported in absolute values. Life expectancy at birth and age 35 reported as mean annual losses per person. Economic losses reported in absolute values (in 2018 US$ billions).

India versus Indonesia - Economic Losses

In India, if the vaccine was introduced in 2020, US$2.01 trillion in economic losses could have been avoided (vaccinating the 18-49-year-old population). The savings can be retained even if vaccination is delayed until 2025, by vaccinating individuals of all ages. By delaying vaccine introduction until 2030, but by vaccinating individuals of all ages, the 2025 savings can even be exceeded (by US$10 billion) (Fig. 3A-3C).

The same is true in Indonesia. If introduced in 2020, US$550 billion in economic losses can be avoided (limiting vaccination to the18-49-year-old population). By introducing the vaccine in 2025, to individuals of all ages, the 2020 savings can be surpassed (US$680 billion compared to the US$550 billion in 2020). Similarly, if introduced in 2030 to individuals of all ages, the 2025 savings can be surpassed (US$490 billion as compared to the US$380 billion in 2025) (Fig. 4A-4C).

In both countries, irrespective of whether vaccination is initiated in 2020, 2025 or 2030, if individuals of all ages are vaccinated, then by 2050, the economic losses converge. In Indonesia in particular, the economic losses overlap in 2050 for the 2020 and 2025 vaccination initiation scenarios. If the population

aged 18–49 were vaccinated however, the economic losses do not converge in either country. They instead remain parallel (Figs. 3A-3C; Fig. 4A-4C; SI Appendix-2 Sect. 1 and Sect. 2).

India versus Indonesia - Life Expectancy Losses

In India, the average annual gain in life expectancy at birth declines as vaccination is delayed. However, the average annual gain in life expectancy at age 35 more than triples if vaccination is initiated in 2030 instead of 2025. The same is true in Indonesia: the average annual gains in life expectancy are nearly four-fold higher if vaccination is initiated in 2030 instead of 2025. This finding is in agreement with our other finding that peak incidence and mortality shift towards higher ages from 2020 to 2050 in both countries (Fig. 3A-3C).

If the duration of protection is limited to 10 years instead of lifetime, then in both countries, vaccinating with such a vaccine is comparable to waiting until 2025 but vaccinating with a vaccine that provides lifetime protection. Though this is the case from the perspective of TB deaths averted, from the perspective of economic gains, vaccinating with a vaccine that provides 10 years of protection is comparable to delaying vaccinating with a vaccine that provides lifetime protection, until 2030 (Figs. 3A-3C; Fig. 4A-4C; SI Appendix-2 Sect. 1 and Sect. 2).

Figure 3: Impact of M72 vaccine on (D) TB deaths, (E) life expectancy at birth, and (C) economic losses in India, by vaccine efficacy, duration of protection and age of vaccination. Vaccination assumed to be initiated in 2020. TB deaths reported in absolute values. Life expectancy at birth reported as total gains in individual life expectancy at birth from 2020–2050. Economic losses reported total economic losses from 2020–2050 (in 2018 US$ billions).

Figure 4: Impact of M72 vaccine on (D) TB deaths, (E) life expectancy at birth, and (C) economic losses in Indonesia, by vaccine efficacy, duration of protection and age of vaccination. Vaccination assumed to be initiated in 2020. TB deaths reported in absolute values. Life expectancy at birth reported as total gains in individual life expectancy at birth from 2020–2050. Economic losses reported total economic losses from 2020–2050 (in 2018 US$ billions).

Table 1: Impact of vaccination on TB deaths, life expectancy at birth and full-income, in India and Indonesia, by vaccine introduction year, vaccinated age group and vaccine's duration of protection. TB deaths reported as the total between 2020 and 2050. Life expectancy at birth reported as the mean annual gain per person (in years). Full-income reported as total losses from 2020–2050 in 2018 US$ Billions.

Discussion

Our analysis sought to answer two questions: first, whether there is sufficient health and economic value in making the vaccines available in India and Indonesia, given what is currently known about the vaccine; secondly, how soon the vaccine should be made available, to yield its highest health and economic benefits. The answer to the first question is promising. The economic value of the vaccine can be substantial: in the best case, where we assumed that the efficacies demonstrated for populations aged

18–49 years are transferable to populations of all ages: 30.3% and 23.1% of economic losses can be averted in India and Indonesia (respectively), if initiated in 2025, and 22.6% and 16.0% if initiated in 2030. Our assumption regarding the transferability of efficacies is reasonable as the 3-year final analysis of the M72 phase 2b trial did not show differential efficacy by age[16].

The answer to the second question is less clear, however. The health and economic losses due to not initiating vaccination in 2020 could be fully recovered even if vaccination is initiated in 2025, provided all who are latently infected are vaccinated. Indeed, in Indonesia, vaccinating all who are latently infected in 2025 is a better option than vaccinating the 18–49 year age group in 2020 (23.05% of the projected economic losses averted compared to 18.64%, respectively), as a large proportion of the latently infected are ≥ 50 years of age. This conclusion, however, is contingent on the vaccine providing a lifetime of protection. Whether the vaccine can provide such protection is still unknown. Knowing the duration of protection is important as our results demonstrate that in both countries, 10 years of protection at the lower efficacy bound, results in a greater number of TB deaths averted if the individuals of all ages are vaccinated (Figs. 1D and 2D).

We also find that there are specific windows within each country that can yield a demographic dividend, in addition to an economic dividend, given when vaccination is initiated. In India, the total dependency ratio declines from 2020 to 2040, then begins a steady upward trajectory[13]. Initiating vaccination early will allow capturing this window by reducing the burden of TB on the productive population. If vaccination is initiated in 2020 or 2025, then the highest number of deaths are averted in the 30–35 age group. Incidence is more sensitive to early initiation; if initiated in 2020, then the highest incidence is averted in the 30–35 age group. Waiting until 2030, moves the age group likely to experience the greatest benefit to 40–45 years. In Indonesia, unlike in India, the total dependency ratio steadily increases. Therefore, in Indonesia there is no optimal window during which a demographic dividend can be gained. The earlier vaccination is initiated, the greater the burden on the productive population that can be averted, especially as the contribution towards life expectancy at birth is greater in Indonesia when compared to India (Table 1).

This argument, however, does not account for the exogenous shock of COVID-19 in deterring economic growth. The projected upswing in the per capita income growth (7.4% and 8.2% in India and Indonesia, respectively, in 2021[22]) is largely uncertain now. Though population age structure can fuel economic growth, effective policies are needed to capitalize on the working population. Without such policies, countries can end up with large pools of unemployed or underemployed working age populations. COVID-19 has reframed the context for social policy and it is indeed why vaccination is all the more important now. Pre-COVID projections of TB incidence likely underestimates current levels as well. Recent estimates by Cilloni and colleagues show that a two-month lockdown with two months of recovery, gave rise to 473,000 additional TB cases and 130,000 additional TB deaths in India[23]. Our recent estimates show that the additional incident cases due to a 3-month lockdown with 10-months of recovery can give rise to significant increases in additional government spending and additional out-of-pocket spending[24]. In

India, where out-of-pocket spending already accounts for as much as 43.8% of total spending, the economic and social consequences of COVID-19 only stand to aggravate the burden on patients and households.

Notwithstanding the unknowns, our results provide compelling epidemiological and economic justification for making the vaccine available as soon as scientifically justifiable. In Indonesia, 5,496,793 incident cases can be averted if the vaccine is introduced in 2030 to all ages. Fuady et al. find that 36% of households in Indonesia with a case of active drug-susceptible TB, experienced catastrophic costs [25] . If generalizable, then by introducing the vaccine in 2030, 1,978,845 households can be prevented from experiencing catastrophic losses. India had a higher estimated percentage of new TB cases with rifampicin resistant TB compared to Indonesia (2.8% versus 2.4%), which means that the gains in India can be even higher. Recent estimates from Su et al. show that India's total tuberculosis spending per incident case in 2017 is double that of Indonesia's (US$644; 95% CI: US$489–852, versus US$322; 95% CI: US$258–403) [26] . In India, 43.8% (95% CI: 28.9%-59.6%) of the spending is borne by the patient as out of pocket spending, whereas In Indonesia, the share is 14.5% (95% CI: 6.4%-26.8%). India's TB spending is also projected to grow at 7.9% annually whereas Indonesia's is projected to grow at 2.6%[26].

The applicability of the efficacies demonstrated in Kenya, South Africa, and Zambia, to populations in India and Indonesia is a central assumption of our analysis and thereby potentially a limitation. We assumed that latency can be established in a reliable and cost effective manner, which in countries like India with large high risk populations[12], can be expensive. Vaccinating irrespective of exposure status is therefore a better option, provided the safety of the vaccine in individuals previously unexposed to Mtb is known. Our estimates of incidence and consequent mortality are contingent on assumptions inherent in our natural history model. While these assumptions reflect the most recent thinking and findings, they are nonetheless limitations. We also assumed that the efficacies remained stable over the duration of protection, which is yet to be established. Our full-income estimates are limited by our projections of per capita income, which are now all the more uncertain. Equally uncertain due to COVID-19 are the empirically established VSL values. Though the literature is scarce, it is plausible that the mean individual valuation of mortality risk reduction is influenced by the presence of a global scale pandemic. Our estimates are also limited by WPP's projections of populations in India and Indonesia, as well as the abridged life tables through 2050 for both countries.

As much as our results point towards substantial economic benefits, that conclusion is still contingent on unknowns - primarily, the safety of the vaccine in young adolescents and older adults, and the duration of protection. Our results are all the more reason to invest in a phase 3 trial that could resolve these unknowns and thereby pave the way towards realizing the potentially substantial health and economic benefits. Excess cases due to disruption of routine TB services from COVID-19 lockdowns, will undoubtedly add to the dividends achievable with a vaccine, though possibly moderated by COVID-19 prevention measures given the common routes of transmission[27]. The optimal window for vaccination is fast approaching. Investment is needed now more than ever.

Declarations

Author Contributions

SS conceived the study, developed the economic model and the demographic model, completed the economic and demographic analysis, wrote the initial draft and contributed to finalizing the manuscript.

Author Contributions

SS conceived the study, developed the economic model and the demographic model, completed the economic and demographic analysis, wrote the initial draft and contributed to finalizing the manuscript.

SFA developed the epidemiological model, completed the epidemiological analysis and contributed to finalizing the manuscript.

LJA developed the epidemiological model, oversaw the epidemiological analysis and contributed to finalizing the manuscript.

RA advised SS on the economic and demographic analysis and contributed to finalizing the manuscript.

EG contributed to the finalizing the manuscript.

MJR conceived the study with SS, contributed to the design of the study, wrote the initial draft with SS and contributed to finalizing the manuscript.

All authors have approved the final version submitted.

Competing Interest Statement

We declare that we have no competing interests.

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Table

Table 1: Impact of vaccination on TB deaths, life expectancy at birth and full-income, in India and Indonesia, by vaccine introduction year, vaccinated age group and vaccine's duration of protection. TB deaths reported as the total between 2020 and 2050. Life expectancy at birth reported as the mean annual gain per person (in years). Full-income reported as total losses from 2020-2050 in 2018 US$ billions.

A. Impact on TB death

Scenario	Vaccinated Age-Group	Duration of Protection (years)	India			Indonesia		
			TB Deaths	TB Deaths Averted	TB Deaths Averted %	TB Deaths	TB Deaths Averted	TB Deaths Averted %
Counterfactual: Annual TB mortality declined as predicted by epidemiological model			8,763,539			3,229,266		
Vaccine introduced in 2020	All	lifelong	5,667,078	3,096,461	35.33%	2,278,776	950,490	29.43%
Vaccine introduced in 2020	18-49	lifelong	6,378,267	2,385,272	27.22%	2,655,384	573,882	17.77%
Vaccine introduced in 2025	All	lifelong	6,504,006	2,259,533	25.78%	2,534,504	694,762	21.51%
Vaccine introduced in 2025	18-49	lifelong	7,100,360	1,663,179	18.98%	2,838,735	390,531	12.09%
Vaccine introduced in 2030	All	lifelong	7,166,039	1,597,500	18.23%	2,740,050	489,216	15.15%
Vaccine introduced in 2030	18-49	lifelong	7,642,127	1,121,412	12.80%	2,971,423	257,843	7.98%
Vaccine introduced in 2020	18-49	10	7,045,671	1,717,868	19.60%	2,829,698	399,568	12.37%

B. Impact on life expectancy

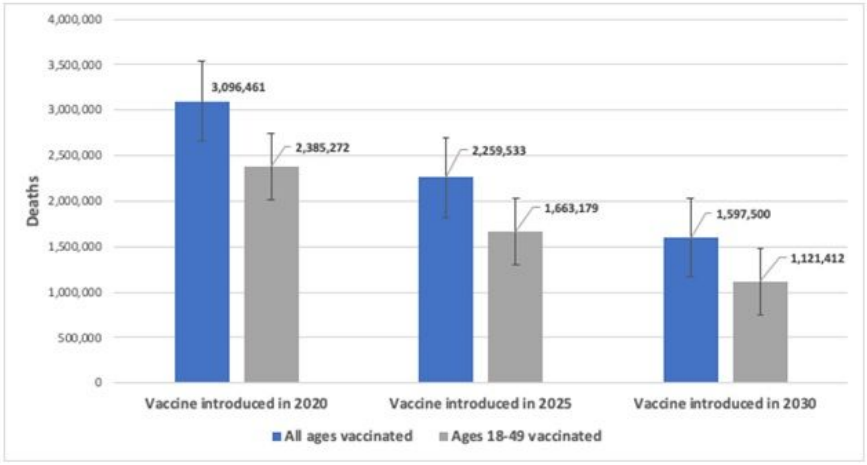
	Vaccinated Age-Group	Duration of Protection (years)	India			Indonesia		
			Life Expectancy at Birth (Mean Annual Gain)	Contribution to Life Expectancy at Birth	% Contribution to Life Expectancy at Birth	Life Expectancy at Birth (Mean Annual Gain)	Contribution to Life Expectancy at Birth	% Contribution to Life Expectancy at Birth
Counterfactual: Annual TB mortality declined as predicted by epidemiological model			*0.51*			*0.82*		
Vaccine introduced in 2020	All	lifelong	*0.33*	*0.18*	*35.29%*	*0.58*	*0.24*	*29.27%*
Vaccine introduced in 2020	18-49	lifelong	*0.37*	*0.14*	*27.45%*	*0.68*	*0.14*	*17.07%*
Vaccine introduced in 2025	All	lifelong	*0.42*	*0.09*	*17.65%*	*0.65*	*0.17*	*20.73%*
Vaccine introduced in 2025	18-49	lifelong	*0.38*	*0.13*	*25.49%*	*0.72*	*0.10*	*12.20%*
Vaccine introduced in 2030	All	lifelong	*0.42*	*0.09*	*17.65%*	*0.70*	*0.12*	*14.63%*
Vaccine introduced in 2030	18-49	lifelong	*0.45*	*0.06*	*11.76%*	*0.75*	*0.07*	*8.54%*
Vaccine introduced in 2020	18-49	10	*0.41*	*0.10*	*19.61%*	0.72	*0.10*	*12.20%*

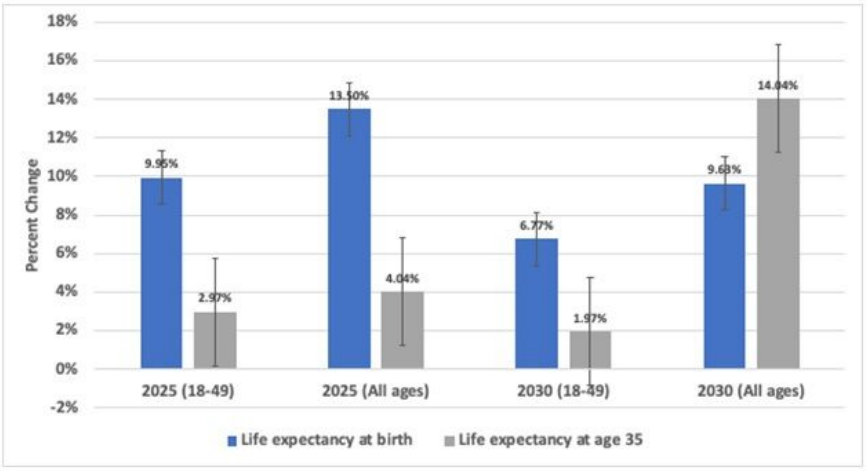
C. Impact on full-income

Scenario	Vaccinated Age-Group	Duration of Protection (years)	India			Indonesia		
			*Full-Income Losses	*Full-Income Losses Averted	Full-Income Losses Averted %	*Full-Income Losses	*Full-Income Losses Averted	Full-Income Losses Averted %
Counterfactual: Annual TB mortality declined as predicted			6,630			2,950		

by epidemiological model								
Vaccine introduced in 2020	All	lifelong	4,050	2,580	38.91%	2,040	910	30.85%
Vaccine introduced in 2020	18-49	lifelong	4,620	2,010	30.32%	2,400	550	18.64%
Vaccine introduced in 2025	All	lifelong	4,620	2,010	30.32%	2,270	680	23.05%
Vaccine introduced in 2025	18-49	lifelong	5,140	1,490	22.47%	2,570	380	12.88%
Vaccine introduced in 2030	All	lifelong	5,130	1,500	22.62%	2,460	490	16.61%
Vaccine introduced in 2030	18-49	lifelong	5,570	1,060	15.99%	2,690	260	8.81%
Vaccine introduced in 2020	18-49	10	5,210	1,420	21.42%	2,570	380	12.88%

Figures





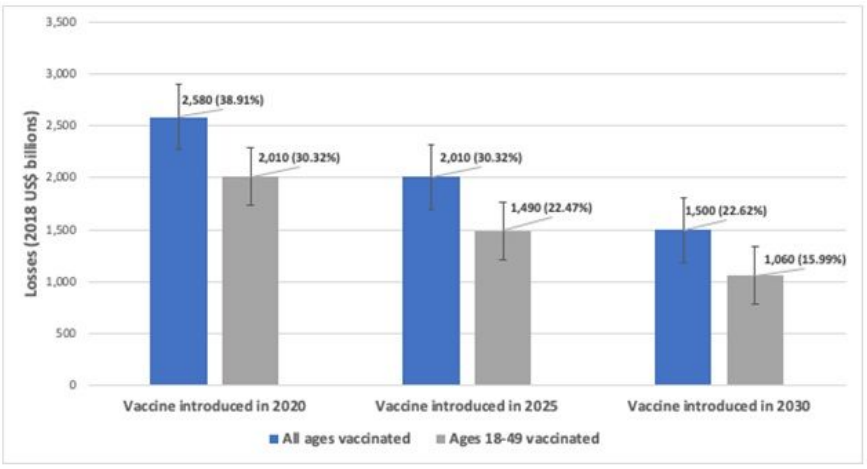
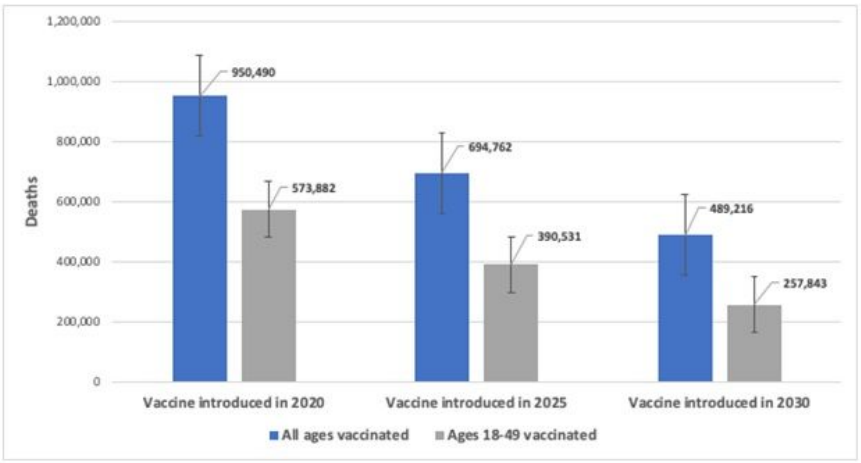
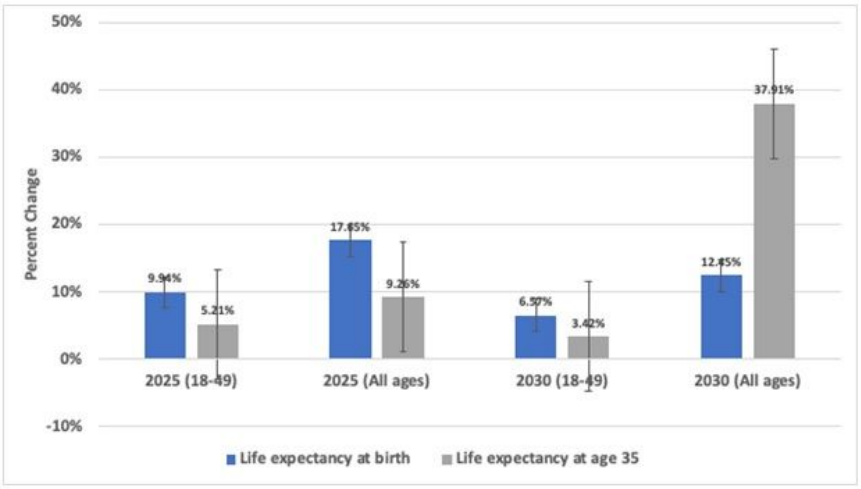


Figure 1

Impact of M72 vaccine in India between 2020-2050, on (A) TB deaths, (B) life expectancy at birth and at age 35, and (C) economic losses, by year of initiation and age of vaccination. Vaccine efficacy assumed to be 54.1% with lifetime protection. TB deaths are reported in absolute values. Life expectancy at birth and age 35 reported as mean annual losses per person. Economic losses reported in absolute values (in 2018 US$ billions).





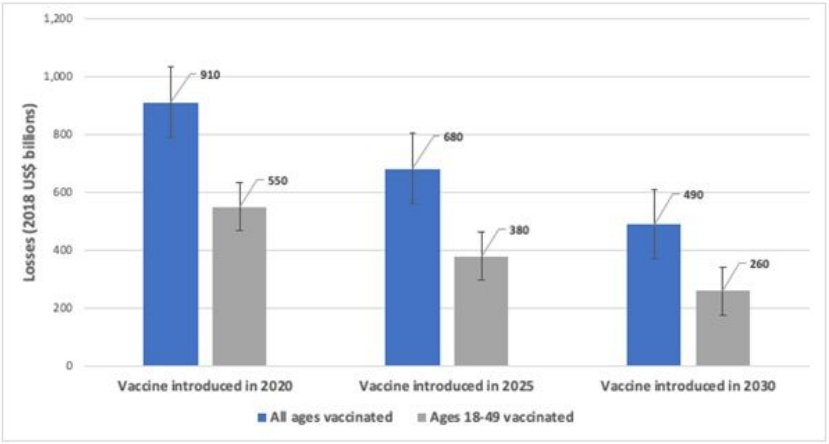
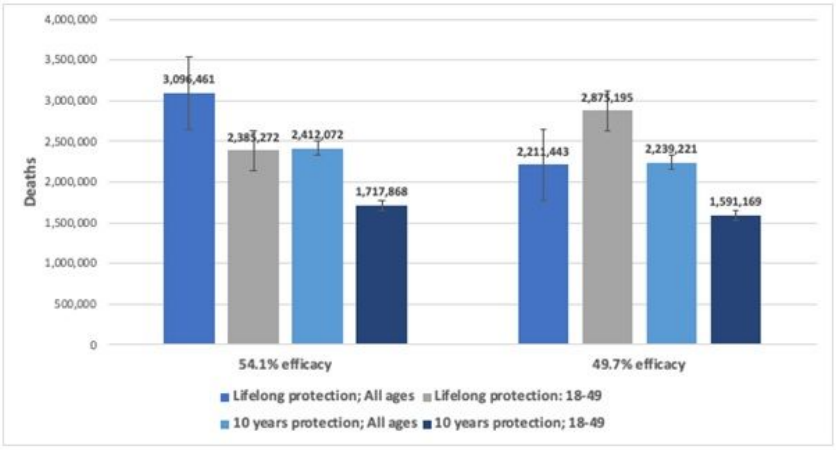
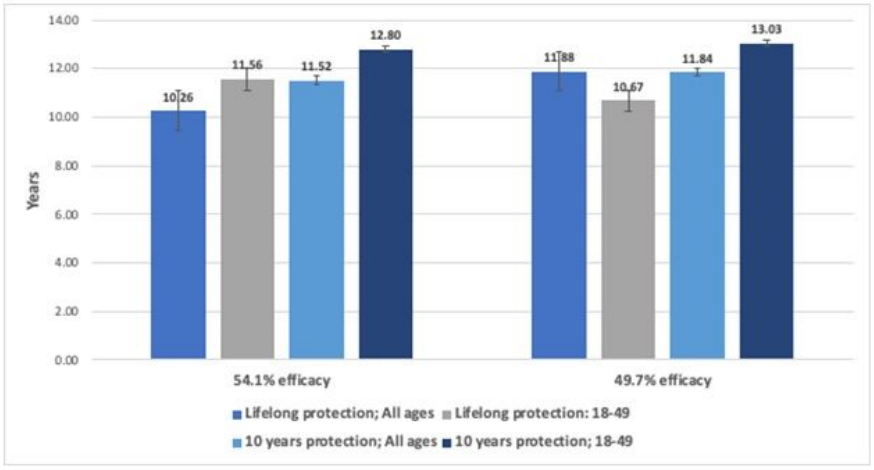


Figure 2

Impact of M72 vaccine in Indonesia between 2020-2050, on (A) TB deaths, (B) life expectancy at birth and at age 35, and (C) economic losses, by year of initiation and age of vaccination. Vaccine efficacy assumed to be 54.1% with lifetime protection. TB deaths are reported in absolute values. Life expectancy at birth and age 35 reported as mean annual losses per person. Economic losses reported in absolute values (in 2018 US$ billions).





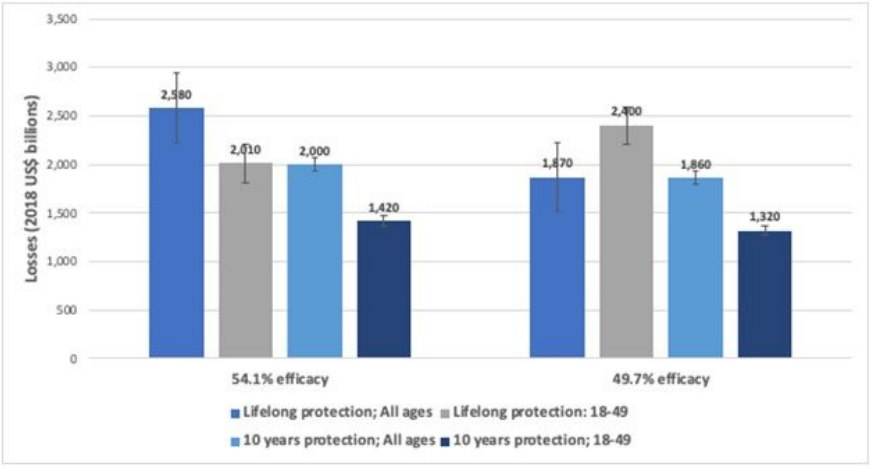


Figure 3

Impact of M72 vaccine on (A) TB deaths, (B) life expectancy at birth, and (C) economic losses in India, by vaccine efficacy, duration of protection and age of vaccination. Vaccination assumed to be initiated in 2020. TB deaths reported in absolute values. Life expectancy at birth reported as total gains in individual life expectancy at birth from 2020-2050. Economic losses reported total economic losses from 2020-2050 (in 2018 US$ billions).

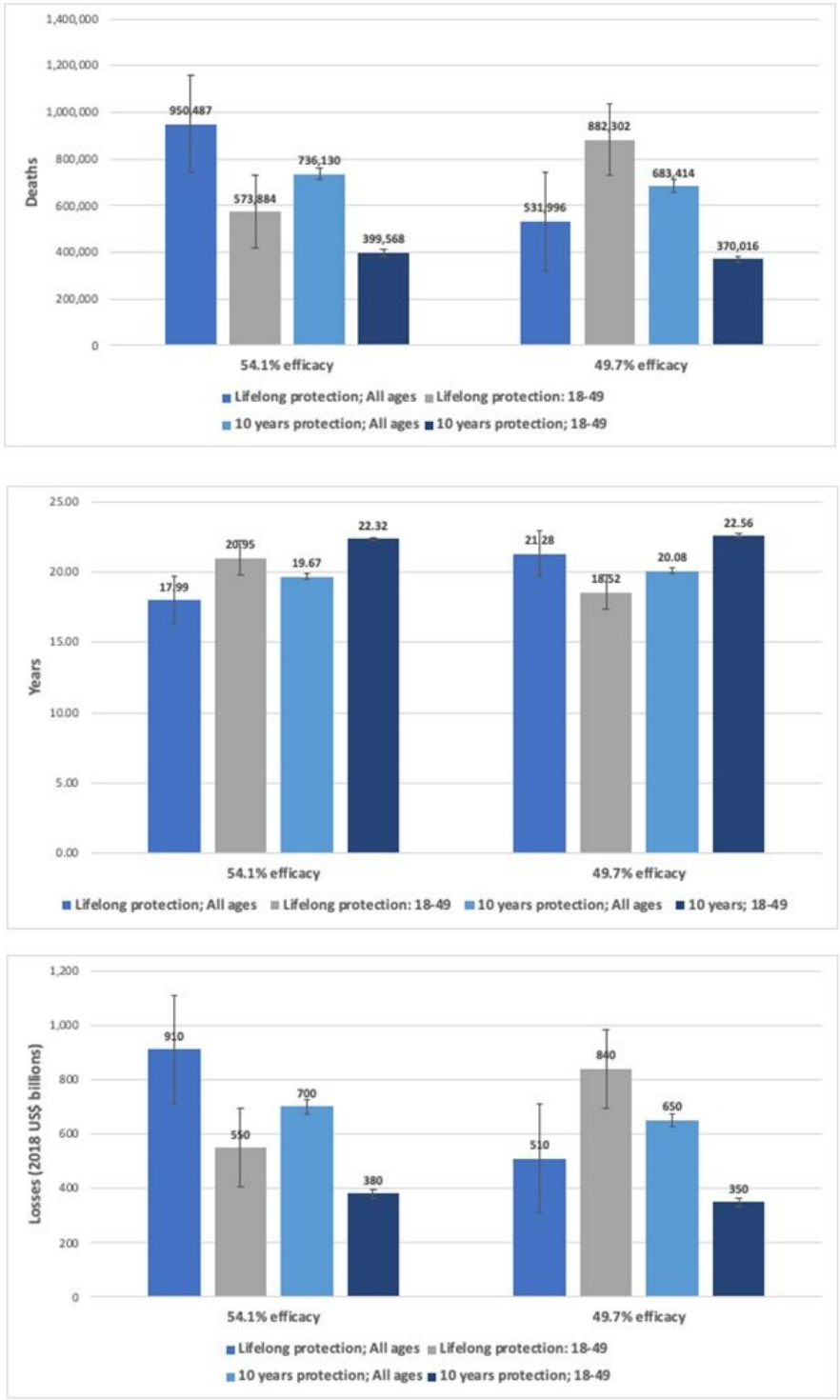


Figure 4

Impact of M72 vaccine on (A) TB deaths, (B) life expectancy at birth , and (C) economic losses in Indonesia, by vaccine efficacy, duration of protection and age of vaccination. Vaccination assumed to be initiated in 2020. TB deaths reported in absolute values. Life expectancy at birth reported as total gains in individual life expectancy at birth from 2020-2050. Economic losses reported total economic losses from 2020-2050 (in 2018 US$ billions).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SIAppendix1.docx
- SIAppendix2.docx
- SIAppendix3.xlsx