

# New Tuberculosis Vaccines: The Potential Cost and Cost-Effectiveness of M72/AS01<sub>E</sub> and BCG- revaccination in India and South Africa

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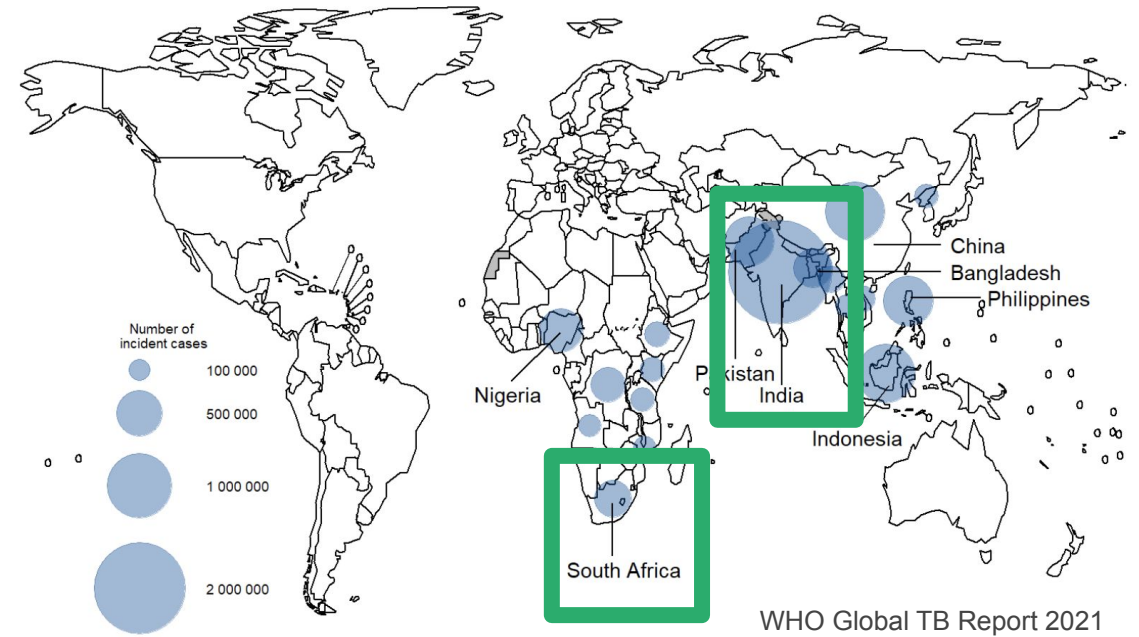
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# Background

India and South Africa accounted for 31% of TB cases and 36% of TB deaths globally in 2021

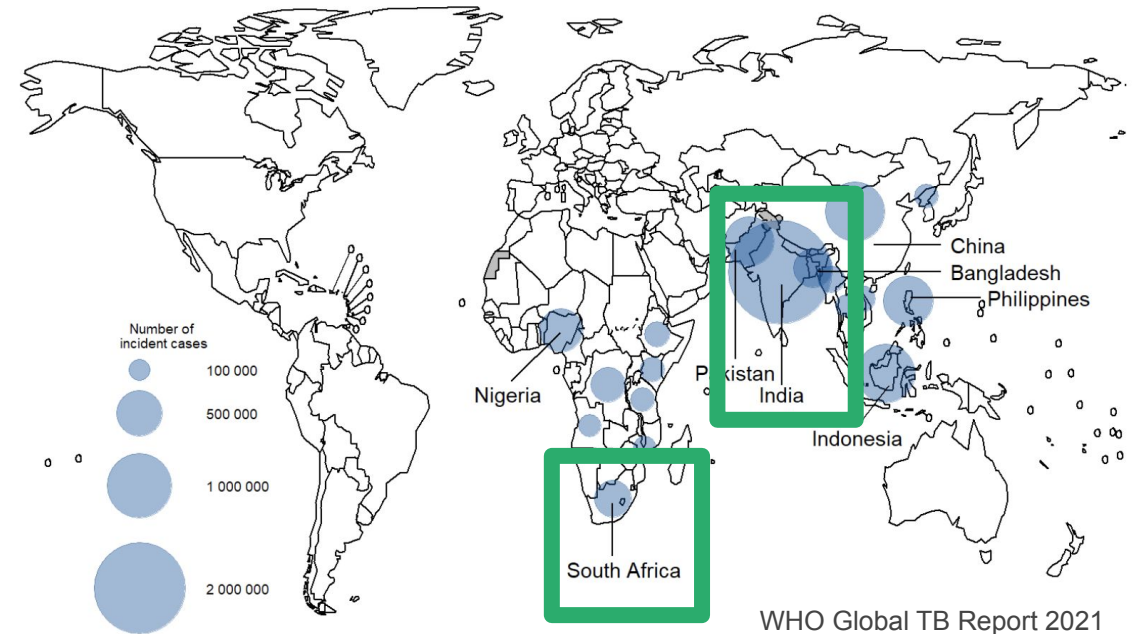


# Background

India and South Africa accounted for 31% of TB cases and 36% of TB deaths globally in 2021

Vaccines likely to be key to reaching TB elimination:

- Novel TB vaccine candidates and policy recommendations, such as M72/AS01<sub>E</sub> and BCG-revaccination, have had promising results from Phase IIb trials
- But lack of incentive to invest



# Objectives

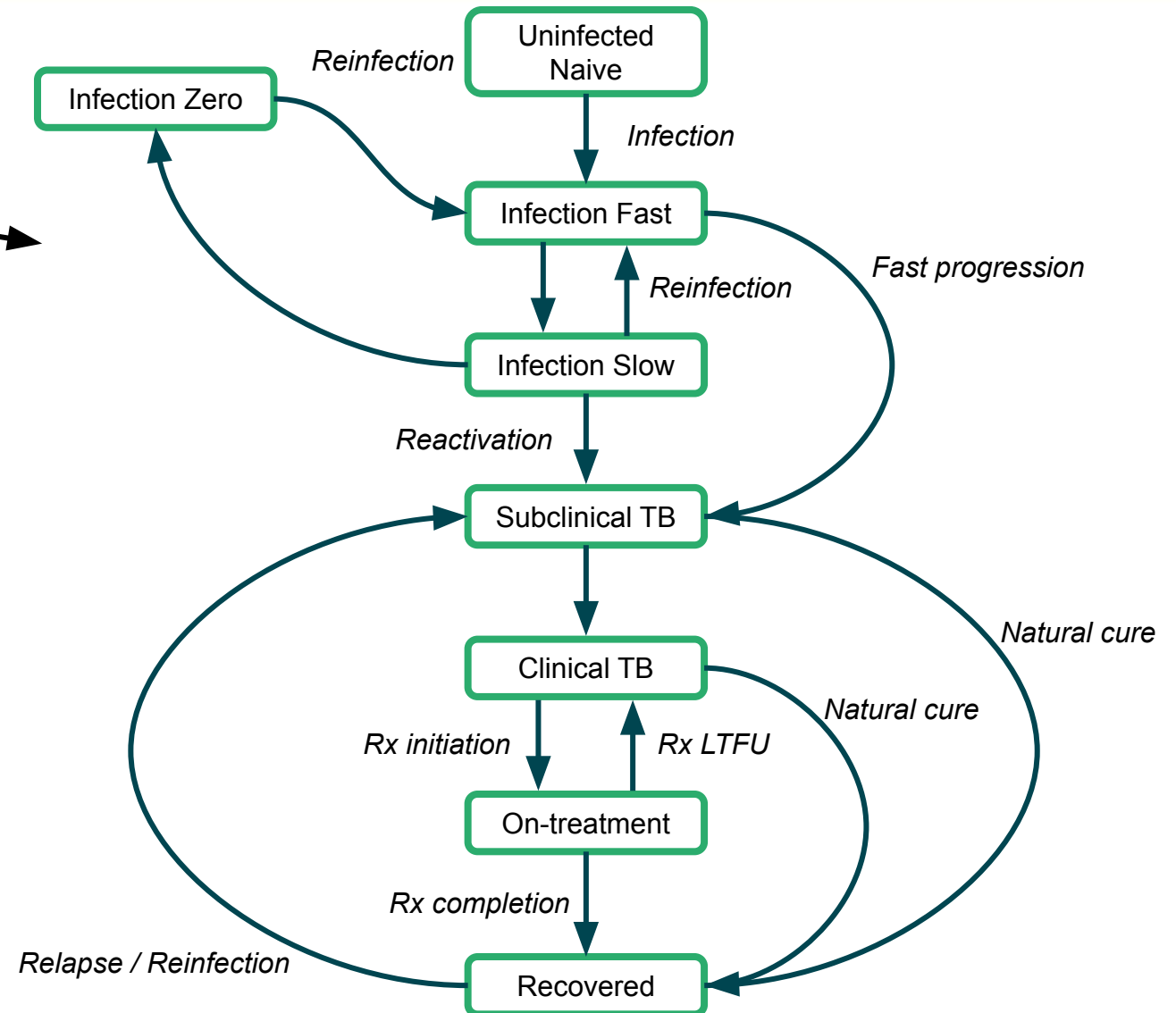
- Evaluate the impact of M72/AS01<sub>E</sub> and BCG-revaccination in India and South Africa with a mathematical modeling framework
- Estimate the cost-effectiveness of M72/AS01<sub>E</sub> and BCG-revaccination
- Vary unknowns in vaccine product characteristics to investigate differences in impact, and how the decision to introduce a vaccine into India or South Africa might change based on the realised product characteristics

# Methods: Model structure

TB natural history model structure for both India and South Africa

HIV structure included for South Africa only to allow for vaccine targeting by HIV status

Modelled single ages from 0–79, and categories for ages 80–89 and 90–99



1. Calibrated using history matching with emulation (R package: *hmer*) and ABC-MCMC until we had at least 1000 parameter sets that fit all country-specific targets
2. Used the fitted parameter sets to run the model to 2050 to simulate the trends in epidemiology in each country (the “no-new-vaccine baseline”)
3. Ran the model assuming vaccines were introduced
  - One “Basecase” vaccine scenario for each vaccine product
  - Varied vaccine characteristics univariately from the Basecase scenarios to evaluate uncertainty
4. Compared the number of TB cases, TB deaths, DALYs, and costs from running the vaccine scenarios versus the no-new-vaccine baseline

# Methods: Vaccine characteristic scenarios

Characteristic	M72/AS01 <sub>E</sub>		BCG-revaccination	
	Basecase	Varied in univariate	Basecase	Varied in univariate
<b>Vaccine efficacy</b>	50%		45%	
<b>Duration of protection</b>	10 years		10 years	
<b>Host infection status</b>	Any infection		No current infection	
<b>Mechanism of effect</b>	Prevents disease		Prevents infection	
<b>Introduction year (repeat campaigns)</b>	2030 (2040)		2025 (2035, 2045)	
<b>Achieved vaccine coverage</b>	Campaign = 70% / Routine = 80%		80%	

# Methods: Vaccine characteristic scenarios

Characteristic	M72/AS01 <sub>E</sub>		BCG-revaccination	
	Basecase	Varied in univariate	Basecase	Varied in univariate
<b>Vaccine efficacy</b>	50%	60%, 70%	45%	70%
<b>Duration of protection</b>	10 years	5, 15, 20 years	10 years	5, 15, 20 years
<b>Host infection status</b>	Any infection	Current infection	No current infection	Any infection
<b>Mechanism of effect</b>	Prevents disease	Prevents infection and disease	Prevents infection	Prevents infection and disease
<b>Introduction year (repeat campaigns)</b>	2030 (2040)	2036 (2046) [India] 2034 (2044) [SA]	2025 (2035, 2045)	2031 (2041) [India] 2029 (2039) [SA]
<b>Achieved vaccine coverage</b>	Campaign = 70% / Routine = 80%	Campaign = 50% / Routine = 70%  Campaign = 90% / Routine = 90%	80%	70%  90%

# Methods: Policy scenarios

Characteristic	M72/AS01 <sub>E</sub>		BCG-revaccination	
	Basecase	Varied in univariate	Basecase	Varied in univariate
<b>Age targeting</b>	Routine for age 15, campaign for ages 16–34		Routine for age 10, campaign for ages 11–18	

# Methods: Policy scenarios

Characteristic	M72/AS01 <sub>E</sub>		BCG-revaccination	
	Basecase	Varied in univariate	Basecase	Varied in univariate
<b>Age targeting</b>	Routine for age 15, campaign for ages 16–34	Campaign for ages 18–55  Routine for age 60, campaign for ages 61+ ( <i>India</i> )  Routine for age 10, campaign for ages 11–34 ( <i>South Africa</i> )	Routine for age 10, campaign for ages 11–18	Routine for age 15, campaign for ages 16–34  Routine for age 60, campaign for ages 61+ ( <i>India</i> )

# Methods: HIV-targeting vaccine scenarios

In South Africa, the Basecase BCG-revaccination scenario is delivered to those without HIV only as a campaign for ages 11-18 and routinely to age 10

We created scenarios where **in addition** to targeting HIV-, we added targeting to PLHIV as follows:

1. PLHIV on ART: campaign for ages 11-18
2. PLHIV on ART: campaign for ages 10+
3. PLHIV on ART and virally suppressed: campaign for ages 10+

## Delivery costs

One-time vaccine introduction costs per targeted person:

\$2.40 (\$1.20–\$4.80)

Recurrent vaccine delivery cost per person per dose:

\$2.50 (\$1.00–\$5.00)

Vaccine supply costs per person per dose:

\$0.11 (\$0.06–\$0.22)

## Vaccine price

M72/AS01<sub>E</sub>

- Price per dose: \$2.50
- Two doses per course

BCG-revaccination

- Price per dose: \$0.17
- One dose per course

# Methods: Cost-effectiveness analyses

In CEA, we present an 'efficient frontier' curve for the **Policy scenarios**

Points along the frontier represent an efficient strategy with an associated incremental cost-effectiveness ratio (ICER), defined as costs per disability-adjusted life year (DALY) averted

A strategy is considered cost-effective based on the 'willingness-to-pay' for health gains in a specified setting

- In India, the threshold ranged from US\$264–US\$1,928
- In South Africa, the threshold ranged from US\$2,480–US\$5,742

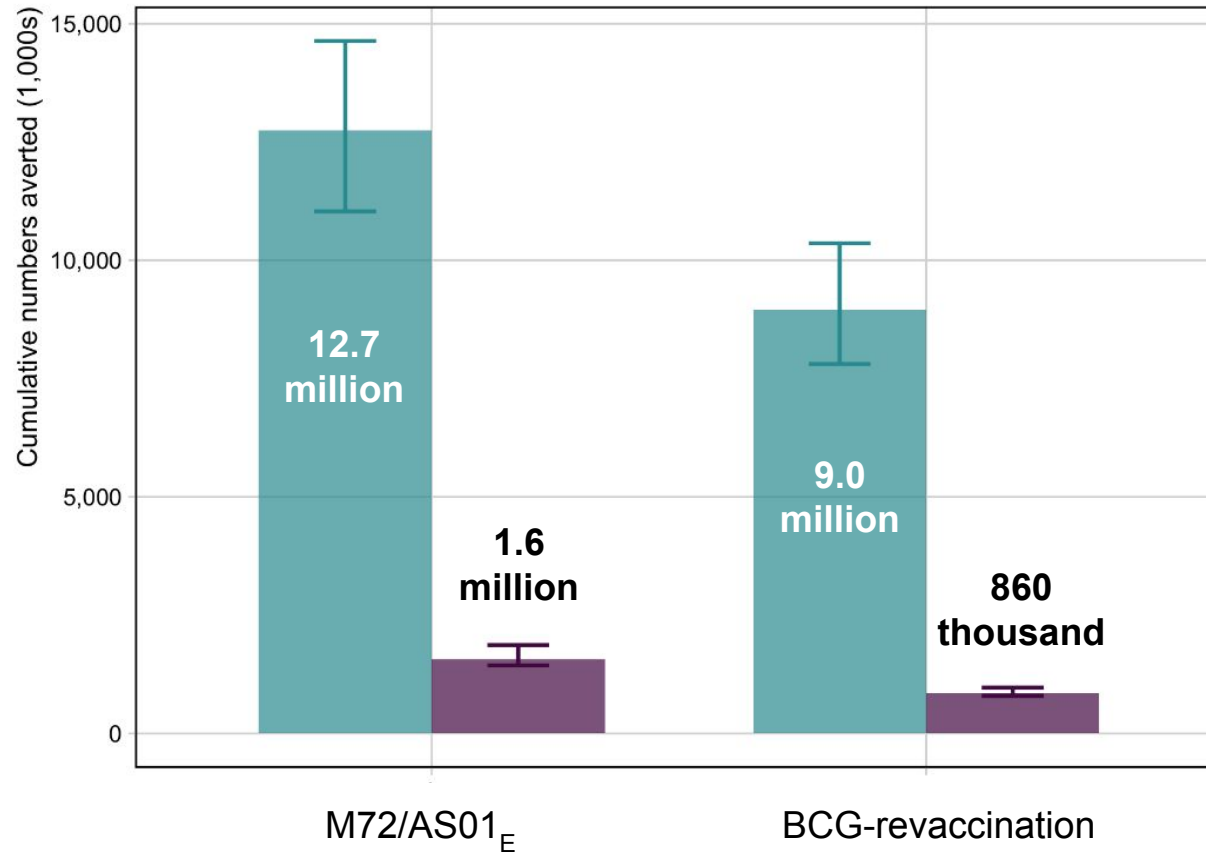
For each scenario, we estimated

- Cumulative TB cases and deaths averted between vaccine introduction and 2050
- TB costs (including cost-savings from averted cases) and vaccine costs, DALYs averted, and ICERs

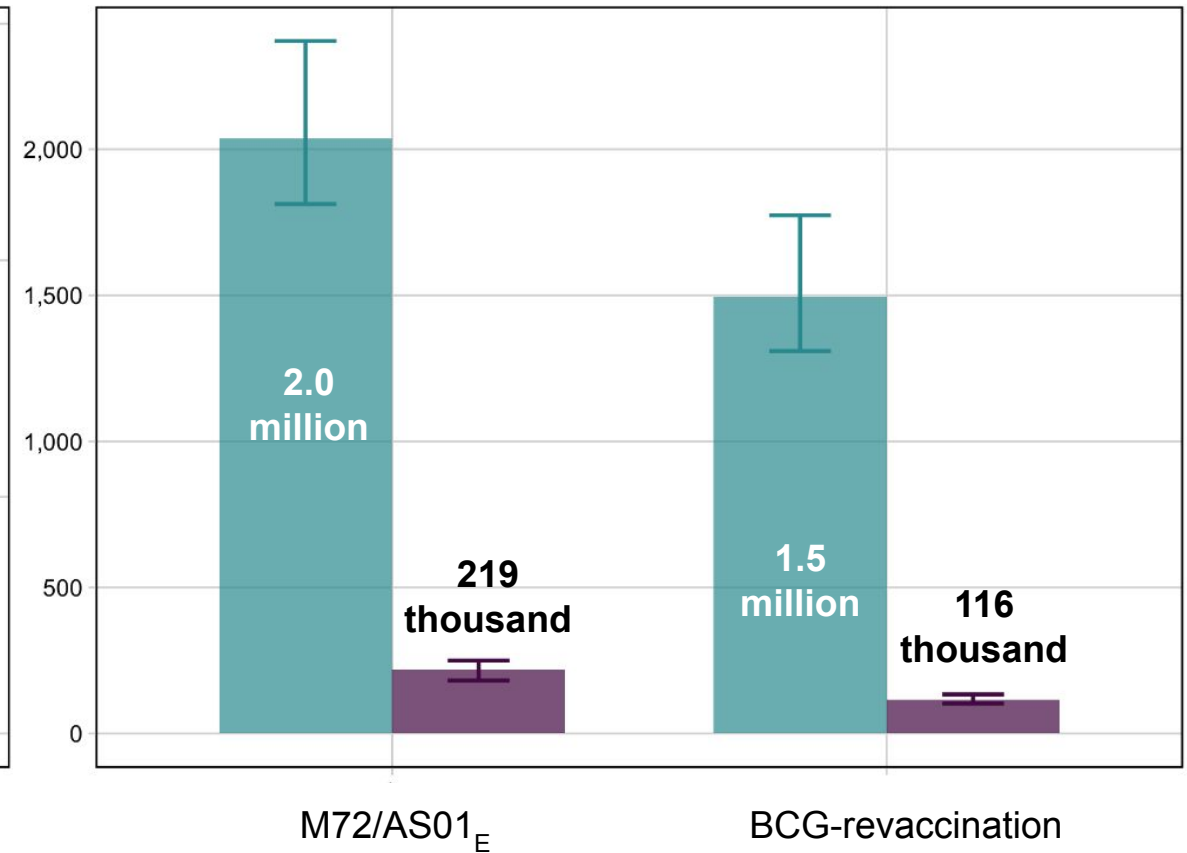
Outcomes were assessed over 2023–2050, with cost outcomes discounted at 3% per year

# Results: Health impacts

## TB Cases Averted



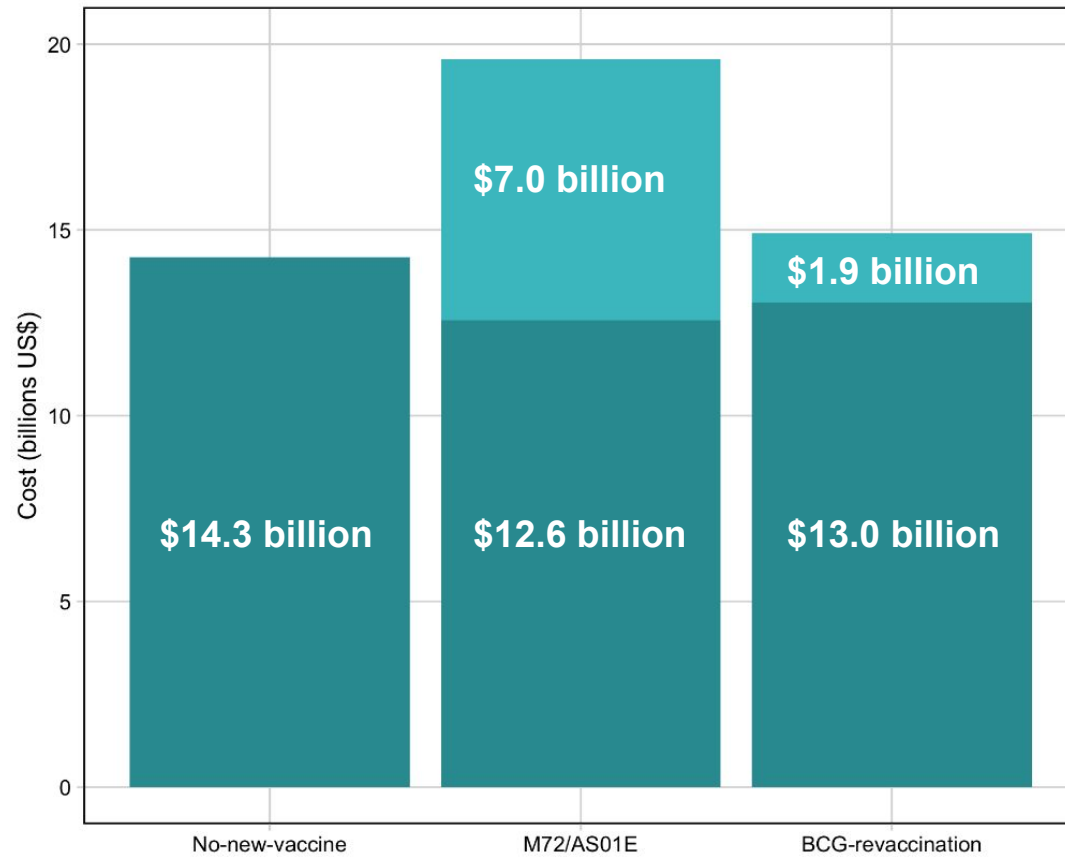
## TB Deaths Averted



Country ■ India ■ South Africa

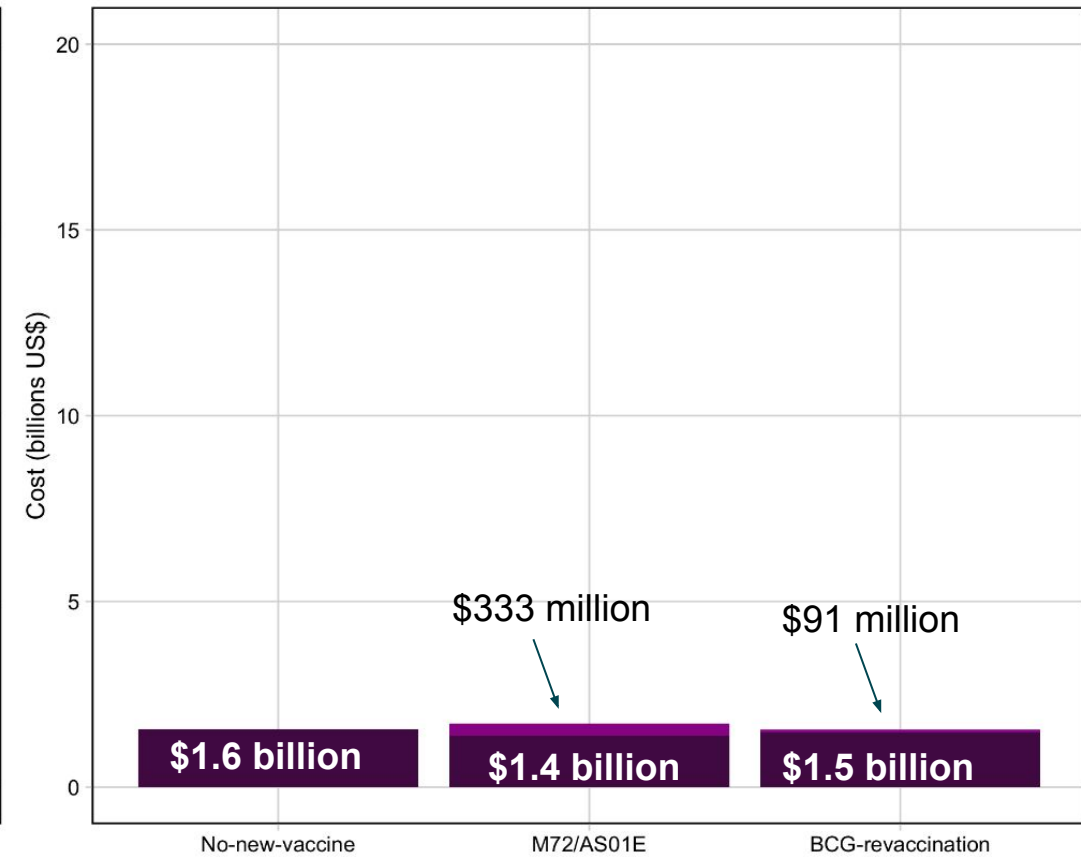
# Results: Vaccine and disease costs

## India



Type of Cost ■ Disease Cost ■ Vaccination Cost

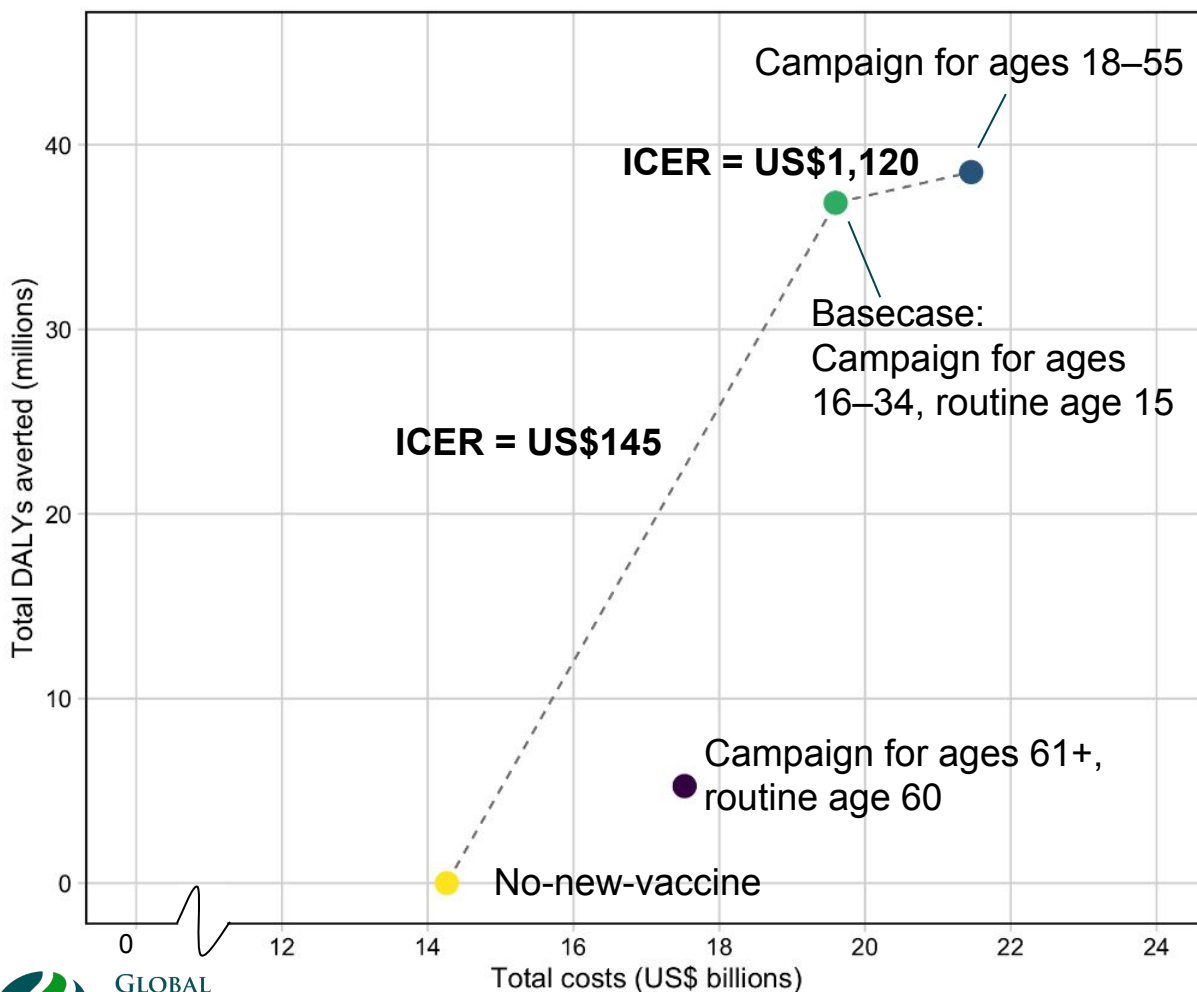
## South Africa



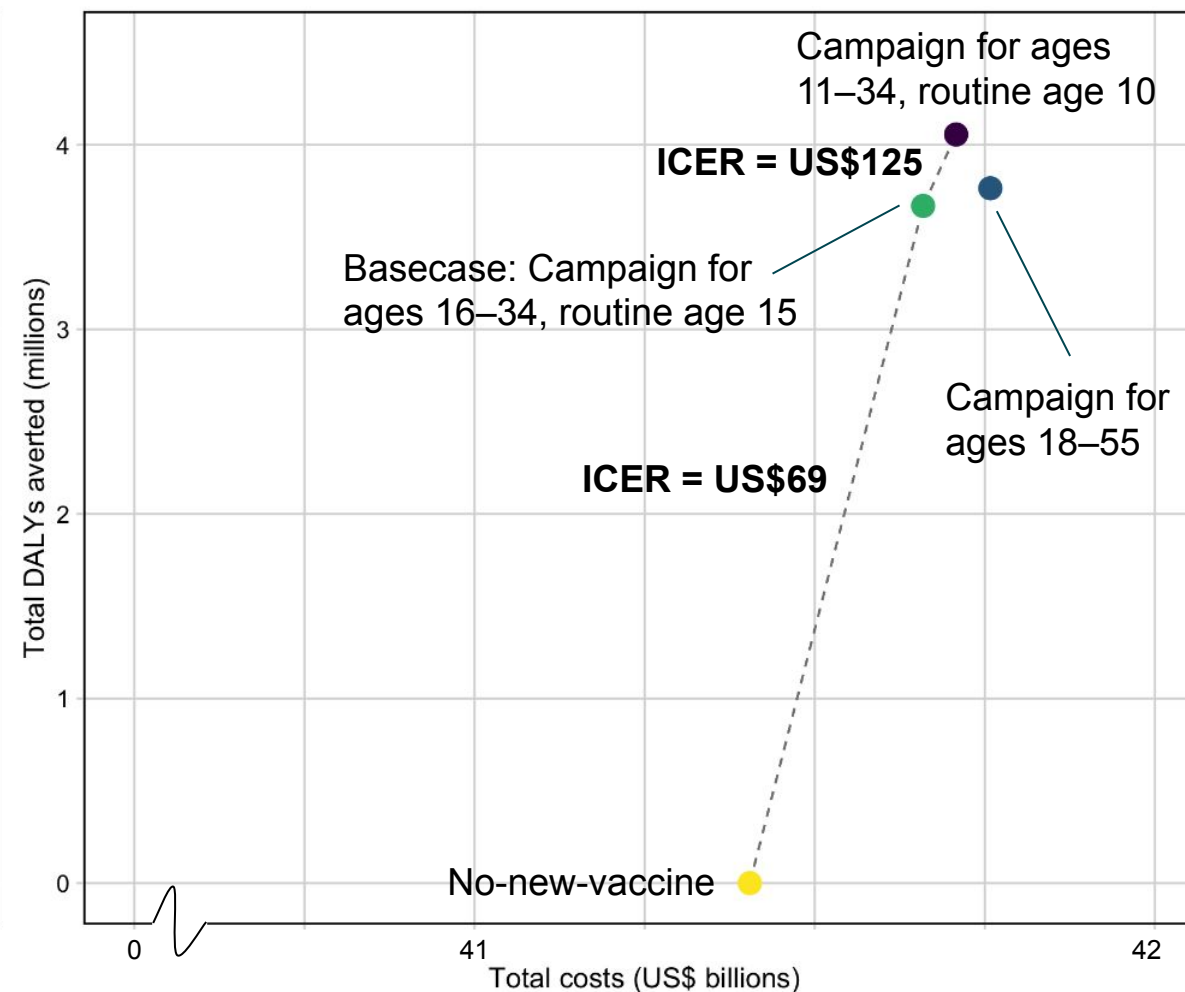
Type of Cost ■ Disease Cost ■ Vaccination Cost

# Results: Cost-effectiveness (M72/AS01<sub>E</sub>)

## India

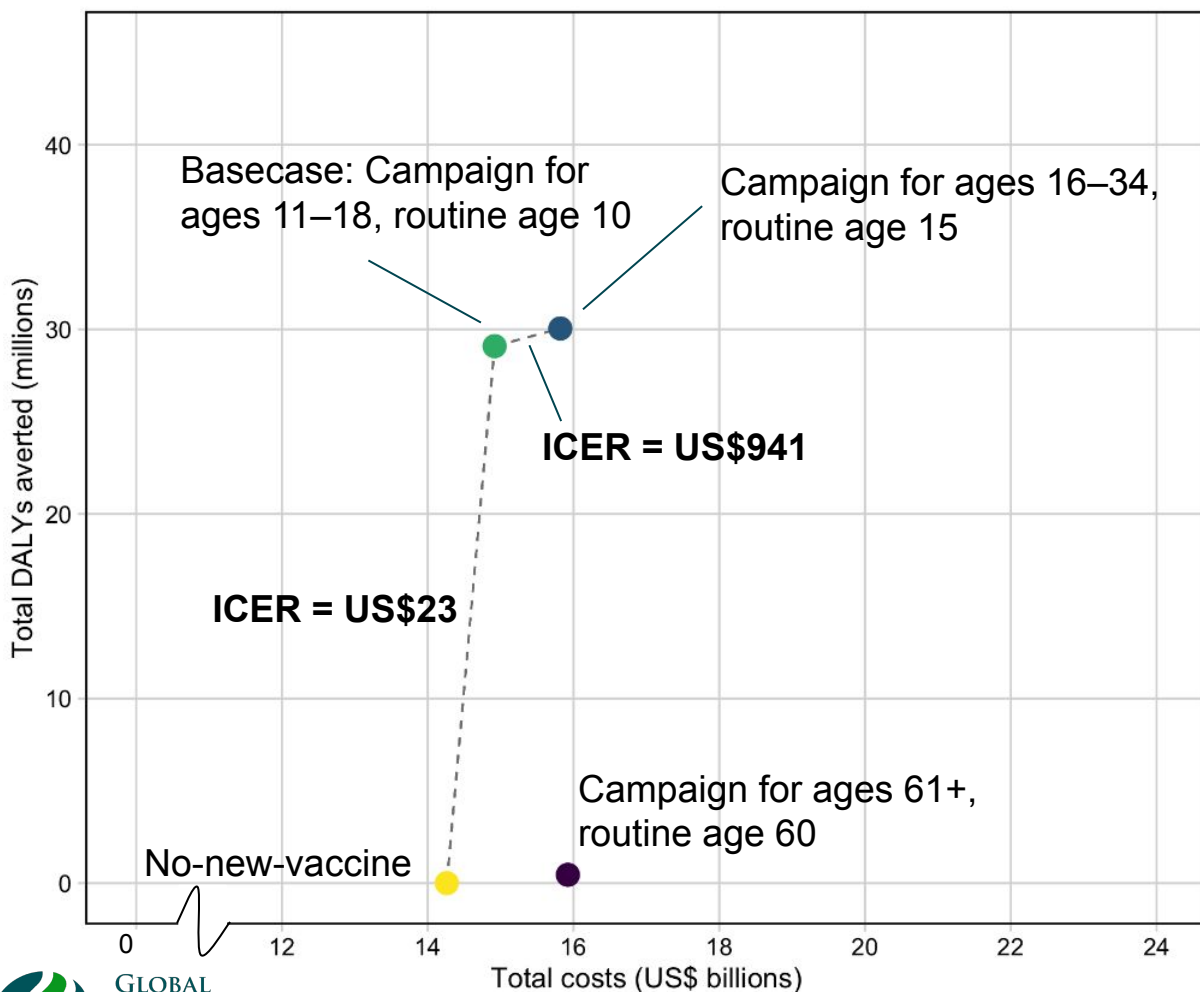


## South Africa

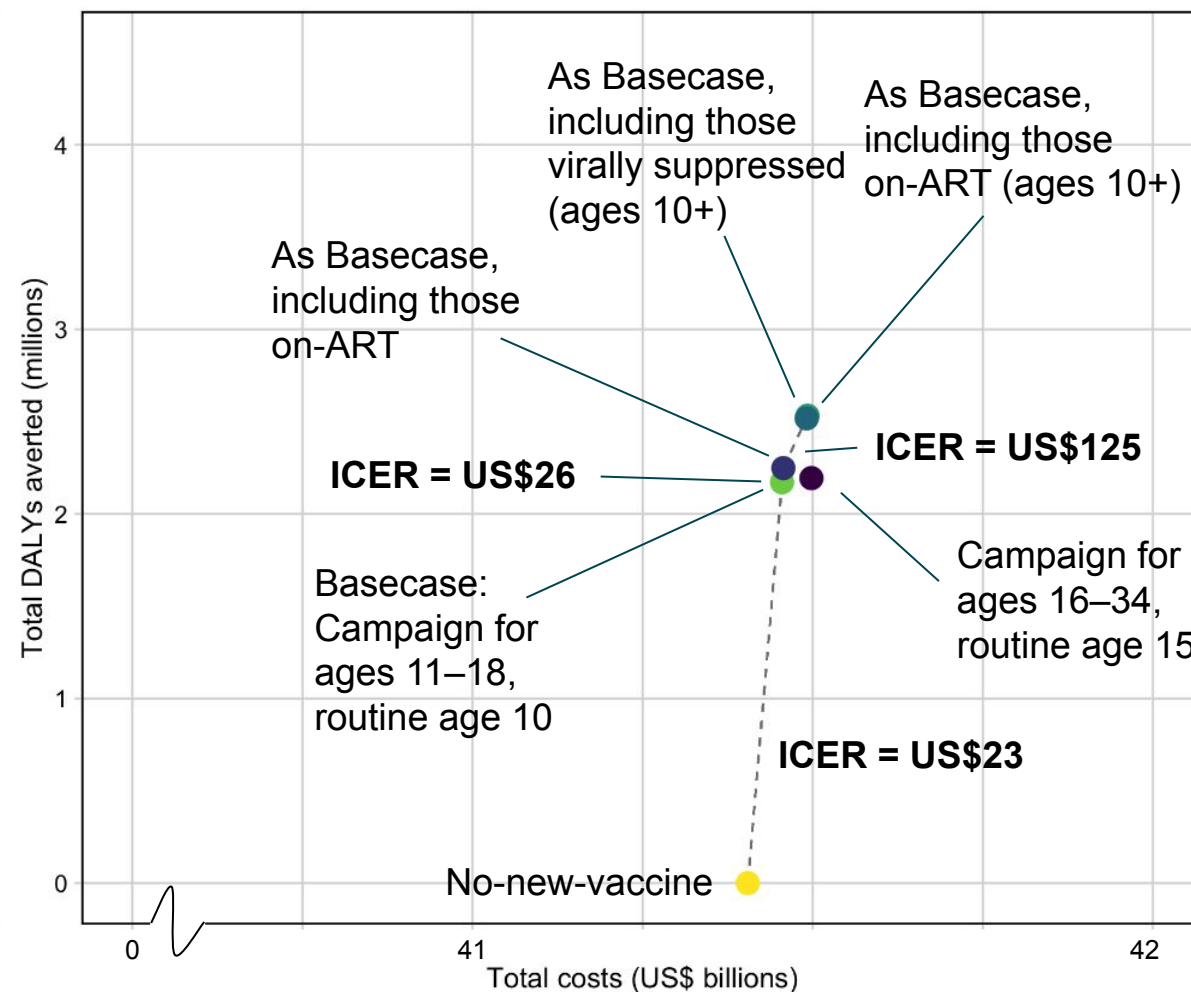


# Results: Cost-effectiveness (BCG-revaccination)

## India



## South Africa



In both India and South Africa, M72/AS01<sub>E</sub> was more expensive than BCG-revaccination (~4x more)

- Due to the higher assumed cost-per-dose (\$2.5 vs \$0.17) and requiring two doses per course

If the realised vaccine characteristics align with what we modelled, both vaccines are likely to be cost-effective in India and South Africa at the thresholds evaluated

In South Africa, including those on-ART when delivering BCG-revaccination would be cost-effective at the thresholds evaluated

# Key findings

In both countries, higher cost-effectiveness ratios for M72/AS01<sub>E</sub> compared to BCG-revaccination

→ Higher costs for M72/AS01<sub>E</sub> than BCG-revaccination

For both vaccines, higher cost-effectiveness ratios for India compared to South Africa

→ Higher TB burden in South Africa than India

Given our assumptions, introducing M72/AS01<sub>E</sub> or BCG-revaccination in India and South Africa would

- Likely have a positive health impact on the TB burden, and
- Likely be cost-effective (or even cost-saving) regardless of the resulting product characteristics at the thresholds evaluated

Results can help support country-level decision makers with forward planning for introducing vaccines

# Acknowledgements

## Contributors/Advisors:

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And many, many others...

