

# Cost-effectiveness of routine adolescent vaccination with an M72/AS01E-like tuberculosis vaccine in South Africa and India

Rebecca C Harris<sup>+</sup>, **Matthew Quaife<sup>+</sup>**, Chathika Weerasuriya, Gabriela B Gomez, Tom Sumner, Fiammetta Bozzani, Richard G White

*TB Modelling Group, Centre for Mathematical Modelling of Infectious Diseases, London School of Hygiene and Tropical Medicine*

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# Conflicts of interest

- Rebecca C Harris and Gabriela B Gomez report current employment at Sanofi Pasteur, but do not work on TB or TB vaccines in their roles.
- Matthew Quaife, Chathika Weerasuriya, Tom Sumner, Fiammetta Bozzani, and Richard G White have no conflicts of interest to declare

# Introduction

- Over the last decade tuberculosis has killed more people globally than any other single infectious pathogen
- Over 100 years being developed, bacille Calmette–Guérin (BCG) remains the only licensed vaccine against tuberculosis. BCG is good at preventing extra-pulmonary tuberculosis in children, but the majority of burden is in adolescents and adults
- The End-TB targets set ambitious goals for 2030 – progress is slow, and unlikely to be met without an effective vaccine
- In 2018, the novel vaccine candidate M72/AS01<sub>E</sub> was shown 50% (95% CI: 2-74%) efficacious in preventing pulmonary tuberculosis disease in *M.tb* infected adults aged 18-50

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- In 2018, the novel vaccine candidate M72/AS01<sub>E</sub> was shown 50% (95% CI: 2-74%) efficacious in preventing pulmonary tuberculosis disease in *M.tb* infected adults aged 18-50
- Previous work has:
  - Estimated only the epidemiological impact of vaccine candidates
    - Not cost-effectiveness
  - Estimated impact of vaccines delivered routinely to nine-year-olds, and in mass campaigns
    - Not adolescents, among whom delivery could be most cost-effective
  - Estimated impact of vaccine with post-infection efficacy only
    - Not vaccine with pre- and post-infection efficacy only

- We used a previously calibrated age-structured compartmental dynamic *M.tuberculosis* transmission model to assess the population-level impact and cost-effectiveness of a new M72/AS01<sub>E</sub>-like vaccine
- Assumed delivery during 2025-2050 to adolescents in South Africa and India.

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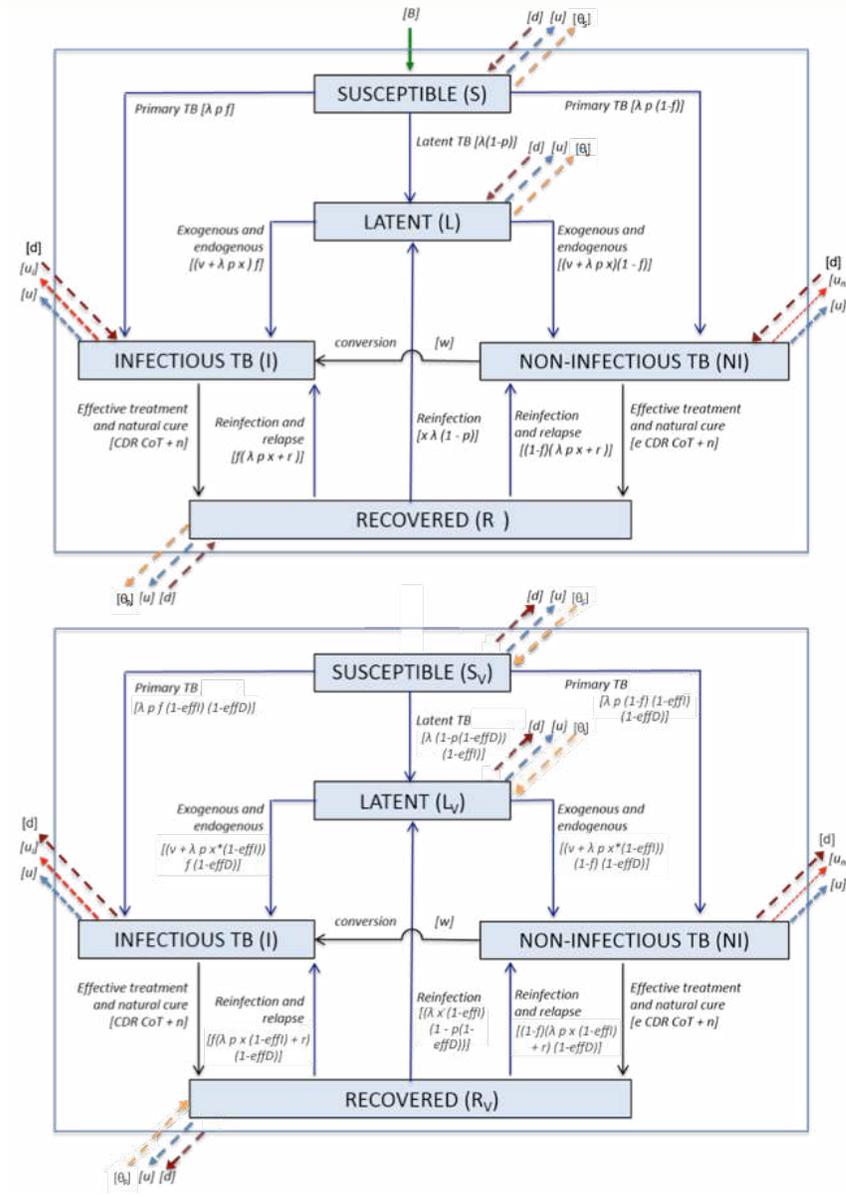
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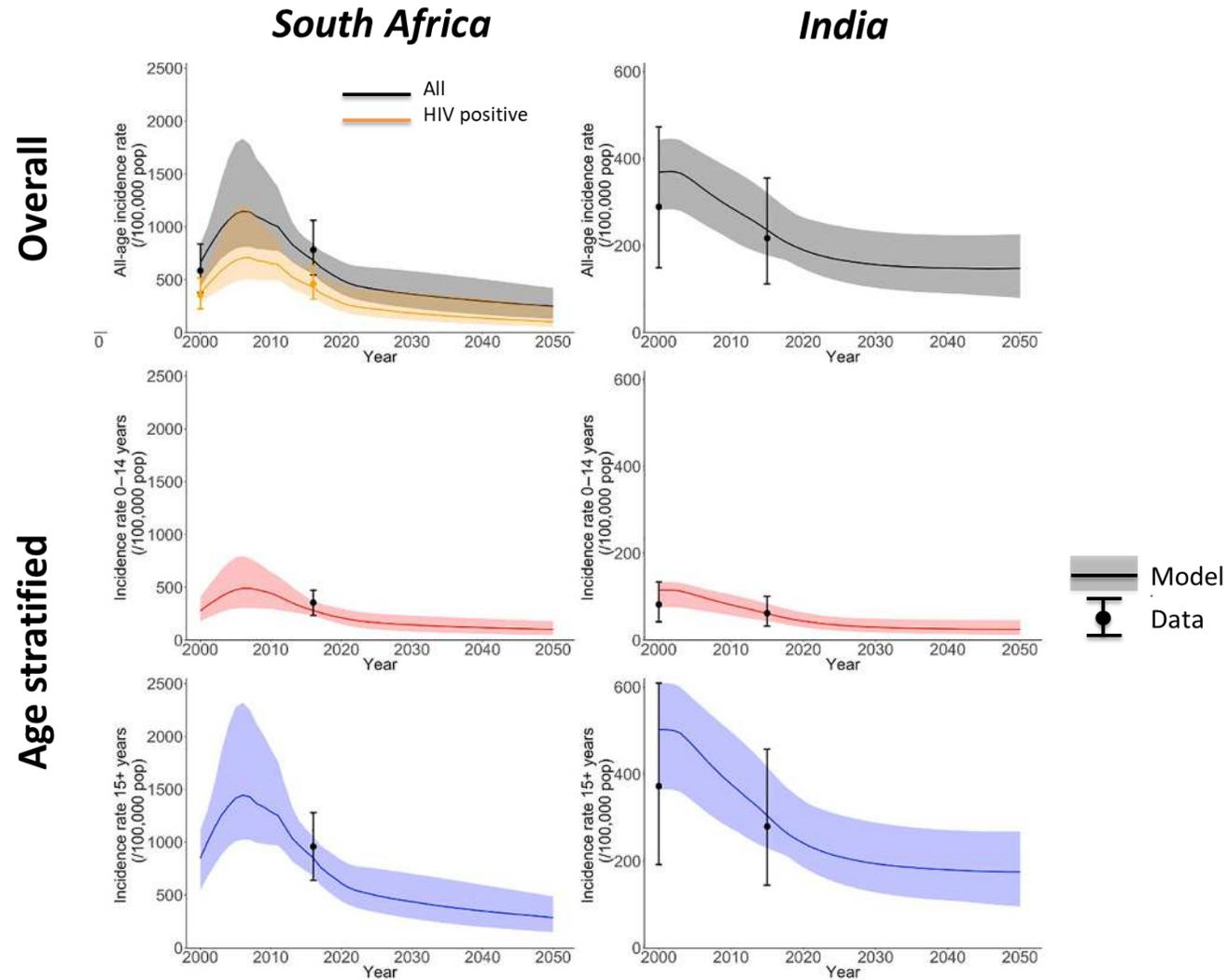
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- Assumed delivery during 2025-2050 to adolescents in South Africa and India.
- Estimated impact on mortality and morbidity, alongside health service costs of routine vaccination and health service and patient costs averted from preventing tuberculosis disease.
- Assessed cost-effectiveness using country-specific cost-effectiveness thresholds (Ochalek et al.)
- We simulated three scenarios of routine adolescent vaccination, assuming:
  - a coverage of 80% is reached among 10-year-olds and 15-year-olds,
  - a lower coverage of 50% is reached among 18-year-olds, to reflect potential difficulties in reaching older adolescents in vaccination campaigns.

# Methods – transmission model

- Age-structured compartmental dynamic M.tb transmission model
- Accounted for differential treatment initiation & success in the private sector in India & impact of HIV co-infection in SA
- Calibrated to age- and HIV-stratified country-level TB prevalence, incidence, mortality and notifications data for South Africa and India

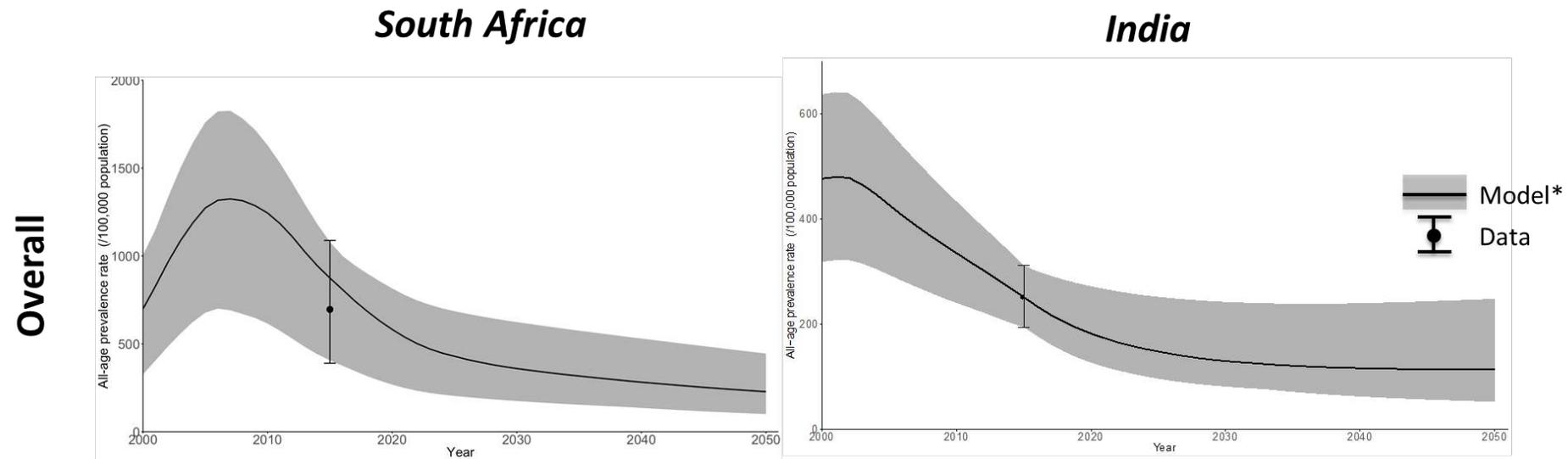


# Methods – transmission model



**Incidence rate projection from calibrated models.** Incidence rates shown over time for South Africa and India. Median (line) and ranges (shaded area) summarise 1000 calibrated parameter sets for each country. NB. Axes differ to aid visualisation.

# Methods – transmission model



**TB prevalence projection from calibrated models.** Incidence rates shown over time for South Africa and India. Median (line) and ranges (shaded area) summarise 1000 calibrated parameter sets for each country. NB.. Axes differ to aid visualisation.

- Ingredients-based approach estimating the net cumulative costs of routine vaccination from a health service perspective, including vaccination costs incurred and tuberculosis services costs averted.
  - Societal perspective: Additional analysis included patient-incurred costs of tuberculosis treatment. Adolescent patient cost data were not available, so we
    - assumed that patient-incurred direct medical and non-medical costs were the same as those faced by adults
    - omit indirect costs which could feasibly differ among adolescents, in particular income losses

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    - assumed that patient-incurred direct medical and non-medical costs were the same as those faced by adult
    - omit indirect costs which could feasibly differ among adolescents, in particular income losses.
- Given the close relationship between HIV and tuberculosis epidemics in South Africa, we also estimated additional costs of HIV treatment as a result of increased life-expectancy due to reduced tuberculosis mortality. In the South Africa epidemiological model, we assume that antiretroviral therapy scale-up is consistent with UNAIDS 90-90-90 targets.
- Vaccine purchasing and delivery costs were unknown, so were drawn from a distribution of  $\text{Gamma}(6,0.83)$  - equating to a central estimate of \$5 per person, based on information provided by potential funders.

# Methods – economic evaluation

- Estimated the cumulative number of disability-adjusted life years (DALYs) incurred by tuberculosis disease using DALY weights and accounting for HIV co-infection.
- MDR-tuberculosis modelled as a constant proportion of all tuberculosis: 6.2% in India and 4.6% in South Africa. We assume rifampicin-resistant tuberculosis received MDR regimens as it is generally treated with the same drugs for the same duration as MDR-tuberculosis, including in South Africa.
- We assume no changes to other prevention and control measures over the future time horizon modelled.

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- We assume no changes to other prevention and control measures over the future time horizon modelled.
  
- Ran probabilistic sensitivity analysis with 1000 draws to explore the impact of epidemiological and economic parameter uncertainty on results
- Costs and DALYs were discounted by 3% per year as standard.
- Cost-effectiveness assessed relative to lower-bound supply-side country-specific cost-effectiveness thresholds - \$264/DALY averted in India and \$2 480/DALY averted in South Africa (Ochalek et al.)

# Methods – vaccine assumptions



	<b>Scenario 1</b>	<b>Scenario 2</b>	<b>Scenario 3</b>
Efficacy by infection status	Pre and post infection	Pre and post infection	Pre and post infection
Vaccination age	10 years	15 years	18 years
Coverage	80%	80%	50%

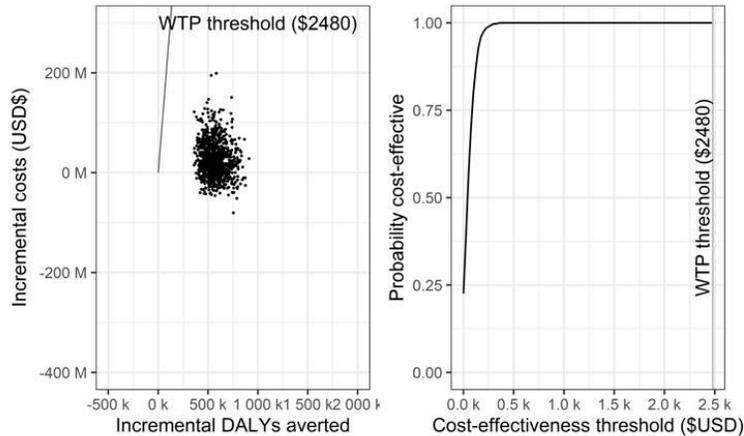
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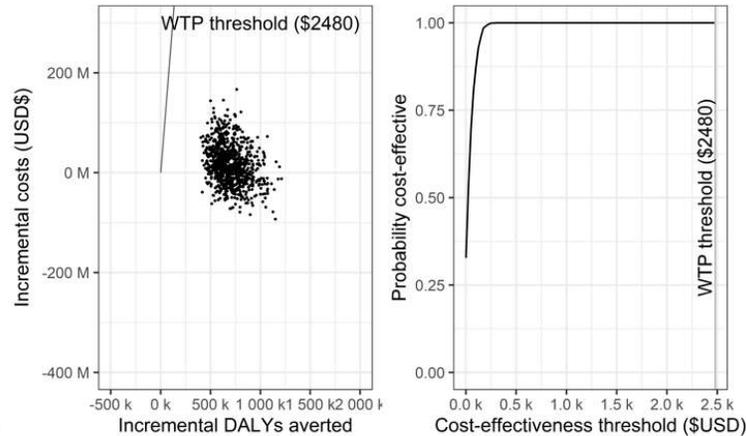
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	<b>Scenario 4</b>	<b>Scenario 5</b>	<b>Scenario 6</b>
	Post infection only	Post infection only	Post infection only
	10 years	15 years	18 years
	80%	80%	50%

# Results – South Africa

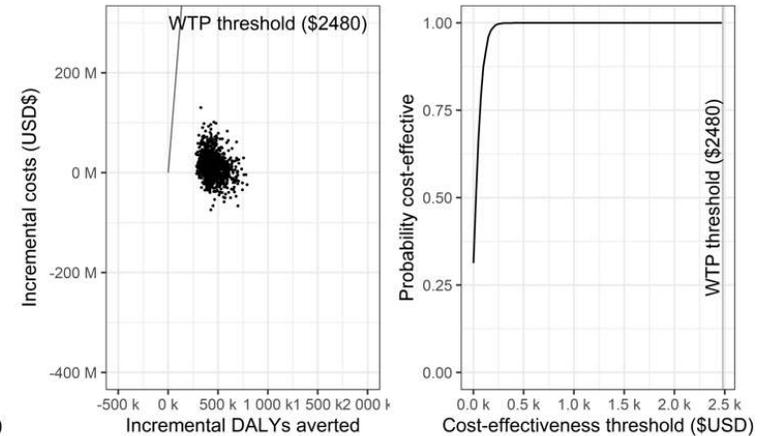
1 - P&PI, 10 year-olds, 80% coverage



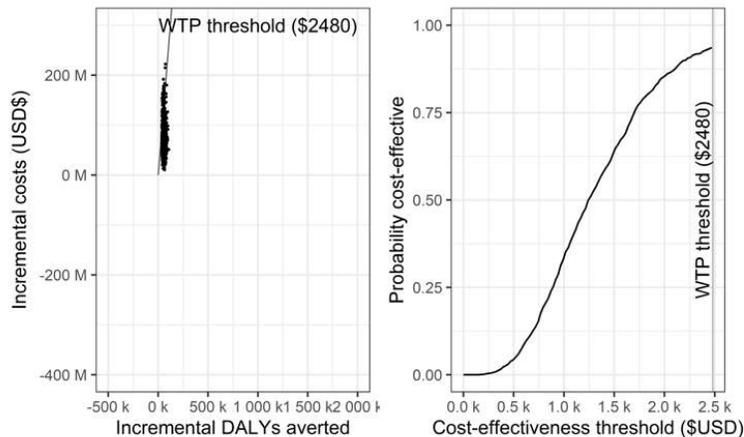
2 - P&PI, 15 year-olds, 80% coverage



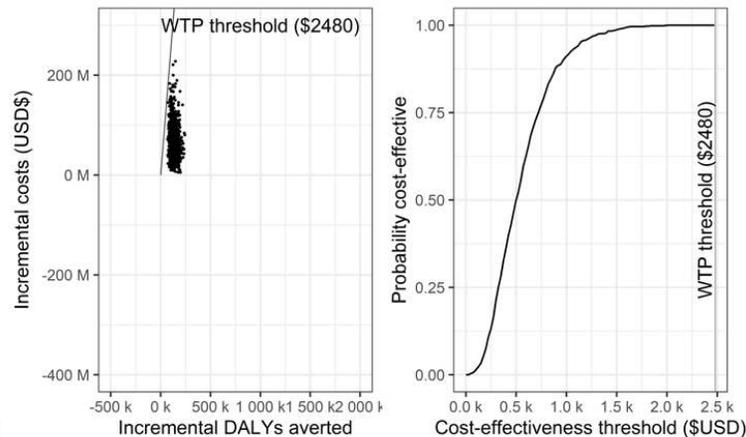
3 - P&PI, 18 year-olds, 50% coverage



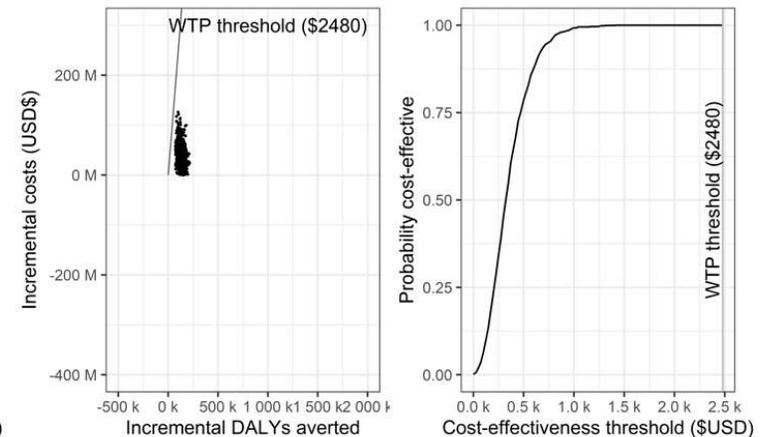
4 - PI, 10 year-olds, 80% coverage



5 - PI, 15 year-olds, 80% coverage



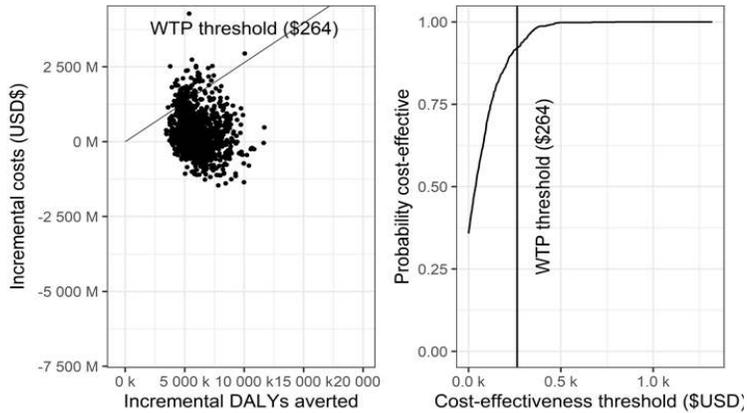
6 - PI, 18 year-olds, 50% coverage



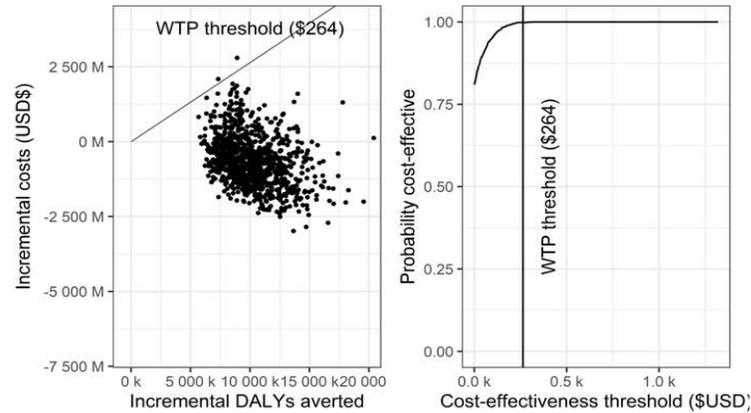
- Any routine vaccination scenario with either vaccine type would be highly cost-effective from the health system perspective
  - 94-100% probability of being cost-effective across scenarios modelled

# Results – India

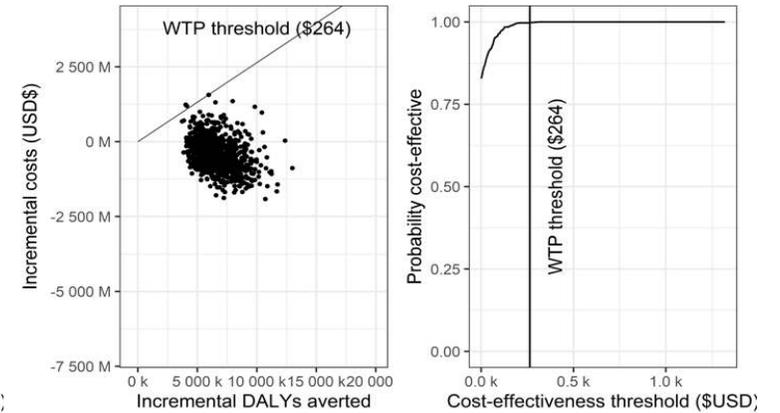
1 - P&PI, 10 year-olds, 80% coverage



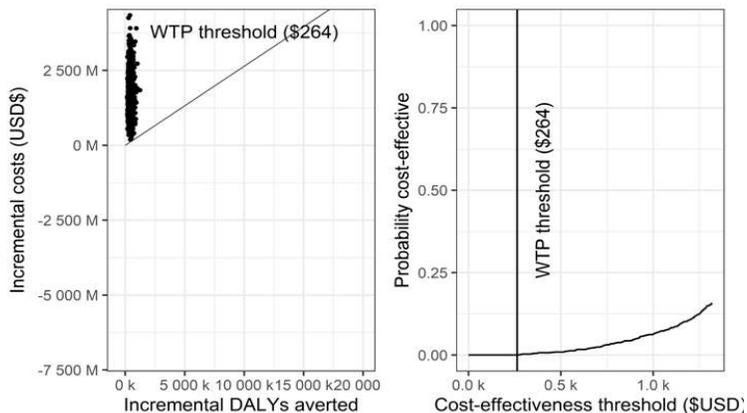
2 - P&PI, 15 year-olds, 80% coverage



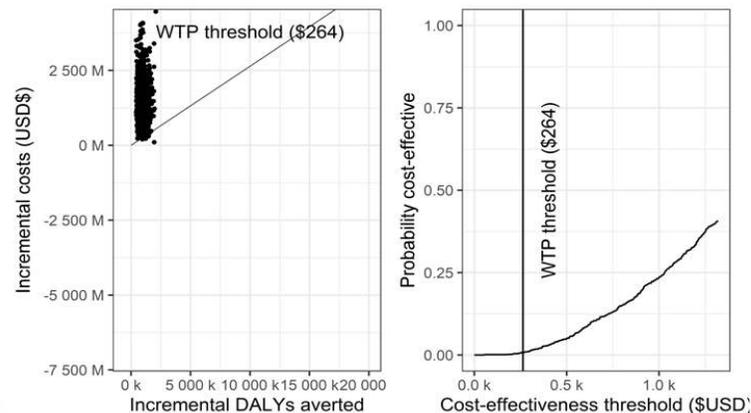
3 - P&PI, 18 year-olds, 50% coverage



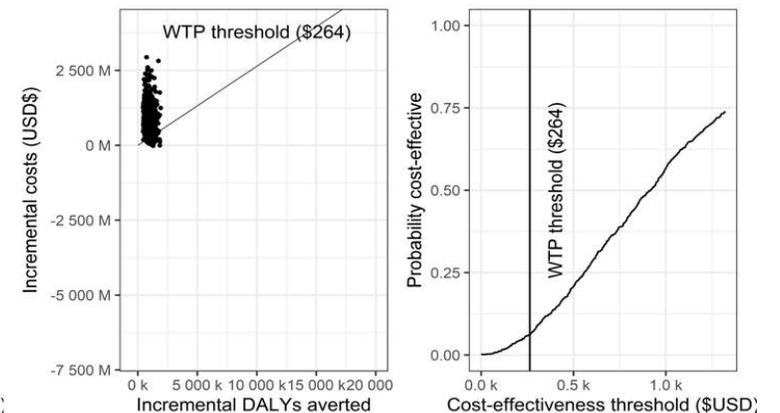
4 - PI, 10 year-olds, 80% coverage



5 - PI, 15 year-olds, 80% coverage



6 - PI, 18 year-olds, 50% coverage



- Routine vaccination with pre- and post-infection efficacy (top row) likely to be cost-effective from the health system perspective (92-100% probability of cost-effectiveness)
- Unlikely a vaccine with post-infection efficacy (bottom row) only will be cost-effective (0-6% probability of cost-effectiveness)

# Results – by vaccination type

- A vaccine with pre- and post-vaccination efficacy had a much greater impact on 2050 incidence rate than a vaccine with post-infection efficacy only.
- Depending on the vaccination scenario modelled, a pre- and post-infection vaccine had between a nine- and 23-fold greater impact on incidence rate than post-infection only in India, and between five- and 13-fold greater impact in South Africa.
- Similarly, a vaccine with pre- and post-infection efficacy averted between seven and 15-times more DALYs than a post-infection vaccine only in India, and between four and ten times more DALYs in South Africa.
- The greatest difference in impact between vaccines of different efficacy types was in the scenarios vaccinating 10-year-olds
- **Societal perspective** – all scenarios became more cost-effective, though cost-ineffective scenarios did not become substantially better value

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# (Some) Limitations

- As in any model-based analysis of technologies in development, we make assumptions about vaccine characteristics and implementation.
  - Time horizon (26 years), MDR constant, ART scale-up assumptions in South Africa, duration of protection offered by the M72/AS01E vaccine (15 years).
- Detailed routine vaccine implementation not modelled – likely omitting dynamics which could improve or lessen the cost-effectiveness of M72/AS01E introduction. E.g. health service capacity to absorb a new campaign, non-financial constraints.
- Assume no changes to other TB prevention and control measures over the period modelled.
- **Societal perspective:** Direct costs to patients (i.e. omitting earning losses) collected among adult TB patients are the same among adolescents.

# Summary

- This is the first cost-effectiveness analysis to use M72/AS01<sub>E</sub> efficacy data to explore routine adolescent vaccination.
- We estimate that routine adolescent vaccination with a M72/AS01<sub>E</sub>-like vaccine would be cost-effective in South Africa, and would be cost-effective and potentially cost-saving in India if it provided efficacy pre- and post-infection.
- We also find that, in both settings, vaccinating fewer 18-year-olds (50%) through routine vaccination is as cost-effective as vaccinating 80% of 15-year-olds.
- These findings are important to inform decisions of where and how phase III trials of vaccines could be best conducted to maximise value, and how vaccines could be implemented most efficiently.

# Implications

- Strengthens the case for continued investment in M72/AS01E development
- Clear need to include adolescent populations in clinical trials of tuberculosis vaccines
- Also need to include pre- and post-infection participants in trials, to assess vaccine efficacy in these groups
- Vaccinating fewer 18-year-olds (50%) through routine vaccination is as cost-effective as vaccinating 80% of 15-year-olds
  - More or less feasible?
- For adolescent vaccination in India, important to understand if and how much M72/AS01E provides efficacy in pre-infection populations

# Acknowledgements and conflicts of interest

- We are grateful to the Bill and Melinda Gates foundation for funding this work

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Questions?

[Link to publication](#)