Using the FVVA framework to estimate the potential health and economic impacts of novel TB vaccines in low- and middle-income countries

Richard White, Nick Menzies, Rebecca Clark, Allison Portnoy, and many, many others
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LONDON SCHOOL of HYGIENE &TROPICAL MEDICINE

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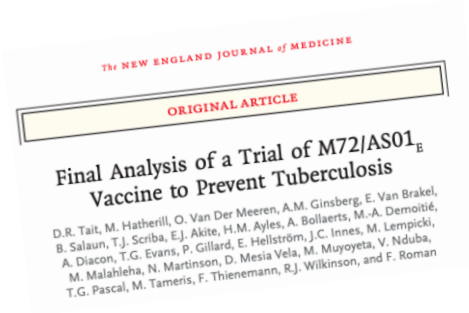
Background

Tuberculosis (TB) is a serious global health issue:

- Causes significant morbidity and mortality
- Leading cause of death in 2019 from a single infectious agent
- Burden is highest in low- and middle-income countries (LMICs)

Promising vaccine candidates in late stage trials:

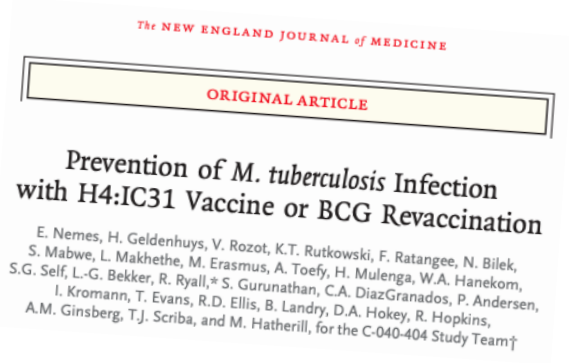
- Will be key to reaching elimination goals
- But development expensive and long
- Lack of market incentives to invest


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Final Analysis of a Trial of M72/AS01$_E$ Vaccine to Prevent Tuberculosis

D.R. Tait, M. Hatherill, O. Van Der Meeren, A.M. Ginsberg, E. Van Brakel, B. Salaun, T.J. Scriba, E.J. Akite, H.M. Ayles, A. Bollaerts, M.-A. Demoitié, A. Diacon, T.G. Evans, P. Gillard, E. Hellström, J.C. Innes, M. Lempicki, M. Malahleha, N. Martinson, D. Mesia Vela, M. Muyoyeta, V. Nduba, T.G. Pascal, M. Tameris, F. Thienemann, R.J. Wilkinson, and F. Roman


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Prevention of *M. tuberculosis* Infection with H4:IC31 Vaccine or BCG Revaccination

E. Nemes, H. Geldenhuys, V. Rozot, K.T. Rutkowski, F. Ratangee, N. Bilek, S. Mabwe, L. Makhethe, M. Erasmus, A. Toefy, H. Mulenga, W.A. Hanekom, S.G. Self, L.-G. Bekker, R. Ryall,* S. Gurunathan, C.A. DiazGranados, P. Andersen, I. Kromann, T. Evans, R.D. Ellis, B. Landry, D.A. Hokey, R. Hopkins, A.M. Ginsberg, T.J. Scriba, and M. Hatherill, for the C-040-404 Study Team†

Objectives: Estimate the potential health impact in LMICs of vaccines meeting the technical specifications of the WHO Preferred Product Characteristics for New Tuberculosis Vaccines,

using the FVVA framework

Full Value of Vaccines Assessment Framework

	Health		Non-health (Societal/Economic)	
	Direct	Indirect	Direct	Indirect
Individual	Traditional Direct Risk/Benefit	Full Public Value		
Population				

→ Express the global public health rationale for developing a vaccine

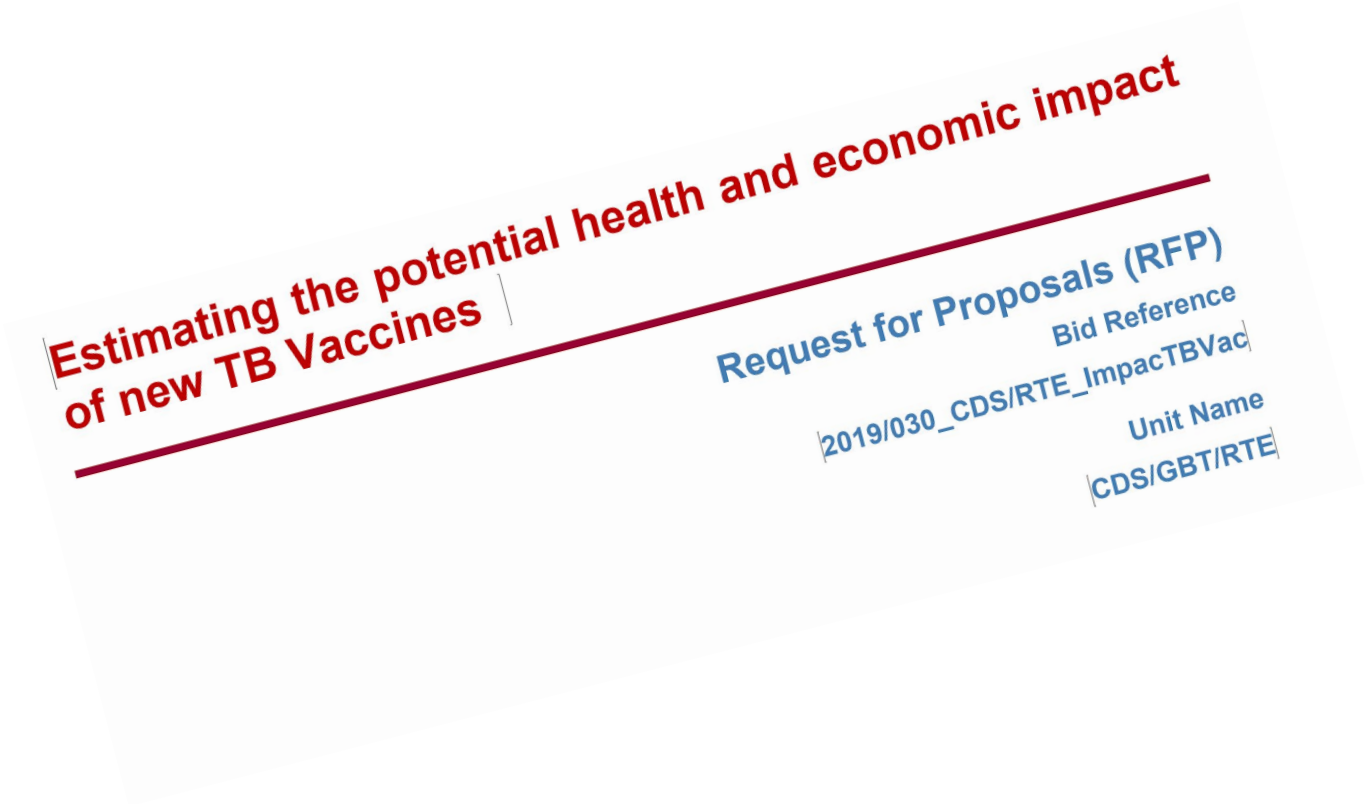
→ Inform decision-making across the duration of vaccine development and uptake

Consultation and operationalized by WHO GTB into request for 9 ‘buckets’ of evidence

- Consultation including technical experts, funders and countries

1. Health impact
2. Value for money
3. Equity and social protection impact
4. Economic impact
5. Global health security impact
6. Market and implementation scenarios
7. Vaccine cost
8. Alternative strategies
9. Implementation feasibility

- WHO put out to tender as open RFA



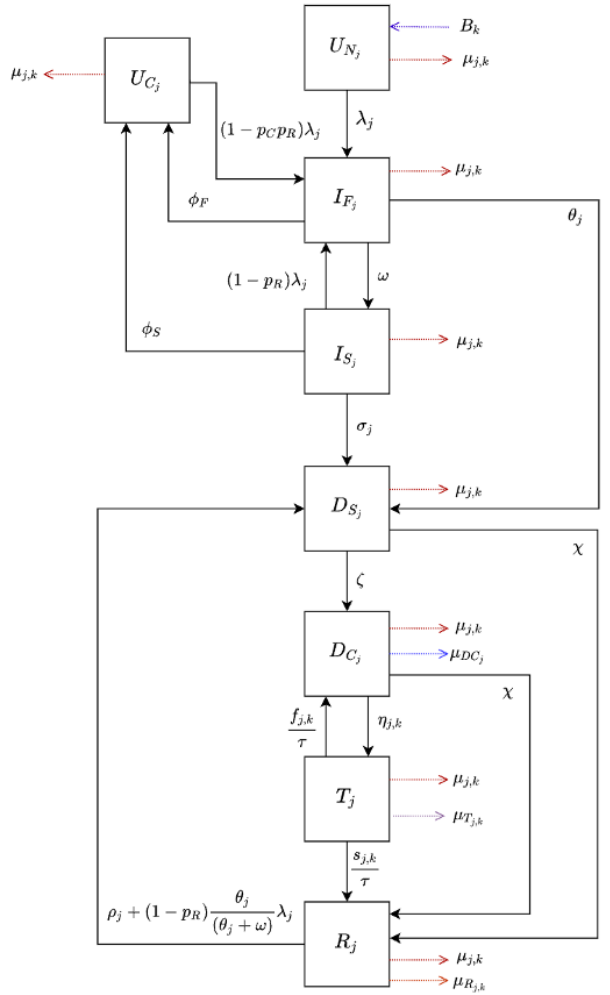
Health estimation methods

- **135** LMICs based on 2019 World Bank Income group
- Missing data for **20** countries
- Attempted calibration on **115** countries

Project to 2050 assuming no novel vaccine introduction (“*No-New-Vaccine*” baseline), then compared to scenarios with a vaccine implemented

Outcomes:

- Countries grouped by WHO region, World Bank Income Group, and for WHO high TB burden countries
- Calculated cumulative cases/treatments/deaths averted between vaccine introduction and 2050 for scenarios with new TB vaccines compared to the *No-New-Vaccine* baseline



D_C = Clinical Disease, D_S = Subclinical Disease; I_F = Infection-Fast, I_S = Infection-Slo
R = Resolved, T = On-Treatment, U_C = Uninfected-Cleared, U_N = Uninfected-Naive

Vaccine profile methods

Informed by WHO Preferred Product Characteristics for New Tuberculosis Vaccines

Vaccine Age Group	Infection status at time of vaccination required for vaccine efficacy	Prevents	Vaccine Efficacy	Duration of Protection
Adolescent / Adult	Pre and Post Infection with *Mtb*	Disease	50% 75%	10 years Lifelong
Infant	Pre Infection with *Mtb*	Disease	80%	10 years Lifelong

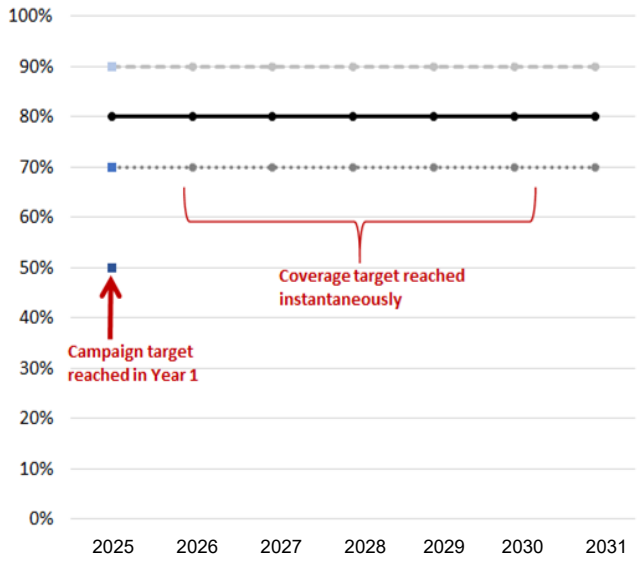
Clark RA, Mukandavire C, Portnoy A, et al. The impact of alternative delivery strategies for novel tuberculosis vaccines in low-income and middle-income countries: a modelling study. *Lancet Glob Health*, 2023: doi: https://doi.org/10.1016/S2214-109X(23)00045-1

Vaccine delivery methods

Vaccine coverage at 5 years (low / medium / high)
Neonatal: 75% / **85%** / 95%
9-year-olds: 70% / **80%** / 90%
10+: 50% / **70%** / 90%

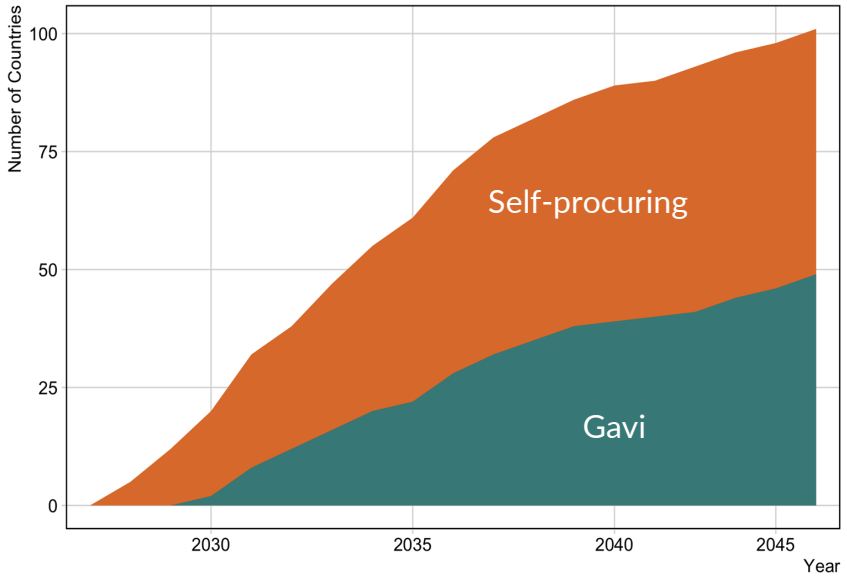
Accelerated Scale-up

- All countries introduce in 2025
- Instant scale-up to coverage
- Infant vaccine: Routine neonatal
- Adolescent/adult vaccine: routine 9-year-olds; 1 campaign ages 10+



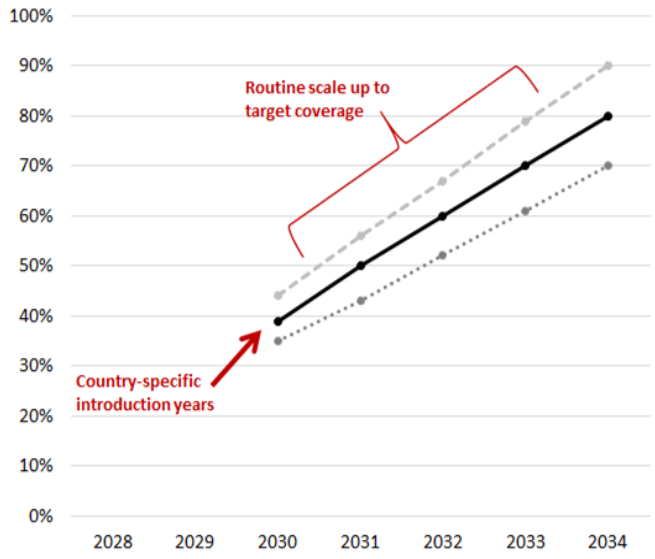
Basecase

- Country-specific intro years
- Scale-up to coverage over 5 years
- Infant vaccine: Routine neonatal
- Adolescent/adult vaccine: routine 9-year-olds; 1 campaign ages 10+



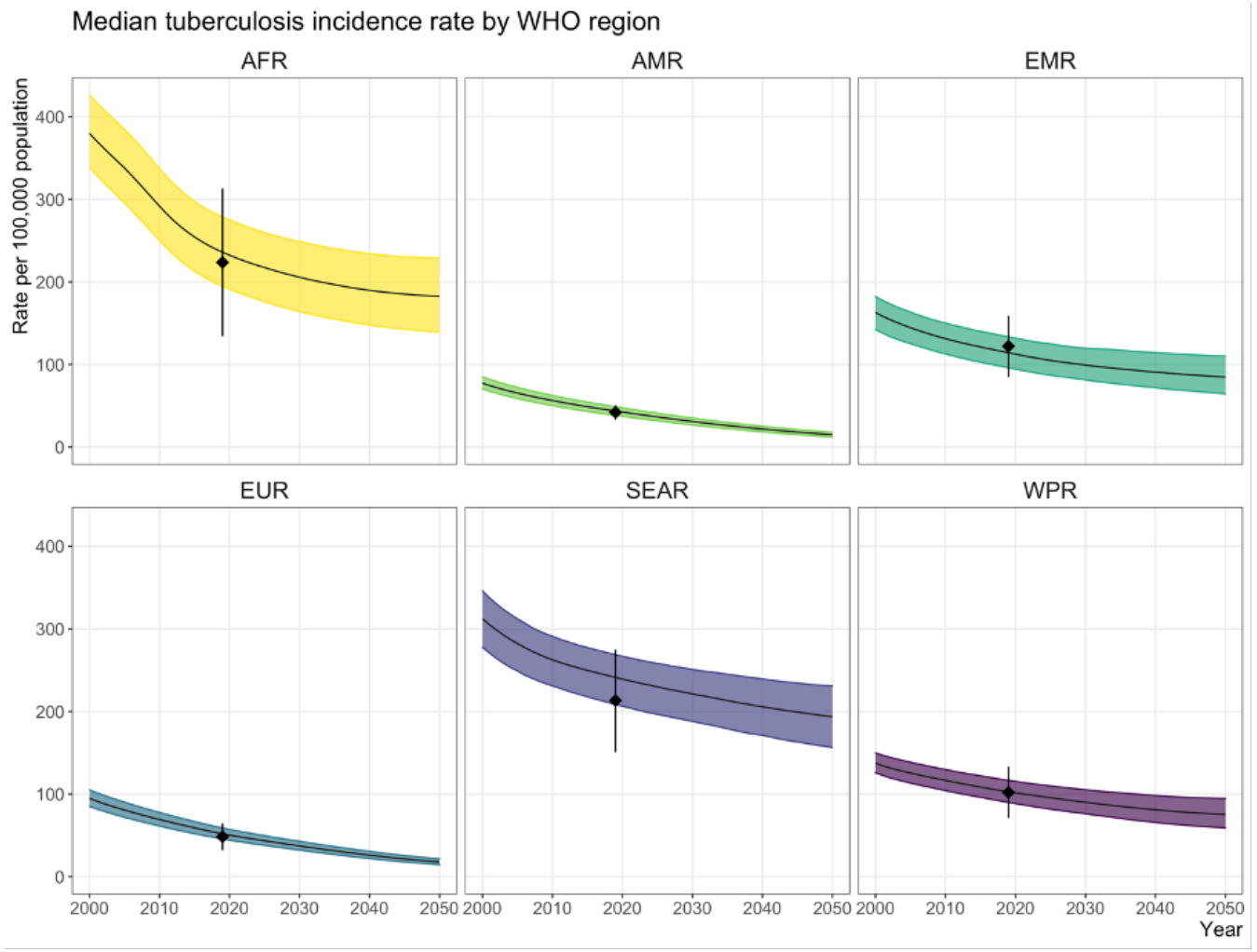
Routine Only

- Country-specific intro years
- Scale-up to coverage over 5 years
- Adolescent/adult vaccine: routine 9-year-olds



Calibration results

- **105** countries successfully calibrated
- Account for 93% of global TB cases and 94% of deaths in 2019
- **10** countries that we were unable to calibrate were further explored by Scarponi et al



Scarponi D, Iskauskas A, Clark RA, et al. Demonstrating Multi-Country Calibration of a Tuberculosis Model Using New History Matching and Emulation Package - hmer. *Epidemics,* 2023: doi: https://doi.org/10.1016/j.epidem.2023.100678

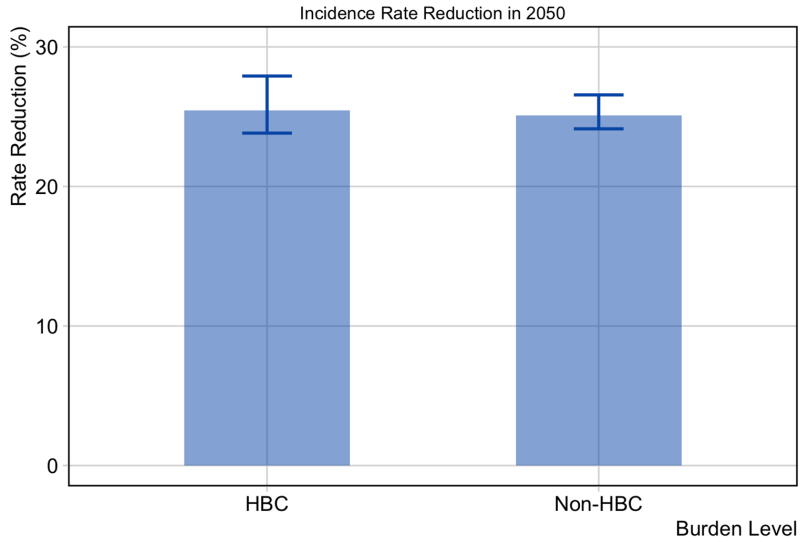
An adolescent/adult TB vaccine may reduce incidence rates in 2050 by 25%

Adol/Adult, 50% efficacy, Basecase delivery, 10y protect, med coverage

In line with previous LMIC modelling (Knight 2014)

- Important health impact

  → **~25%** reduction in cases in 2050

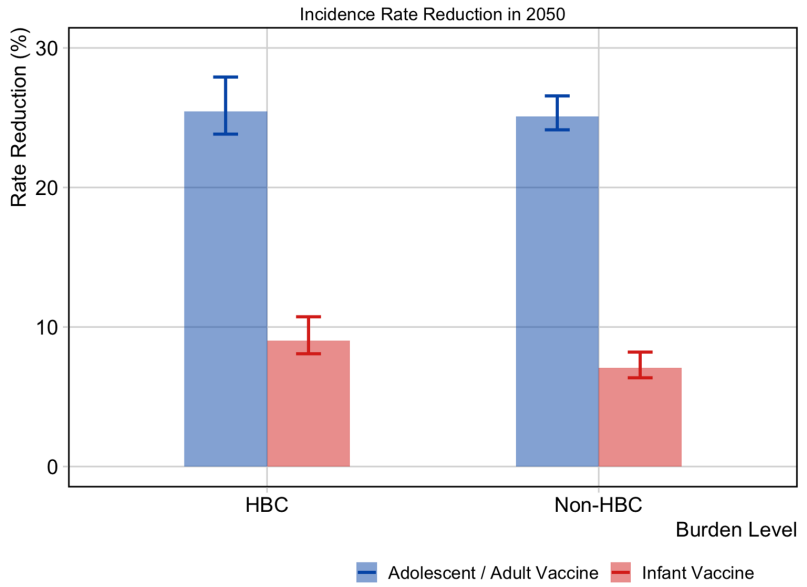


Vaccination adolescent/adults may lead to greater/more rapid incidence rate reductions in 2050, than vaccinating infants

vs Infant, 80% efficacy, Basecase delivery, 10y protect, med coverage

Greater impact from an adolescent / adult vaccine vs. infant vaccine before 2050

→ Targeting the age group with the largest burden



An adolescent/adult vaccine may avert ~44m cases, ~25m treatments, and ~5m deaths by 2050

Adol/Adult, 50% efficacy, Basecase delivery, 10y protect, med coverage

Cumulative cases averted between vaccine introduction and 2050

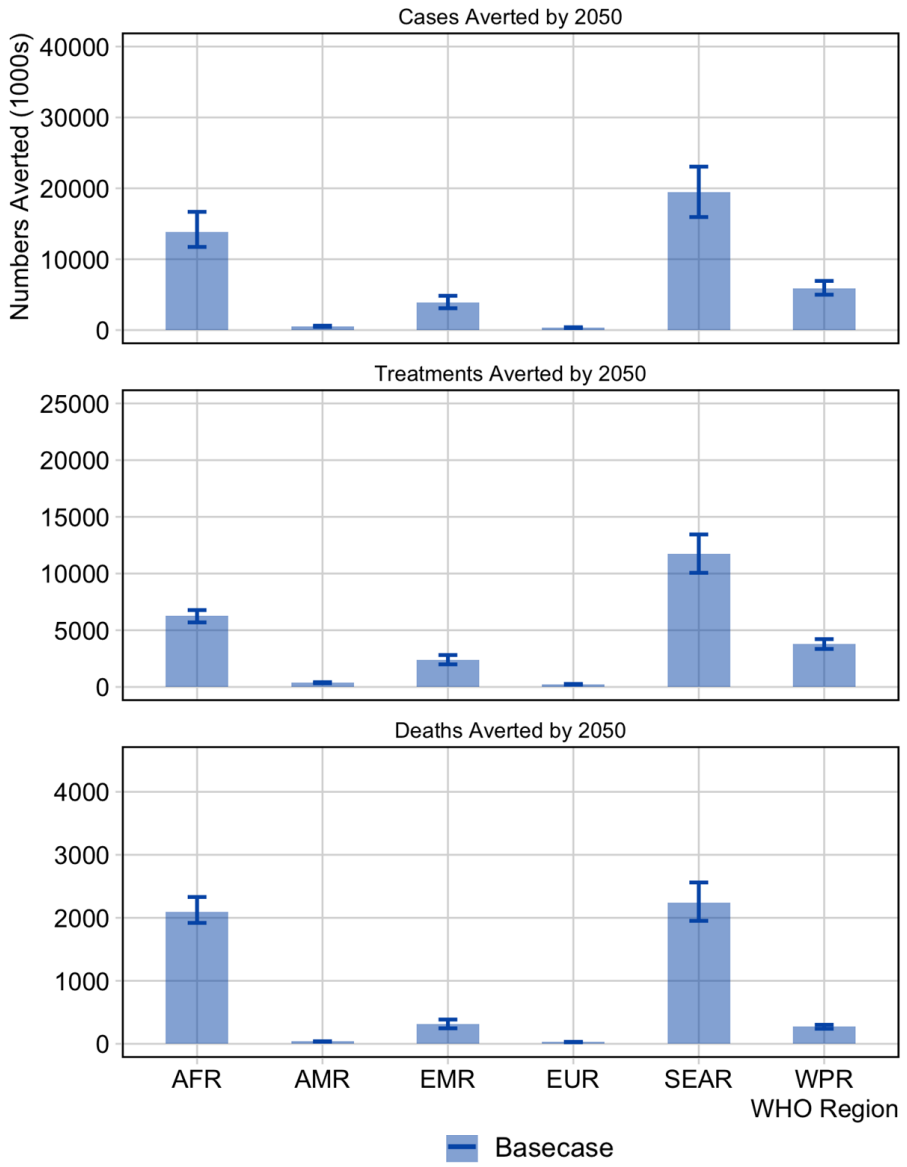
- Potential to avert **~44 million** cases
  - Particularly in AFR and SEAR

Cumulative treatments averted between vaccine introduction and 2050

- Potential to avert **~25 million** treatments by 2050
  - Valuable contribution to averting antimicrobial resistance

Cumulative deaths averted between vaccine introduction and 2050

- Potential to avert **~5 million** deaths by 2050



Introducing at rate ~COVID vx may avert ~50-60% more cases/deaths, than introducing at rate ~PCV vx

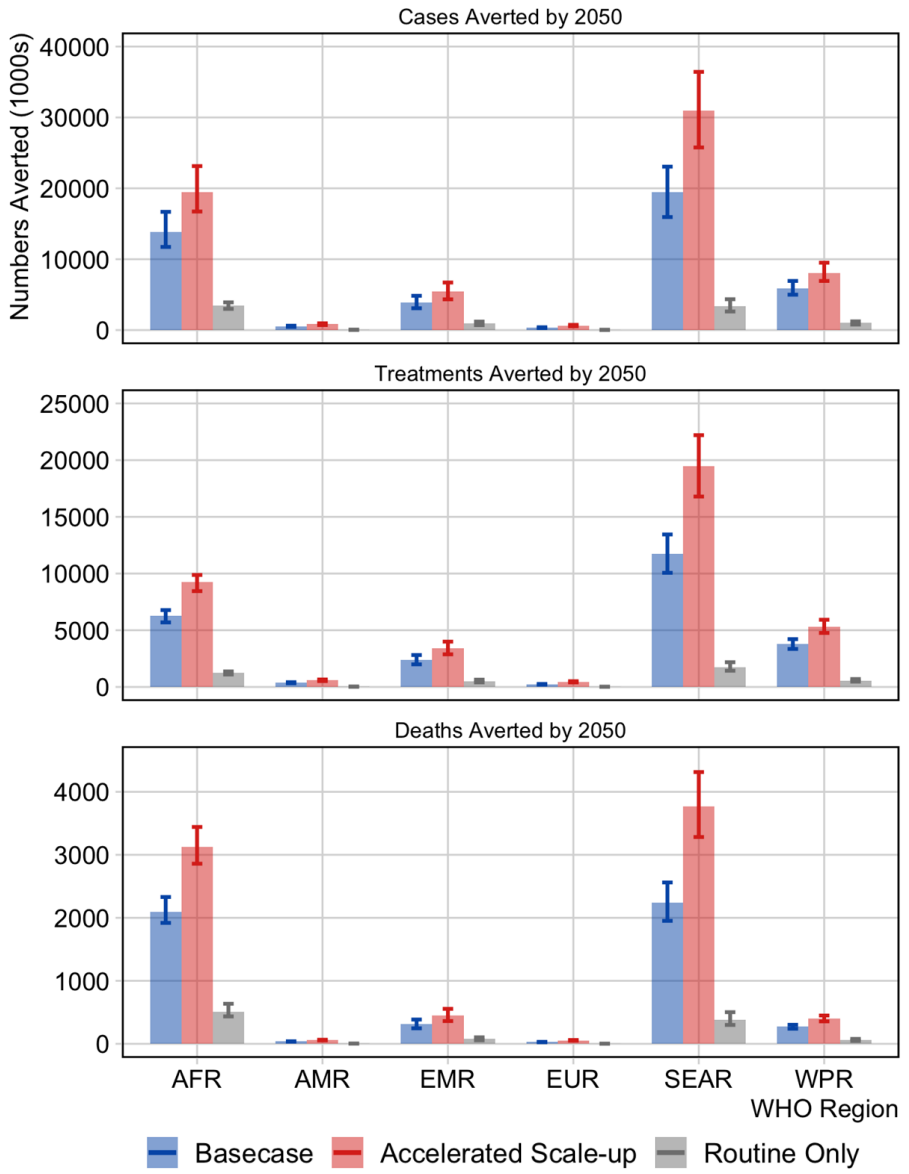
Adol/Adult, 50% efficacy, varying delivery, 10y protect, med coverage

Cases, treatments, and deaths averted by delivery:

We assumed more 'realistic' introduction & scale up scenarios than previous modelling

In the *Basecase* scenario, **~44 million** cases, **~25 million** treatments, and **~5 million** deaths were averted.

An increased scale-up speed (*Accelerated Scale-up*) could prevent **~21 million additional** cases, **~14 million additional** treatments, and **~3 million additional** deaths **(~50-60% more)**



Routine only delivery may avert ~80-90% fewer cases/deaths, than the routine & campaign

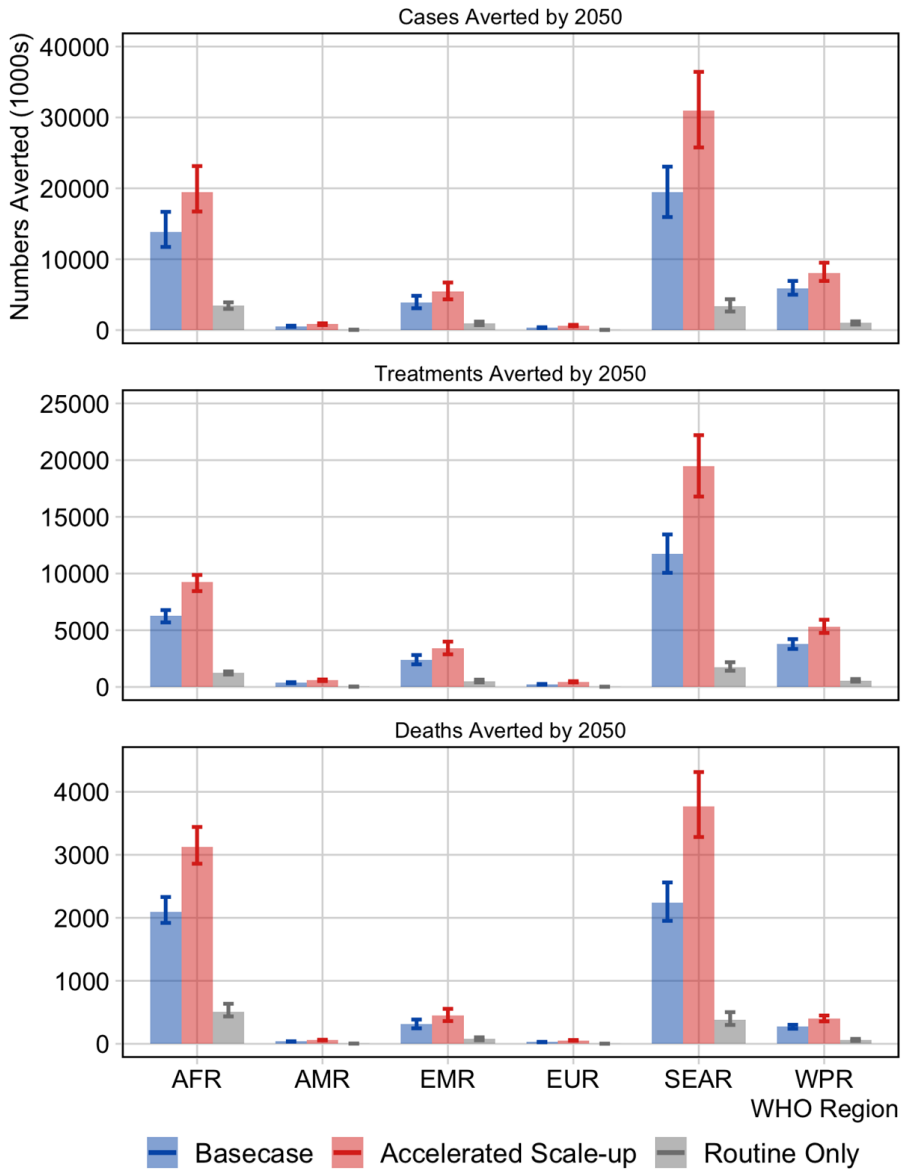
Adol/Adult, 50% efficacy, varying delivery, 10y protect, med coverage

Cases, treatments, and deaths averted by delivery:

We assumed more 'realistic' introduction & scale up scenarios than previous modelling

In the *Basecase* scenario, **~44 million** cases, **~25 million** treatments, and **~5 million** deaths were averted.

- An increased scale-up speed (*Accelerated Scale-up*) could prevent **~21 million additional** cases, **~14 million additional** treatments, and **~3 million additional** deaths **(~50-60% more)**
- By only offering this new TB vaccine routinely to adolescents (*Routine Only*), **~35 million fewer** cases, **~22 million fewer** treatments, and **~4 million** fewer deaths would be averted **(~80-90% fewer)**



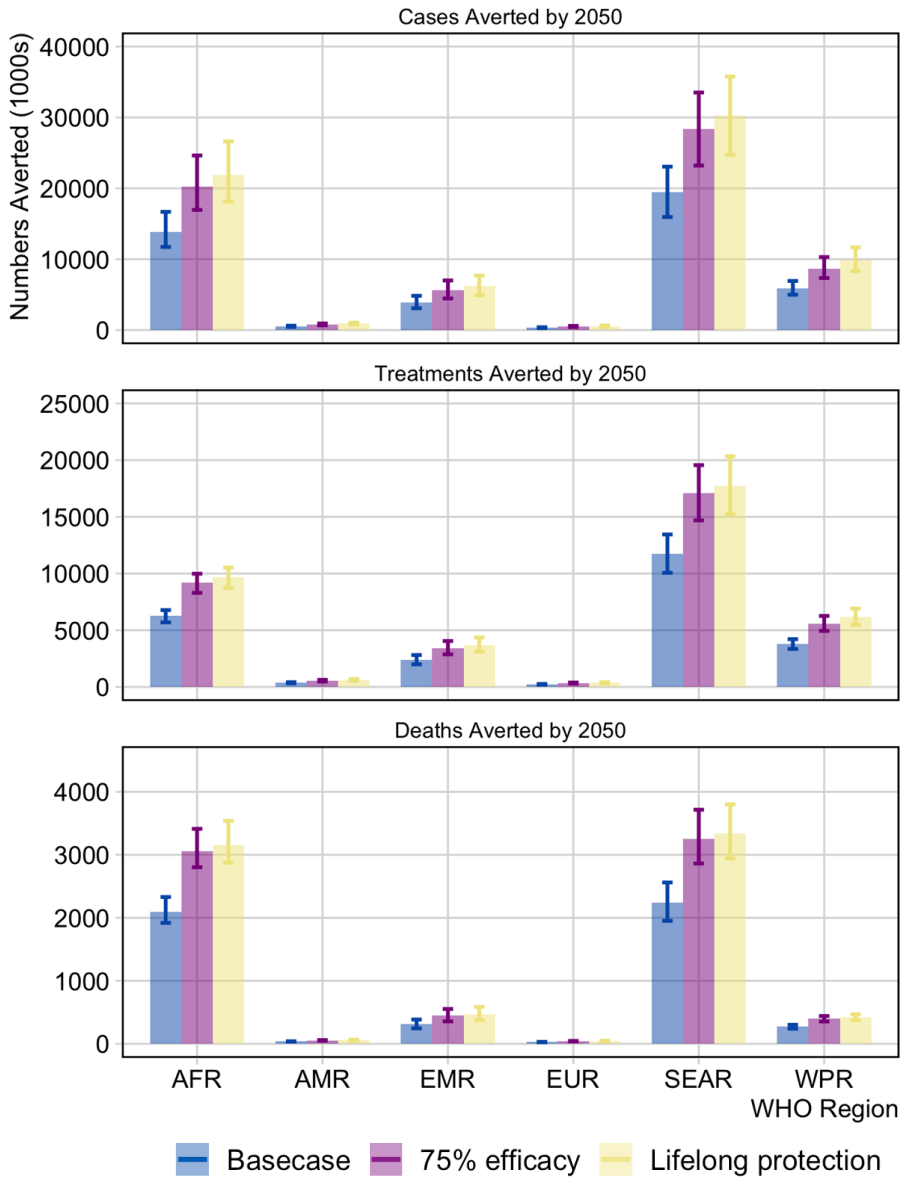
A 75% efficacy vaccine may avert ~50% more cases/deaths, than a 50% efficacy vaccine

Adol/Adult, 50% / 75% efficacy, Basecase, 10y protect vs LL, med coverage

Cases, treatments, and deaths averted by Basecase delivery with 50% vs 75% efficacy and 10 years vs lifelong protection

In the *Basecase* scenario, **~44 million** cases, **~25 million** treatments, and **~5 million** deaths were averted.

- A vaccine with 75% efficacy could prevent **~20 million additional** cases, **~14 million additional** treatments, and **~2 million additional** deaths **(~50% more)**



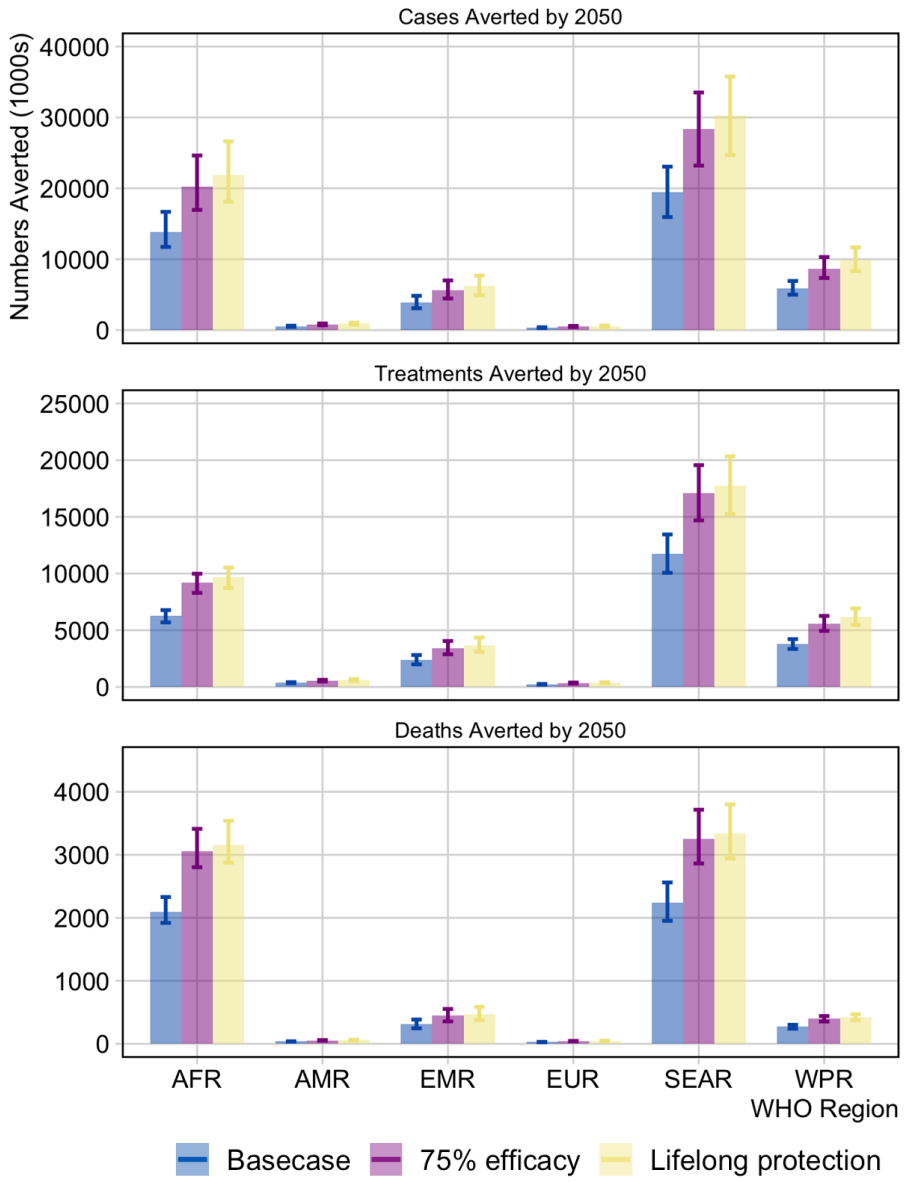
A lifelong protection vaccine may avert ~50% more cases/deaths, than a 10-year protection vaccine

Adol/Adult, 50% / 75% efficacy, Basecase, 10y protect vs LL, med coverage

Cases, treatments, and deaths averted by Basecase delivery with 50% vs 75% efficacy and 10 years vs lifelong protection

In the *Basecase* scenario, **~44 million** cases, **~25 million** treatments, and **~5 million** deaths were averted.

- A vaccine with 75% efficacy could prevent **~20 million additional** cases, **~14 million additional** treatments, and **~2 million additional** deaths **(~50% more)**
- A lifelong duration of protection vaccine could prevent **~26 million additional** cases, **~13 million additional** treatments, and **~2.5 million additional** deaths **(~50% more)**



Approach for economic evaluation

- Estimated a range of economic outcomes relevant to different decision-makers or for different goals

Cost-effectiveness (health system perspective)	Budget impact	Health equity & financial risk protection
Cost-effectiveness (societal perspective)	Return on investment (Net Monetary Benefit)	Macroeconomic impact

- Same countries, time period, introduction scenarios, and vaccine profiles (infant 80% efficacy, adult 50% efficacy) as health impact analyses

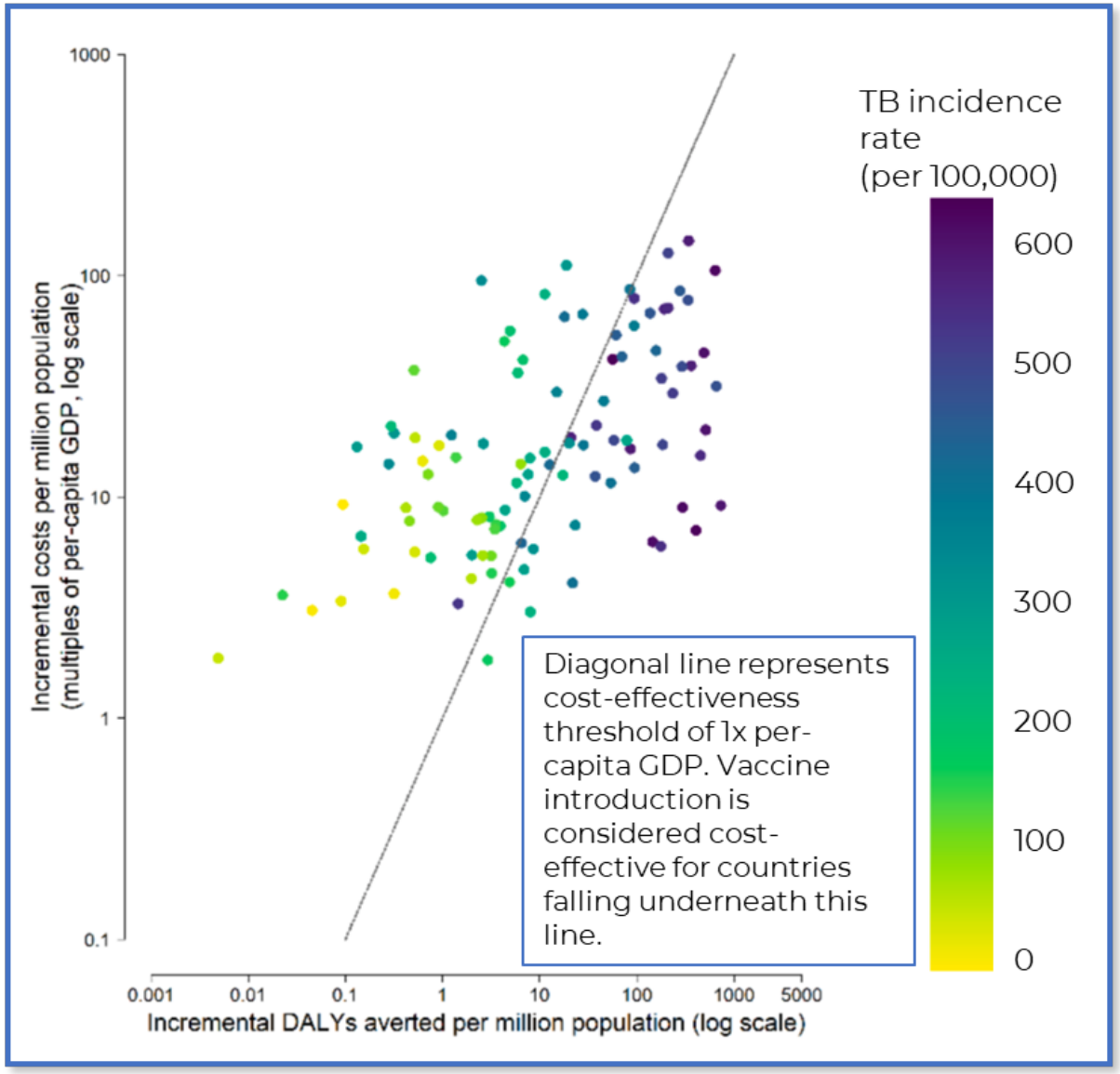
Cost-effectiveness analysis methods

- Health outcome: Disability-adjusted life years (DALYs) averted
- Costs (health system perspective): Costs of vaccine program, costs of TB and HIV services indirectly affected by vaccine introduction
- Costs (societal perspective): As above, plus patient out-of-pocket costs, productivity losses
- Outcomes assessed over 2028–2050, discounted at 3%
- Incremental cost-effectiveness ratios (ICERs) compared to cost-effectiveness thresholds defined as multiples of per-capita GDP for each country

Infant TB vaccines cost-effective in 45% of countries (89% high-burden countries)

- Higher country incidence rate associated with higher impact per capita, more favorable CE

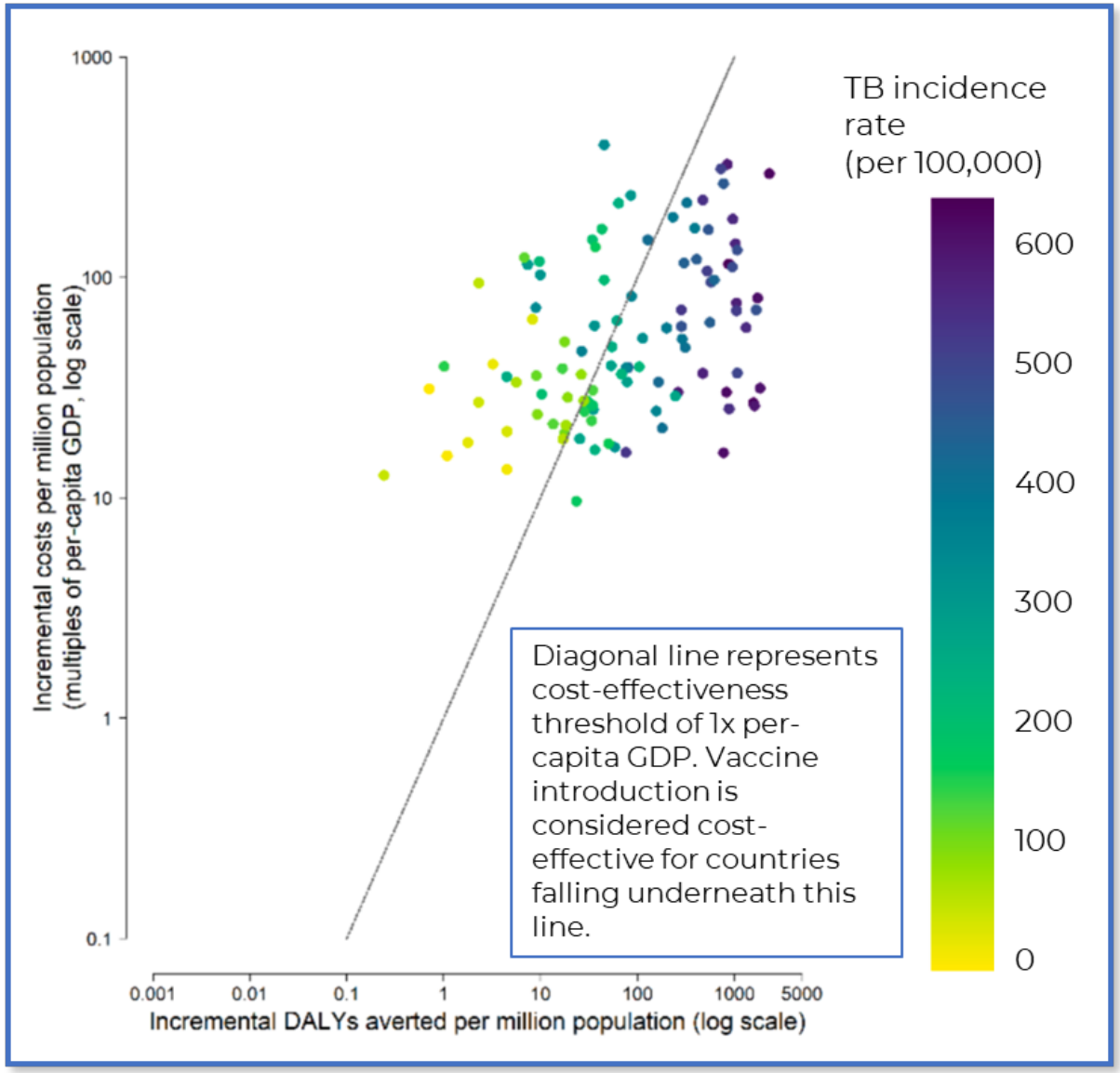
Health system perspective



Portnoy A, Clark RA, Quaife M et al. The cost and cost-effectiveness of novel tuberculosis vaccines in low- and middle-income countries: A modeling study. *PLOS Med,* 2023; doi: https://doi.org/10.1371/journal.pmed.1004155.

Adult TB vaccines cost-effective in 61% of countries (100% high-burden countries)

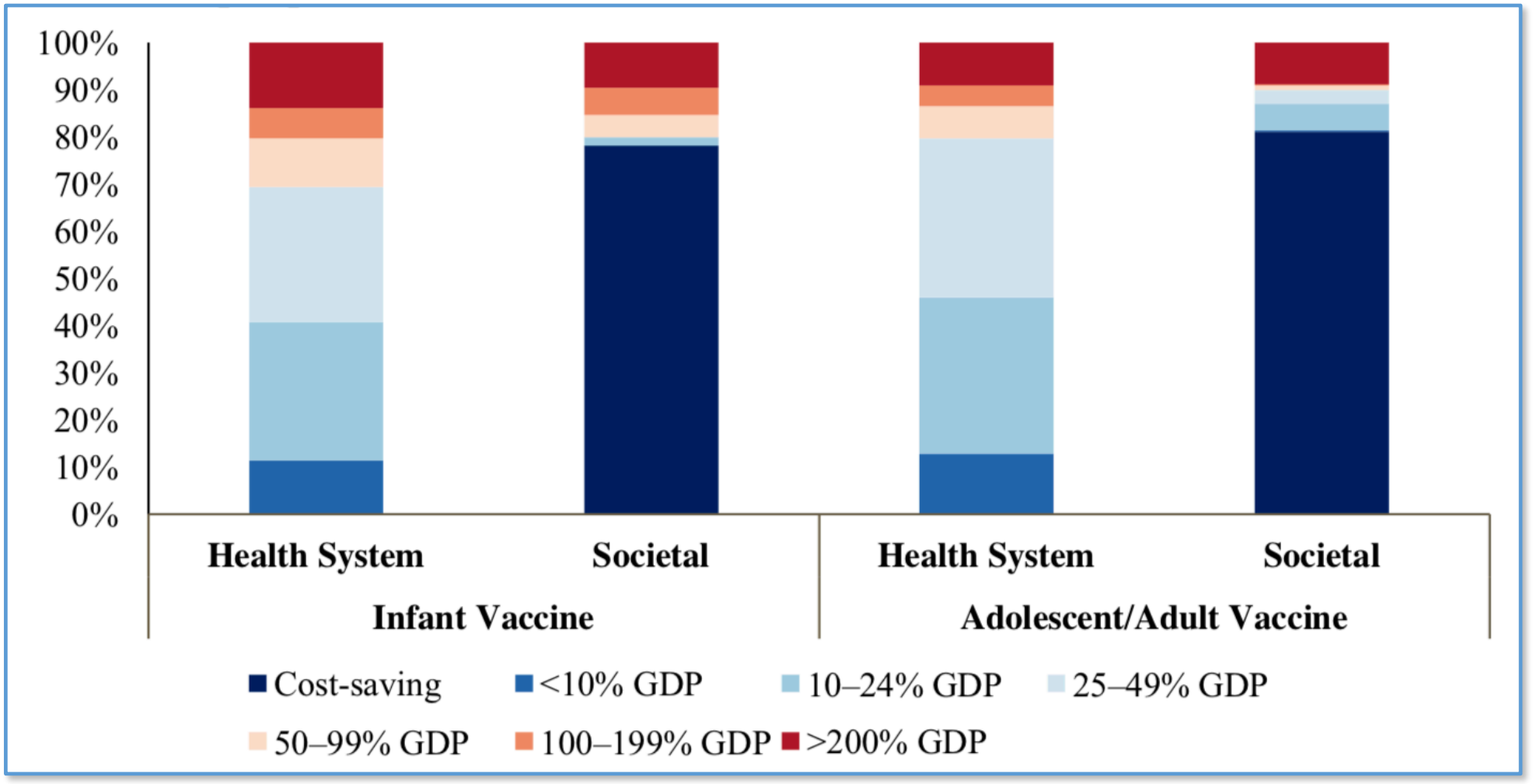
Health system perspective



- Higher country incidence rate associated with higher impact per capita, more favorable CE
- Same story for adult vaccine, with higher average costs and impact

Portnoy A, Clark RA, Quaife M et al. The cost and cost-effectiveness of novel tuberculosis vaccines in low- and middle-income countries: A modeling study. *PLOS Med,* 2023; doi: https://doi.org/10.1371/journal.pmed.1004155.

TB vaccines may be cost-saving (*societal perspective*)



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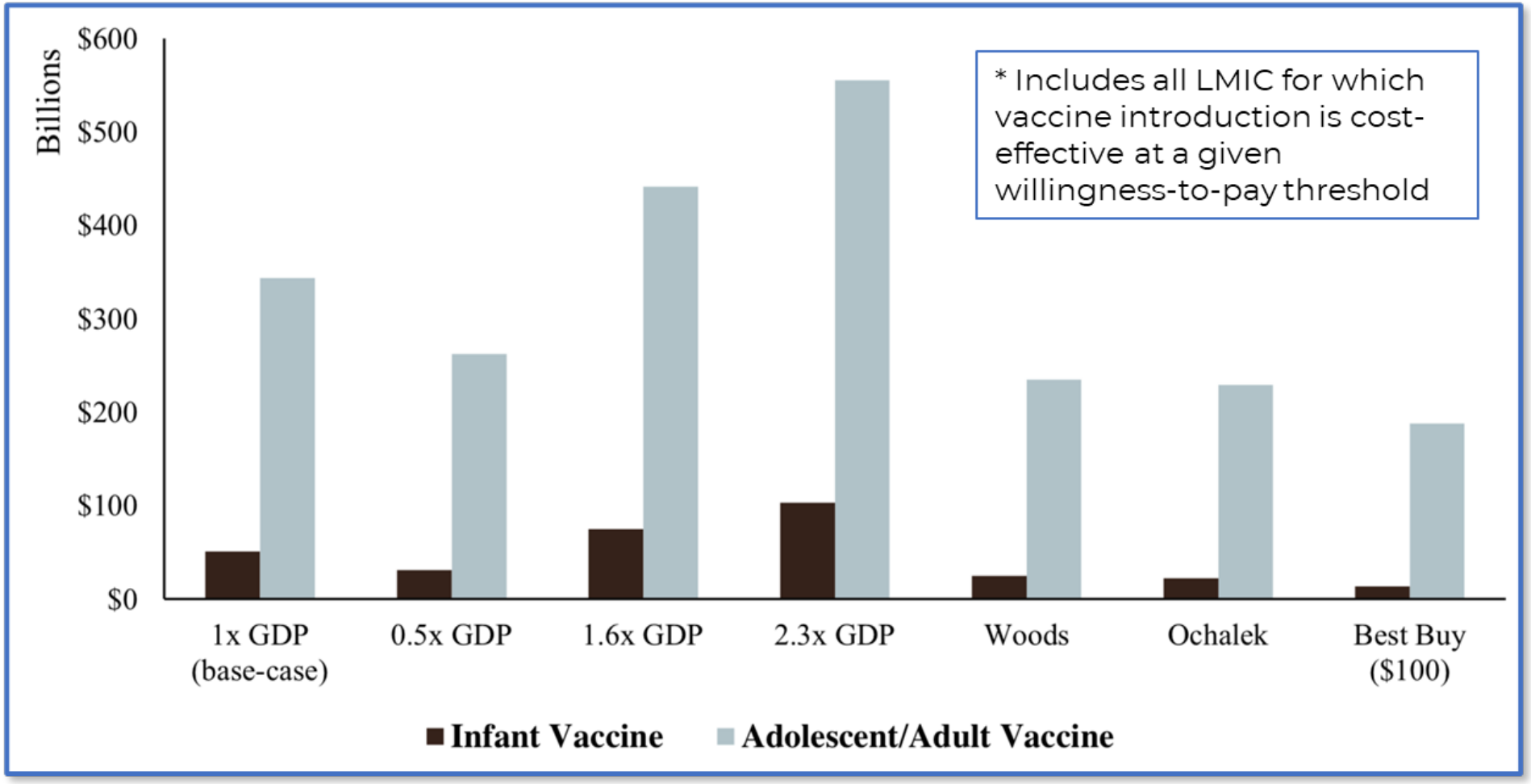
Return on investment

Net Monetary Benefit (NMB) = health benefits * CE threshold – costs

- Health benefits = DALYs averted
- CE threshold = multiples of per-capita GDP, assessed range of values
- Costs assessed from societal perspective

$7 in health and economic benefits, for every $1 invested in adolescent/adult TB vaccines



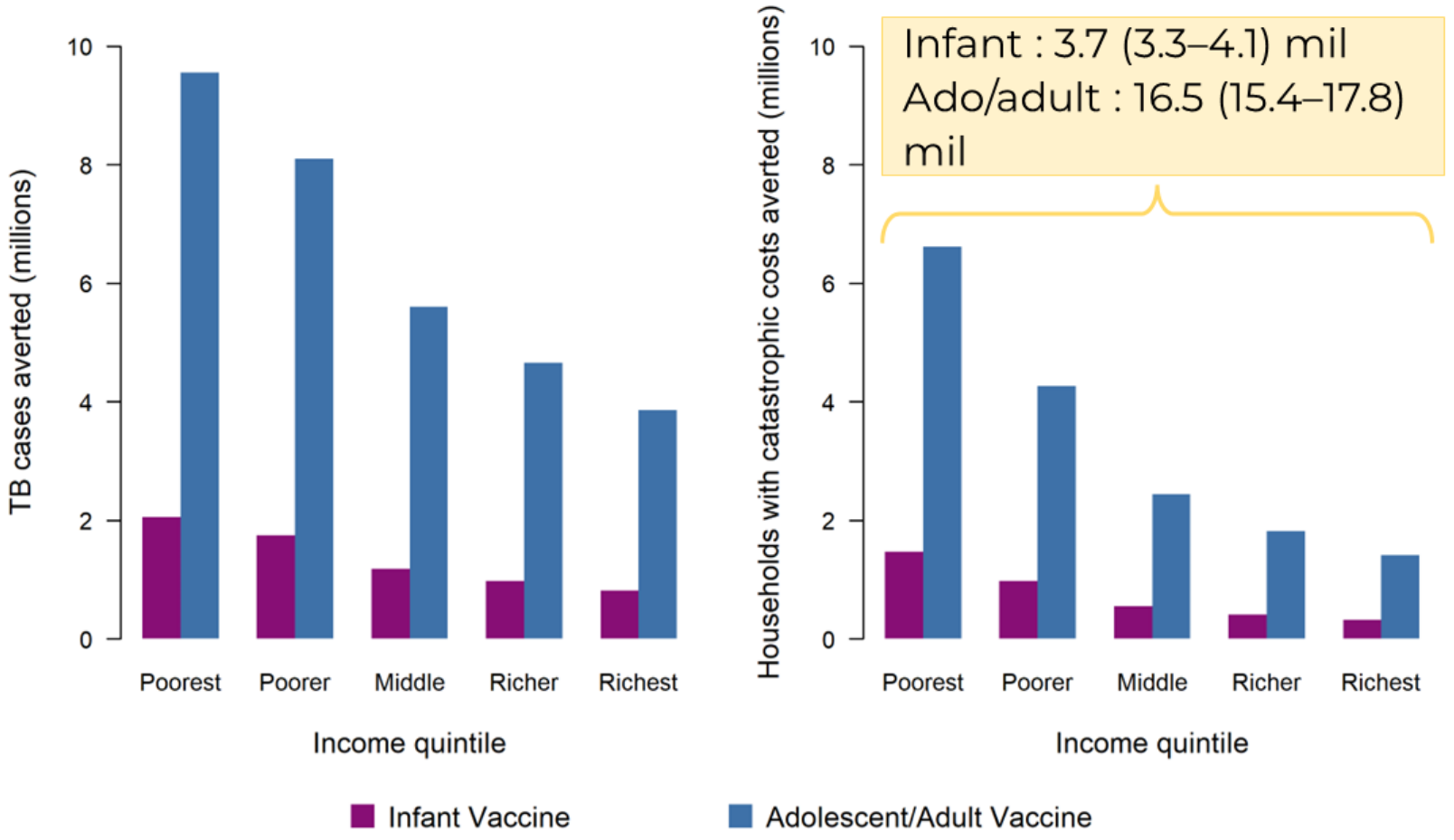
Health equity and financial risk protection methods

- Stratified outcomes across 5 income quintiles within each modeled country, based on current distribution of TB burden
- For each country and quintile, costs incurred by patients estimated by extrapolating from national TB patient cost survey data (N=20 surveys)
- Catastrophic costs of TB defined as patient costs per TB episode > 20% of household annual income

TB vaccines may advance health equity, with ~56% of benefits in poorest 40% of the population

Lower income quintiles:

- Higher TB incidence
- Greater fraction with catastrophic costs, per case



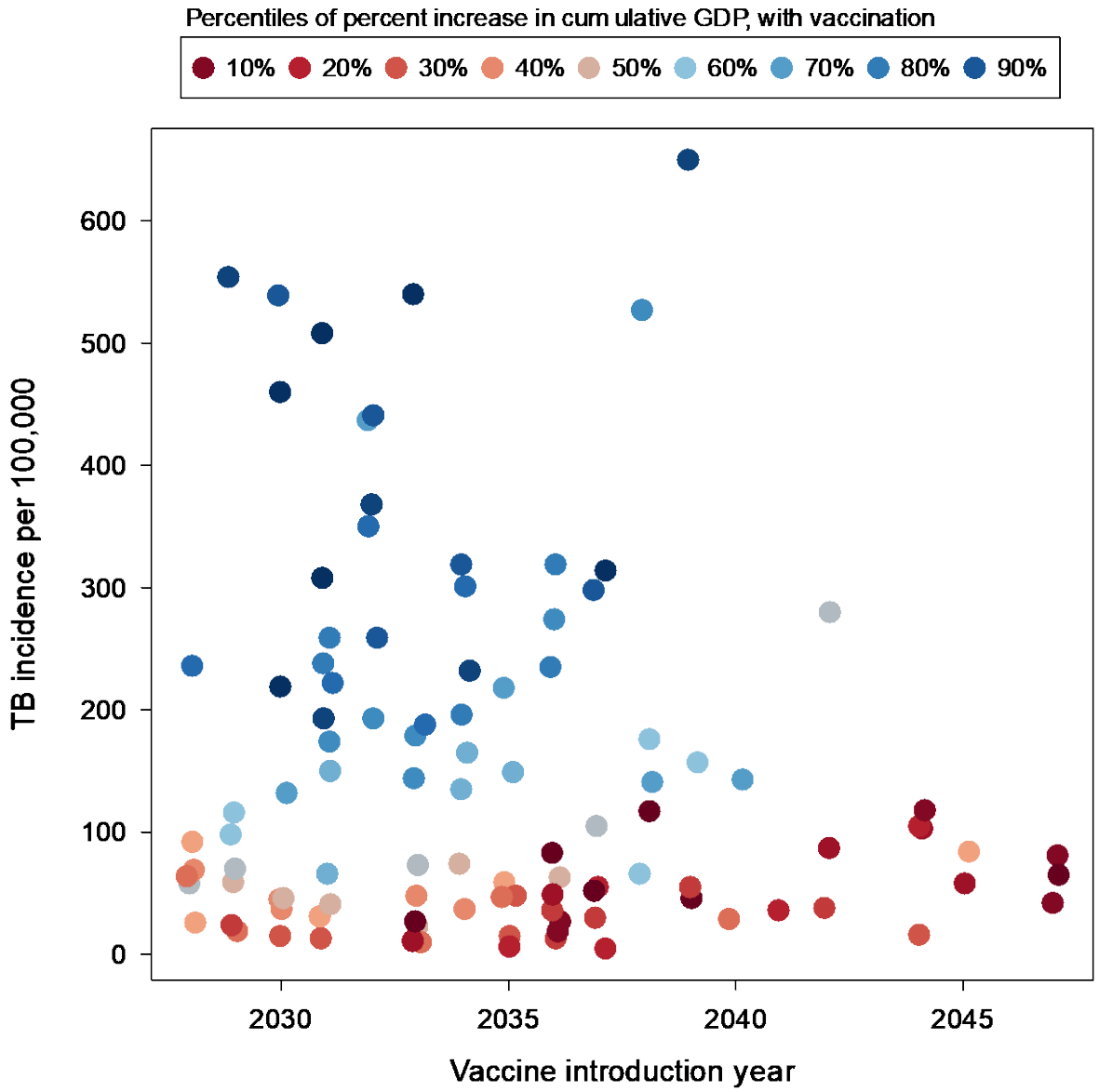
Portnoy A, Clark RA, Weerasuriya CK et al. The potential impact of novel tuberculosis vaccines on health equity and financial protection in low- and middle-income countries. *medRxiv,* 2022; doi: https://doi.org/10.1101/2022.10.29.22281678

Macroeconomic impact methods

- Health and cost outcomes used to parameterize published macroeconomic model (EPIC model) to estimate impact of TB vaccination on country GDP
- Timeline extended to 2080 to capture long-term effects

Adult TB vaccines may increase GDP by $1.6 trillion by 2080

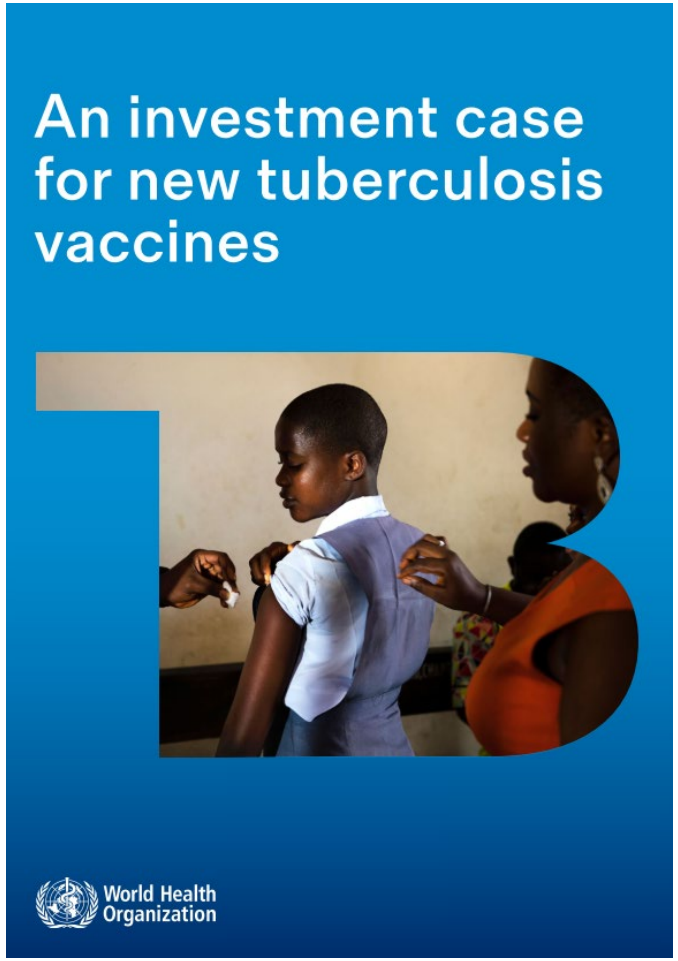
- Macroeconomic impact strongly related to current TB incidence level
- Earlier vaccine introduction, lower current GDP per capita also related to greater % impact



Portnoy A, Arcand J-L, Clark RA, et al. The potential impact of novel tuberculosis vaccine introduction on economic growth in low- and middle-income countries. *medRxiv,* 2022; doi: https://doi.org/10.1101/2022.11.23.22282690

Outputs

Policy Brief



Health Impact

The impact of alternative delivery strategies for novel tuberculosis vaccines in low-income and middle-income countries: a modelling study

Rebecca A Clark, Christinah Mukandavire, Allison Portnoy, Chathika K Weerasuriya, Arminder Deol, Danny Scarponi, Andrew Iskauskas, Roel Bakker, Matthew Quaife, Shelly Malhotra, Nebiat Gebreselassie, Matteo Zignol, Raymond C W Hutubessy, Birgitte Giersing, Mark Jit, Rebecca C Harris, Nicolas A Menzies, Richard G White

Summary

Background Tuberculosis is a leading infectious cause of death worldwide. Novel vaccines will be required to reacl global targets and reverse setbacks resulting from the COVID-19 pandemic. We estimated the impact of nove tuberculosis vaccines in low-income and middle-income countries (LMICs) in several delivery scenarios.

Cost and cost effectiveness

PLOS MEDICINE

RESEARCH ARTICLE

The cost and cost-effectiveness of novel tuberculosis vaccines in low- and middle-income countries: A modeling study

Allison Portnoy[1*], Rebecca A. Clark[2,3,4], Matthew Quaife[2,3,4], Chathika K. Weerasuriya[2,3,4], Christinah Mukandavire[2,3,4], Roel Bakker[2,3,4,5], Arminder K. Deol[2,3,4,6], Shelly Malhotra[7,8], Nebiat Gebreselassie[9], Matteo Zignol[9], So Yoon Sim[10], Raymond C. W. Hutubessy[10], Inés Garcia Baena[9], Nobuyuki Nishikiori[9], Mark Jit[3,4,11], Richard G. White[2,3,4‡], Nicolas A. Menzies[1,12‡]

Equity and financial protection

The potential impact of novel tuberculosis vaccines on health equity and financial protection in low- and middle-income countries

Authors

Allison Portnoy, ScD[1], Rebecca A. Clark, MSc[2-4], Chathika K. Weerasuriya, PhD[2-4], Christinah Mukandavire, PhD[2-4], Matthew Quaife, PhD[2-4], Roel Bakker, PhD[2-5], Inés Garcia Baena, MSc[6], Nebiat Gebreselassie, PhD[6], Matteo Zignol, MD[6], Mark Jit, PhD[3,4,7], Richard G. White, PhD[2-4], Nicolas A. Menzies, PhD[1,8]

Macroeconomic growth

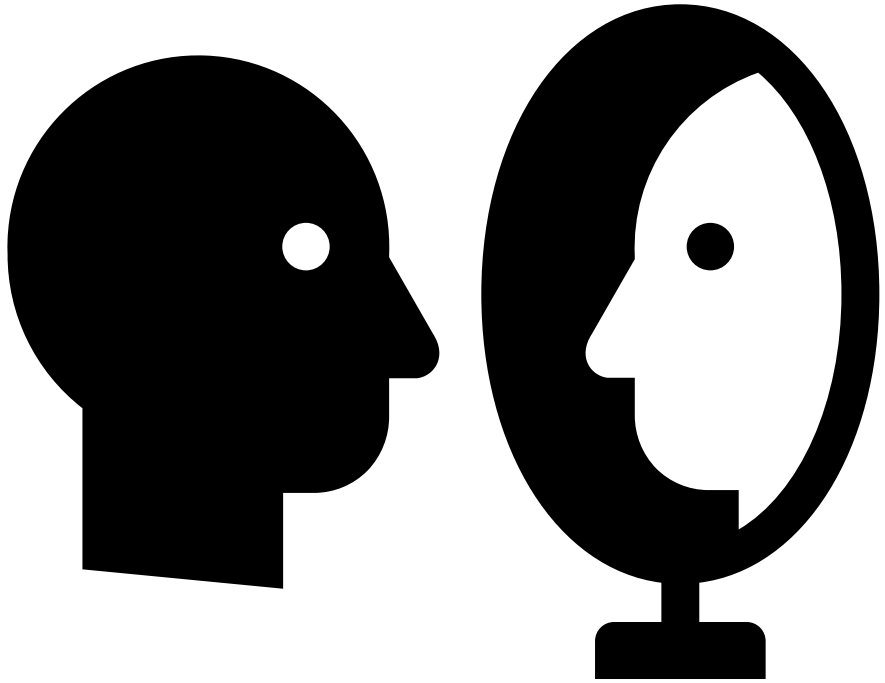
The potential impact of novel tuberculosis vaccine introduction on economic growth in low- and middle-income countries

Authors

Allison Portnoy[1,*], Jean-Louis Arcand[2,3], Rebecca A. Clark[4-6], Chathika K. Weerasuriya[4-6], Christinah Mukandavire[4-6], Roel Bakker[4-7], Edith Patouillard[8], Nebiat Gebreselassie[9], Matteo Zignol[9], Mark Jit[5,6,10], Richard G. White[4-6], Nicolas A. Menzies[1,11]

Reflections

- Very useful guiding framework
- ‘Pushed’ to think how we might create evidence in these
- Used to support case for TB Vaccine Accelerator launch at Davos
- Likely utility for GAVI VIS this year
- Being used by multiple advocates in run up to UNHLM later in year
- Looking forward to feedback on utility and what other evidence might be useful



Acknowledgments

Rebecca Clark
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Thanks to funding provided by the World Health Organization (WHO)

Using the FVVA framework to estimate the potential health and economic impacts of novel TB vaccines in low- and middle-income countries

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