Modelling to support new TB vaccines and immunisation decisions

Mathematical Modelling for New TB Vaccine Decision-Making in Africa
NISH-WHO Webinar 18
08 April 2026

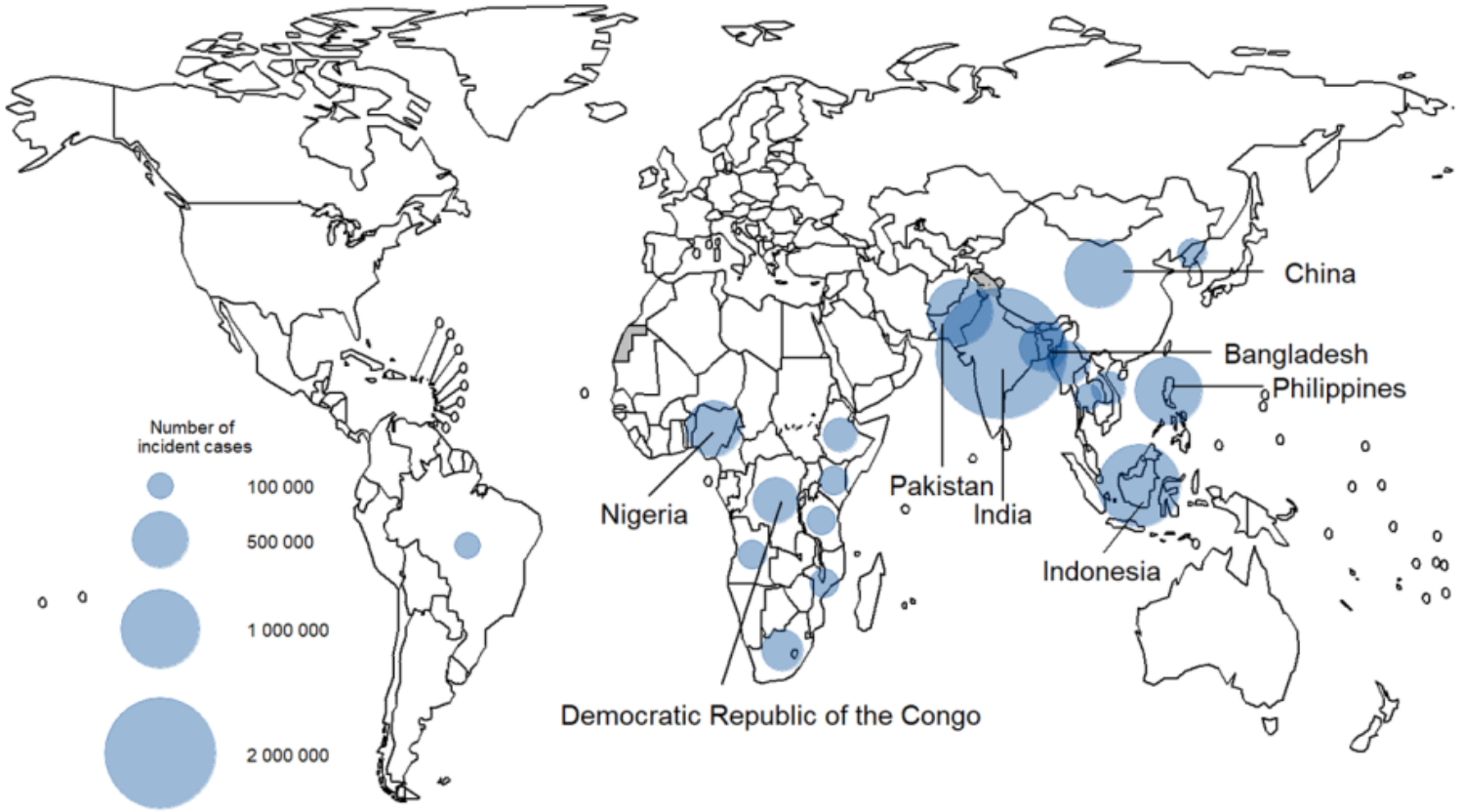
Mmamapudi Kubjane

Health Economics and Epidemiology Research Office

Health Economics and Epidemiology Research Office
HE²RO
Wits Health Consortium
University of the Witwatersrand

Background

- Globally: 10.7 million fell ill and ~1.23 million die of TB annually
- African region: 2.62 million fell ill, 400,000 die of annually



Source: WHO TB Report, 2024 estimates

End TB Strategy milestones for 2025, WHO African region

TB DEATHS 2024 VS 2015
46% reduction
(Target is 75% reduction by 2025)

TB INCIDENCE 2024 VS 2015
28% reduction
(Target is 50% reduction by 2025)

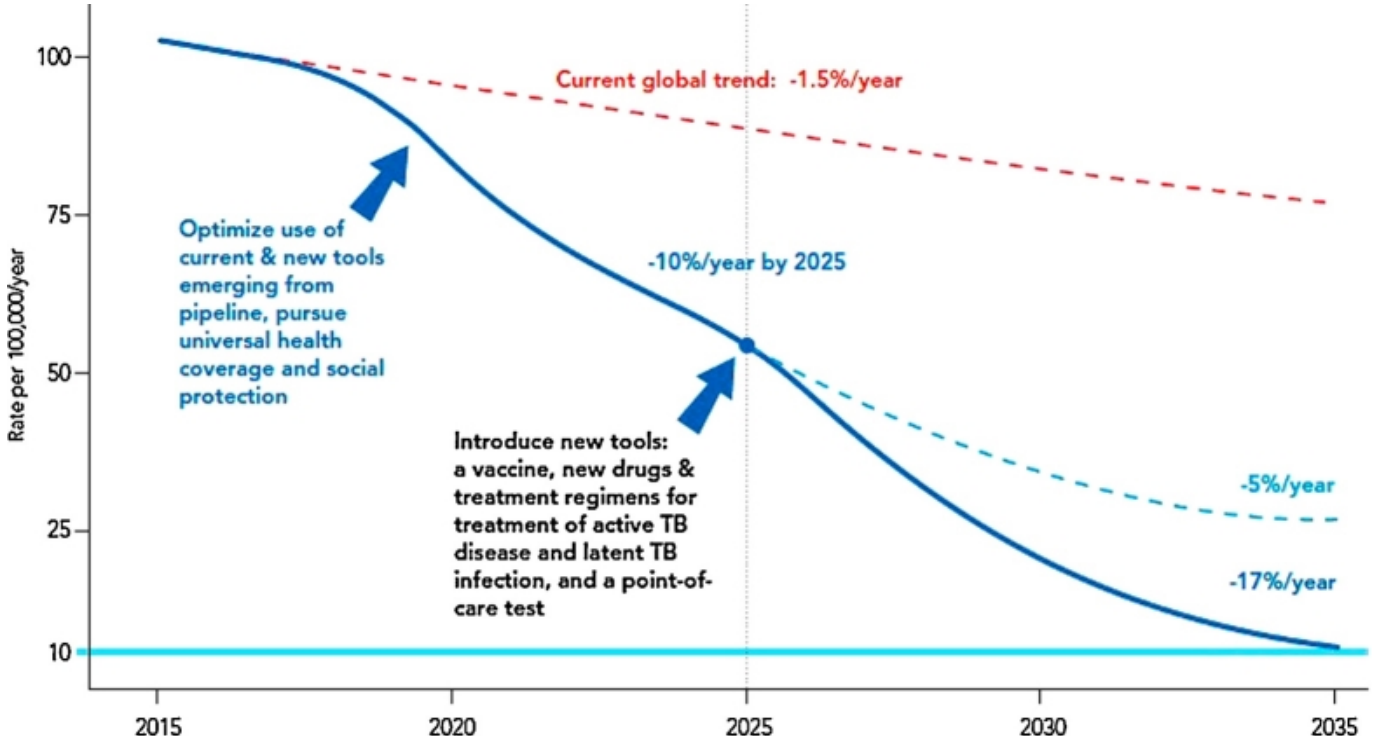
CATASTROPHIC COSTS
54%
(Target is 0% of people with TB facing catastrophic costs by 2020)

Global targets for TB elimination

End TB targets

	MILESTONES		TARGETS	
			SDG*	END TB
	2020	2025	2030	2035
Reduction in number of TB deaths compared with 2015 (%)	35%	75%	90%	95%
Reduction in TB incidence rate compared with 2015 (%)	20%	50%	80%	90%
TB-affected families facing catastrophic costs due to TB (%)	0%	0%	0%	0%

Projected acceleration of TB decline to reach target levels



Source: The End TB Strategy. Global strategy and targets for TB prevention, care and control after 2015

TB vaccine pipeline

TB vaccine candidates in active clinical trials

There are 9 candidates in active clinical trials as of January 2026.

Platform

- Mycobacterial - Live attenuated
- Mycobacterial - Inactivated
- Viral vector
- Protein/Adjuvant
- RNA

Trial target population

- Elderly
- Adults
- Adolescents
- Children
- Infants
- +HIV — People living with HIV
- -HIV — People without HIV infection
- -Mtb — People without Mtb infection
- +Mtb — People with Mtb infection
- aTBd — People with active TB disease
- MDR — People with MDR-TB
- cTB — People cured of active TB

Primary endpoint

- *Sf* — Safety
- *Im* — Immunogenicity
- *POI* — Prevention of Infection
- *POD* — Prevention of Disease
- *POR* — Prevention of Recurrence
- *Thp* — Therapeutic

Information reported by trial sponsors or found in clinical trial registries or other public sources

Institutions listed are the trial sponsors

Additional information about each candidate can be accessed via the QR code or at newtbvaccines.org/tb-vaccine-pipeline/

Last update: 6 January 2026

Stop TB Partnership
WORKING GROUP ON NEW TB VACCINES

Mathematical modelling

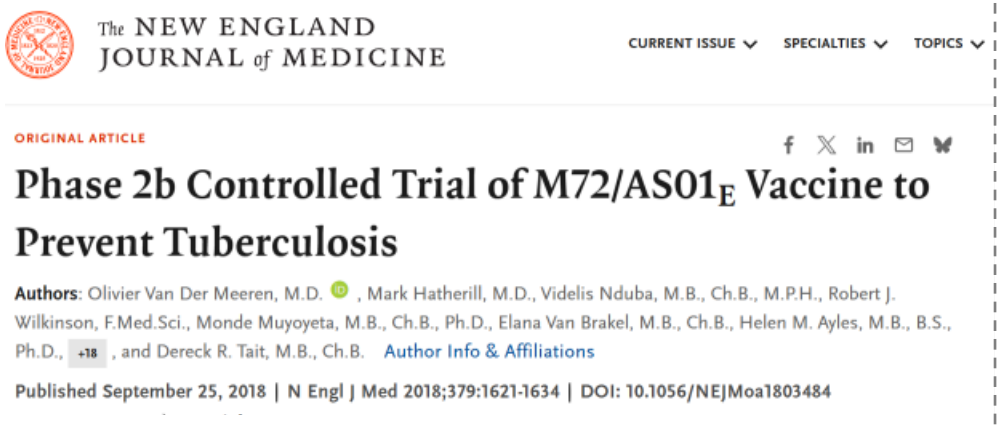
- A simplified representation of the real-world systems using mathematical expressions/equations
- Extrapolate from trial efficacy studies to estimate population-level impact
- Simulate how TB spreads and responds to interventions (i.e. a TB vaccine)
- Can build models that capture TB transmission dynamics and economics
- Questions we can address:
  - Impact on TB morbidity: new cases, deaths, disability adjusted life years averted
  - Overall budget required
  - Efficiency (who to prioritise for vaccination)
  - What gives value for money
  - Downstream impact on other TB/health services demands/requirements
- What models cannot do:
  - Predict exact future -> they estimate plausible scenarios
- Interpretation of results:
  - Understand the input data and sources of uncertainty
  - Understand key simplifying assumptions
  - All limitations need to be acknowledged

Some assumptions in TB vaccine modelling

To bear in mind

- TB natural history: disease states considered, what informs this?
- Vaccine efficacy (pV)
- Mechanism of vaccine effect**:** Prevention of disease (POD)/infection (POI)?
- Administered to who: Everyone without disease receives the vaccine regardless infection status?
- Duration of protection?
- Model time horizon: long enough to show lasting impact?
- The data that informed the model
- Calibration: to country specific data and their sources (**important!**)?

… commonly cited evidence on efficacy



The NEW ENGLAND JOURNAL of MEDICINE

CURRENT ISSUE SPECIALTIES TOPICS

ORIGINAL ARTICLE

Phase 2b Controlled Trial of M72/AS01$_E$ Vaccine to Prevent Tuberculosis

Authors: Olivier Van Der Meeren, M.D., Mark Hatherill, M.D., Videlis Nduba, M.B., Ch.B., M.P.H., Robert J. Wilkinson, F.Med.Sci., Monde Muyoyeta, M.B., Ch.B., Ph.D., Elana Van Brakel, M.B., Ch.B., Helen M. Ayles, M.B., B.S., Ph.D., +18, and Dereck R. Tait, M.B., Ch.B. Author Info & Affiliations

Published September 25, 2018 | N Engl J Med 2018;379:1621-1634 | DOI: 10.1056/NEJMoa1803484

☐☐ Efficacy	54.1% (95% CI 11.5–76.2%) Prevents progression to active TB
☐☐ Population	HIV-negative adults (18–50) Latent TB infection

Evidence from TB vaccine modelling studies

Over 2025-2050, prevention of disease vaccines would provide faster and greater impact than POI vaccines; but the impact of POI vaccines increases in higher transmission settings, e.g., India and South Africa.
Harris, *Sci Trans Med.* 2020.

Potential impact of tuberculosis vaccines in China, South Africa, and India

Chathika K Weerasuriya, PhD [a,b,] · Andrew Iskauskas, PhD [g] · Roel B
Nebiat Gebreselassie, PhD [j] · Ma
Mark Jit, PhD [b,c] · Rebecca C Har

REBECCA C. HARRIS, TOM SUMNER, GWENAN M. KNIGHT, HUI ZHANG, AND RICHARD G. WHITE Authors Info & Affiliations

Article | Open access | Published:

Vaccine of 50% efficacy, with 10 year duration of protection, prevention of disease vaccine, could be cost-effective at the price US$6-8 per dose if delivered to adolescents and adults.
Knight, *PNAS*, 2014.

Sumner, Tom[a,b,c]; Clark, Rebecca A.[a,b,c]; Prys-Jones, Tomos O.[a,b,c]; Bakker, Roel[a,b,c,d]; Churchyard, Gavin[e,f,g]; White, Richard G.[a,b,c]

Tameris, Dereck Tait, Richard G. Wh

▸ Front Public Health. 2024 Feb 23;12:1302688. doi: 10.3389/fpubh.2024.1302688

Model-based impact evaluation of new tuberculosis vaccines in aging populations under different modeling scenarios: the case of China

Mario Tovar [1,2,*], Joaquín Sanz [1,2], Yamir Moreno [1,2,3]

RESEARCH ARTICLE | BIOLOGICAL SCIENCES

Impact and cost-eff tuberculosis vaccine income countries

Gwenan M. Knight, Ulla K. Griffiths, Tom Sumner, +4

Edited* by Barry R. Bloom, Harvard School of Public Health, Boston, MA, and approved September 8, 2014 (received for review March 7, 2014)

WHO TB Vaccine Investment case

1 TB vaccines save lives

Over 2025–2050, a TB vaccine for infants could avert 5.8–18.8 million cases and 0.8–2.6 million deaths, while a vaccine for adolescents and adults that is 50% effective in preventing disease could cumulatively avert 37.2–76.0 million cases and 4.6–8.5 million deaths. A vaccine that is 75% effective could avert 54–110 million new TB cases and 6.7–12·3 million TB deaths.

2 TB vaccines can help fight antimicrobial resistance

A TB vaccine for infants could avert an estimated 2.4–8.6 million treatments (up to US$ 299 million in treatment costs saved), while one for adolescents and adults could avert 21.9–42.3 million treatments, saving up to US$ 3.2 billion in treatment costs.

3 TB vaccines can be highly cost-effective and cost-saving

Vaccine products for both infants and adolescents/adults were estimated to be cost–effective in nearly all high TB-burden countries and cost-saving from a societal perspective.

4 TB vaccines offer a substantial return on investment

The value of novel TB vaccines in monetary terms was estimated globally as US$ 68.6 (44.5–100.0) billion for introduction of a vaccine for infants and US$ 372 (283–474) billion for one for adolescents and adults.

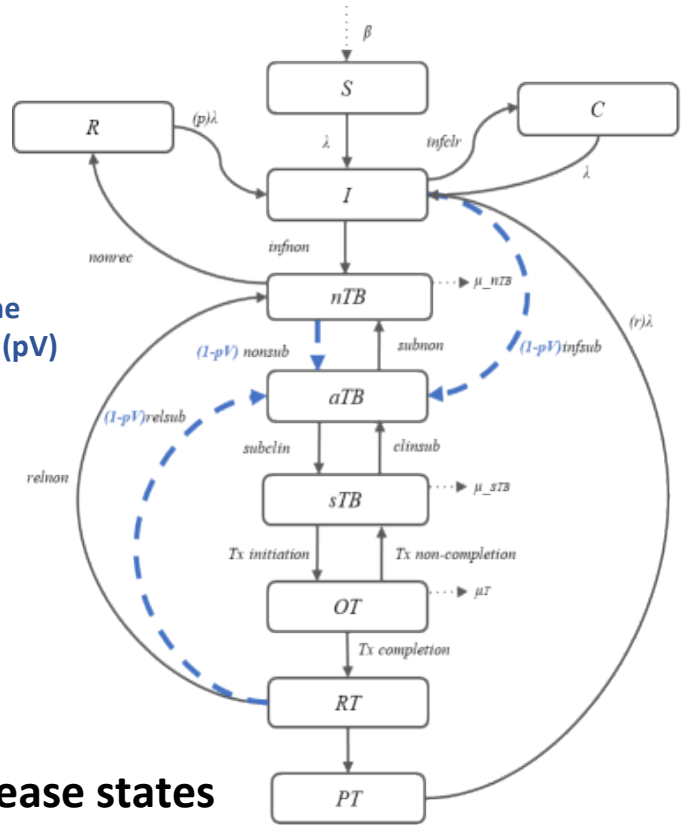
Example of ongoing work, using mathematical modelling to inform decision-making in South Africa (The WellMod Study)

Wellmod study: Mmamapudi Kubjane, Rebecca A. Clark, Tom Sumner, Elena Venero-Garcia, Lily O'Brien, Thobani Ntshiqa, Mthokozisi Dube, Katherine A. Thomas, Tomos Prŷs-Jones, Roel Bakker, Salome Charalambous, Richard G. White

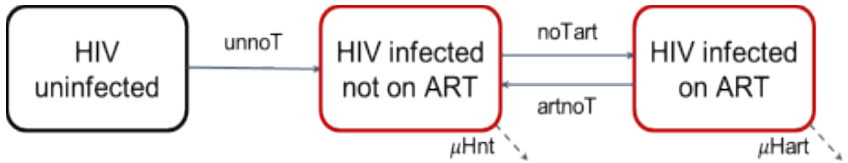
Mathematical modelling: data inputs and assumptions

TB model with a TB vaccine (tbmod)

Vaccine effect (pV)



HIV disease states



Some key assumptions that require real world data -> clinical trials and effectiveness studies

- Vaccine efficacy (pV):= 50%
- Efficacious irrespective of an individual's prior exposure
- Mechanism of effect**:** Prevention of disease (POD)
- Reduces the rate of progressing to TB disease states, by (1-pV))
- Everyone without disease receives the vaccine regardless infection status – i.e., no test before vaccination
- Duration of protection: 10 years on average
- Model time horizon: 20 years
- Stakeholder inputs: vaccine coverage, strategy, population,
- Cost data for economic evaluation: HE2RO
- Calibrated to TB (WHO) and HIV (UNAIDS) epidemiology estimates

Source: LSHTM, tbmod

Key factors that would influence TB vaccine adoption

- A wide range of country stakeholders were consulted to get a holistic position on future TB vaccination
- May-April, one-on-one small groups and a workshop

Stakeholders represented:

- National Department of Health
- South African Health Products Regulatory Authority
- National Advisory Group on Immunisation
- National Treasury
- Affordable Medicines Directorate
- WHO, South Africa
- Gates Foundation
- TB Proof
- Researchers: MRC, NICD, AHRI, WRHI, UCT

Figure 1: Factors influencing TB vaccine introduction

Thomas et al, 2026. Plos Global Health

Stakeholder-informed implementation strategies for the priority populations

Target population	Adolescents	People living with HIV	Health care workers	Adults	Household contacts of TB
Geographical scope	Nationwide, phased subnational among high burden provinces	Nationwide and regional	Nationwide	Nationwide and regional	Nationwide
Delivery strategy	Campaign and routine run parallel	Both campaign and routine	Campaign and routine	Campaign and routine run parallel	Campaign
Coverage target					
Low	Campaign: 50% Routine: 60%	Campaign: 40% Routine: 40%	Campaign: 50% Routine: 50%	Campaign: 50% Routine: 60%	Campaign = 50% Routine = 50%
Medium	Campaign: 60% Routine: 70%	Campaign: 55% Routine: 65%	Campaign: 60% Routine: 60%	Campaign: 55% Routine: 65%	
High	Campaign: 80% Routine: 90%	Campaign: 70% Routine: 90%	Campaign: 80% Routine: 80%	Campaign: 60% Routine: 70%	
Years to achieve coverage	1-5 years	1-5 years	3-5 years	1-10 years	
Age	12–17 years	18-64 years		18-64 years	
Feasibility	Can reach population through schools, majority of adolescents are in school	Easy to reach those who are diagnosed through HIV clinics for ARV collection & annual blood tests	Easy to reach through workplace	A hard-to-reach population due to no existing infrastructure that vaccinates adults	Could be reached through contact tracing, although the logistics would be challenging

Thomas et al, 2026. Plos Global Health

TB interventions and populations for costing

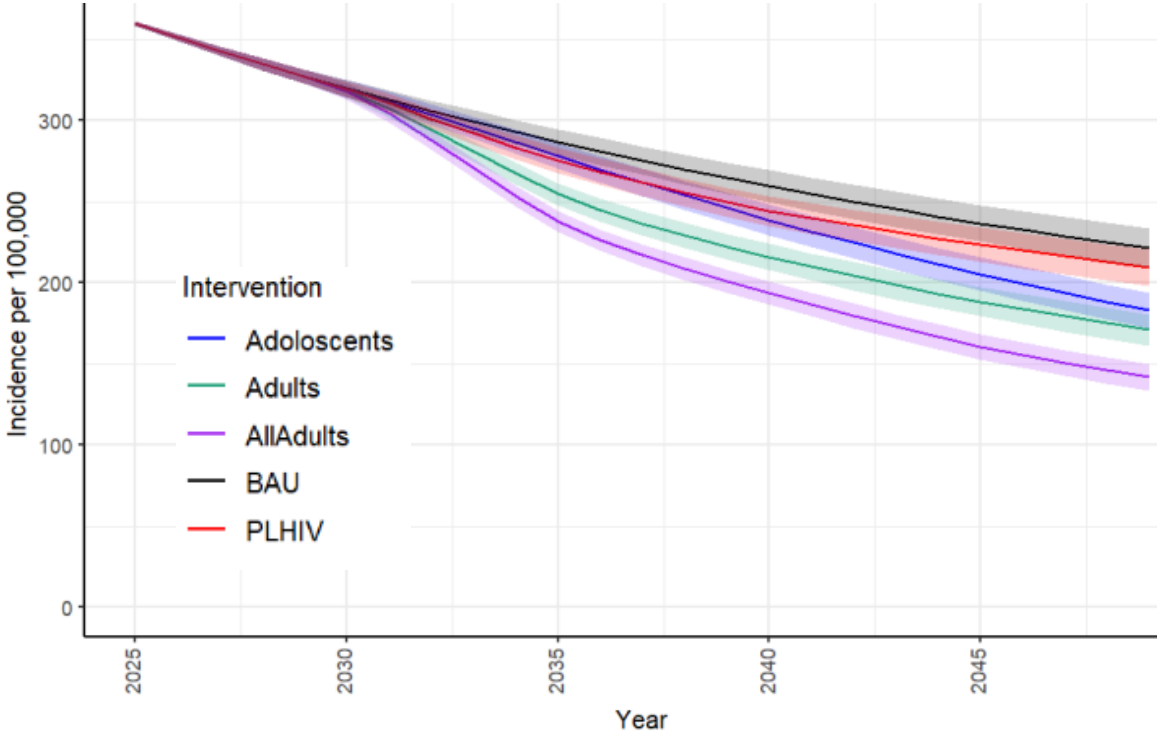
Intervention area	Population targeted	Cost item	Average cost (US$)	Unit
Prevention: TB vaccination	PLHIV in care (18–64 yrs) Adolescents (12–17 yrs) Adults (18–64 yrs; and 15–90 yrs)	**Vaccine cost**	**12.88**	**per course**
		Vaccine introduction	2.40	per course
		Vaccine delivery / administration	2.61	per dose (x2)
		Vaccine product (M72/AS01E)	2.63	per dose (x2)
Symptom screening & testing	**Symptom screening**		**0.74**	**per screen**
	Xpert/NAAT test		**16.82**	**per test**
Treatment initiations	Individuals initiating TB treatment	**Drug-susceptible TB (outpatient)**	**128.71**	**per course**
	~5% of treatment initiators	**Drug-resistant TB (in-/out outpatient)**	**5,287.88**	**per course**
	Children with TB	**Paediatric TB treatment**	**100.58**	**per course**

Intervention area	Population targeted	Cost item	Average cost (US$)	Unit
Prevention: TB vaccination	PLHIV in care (18–64 yrs) Adolescents (12–17 yrs) Adults (18–64 yrs; and 15–90 yrs)	**Vaccine cost**	**12.88**	**per course**
		Vaccine introduction	2.40	per course
		Vaccine delivery / administration	2.61	per dose (x2)
		Vaccine product (M72/AS01E)	2.63	per dose (x2)
Symptom screening & testing	Individuals presenting at public facilities	**Symptom screening**	**0.74**	**per screen**
	Approximated from treatment initiations: • Number of diagnoses = treatment initiations ÷ (1.0– %lost to follow-up) • Test-to-Diagnosis (TDR) = 15 in South Africa Number of tests = Number of diagnoses × TDR	**Xpert/NAAT test**	**16.82**	**per test**
Treatment initiations	Individuals initiating TB treatment	**Drug-susceptible TB (outpatient)**	**128.71**	**per course**
	~5% of treatment initiators	**Drug-resistant TB (in-/out outpatient)**	**5,287.88**	**per course**
	Children with TB	**Paediatric TB treatment**	**100.58**	**per course**

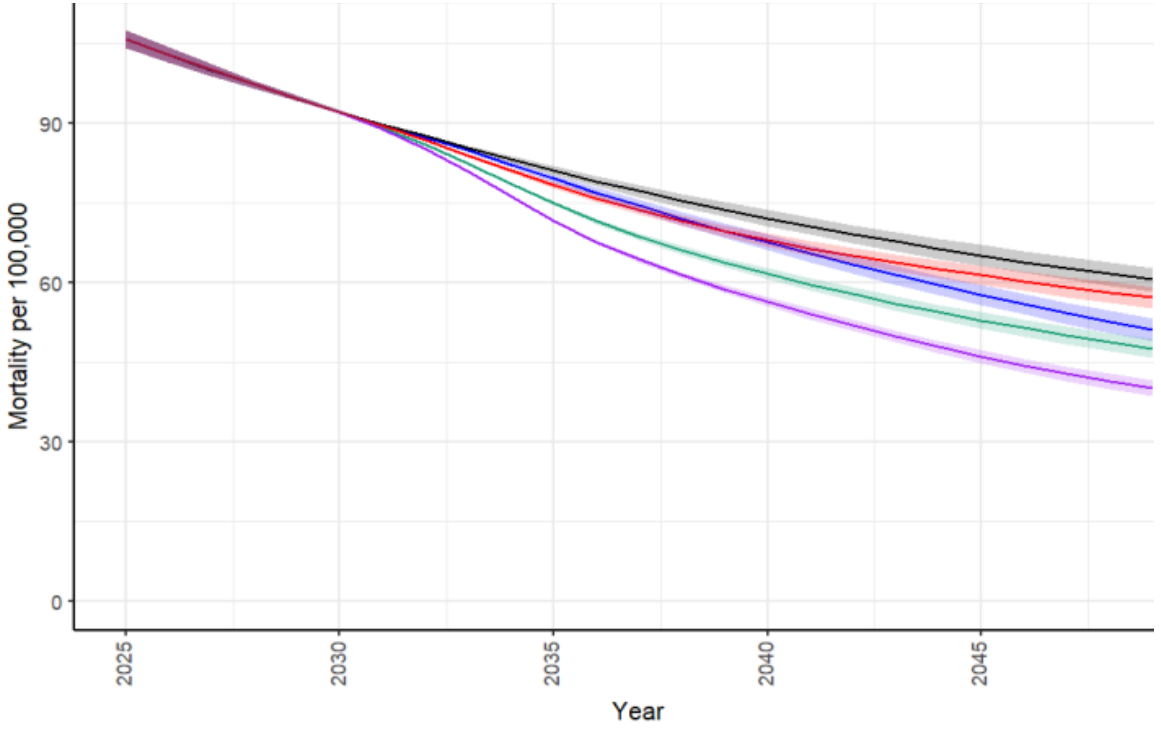
*The cost of current preventative therapy interventions: 3HP=US$22.8; IPT=US$10.75. Source: Health Economics and Epidemiology Research Office

Estimated impact on TB incidence and mortality, 2025-49

Impact on population-level incidence by strategy



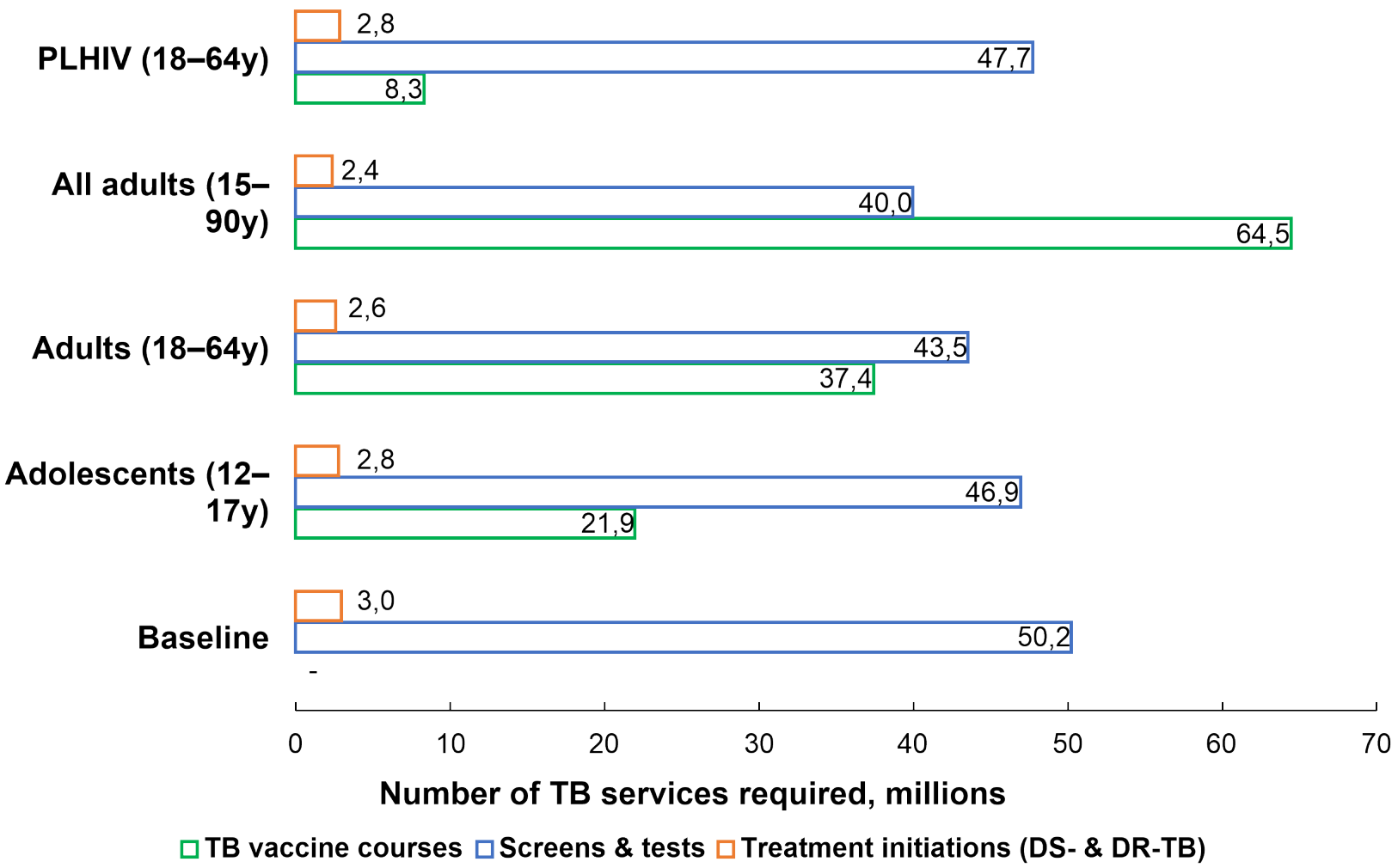
Impact on population-level mortality by strategy



	New TB episodes averted (2030-3049), millions (95%CI)	(Δ%)
--- Baseline (BAU)	3.64 (3.51 – 3.77)	
--- Adolescents (12-17yrs)	0.35 (0.28 – 0.45)	(-10%)
--- Adults (18-64yrs)	0.63(0.52 – 0.79)	(-17%)
--- All Adults (15-90yrs)	1.0 (0.8 – 1.22)	(-27%)
--- PLHIV (18-64yrs)	0.19 (0.14 – 0.22)	(-5%)

	TB deaths averted (2030-3049), millions (95% CI)	(Δ%)
--- Baseline (BAU)	1.02 (1.0 – 1.04)	
--- Adolescents (12-17yrs)	0.07 (0.05 – 0.09)	(-7%)
--- Adults (18-64yrs)	0.13 (0.10 – 0.17)	(-13%)
--- All Adults (15-90yrs)	0.20 (0.176 – 0.19)	(-20%)
--- PLHIV (18-64yrs)	0.05 (0.03 – 0.06)	(-4.6%)

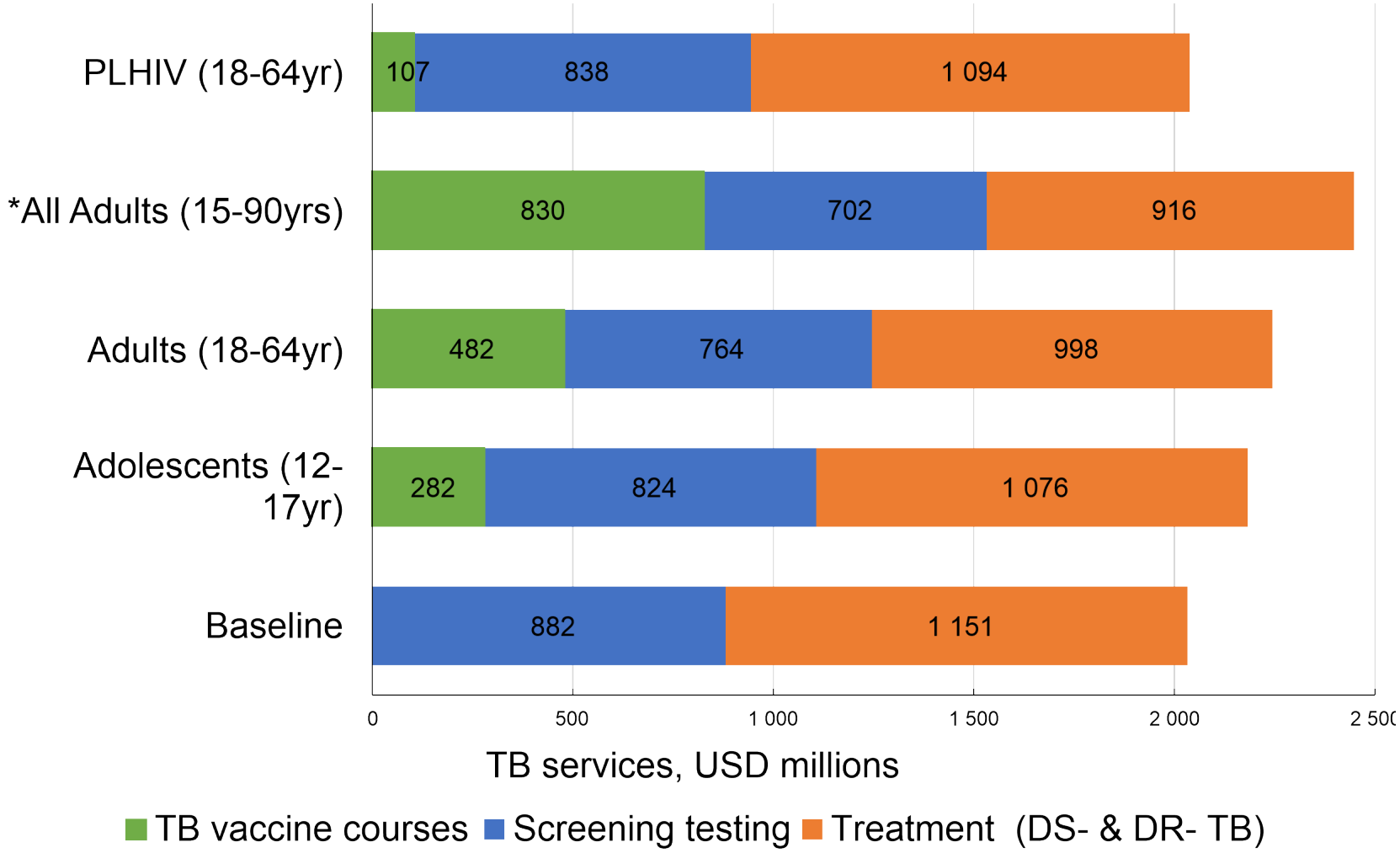
Estimated total number of TB services required, millions, 2030-49



- More vaccines needed when targeting broader groups (adults)
- Greater reductions in downstream TB services (testing and treatment) when targeting broader populations i.e., adults

Total reductions in treatment initiations, thousands	
Adolescents (12-17yr)	↓ 220K
Adults (18-64yr)	↓ 430K
All Adults (15-90yrs)	↓ 670K
PLHIV (18-64yr)	↓ 150K

Estimated budget for TB services required, millions, 2030-49



- Treatment (DS-TB and DR-TB) is the driver of costs
- Greater investment would be required for broader population-targeted vaccination (adults)
- However, downstream testing and treatment costs reduce (relative to the baseline)

Modelling insights: Targeting for maximising impact

Target group	***Insights***
Age: adolescents & adults	❑ Greatest health impact when targeting adolescents and adults. ❑ Vaccinating all ages leads to greater health impact ▪ But, requires more people to be vaccinated (↑ cost).
People living with HIV (PLHIV)	❑ Strategies targeting irrespective of HIV-status may have greater population-level impact. ▪ But, requires more people to be vaccinated (↑ costs). ❑ More efficient and cost-effective to target PLHIV alone than target people without HIV alone. ❑ Vaccinating people without HIV alone may provide indirect benefits to PLHIV.
High risk populations: miners	❑ Venue-based delivery to high-risk groups (i.e. miners and miner-sending community) may improve feasibility and impact.

Some identified gaps in evidence

Epidemiological Impact

- Does infection prevention (e.g., BCG-like) translate to TB morbidity reduction? (longer trials needed)
- How does LTBI status at vaccination affect efficacy/effectiveness?
- What is the safety, efficacy, and protection duration in priority sub-groups (e.g. PLHIV, comorbidities, …)?
- What is the impact of targeting additional priority groups (e.g., healthcare workers, comorbidities, prisons, high-burden regions, …)?
- What is the optimal timing of vaccination to maximise impact?

Implementation Strategies

- What are the feasibility and resource needs for different delivery strategies?
- What is the likely TB vaccine acceptance in various target populations?
- How can TB vaccines be efficiently integrated into existing public health programs/interventions?

Acknowledgement: Zsofia Hesketh

Some identified gaps in evidence

Health Economic Impact

- What are the economic implications of offering vaccines regardless of LTBI status?
- What are the costs of alternative delivery strategies (e.g. out-of-school adolescents, the elderly)?
- How will evolving treatments & preventive therapy affect economic projections (timing of spending, savings, productivity)?
- How do TB vaccines cost and cost-effectiveness compare to existing TB programme interventions: preventive therapy, diagnostics, treatment)?
- Need national TB investment cases that include TB vaccines.

Empirical Data & Modelling

- More local data to inform modelling and decision -making needed.
- More in-country/local-driven modelling needed.
- Need subnational modelling
- Country level costing data needed.

Conclusions

- Mathematical modelling is a valuable tool for informed decision-making in TB vaccine planning.
- Collaboration between NITAGs, policymakers, and modellers is essential for integrating modelling evidence into immunization strategies.
- Adapting models to local contexts is critical for effective vaccine implementation.
- Strengthening data collection is necessary to improve model inputs and accuracy.
- Building local capacity in mathematical modelling will enhance vaccine decision-making and support global TB control efforts.

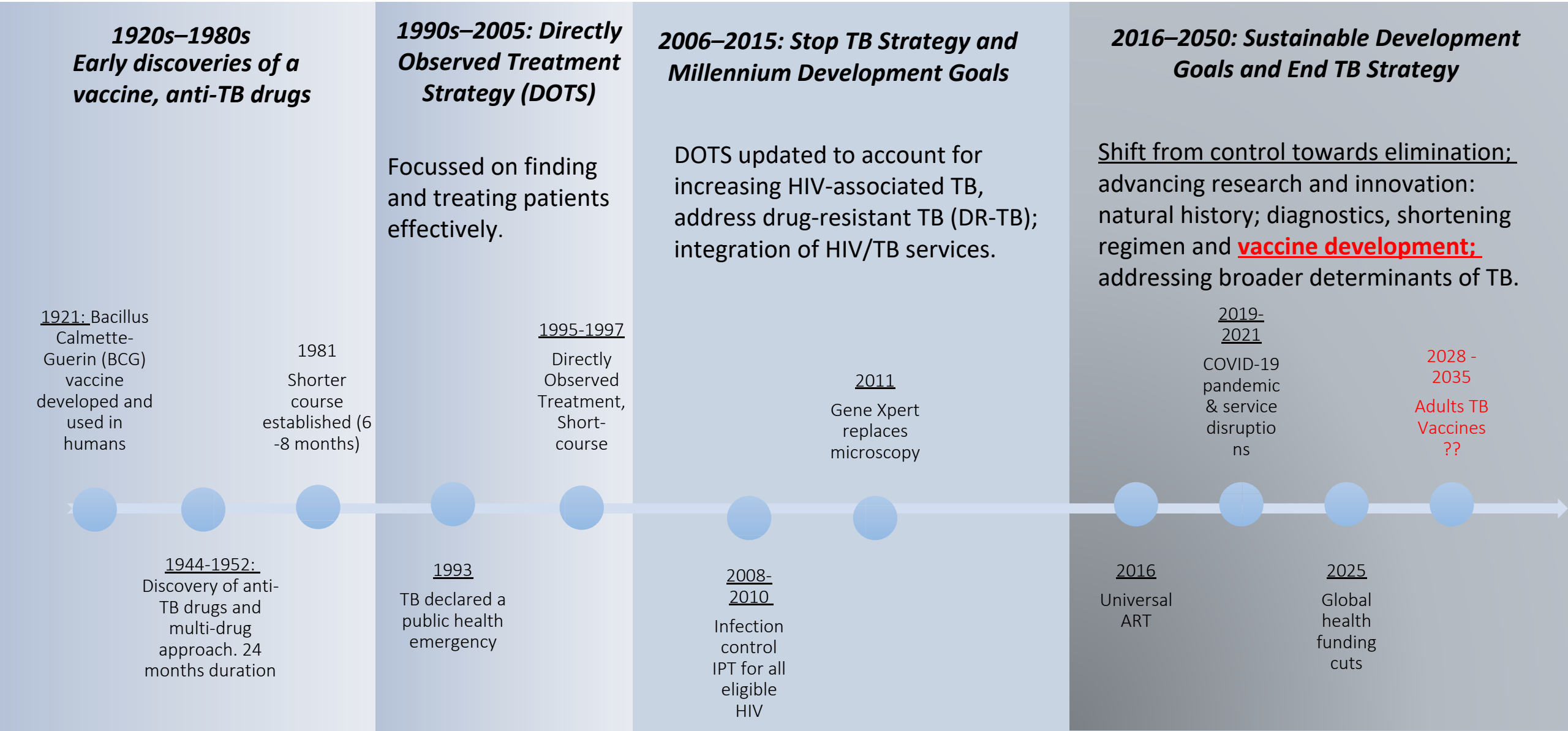
Acknowledgements

- Wellcome Trust
- TIMBER project
- WellMod project

From modelling to policy

- TB vaccines could be
  - Highly impactful and cost-effective in Africa
- Strategic insights
  - Adult/adolescent vaccination → biggest population impact
  - Targeted strategies (e.g., PLHIV) → high efficiency
  - Early and high coverage → critical
- Modelling supports
  - Prioritisation
  - Compare to other programme interventions
  - Investment cases
  - Introduction strategies
- Considerations
  - Integration with HIV programs
  - Health system constraints
  - Financing and donor alignment
  - Data needs for country-specific modelling

Intervention (from most cost-effective to least cost effective	**Incremental cost-effectiveness ratio Cost/LYS (USD)**
Testing for symptomatic: 3.7 million Xpert tests	*cost saving*
TPT for PLHIV on ART: 0.065 million IPT initiations; 0.35 million 3HP initiations	*cost saving*
Symptom screening for household contacts 0.25 million screens	12
Reduce ILTFU by 42%	13
TUTT for household contacts: 0.25 million Xpert tests	84
TPT for household contacts: 0.02 IPT million initiations, 0.10 3HP million initiations	106
TUTT for previous TB irrespective of symptoms 0.34 million Xpert tests	255
Door-to-door symptom 5 million symptom screens	312
Culture testing for PLHIV 0.9 million culture tests	703
TUTT for PLHIV on ART 3.2 million Xpert tests	2,100
digital chest X-ray screening 0.49 million screens	2,933

Kubjane M, Jamieson L, Hirasen K, Coetzee L, Ramushu C, Evans D, Naidoo P, Johnson L, Meyer-Rath G. Preprint. 2026

Evolution of TB control and response eras - an effective TB vaccine is needed!