Rationale for using modelling to inform future TB vaccine introductions

WHO National Immunisation Technical and Advisory Group Support Hub webinar,
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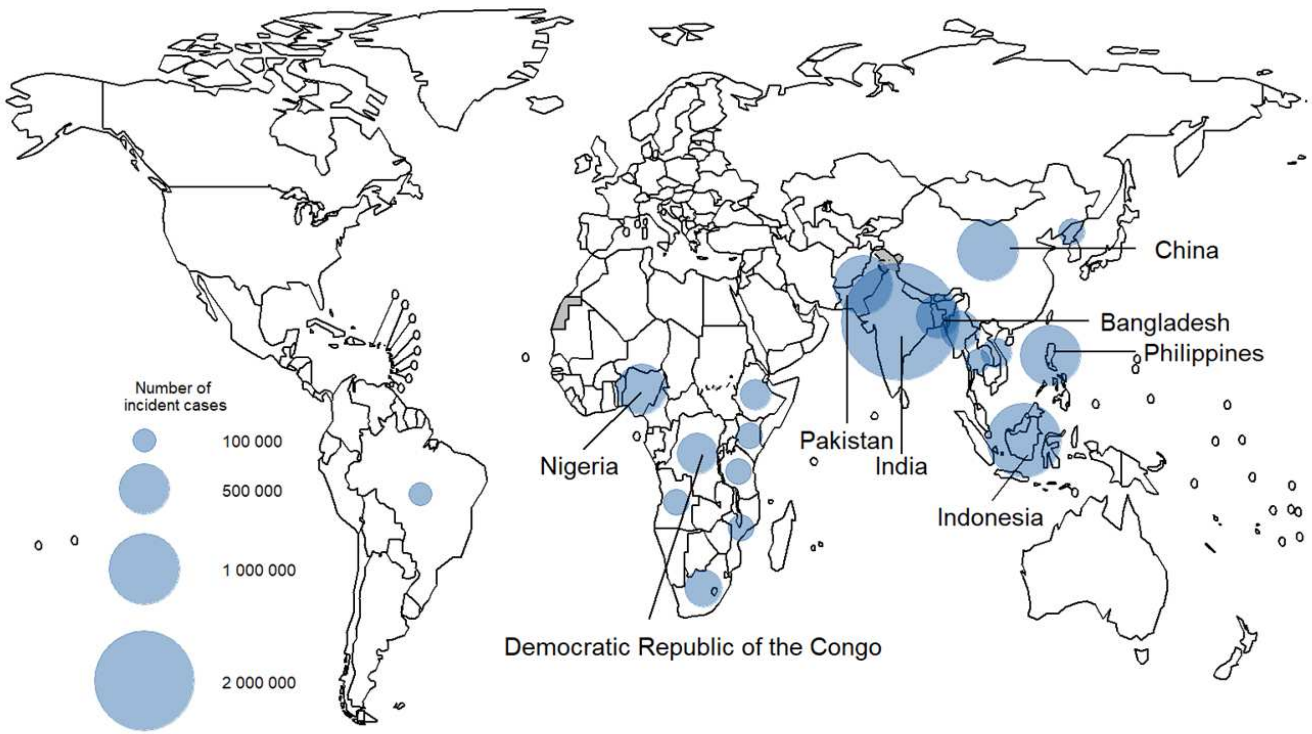
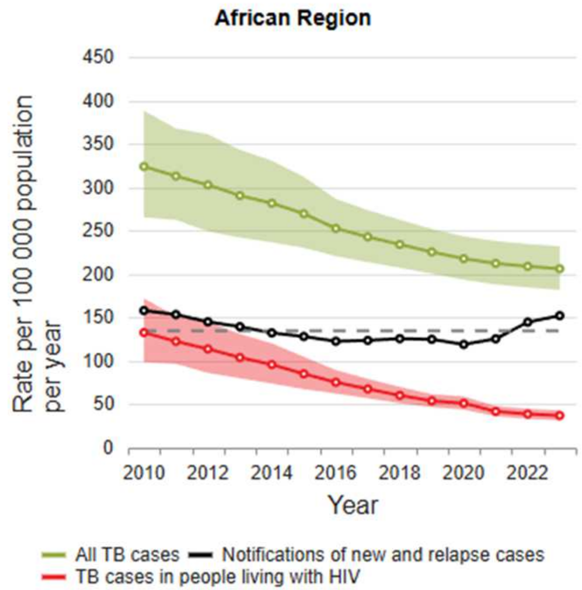
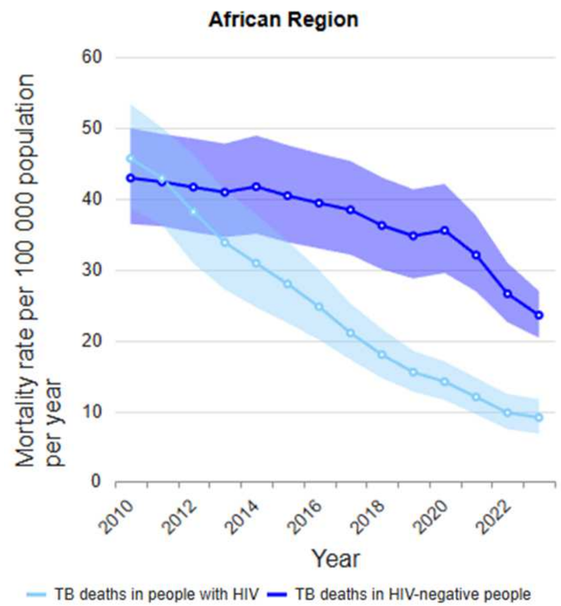
Background

➢ Globally, 10.1 million fell ill with TB in 2023; 1.25 million died.



WHO TB Report, 2023





Background

- Control strategies over time, pre 1980s

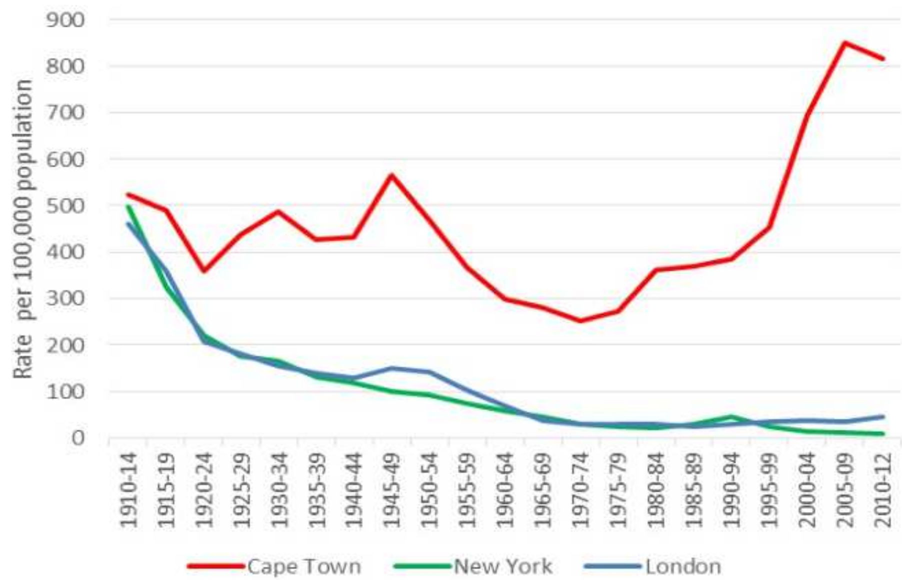
1882
Bacillus identified

1921
Bacillus Calmette-Guerin (BCG) vaccine developed and used in humans

1944-1952
Discovery of anti-TB drugs and multi-drug approach. 24 months duration

1981
Shorter course established (6-8 months)

TB notification rates over time, cities in the northern vs. southern hemisphere



Hermans et al, Plos One. 2015

Evolution of TB control and response eras

1994–2005: Directly Observed Treatment Strategy (DOTS)

Focussed on finding and treating patients effectively.

2006–2015: Stop TB Strategy and Millennium Development Goals

DOTS updated to account for increasing HIV-associated TB, address drug-resistant TB (DR-TB); integration of HIV/TB services.

2016–2050: Sustainable Development Goals and End TB Strategy

Shift from control towards elimination; advancing research and innovation: natural history; diagnostics, shortening regimen and **vaccine development;** addressing broader determinants of TB.

1993
TB declared a public health emergency

1995-1997
DOTS strategy adopted; National TB

2008-2010
Infection control IPT for all eligible HIV irrespecstive of TST

2011
Gene Xpert replaces microscopy

2016
Universal ART

2019-2021
COVID-19 pandemic & service disruptions

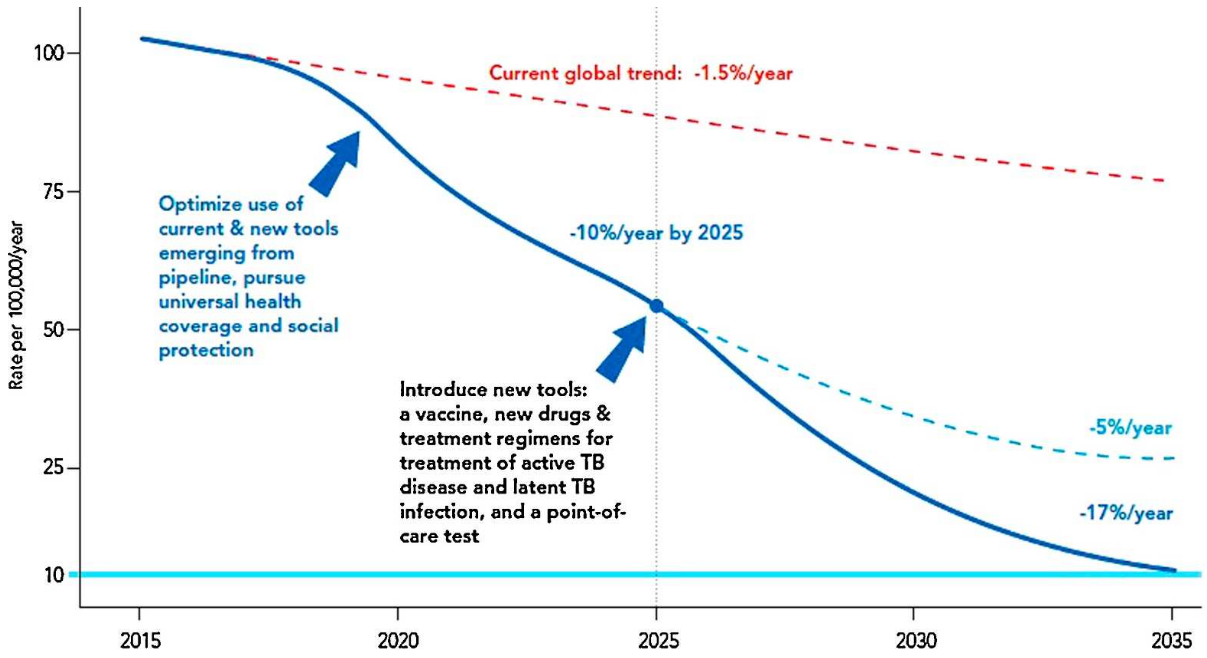
2025
Global health funding cuts

Evolution of TB control and response eras

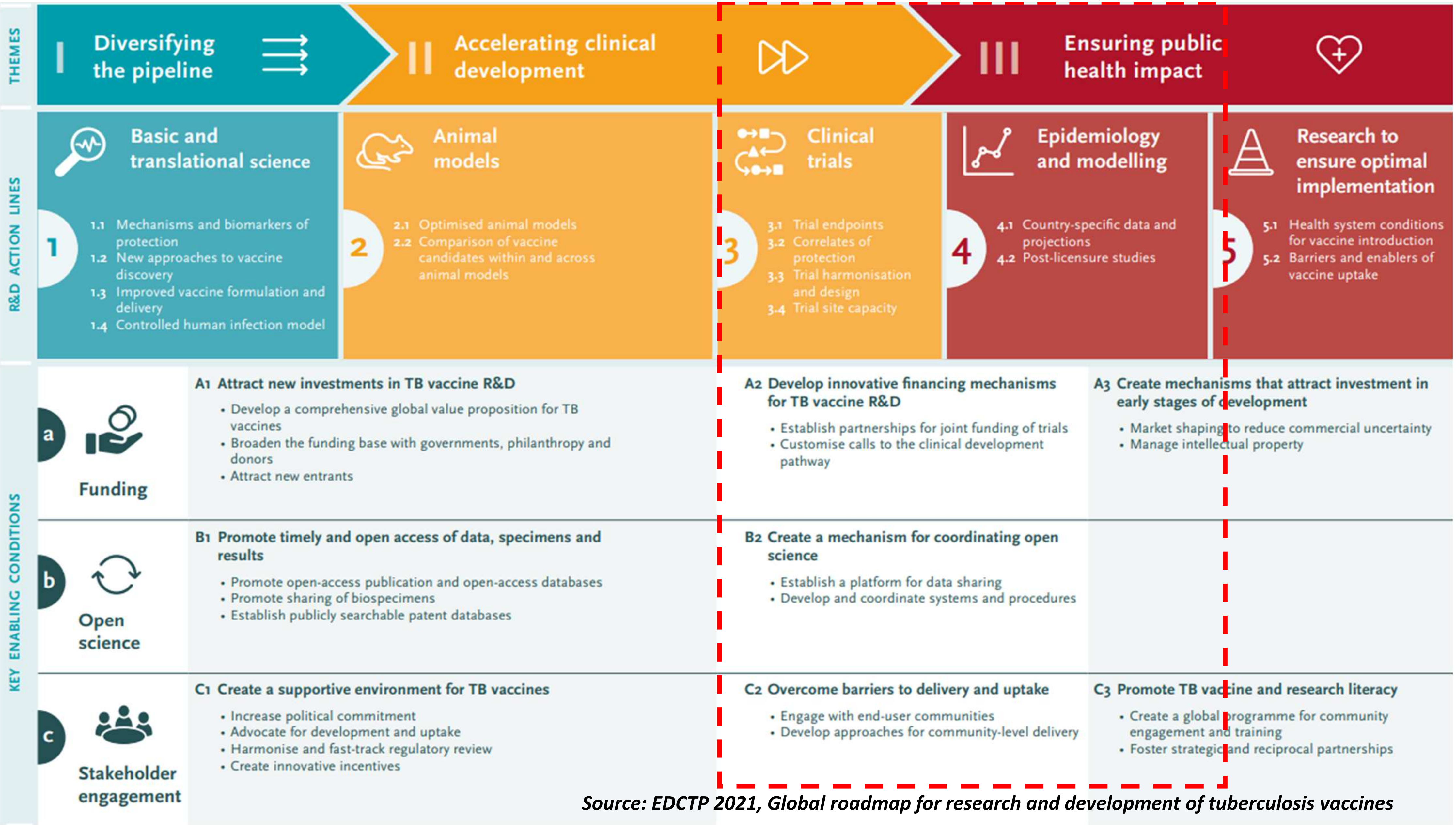
End TB targets

	MILESTONES 2020	MILESTONES 2025	TARGETS SDG* 2030	TARGETS END TB 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



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



Source: EDCTP 2021, Global roadmap for research and development of tuberculosis vaccines

TB Vaccine Pipeline

TB vaccine candidates in active clinical trials

There are 12 candidates in active clinical trials as of September 2024.

Platform

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

Trial target population

	Elderly
	Adults
	Adolescents
	Children
	Infants
+	People living with 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

Phase 1

BNT164a1
BioNTech
Sf

BNT164b1
BioNTech
Sf

TB/FLU-05E
Res Inst of Influenza
Sf

H107/CAF10b
SSI
Sf *-Mtb* *+Mtb*

Phase 2a

AEC/BC02
Anhui Zhifei Longcom
Sf *+Mtb*

MTBVAC
HVTN
Sf *Im* + -

Phase 2b

RUTI®
Archivel Farma
Thp *aTBd* *MDR*

Phase 3

BCG (traveler vaccine)
HJF
POI *-Mtb*

GamTBvac
Gamaleya Res Centre
POD *-Mtb*

MTBVAC
Biofabri
POD

Immuvac (MIP)
ICMR
POD

VPM1002
SIIPL
POD
POI
POR *cTB*

M72/AS01E
Gates MRI
POD *+-Mtb* *+Mtb* +

StopTB Partnership
WORKING GROUP ON NEW TB VACCINES

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

Institutions listed are the trial sponsors

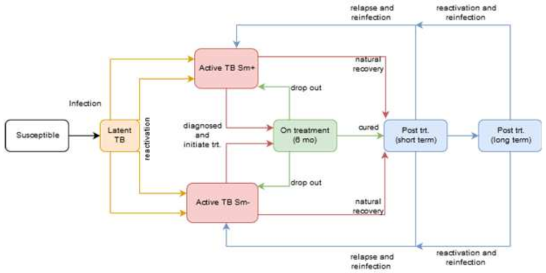
Additional information about each candidate can be accessed via the QR code or at newtbvaccines.org/tb-vaccine-pipeline/

Last update: 2 September 2024

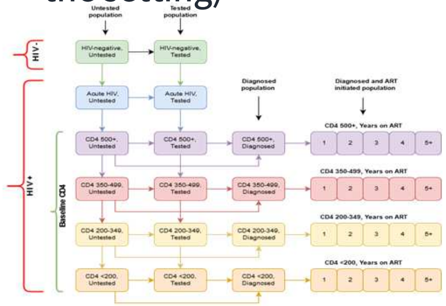
Mathematical modelling

TB model

TB natural history



HIV natural history (important co-morbidities for the setting)



Country specific model inputs: Demographic and epidemiological

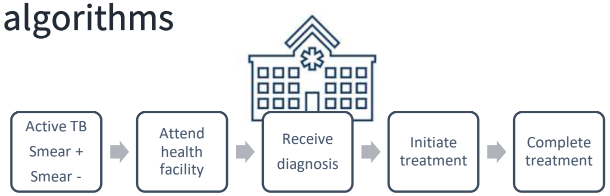
- **Demographic data**
  Age, sex-structures
- **Effects of risk factors/interventions**
- **Epidemiological parameters**

Calibration to local data

- TB treatment initiations
- TB deaths from the vital register
- Microbiological tests
- TB prevalence

Transmission dynamics – age & sex social mixing

TB care cascade and diagnostic algorithms



Stakeholder and expert inputs

Mathematical modelling

Target population	• The population group prioritised for the vaccine e.g., elderly, adolescents, adults; HIV positive/negative
Implementation strategy	• How the vaccine will be rolled out • What % of target population should receive it • How to integrate the vaccine program in health system
Population health impact	• Estimate and predict the future population-level health related outcomes (e.g., incidence, mortality,) as a result of the vaccine
Cost effectiveness	• What is the cost of implementing the vaccine programme in relation to changes in health outcomes. • What is the optimal combination of TB interventions (the vaccine, preventative therapy, screening, diagnostic, treatment regimen)

Recent TB vaccine modelling studies

Science Translational Medicine Current Issue First rele

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RESEARCH ARTICLE | TUBERCULOSIS

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

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

ARTICLES · Volume 11, Issue 4, E546-E555, April 2023 · Open Access Download Full Issue

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

Rebecca A Clark, MSc [a,b,c,d] · Christinah Mukandavire, PhD [a,b,c] · Allison Portnoy, ScD [e] · Chathika K Weerasuriya, PhD [a,b,c] · Arminder Deol, PhD [a,b,c] · Danny Scarponi, PhD [a,b,c] · Andrew Iskauskas, PhD [g] · Roel Bakker, PhD [a,b,c,h] · Matthew Quaife, PhD [a,b,c] · Shelly Malhotra, MA [i] · Nebiat Gebreselassie, PhD [j] · Matteo Zignol, MD [j] · Raymond C W Hutubessy, PhD [k] · Birgitte Giersing, PhD [l] · Mark Jit, PhD [b,c] · Rebecca C Harris, PhD [a,b,c,m] · Nicolas A Menzies, PhD [e,f] · Richard G White, PhD [a,b,c]

EPIDEMIOLOGY AND SOCIAL

The potential impact of new tuberculosis vaccines on the burden of tuberculosis in people with HIV in South Africa

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]

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

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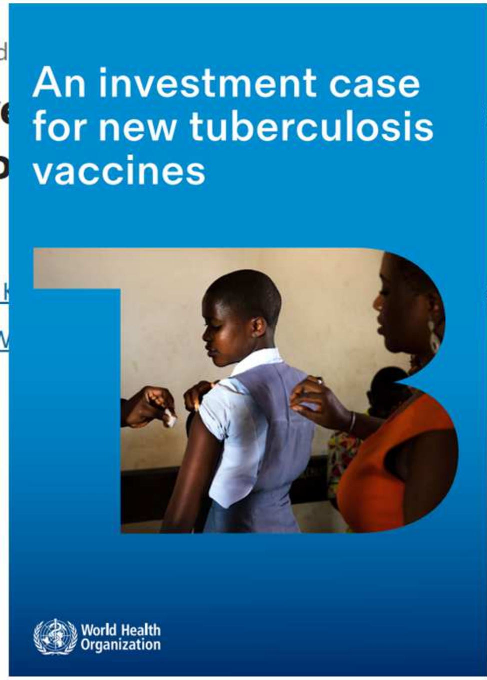
Feasibility of nove … cination in South Africa: a co … dget impact analysis

Sahan Jayawardana, Chathika K … ebecca C. Harris, Michele Tameris, Dereck Tait, Richard G. W

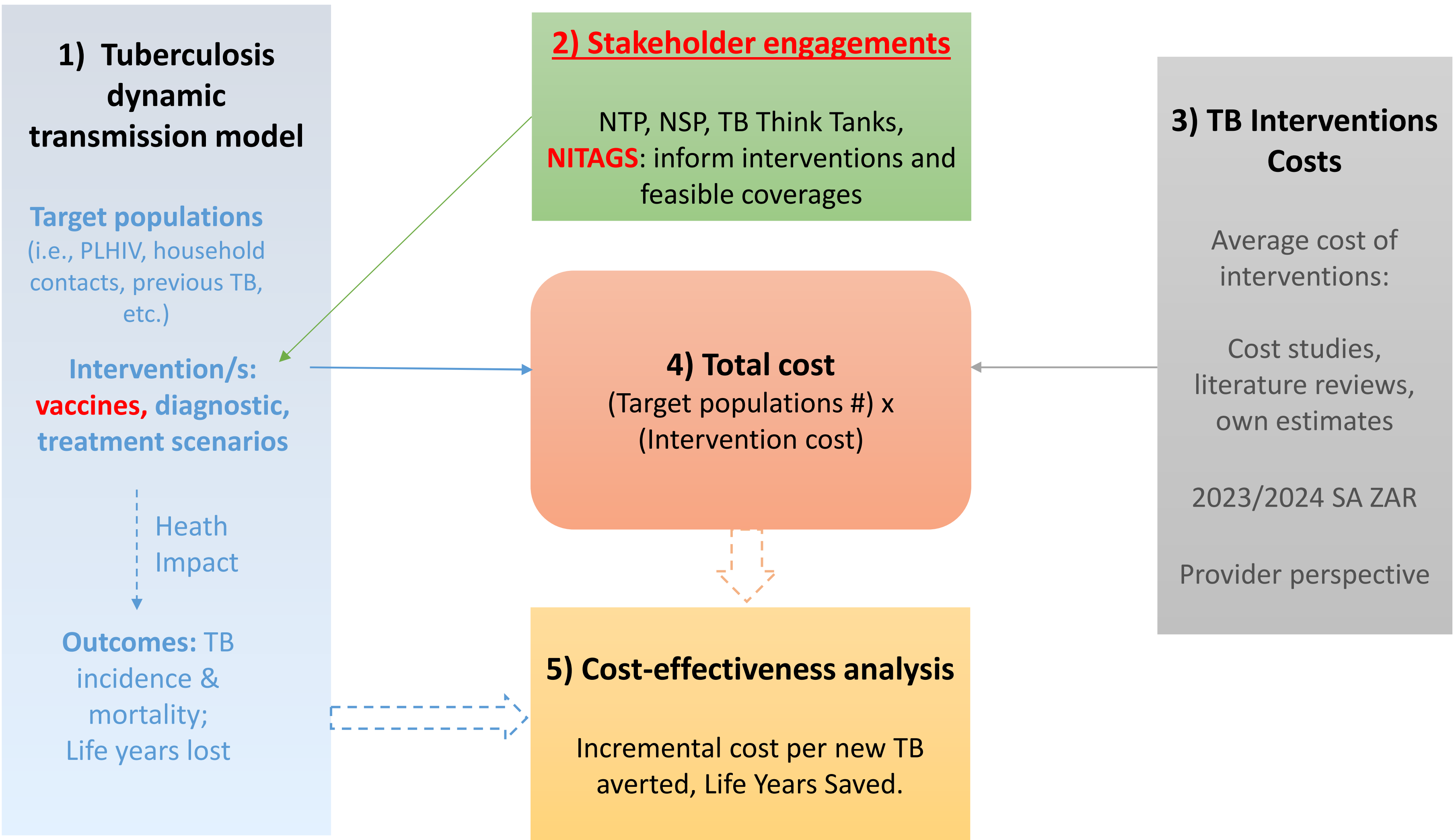


Model-based impact evaluation of new tuberculosis vaccines in aging populations under different modeling scenarios: the case of China

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

Case study of using mathematical modelling to inform TB national planning

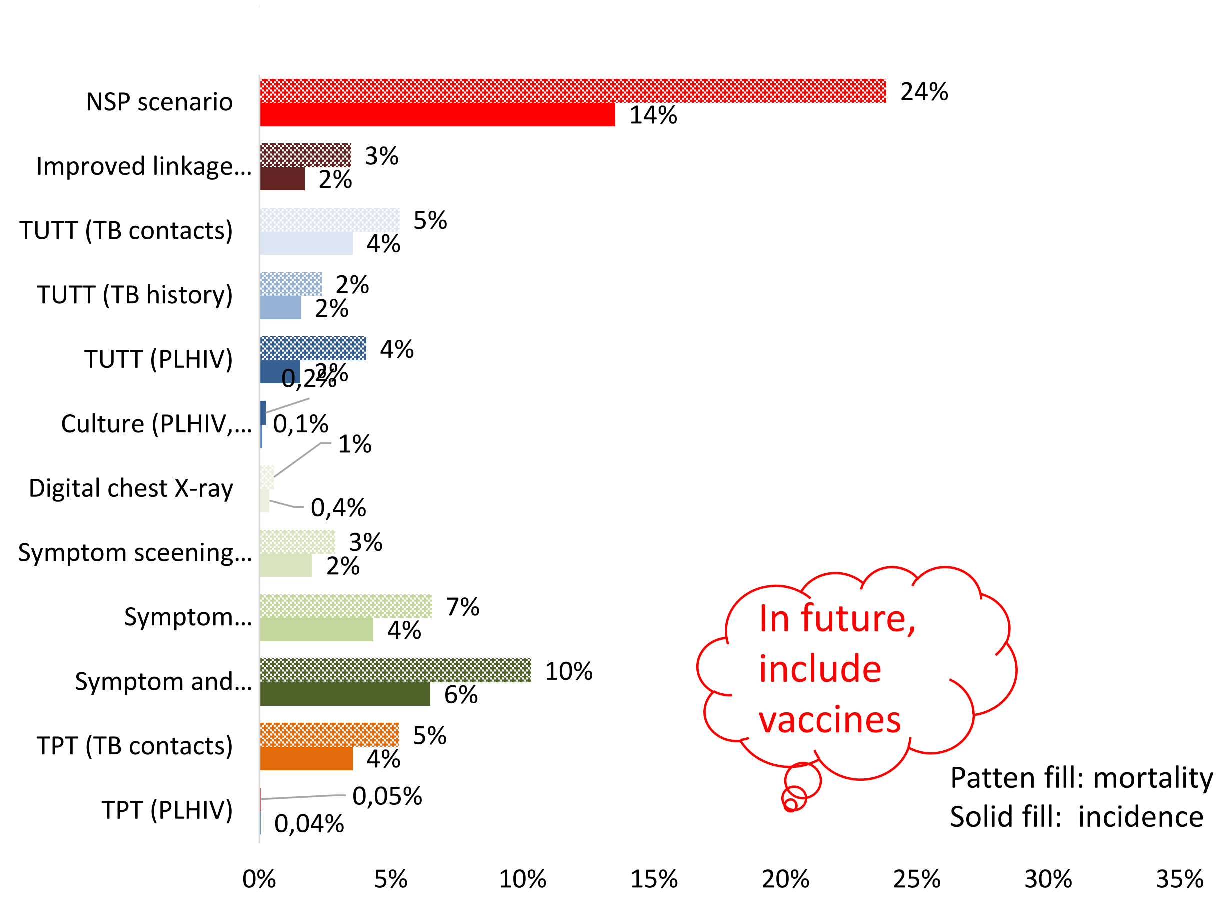
Estimating TB programme costs and health impact

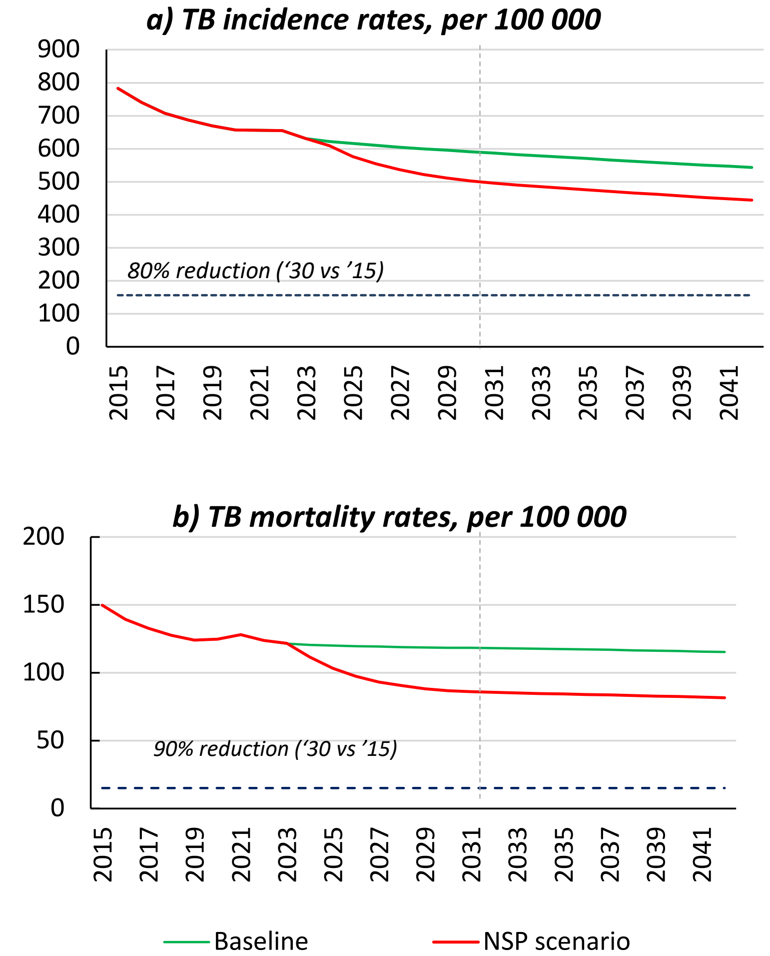


Health Economics & Epidemiology Research Office, 2023 Kubjane M, Jamieson L, Hirasen K, Coetzee L, Ramushu C, Evans D, Naidoo P, Johnson L, Meyer-Rath G

Projected impact of TB interventions under National Strategic Plans, South Africa

Percent reductions in TB incidence and mortality due to interventions, (2023-2042)





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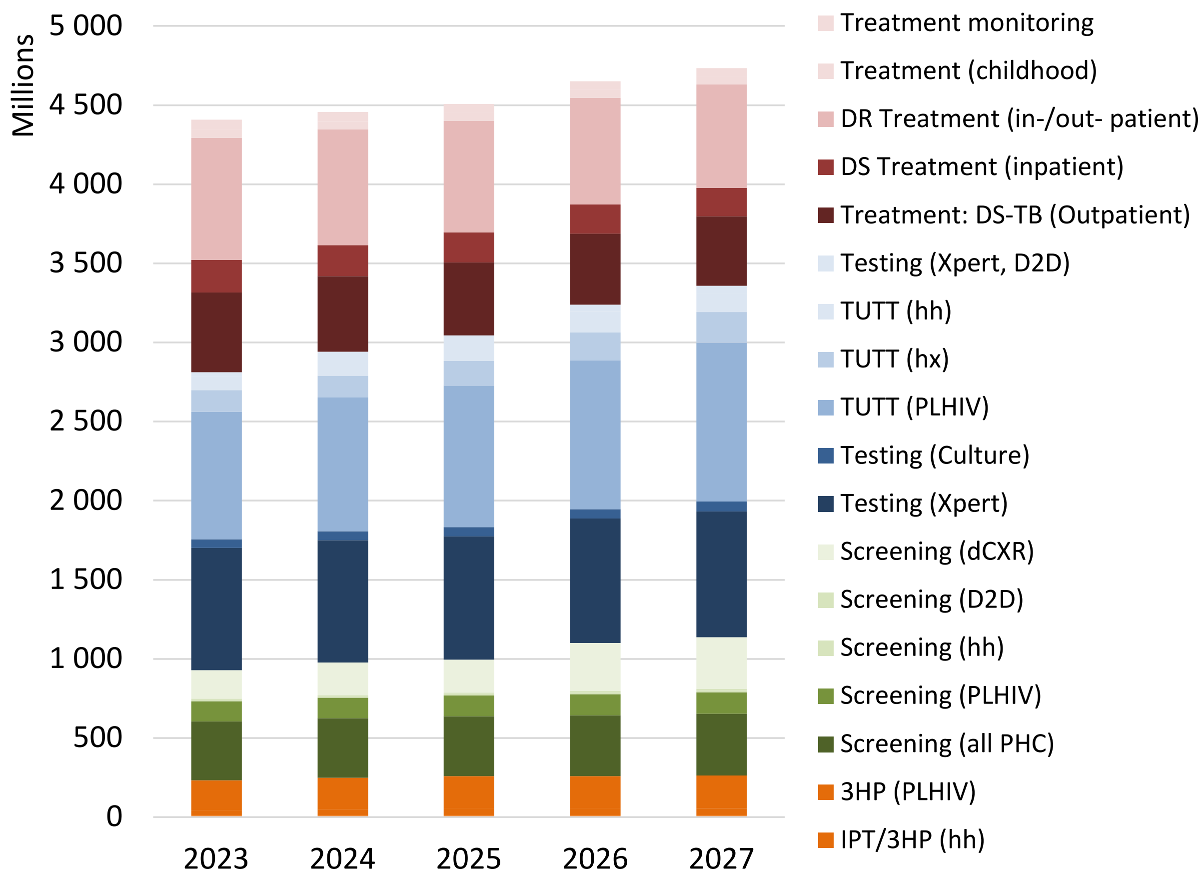

- R4.4-R4.7 B/year; R22.8 B over 2023-2027
- Testing and Treatment driver of costs

Interventions (average coverage per year) – from most cost-effective to least cost-effective	**Cost/LYS (2021/2022 ZAR)**
Symptom (38 million screens) and Xpert (3.9 million tests)	2160
TUTT for TB contacts (+0.49 million Xpert tests)	2 385
Symptom screening for TB contacts (+0.49 million screens)	2 446
Improved linkage to treatment (reduce ILTFU by 50%)	2 505
TPT for TB contacts (0.23 million initiated)	3 900
TUTT for those with TB history (+0.37 million Xpert tests)	5 400
Door-to-door symptom screening (5.8 million screens)	7575
TUTT for PLHIV (+3.7 million Xpert tests)	20 970
Culture testing for PLHIV with negative result on Xpert (0.67 million)	40 095
Door-to-door screening with digital chest X-ray (0.55 million)	67 200
TPT for PLHIV (0.41 million initiated)	133 732
NSP scenario: all individual interventions above combined	8 855

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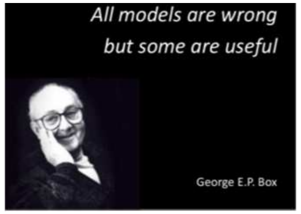
Conclusions



- 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 deployment.
- Strengthening data collection is necessary to improve model inputs and accuracy.
- Building capacity in mathematical modelling will enhance vaccine decision-making and support global TB control efforts.