Advancing evidence-informed in-country decision-making for new TB vaccine introduction: A responsive and integrated vaccine modelling approach from India

Jessy Joseph, IAVI

10th October 2024

Presentation outline

- Country context for evidence need
- National modelling efforts and value addition
- Demonstration of model outputs and way forward

Partners and donors

ICMR NIRT — Indian Council of Medical Research | National Institute for Research in Tuberculosis

World Health Organization

iavi

thsti — ट्रांसलेशनल स्वास्थ्य विज्ञान एवं प्रौद्योगिकी संस्थान

Ministry of Health & Family Welfare
Government of India

Central Tuberculosis Division
National Tuberculosis Elimination Programme
राष्ट्रीय तपेदिक उन्मूलन कार्यक्रम

birac

KnIT — Knowledge Integration and Translational Platform
Evidence for health policy

Grand Challenges India

Gates Ventures

A lot is being done……………………………

ORIGINAL ARTICLE

Estimating the Burden of Tuberculosis in India: A Modelling Study

Mandal, Sandip; Rao, Raghuram[1]; Joshi, Rajendra[1]

Author Information

Indian Journal of Community Medicine 48(3):p 436-442, May
10.4103/ijcm_160_23

Emergence of drug resistance in patients with tuberculosis cared for by the Indian health-care system: a dynamic modelling study

Stephanie Law, Amy S Piatek, Cheri Vincent, Olivia Oxlade, Dick Menzies**

SCIENTIFIC REPORTS

OPEN

Modelling the impact of effective private provider engagement on tuberculosis control in urban India

Received: 23 May 2018
Accepted: 31 January 2019
Published online: 07 March 2019

Nimalan Arinaminpathy[1], Sarang Deo[2], Simrita Singh[2], Sunil Khaparde[3], Raghuram Rao[3], Bhavin Vadera[3], Niraj Kulshrestha[3], Devesh Gupta[3], Kiran Rade[4], Sreenivas Achuthan Nair[5] & Puneet Dewan[6]

BMC Medicine

RESEARCH ARTICLE Open Access

New tuberculosis vaccines in India: modelling the potential health and economic impacts of adolescent/adult vaccination with M72/AS01$_E$ and BCG-revaccination

Rebecca A. Clark[1,2,3,4*], Chathika K. Weerasuriya[1,2,3], Allison Portnoy[5,6], Christinah Mukandavire[1,2,3], Matthew Quaife[1,2,3], Roel Bakker[1,2,3,7], Danny Scarponi[1,2,3], Rebecca C. Harris[1,2,3,8], Kirankumar Rade[9], Sanjay Kumar Mattoo[10], Dheeraj Tumu[9,10], Nicolas A. Menzies[5,11] and Richard G. White[1,2,3,4]

PA-50

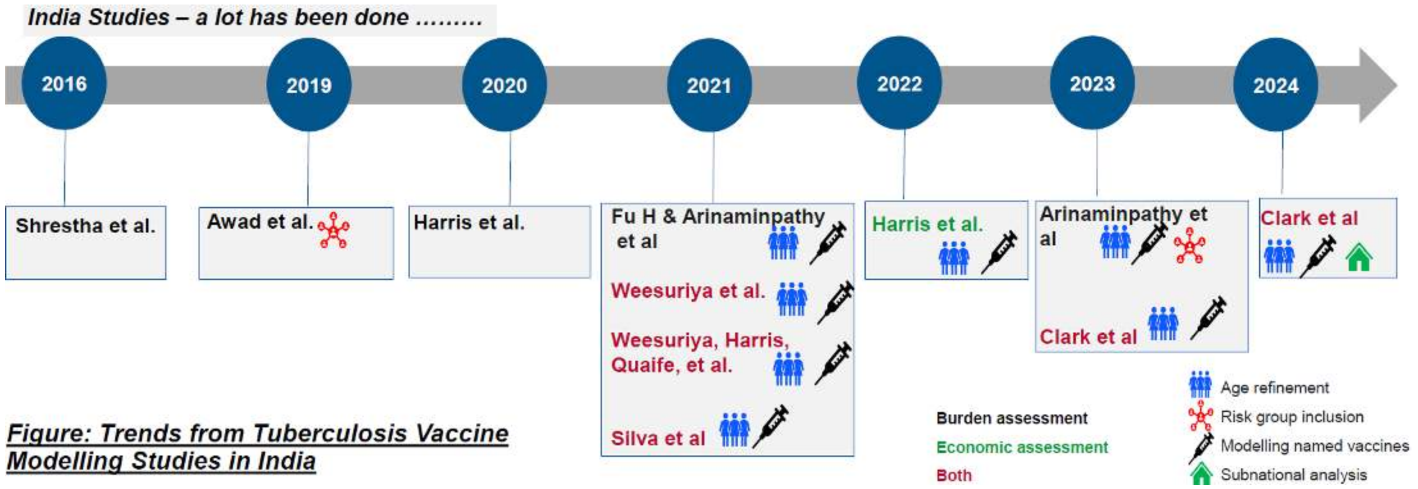
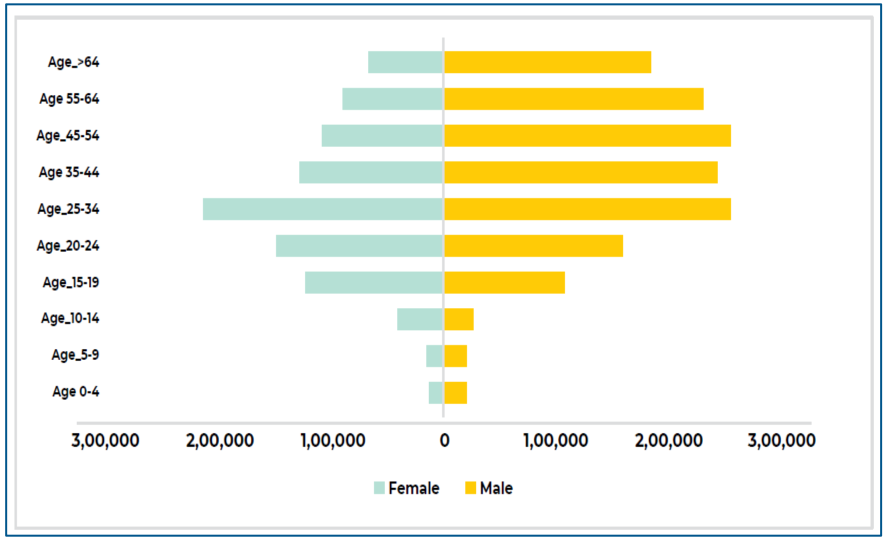


Figure: Trends from Tuberculosis Vaccine Modelling Studies in India

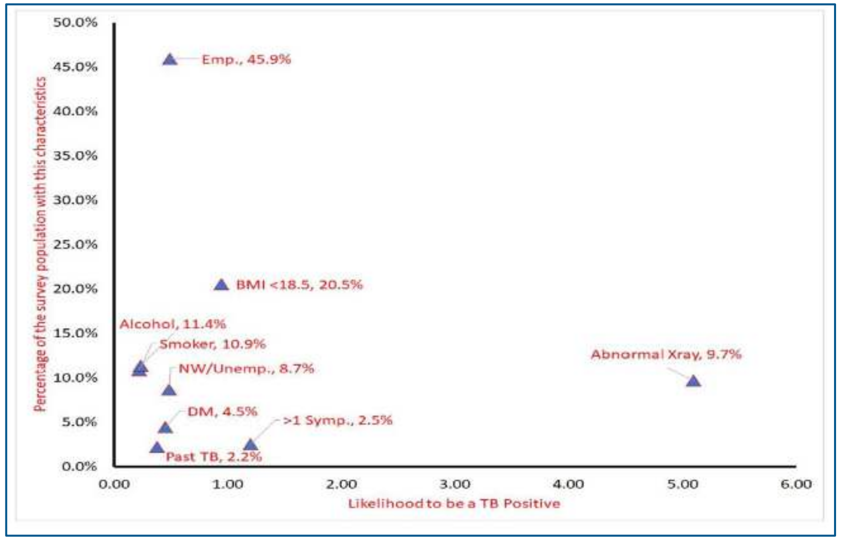
Reinforcing the need for in-country evidence…

Tuberculosis remains a public health crisis in India

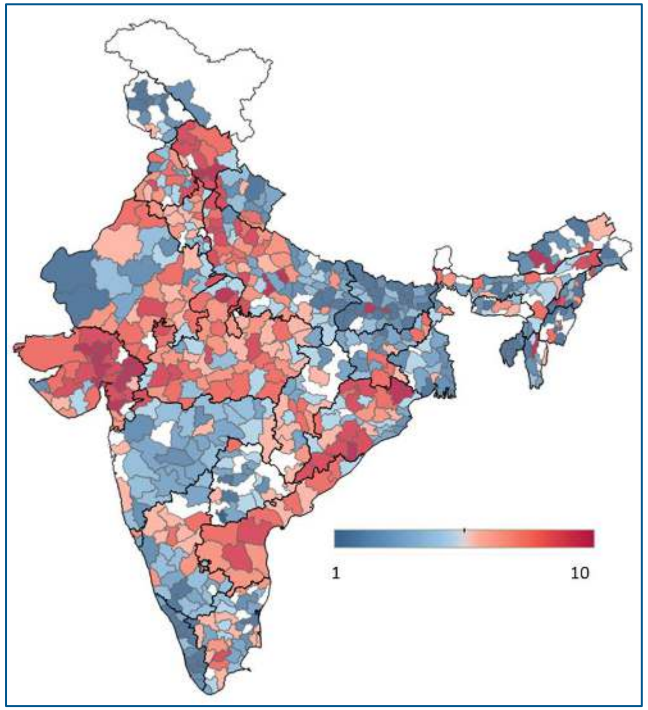
Accounting for about a quarter of the global TB burden with about 2.7 million cases and 0.3 million deaths estimated in 2022



Age-sex distribution in TB case notifications (2022); India TB report 2023



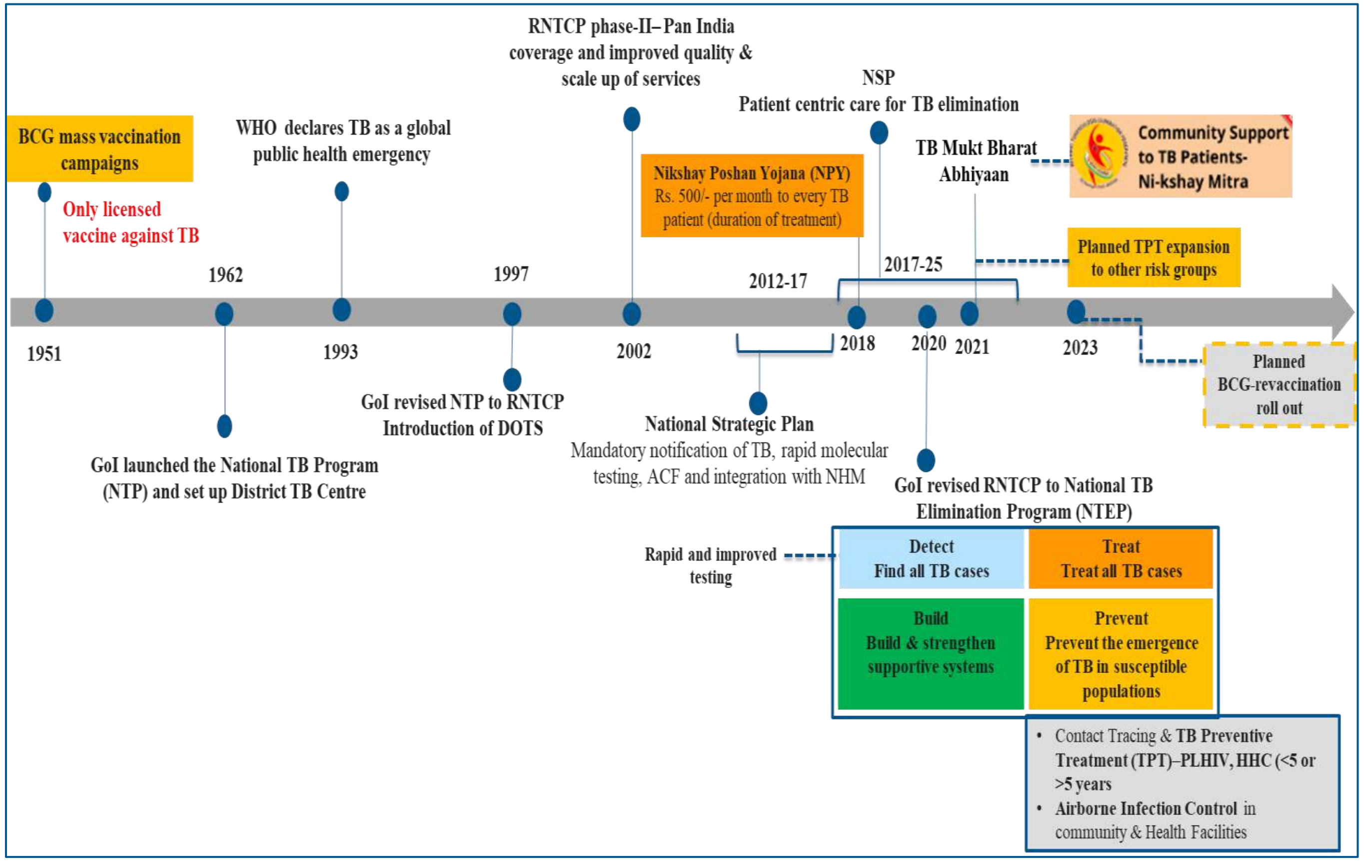
Risk factors associated with TB; National TB prevalence report 2019-21



Sub-national variation based on district wise case notification rate (per lakh population)

Disproportionately high TB burden in India is intermingled with huge variations across age, risk profile, and geographies

India is committed to decrease TB burden in the country with an evolving prevention and management landscape



TB prevention & management landscape in India

Need for innovative tools like vaccines to accelerate fall in TB incidence and achieve the End TB Strategy targets is well recognized

For three potential vaccines entering late-stage trial, the **Government Of India** is expected to make critical decisions on development, introduction, and delivery in the **next 2-3 years - focussing on "Make In India" products**

With new TB vaccines in late-stage clinical development, timely evidence enables a state of readiness for new TB vaccine roll-out

iavi

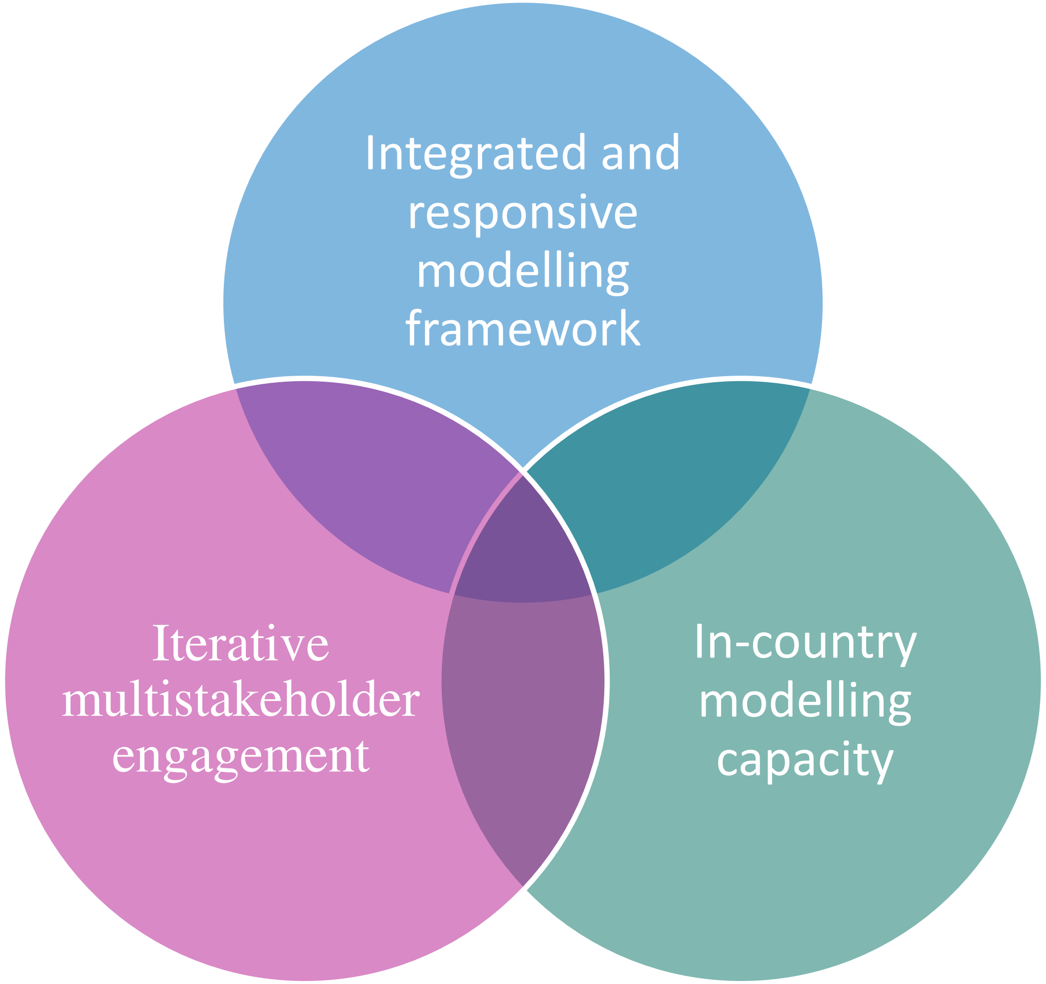
Target population	Vaccine Delivery scenarios	Resource availability
• Disease epidemiology • Geographical variation	• Disease management *(preventive)* landscape • Vaccine Pipeline • Health system considerations	• Programmatic costs of vaccine introduction • Disease management costs • Program integration pathways

Pathways for maximal impact

In-country vaccine mathematical modelling effort in India

How are we adding value?

Fostering an ecosystem within the country for model-based decision-making

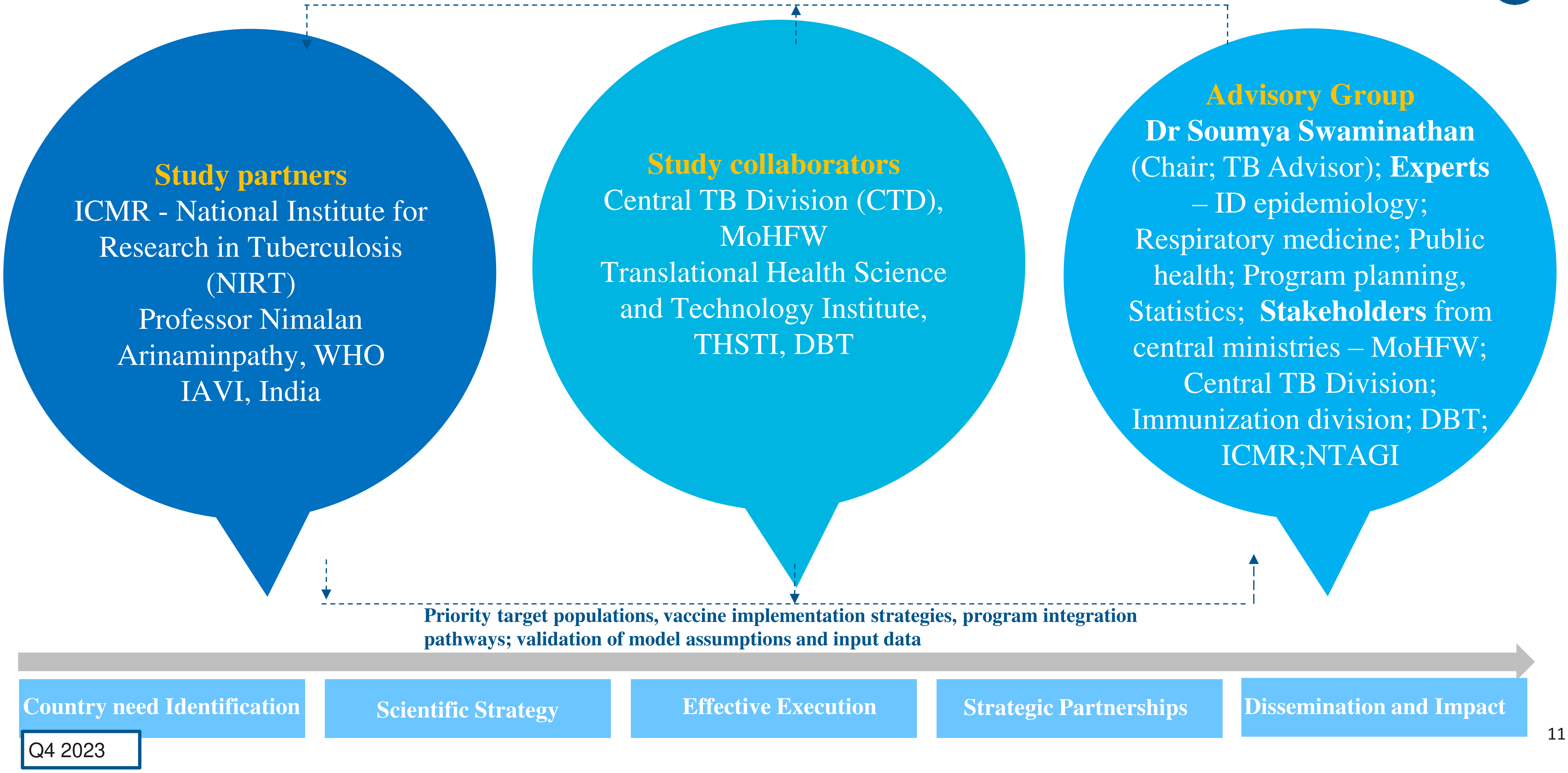


Potential health impact

Potential programmatic cost and cost-effectiveness analysis

Potential impact on equity

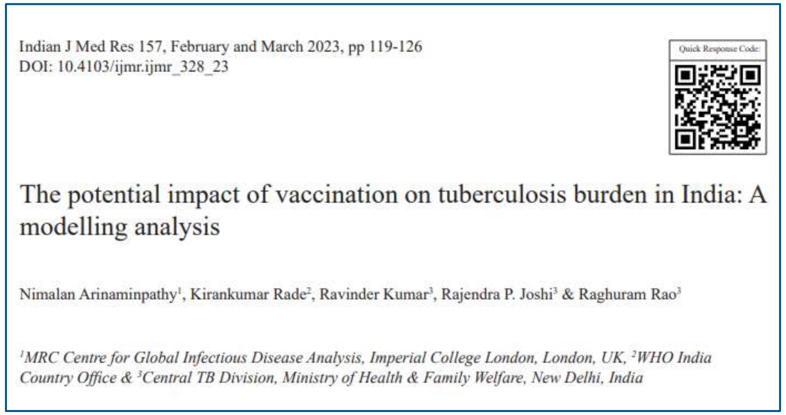
Iterative multistakeholder engagement…



In-country modelling capacity….

TBI-MIG ("TB India – Modelling Interest Group) led by Prof Nimalan – in-country capacity strengthening in infectious disease modelling

Integrated and responsive modelling framework…


Indian J Med Res 157, February and March 2023, pp 119-126
DOI: 10.4103/ijmr.ijmr_328_23

Quick Response Code:

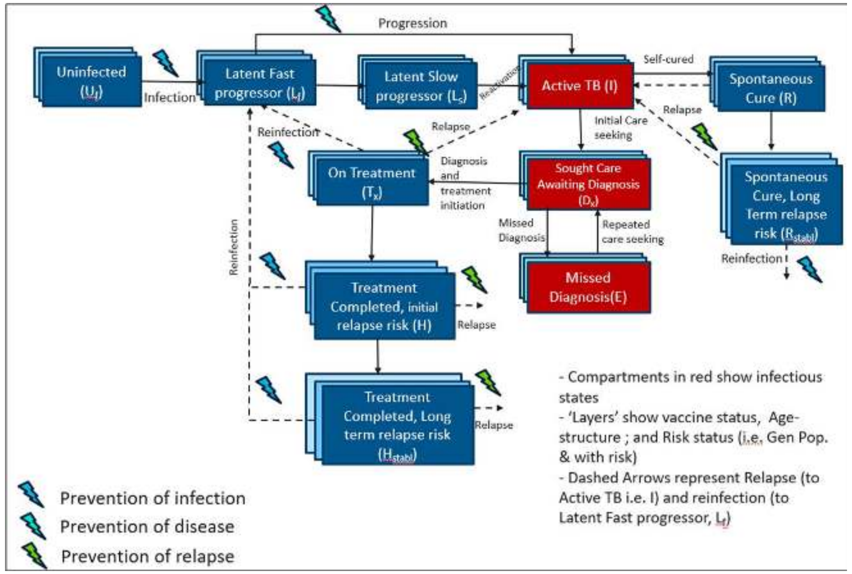
The potential impact of vaccination on tuberculosis burden in India: A modelling analysis

Nimalan Arinaminpathy[1], Kirankumar Rade[2], Ravinder Kumar[3], Rajendra P. Joshi[3] & Raghuram Rao[3]

[1]MRC Centre for Global Infectious Disease Analysis, Imperial College London, London, UK, [2]WHO India Country Office & [3]Central TB Division, Ministry of Health & Family Welfare, New Delhi, India

Compartmental deterministic model of TB in India - Arinaminpathy in collaboration with Central TB Division (CTD), India

Incorporates
- Risk status along with age-structure and vaccine status
- Reinfection and relapse status
- Allows capturing impact of post-treatment vaccine intervention and combination of preventive interventions along with POI and POD vaccine



Target population
- General population
- Age-groups
- High-risk groups: Under nutrition, DM, Smoking, Alcohol Status, pats history of TB, elderly, PLHIV, HHC

Preventive Interventions

Vaccination -
- POI
- POD
- POR

Other preventive strategies -
- TPT, nutrition supplementation, AIC

Delivery scenarios
- Mass campaign
- Routine immunization
- Targeted approach

Cost consideration
- Program and patient (Disease and vaccine introduction)

Timeline for roll-out - roll-out in 2025, yearly impact estimated over 25 years

Sensitivity analysis –
- Vaccine efficacy (min 35%, WHO TPP)
- Duration (~10 years) of immunity
- Mechanism of effect (POI, POD, POR)
- Vaccine coverage, vaccine pricing
- Sub-national variations

Model additions

Integrated and responsive modelling framework…

Proposed delivery scenarios

Line item	Strategies	Interventions	Population
Comparator	Status-quo, no new vaccination	TB diagnostics	All presumptive TB patients aged < 15 years and ≥15 years
		TB treatment (DS)	All diagnosed TB patient aged < 15 years and ≥15 years
		TB preventive therapy	PLHIV; all HCC of pulmonary TB patients (current coverage rates)
		Nutritional support	TB patients
		BCG vaccination	Infants and neonates
Scenario 1	New vaccination in place of existing BCG vaccination at birth	New POI vaccination in place of BCG vaccination	BCG naive infants at birth
Scenario 2	New vaccination in **LTBI negative population (symptom free)**	POI vaccination after LTBI testing	LTBI negative general population
Scenario 3		POI vaccination after LTBI testing	LTBI negative high-risk population
Scenario 4	New vaccination in **LTBI positive population (symptom free)**	POD vaccination after LTBI testing	LTBI positive general population
Scenario 5		POD vaccination after LTBI testing	LTBI positive high-risk population
Scenario 6	New vaccination in TB disease negative population (symptom positive)	POD vaccination after TBD testing	TBD negative population
Scenario 7		POD vaccination after TBD testing	TBD negative high-risk population
Scenario 8	New vaccination on TB treatment completion	**POR vaccination in TB treatment completed**	General population or high-risk group
Scenario 9	Scale up of TPT for prevention of disease	**Any newer minimal duration of TPT regimen (<6 months) for POD**	Scale up of coverage to all PLHIV, HHC, and other people at risk like clinical risk groups or high transmission settings with minimal duration TPT regimens
Scenario 10	Scale up of nutrition supplementation for prevention of disease	**Nutrition supplementation for POD**	Scale up of nutrition supplementation in HHCs, other high-risk groups
Scenario 11	Strengthening of infection control measures for prevention of infection	**Airborne control (ABC) measures, masking, smoking cessation etc. for POI**	Strengthening based on population groups and/or setting
Scenario 12	Vaccination and preventive strategies (as combination)	**Combination of interventions (scenarios 1-7 plus scenario 8-10)**	All population or high-risk group
Scenario 13	POI + POD + POR	**Combination of vaccination interventions**	All population or high-risk group

***For all scenarios we will consider WHO symptom screening before vaccination**; if symptom positive tested for TB disease and treated
POI – Prevention of Infection, POD – Prevention of Disease, POR - Prevention of recurrence, LTBI – Latent TB Infection, TBD – TB disease

‘**Living model**, based on scenario related assumptions’, designed to be updated rapidly based on policy needs and as new evidence comes to light – through collaborations and expert consensus

Integrated and responsive modelling framework…

Model Input and calibration data

Line item	Data validation and evidence gap identification (ongoing)
Natural history (disease transmission) parameters	Review of literature
Disease burden (prevalence, mortality, % on treatment etc.,) **including relative risk (RR) by risk groups**	RR for TBD across risk groups (DM, Smoking, and low BMI) – **National TB prevalence survey, NIRT** **Nikshay data (CTD** Programmatic data) for **TB mortality by risk groups*** (assuming excess risk of mortality in undiagnosed is similar to excess mortality risk in diagnosed; not included in the current analysis)
Demographics (at birth population, background mortality, **Per cent of population by age groups and risk group**)	Population proportions through literature review and from **National TB prevalence survey, NIRT**
Health services (healthcare seeking)	**Nikshay data (CTD)** to be leveraged (not included in the current analysis) • **Care seeking data for specific risk groups** (Current analysis would assume similar care seeking rates in risk groups, exploratory analysis of prevalence data from CTD and NIRT to estimate care seeking rates by risk groups will be helpful to refine model outputs in the second phase)
Intervention specific data • Vaccine efficacy (PoI, PoD, PoR) • Vaccination status/coverage data • Duration of vaccine-induced immunity • **Relative risk by other preventive strategies**	**Coverage rates for ongoing BCG revaccination in risk groups** (extrapolated for assessing rate of transmission between unvaccinated and vaccinated; not included in the current analysis)
Cost parameters • Disease management - **Unit costs for routine programmatic activities and Unit patient costs** • Programmatic vaccination cost **and patient cost**	Literature review ongoing, additional data to be collected through CTD and NIRT's support

Literature review
Secondary data analysis
Expert opinion

↓

Updated estimates for TB burden, population proportions through the national prevalence survey (NIRT)

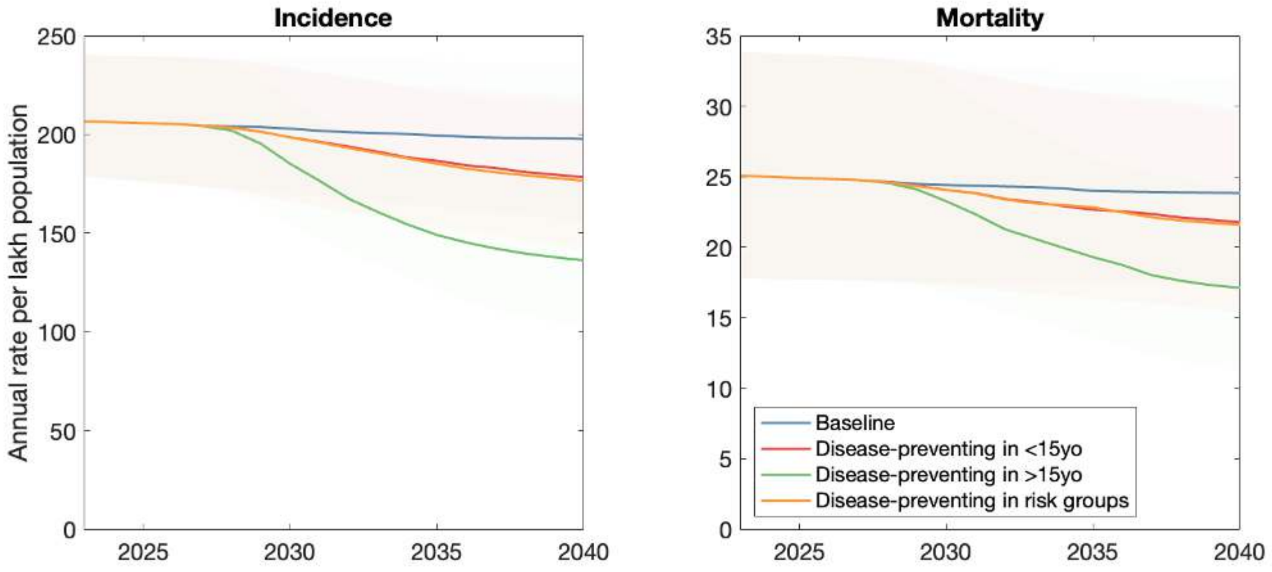
Leveraging programmatic data

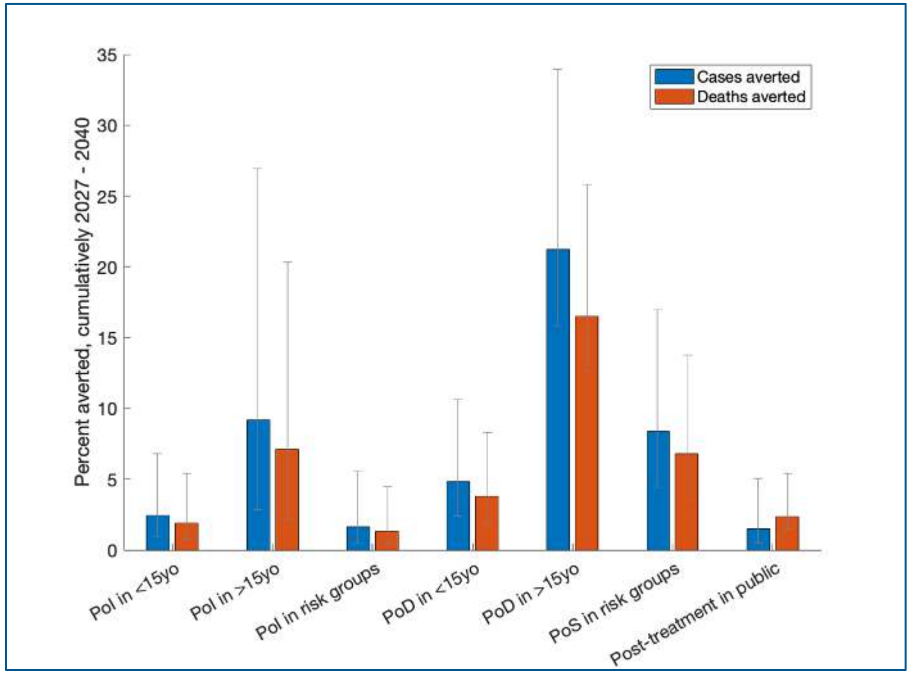
Understanding evidence gaps

What can the model do?

Demonstrative scenarios….

Disease-preventing vaccine + DM as risk group

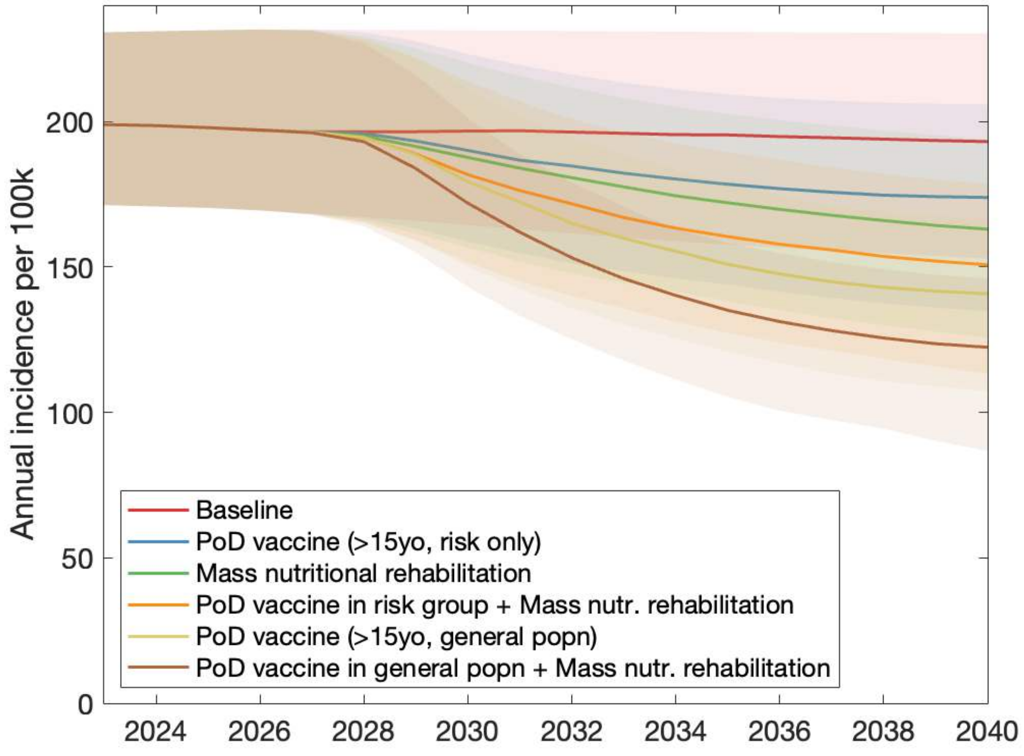




- Impact alone - the greatest reductions in burden achieved by a PoD vaccine in >15-year-olds, regardless of risk

Demonstrative combination scenarios….

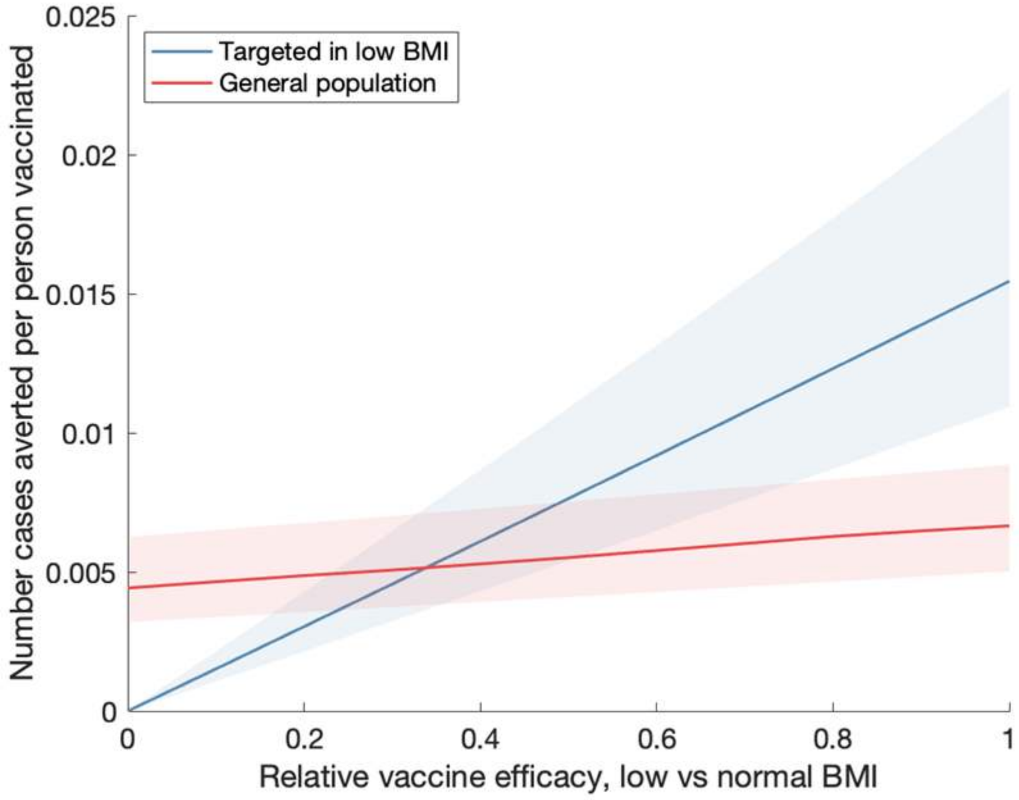
Undernutrition - modelling for vaccine and nutritional rehabilitation impact



- Combined preventive measures, such as nutritional interventions together with vaccination, can have important synergistic effects.

Modelling analysis to answer key policy questions….

Example: when to prioritize vulnerable populations?



- If vaccine efficacy is <35% less effective in low BMI than in general population, then *untargeted* vaccination strategy is more efficient than *risk-prioritized*

To conclude..

- The model outputs currently being be updated and refined in collaboration with key stakeholders to address critical policy relevant questions for vaccine roll-out.
- Apply model to help inform the most pressing priorities for evidence generation during vaccine development and rollout.
- This work accompanies a new, ongoing initiative to build new modelling capacity in India for helping address nationally relevant policy questions in India
- Momentum generated by the study in India has enabled expansion and linkage to new opportunities with global modelling efforts (Wellcome Trust, LSHTM)

The development of this comprehensive, integrated modelling framework offers an example of how high burden countries can generate their own **nationally-relevant evidence through a multi-stakeholder, integrated approach**, to optimize planning for vaccine rollout. Performed in advance of deployment of a future vaccine, such preparations will help **accelerate policy decisions and adoption for maximal impact with available resources.**

Acknowledgements

NIRT-ICMR	WHO	IAVI	THSTI, GoI	CTD, GoI
Dr Adhin Bhaskar	Professor Nimalan Arinaminpathy	Dr Jessy Joseph	Dr Samrat Chatterjee	Dr Raghuram Rao
Dr M. Muniyandi	Dr Ranjani Ramachandran	Ms Ruchita Jalal	Dr Jayanta Bhattacharya	Dr Urvashi B Singh
Ms Basilea Watson		Dr Rajat Goyal		Dr Dheeraj Tumu
		Mr Saif ul Had		
		Dr Gabriella Gomez		
		Dr Surabhi Pandey, Consultant, Mathematical modelling		