

The potential impact of nutritional interventions in the South-East Asia Region: A modelling analysis

Sandip Mandal

John Snow India, New Delhi, India

Indian Institute of Technology-Bombay, India



Outline

- Outcome from RATIONS trial in India
- Modelling approach
- Findings
- Summary

ARTICLE IN PRESS

Articles

The potential impact on tuberculosis of interventions to reduce undernutrition in the WHO South-East Asian Region: a modelling analysis

Sandip Mandal,^{1,2*} Vineet Bhatia,³ Anurag Bhargava,⁴ Suman Rijal,³ and Nimalan Arinaminpathy¹

¹John Snow India, New Delhi, India

²World Health Organization, South-East Asia Regional Office, New Delhi, India

³Department of General Medicine, Yenepoya Medical College, Karnataka, India

⁴MRC Centre for Global Infectious Disease Analysis, Imperial College London, London, UK

Summary

Background Undernutrition is a major risk factor for TB incidence in the WHO South-East (SE) Asia Region. We examined the potential impact of addressing undernutrition as a preventive measure, for reducing TB burden in region.

Methods We developed a deterministic, compartmental mathematical model, capturing undernutrition and its



The Lancet Regional Health - Southeast Asia 2024;■ 100423
Published Online XXX
<https://doi.org/10.1016/j.lansea.2024.100423>

RATION TRIALS

Nutritional supplementation to prevent tuberculosis incidence in household contacts of patients with pulmonary tuberculosis in India (RATIONS): a field-based, open-label, cluster-randomised, controlled trial

Anurag Bhargava, Madhavi Bhargava, Ajay Meher, Andrea Benedetti, Banurekha Velayutham, G Sai Teja, Basilea Watson, Ganesh Barik, Rajeev Ranjan Pathak, Ranjit Prasad, Rakesh Dayal, Adarsh Kibballi Madhukeshwar, Vineet Chadha, Madhukar Pai, Rajendra Joshi, Dick Menzies, Soumya Swaminathan



Nutritional support for adult patients with microbiologically confirmed pulmonary tuberculosis: outcomes in a programmatic cohort nested within the RATIONS trial in Jharkhand, India

Anurag Bhargava, Madhavi Bhargava, Ajay Meher, G Sai Teja, Banurekha Velayutham, Basilea Watson, Andrea Benedetti, Ganesh Barik, Vivek Pratap Singh, Dhananjay Singh, Adarsh Kibballi Madhukeshwar, Ranjit Prasad, Rajeev Ranjan Pathak, Vineet Chadha, Rajendra Joshi

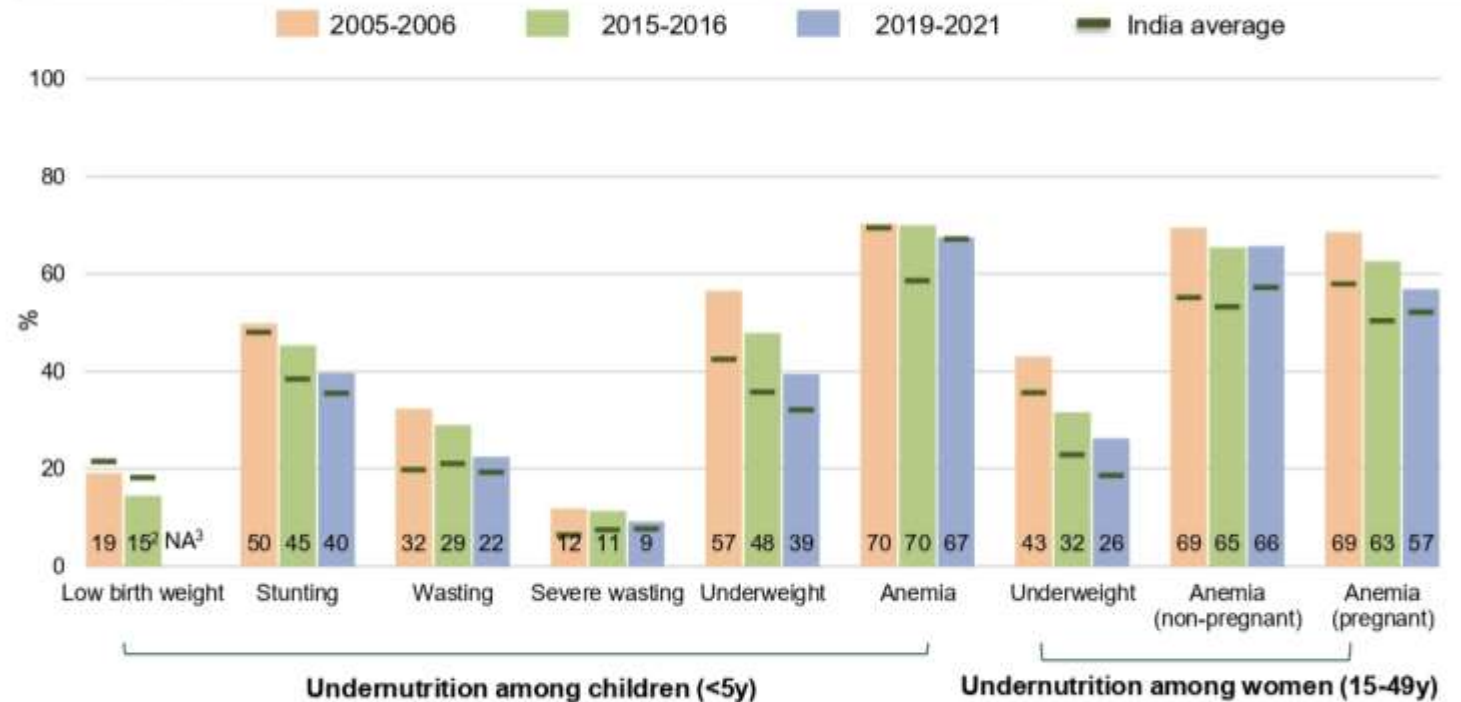


- Nutritional supplementation in household contacts could reduce tuberculosis incidence by 40–50% (observed 2 years of follow-up period)
- A reduced hazard of death (adjusted HR 0.39, 95% CI 0.18–0.86) was associated with a 5% weight gain at 2 months.

Status of undernutrition in Jharkhand, India



Figure 1. Trends in undernutrition outcomes 2005-2006, 2015-2016, 2019-2021

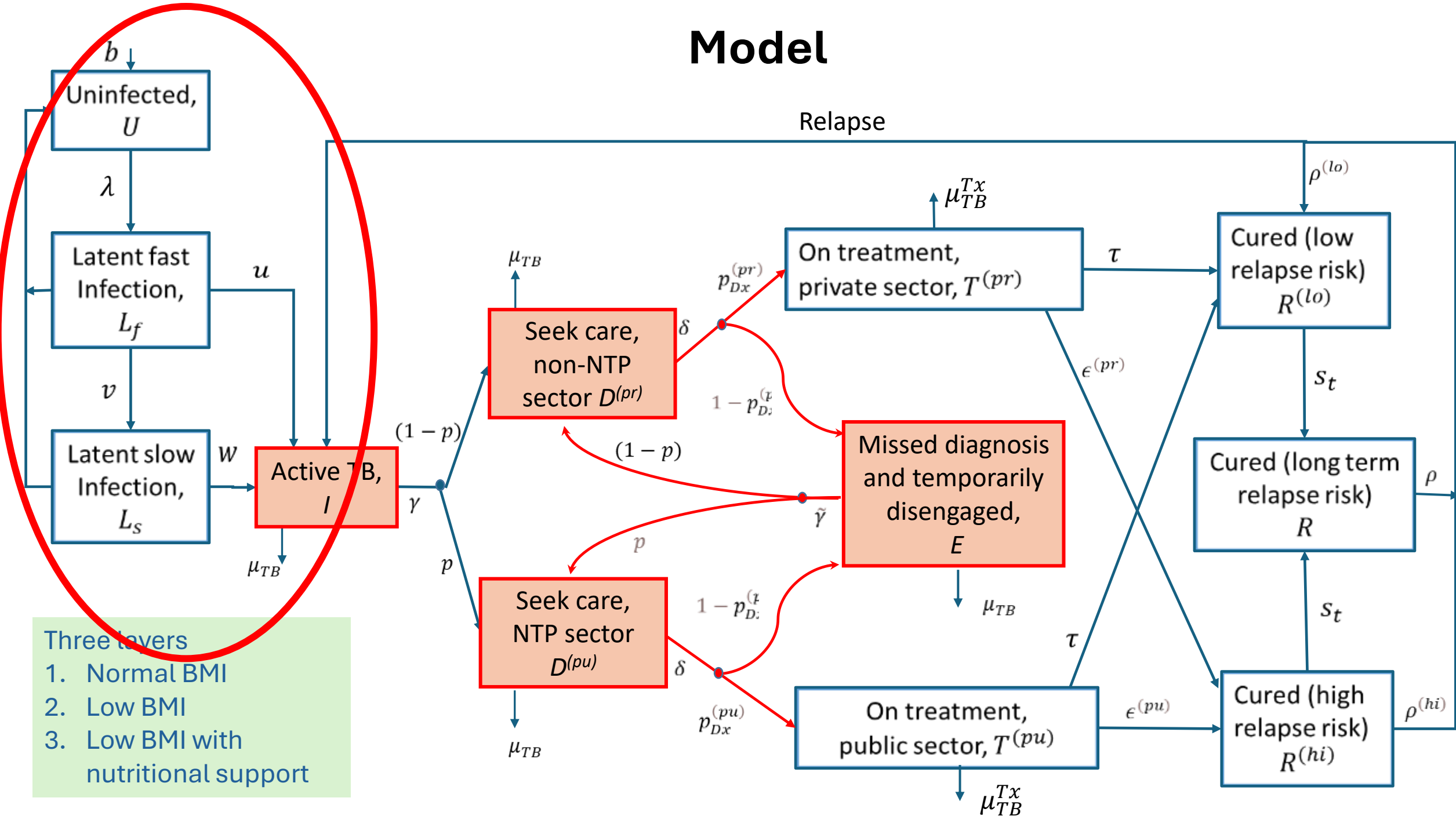


Source: NFHS-3 (2005-2006) national report and data [IFPRI estimates] and NFHS-5 (2019-2021) national and state factsheets. Anemia among non-pregnant and pregnant women for 2005-2006 are IFPRI estimates using woman dataset. ¹WHO. Nutrition Landscape Information System (NLIS). Help Topic: Malnutrition in children. Stunting, wasting, overweight and underweight. (<https://apps.who.int/nutrition/landscape/help.aspx?menu=0&helpid=391&lang=EN>); ²In NFHS-3, 79.5% of data were missing and 30.7% of data were missing in NFHS-4. ³NA refers to the unavailability of data for a particular indicator in the specified NFHS round.

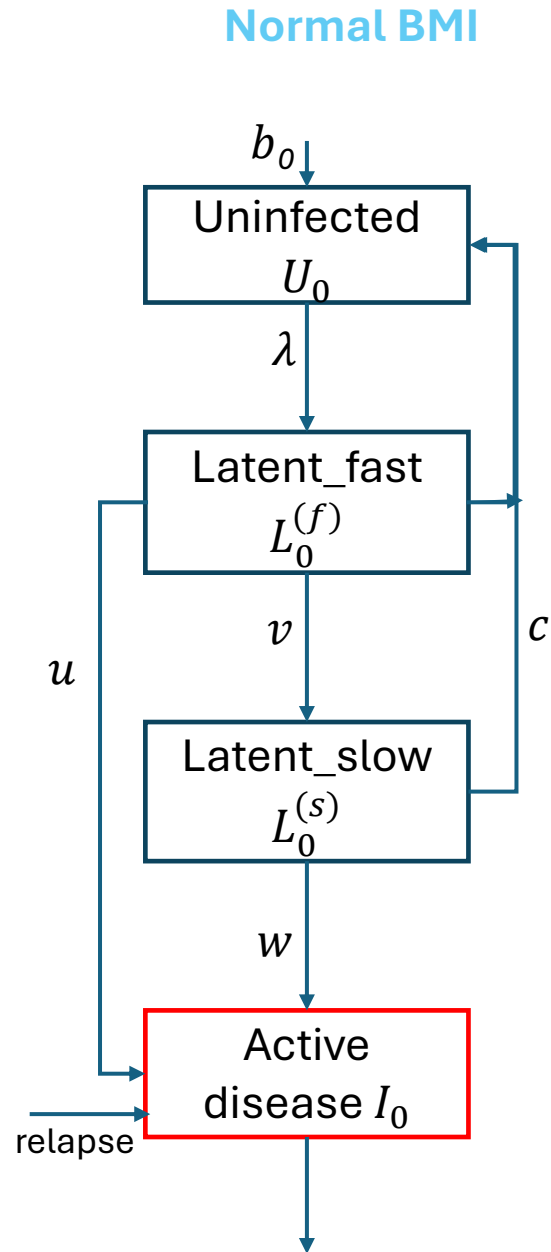
Country specific prevalence of underweight among adults

Country	Prevalence of underweight among adults, BMI < 18.5 (age-standardized estimate) (%) in 2016
Bangladesh	21.5 [16.8 – 26.7]
Bhutan	10.9 [6.6 – 16.2]
DPR Korea	6.6 [3.1 – 12.2]
India	23.6 [19.9 – 27.6]
Indonesia	12.9 [9.3 – 16.9]
Maldives	9.2 [5.7 – 13.8]
Myanmar	14.6 [10.4 – 19.5]
Nepal	16.8 [12.6 – 21.3]
Sri Lanka	14 [9.8 – 18.8]
Thailand	8.6 [5.6 – 12.3]
Timor -Leste	16.1 [11.2 – 21.7]

Model



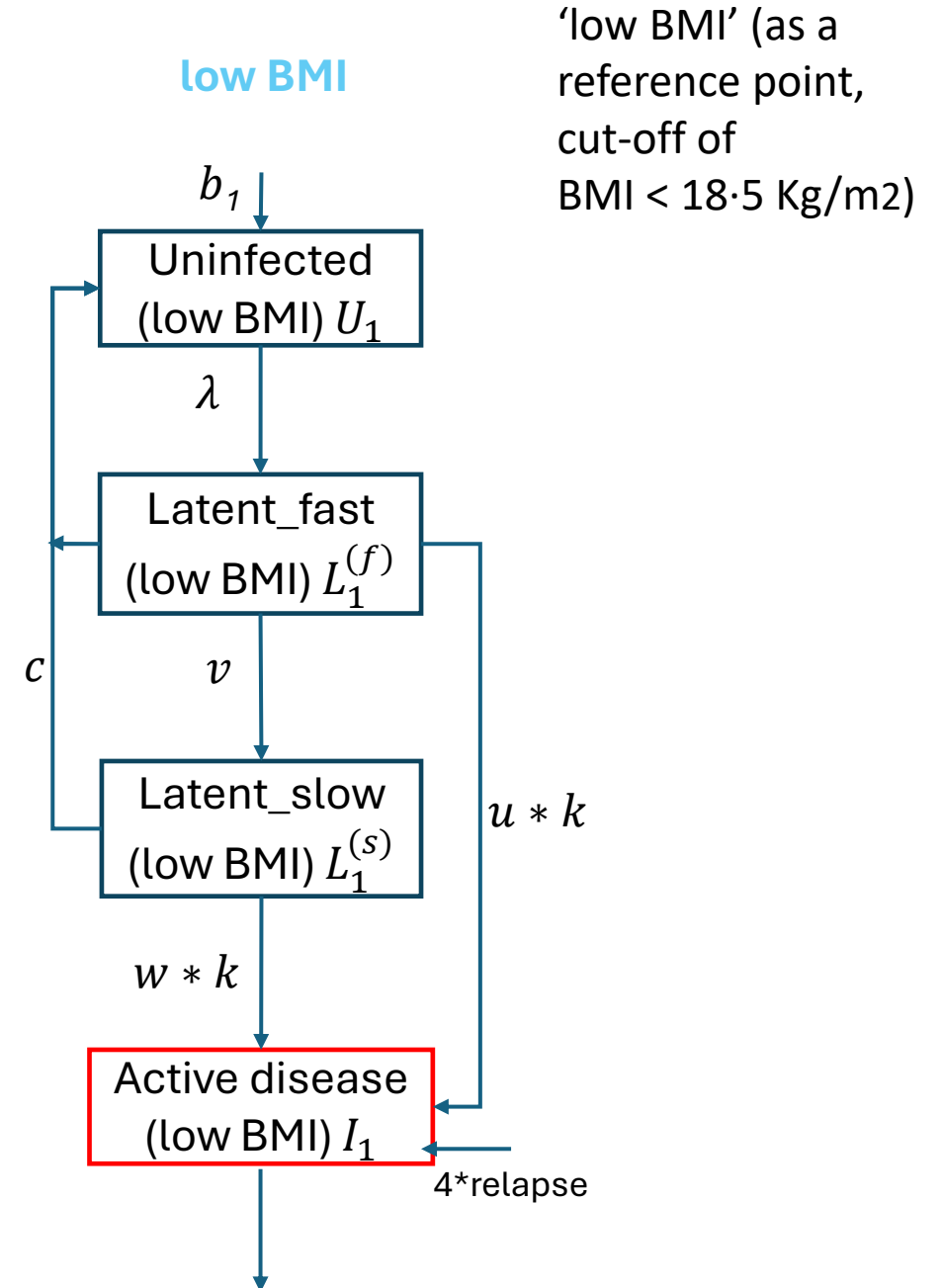
Model



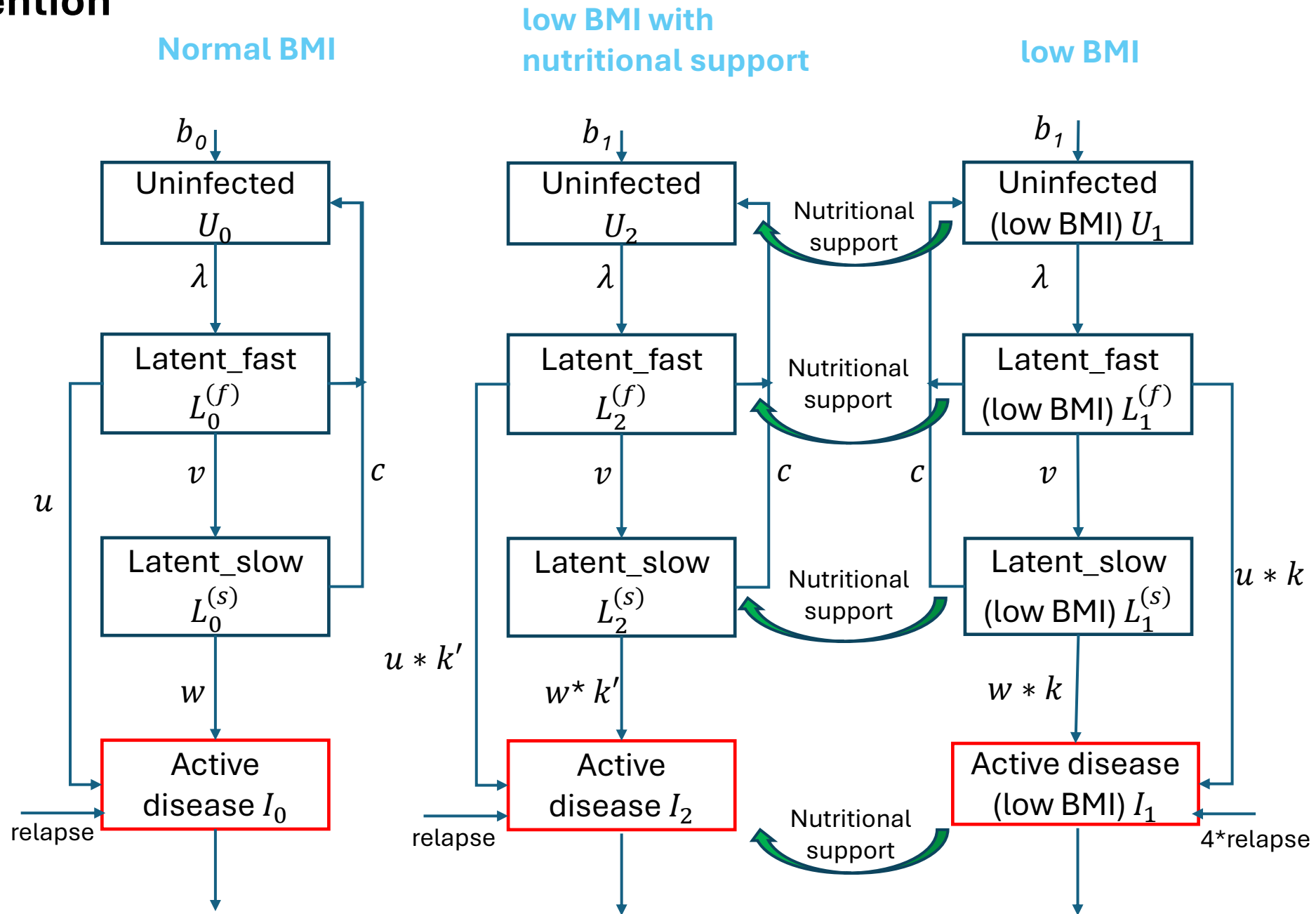
Relative risk of TB amongst undernourished = 3.2 [3.1 – 3.3]

The effect of undernutrition is to amplify the rates at which TB-infected individuals progress to active disease

k is estimated to fulfil this condition



Intervention



Assumptions

Before intervention

- Amongst TBI, progression/reactivation rate is higher amongst low-BMI than normal BMI
- Relapse rate is 4 –times higher among low-BMI relative to normal BMI
- Untreated TB mortality hazard among low-BMI is twice as high as in normal BMI
- CFR during treatment is around 4% for normal BMI, vs 6% for low-BMI
- Ignored any nutritional shocks related to COVID-19 pandemic

Effect of nutritional support

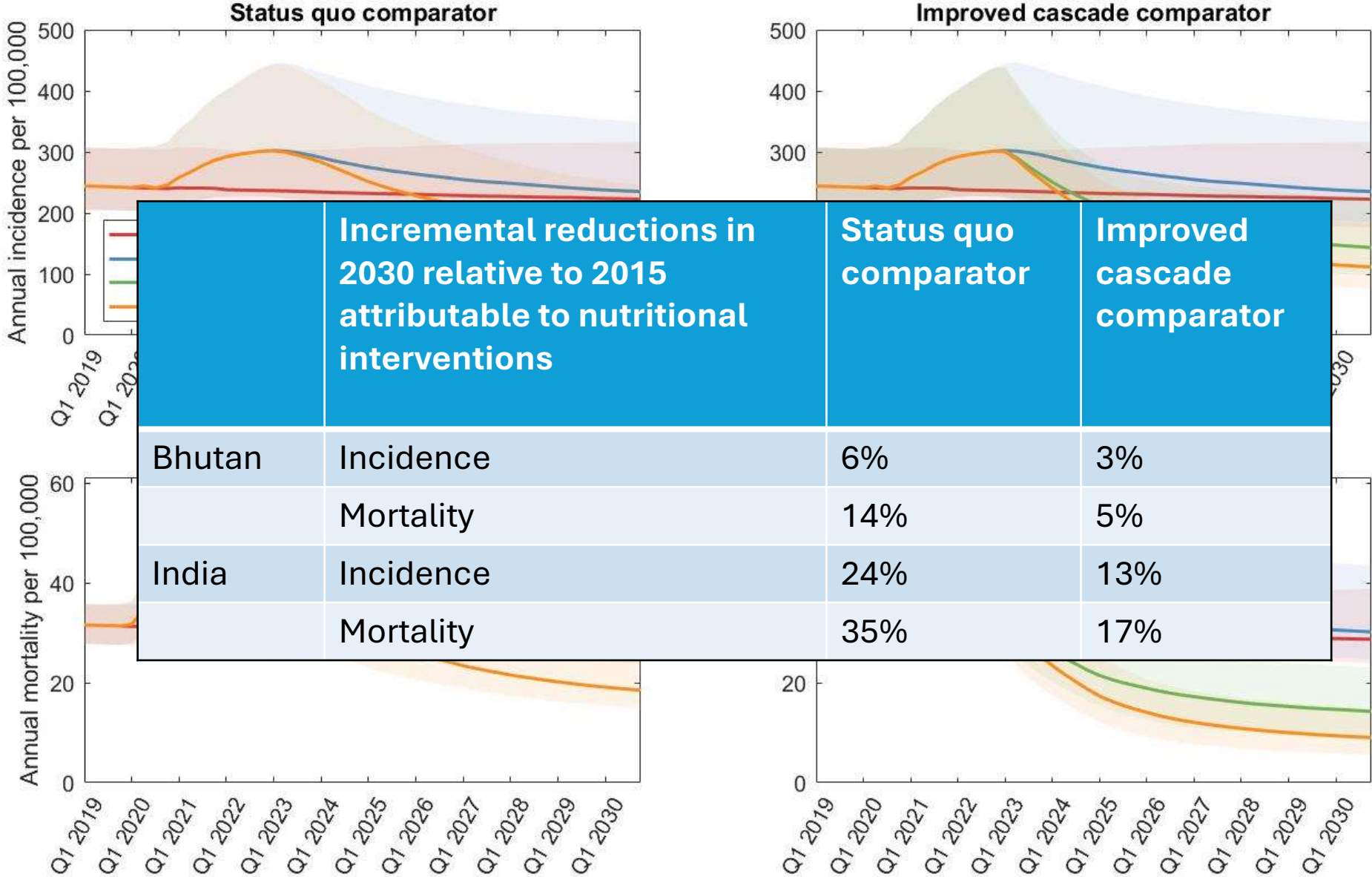
- Amongst TBI, reduces cumulative incidence by 40% by lowering progression/reactivation rates.
- Restore relapse hazards to same level as normal BMI (assumption)
- Restore untreated mortality hazards to same level as normal BMI (assumption)
- Restore CFR during treatment to same level as normal BMI

Modelling interventions

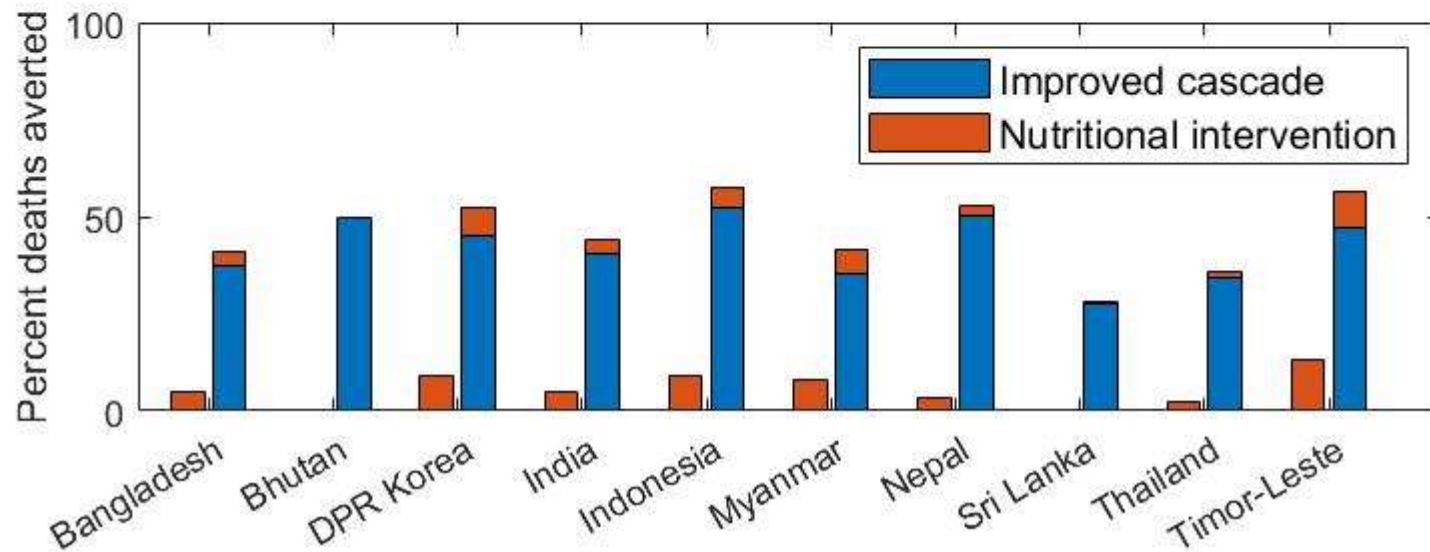
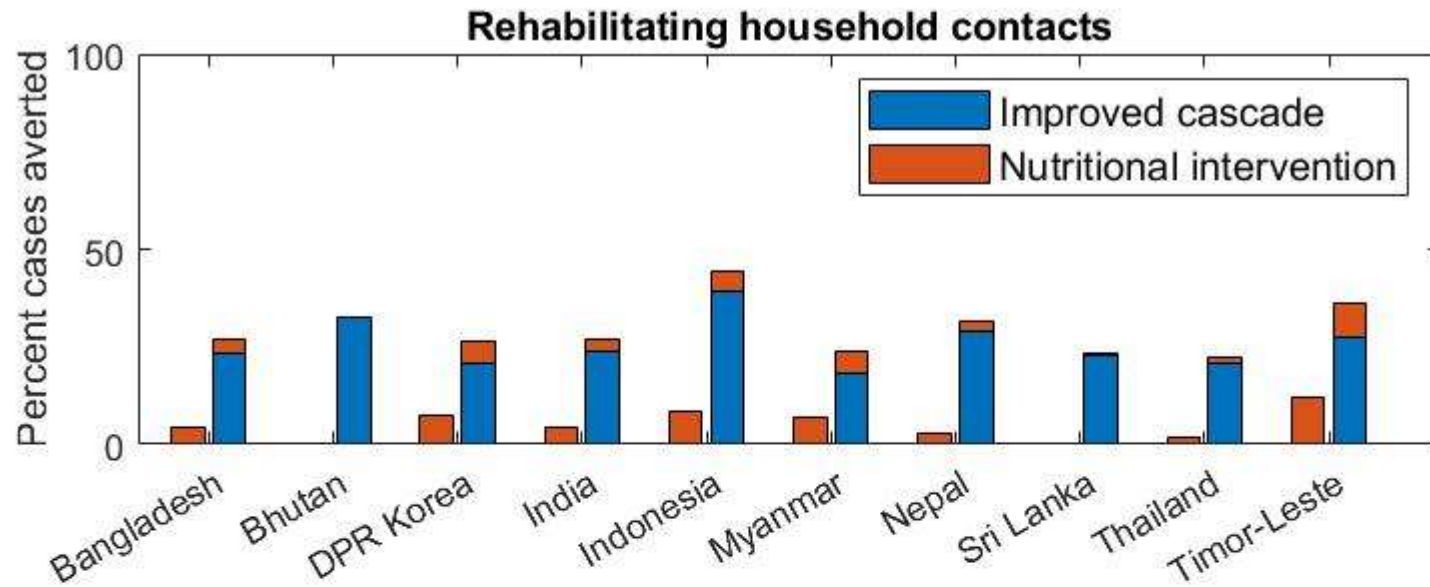
- Among all contacts of index cases, regardless of nutritional status
- Intervention that provides nutritional support to 30% of undernourished people each year
 - Modelled these interventions as shifting individuals from ‘low’ BMI to ‘low BMI with nutritional support’ status
 - Intervention scaled up in a linear way between 2023 and 2025.
 - Those having ‘low BMI with nutritional support’ status would show the same incidence reductions as amongst undernourished contacts in the RATIONS study, i.e. of 40%.

Incidence and mortality with nutritional intervention

WHO South-East Asia Region



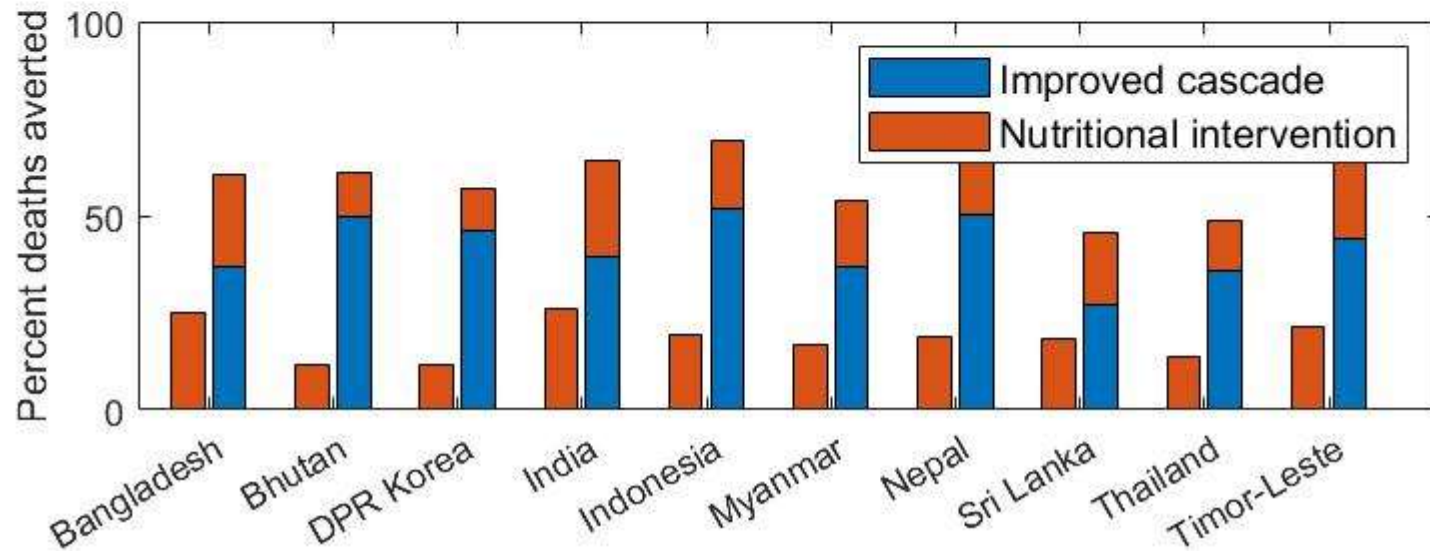
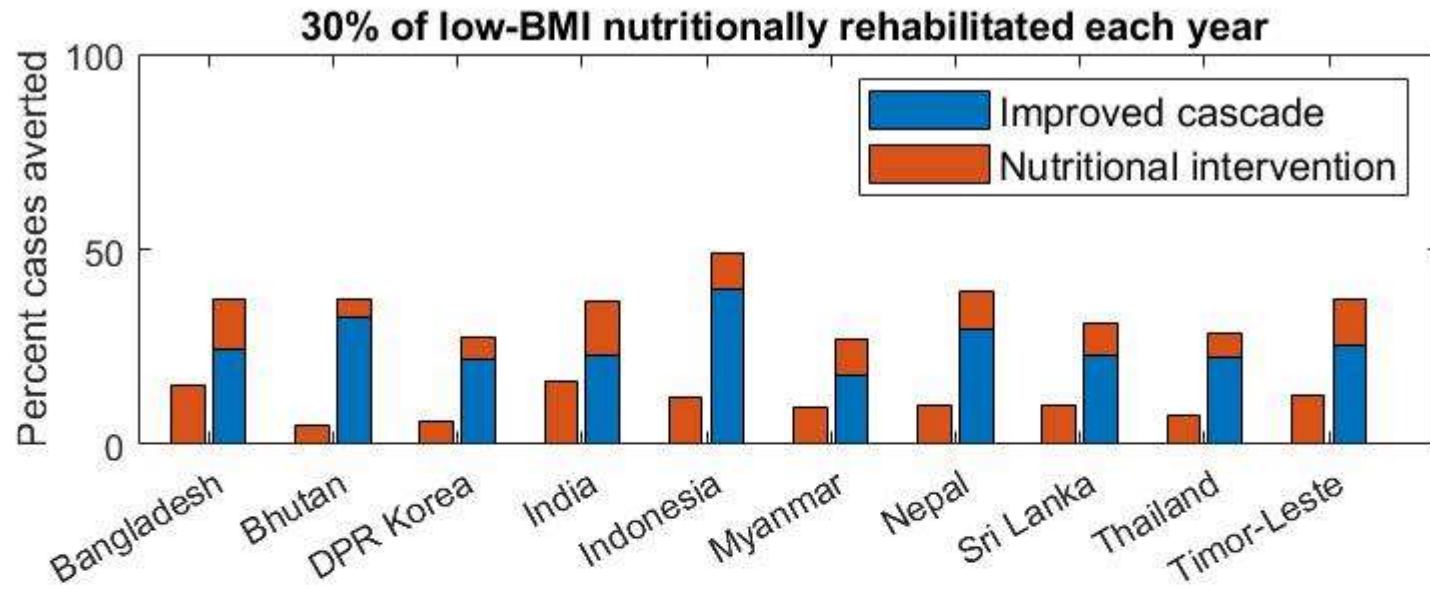
Impact: percent cases and deaths averted between 2023 – 2030



**Improved cascade
Includes:**

PPM, improved
diagnostic outcomes in
routine programmatic
settings,
Case finding efforts

Impact: percent cases and deaths averted between 2023 – 2030



**Improved cascade
Includes:**

PPM, improved
diagnostic outcomes in
routine programmatic
settings,
Case finding efforts

Limitations

- Every model is a simplification. Ignoring:
 - Age structure
 - Pulmonary/extrapulmonary TB
 - Drug resistance
 - HIV (although not a major driver in most countries in the Region)
 - Subnational variations in nutritional status
- Impact of intervention: need evidence from wider range of geographies than Jharkhand
- Impact in general population: extrapolated efficacy from RATIONS trial (which was based on household contacts)
 - Further evidence needed on potential efficacy in general population: although may be expensive to generate! Comparable to vaccine phase 3 trial

Summary

- The impact of nutritional interventions varies substantially by country.
- Nutritional support in low-BMI in the general population: between 2023 and 2030, strong reductions were observed in cumulative incidence (5% in Bhutan to 16% in India) and cumulative mortality (12% in Bhutan to 26% in India) by providing annual nutritional support to 30% of people with low BMI per year.
- Nutritional support among household contacts: cumulative incidence and mortality is <1% in Bhutan to ~5% in India.
 - Potential for important synergies with other interventions, e.g. PPM increasing the number of eligible contacts of notified cases.
- *Overall*: Nutritional support could have an important impact on the TB epidemic in countries in WHO/SEA Region, but is unlikely to be sufficient, by itself, to reach the End TB goals

Acknowledgements

- **Vineet Bhatia**, WHO-South-East Asia Regional Office, New Delhi, India
- **Anurag Agarwal**, Yenepoya Medical College, Karnataka, India
- **Suman Rijal**, WHO-South-East Asia Regional Office, New Delhi, India
- **Nimalan Arinaminpathy**, WHO, Geneva, Switzerland

Thank you