## Title

TB and nutrition: what gets measured gets managed

## Authors

C. Finn McQuaid<sup>1</sup>, Pranay Sinha<sup>2</sup>, Madhavi Bhargava<sup>3,4</sup>, Chathika Weerasuriya<sup>1</sup>, Rein M.G.J. Houben<sup>1</sup>, Anurag Bhargava<sup>4,5,6</sup>

## Corresponding author

Christopher Finn McQuaid, London School of Hygiene & Tropical Medicine, Keppel Street, London, WC1E 7HT, UK. Email: finn.mcquaid@lshtm.ac.uk

## Affiliations

<sup>1</sup>TB Modelling Group, TB Centre and Centre for Mathematical Modelling of Infectious Diseases, Department of Infectious Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, UK

<sup>2</sup>Section of Infectious Diseases, Department of Medicine, Boston University Chobanian & Avedisian School of Medicine, Boston, USA

<sup>3</sup>Department of Community Medicine, Yenepoya Medical College, Mangalore, India <sup>4</sup>Center for Nutrition Studies, Yenepoya University, Mangalore, India

<sup>5</sup>Department of Medicine, Yenepoya Medical College Hospital, Mangalore, India <sup>6</sup>Department of Medicine, McGill University, Montreal, QC, Canada

While *Mycobacterium tuberculosis* transmission is primarily airborne, tuberculosis (TB) disease is also a structural problem, requiring non-biomedical solutions. Nutritional status, approximated by indicators such as body mass index (BMI), is a widely prevalent comorbidity and risk factor for TB disease and mortality(1, 2). More than one in five cases globally are attributable to undernutrition(3), where in many settings, such as India, there is no factor more important in driving the TB epidemic(4). With COVID-19(5), climate change, and war in Ukraine threatening global food security(6), nutrition is likely to take on even greater salience for TB elimination efforts.

However, current programmatic guidance for nutritional support to people with TB (PWTB) remains limited, founded on conclusions drawn from a small number of methodologically-flawed studies(7), and many influential epidemiological analyses of TB have not included undernutrition as a covariate(8). As a consequence, most programs do not provide nutritional support or mandate systematic nutritional assessment at diagnosis, during therapy, or at treatment completion(9). This leaves a critical gap in the comprehensive care of the patient, as well as a lack of ability to create data and evidence for much needed change.

Simply put, 'what gets measured gets managed'. BMI is one indicator that is quick, inexpensive, and extensively used in primary maternal and child health, but seldom used, let alone reported, for PWTB. However, such data is necessary to highlight the magnitude of undernutrition's impact on TB, and advocate for action (Figure 1 – panel 1).

We therefore advocate that National TB Programmes should record nutritional status routinely as a part of TB notification data and prevalence surveys, including relating undernutrition

# distribution in PWTB back to that of the general population, and the World Health Organization should include these recorded data in their regular reports.

Measuring and reporting BMI represents an important starting point, even if it has limitations (7). We recognise the existence of potential alternatives, although these too have limitations, and are more challenging to implement at scale(10). Instead, BMI is simple to measure, well-understood, and has well-established cut-offs. Capacity to measure height and weight is also uniformly useful in all age groups to estimate further indicators. While ambiguities appear in interpretation of mid-range BMIs, these may be less concerning for TB programs as the majority of PWTB are at the lower extreme. As BMI has been widely used in the TB literature, new data generated would have the added benefit of comparability.

*Prioritisation:* Programmatic BMI data would help us appropriately prioritise high-risk PWTB and both visualise and understand the contribution of undernutrition to TB burden (Figure 1 – panel 2). In a recent example, discussion of the COVID-19 pandemic's detrimental effect on TB elimination has focused primarily on case finding, largely because notification data are 'measured' and are therefore part of management targets. However, the effect of declining nutritional status in the populations of high TB burden countries, PWTB, and their household contacts, has not been measured, and not managed. With standardised collection of BMI data nutrition could be appropriately prioritised.

*Monitoring and Evaluation:* Including BMI in annual reporting and TB incidence estimation would help to monitor the impact of nutritional interventions, or highlight the need to improve them. In a welcome step in the right direction, the World Health Organization Regional Office for South-East Asia recently recommended the inclusion of a nutritional monitoring indicator(11). Selected programmes like India's have implemented nutritional interventions, including cash-transfers and in-kind support, but lack data on effectiveness of these interventions. Routine collection of programmatic data would help monitor and evaluate the impact of these programmes.

*Advocacy:* Availability of BMI data would allow for much-needed advocacy. For example, a 2013 study in India found that a staggering 67% of male and 80% of female PWTB had moderate- to severe undernutrition, with double the mortality rate in these groups (12). Nutritional support interventions could significantly improve these treatment outcomes(13). Similarly, data from a Myanmar survey showed a near six-fold increased risk of TB disease in those with severe undernutrition(14). Only when we measure, we know, and action becomes imperative.

Severe undernutrition has been referred to as nutritionally-acquired immunodeficiency syndrome (N-AIDS). If we don't allow HIV/AIDS, driving ~2% of TB in India, to go untested and untreated in PWTB, it seems just the absence of data is enabling us to tolerate the neglect of N-AIDS, to which nearly 50% of all TB in India is attributable, and which is contributing to preventable TB mortality (see Figure 1). Data on undernutrition in patients and populations would help assess and address this reversible risk factor for TB incidence and TB mortality.

The value of information of our proposal offers policy makers an easy win, especially for geographies such as India where nutrition plays a near-dominant role in TB epidemiology and care. Undernutrition and TB are the result of a multitude of social determinants(15). Measuring

BMI would enable advocacy where it is needed, and drive much-needed intersectoral links between health and agricultural ministries to provide more holistic care. Measuring and reporting nutritional status through a straightforward indicator such as BMI should be a no-brainer for the TB community.

We declare no competing interests.

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### References

1. Lönnroth K, Williams BG, Cegielski P, Dye C. A consistent log-linear relationship between tuberculosis incidence and body mass index. International journal of epidemiology. 2010;39(1):149-55.

2. Waitt CJ, Squire SB. A systematic review of risk factors for death in adults during and after tuberculosis treatment. Int J Tuberc Lung Dis. 2011;15(7):871-85.

3. World Health Organization. Global Tuberculosis Report 2022. Geneva, Switzerland; 2022.

4. Bhargava A, Bhargava M, Beneditti A, Kurpad A. Attributable is preventable: Corrected and revised estimates of population attributable fraction of TB related to undernutrition in 30 high TB burden countries. J Clin Tuberc Other Mycobact Dis.27(100309):1-8.

5. Bhargava A, Shewade HD. The potential impact of the COVID-19 response related lockdown on TB incidence and mortality in India. Indian Journal of Tuberculosis. 2020;67(4, Supplement):S139-S46.

6. 2021 Global Nutrition Report: The state of global nutrition. Bristol, UK: Development Initiatives; 2021.

7. Sinha P, Davis J, Saag L, Wanke C, Salgame P, Mesick J, et al. Undernutrition and Tuberculosis: Public Health Implications. J Infect Dis. 2019;219(9):1356-63.

8. Sinha P, Hochberg NS. Controlling for undernutrition in epidemiological studies of tuberculosis. Lancet Infect Dis. 2020;20(5):540-1.

9. Guidance for national strategic planning for tuberculosis. Geneva: World Health Organization; 2022.

10. Kehoe SH, Krishnaveni GV, Lubree HG, Wills AK, Guntupalli AM, Veena SR, et al. Prediction of body-fat percentage from skinfold and bio-impedance measurements in Indian school children. Eur J Clin Nutr. 2011;65(12):1263-70.

11. Regional strategic plan towards ending TB in the WHO South-East Asia Region: 2021–2025. India: World Health Organization Regional Office for South-East Asia; 2021.

12. Bhargava A, Chatterjee M, Jain Y, Chatterjee B, Kataria A, Bhargava M, et al. Nutritional status of adult patients with pulmonary tuberculosis in rural central India and its association with mortality. PloS one. 2013;8(10):e77979.

13. Reis-Santos B, Locatelli R, Oliosi J, Sales CM, do Prado TN, Shete PB, et al. A Matter of Inclusion: A Cluster-Randomized Trial to Access the Effect of Food Vouchers Versus Traditional Treatment on Tuberculosis Outcomes in Brazil. Am J Trop Med Hyg. 2022.

 Aung ST, Nyunt WW, Moe MM, Aung HL, Lwin T. The fourth national tuberculosis prevalence survey in Myanmar. PLOS Global Public Health. 2022;2(6):e0000588.
Sinha P, Lonnroth K, Bhargava A, Heysell SK, Sarkar S, Salgame P, et al. Food for thought: addressing undernutrition to end tuberculosis. Lancet Infect Dis. 2021;21(10):e318e25.

Figure 1: Potential uses of routinely reported body mass index data over time. Dashed lines indicate illustrative future projections of tuberculosis incidence. Rate per 100,000 population per year.

