

Reducing undernutrition in persons with TB and populations is important to achieve END TB targets

Written by The Union Nutrition-TB Working Group

Key messages and recommendations

- Problem: Undernutrition receives inadequate attention despite being the top risk factor for TB globally and an important comorbidity in high TB burden countries. The WHO's end-TB strategy has not met its targets. Investments in undernutrition may accelerate TB elimination efforts.
- Recommendation 1: Integrate assessment, counseling, and care for undernutrition into existing TB treatment guidelines. (Intersects with pillar 1 of END TB strategy)
- Recommendation 2: Reduction in population-level food insecurity in high TB burden countries (Intersects with pillar 2 of END TB strategy)
- Recommendation 3: Increase funding for undernutrition-TB research

Executive statement

Tuberculosis (TB) is the second leading infectious killer worldwide after COVID-19. More TB cases have been attributed to undernutrition than any other population-based, modifiable risk factor. Addressing undernutrition at the population level and integrating care for TB and undernutrition would have a meaningful impact on the world's TB burden. Undernutrition is also a cross-cutting issue in global health and impacts numerous sustainable development goals (SDG): SDG1 (no poverty), SDG2 (zero hunger), SDG3 (good health and well-being), SDG8 (decent work and economic growth), SDG10 (reduced inequalities), SDG16 (peace, justice, and strong institutions). As such, it deserves a robust multisectoral response.

An overview of TB

Tuberculosis is caused by *Mycobacterium tuberculosis*, and it is spread through the air by coughing, sneezing, shouting, singing, and even talking. After infecting an individual, *Mtb* can lie dormant for years before causing disease. One in four human beings are infected with the mycobacteria, more than 10 million individuals suffer symptomatic disease annually, and approximately 1.5 million die of TB. The effects of TB extend beyond the initial period of disease—as many as 1 in 4 TB survivors can develop chronic lung disease. A large fraction of persons living with TB (PLWTB) suffers catastrophic costs due to TB even when the government provides free TB diagnosis and care. Moreover, as TB predominantly affects working-age individuals, the disease has an outsized economic impact globally.



Relationship between TB and undernutrition

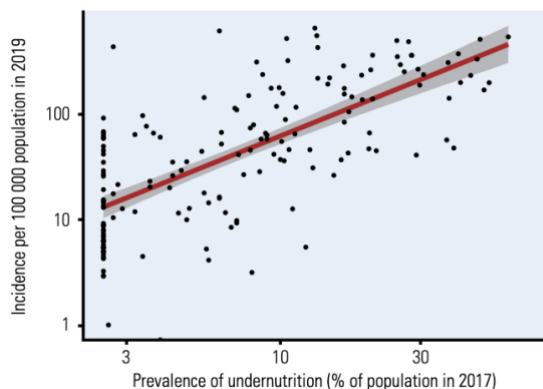


Figure 1: Risk of TB disease increases with prevalence of undernutrition (Global TB report 2020). Decades of research in diverse populations have demonstrated the relationship between undernutrition and TB. As the prevalence of undernutrition rises, so does the incidence of TB disease (see figure 1). Approximately one in five cases of TB worldwide is attributable to undernutrition. Not only does undernutrition increase the risk of TB progressing from its dormant state to active disease, but it also increases severity of TB disease, risk of dying of TB, risk of adverse drug effects, and possibly the risk of having long-term lung complications after recovering from TB. In the pre-antibiotic era, nutrition was considered central to both treatment and prevention of

tuberculosis. While advances have been made in new TB drugs and vaccines, little attention has been paid to this modifiable risk factor by funding agencies. Undernutrition as a comorbidity is easy to assess, and potentially reversible. In high TB burden countries, numerous studies have shown that PLWTB experience life-threatening levels of undernutrition, which in the absence of nutritional support, persists even after microbiological cure, impairing the PLWTB's return to normal function, while also increasing the risk of recurrence of TB.

The Impact of Nutritional Interventions

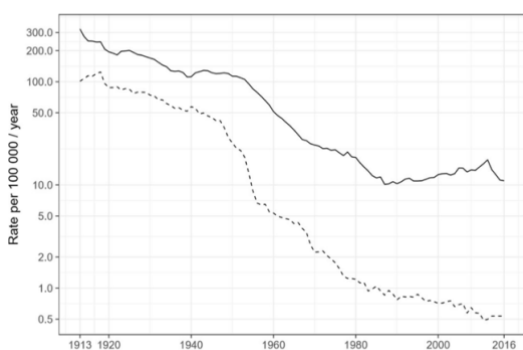


Figure 2: TB incidence (solid line) and mortality (dashed line) rates per 100,000 populations per year in England and Wales in 1913-2016 show marked declines even in pre-antibiotic era. (Glaziou et al., 2016)

Even before antibiotics for TB became available, large reductions in TB incidence and mortality occurred in the United States and wealthy European countries primarily due to improved socioeconomic status of the population with better nutrition likely playing a major role. Nutritional supplementation is likely to reduce TB morbidity and mortality and secondarily prevent transmission to others. Numerous historical data support this idea. For instance,

during World War II, British prisoners received Red Cross supplements doubling the number of calories compared to Soviet prisoners in the same prison camps. Despite similar living conditions, Soviet prisoners had a sixteen-fold higher incidence of TB and a higher mortality rate compared to their British contemporaries. In a well-documented cohort, social interventions that emphasized adequate nutrition reduced, by six-fold, the occurrence of TB in close household contacts of PLWTB with tuberculosis at a time when drugs for TB were not available and vaccines were not used. Large field studies, currently underway in India, will provide evidence on the immunological and clinical impact of nutritional supplementation among PLWTBs and their household contacts. It is expected that improving the nutritional status of people infected asymptotically with the mycobacteria can prevent them from progressing to symptomatic disease. Nutritional supplementation increases treatment adherence and treatment success for persons who already have active TB disease. Currently, one in three individuals emerge from TB therapy undernourished – nutritional supplementation may reduce this proportion of individuals who would have reduced economic productivity and be at increased risk of recurrent TB disease as well as other infections.

Implication and Recommendations

The COVID-19 pandemic has reduced income and decreased food security around the world which may further fuel the TB pandemic. In 2020, TB deaths worldwide increased from 1.4 million in 2019 to 1.5 million-- the first increase in ten years. Additionally, factors such as climate change, forced migration, and political instability also impact the nutritional status of populations. The WHO's goal of eliminating TB by 2035 is becoming less realistic. Urgent action on undernutrition and other social determinants may prevent loss of hard-won progress in the global TB elimination efforts as well as the SDGs.

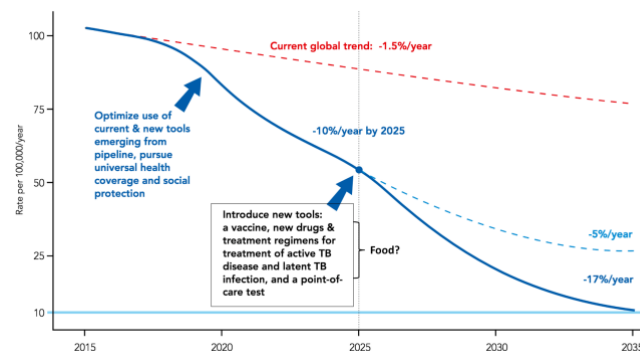


Figure 3: Nutritional interventions may be a catalyst for change in TB elimination efforts (recreated and adapted with permission from the WHO (Creative Commons license: CC BY-NC-SA 3.0 IG)

Recommendation 1: Integrate nutritional assessment & care for into extant TB care protocols

Leaving undernutrition untreated among PLWTB increases risk of treatment failure, treatment toxicity, and mortality. Persons who remain undernourished at the end of TB therapy are at elevated risk of recurrent TB disease. Moreover, studies show that nutritional supplementation may enhance treatment adherence. Lastly, as food costs are a significant component of TB-related costs, nutritional supplements may also achieve the WHO's goal of eliminating catastrophic costs among PLWTB. Pillar 1 of the End TB strategy prioritizes integration of patient-centered TB care and prevention. Action on undernutrition would contribute meaningfully towards this goal.

Recommendation 2: Reduce population-level food insecurity in high TB burden countries

As suggested in the Copenhagen Consensus, undernutrition results in economic losses directly through reduction in physical productivity, indirectly through cognitive losses and missed schooling, and through increased health care costs. Modeling studies have suggested that reducing undernutrition in high TB burden countries could decrease TB incidence and mortality while being highly cost effective. Improved nutrition would also reduce health costs from the many diseases caused by undernutrition and improve economic productivity. Mitigating undernutrition would directly benefit SDG2 (zero hunger) and SDG3 (good-health and well being) and also have indirect effects on SDG8 (decent work and economic growth), SDG10 (reduced inequalities), SDG16 (peace, justice, and strong institutions). Pillar 2 of the End TB strategy calls for building bold policies and supportive systems. Wielding nutritional policy to aid TB elimination would dovetail with this aspect of the End TB strategy.

Recommendation 3: Increased funding for undernutrition-TB research

While a robust body of historical research supports the idea that undernutrition is a risk factor for TB, undernutrition receives inadequate attention currently despite being the leading TB risk factor. More research is needed to understand which nutrients are the most important for PLWTB, which population groups would benefit the most, and what formulation of macronutrients and micronutrient supplementation would be most cost-effective in reducing incidence, mortality, and morbidity of TB among vulnerable populations such as children and pregnant women as well as the general population.

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