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

Summary

Background Undernutrition is a common comorbidity of tuberculosis in countries with a high tuberculosis burden, such as India. RATIONS is a field-based, cluster-randomised controlled trial evaluating the effect of providing nutritional support to household contacts of adult patients with microbiologically confirmed pulmonary tuberculosis in Jharkhand, India, on tuberculosis incidence. The patient cohort in both groups of the trial was provided with nutritional support. In this study, we assessed the effects of nutritional support on tuberculosis mortality, treatment success, and other outcomes in the RATIONS patient cohort.

Methods We enrolled patients (aged 18 years or older) with microbiologically confirmed pulmonary tuberculosis across 28 tuberculosis units. Patients received nutritional support in the form of food rations (1200 kcal and 52 g of protein per day) and micronutrient pills. Nutritional support was for 6 months for drug-susceptible tuberculosis and 12 months for multidrug-resistant tuberculosis; patients with drug-susceptible tuberculosis could receive an extension of up to 6 months if their BMI was less than 18·5 kg/m² at the end of treatment. We recorded BMI, diabetes status, and modified Eastern Cooperative Oncology Group (ECOG) performance status at baseline. Clinical outcomes (treatment success, tuberculosis mortality, loss to follow-up, and change in performance status) and weight gain were recorded at 6 months. We assessed the predictors of tuberculosis mortality with Poisson and Cox regression using adjusted incidence rate ratios (IRRs) and adjusted hazard ratios (HRs). The RATIONS trial is registered with the Clinical Trials Registry of India (CTRI/2019/08/020490).

Findings Between Aug 16, 2019, and Jan 31, 2021, 2800 patients (mean age 41·5 years [SD 14·5]; 1979 [70·7%] men and 821 [29·3%] women) were enrolled. At enrolment, 2291 (82·4%) patients were underweight (BMI <18·5 kg/m²), and 480 (17·3%) had a BMI of less than 14 kg/m². The mean weight and BMI were 42·6 kg (SD 7·8) and 16·4 kg/m² (2·6) in men and 36·1 kg (7·3) and 16·2 kg/m² (2·9) in women. During the 6-month follow-up, treatment was successful in 2623 (93·7%) patients, 108 (3·9%) tuberculosis deaths occurred, 28 (1·0%) patients were lost to follow-up, and treatment failure was experienced by five (0·2%) patients. The median weight gain was 4·6 kg (IQR 2·8–6·8), but 1441 (54·8%) of 2630 patients remained underweight. At 2 months, 1444 (54·0%) of 2676 patients gained at least 5% of baseline weight. Baseline weight (adjusted IRR 0·95, 95% CI 0·90–0·99), BMI (0·88, 0·76–1·01), poor performance status (ECOG categories 3–4; 5·33, 2·90–9·79), diabetes (3·30, 1·65–6·72), and haemoglobin (0·85, 0·71–1·00) were predictors of tuberculosis mortality. 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.

Interpretation In this study, nutritional support was provided to a cohort with a high prevalence of severe undernutrition. Weight gain, particularly in the first 2 months, was associated with a substantially decreased hazard of tuberculosis mortality. Nutritional support needs to be an integral component of patient-centred care to improve treatment outcomes in such settings.

Funding India Tuberculosis Research Consortium, Indian Council of Medical Research.

Introduction

Tuberculosis is a global public health problem. India had an estimated 3 million cases of tuberculosis and 494 000 tuberculosis deaths among HIV-negative people in 2021.[1] The National Strategic Plan for Tuberculosis Elimination in India has targets of an 80% reduction in

Lancet Glob Health 2023

Published Online August 8, 2023 https://doi.org/10.1016/S2214-109X(23)00324-8

Department of Medicine (Prof A Bhargava MD), **Department of Community Medicine** (M Bhargava MD), **and Department of Radiology** (Adarsh KM MD), **Yenepoya Medical College, Mangalore, India; Center for Nutrition Studies, Yenepoya (Deemed to be University), Mangalore, India** (Prof A Bhargava, M Bhargava, G S Teja MPhil, A Benedetti PhD); **Department of Medicine** (Prof A Bhargava, A Benedetti) **and Department of Epidemiology, Biostatistics and Occupational Health** (A Benedetti), **McGill University, Montreal, QC, Canada; Indian Council of Medical Research–National Institute for Research in Tuberculosis, Chennai, India** (A Meher MPH, B Velayutham MPH, B Watson MSc, G Barik PGDCA, V P Singh MPH, D Singh MPH); **State TB Cell, National Tuberculosis Elimination Programme, Ranchi, India** (R Prasad MD); **WHO Technical Support Network, Ranchi, India** (R R Pathak MPH); **National Tuberculosis Institute, Bangalore, India** (V Chadha MD); **National Tuberculosis Elimination Programme, Ministry of Health and Family Welfare, New Delhi, India** (R Joshi DNB)

Correspondence to: Prof Anurag Bhargava, Department of Medicine, Yenepoya Medical College, Center for Nutrition Studies, Yenepoya (Deemed to be University), Mangalore 575018, India
anuragb17@gmail.com

Research in context

Evidence before this study

Undernutrition in patients with active tuberculosis is a risk factor for tuberculosis mortality, drug toxicity, and relapse. We searched for evidence of nutritional support (macronutrients, micronutrients, or both) on treatment outcomes in MEDLINE, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews on Nov 15, 2022, using the terms "macronutrients", "micronutrients", "food supplement", "diet supplement", "nutrition support", "nutritional supplementation", and "tuberculosis". Search strings were developed using "OR" and "AND" Boolean operators. We searched for observational studies, clinical trials, and key review articles published between Jan 1, 1950, and Aug 1, 2019, in English. We also retrieved additional studies from the bibliography of articles, and identified 35 relevant publications. A Cochrane review on the effect of macronutrient supplementation on tuberculosis outcomes was inconclusive because randomised controlled trials of macronutrient supplementation were few, small, and unable to achieve an optimal intake of calories and proteins. A relative risk of tuberculosis mortality of 0·34 (95% CI 0·10–1·20) was seen in four randomised controlled trials with 567 participants, indicating a possibly effective intervention. The generation of evidence based on randomised controlled trials is ethically problematic in settings such as India, where severe undernutrition and food insecurity are widely prevalent in patients with tuberculosis.

Added value of this study

To our knowledge, this is the largest single programmatic cohort of predominantly HIV-negative patients with drug-susceptible tuberculosis who underwent comprehensive evaluation of clinical, nutritional, and performance status at enrolment and in whom the effect of a food rations-based nutritional intervention on clinical and nutritional outcomes was documented. The study shows high levels of severe and extremely severe undernutrition in patients at diagnosis, which is a contributor to tuberculosis mortality that is currently unaddressed in most national tuberculosis programmes. Most deaths occurred in the first 2 months, 80% occurred at home, and performance status, nutritional status, haemoglobin, and diabetes were identified to be predictors of death. The effect of nutritional support on tuberculosis mortality in this cohort can be inferred from the survival, with nutritional support, of more than 85% of patients with potentially fatal undernutrition (BMI <13 kg/m² in men and <11 kg/m² in women), and the 61% reduced hazard of death in those with desirable (5%) weight gain in 2 months. The case fatality ratio was considerably lower than in another National Tuberculosis Elimination Programme cohort with a similar patient population that had no nutritional support. The nutritional intervention was well accepted and was associated with high rates of adherence to treatment and low rates of treatment failure. However, nutritional recovery was incomplete at 6 months in patients with severe undernutrition at enrolment.

Implications of all the available evidence

Nutritional assessment, counselling, and support need to be implemented in settings with a high burden of tuberculosis and undernutrition, such as India, to improve tuberculosis treatment outcomes. Food-based nutritional support during treatment is associated with weight gain, improved performance status, and a decreased hazard of tuberculosis mortality. However, nutritional recovery in patients with severe undernutrition might require graded support for a longer period.

incidence and a 90% reduction in tuberculosis mortality by 2025, compared with the baseline estimates for 2015.[2] The modest progress in reducing tuberculosis mortality since 2015 was reversed during the COVID-19 pandemic.[3]

Preventing tuberculosis mortality requires early diagnosis, provision of high-quality care with comprehensive evaluation, and management of comorbidities.[4] In countries with a high tuberculosis burden such as India, undernutrition is a common comorbidity due to disease-related weight loss acting on a substrate of pre-existing chronic undernutrition. In patients with tuberculosis, undernutrition is often severe, potentially lethal, and, in the absence of nutritional support, persists even after treatment.[5,6] Undernutrition is a consistent risk factor for mortality, drug toxicity, delayed sputum conversion, and recurrence.[5,7,8]

WHO recommends nutritional assessment, counselling, and support as integral components of tuberculosis care.[9,10] These recommendations await adoption in most national programmes.[11] Although modelling studies indicate that addressing undernutrition could reduce tuberculosis mortality,[12] the impact of macronutrient and micronutrient supplementation on treatment outcomes in clinical trials has been inconclusive due to small numbers of participants, heterogeneity, and not reaching optimal intake of calories and proteins.[13] However, a possible reduction in tuberculosis mortality in HIV-negative patients has been noted in small randomised controlled trials of nutritional support.[13]

Reducing Activation of Tuberculosis Through Improvement of Nutritional Status (RATIONS) is an open-label, parallel-arm, cluster-randomised controlled trial involving household contacts of adult patients with microbiologically confirmed pulmonary tuberculosis in Jharkhand state in eastern India.[14] The primary objective of the trial was to estimate the effect of nutritional support in reducing tuberculosis incidence among household contacts of patients in a setting with high prevalence of undernutrition. In this report, we describe

tuberculosis mortality, treatment success, and changes in nutritional and performance status in the patient cohort receiving nutritional support within the RATIONS trial, over the intervention period of 6 months.[14]

Methods

Study design

The RATIONS trial design, detailed methods, recruitment, intervention, follow-up, and outcomes have been described previously.[14] The trial population in this cluster-randomised controlled trial consisted of the household contacts of 2800 patients with microbiologically confirmed pulmonary tuberculosis drawn from 28 tuberculosis units (trial clusters) across four districts of Jharkhand. The 28 clusters were randomly assigned in a 1:1 ratio to receive the intervention of nutritional support (food baskets and micronutrients) for household contacts or no nutritional support for household contacts. The primary outcome in this population was the difference in tuberculosis incidence among household contacts of the two groups over a follow-up period of 2 years from the treatment of the index patient with microbiologically confirmed pulmonary tuberculosis. The trial found a 39% reduction in the incidence of tuberculosis (for all forms of tuberculosis), and a 48% reduction in incidence of microbiologically confirmed pulmonary tuberculosis in household contacts in the intervention group compared with the control group.[14]

All 2800 patients with microbiologically confirmed pulmonary tuberculosis were provided with nutritional support (food baskets and micronutrients) for the treatment period, regardless of their baseline nutritional status or assignment group. They were followed up for the treatment period for the secondary treatment outcomes of tuberculosis mortality (all-cause mortality during the treatment period), treatment success, changes in nutritional and performance status, and occurrence of severe adverse effects (appendix p 2).

The RATIONS trial was embedded within the National Tuberculosis Elimination Programme (NTEP) in four districts of Jharkhand: Saraikela-Kharsawan, West Singhbhum, East Singhbhum, and Ranchi (appendix pp 2–3). Jharkhand (meaning land of trees) has substantial forest cover and a population of 33 million; the population is predominantly rural (75%) and almost a quarter is indigenous, known as scheduled tribes. The state has one of the highest proportions (46%) of population living in multidimensional poverty in India.[15] The prevalence of underweight is 26·2% in women (aged 15–49 years) and 39·4% in children younger than 5 years, compared with the national average of 18·7%.[16] In 2021, the tuberculosis case notification rate was 130 per 100 000 population,[17] and the prevalence of microbiologically confirmed pulmonary tuberculosis was 352 per 100 000 population compared with 316 per 100 000 population for India overall.[18]

Participants

Patients and their household contacts from 28 tuberculosis units of the NTEP were enrolled between Aug 16, 2019, and Jan 31, 2021. The trial ended on Aug 13, 2022. A district is an administrative unit, and a tuberculosis unit is a programme management unit at the subdistrict level that covers 0·15–0·25 million population. All patients aged 18 years or older with microbiologically confirmed pulmonary tuberculosis and initiated on treatment within the previous 2 weeks were considered eligible for inclusion, regardless of their HIV or drug susceptibility status, if they had at least one eligible household contact.[14] An eligible household contact was a person living in the same house as the index patient, and eating from the same kitchen for at least one night or for frequent or extended periods during the day during the 3 months before diagnosis of the index patient; household contacts were ineligible if they were currently on treatment for microbiologically confirmed or clinically diagnosed active tuberculosis (appendix p 4).[14,19]

Ethics approval was obtained from the Institutional Ethics Committee of the Indian Council of Medical Research–National Institute for Research in Tuberculosis (number 2018020). Local oversight was provided by the ethics committee of Ekjut, a non-profit organisation involved in field-based research. Field staff obtained written informed consent from participants.

Procedures

Patients were diagnosed by the NTEP and received antituberculosis treatment and supervision as per the guidelines.[19] Patients in both groups received an identical monthly food basket supplying 1200 kcal and 52 g protein per day, and a micronutrient pill containing the recommended dietary allowance based on national recommendations (appendix pp 4, 6),[20] which cost US$0·49 per day, inclusive of delivery costs. The food rations were delivered at home by the field staff for 6 months for drug-susceptible tuberculosis and 12 months for multidrug-resistant tuberculosis. Delivery was challenging due to the difficult terrain and poor connectivity, and was further complicated by restrictions related to the COVID-19 pandemic. The food rations for an individual patient in the cohort with drug-susceptible tuberculosis were extended by up to 6 months if the BMI was less than 18·5 kg/m² at the end of treatment. All patients received INR 500 per month ($6·1 per month) under the direct benefit transfer scheme of NTEP during treatment.[21]

See Online for appendix

Demographic characteristics, household assets (appendix p 4), and risk factors were assessed at baseline, along with anthropometry, blood pressure, pulse oximetry for oxygen saturation (SpO_2), performance status using a modified Eastern Cooperative Oncology Group (ECOG) scale, and oedema assessed by pressure over shins.[22] The ECOG scale is categorised from 0 to 4, with a score of

0 representing no restriction of physical activity and 4 representing complete confinement to a bed or chair (appendix p 5). Haemoglobin was estimated with use of the Hemocue Hb 201+ system (HemoCue, Ängelholm, Sweden) and severe anaemia was defined as haemoglobin less than 80 g/L. Nutritional status was defined according to BMI as per WHO guidelines, with a BMI of less than 16 kg/m² classified as severe underweight and an additional category of BMI less than 14 kg/m² classified as extremely severe underweight (appendix p 5).[23] HIV status and random blood sugar were retrieved from NTEP data. Participants with random blood sugar greater than 11·1 mmol/L, those with self-reported diabetes, and those on diabetes medication were categorised as having diabetes. Hypoxia was defined as SpO_2 of less than 94% and hypotension was defined as systolic blood pressure of less than 90 mm Hg.

At monthly follow-ups for 6 months, we monitored symptoms, treatment adherence, consumption of food rations, adverse drug reactions, anthropometry, and ECOG performance status. We referred patients with critical values of BMI, blood pressure, oxygen saturation, and ECOG performance status, and those with adverse drug reactions to the nearest public health facility (appendix p 6).[20] Mortality and adverse drug reactions were reported to the field staff during follow-up visits or by telephone. Data collection was done using REDCap (version 12.2.7), hosted by the National Institute of Research in Tuberculosis (Chennai, India).

	Overall (n=2800)	Underweight (BMI <18·5 kg/m²; n=2291)*	Not underweight (BMI ≥18·5 kg/m²; n=489)*
Sex			
Male	1979 (70·7%)	1603 (70·0%)	362 (74·0%)
Female	821 (29·3%)	688 (30·0%)	127 (26·0%)
Age, years, mean (SD)	40·3 (14·5)	40·1 (14·6)	40·4 (13·6)
Men	41·5 (14·3)	41·3 (14·5)	41·7 (13·6)
Women	37·3 (14·5)	37·2 (14·5)	36·5 (13·2)
Caste			
Scheduled tribe	1896 (67·7%)	1613 (70·4%)	270 (55·2%)
Scheduled caste	258 (9·2%)	200 (8·7%)	57 (11·7%)
Other backward classes	551 (19·7%)	424 (18·5%)	121 (24·7%)
Other	95 (3·4%)	54 (2·4%)	41 (8·4%)
Education			
None	1109 (39·6%)	968 (42·3%)	127 (26·0%)
<10 years	1064 (38·0%)	873 (38·1%)	186 (38·0%)
≥10 years	627 (22·4%)	450 (19·6%)	176 (36·0%)
PDS beneficiary†	2356 (84·1%)	1962 (85·6%)	376 (76·9%)
History of alcohol use	1405 (50·2%)	1123 (49·0%)	207 (54·6%)
History of tobacco use	1021 (36·5%)	841 (36·7%)	169 (34·6%)
History of previous tuberculosis	262 (9·4%)	206 (9·0%)	55 (11·3%)
History of previous tuberculosis in family member	395 (14·1%)	312 (13·6%)	83 (17·0%)
Diabetes	139 (5·0%)	80 (3·5%)	57 (11·6%)
HIV infection‡	6/2264 (0·3%)	6/2264 (0·3%)	0/489
Multidrug-resistant tuberculosis at diagnosis§	38/1258 (3·0%)	30/985 (3·0%)	8/264 (3·0%)

Data are n (%) or n/N (%), unless specified otherwise. PDS=public distribution system. *Patient numbers in the columns related to nutritional status might not add up to the overall prevalence of the characteristic because of missing BMI values in 20 patients. †The PDS provides subsidised rations to Indians living below the poverty line. ‡HIV testing was done in 2264 patients. §Multidrug-resistant tuberculosis was diagnosed based on cartridge-based nucleic acid amplification test; 1258 tests were done.

Table 1: **Demographic characteristics and comorbidities in patients with microbiologically confirmed pulmonary tuberculosis in the RATIONS trial**

Outcomes

The following outcomes of treatment documented by the NTEP were noted: cure or treatment completion (treatment success), deaths during treatment, loss to follow-up, and treatment failure. In addition, minor adverse effects during treatment were noted by field staff. The diagnosis of adverse effects such as drug-induced hepatitis was based on evaluation by physicians in health facilities. We defined treatment outcomes as per NTEP definitions (appendix pp 4–5).[19] Loss to follow-up during the treatment period was defined as patients who interrupted treatment for 1 month or longer. Loss to follow-up for the purpose of trial intervention was considered non-availability for follow-up for 2 months or longer during the treatment period (appendix p 5).[19] Tuberculosis mortality was defined as all-cause mortality in HIV-negative patients during treatment.[3] The case fatality ratio was defined as the number of patients with tuberculosis mortality divided by the number of patients forming the cohort at the beginning of the observed period.[24] The diagnosis of tuberculosis involved smear microscopy (graded as scanty, 1+, 2+, or 3+) and cartridge-based nucleic acid amplification tests (GeneXpert [Cepheid, Sunnyvale, CA, USA] or Truenat [Molbio Diagnostics/Bigtec Labs, Goa/Bengaluru, India]) and the end of treatment evaluation was by smear microscopy as per NTEP guidelines.[19]

Statistical analysis

Continuous variables were summarised as mean (SD) or median (IQR). Differences between groups were assessed using Student's *t* test or Mann-Whitney *U* test, as appropriate. The association between categorical variables was assessed using the χ^2 test or Fisher's exact test. We estimated the 6-month tuberculosis mortality rate and case fatality ratio with 95% CIs and compared these outcomes via adjusted incidence rate ratios (IRRs) among key subgroups (sex, bodyweight, BMI category, and ECOG performance status). Baseline ECOG performance status was dichotomised as poor (score of 3–4) or better (score of 0–2). All of the aforementioned analyses used a marginal Poisson regression model with independence correlation structure, and the results are presented based on the empirical standard errors to account for clustering by tuberculosis unit and using the log of person-time at risk as the offset. The model was adjusted for potential confounders that are known to be associated with the exposure of undernutrition and are independent

predictors of outcomes such as tuberculosis mortality: age, sex, caste, family history of tuberculosis, alcohol use, tobacco use, diabetes, cough duration, sputum smear grade, ECOG category, haemoglobin, and log of value of household assets as a measure of standard of living. We included interactions between baseline bodyweight, and age, sex, and ECOG score in the regression model and used the p value for the regression coefficient to test the interaction. Participants were censored at 180 days. We estimated the change in weight and BMI (absolute and relative), stratified by sex. With use of a Cox proportional hazards model, we compared time to death (via adjusted hazard ratios [HRs]) over 6 months in participants who gained and did not gain weight over the first 2 months. In this analysis, we considered weight gain as a time-dependent covariate, which started at zero for all patients and changed to one if there was desirable (≥5%) weight gain at 2 months.[25] Missing values were imputed via chained equations,[26] using the missingness-at-random assumption. In sensitivity analyses, we also considered a complete case analysis. We assessed the proportional hazards assumption and used a stratified model in the case of violations. Kaplan-Meier survival curves, stratified by ECOG status and bodyweight category at enrolment, were estimated. The analyses were done with STATA (version 17.0) and R (version 4.1.2).

The RATIONS trial is registered with the Clinical Trials Registry of India (CTRI/2019/08/020490).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

The patient cohort (n=2800) was recruited between Aug 16, 2019, and Jan 31, 2021 (appendix p 7). At enrolment, the mean age was 41·5 years (SD 14·5) in men and 37·3 years (14·5) in women (table 1). Most individuals belonged to indigenous communities (scheduled tribes), were engaged in manual labour (appendix p 6), and were beneficiaries of subsidised food rations from the public distribution system; almost 40% had no schooling. HIV–tuberculosis co-infection was found in six (0·3%) of 2264 tested participants, and 139 (5·0%) of 2800 participants had diabetes.

The mean bodyweight at enrolment was 42·6 kg (SD 7·8) in men and 36·1 kg (7·3) in women, and mean BMI was 16·4 kg/m² (2·6) and 16·2 kg/m² (2·9), respectively (table 2). More than 80% of participants were underweight, almost half were severely underweight, and 17% had a BMI of less than 14 kg/m². Almost a quarter of participants had a bodyweight of less than 35 kg, and the cohort included 143 men with a BMI of less than 13 kg/m² and ten women with a BMI of less than 11 kg/m². The lowest recorded bodyweight and BMI were 22·0 kg and 8·3 kg/m² in men, and 18·8 kg and 8·6 kg/m² in women.

Only 29 (1·0%) of 2780 patients were overweight or obese

	Patients with available data, n	Characteristic
Bodyweight, kg	2785	..
Men	1968	42·58 (7·76)
Women	817	36·08 (7·25)
Bodyweight category, kg	2785	..
18·0–24·9	..	27 (1·0%)
25·0–29·9	..	172 (6·2%)
30·0–39·9	..	1211 (43·5%)
40·0–54·9	..	1233 (44·3%)
55·0–70·0	..	129 (4·6%)
>70·0	..	13 (0·5%)
Height, cm	2780	..
Men	1965	160·78 (6·38)
Women	815	149·36 (6·00)
Stunting*	2780	..
Men	1965	1067 (54·3%)
Women	815	431 (53·9%)
BMI, kg/m²	2780	..
Men	1965	16·44 (2·59)
Women	815	16·15 (2·90)
BMI category, kg/m²	2780	..
≥25·0 (overweight or obese)	..	29 (1·0%)
18·5–24·9 (normal)	..	460 (16·5%)
<18·5 (underweight)	..	2291 (82·4%)
17·0–18·4 (mild underweight)	..	485 (17·4%)
16·0–16·9 (moderate underweight)	..	455 (16·4%)
14·0–15·9 (severe underweight)	..	871 (31·3%)
<14·0 (extremely severe underweight)	..	480 (17·3%)
Haemoglobin, g/L	2734	104·5 (18·9)
Anaemia†	2734	2411 (88·2%)
Haemoglobin <80 g/L	2734	204 (7·5%)
Sputum smear examination as basis of diagnosis‡	..	2025
Grade scanty to 1+	2025	910 (44·9%)
Grade 2+ to 3+	2025	1115 (55·1%)
CB-NAAT as basis of diagnosis‡	..	775
Modified ECOG performance status	2800	..
0 (able to carry out normal activity)	..	79 (2·8%)
1 (ambulatory but not able to do strenuous activity)	..	1202 (42·9%)
2 (can do self-care, cannot work, up and about <50% of waking hours)	..	1194 (42·6%)
3 (self-care only, confined to bed or chair >50% of waking hours)	..	271 (9·7%)
4 (no ability to carry out self-care, confined to bed or chair)	..	54 (1·9%)
Systolic blood pressure, mm Hg	2753	110·2 (16·7)
Diastolic blood pressure, mm Hg	2753	77·9 (11·9)
Hypotension (systolic blood pressure <90 mm Hg)	2753	286 (10·4%)
Hypoxia (SpO_2 <94%)	2797	249 (8·9%)
Oedema	2800	130 (4·6%)

Data are mean (SD) or n (%). Percentages might not add to 100% due to rounding. Some patients could not be assessed for height or weight due to a disability or an inability to stand. CB-NAAT=cartridge-based nucleic acid amplification test. ECOG=Eastern Cooperative Oncology Group. SpO_2=oxygen saturation. *Stunting in men and women was assumed if the height measured was more than 2 SD below the WHO standards for boys and girls aged 18 years. †Anaemia was defined as haemoglobin <13 g/dL in men and <12 g/dL in women. ‡Some patients underwent both sputum smear examination and CB-NAAT.

Table 2: **Anthropometric and clinical characteristics of patients in the RATIONS trial at enrolment**

(BMI ≥25 kg/m²). Diagnosis was based on smear microscopy in 2025 patients and on cartridge-based nucleic acid amplification tests in 775 patients. Severe anaemia was noted in 204 (7·5%) of 2734 patients screened, 325 (11·6%) of 2800 had poor performance status, 286 (10·4%) of 2753 had hypotension (systolic blood pressure <90 mm Hg), and 249 (8·9%) of 2797 had hypoxia. Weight data were missing for 15 patients and height data were missing for 20 patients due to difficulty standing or disabilities rendering height measurements inaccurate (appendix p 4); all of these patients had mid-upper arm circumference measurements, with a mean of 16·3 cm (SD 2·2). The total follow-up time was 1337·32 person-years. Treatment was successful (cure or treatment completed) for 2623 (93·7%) of 2800 patients. Of these, 1382 (49·4%) were smear-negative at 6 months (cured) and 1241 (44·3%) completed treatment with clinical improvement without smear examination. At 6 months, 28 (1·0%) patients were lost to follow-up, which was mostly due to relocation during the COVID-19 pandemic; 13 of the 28 patients withdrew from the study, mostly due to migration or personal reasons. Five (0·2%) patients had treatment failure and 36 (1·3%) of 38 patients with multidrug-resistant tuberculosis continued their treatment (two were lost to follow-up).

The most common adverse drug reactions were joint pains in 1259 (45·0%) participants, further loss of appetite in 589 (21·0%), itching in 520 (18·6%), abdominal pain in 485 (17·3%), tingling sensation in limbs in 343 (12·3%), and vomiting and nausea in 311 (11·1%; appendix p 11). Eight (0·3%) patients developed drug-induced hepatitis. None of the adverse drug reactions led to loss to follow-up.

108 deaths occurred during follow-up, including 81 (75%) in men and 27 (25%) in women. No deaths occurred in patients with multidrug-resistant tuberculosis or HIV–tuberculosis co-infection. One death at 187 days in a patient who interrupted and then resumed therapy was omitted in the survival analysis that was censored at 180 days. The overall incidence of tuberculosis mortality was 8·00 per 100 person-years (95% CI 6·41–9·99); the incidence was 8·49 per 100 person-years (6·65–10·83) in men and 6·84 per 100 person-years (4·70–9·95) in women. The overall case fatality ratio was 3·9% (95% CI 3·2–4·6).

The median time to death was 46 days (IQR 18–96) and 58 (54%) deaths occurred in the first 2 months of treatment. Although most patients (83 [77%] of 108) died at home, 54 patients who died had a history of

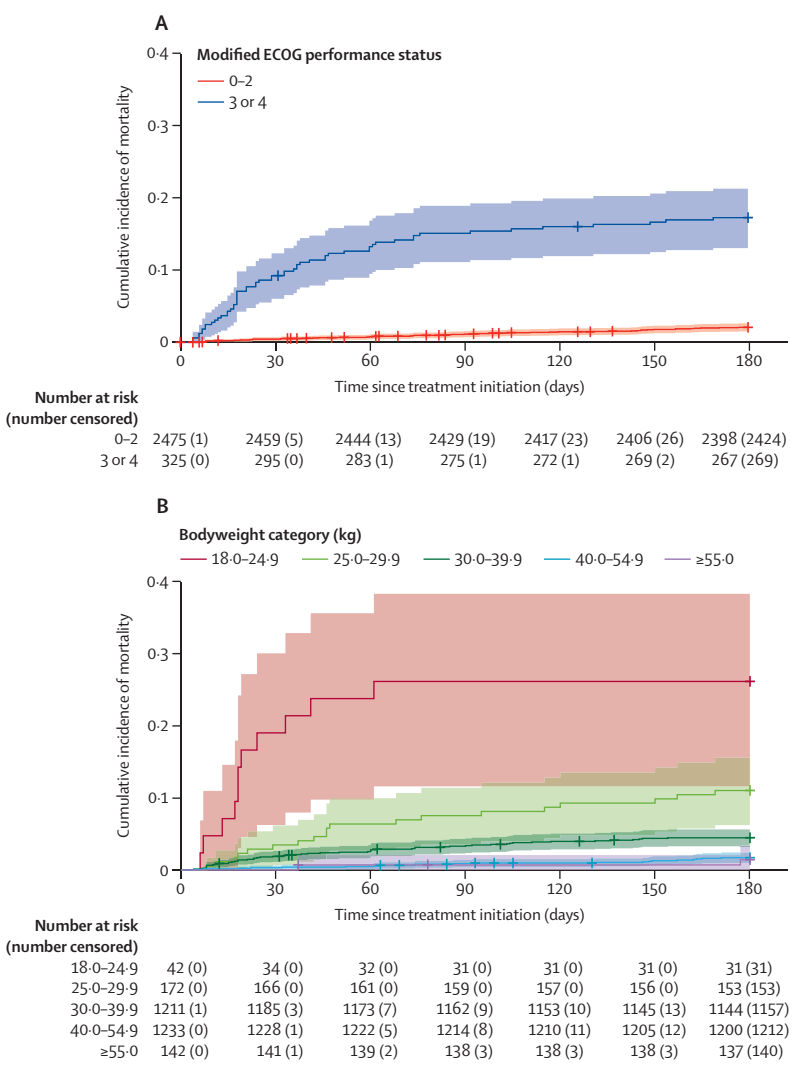

Figure: **Kaplan-Meier plots of cumulative incidence of tuberculosis mortality over 6 months of treatment according to performance status (A) or bodyweight category (B) at enrolment**
ECOG scores were dichotomised into better (score of 0–2) or poor (score of 3 or 4) performance status. The definitions of each ECOG category are described in the appendix (p 5).The number censored is the number of patients who were lost to follow-up or withdrew from the study during the 6-month treatment period. ECOG=Eastern Cooperative Oncology Group.

	Unadjusted IRR (95% CI)	Adjusted IRR (95% CI)
Bodyweight (per kg increase)	0·91 (0·88–0·94)	0·95 (0·90–0·99)
BMI (per kg/m² increase)	0·73 (0·67–0·81)	0·88 (0·76–1·01)
Haemoglobin (per g/dL increase)	0·72 (0·61–0·84)	0·85 (0·71–1·00)
Male sex (*vs* female sex)	1·24 (0·83–1·86)	1·72 (0·89–3·35)
Age (per year increase)	1·03 (1·02–1·05)	1·01 (1·00–1·03)
Poor performance status (*vs* better performance status)*	9·50 (5·25–17·19)	5·33 (2·90–9·79)
Diabetes	3·22 (1·76–5·88)	3·30 (1·65–6·72)
Alcohol use	1·70 (1·11–2·61)	1·18 (0·64–2·17)
Tobacco use	0·62 (0·43–0·90)	0·69 (0·43–1·10)

IRRs were estimated using Poisson regression. The model was adjusted for sex, age, caste, bodyweight, log of value of household assets, trial group, ECOG category, diabetes status, cough duration, sputum smear grade, family history of tuberculosis, haemoglobin, alcohol use, and tobacco use. IRR=incidence rate ratio. ECOG=Eastern Cooperative Oncology Group. *Poor performance status was defined as modified ECOG categories 3 and 4, and better performance status was defined as categories 0–2 (appendix p 5).

Table 3: **IRRs of covariates for the event of tuberculosis death in the RATIONS trial**

hospitalisation. No deaths were attributable to COVID-19. In patients with bodyweight of less than 35 kg (n=680), the case fatality ratio was 7·2% (95% CI 5·4–9·4). The lowest weight and BMI at initiation of treatment in survivors were 24·2 kg and 10·7 kg/m² in men and 18·8 kg and 8·6 kg/m² in women, respectively. In men with a BMI of less than 13 kg/m², 123 (86%) of 143 survived, and in women with a BMI of less than 11 kg/m², nine (90%) of ten survived. The case fatality ratios for different categories of ECOG, baseline bodyweight, and BMI are presented in the appendix (p 9).

In univariable analysis, bodyweight, BMI, age, poor performance status, diabetes, alcohol use, haemoglobin, blood pressure, and oxygen saturation were associated with risk of death during treatment (appendix p 10). At enrolment, the bodyweight of patients who died was 5–6 kg lower, their BMI was 2 kg/m² lower, and their performance status was more frequently poor compared with those who survived. The survivors also had higher weight gain at 1 month and 2 months. Kaplan-Meier survival curves (figure) show that the survival in those with lower bodyweight categories or with poor performance status was lower than those in the higher bodyweight categories and with better performance status.

In the adjusted analysis using marginal Poisson regression, nutritional status, diabetes, and ECOG performance status at enrolment were associated with a higher incidence of tuberculosis mortality, when adjusted for important covariates (table 3). The presence of diabetes or a poor performance status was associated with a substantially increased incidence of tuberculosis death (IRR 3·30 [95% CI 1·65–6·72] for diabetes and 5·33 [2·90–9·79] for poor performance status). As a sensitivity analysis, we considered a complete case analysis, which makes a missing-at-random assumption, and the results were similar. The incidence of tuberculosis deaths with 1-kg or 5-kg higher baseline bodyweight was 5% and 23% lower, respectively, independent of other variables. For baseline BMI, the incidence of tuberculosis deaths decreased by 12% with a one-unit increase in BMI, or by 23% for a two-unit increase in BMI (table 3). The interaction of weight with age was statistically significant (p=0·037), suggesting that the protective effect of weight at baseline decreased for older patients. There was no significant interaction with sex or baseline ECOG score.

The overall median weight gain at 6 months was 4·6 kg (IQR 2·8–6·8), and weight gain was higher in men than in women (table 4). A median gain of two units of BMI was recorded in both sexes. At

	All participants	Men	Women	p value
Bodyweight				
Available data, n	2626	1850	776	..
Baseline bodyweight, kg	40·9 (8·1)	42·8 (7·7)	36·2 (7·2)	<0·0001*
Bodyweight at 6 months, kg	45·8 (8·1)	47·9 (7·5)	40·7 (7·0)	<0·0001*
Weight gain in 6 months, kg	4·6 (2·8–6·8)	4·8 (2·9–7·0)	4·2 (2·5–6·2)	<0·0001†
Percentage weight gain over 6 months	11·3% (6·4–17·4)	11·2% (6·4–17·3)	11·6% (6·5–17·6)	0·42†
BMI, kg/m²				
Available data, n	2621	1847	774	..
Baseline BMI	16·4 (2·7)	16·5 (2·6)	16·2 (2·9)	0·0049*
BMI at 6 months	18·4 (2·6)	18·5 (2·5)	18·2 (2·8)	0·0042*
Change in BMI over 6 months	1·9 (1·1–2·7)	1·8 (1·1–2·7)	1·9 (1·1–2·7)	0·72†
Nutritional status at 6 months (BMI category, kg/m²)	..	..	..	0·003‡
Obese or overweight (≥25·0)	45/2630 (1·7%)	28/1853 (1·5%)	17/777 (2·2%)	..
Normal (18·5–24·9)	1144/2630 (43·5%)	845/1853 (45·6%)	299/777 (38·5%)	..
Underweight (<18·5)	1441/2630 (54·8%)	980/1853 (52·9%)	461/777 (59·3%)	..
Mild underweight (17·0–18·4)	670/2630 (25·5%)	473/1853 (25·5%)	197/777 (25·4%)	..
Moderate underweight (16·0–16·9)	361/2630 (13·7%)	247/1853 (13·3%)	114/777 (14·7%)	..
Severe underweight (14·0–15·9)	350/2630 (13·3%)	226/1853 (12·2%)	124/777 (16·0%)	..
Extremely severe underweight (<14·0)	60/2630 (2·3%)	34/1853 (1·8%)	26/777 (3·3%)	..
Modified ECOG performance status at 6 months§	..	..	..	0·17‡
0	2000/2651 (75·4%)	1430/1867 (76·6%)	570/784 (72·7%)	..
1	558/2651 (21·0%)	377/1867 (20·2%)	181/784 (23·1%)	..
2	74/2651 (2·8%)	47/1867 (2·5%)	27/784 (3·4%)	..
3	13/2651 (0·5%)	10/1867 (0·5%)	3/784 (0·4%)	..
4	6/2651 (0·2%)	3/1867 (0·2%)	3/784 (0·4%)	..

Data are mean (SD), median (IQR), or n/N (%), unless specified otherwise. Percentages might not add to 100% due to rounding. ECOG=Eastern Cooperative Oncology Group. *Calculated by Student's *t* test. †Calculated by Mann-Whitney *U* test. ‡Calculated by χ^2 test. §Modified ECOG categories are described in the appendix (p 5).

Table 4: **Nutritional status and performance status at enrolment and after 6 months of nutritional support in patients in the RATIONS trial**

	Adjusted hazard ratio (95% CI)
Bodyweight at enrolment (per increment of 1 kg)	0·92 (0·87–0·97)
Percentage weight gain at month 2 (per 1% increase from enrolment bodyweight)	0·87 (0·81–0·93)
Weight gain of ≥5% at month 2	0·39 (0·18–0·86)

Models were adjusted for sex, age, and haemoglobin, and were stratified by baseline modified ECOG category and diabetes. Results were similar when adjusting only for sex, age, and haemoglobin. The proportionality hazard assumption was tested; it was often violated by diabetes and modified ECOG category at baseline. In that case, Cox proportionality hazard models were stratified, which was sufficient to ensure that the proportionality hazard assumption held. Missing data were addressed with multiple imputation via chained equations; results of a sensitivity analysis using complete case analysis were similar. ECOG=Eastern Cooperative Oncology Group.

Table 5: **Results of multivariable Cox proportional hazards model examining weight as a time-dependent covariate up to the end of month 2 for the risk of tuberculosis mortality over a treatment period of 6 months**

2 months, the median change in weight was 2·2 kg (1·2–3·6) and in BMI was 0·89 kg/m² (0·49–1·46); 1444 (54·0%) of 2676 patients gained at least 5% of their baseline weight. In 206 (7·7%) of 2674 patients, BMI was unchanged or reduced at 2 months. At 6 months, the proportion of those with normal BMI increased from 16·5% to 43·5%, but 1441 (54·8% remained underweight; this included more than half of men and almost 60% of women. Of the 48·6% of patients who were severely underweight at baseline, 15·6% continued to be so at the end of treatment. In terms of ECOG performance status, the proportion of patients in category 0 (able to carry out normal activity) increased from 2·8% at baseline to 75·4% at the end of treatment (table 3, appendix p 8).

Absolute and relative weight gain in the initial 2 months was associated with a reduced risk of tuberculosis mortality in Cox regression analysis. The adjusted HR of baseline weight was 0·92 (95% CI 0·87–0·97) per 1-kg increment, with adjustment for male sex, age, baseline ECOG category, diabetes, and haemoglobin (table 5). The adjusted HR of bodyweight at 2 months for death during treatment was 0·68 (0·56–0·82) per 1-kg increment. The adjusted HR of percentage weight gain at 2 months for death was 0·87 (0·81–0·93) per 1% increase. We considered a 5% weight gain by 2 months to be desirable;[22] in Cox proportional hazards analysis, a desirable weight gain reduced the hazard (instantaneous risk) of death compared with those who gained less weight (adjusted HR 0·39 [0·18–0·86]; table 5). The results of Cox regression using complete case analysis and multiple imputation using a missing-at-random assumption were almost identical (data not shown).

Discussion

In our cohort of 2800 patients with microbiologically confirmed pulmonary tuberculosis, we observed a high prevalence of undernutrition. Severe undernutrition was seen in almost half of patients, and BMIs that were low enough to pose an immediate threat to life in the absence of nutritional intervention (<13 kg/m² in men and <11 kg/m² in women)[27] were seen in 153 (5·5%) patients at baseline. Most deaths occurred in the intensive phase of treatment, with an overall case fatality ratio of 3·9%. At diagnosis, several indicators that can be easily assessed, such as bodyweight, BMI, haemoglobin, diabetes, and ECOG performance status, were predictors of tuberculosis mortality. Previous cohort studies have reported an association between these predictors and tuberculosis mortality.[5,28–30] Weight gain during treatment, especially at 2 months, was associated with reduced mortality, with the instantaneous risk of death over the treatment period reducing by 13% for a 1% weight gain and by 61% for a 5% weight gain at 2 months.

The nutritional support delivered to patients in the form of food rations and micronutrient pills as an adjunct to antituberculosis treatment was feasible, cost less than $0·5 per day, and was associated with high rates of treatment success, lower loss to follow-up and treatment failure, more than 10% weight gain, and a marked improvement in performance status. These are an improvement over the outcomes reported by the NTEP. In 2022, the NTEP reported the following outcomes for patients notified in the public sector in 2020: treatment success of 83%, tuberculosis mortality of 4·4%, loss to follow-up of 2·5%, treatment failure of 0·6%, regimen changes of 1·8%, and outcomes not evaluated of 1·9%.[17] The national case fatality ratio appears similar to that seen in our study, but states with better health infrastructure, such as Kerala, had higher case fatality ratios (7·9%) than Jharkhand (2·9%).[17] A cohort from NTEP during the COVID-19 pandemic, reported in 2022, had a case fatality ratio of 6·5% in the first 2 months, which was much higher than in our cohorts.[31]

Our study did not randomly assign patients to a control group without nutritional support for ethical reasons. Nevertheless, our results show a predictive effect for undernutrition at enrolment, and a protective effect of weight gain for tuberculosis mortality. Outcomes from two previous large multicentre cohort studies in patients with pulmonary tuberculosis that did not provide nutritional support are relevant because they had similar inclusion criteria, and a low prevalence of HIV and multidrug-resistant tuberculosis. One of these studies was conducted in southern and western India and included private-sector patients,[30] and the other was an NTEP cohort that included participants from states such as Madhya Pradesh with similar socioeconomic indicators to Jharkhand.[32] In the private-sector study, the loss to follow-up was 12%, and 78·5% completed treatment.[30] The NTEP cohort study reported a 6% (93 of 1565) case fatality ratio, 6% loss to follow-up, and 8% treatment failure.[32] However, that study defined treatment failure with documentation of negative cultures at the end of

treatment, unlike in RATIONS.[32] A case fatality ratio of 16 (15%) of 104 in patients with bodyweight of less than 35 kg was reported in another cohort study from the NTEP.[28] Improved treatment success with nutritional support was also seen in a 2021 pilot study in India.[33]

The NTEP reports a high prevalence of undernutrition in people in India with tuberculosis, with median bodyweights of 43 kg in men and 38 kg in women.[34] The weight of men in our cohort was similar, whereas those of women were lower than the NTEP data. A mean weight gain of 3·2 kg was reported in an NTEP cohort,[35] and it was 1·5 times higher in our cohort with nutritional support. An unchanged or decreased BMI at 2 months, associated with a five-fold higher risk of tuberculosis mortality, was observed in 59% of patients in a recent study in which patients did not receive nutritional support.[30] Static or decreasing BMIs at 2 months were observed in only 7% of our cohort, indicating better weight gains. Overall, almost 45% of our patients had a normal BMI (18·5–24·9 kg/m²) at the end of 6 months. The dietary energy surplus over expenditure required to gain 1 kg of weight is approximately 7500 kcal.[36] Not reaching a normal BMI could be due to a high prevalence of severe and extremely severe undernutrition at enrolment, the inability to reach an adequate dietary surplus in view of poverty, COVID-19-induced disruptions, early return to activity, and physiological limits to nutritional recovery over 6 months. In a smaller study of nutritional support from 2021, weight gains were satisfactory but 13% of patients continued to be severely underweight at the end of intervention.[33]

The current study has some limitations. The study design did not include a control patient group without nutritional support because this was deemed unethical in view of the high prevalence of severe undernutrition[5,33] and its association with mortality reported in Indian patients with tuberculosis.[5,25] Our intervention was based on national guidelines and was standardised, rather than being individualised and graded with reference to nutritional status. Our assessment of adherence to food intervention was indirect,[14] and food sharing could have occurred between patients and their contacts without tuberculosis, although nutritional counselling included advice to families that the food basket should be consumed by the patient alone. Tuberculosis cure, which is defined in the national guidelines as a negative smear examination at end of treatment, was not assessed in almost half of patients due to COVID-19-related disruptions.

A strength of this study is that the patient cohort was more than four times larger than has been studied in previous trials, and we evaluated implementation of nutritional support in a real-world, programmatic setting. The intervention was delivered despite a challenging terrain, poor road connectivity, and forest cover, and without interruption during the COVID-19 pandemic. The food basket was developed after discussion with community workers in the preparatory phase and was well accepted. We had low loss to follow-up and few missing values in our anthropometric measurements.

A primarily food-based nutritional support intervention was feasible, low-cost, and was associated with improved clinical outcomes. These findings have implications for the tuberculosis programme in India and other countries with a large burden of tuberculosis and undernutrition. We suggest that national programmes routinely assess nutritional status, haemoglobin, and performance status at diagnosis, in addition to HIV and diabetes screening; implement graded nutritional support as part of patient-centred care; and provide close supervision with the option of referral for inpatient care in the intensive phase, the period with the highest risk of tuberculosis mortality.

Undernutrition is a widely prevalent, serious, and potentially lethal comorbidity in Indian patients with pulmonary tuberculosis. Baseline bodyweight was a risk factor for tuberculosis mortality, and weight gain in the first 2 months, with nutritional support, was associated with a significantly reduced hazard of death during treatment. The provision of nutritional support with food baskets and micronutrients was feasible and was associated with normalisation of performance status in the majority, as well as higher rates of treatment success, lower rates of loss to follow-up, and better weight gain compared with NTEP data.

Contributors

ABh, MB, and BV were involved in funding acquisition. ABh, MB, BV, and ABe were involved in conceptualisation. ABh, MB, AM, GST, BW, GB, and AKM curated the data, and along with them ABe, VPS, DS, and RRP contributed to formal analysis. Investigations were done by ABh, MB, AM, BV, VPS, AKM, and RRP. The methodology was the responsibility of ABh, MB, AM, BV, BW, ABe, and VC. ABh, MB, AM, BV, BW, GB, GST, VPS, DS, RP, and RJ were involved in supervision and project administration. The software was the responsibility of ABh, MB, AM, GST, BW, GB, VPS, and DS. Validation was done by ABh, MB, AM, GST, BW, and ABe, and visualisation was done by ABh, MB, GST, and ABe. ABh, MB, ABe, VC, and RJ were involved in the writing of the original draft and all authors were involved in reviewing and editing the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

We declare no competing interests.

Data sharing

Data will be made available upon reasonable request (made to the corresponding author) after planned analyses and reporting have been completed.

Acknowledgments

This work was supported by grants from the India Tuberculosis Research Consortium, Indian Council of Medical Research (India vide grant number 5/8/5/57/TB consortium/Call India Project/2017/ECD-1). We appreciate the tremendous efforts of the entire field team who worked in a difficult terrain, and continued work without any interruption during the COVID-19 pandemic. The cooperation of the district tuberculosis officers of Ranchi, East Singhbhum, West Singhbhum, and Seraikela-Kharsawan and their teams is gratefully acknowledged. We acknowledge the support of Central Coalfields for making available laboratory space and equipment in Ranchi, and the Letzdream Foundation for providing support for handheld devices for data entry and two-wheelers for the supervisory team. We acknowledge Anika Juneja (Institute of Public Health, Bengaluru, India) and Carl Britto (Boston Children's Hospital, Boston, MA, USA) for their contributions to the launch of substudies and the trial, and

Kannan Thiruvengadam (National Institute for Research in Tuberculosis, Chennai, India) for maintenance of the RedCap database. We thank Madhukar Pai (McGill University, Montreal, QC, Canada) and Shriprakash Kalantri (Mahatma Gandhi Institute for Medical Sciences, Wardha, India) for their critical input on earlier drafts of this report.

References

1 WHO. Global tuberculosis report 2022. Geneva: World Health Organization, 2022.
2 Ministry of Health with Family Welfare, Government of India. National strategic plan for tuberculosis: 2017–25. March, 2017. https://tbcindia.gov.in/WriteReadData/National%20Strategic%20Plan%202017-25.pdf (accessed Nov 1, 2022).
3 WHO. Global tuberculosis report 2021. Geneva: World Health Organization, 2021.
4 Bhargava A, Bhargava M. Tuberculosis deaths are predictable and preventable: comprehensive assessment and clinical care is the key. *J Clin Tuberc Other Mycobact Dis* 2020; **19:** 100155.
5 Bhargava A, Chatterjee M, Jain Y, et al. Nutritional status of adult patients with pulmonary tuberculosis in rural central India and its association with mortality. *PLoS One* 2013; **8:** e77979.
6 Zachariah R, Spielmann MP, Harries AD, Salaniponi FML. Moderate to severe malnutrition in patients with tuberculosis is a risk factor associated with early death. *Trans R Soc Trop Med Hyg* 2002; **96:** 291–94.
7 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:** 871–85.
8 Sinha P, Lönnroth K, Bhargava A, et al. Food for thought: addressing undernutrition to end tuberculosis. *Lancet Infect Dis* 2021; **10:** e318–25.
9 WHO. Guideline: nutritional care and support for patients with tuberculosis. Geneva: World Health Organization, 2013.
10 WHO. Management of severe malnutrition: a manual for physicians and other senior health workers. Geneva: World Health Organization, 1999.
11 Darnton-Hill I, Mandal PP, de Silva A, Bhatia V, Sharma M. Opportunities to prevent and manage undernutrition to amplify efforts to end TB. *Int J Tuberc Lung Dis* 2022; **26:** 6–11.
12 Oxlade O, Huang CC, Murray M. Estimating the impact of reducing under-nutrition on the tuberculosis epidemic in the central eastern states of India: a dynamic modeling study. *PLoS One* 2015; **10:** e0128187.
13 Grobler L, Nagpal S, Sudarsanam TD, Sinclair D. Nutritional supplements for people being treated for active tuberculosis. *Cochrane Database Syst Rev* 2016; **6:** CD006086.
14 Bhargava A, Bhargava M, Meher A, et al. 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. *Lancet* 2023; published online Aug 8. https://doi.org/10.1016/S0140-6736(23)01231-X.
15 NITI Aayog. India national multidimensional poverty index: baseline report. 2021. https://www.niti.gov.in/sites/default/files/2021-11/National_MPI_India-11242021.pdf (accessed Nov 1, 2022).
16 International Institute for Population Sciences. National Family Health Survey (NFHS-5) 2019–21: compendium of fact sheets. 2021. https://main.mohfw.gov.in/sites/default/files/NFHS-5_Phase-II_0.pdf (accessed Nov 1, 2022).
17 Ministry of Health with Family Welfare, Government of India. India TB report 2022. March, 2022. https://tbcindia.gov.in/WriteReadData/IndiaTBReport2022/TBAnnaulReport2022.pdf (accessed Nov 1, 2022).
18 Indian Council of Medical Research, National Institute for Research in Tuberculosis, National Health Mission, Ministry of Health and Family Welfare, Government of India, National Tuberculosis Elimination Programme, WHO. National TB prevalence survey in India (2019-2021): summary report. New Delhi: India Office, 2022. https://tbcindia.gov.in/WriteReadData/l892s/25032022161020NATBPSReport.pdf (accessed Nov 1, 2022).
19 Ministry of Health and Family Welfare, Government of India. Revised national TB control programme: technical and operational guidelines for tuberculosis control in India. 2016. https://tbcindia.gov.in/index1.php?sublinkid=4573&level=2&lid=3177&lang=1 (accessed Nov 1, 2022).
20 Ministry of Health and Family Welfare, Government of India. Guidance document: nutritional care and support for patients with tuberculosis in India. 2017. https://tbcindia.gov.in/WriteReadData/Guidance%20Document%20-%20Nutritional%20Care%20%26%20Support%20for%20TB%20patients%20in%20India.pdf (accessed Nov 1, 2022).
21 Ministry of Health and Family Welfare, Government of India. Government of India gazette notification for DBT with NIKSHAY. https://tbcindia.gov.in/showfile.php?lid=3286 (accessed Nov 1, 2022).
22 de Vallière S, Barker RD. Poor performance status is associated with early death in patients with pulmonary tuberculosis. *Trans R Soc Trop Med Hyg* 2006; **100:** 681–86.
23 Alpers DH, Taylor BE, Beir DM, Klein S. Manual of nutritional therapeutics, 6th edn. Philadelphia, PA: Lippincott Williams & Wilkins, 2015.
24 Huddart S, Svadzian A, Nafade V, Satyanarayana S, Pai M. Tuberculosis case fatality in India: a systematic review and meta-analysis. *BMJ Glob Health* 2020; **5:** e002080.
25 Khan A, Sterling TR, Reves R, Vernon A, Horsburgh CR. Lack of weight gain and relapse risk in a large tuberculosis treatment trial. *Am J Respir Crit Care Med* 2006; **174:** 344–48.
26 Van Buuren S, Groothuis-Oudshoorn K. mice: multivariate imputation by chained equations in R. *J Stat Softw* 2011; **45:** 1–67.
27 Henry CJK. The biology of human starvation: some new insights. *Nutr Bull* 2001; **26:** 205–11.
28 Santha T, Garg R, Frieden TR, et al. Risk factors associated with default, failure and death among tuberculosis patients treated in a DOTS programme in Tiruvallur district, south India, 2000. *Int J Tuberc Lung Dis* 2002; **6:** 780–88.
29 Huangfu P, Ugarte-Gil C, Golub J, Pearson F, Critchley J. The effects of diabetes on tuberculosis treatment outcomes: an updated systematic review and meta-analysis. *Int J Tuberc Lung Dis* 2019; **23:** 783–96.
30 Sinha P, Ponnuraja C, Gupte N, et al. Impact of undernutrition on tuberculosis treatment outcomes in India: a multicenter, prospective, cohort analysis. *Clin Infect Dis* 2023; **76:** 1483–91.
31 Shewade HD, Nagaraja SB, Vanitha B, et al. Screening for severe illness at diagnosis has the potential to prevent early TB deaths: programmatic experience from Karnataka, India. *Glob Health Sci Pract* 2022; **10:** e2100736.
32 Velayutham B, Chadha VK, Singla N, et al. Recurrence of tuberculosis among newly diagnosed sputum positive pulmonary tuberculosis patients treated under the Revised National Tuberculosis Control Programme, India: a multi-centric prospective study. *PLoS One* 2018; **13:** e0200150.
33 Singh AK, Siddhanta A, Goswami L. Improving tuberculosis treatment success rate through nutrition supplements and counselling: findings from a pilot intervention in India. *Clin Epidemiol Glob Health* 2021; **11:** 11.
34 Padmapriyadarsini C, Shobana M, Lakshmi M, Beena T, Swaminathan S. Undernutrition & tuberculosis in India: situation analysis & the way forward. *Indian J Med Res* 2016; **144:** 11–20.
35 Vasantha M, Gopi PG, Subramani R. Weight gain in patients with tuberculosis treated under directly observed treatment short-course (DOTS). *Indian J Tuberc* 2009; **56:** 5–9.
36 Wakabayashi H, Yoshimura Y, Maeda K, Fujiwara D, Nishioka S, Nagano A. Goal setting for nutrition and body weight in rehabilitation nutrition: position paper by the Japanese Association of Rehabilitation Nutrition (secondary publication). *J Gen Fam Med* 2021; **23:** 77–86.