Title

Estimating the epidemiological and economic impact of providing nutritional care for Tuberculosis-affected households across India

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Abstract

Background

Approximately 20% of global tuberculosis (TB) incidence is attributable to undernutrition, increasing to more than a third in India. Targeting nutritional interventions to TB affected households is a policy priority, but understanding of epidemiological and economic impact is limited.

Methods

We developed a transmission model of TB with explicit body mass index strata linked to disease progression and treatment outcomes. We used results from a recent trial of nutritional support to people initiating TB treatment and their households to inform estimates of impact and costs.

Findings

Compared to a baseline with no nutritional intervention, at 50% coverage of adults on TB treatment (~23% of incident TB) and their households, providing nutritional support could prevent 361,200 (318,000–437,700) TB deaths and 880,700 (802,700-974,900) disease episodes over 2023-2035. This would be equivalent to averting approximately one in 20 (4.2%–5.5%) TB deaths and over one in 50 (2.1%–2.4%) TB episodes. The additional health system cost would be $1,349 million (1,221–1,492 million), with an incremental cost-effectiveness ratio of $167 (147-187) per disability-adjusted life year averted. To prevent one TB death or episode, a median 24.4 and 10.0 households needed to receive nutritional support, respectively. If 80% coverage (37% of incident TB) was reached, over one in 14 deaths and one in 30 episodes could be averted, with a total incremental cost of $2,139 million.

Interpretation

A nutritional intervention for TB-affected households could avert a substantial amount of TB disease and death in India, and on TB-specific benefits alone would be highly likely to be cost-effective.

Funding

This work was unfunded.

Research in context

Evidence before this study

We searched PubMed with the terms ("TB" OR "tubercul*") AND ("nutrition*" OR “nutrient*” OR "diet*" OR "vitamin*") AND ("household") AND ("model*" OR "cost-effect*") for articles published from database inception to May 30, 2024, in English. We found 55 studies, from which we identified two studies that had estimated the cost-effectiveness of nutritional supplementation. One modelling study estimated the potential impact of nutritional interventions including at a household level. One cluster-randomised controlled trial estimated the number needed to treat to prevent TB incidence. Sinha and colleagues (2022) used a Markov model from the provider perspective to estimate the effect of providing nutritional support to undernourished individuals in India, finding that a substantial burden of TB in this population could be averted through this likely cost-effective intervention. Focusing on undernutrition in household contacts alone was found to have a lower incremental cost-effectiveness ratio than the general population. Sinha and colleagues (2024) in a preprint took a similar approach but considered household contacts in general, and also found this intervention to be cost-effective at most willingness-to-pay thresholds. Mandal and colleagues used a transmission model to estimate the epidemiological effect of providing nutritional support to undernourished household contacts of TB patients, finding a sizeable proportion of TB could be averted. Meanwhile, Bhargava and colleagues (2023) demonstrated in a trial of nutritional supplements that around 30 households needed to receive the intervention to prevent one case of incident TB in 2 years.

Added value of this study

Our study was the first to evaluate the impact and cost-effectiveness of a nutritional intervention for TB-affected households while considering the effect on onward transmission of reduced TB disease. We compared different recipients of the intervention (both individuals on TB treatment and their household contacts), providing national-level estimates of the health benefits, costs to both the health system and to wider society, and incremental cost-effectiveness ratios for India.

Implications of all the available evidence

We find that if India can deliver a nutritional intervention to 80% of households where individuals are receiving TB treatment, nearly 1.4 million episodes of TB would be averted, and over half a million deaths, at a cost of $168 per disability-adjusted life-year averted. Nutritional supplementation is likely to have substantial TB-related health benefits and be cost-effective at most willingness-to-pay thresholds, even at the national level. A focus on states with high levels of undernutrition is likely to avert a higher proportion of the TB burden, further improving the value for money. Considering the equity and health benefits beyond TB, our study likely underestimates both impact and cost-effectiveness.

Introduction

Globally tuberculosis (TB) disease remains one of the leading causes of mortality due to a single pathogen. Exposure to *M.tb* is widespread in high burden countries,[1] however most individuals contain or clear their infection.[2,3] Co-morbidities like HIV, diabetes and undernutrition can impair the control of *M.tb*, increasing the risk of progressing to disease[4] and unfavourable outcomes.[5] Of these, undernutrition is the leading risk factor for TB globally, accounting for 20% of annual TB incidence, and is a leading comorbidity in TB patients.[6]

In many high TB burden countries, TB and undernutrition constitute a syndemic, with significant prevalence of undernutrition as well as TB infection and disease. India has a low prevalence of HIV infection (0.21% in 2021)[7] but the prevalence of undernutrition is high (16-19%),[8] with between 34 and 45% of TB directly attributable to this risk factor alone.[9] In recent years, the number of food insecure people has increased globally, highlighting the urgent need to incorporate nutritional interventions in TB elimination efforts.

Ecological observations and evidence from well-documented cohorts have supported the benefit of improved nutrition in the decline of TB incidence in what are now low TB burden countries.[10,11] Although there was insufficient research on the effect of nutritional interventions on treatment outcomes,[12] in 2013 the WHO recommended nutritional assessment, counselling and support in selected groups as integral components of TB care.[13] Globally, programmatic implementation of this recommendation is sparse,[14] however in India the TB elimination programme established a direct benefit transfer to enable a nutritious diet to begin to address the issue in 2018.[15] A recent cluster-randomised controlled trial in the state of Jharkhand, India (a setting with high prevalence of poverty, undernutrition and TB) the Reducing Activation of Tuberculosis by Improvement of Nutritional Status (RATIONS) trial, demonstrated for the first time evidence of the effect of a macro nutritional support intervention in reducing TB incidence in the household contacts of adult TB patients[16] as well as improving treatment outcomes for the patients themselves.[17]

Here we modelled the effect of scaling up such an intervention nationally, to estimate the potential impact of the intervention on TB incidence and mortality in the longer term including averted transmission, as well as the cost and cost-effectiveness of introducing nutritional support to those receiving TB treatment and their household contacts.

Methods

We used a previously-published compartmental transmission model of TB in India which included explicit body mass index (BMI) strata.[18] The model structure and calibration were identical to previous,[18] reproduced here with minor modifications described below to simulate the intervention.

Data

We obtained demographic data for India from the United Nations Population Division (2019 revision),[19] the Global Health Observatory,[20] and India National Family Health Surveys.[8,21,22] TB disease and infection prevalence estimates were derived from the National TB Prevalence Survey in India 2019–2021.[23] TB disease incidence, case notifications (accounting for public and private sector differences, see supplementary material), mortality, and number of previous treatments were obtained from data available from the World Health Organization (WHO).[24] Estimates of the population attributable fraction (PAF) of undernutrition for TB were obtained from WHO and recent revised estimates for 30 high TB burden countries.[9,24] Data to inform the BMI specific-risk of progressing to TB disease and TB treatment outcomes were re-estimated from previous estimates,[4,5,25] and future BMI projections were obtained from the LandSyMM food system model.[26] The LandSyMM scenario assumed future socioeconomic dynamics, such as population and GDP changes, were in line with the 'middle of the road' shared socioeconomic pathway (SSP2), while the representative concentration pathway (RCP) 4.5 was used for the climate projections.[27]

Model

We extended a previously published and described age-stratified, compartmental transmission model for TB.[28] We defined four BMI strata: moderate to severe thinness (BMI < 17.0 kg/m^2), mild thinness (17.0 kg/m^2 ≤ BMI < 18.5 kg/m^2), normal BMI (18.5 kg/m^2 ≤ BMI < 25.0 kg/m^2) and overweight to obese BMI (BMI ≥ 25.0 kg/m^2). We used weight-for-height standard deviations for children<5 years and BMI standard deviations for children and adolescent 5-19 years. The risk of TB infection[29,30] and time to diagnosis[31] were assumed to be the same across BMI strata. We varied the risks of progression and reversion to TB disease (similar to methods used elsewhere[32]) and treatment outcomes[5] by BMI strata as in Table S3. Further information on our calculations of varying TB risk by BMI strata are included in the online supplement, as well as comparisons to other available estimates.

Calibration and uncertainty

The model was fitted to 15 calibration targets to represent the TB epidemic in India: the TB incidence rate (overall and by age) in 2000 and 2020,[24] the TB mortality rate (overall) in 2000 and 2020,[24] the TB case notification rate (overall and by age) in 2000 and 2020,[24] the TB disease prevalence (overall and for adults) in 2015 and 2021,[23,33] the TB infection prevalence overall in 2021,[23] and the fraction of subclinical TB among active TB.[34] The model was calibrated using history matching with emulation and Approximate Bayesian Computation Markov Chain Monte Carlo (ABC-MCMC).[35,36] We validated our calibration by comparing estimates of PAF due to undernutrition from our model to recent estimates.[9,24]

We calibrated 1000 parameter sets, using these with the mechanistic TB model to simulate the future, and to quantify the uncertainty in TB natural history (e.g., risks of infection and progression to disease) based on previously published literature (see Supplementary Table S1).

Intervention scenarios
We considered four mechanisms of action of a nutritional support intervention, based on the recent RATIONS trial.[16,17] These included improvements in 1) treatment outcomes, and 2) BMI, for people with TB on treatment, and 3) reductions in incidence, and 4) improvements in BMI, for household contacts. We assumed that improvements in BMI lasted for two years. We assumed instant scale-up of the intervention to reach 50% of the adult population notified and started on treatment each year from 2023–2035, where we did not separate out public versus private providers. We assumed that the coverage and quality of existing interventions in the TB programme remained constant.

For improvements in treatment outcomes for people with TB, we assumed that those who received nutritional support experienced a reduced hazard of death of 0.67 that of those who did not receive nutritional support (where the probability of death on treatment was dependent on factors such as age and BMI). This reflects the 54% of patients in the trial who experienced weight gain ≥5% at 2 months, which was associated with a reduced hazard of death (adjusted HR 0·39, 95% UI 0·18–0·86).[17] Improvements in the trial were also suggested for loss to follow up, treatment failure, recurrence, and drug toxicity, which we did not include in our model as they were not reported dependent on weight gain, although further analysis is planned.

Separately, we assumed an increase in BMI in line with the trial[17] for a proportion of adults on treatment equivalent to the intervention coverage.

For reductions in TB incidence in household contacts, we estimated the number of household contacts (both children and adults) who were expected to develop TB disease, and reduced this using the trial incident rate ratio. We estimated the number at risk using the number of households receiving the intervention, the average household size minus one (the person with TB on treatment)[8] and the proportion of those that would be expected to develop TB disease (3,419 [95% UI 1,569–5,132] per 100,000 [based on a previous review[37] using the first 3 years for low and middle income countries only]). We multiplied this by the protective effect of the trial (1 - 0·61) to identify those who would have gone on to develop TB disease in the absence of the intervention, and assumed that they remained infected with TB only.

We assumed an increase in BMI in household contacts (both adult and children) in line with the trial.[16] However, household contacts are at an increased risk of TB disease.[37] We therefore assumed that 3.1% (95% UI 2.2–4.4%) of contacts would have TB disease, and used the estimated number of household contacts and the intervention coverage to increase the BMI of those with disease in the household.[37] We then assumed that the remaining contacts had the same BMI distribution (and distribution of TB infection status other than disease) as the general population, which we again increased in line with the trial results. We assumed a similar increase in weight-for-height and BMI for children and adolescents. We did not consider the impact of TB screening for co-prevalent TB among household contacts.

Costs
We assumed TB diagnostic and treatment costs from the health system perspective per patient and episode in previous work.[28] In addition, from the societal perspective we accounted for indirect and non-medical patient costs including productivity loss and transportation while receiving treatment.[38-40] We assumed a total intervention cost (cost of food basket and

delivery) per person receiving TB treatment of $92.02, and $33.23 per household contact, based on the cost per month reported in the trial[16] and assuming six months of treatment. Further details are included in Supplementary Table 5.

Outcomes

We estimated TB incidence, mortality rates, and the number of people developing TB disease and dying as a result for each year from 2023 to 2035 for each of the scenarios. We estimated the relative difference in incidence and mortality rates in 2035 compared to 2023, and the cumulative difference in the number of people developing or dying of TB disease between 2023 and 2035.

For each scenario, we calculated the total TB diagnostic, treatment, and intervention costs from the health system and societal perspectives, including indirect and non-medical costs, and the total savings in diagnostic and treatment costs compared to the no-intervention scenario. We discounted both costs and outcomes to 2023 at 3% per year.[41] We calculated the difference in total disability-adjusted life years (DALYs) from each scenario compared to a scenario with no intervention. For individuals currently with TB, we used the disability weight from the Global Burden of Disease 2019 study of 0.333 (0.224, 0.454)[42], and age-specific life expectancy estimates from the United Nations Development Programme[43] to estimate years lived with a disability. We did not incorporate any disability weights for different BMI categories.

We performed cost-effectiveness analyses for scenarios delivering the intervention to different groups (those receiving TB treatment, household contacts of those receiving TB treatment, or both) and compared incremental cost-effectiveness ratios (ICERs) against three cost thresholds: 1 × gross domestic product (GDP) per capita ($2,411 in 2022[44]), and two India-specific cost thresholds[45] (upper [$555] and lower [$410] bounds, representing 23% and 17% of GDP per capita respectively).

Sensitivity analyses

We varied the duration of protection in our model (i.e. how long individuals had an improved BMI or treatment outcome for), comparing if they (i) returned to their prior state immediately after treatment, (ii) remained in an improved state for an average of 1 year waning exponentially, (iii) remained for an average of 5 years, or (v) remained in an improved state for life.

Separately, we varied the coverage of the intervention, assuming the intervention reached either 20% or 80% of the adult population on treatment each year from 2023–2035.

Finally, we varied the intervention impact by BMI status, comparing if (i) the adjusted hazard ratio was higher in those with a low BMI (0.62 for BMI < 17.0 kg/m^2, 0.72 for BMI 17.0-18.4 kg/m^2, 0.80 for BMI 18.5-24.9 kg/m^2 and 0.98 for BMI ≥ 25.0 kg/m^2, based on the same adjusted hazard ratio and the proportion in each group who experienced a weight gain ≥5% at 2 months), (ii) the protective effect of the trial in terms of a incident rate ratio for household contacts varied by BMI status as in the trial (where those with a normal BMI had a larger reduced incident rate ratio than those who were underweight), or (iii) both the adjusted hazard ratio and the incident rate ratio varied by BMI status.

Results

If nutritional support is provided to 50% of adults notified and started on TB treatment in India and their households between 2023 and 2035, we project that a cumulative 880,700 (802,700–974,800) fewer people would develop TB disease and 361,200 (317,900–437,700) fewer would die as a result (see Table 1). This is equivalent to averting 2.2% (2.1–2.54) of all TB disease and 4.6% (4.2–5.5) of all TB deaths. This effect scales linearly with coverage, where at 80% coverage as many as 1,396,800 (1,273,700–1,545,400) fewer people would develop TB and 570,900 (502,300–691,400) fewer would die (see Figure 1 and supplementary material for additional results). Providing nutritional support to 50% of adults on TB treatment only could prevent 46,700 (27,800–71,600) people developing disease, and 234,300 (193,700–305,700) people dying as a result.

The duration of protection did not have a significant effect on our results; given an intervention coverage of 50%, assuming that improvements in BMI (for both patients and their household contacts) and treatment outcomes last only while the patient was on treatment reduces the overall effect of the intervention, but still prevents 868,500 (791,800–961,200) people developing TB disease and 350,200 (308,400–432,5000) deaths. Waning protection between 5 years and lifelong provided slightly improves outcomes (see Supplementary Figure S3). Varying the intervention impact by BMI status does not qualitatively change our results; varying the intervention effect on treatment outcomes by BMI reduces the number of TB deaths averted but makes very little difference to TB disease prevented, while varying the intervention effect on TB incidence in household contacts by BMI increases both the number of TB deaths averted and the number of TB disease episodes prevented (see Supplementary Figure S4).

To prevent one person developing TB disease or dying as a result, a median 10.0 and 24.4 households needed to receive nutritional support, respectively. The number needed to treat remained stable irrespective of intervention coverage, with some variability due to model uncertainty (see Figure 2). Reducing the duration of protection increased the number needed to treat.

Providing nutritional support for TB patients only is likely to be cost-effective at most willingness-to-pay thresholds, with an ICER of $139 (113–167) per DALY averted (see Table 2 and Figures 3) and total budget impact of $664 million (605–733 million, see Supplementary Figure S7). Providing nutritional support additionally to household contacts of TB patients is also likely to be cost-effective at most thresholds, with an ICER of $208 (181–234) per DALY averted and a budget impact of an additional $685 million (615–759 million) compared to providing nutritional support to TB patients only. Both the intervention and treatment costs reduce over time. Compared to no nutritional support, provision of the full intervention has an ICER of $167 (147-187) per DALY averted, which remains consistent with increasing coverage at $168 (147-188) per DALY averted for 80% coverage. Results are qualitatively similar from a societal perspective.

Discussion

Compared to a baseline with no TB nutritional intervention, at 50% coverage of those on TB treatment (~23% of all TB-affected households), providing nutritional support to people with TB would prevent 234,300 people dying of TB in India between 2023–2035, and prevent 46,700 developing disease. This would cost $664 million, with an ICER of $139 per DALY averted. Extending support to household contacts would prevent an additional 126,500 TB deaths and 831,500 developing disease, equivalent to averting a total 2.2% and 4.6% of all TB deaths and disease respectively, over 2023-2035. The additional cost was $685 million, with an ICER of $208 per DALY averted. To prevent one person developing or dying of TB would require nutritional support to 10.0 and 24.4 TB-affected households, respectively.

Our results demonstrate that the majority of intervention benefit in terms of TB disease averted is a result of reduced TB incidence in household contacts of TB patients; indeed an improvement in treatment outcomes for TB patients paradoxically leads to a slight increase in incidence, as these individuals may be more likely to experience recurrent TB. This may no longer be the cases if the nutritional intervention is shown to decrease recurrence rates, for which undernutrition is a risk factor.[46] In contrast, intervention benefit in terms of TB deaths averted is a result of both reduced TB incidence in household contacts (who are therefore less likely to die of TB) and improved outcomes in TB patients. This demonstrates the importance of nutritional support for TB patients as well as their household contacts in reducing TB deaths.

The duration of protection we assumed in our intervention did not affect our results significantly. As improvements in BMI were not important drivers in the intervention, the rate at which these improvements waned did not affect results. However, due to the structure of our model we were unable to vary the duration of protection against progression to TB disease in household contacts of people with TB. Given that this accounted for the majority of reduction in TB incidence, and represents a group of individuals likely at higher long-term risk of TB disease than the general population, these results should be interpreted with caution. Varying the intervention effect by BMI status saw a decreased intervention effect when varying treatment outcomes and an increased effect when varying the prevention of incident TB. This is a result of the differing BMI distribution in the model population compared to the trial, with an increase in mean BMI. As a result, while improved outcomes in those with low BMI do have a larger effect in a population at greater risk of poor treatment outcomes, this is not sufficient to make up for the reduced size of the population affected. Similarly, while there was a reduced effect of the intervention in household contacts with low BMI, due to the larger population in our model with a normal BMI the intervention effect size increased overall.

The effect of the intervention is constrained by two elements. First, the proportion of *M.tb* that is transmitted outside of the household, particularly in a high TB burden setting such as India, limits the amount of TB disease as well as subsequent TB deaths that can be prevented through reduced progression.[47] Second, the proportion of TB mortality that occurs in those who remain undiagnosed with TB disease limits the TB deaths that can be averted through improved nutrition while on treatment.[48] As a result, an intervention targeting only those on TB treatment and their households is only able to avert a limited proportion of TB incidence and mortality, as compared to a population-level intervention to improve nutrition which could have a significantly larger effect size (albeit with a significantly larger associated cost).

The number needed to treat in our results was consistently significantly smaller than in the trials (30 households to prevent one incident case[16]), likely a result of future transmission averted in our model. These values are comparable to other TB-affected household-based interventions such as preventive therapy.[49,50] The targeted nature of the intervention, focused on TB-affected households at a higher risk of both TB disease and poor outcomes, meant that the intervention was likely to see a much higher return for effort than a more general population-based intervention, and support evidence of its cost-effectiveness.[51] For example, previous research[52] found a nutritional intervention rehabilitating 30% of the undernourished population (~300,000,000 people) averted ~16% of cumulative incidence between 2023 and 2030. In contrast, our results demonstrated that an intervention with 50% coverage of adult TB patients and their households (~40,000,000 people) averted ~2% of cumulative incidence between 2023 and 2035. Our results are similar in scale to estimates for a household intervention[52], which suggest an intervention improving BMI for all undernourished household contacts would see a 4.5% reduction in cumulative TB incidence and a 4.8% reduction in mortality between 2023 and 2035 given 100% coverage. Our results also demonstrate a similar, although somewhat improved due to additional transmission averted, cost-effectiveness to recent studies.[51,53]

Our model was limited by a number of assumptions for the intervention effect. A lack of comparator arm for index patients in the trial means that we may have overestimated improvements in outcomes due to weight gain, which could also have occurred in part due to TB treatment.[5] A lack of private treatment pathways in our model may have overestimated achievable coverage of the intervention, and similarly our assumption of instant scale-up is highly optimistic, while other improvements in the programme over time would also reduce the potential intervention effect. In contrast, extending the intervention beyond adults on TB treatment to children and adolescents would increase the potential impact. Variation in both prices and implementation across the country could also lead to important regional differences not considered here, as well as indirect benefits to the community of sourcing food locally. We also did not consider any potential case-finding component of the intervention, where household contacts with prevalent TB may have been more likely to have been diagnosed due to the intervention, or the health cost of post-TB lung damage which was averted due to the intervention. Most importantly, however, we did not consider the wider, non-TB-specific benefits of the intervention and improvements in weight in TB-affected households, such as improved general health and ability to function. These benefits could potentially significantly further increase the intervention impact and cost-effectiveness.

Our results demonstrate that widespread coverage of a nutritional support intervention for TB patients and their household contacts in India could prevent nearly 900,000 people developing TB disease and over 350,000 TB deaths by 2035. Such an intervention could have a significant effect on the TB epidemic in India, reducing both incident TB disease and TB deaths, and is likely to be cost-effective at most willingness-to-pay thresholds. These results are likely a significant underestimate, as considering the wider health benefits beyond TB would only further increase the benefit and cost-effectiveness of the intervention. There is an urgent need to further generate evidence to support rapid translation of this intervention into policy and practice.

A nutritional support intervention for TB-affected households could avert a substantial amount of TB incidence and deaths in India, and would be likely to be cost-effective even when considering only the TB-specific benefits.

Contributors

CFM, RAC and RMGJH conceived and designed the study. CFM and PS did the TB data analysis, PA and RH did the food system modelling, and RAC and RB did the TB modelling. CFM and RAC accessed and verified the data. CFM and RAC wrote the first draft of the Article. All authors critiqued the results, and revised and edited the submitted Article. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data sharing

The analytic code will be available here immediately following publication, indefinitely, for anyone who wishes to access the data for any purpose.

Declaration of interests

We declare no competing interests.

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Figures and tables

Table 1: Health outcomes for nutritional support interventions with 50% coverage of adults receiving tuberculosis treatment in India between 2023 and 2035, assuming 2 years duration of protection. BMI= body mass index, TB= tuberculosis, UI= uncertainty interval, DALY=disability-adjusted life years

	No intervention	People with TB			Household contacts			Full intervention
		Improved outcomes	Improved BMI	Combined	Reduced incidence	Improved BMI	Combined	
Total outcomes								
Incident TB per 100,000 in 2035 (95% UI)	157.6 (141.2, 174.6)	158.0 (141.5, 175.1)	156.8 (140.5, 173.5)	157.2 (140.8, 173.9)	152.6 (136.4, 169.1)	157.2 (140.8, 174.1)	152.1 (136.1, 168.6)	151.6 (135.7, 168.0)
TB deaths per 100,000 in 2035 (95% UI)	30.5 (27.9, 33.8)	29.6 (27.1, 32.8)	30.1 (27.6, 33.4)	29.3 (26.8, 32.4)	29.6 (27.0, 32.8)	30.4 (27.9, 33.7)	29.5 (27.0, 32.7)	28.3 (25.9, 31.4)
DALYs incurred in millions (95% UI)	2212 (2207, 2218)	2208 (2203, 2215)	2211 (2206, 2217)	2207 (2202, 2214)	2209 (2204, 2215)	2212 (2207, 2218)	2209 (2204, 2215)	2204 (2199, 2210)
Outcomes averted								
Additional cumulative incident TB in 1000s (95% UI)	-	-42.1 (-65.2, -32.0)	84.2 (66.7, 121.1)	46.7 (27.8, 71.6)	777.1 (718.0, 850.7)	59.2 (51.0, 69.3)	833.7 (768.7, 917.3)	880.7 (802.7, 974.9)
Additional cumulative incident TB in % (95% UI)	-	-0.1 (-0.2, -0.1)	0.2 (0.2, 0.3)	0.1 (0.1, 0.2)	2.0 (1.8, 2.1)	0.2 (0.1, 0.2)	2.1 (2.0, 2.3)	2.2 (2.1, 2.4)
Additional cumulative TB deaths in 1000s (95% UI)	-	184.3 (148.8, 242.4)	59.4 (47.1, 80.8)	234.3 (193.7, 305.7)	120.5 (108.9, 133.8)	8.9 (7.9, 10.2)	129.2 (116.9, 143.1)	361.2 (318.0, 437.7)
Additional cumulative TB deaths in % (95% UI)	-	2.4 (1.9, 3.1)	0.8 (0.6, 1.0)	3.0 (2.6, 4.0)	1.5 (1.4, 1.7)	0.1 (0.1, 0.1)	1.7 (1.5, 1.8)	4.6 (4.2, 5.5)
DALYs averted in millions (95% UI)	-	3.7 (2.9, 4.8)	1.3 (1.0, 1.6)	4.8 (3.9, 6.0)	3.1 (2.8, 3.5)	0.2 (0.1, 0.2)	3.4 (3.0, 3.7)	8.0 (7.1, 9.4)

Table 2: Resources required for nutritional support interventions with 50% coverage of adults receiving tuberculosis treatment in India between 2023 and 2035, assuming 2 years duration of protection. Note the comparator for incremental cost and cost-effectiveness of the

intervention for people with TB, their household contacts, and the full intervention, is no intervention. All costs are discounted at 3% per year. BMI= body mass index, USD=United States Dollar, TB= tuberculosis, UI= uncertainty interval

	No intervention	People with TB	Household contacts	Full intervention
Total resources				
Average total health system cost (millions USD)	8 618 (7 990, 9 355)	9 281 (8 598, 10 093)	9 313 (8 624, 10 127)	9 967 (9 220, 10 846)
Average total societal cost (millions USD)	11 967 (11 096, 12 991)	12 623 (11 695, 13 719)	12 610 (11 677, 13 702)	13 256 (12 271, 14 417)
Additional resources required				
Additional health system cost (millions USD)	-	664 (605, 733)	696 (625, 771)	1 349 (1 221, 1 492)
Additional societal cost (millions USD)	-	656 (599, 724)	643 (574, 715)	1 289 (1 163, 1 426)
People with TB receiving support in 1000s (95% UI)	-	8 947 (8 141, 9 937)	-	8 829 (8 033, 9 807)
Household contacts receiving support in 1000s (95% UI)	-	-	30 101 (27 384, 33 450)	30 018 (27 312, 33 344)
Number of households needed to treat				
To avert one TB case	-	191.6	10.6	10.0
To avert one TB death	-	38.2	68.5	24.4
Cost-effectiveness				
Incremental health system cost-effectiveness (USD per DALY averted)	-	139 (113, 167)	-	167 (147, 187)
Incremental societal cost-effectiveness (USD per DALY averted)	-	137 (112, 164)	-	192 (166, 218)

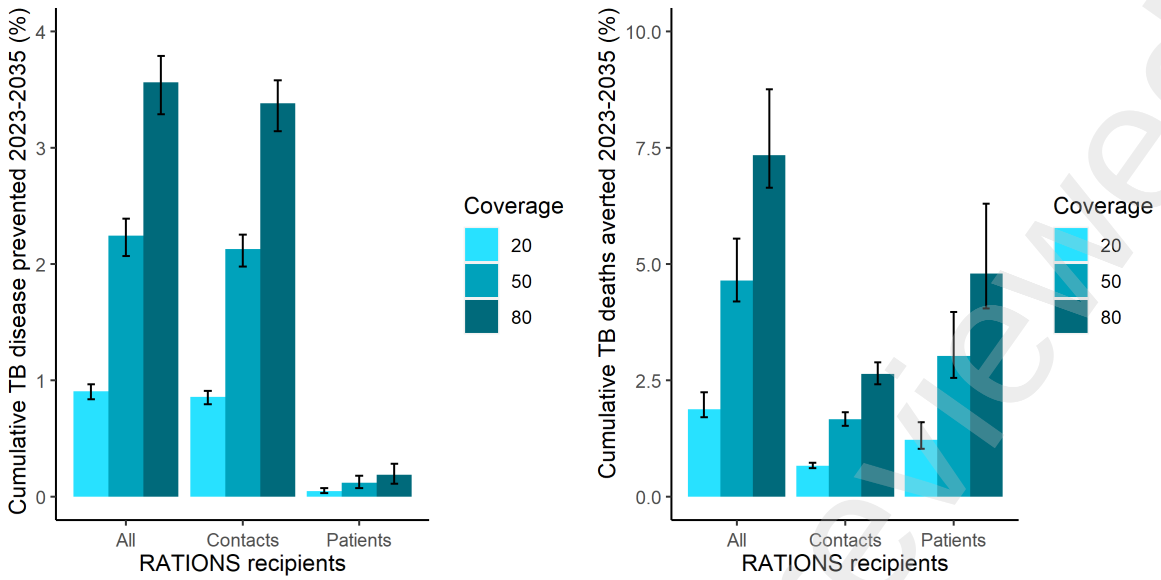


Figure 1: cumulative proportion of tuberculosis (a) disease prevented and (b) deaths averted due to a nutritional support intervention with varying coverage of adults receiving tuberculosis treatment in India between 2023 and 2035, assuming 2 years duration of protection and considering different recipients; all individuals in tuberculosis-affected households, household contacts of people with tuberculosis only, or people with tuberculosis only. TB=tuberculosis

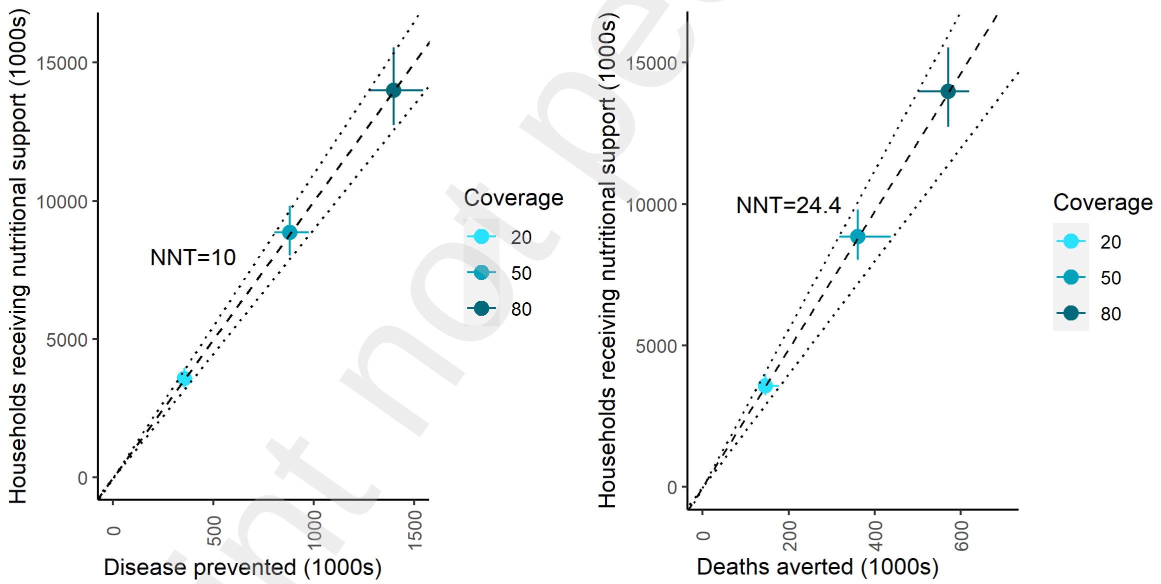


Figure 2: number of households receiving a nutritional support intervention needed to prevent (a) one person developing TB disease and (b) one TB death in India between 2023 and 2035, varying intervention coverage in adults on treatment. NNT=number needed to treat

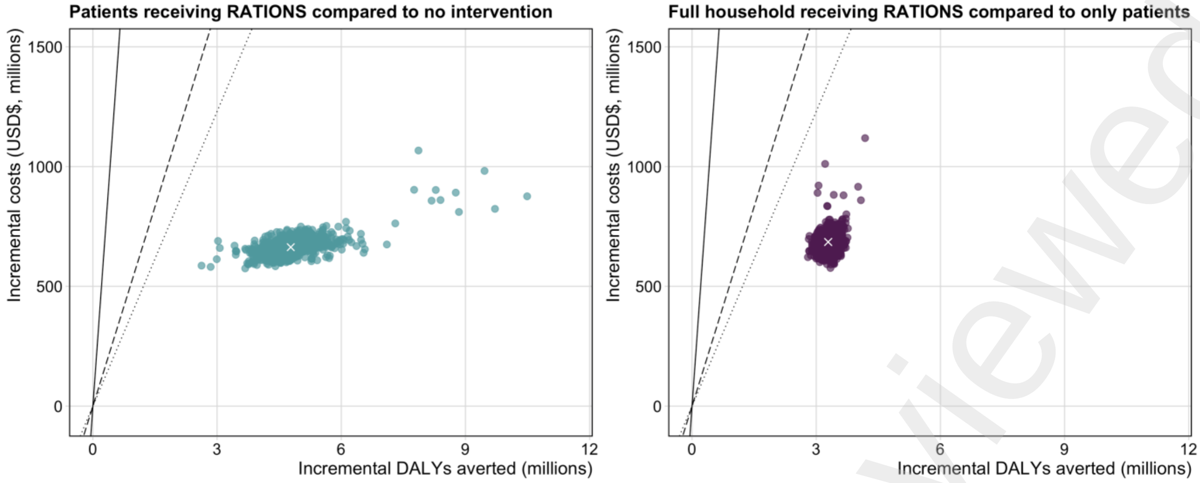
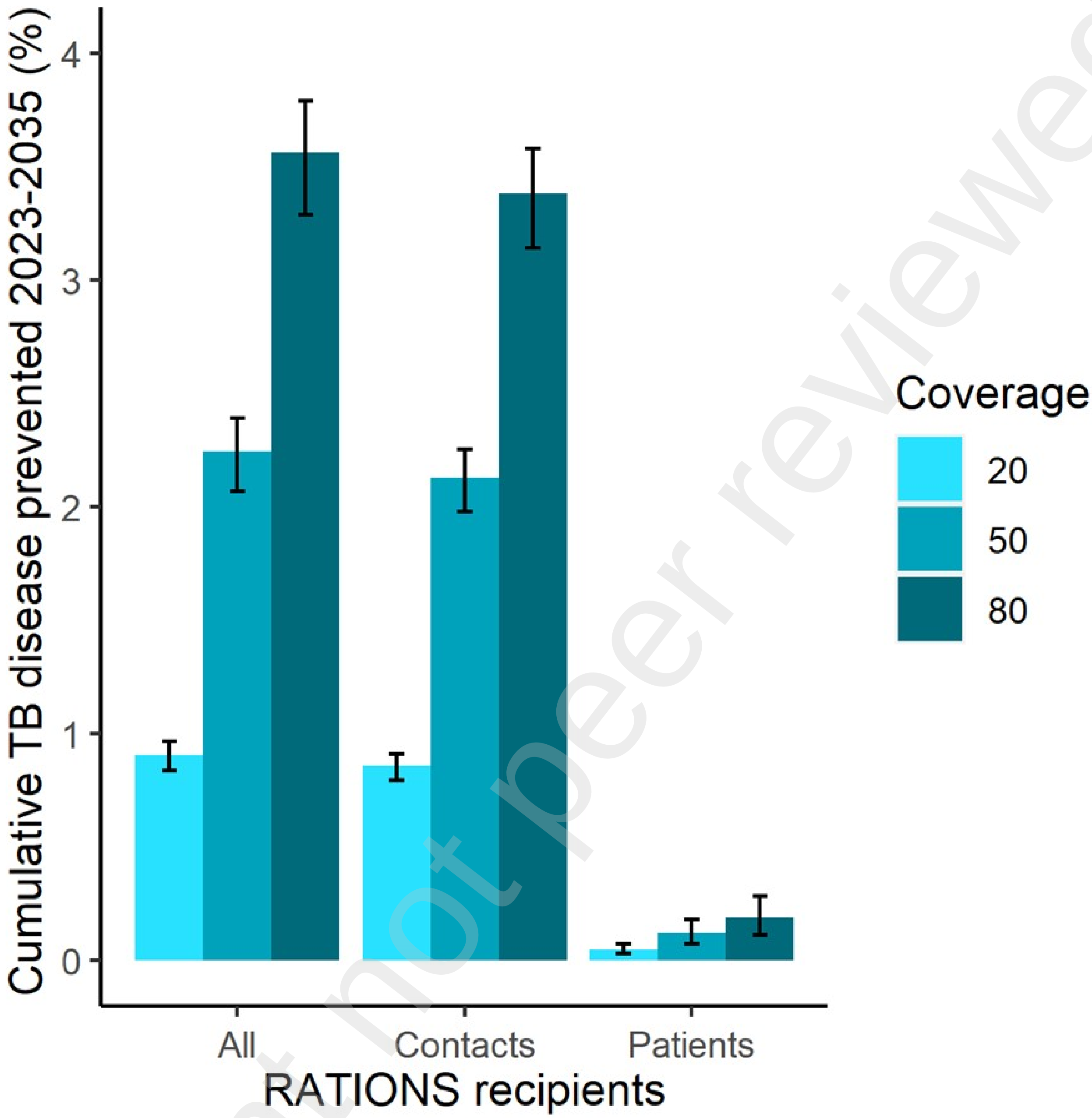
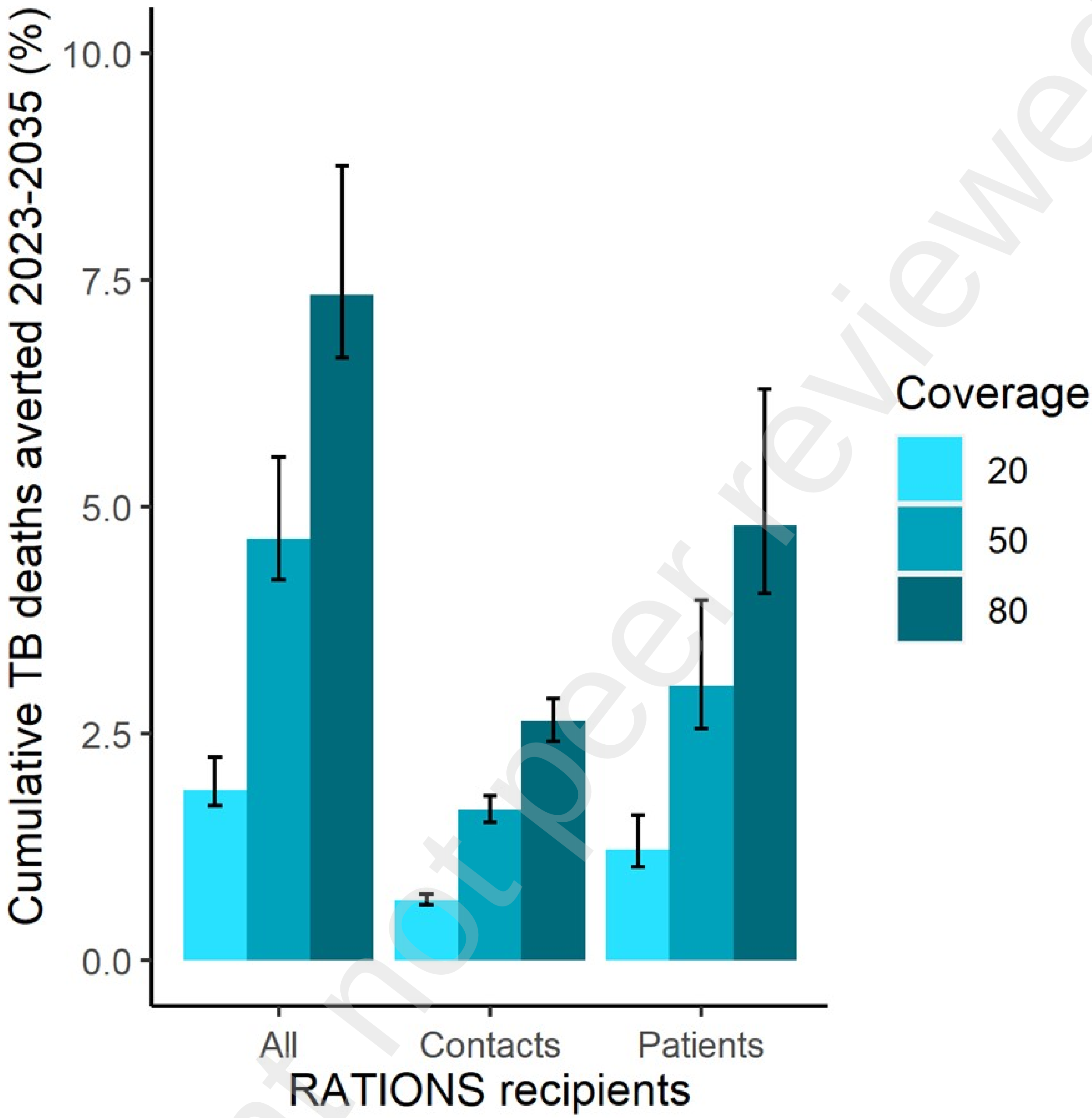
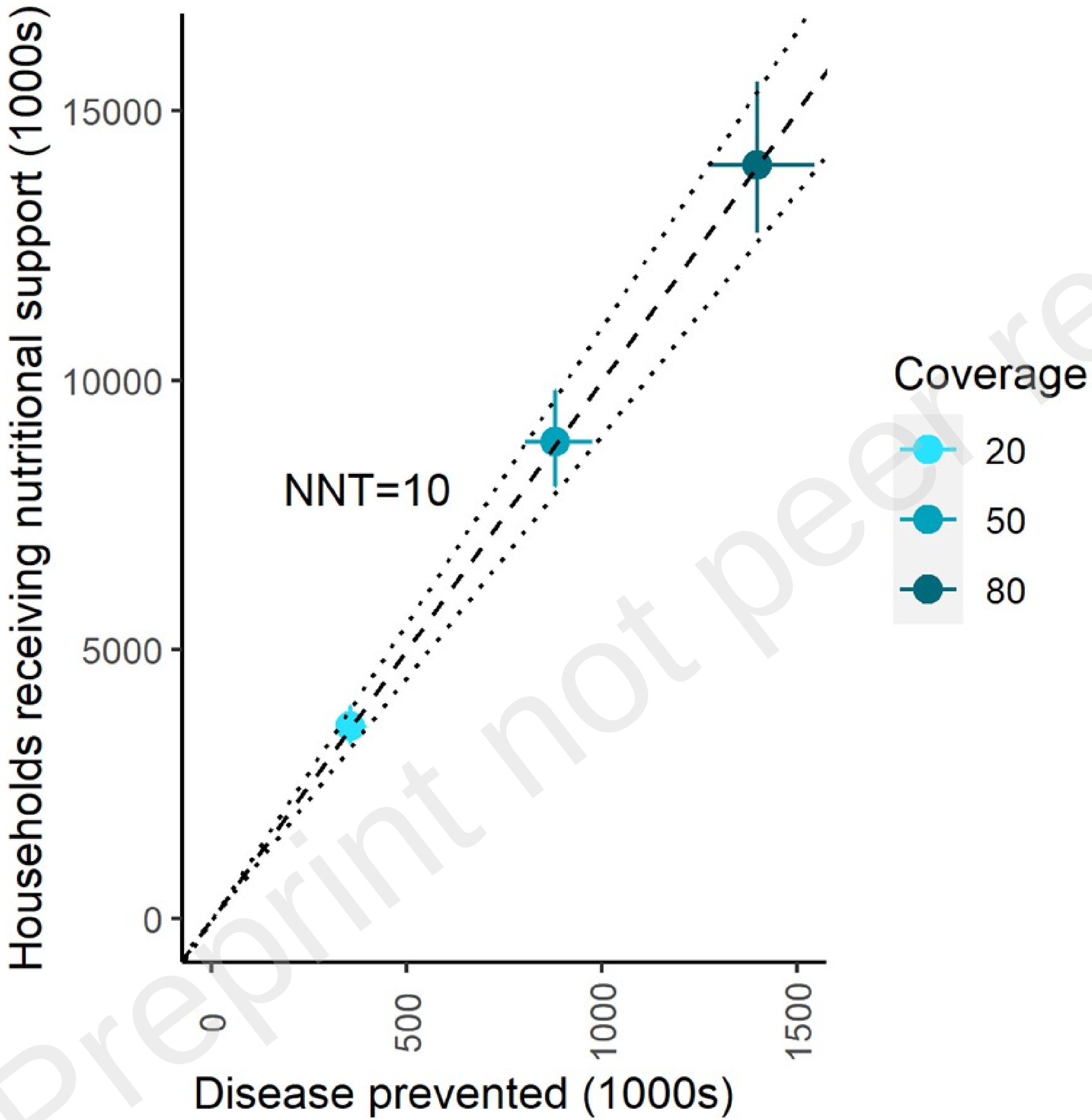


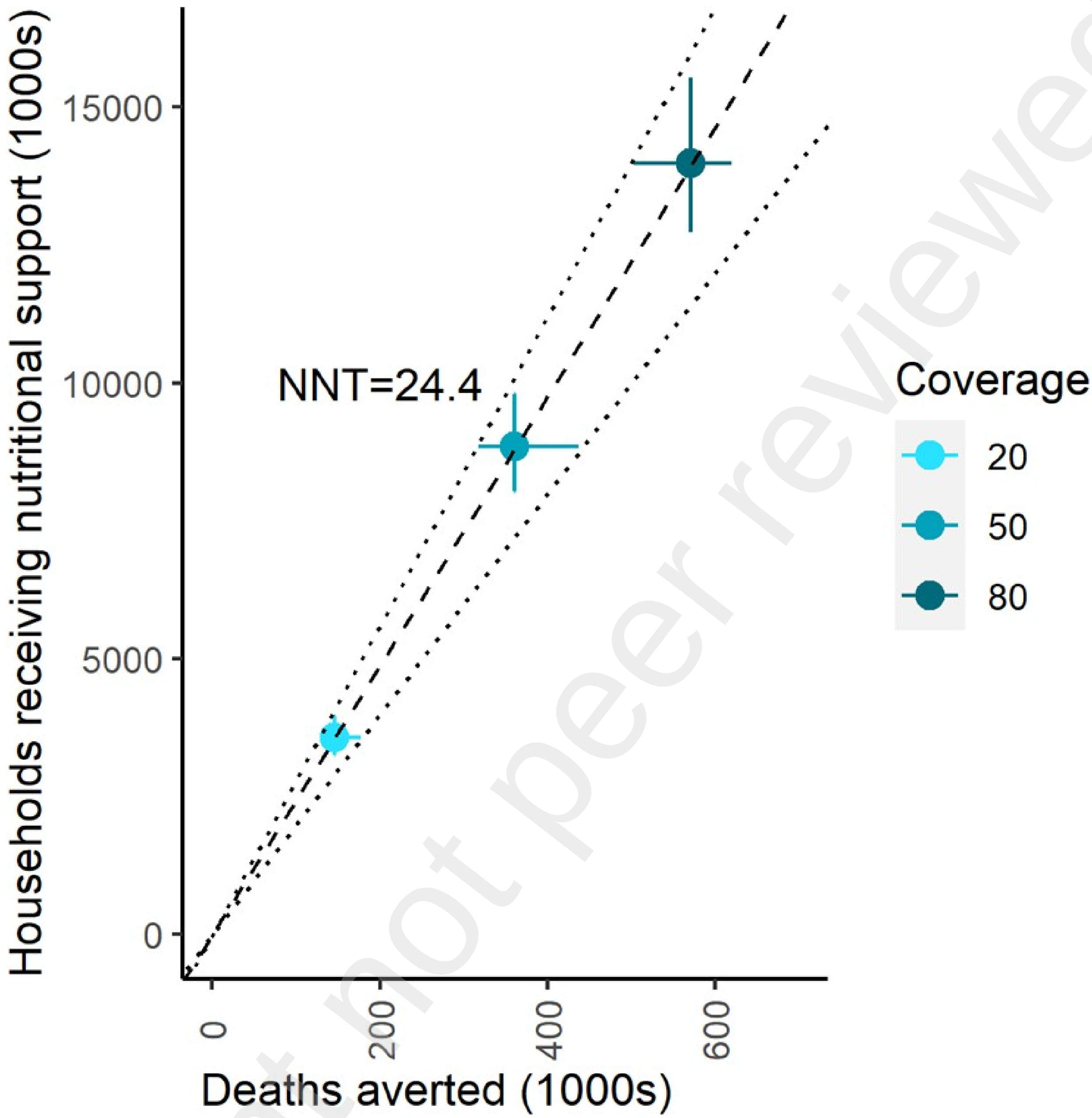
Figure 3: incremental cost-effectiveness of (a) nutritional support for TB patients, and (b) nutritional support for TB patients and their household contacts, from a health system perspective at 50% coverage. Lines indicate willingness-to-pay thresholds; solid line=USD$2,411 (1xIndia GDP), dashed line=USD$555 (Ochalek upper bound), dotted line=USD$410 (Ochalek lower bound). DALYs=disability-adjusted life years


Cumulative TB disease prevented 2023-2035 (%)
0
1
2
3
4
All
Contacts
Patients
RATIONS recipients
Coverage
20
50
80

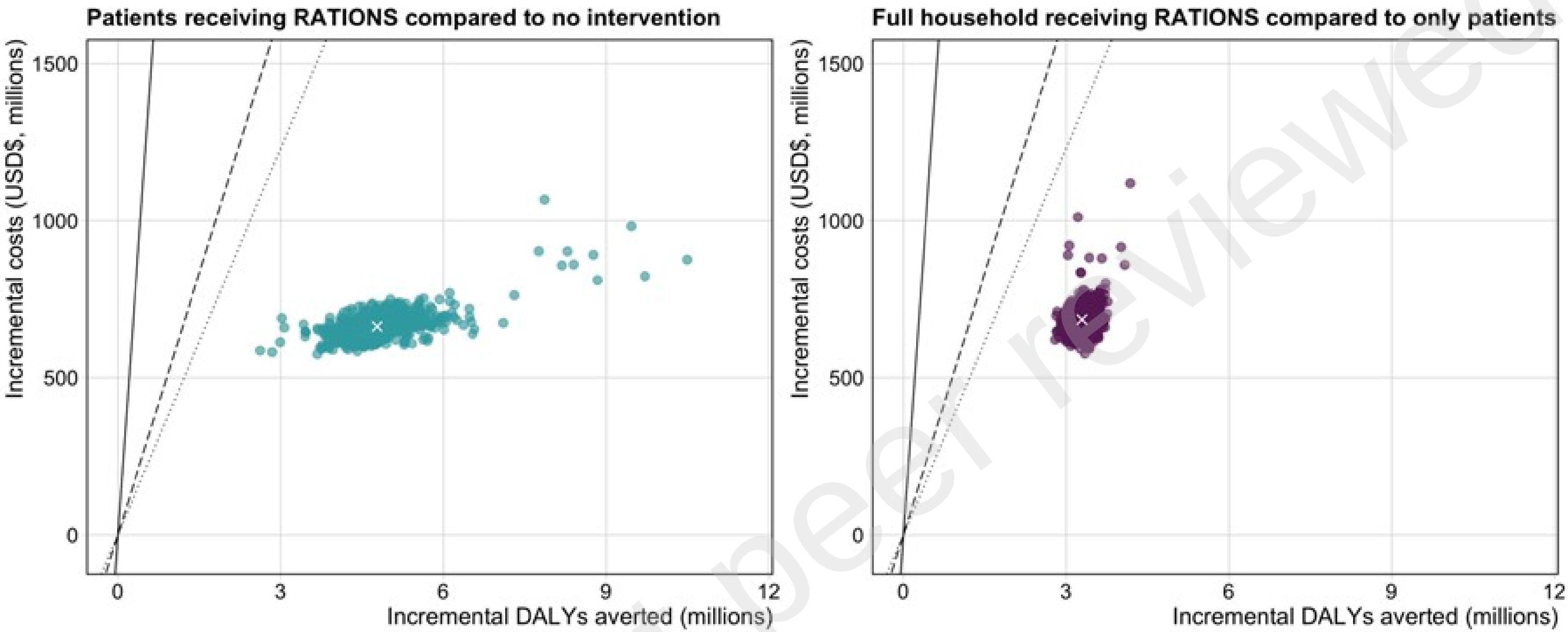

Cumulative TB deaths averted 2023-2035 (%)
10.0
7.5
5.0
2.5
0.0
All
Contacts
Patients
RATIONS recipients
Coverage
20
50
80



Households receiving nutritional support (1000s)
15000
10000
5000
0
NNT=10
0
500
1000
1500
Disease prevented (1000s)
Coverage
20
50
80



Households receiving nutritional support (1000s)
15000
10000
5000
0
NNT=24.4
0
200
400
600
Deaths averted (1000s)
Coverage
20
50
80



Patients receiving RATIONS compared to no intervention
Full household receiving RATIONS compared to only patients
Incremental costs (USD$, millions)
Incremental DALYs averted (millions)
1500
1000
500
0
0
3
6
9
12

Section/item	Item No	Recommendation	Reported on page No/location
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared.	Title page pp 1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	Abstract page p 2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	Introduction section p 4 paragraph 3
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	Methods section p 5 Model paragraph 1
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	Methods section pp 5 Model paragraph 1
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	Methods section p 6

			Costs paragraph 1
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	Methods section p 6 Intervention scenarios paragraphs
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	Methods section p 7 Outcomes paragraphs
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate	Methods section p 7 Outcomes paragraph 2
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	Methods section pp 7 Outcomes paragraphs
Measurement of effectiveness	11a	Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	NA
	11b	Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	NA
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	NA

Estimating resources and costs	13a	Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	NA
	13b	Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	Methods section p 6 Costs paragraph 1, Appendix pp 15-16 Supplementary Methods Economic analysis methods
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	Methods section p 6 Costs paragraph 1, Appendix pp 15-16 Supplementary Methods Economic analysis methods
Choice of model	15	Describe and give reasons for the specific type of decision analytic model used. Providing a figure to show model structure is strongly recommended.	Methods section pp 5 Model paragraph 1 and Appendix pp

			2-13 Supplementary Methods TB transmission model
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	Methods section p 5 modelling approach, Appendix pp 2-13 Supplementary Methods TB transmission model
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	Methods section p 5 modelling approach, Appendix pp 2-13 Supplementary Methods TB transmission model
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all	Appendix pp

		parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	2-13 Supplementary Methods TB transmission model
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Results section tables 1 and 2
Characterising uncertainty	20a	Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).	NA
	20b	Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	Results section tables 1 and 2, Appendix pp 17-22 Supplementary Results
Discussion			
Study findings, limitations, generalisability, and current knowledge	21	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	Discussion section pp 9-11, Research in context section p 3
Other			

Source of funding	22	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	Acknowledgements section p 11, Role of funding source section p 2
Conflicts of interest	23	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	Declaration of interests section p 11