Title: The lifetime burden of disease due to incident tuberculosis: a global re-appraisal including post-TB sequelae.

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Abstract

Background: Many individuals who survive TB disease face ongoing disability and elevated mortality risks. However, the impact of post-TB sequelae is generally omitted from policy analyses and disease burden estimates. We therefore estimated the global burden of TB, inclusive of post-TB morbidity and mortality.

Methods: Lifetime health outcomes were simulated for the cohort developing TB disease globally in 2019, stratified by country, age, sex, HIV status, and treatment status. We used disability-adjusted life-years (DALYs) to summarize fatal and nonfatal health losses attributable to TB, during the disease episode and afterwards. We estimated post-TB mortality and morbidity based on the decreased lung function caused by pulmonary TB disease.

Findings: Globally, we estimated 122 (95% uncertainty interval: 98, 151) million DALYs due to incident TB disease in 2019, with 58 (38, 83) million DALYs attributed to post-TB sequelae, representing 47% (37, 57) of the total burden estimate. The increase in burden from post-TB varied substantially across countries and regions, driven largely by differences in estimated case fatality for the disease episode. We estimated 12.1 (10.0, 14.9) DALYs per incident TB case, of which 6.3 (5.6, 7.0) DALYs were from the disease episode and 5.8 (3.8, 8.3) from post-TB. Per-case post-TB burden estimates were greater for younger individuals, and in countries with high incidence rates. The burden of post-TB was spread over the remaining lifetime of TB survivors, with almost one-third (28% (23, 34)) of total DALYs accruing 15 or more years after incident TB.

Interpretation: Post-TB sequelae add substantially to the overall disease burden caused by TB. This hitherto unquantified burden has been omitted from most prior policy analyses. Future policy analyses and burden estimates should take better account of post-TB, to avoid the

potential misallocation of funding, political attention, and research effort resulting from continued neglect of this issue.

Research in context

Evidence before this study: A growing number of cross-sectional and longitudinal studies have described chronic lung disease, long-term disability, and elevated mortality among individuals surviving TB disease. However, these post-TB sequelae are omitted from disease burden estimations and policy analyses that quantify the health losses caused by TB.

Added value of this study: We quantified the global burden of disease caused by incident TB in 2019, inclusive of post-TB morbidity and mortality over the lifetime of TB survivors. The results of this analysis demonstrate that post-TB burden adds considerably to the health losses caused by incident TB – globally, we estimated 122 (95% uncertainty interval: 98, 151) million DALYs due to TB occurring in 2019, with 58 (38, 83) million DALYs attributed to post-TB sequelae, representing 47% (37, 57) of the total burden estimate.

Implications of all the available evidence: When post-TB sequelae are considered, the disease burden caused by TB is substantially greater than conventional TB burden estimates. Accounting for post-TB in burden estimates and policy analyses will likely lead to revisions in the estimated impact of TB control efforts.

Introduction

Tuberculosis (TB) was estimated to cause 1.4 million deaths in 2019[1]. Individuals who develop TB experience a range of symptoms, including fever, wasting, and cough. Whilst successful treatment prevents death, many TB survivors experience ongoing health problems following the disease episode, and there is increasing evidence of long-term disability and elevated mortality risks in this population[2].

'Post-TB' describes the range of pathological conditions experienced by TB survivors. Pulmonary TB, the commonest disease presentation, causes progressive destruction of lung tissue, and this damage may not fully resolve after treatment[3-5]. While prompt treatment can minimize lung damage, many TB survivors experience residual lung pathology, with cross-sectional studies consistently demonstrating substantial pulmonary impairment—including chronic obstructive pulmonary disease (COPD), spirometric restriction, bronchiectasis and pulmonary hypertension, as well as secondary non-TB lung infections—among TB survivors[3-5]. These results are consistent with longitudinal evidence comparing lung function before and after the TB episode[6,7]. Individuals with chronic respiratory disease experience lower quality of life[8], higher health care utilization[9], and reduced economic productivity[10], while individuals additionally face higher all-cause mortality, even with only mild lung impairment[2,11]. In addition to pulmonary damage, extra-pulmonary TB disease and drug toxicity can cause permanent damage to other organ systems, as well as social and psychological sequelae[5].

Historically, post-TB has not been a major focus of the TB control agenda. However, the healthcare needs of TB survivors are drawing increasing attention[5], and recent modelling has highlighted the large population of TB survivors, estimated at 155 million in 2020[12]. The mortality and morbidity caused by post-TB has not traditionally been included in estimates of TB disease burden[13], nor policy analyses of TB control interventions[14]. For burden estimates, with health losses quantified as disability adjusted life years (DALYs), health outcomes are attributed to

specific diseases using the International Statistical Classification of Diseases (ICD) framework. While ICD-10 includes a code for TB sequelae (B90.9) this is rarely used, and in practice deaths among individuals with post-TB are commonly attributed to their proximal cause. For this reason, contemporary TB burden estimates only include deaths and disability occurring during the TB disease episode.

Disease burden estimates shape the health research agenda and funding landscape, and also determine how interventions are prioritized within disease control budgets. By excluding post-TB, current burden estimates may substantially underestimate the health losses caused by TB, which could lead to misallocation of funding, political attention, and research effort. Burden estimates for individual settings have provided initial evidence of the biases from omitting post-TB burden—an analysis estimating TB burden for India with and without post-TB found total DALYs increased by 62% when post-TB was included[15]. A study of TB burden in Tarrant County, USA, found a similarly large fraction of total burden due to chronic TB sequelae[16]. In this study we estimated the total DALYs caused globally by incident TB disease in 2019, including attributable deaths and long-term disability among TB survivors in subsequent years. We report estimates for each of 186 countries reporting ≥10 TB cases in 2019, to provide a more comprehensive description of the health losses caused by TB.

Methods

We constructed a hypothetical cohort of individuals developing TB in 2019, including pulmonary and extrapulmonary disease, and stratified by factors related to the burden of TB and/or consequences after TB cure, and for which sufficient data were available (country, age, sex, HIV status, and whether the individuals received TB treatment). We synthesized evidence describing quality of life and mortality among individuals with TB, during the disease episode and over their remaining life. Using this evidence, we simulated lifetime health outcomes for the

cohort developing TB disease in 2019. We used DALYs to summarize the total health losses attributable to TB.

Cohort developing TB disease in 2019

The WHO Global TB Programme reports annual estimates of the population developing TB disease, stratified by country, sex, and age-group[1]. For each country and sex, we interpolated these values to estimate incidence by single year of age in 2019. The fraction receiving treatment (by country, sex, and age) was based on reported case notifications[1] divided by estimated incidence. For countries with missing notification data we used WHO-estimated treatment coverage[1]. We removed countries with insufficient data, or with <10 estimated TB cases for 2019. Applying these criteria, we retained 186 countries, representing 10.0 million TB cases, 99.99% of global incidence. To stratify cases by HIV status, we took estimates of age-specific HIV prevalence in the general population[17] and inflated these by a common odds ratio, to match the reported number of TB-HIV cases in each country[1]. For countries for which this value was missing we assumed TB-HIV prevalence was 0%. For each age and sex, the fraction receiving TB treatment was assumed to be independent of HIV status. We did not stratify the cohort by the presence/absence of MDR-TB, extra-pulmonary disease, or other factors that influence the severity of post-TB sequelae. Figure S1 shows the distribution of the cohort across modelled strata.

Mortality during TB disease

We adopted WHO estimates of TB case fatality in 2019[1]. To apply these average mortality risks to individual strata, we specified odds ratios describing differences in survival by age (based on the ratio of age-specific TB cases and deaths in the United States[18,19]), and by HIV and TB treatment status, based on mortality risks used in WHO TB estimations[20]. We applied these odds ratios to each country and calibrated average mortality risks to reproduce WHO country-

level case fatality estimates. Figure S1 Panel D shows the fraction of the cohort estimated to survive the disease episode, by age.

Disability weights for TB disease

TB disability weights were based on current Global Burden of Disease Study (GBD) valuations[21] (Table 1). For HIV-uninfected individuals without TB we assumed no disability. For HIV-infected individuals without TB we averaged the disability weights for *'HIV: symptomatic, pre-AIDS'* and *'HIV/AIDS: receiving antiretroviral treatment'*, weighted by the global fraction of HIV-infected individuals receiving antiretroviral treatment in 2019[17] (67%). We calculated the incremental disability weight associated with TB disease as the difference between individuals with and without TB disease, stratified by HIV status. We assumed disability values applied for the duration of the disease episode, and adopted WHO disease duration estimates[20], stratified by treatment and HIV status (Table 1).

[Table 1]

Mortality among TB survivors

Individuals surviving TB disease face elevated mortality risks. A recent meta-analysis reported a standardized mortality ratio of 2.91 (2.21, 3.84) for TB survivors, compared to individuals without prior TB[2]. These elevated risks reflect a combination of (i) the causal impact of TB on future mortality risks, and (ii) the effect of individual characteristics that are correlated with both mortality rates and TB disease, but not caused by TB. To decompose these two effects, we assumed that the causal effect of TB on future mortality can be estimated from the effects of TB on lung function, and the resulting effects of impaired lung function on mortality rates.

Two systematic reviews have assessed the elevated rates of chronic respiratory disease among TB survivors[22,23]. The more recent of these reviews described a relationship between the odds

of COPD among post-TB individuals and country-level TB incidence. In this context, incidence is likely a proxy for delayed case detection, recurrent disease episodes, and other risk factors for severe disease[5]. We estimated a meta-regression model summarizing this relationship (Figure S2) and used these results to estimate an odds ratio of chronic respiratory disease among post-TB individuals for each country, based on their 2019 TB incidence (Figure S3, Panel A). We used the results of a multi-site observational study[11] to describe the population distribution of lung function, quantified as country-standardized forced expiratory volume in 1 second (FEV1%), and assumed that TB induced a downward shift of this distribution. For each country, the reduction in FEV1% among TB survivors was estimated to match the odds ratios for chronic respiratory disease in TB survivors, defined as FEV1% <80%. To model the relationship between FEV1% and mortality we fit a quadratic function to mortality rate ratios reported for different FEV1% impairment levels[11], and estimated the mortality risk ratio for post-TB as the average mortality rate for the post-TB FEV1% distribution compared to the distribution without post-TB. Country-level mortality rate ratios estimated for post-TB varied between 1.02 and 1.34, with a median of 1.14 (Figure S3, Panel B), and were applied to all modelled strata.

We estimated all-cause mortality rates for each country, sex, age, and calendar year, by interpolating UN Population Division abridged life tables[24]. To account for excess mortality among HIV positive individuals we assumed a mortality rate ratio producing an 8-year shorter life expectancy compared to HIV-negative individuals[25]. To calculate future mortality rates for TB survivors we multiplied all-cause general population mortality rates for each stratum by the standardized mortality ratio reported for TB survivors[2]. To calculate future mortality rates for the cohort under a counter-factual where they had not developed TB, we divided the mortality rates estimated for the TB scenario by the *causal* mortality rate ratio estimated for each country.

Disability weights for TB survivors

We adapted COPD disability weights to account for the reduced quality of life of TB survivors[21]. We adopted a mapping between COPD severity levels and FEV1% impairment level from an earlier study of COPD burden[8], and applied these disability weights to the distribution of TB survivors across FEV1% impairment levels to calculate a post-TB disability weight for each country. Country-level estimates of the incremental disability caused by post-TB varied between 0.006 and 0.088, with a median of 0.036 (Figure S3, Panel C). These were applied to all model strata over the remaining life expectancy.

Outcomes

The primary outcome was DALYs attributable to TB, stratified by TB disease and post-TB periods, using a life-time horizon. DALYs are calculated as the sum of Years of Life Lost (YLLs) and Years Lived with Disability (YLDs)[26]. We computed YLLs by multiplying deaths at each age by age-specific life expectancy, based on the GBD reference life table[27]. We computed YLDs by multiplying total years lived in each health state by the disability weight for that state. As DALYs arising during the TB disease episode are also reported by the GBD Study[28], we validated our results for this outcome against these existing estimates. As a secondary outcome, we calculated the reductions in life expectancy due to TB disease and post-TB, as compared to a no-TB counterfactual.

Uncertainty analysis

We specified probability distributions to represent uncertainty in model parameters (Table 1), and used second-order Monte Carlo simulation to generate 95% uncertainty intervals for study outcomes[29]. To do so, we re-estimated results for 1000 Latin hypercube samples from the parameter probability distributions, and calculated intervals as the 2.5th and 97.5th percentiles of the resulting distributions of each outcome. Analyses were conducted in R v4.0.2[30].

Sensitivity analyses

The mortality rate ratio for post-TB used in the main analysis is conservative, as it only captures one of several mechanisms through which TB impacts future mortality risks. As a sensitivity analysis, we recalculated results using a mortality risk ratio for post-TB of 1.78 (1.61, 1.98), based on a retrospective cohort study of individuals with and without post-TB, controlling for multiple demographic and clinical risk factors for mortality[31]. We also calculated partial rank correlation coefficients (PRCCs) to report the relative influence of individual parameters on study outcomes[32].

Role of the funder

The funder played no role in study design, implementation, or reporting.

Results

Total DALYs attributable to TB and post-TB

Table 2 reports estimates of the total DALYs attributable to incident TB cases from 2019. Globally, we estimate 122 (98, 151) million DALYs, with 64 (54, 75) million attributed to the TB disease episode, and 58 (38, 83) million attributed to post-TB. Globally, DALY estimates for the TB disease episode are 8.3% higher than GBD estimates (Figure S4, Panel A), largely due to greater TB mortality as estimated by WHO[1], compared to the GBD[28]. Results for individual countries are highly consistent (rank correlation 0.97, Figure S4, Panel B). Mortality (reflected in the YLL results) represents the large majority (93% (88, 96)) of DALYs from the TB disease episode.

[Table 2]

DALYs attributable to post-TB have not been included in past TB burden estimates, and their inclusion substantially increases burden estimates, by 91% (59, 132) globally. The increase in total DALYs produced by considering post-TB varies substantially by region, from 60% in Africa to 267% in the Western Pacific. The proportional increase in YLDs (reflecting the burden of non-fatal morbidity) was 383% (154, 755), reflecting the extended duration of post-TB relative to the TB disease episode. The proportional increase in YLLs was 71% (47, 104). Reductions in survival represent the majority (73% (68, 79)) of DALYs from the post-TB period. Table S1 shows estimated DALYs from TB disease and post-TB for the thirty high-TB-burden countries identified by WHO. In these results, the percent increase in DALYs resulting from the inclusion of post-TB varies widely between countries, driven largely by differences in WHO-estimated TB case fatality (Figure S5, rank correlation = -0.74). Figure S6 shows the global distribution of post-TB DALYs. Globally there were 7.5 (5.0, 10.8) post-TB DALYs per 1000 individuals, and 21 countries with >20 post-TB DALYs per 1000 individuals.

Figure 1 reports global estimates for YLLs, YLDs, and DALYs stratified by age, showing the increase in burden associated with post-TB in each age-group. The proportional increase in DALYs from post-TB is smaller in older age-groups, reflecting higher fatality during TB disease among older individuals.

[Figure 1]

DALYs per incident TB case

Figure 2 shows a schematic of the contribution of mortality and disability to the average global DALYs per individual developing TB in 2019, from both the TB disease episode and post-TB period. Globally, we estimate 12.1 (10.0, 14.9) DALYs per incident TB case, of which 6.3 (5.6, 7.0) DALYs are attributable to the disease episode and 5.8 (3.8, 8.3) DALYs attributable to post-TB.

[Figure 2]

Total and per-case DALY estimates varied by individual and country-level factors (Table 3). The average DALYs per incident case are estimated to be higher for younger individuals, HIV positive individuals, individuals who do not receive TB treatment, and individuals living in high-incidence countries.

[Table 3]

Figure 3 decomposes the average DALYs per case according to when the burden (ie the TB-attributable death, or time spent with disability) occurs. The TB disease episode represents a short period of high disability and mortality. In contrast, the DALYs from post-TB are spread over the remaining lifespan, with almost one-third (28% (23, 34)) of total DALYs accruing 15 or more years after an individual first develops TB.

[Figure 3]

Secondary outcomes

Table S2 reports reductions in life-years lived due to TB disease and post-TB, compared to a counterfactual in which individuals do not develop TB. Per incident TB case, we estimate an average 2.92 (2.60, 3.35) year reduction in life expectancy from mortality during the TB disease episode, and an additional 1.87 (1.21, 2.80) year reduction in life expectancy from post-TB mortality. The average reduction in life expectancy attributed to incident TB in 2019 (summing the effects of excess mortality over the life course) was 4.79 (3.94, 5.86) years.

Sensitivity analyses

Table S3 reports results for the alternative model specification with a higher mortality risk ratio for post-TB. In these results, total YLLs from post-TB increase from 42.1 (28.3, 59.8) to 94.1

(78.7, 111.6) million. Table S4 shows PRCCs for each model parameter, for several outcomes. For DALYs due to the TB disease episode, the most influential parameters were the inputs for total global incidence in 2019 (PRCC = 0.89), and case fatality during the disease episode (PRCC = 0.89). For DALYs due to post-TB, the most influential parameters were the odds ratio of respiratory disease with post-TB (PRCC = 0.86), and total global incidence in 2019 (PRCC = 0.46). For both total DALYs and the percentage increase in DALYs from post-TB, the most influential parameter was the odds ratio of respiratory disease with post-TB (PRCC = 0.83 and 0.85 respectively).

Discussion

This study is the first to estimate the global burden of TB inclusive of post-TB morbidity and mortality. Even with conservative assumptions, the inclusion of post-TB substantially increases the total burden estimate. For the 8.5 million individuals surviving incident TB in 2019, we estimate 58 million post-TB DALYs will accrue over the remaining lifetime, representing almost half of the 122 million DALYs estimated for TB.

Our burden estimate is approximately twice the GBD estimate for TB DALYs in the same year[28]. Our results do not represent a proposed 'correction' of the GBD estimates, as the two approaches answer different questions. Firstly, we adopted an 'incidence approach', quantifying DALYs that would accrue over the lifetime due to disease cases arising in a single year. In contrast, the GBD uses a 'prevalence approach' to estimate health losses from disability, summing the DALYs realized in a given year irrespective of when the causative disease case occurred. Secondly, and more fundamentally, the GBD estimates follow ICD disease classification conventions, with the consequence that incremental deaths due to post-TB are attributed to causes such as respiratory or cardiovascular disease, rather than TB. Within the

GBD framework, the role of post-TB is more similar to a risk factor, as it increases the risks of other diseases over the lifetime.

The primary disease burden tabulations produced by the GBD are calculated to be categorical, such that the sum of DALYs for each individual disease equals the total DALYs from all diseases. However, users of disease burden estimates commonly interpret them to be the burden ***caused by*** a given disease, in the sense that they summarize the death and disability avertable through global elimination of that disease. If our results are correct, the causal interpretation of current GBD estimates for TB disease burden substantially under-values the potential impact of TB control efforts. Appropriate valuation of post-TB disease burden may also lead to reprioritization within the TB control portfolio. This could include greater attention to programmatic activities that can prevent TB from occurring in the first place, to active case-finding that may accelerate diagnosis and to interventions that can prevent, mitigate or repair lung damage from TB. We would welcome a broader definition of treatment success rather than simply sterilizing the causative pathogen. This could include a greater role for end-of-treatment assessments of pathological damage and functional deficits in order to implement interventions that meet the healthcare needs of TB survivors, who in any given year represent a much larger group than the individuals newly developing TB[12]. While initial assessment may be done by TB programs, ongoing care will likely require integrated, multi-specialty services[33].

The magnitude of post-TB disease burden also has implications for new research. In particular, further research is needed on the mechanisms of post-TB impairment, the range of conditions experienced by TB survivors, and how the extent of impairment changes over time[34]. Research is also needed to describe management strategies for post-TB symptoms and disability, and their effectiveness at improving long-term outcomes for TB survivors. Policy analyses used to prioritize TB interventions should also take greater account of post-TB burden, which may lead to a reweighting of current intervention priorities and identify a cost-effective portfolio of services

for post-TB individuals. Finally, research is needed to better understand the social and economic implications of post-TB, including healthcare utilization, social exclusion, and household economic outcomes. This is particularly important given the global target of achieving zero households experiencing catastrophic costs from TB, described in the End TB Strategy[35].

Our analysis has several limitations. Firstly, our results may represent an underestimate of post-TB burden, as we only considered one pathway through which TB impacts future health outcomes. TB disease has deleterious effects on multiple organ systems, and some TB survivors experience respiratory symptoms even in the absence of clinically impaired lung function[36]. Chronic post-TB disability can also lead to stigma, social exclusion, and poverty, which themselves predispose to additional health risks. A more comprehensive assessment of these effects could produce a larger estimate of post-TB DALYs. As an indicator of this, the alternative specification using a higher mortality risk ratio for post-TB increased the total TB burden estimate by a further 40%. Secondly, there is substantial uncertainty associated with our estimates, including parameter uncertainty (quantified as uncertainty intervals around major outcomes), and structural uncertainty, which represents uncertainty about the functional form of the analytic model, not captured in the reported intervals. A major source of uncertainty is the weakness around the causal attribution of post-TB health outcomes to TB (as compared to existing risk factors among individuals developing TB). These causal assumptions affect the mortality risk ratios and disability weights for TB survivors. In our analyses, we estimated that the contribution of post-TB to elevated mortality among TB survivors[2] varied between 2% and 27% across countries (median 12%), yet there is substantial uncertainty around the average value as well as inter-country differences. Age-specific odds ratios for TB mortality represent another course of uncertainty. Finally, our analysis did not distinguish conditions for which post-TB outcomes are likely be different, including MDR-TB and XDR-TB, recurrent TB, extra-pulmonary TB, or extensive disease at initial presentation. For most of these conditions the

burden of post-TB may be greater than estimated in this analysis[34]. Similarly, outcomes may be different for children surviving TB, and better evidence on pediatric post-TB is needed.

Many individuals who survive TB disease face ongoing disability, despite achieving microbiological cure. For these TB survivors, post-TB sequelae limit opportunities and enjoyment of life, and increases the risk of early death. Our analysis has quantified these health losses, demonstrating that post-TB adds substantially to the global disease burden caused by TB. Future analyses should take better account of post-TB, to avoid the potential misallocation of funding, political attention, and research effort that would be produced by continued neglect of this issue.

Declaration of interests

The authors declare no conflicts of interest.

Contributors statement

NAM, MQ, RMGJH, and TC conceptualized the study. BWA, ALB, AKC, ADH, FMM, JM, DP, JAS, SS, SCvK, and RSW contributed to study design. NAM implemented the analysis. MQ, BWA, ALB, AKC, ADH, FMM, JM, DP, JAS, SS, SCvK, RSW, RMGJH, and TC reviewed results. NAM drafted the manuscript. MQ, BWA, ALB, AKC, ADH, FMM, JM, DP, JAS, SS, SCvK, RSW, RMGJH, and TC edited the manuscript. NAM, MQ, RMGJH, and TC have verified the underlying data.

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Data sharing statements

Analytic code and data inputs available upon request to the corresponding author (nmenzies@hsph.harvard.edu).

Tables

Parameter	Mean value	Lower bound of interval*	Upper bound of interval*	Prior distribution	Source
Disability weight for TB	0.333	0.224	0.454	Beta	21
Disability weight for TB and HIV	0.408	0.274	0.549	Beta	21
Disability weight for HIV on ART†	0.078	0.052	0.111	Beta	21
Disability weight for symptomatic HIV, no ART†	0.274	0.184	0.377	Beta	21
Disability weight for mild COPD	0.019	0.011	0.033	Beta	21
Disability weight for moderate COPD	0.225	0.153	0.31	Beta	21
Disability weight for severe COPD	0.408	0.273	0.556	Beta	21
Mortality rate ratio for post-TB individuals	2.91	2.21	3.84	Gamma	2
Linear term for log-linear model for mortality by FEV1%	-2.783	-3.908	-1.662	Normal	11 (Function fitted to study data)
Quadratic term for log-linear model for mortality by FEV1%	0.8947	0.2759	1.522	Normal	11 (Function fitted to study data)
Mortality risk ratio for post-TB [alternative specification]	1.78	1.61	1.98	Gamma	31
Intercept term for log-linear model for OR of chronic respiratory disease with post-TB	-1.494	-3.223	0.321	Normal	23 (Function fitted to study data)
Slope term for log-linear model for OR of chronic respiratory disease in post-TB	0.45	0.057	0.831	Normal	23 (Function fitted to study data)
Duration of treated TB	1.1	0.2	2.0	Gamma	1
Duration of untreated TB	2.5	1.0	4.0	Gamma	1
Duration of treated TB, with HIV	0.51	0.01	1.0	Gamma	1
Duration of untreated TB, with HIV	0.11	0.01	0.2	Gamma	1
Total global TB cases in 2019	9.96	8.94	11.00	Gamma	1
Global average TB case fatality rate in 2019	0.14	0.13	0.16	Beta	1
Fraction of TB cases untreated	0.29	0.20	0.35	Beta	1

Table 1: Values and sources for model parameters included in uncertainty analysis.

* Lower and upper bounds represent the 2.5 and 97.5 percentiles of the parameter distribution. Together these represent an equal-tailed 95% interval for the parameter. † Disability weights for HIV without TB are applied to HIV-infected TB survivors.

Country grouping	Outcomes by disease stage (millions)			Percent increase with post-TB (%)*
	TB disease	Post-TB	Total	
Years of life lost (YLLs)				
Eastern Mediterranean	2.52 (2.14, 2.99)	3.55 (2.38, 5.01)	6.07 (4.78, 7.68)	141 (95, 206)
Europe	0.88 (0.75, 1.02)	0.64 (0.41, 0.93)	1.51 (1.23, 1.83)	73 (48, 109)
Africa	25.35 (21.51, 30.03)	12.46 (8.09, 18.11)	37.81 (31.49, 45.26)	49 (32, 73)
Western Pacific	2.87 (2.45, 3.36)	6.91 (4.70, 9.75)	9.78 (7.49, 12.68)	242 (164, 351)
Americas	0.75 (0.65, 0.88)	0.75 (0.50, 1.08)	1.51 (1.21, 1.86)	100 (66, 148)
South-East Asia	26.90 (23.06, 31.50)	17.81 (11.92, 25.38)	44.72 (37.02, 53.84)	66 (44, 97)
WHO High-Burden	50.96 (43.47, 59.89)	37.52 (24.91, 53.46)	88.48 (72.75, 107.52)	74 (49, 109)
Global	59.27 (50.56, 69.63)	42.12 (28.32, 59.77)	101.39 (83.64, 122.78)	71 (47, 104)
Years lived with disability (YLDs)				
Eastern Mediterranean	0.44 (0.22, 0.77)	1.36 (0.75, 2.13)	1.80 (1.13, 2.63)	340 (142, 686)
Europe	0.10 (0.04, 0.19)	0.21 (0.12, 0.35)	0.31 (0.19, 0.49)	262 (96, 596)
Africa	1.13 (0.57, 1.94)	3.43 (1.80, 5.44)	4.56 (2.83, 6.65)	331 (136, 659)
Western Pacific	0.78 (0.36, 1.44)	2.75 (1.54, 4.28)	3.53 (2.20, 5.18)	394 (153, 809)
Americas	0.11 (0.05, 0.21)	0.33 (0.19, 0.52)	0.44 (0.28, 0.67)	327 (126, 691)
South-East Asia	1.96 (0.92, 3.52)	7.57 (4.13, 11.99)	9.53 (5.73, 14.04)	432 (167, 886)
WHO High-Burden	3.91 (1.90, 6.93)	14.02 (7.65, 22.14)	17.94 (10.90, 26.25)	397 (156, 789)
Global	4.53 (2.21, 8.00)	15.64 (8.61, 24.43)	20.17 (12.48, 29.52)	383 (154, 755)
Disability adjusted life-years (DALYs)				
Eastern Mediterranean	2.96 (2.47, 3.54)	4.90 (3.27, 7.02)	7.87 (6.05, 10.21)	167 (106, 244)
Europe	0.97 (0.82, 1.14)	0.85 (0.55, 1.26)	1.82 (1.45, 2.27)	88 (56, 134)
Africa	26.48 (22.46, 31.29)	15.89 (10.19, 23.31)	42.37 (35.01, 51.52)	60 (38, 90)
Western Pacific	3.65 (2.98, 4.50)	9.66 (6.50, 13.84)	13.31 (9.89, 17.63)	267 (169, 388)
Americas	0.87 (0.73, 1.03)	1.08 (0.71, 1.58)	1.94 (1.51, 2.49)	125 (82, 186)
South-East Asia	28.87 (24.47, 33.66)	25.38 (16.67, 36.84)	54.25 (43.87, 67.66)	88 (56, 130)
WHO High-Burden	54.88 (46.34, 64.69)	51.54 (33.78, 74.85)	106.42 (85.74, 132.97)	94 (61, 140)
Global	63.79 (53.87, 75.16)	57.76 (38.37, 82.97)	121.55 (98.29, 151.19)	91 (59, 133)

Table 2: Burden of disease caused by incident TB in 2019, globally and by WHO region.

* Compares outcomes with vs. without the inclusion of post-TB. Values in parentheses represent 95% uncertainty intervals.

Group	Total TB cases (thousands)	Absolute DALYs (millions)			DALYs per incident TB case		
		TB disease	Post-TB	Total	TB disease	Post-TB	Total
All	9954 (8952, 11003)	63.79 (53.87, 75.16)	57.76 (38.37, 82.97)	121.55 (98.29, 151.19)	6.41 (5.69, 7.20)	5.80 (3.83, 8.34)	12.21 (10.02, 14.85)
Age group							
Age 0-14	1185 (1065, 1309)	10.75 (8.97, 13.02)	10.26 (6.51, 15.03)	21.00 (16.61, 26.56)	9.07 (7.92, 10.80)	8.66 (5.52, 12.92)	17.73 (14.16, 21.99)
Age 15-34	3307 (2974, 3655)	14.43 (12.16, 17.06)	24.32 (16.14, 35.07)	38.75 (29.76, 50.70)	4.36 (3.85, 4.97)	7.36 (4.82, 10.71)	11.72 (9.12, 15.03)
Age 35-54	3039 (2733, 3359)	22.06 (18.72, 25.77)	16.32 (10.85, 23.19)	38.37 (31.55, 46.87)	7.26 (6.47, 8.18)	5.37 (3.59, 7.65)	12.63 (10.61, 15.02)
Age 55-74	1998 (1797, 2208)	14.41 (12.26, 16.76)	6.29 (4.27, 9.00)	20.69 (17.61, 24.29)	7.21 (6.41, 8.01)	3.15 (2.17, 4.45)	10.36 (9.09, 11.79)
Age 75+	426 (383, 471)	2.15 (1.83, 2.51)	0.58 (0.40, 0.83)	2.73 (2.33, 3.19)	5.05 (4.47, 5.65)	1.36 (0.95, 1.92)	6.41 (5.77, 7.17)
Sex							
Male	6158 (5538, 6807)	39.75 (33.58, 46.81)	35.61 (23.69, 51.05)	75.36 (61.12, 93.50)	6.45 (5.73, 7.24)	5.78 (3.85, 8.26)	12.24 (10.10, 14.82)
Female	3796 (3414, 4196)	24.04 (20.29, 28.35)	22.15 (14.63, 32.05)	46.19 (37.13, 57.77)	6.33 (5.62, 7.13)	5.84 (3.81, 8.50)	12.17 (9.93, 14.84)
TB incidence level							
<10 per 100,000	51 (46, 56)	0.13 (0.11, 0.15)	0.08 (0.03, 0.18)	0.21 (0.15, 0.31)	2.48 (2.15, 2.87)	1.60 (0.50, 3.68)	4.08 (2.93, 6.30)
10-49 per 100,000	331 (298, 366)	1.05 (0.89, 1.25)	1.02 (0.58, 1.58)	2.07 (1.58, 2.69)	3.19 (2.78, 3.62)	3.08 (1.82, 4.84)	6.27 (4.92, 8.02)
50-199 per 100,000	4726 (4250, 5224)	29.43 (24.90, 34.33)	23.70 (16.26, 34.37)	53.13 (43.57, 64.51)	6.23 (5.53, 6.95)	5.02 (3.47, 7.10)	11.24 (9.53, 13.53)
>200 per 100,000	4846 (4359, 5357)	33.19 (28.02, 39.07)	32.96 (20.25, 49.02)	66.14 (52.32, 83.97)	6.85 (6.05, 7.81)	6.80 (4.09, 10.14)	13.65 (10.79, 17.05)
HIV status							
HIV positive	999 (899, 1104)	11.84 (10.12, 13.84)	5.81 (3.78, 8.44)	17.65 (14.84, 21.04)	11.85 (10.59, 13.39)	5.82 (3.79, 8.51)	17.67 (15.27, 20.45)
HIV negative	8955 (8053, 9898)	51.95 (43.86, 61.16)	51.95 (34.55, 74.36)	103.90 (83.26, 130.27)	5.80 (5.13, 6.54)	5.80 (3.83, 8.36)	11.60 (9.44, 14.24)
TB treatment							
Treated	7224 (6230, 8270)	17.43 (9.75, 28.92)	43.84 (28.17, 64.45)	61.27 (40.87, 86.32)	2.39 (1.48, 3.59)	6.07 (4.09, 8.76)	8.46 (6.10, 11.35)
Untreated	2730 (1999, 3530)	46.36 (33.70, 60.53)	13.92 (8.04, 22.31)	60.28 (43.59, 79.15)	16.99 (15.24, 18.81)	5.10 (3.27, 7.55)	22.09 (19.51, 24.84)

Table 3: Total and per-person estimates of the burden of disease caused by incident TB in 2019*.

* Values in parentheses represent 95% uncertainty intervals.

Figures

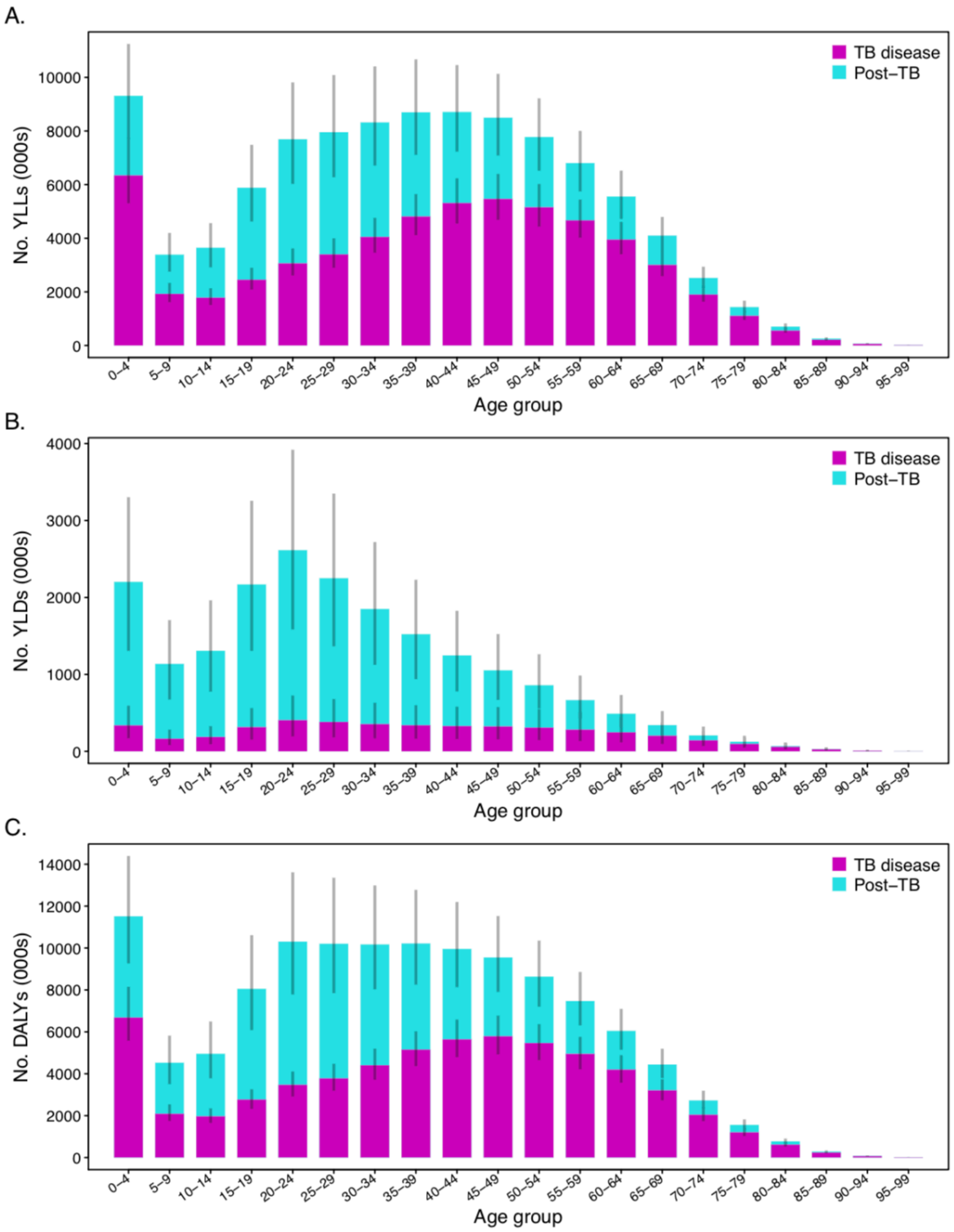

Figure 1: Estimates of YLLs (Panel A), YLDs (Panel B) and DALYs (Panel C) attributable to TB disease in 2019, stratified by age group of disease incidence, and disease period*.

* Shaded bands represent 95% uncertainty intervals.

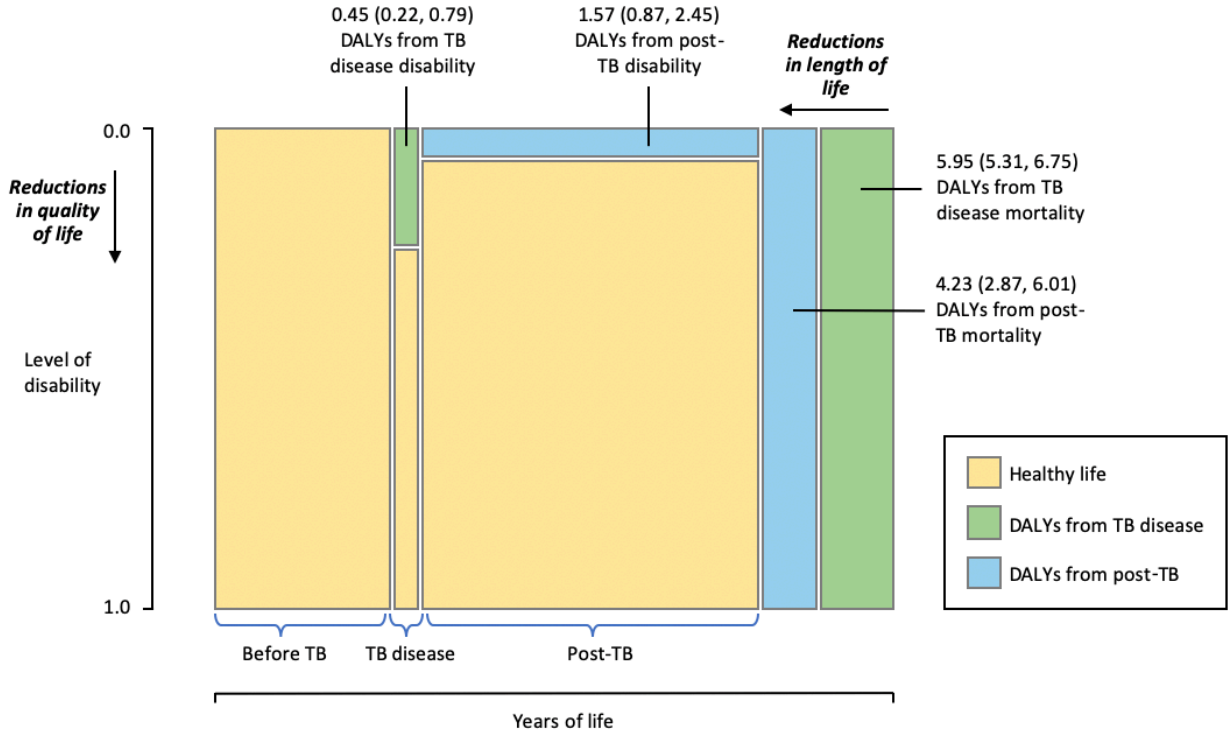

Figure 2: DALYs per incident TB case from increase disability and mortality rates attributable to TB, stratified by TB disease and post-TB period*.

* Total DALYs per incident TB case are equal to the sum of these values. Area of each green and blue rectangle proportional to the number of DALYs indicated, other dimensions not to scale. Values in parentheses represent 95% uncertainty intervals.

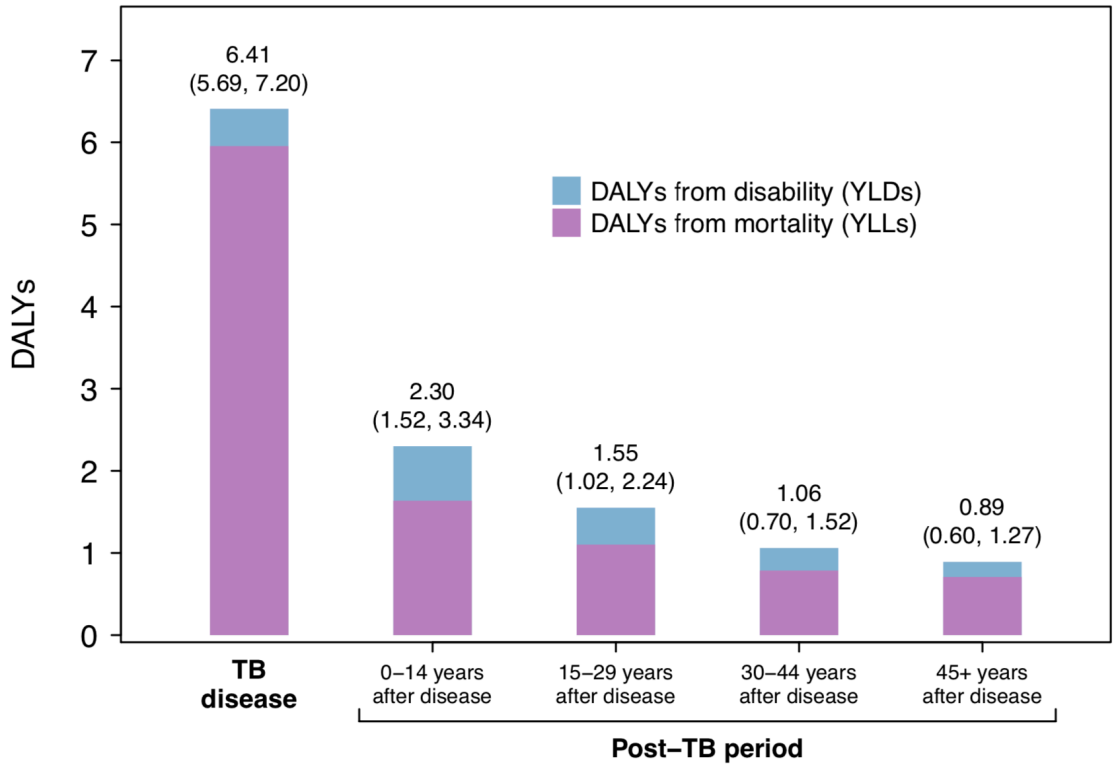

Figure 3: DALYs per incident TB case, stratified by TB disease and post-TB period*.

* Total DALYs per incident TB case equal to the sum of these values. Values in parentheses represent 95% uncertainty intervals.

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