TB morbidity estimates overlook the contribution of post-TB disability: evidence from urban Malawi

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ABSTRACT

Introduction Despite growing evidence of the long-term impact of tuberculosis (TB) on quality of life, Global Burden of Disease (GBD) estimates of TB-related disability-adjusted life years (DALYs) do not include post-TB morbidity, and evaluations of TB interventions typically assume treated patients return to pre-TB health. Using primary data, we estimate years of life lost due to disability (YLDs), years of life lost due to premature mortality (YLL) and DALYs associated with post-TB cardiorespiratory morbidity in a low-income country.

Methods Adults aged ≥15 years who had successfully completed treatment for drug-sensitive pulmonary TB in Blantyre, Malawi (February 2016–April 2017) were followed-up for 3 years with 6-monthly and 12-monthly study visits. In this secondary analysis, St George’s Respiratory Questionnaire data were used to match patients to GBD cardiorespiratory health states and corresponding disability weights (DWs) at each visit. YLDs were calculated for the study period and estimated for remaining lifespan using Malawian life table life expectancies. YLL were estimated using study mortality data and aspirational life expectancies, and post-TB DALYs derived. Data were disaggregated by HIV status and gender.

Results At treatment completion, 222/403 (55.1%) participants met criteria for a cardiorespiratory DW, decreasing to 15.6% after 3 years, at which point two-thirds of the disability burden was experienced by women. Over 90% of projected lifetime-YLD were concentrated within the most severely affected 20% of survivors. Mean DWs in the 3-years post-treatment were 0.041 (HIV-) and 0.025 (HIV+), and beyond 3 years estimated as 0.025 (HIV-) and 0.010 (HIV+), compared with GBD DWs of 0.408 (HIV+) and 0.333 (HIV-) during active disease. Our results imply that the majority of TB-related morbidity occurs post-treatment.

Conclusion TB-related DALYs are greatly underestimated by overlooking post-TB disability. The total disability burden of TB is likely undervalued by both GBD estimates and economic evaluations of interventions, particularly those aimed at early diagnosis and prevention.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ It is increasingly clear that tuberculosis (TB) disease is associated with long-term physical and psychosocial sequelae, affecting patient health-related quality of life (HRQoL) long after treatment completion and microbiological cure.

⇒ While Global Burden of Disease estimates were updated in 2019 to include a longer period of TB illness duration and excess mortality prior to treatment completion, they remain focused on morbidity during TB illness and treatment only and do not include morbidity in the post-TB period.

⇒ Using a hypothetical cohort, a 2021 modelling study estimated that approximately half the global TB burden occurs post-treatment; however, morbidity data from longitudinal post-TB cohorts are needed to provide empirical evidence to support post-TB disability estimates.

WHAT THIS STUDY ADDS

⇒ Using HRQoL data from a prospective cohort study, we have quantified TB-related disability occurring beyond treatment completion, demonstrating that—even with conservative estimates—the inclusion of the post-TB period would dramatically increase TB morbidity estimates.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ To accurately capture TB’s impact, researchers must ensure the inclusion of TB-related morbidity occurring in the post-TB period, a vital adjustment for ensuring appropriate allocation of resources to and within TB services, emphasising interventions which support disease prevention and early diagnosis.

⇒ Mitigating post-TB morbidity should be highlighted as a priority for TB programmes, requiring programmatic guidelines for the clinical management of sequelae, alongside investment in post-TB data collection, reporting mechanisms, rehabilitation and social and economic support.
INTRODUCTION

Tuberculosis (TB) remains an important cause of morbidity and mortality worldwide with an estimated 10 million incident cases of TB disease in 2020, causing 1.5 million deaths. Those who survive TB disease face a considerable but under-recognised burden of ongoing morbidity including respiratory impairment, psychosocial challenges and reduced health-related quality of life (HRQoL) after treatment completion. Guidelines for TB management define ‘treatment success’ using microbiological outcomes and survival only, and measures of TB-associated morbidity remain solely focused on the period prior to and during treatment.

The most widely used measure of disease burden-associated morbidity is the disability-adjusted life year (DALY). This combines ‘years of life lost due to premature mortality’ (YLL) from a disease, with ‘years of life lost due to disability’ (YLD), with the latter calculated by multiplying the number of years lived in a certain health state by a ‘disability weight’ (DW) attributed to this state. The WHO recommends the use of DALYs in generalised cost-effectiveness analysis, prioritising interventions which offer a favourable ratio of DALYs averted to cost.

Although there were an estimated 155 million TB-survivors alive in 2020, measures of YLD due to TB disease do not include post-TB sequelae, and consider disability during TB disease and treatment only. The Global Burden of Disease (GBD) study’s estimates assume that health returns to normal at treatment completion, with the time taken to reach this point weighted by each country’s Health Access and Quality Index. The DWs allocated to active TB disease, with and without HIV coinfection, in the 2019 GBD study are 0.408 (0.274–0.549) and 0.333 (0.224–0.454), respectively (online supplemental appendix table A1). These DWs lead to an annual estimate of YLD for drug-sensitive TB disease of 4.8 million years globally.

Given the growing body of evidence for post-TB sequelae, we hypothesised that by not accounting for residual disability after treatment completion, the GBD study and TB-related economic evaluations underestimate both the YLD from each case of TB disease, and the value of interventions to prevent TB disease or optimise the care-cascade.

Post-TB lung damage is a key form of post-TB morbidity, seen in over a third of TB survivors, and associated with chronic respiratory symptoms, functional impairment and health seeking. Recent work aiming to calculate the YLD for HIV-negative TB survivors has estimated DWs associated with post-TB morbidity based on cross-sectional prevalence estimates of Chronic obstructive pulmonary disease (COPD) and chronic respiratory diseases among recovered patients with TB. While one further 2010 American study has also suggested post-TB DWs, to date, there have been no studies which directly derive post-TB DWs from longitudinal HRQoL data from patients in a high-TB incidence, low-income setting. The aim of this study is to address this evidence gap.

In this study, we use data from a prospective cohort of adult pulmonary tuberculosis (PTB) survivors in Malawi to directly quantify the burden of cardiorespiratory YLD associated with each case of PTB, in the period after TB treatment completion. We derive post-TB cardiorespiratory DWs, YLDs and DALYs for HIV-positive and HIV-negative members of this population and highlight the considerable global implications for post-TB care.

METHODS

Study population

This study is a secondary analysis of post-TB respiratory morbidity data from a prospective cohort study of adults completing treatment for drug-sensitive PTB in urban Blantyre, Malawi. The full study design and respiratory findings are published elsewhere. In brief, participants aged ≥15 were prospectively recruited at TB treatment completion (T0) (February 2016–April 2017). Demographic data and HIV status were recorded at T0, and questionnaire data and respiratory measurements collected at 6-month and 12-month intervals (T6, T12, T24, T30, T36) over 3 years. HRQoL was assessed at each time point using a Chichewa translation of the St George’s Respiratory Questionnaire (SGRQ), a respiratory-focused specific instrument validated for use in post-TB populations, which provides a score from 0 to 100. A validated Chichewa version of the EQ-5D-3L—a generic HRQoL tool—was also administered at T0, T6, and T12.

Study design

Examining HRQoL changes

Data were disaggregated by HIV status and gender. The proportion of participants who experienced deterioration, improvement or ‘no change’ in health between consecutive study visits was determined using a minimal clinically important difference of 4 points in SGRQ ‘total score’ (hereafter SGRQ score). Participants were divided into severity quintiles based on SGRQ score at T0, to observe trends in HRQoL over time.

Calculating DWs: 3-year period

GBD methodology assigns DWs to health states in a process that uses ‘lay-descriptions’ which ‘emphasise the major functional consequences and symptoms associated with each health state’ rather than specifying underlying diseases or diagnoses, such that DWs can reasonably be applied across disease entities based on the presence of symptoms and impairment alone. All 235 health states described within the GBD study were reviewed (online supplemental appendix A). Twelve cardiorespiratory states were identified for which corresponding SGRQ symptom data were available from our cohort, with DWs ranging from 0.015 to 0.408. Health state mapping was performed for each participant at each time point (T0→Tn), by relating the symptoms detailed in these lay descriptions, to those collected by the SGRQ and allocating the corresponding...
DW (DW₀→DW₃₀₆). A conservative approach was taken, whereby only patients reporting all symptoms described for each health state were allocated the corresponding DW (online supplemental appendix B), with sensitivity analyses conducted using less stringent criteria. Where participants satisfied criteria for two or more DWS at a given time point, the ‘maximum limit method’ was followed assigning the largest DW among satisfied states, to give their ‘maximum DW’.

Mean DWS were calculated for each severity quintile at each time point and trends in progression compared with those seen in SGRQ. Visual Analogue Scale (EQ-5D-3L index values.

Calculating YLD: 3-year period

YLD were directly derived from study data for the 3-year period of cohort follow-up. DWS at discrete study visits were translated to a continuous measure of 3-year YLD using an approach equivalent to calculating the ‘area under the curve’ transitions between DWS at consecutive time points were assumed to happen at a constant rate, and YLD in each interval calculated by multiplying the intermediary period length (typically 0.5 years) by the mean of the DWS at adjacent visits. In a small number of cases where HRQoL data were not available for a single time point, DWS were averaged from the nearest available time points. The 3-year YLD for each participant was calculated as the sum of YLD across all intervals (online supplemental appendix figure C1). Variances in disability progression by HIV status and gender were explored, with differences evaluated using t tests. Primary YLD analyses were completed using a ‘core sample’ of those who completed the full 3-year follow-up and for whom baseline data were available (n=299), with sensitivity analyses conducted using aggregated population means of all participants.

Estimating YLD: lifetime

Lifetime YLD were projected for the period after the 3-year study follow-up, for the core sample only. To explore the trajectory in HRQoL, various models were fit to mean SGRQ scores from T₀ to T₃₀₆ (online supplemental appendix D). A quadratic plateau model provided the best fit, which—along with decreasing clinically significant SGRQ changes between subsequent time points—supported stability of morbidity by T₃₀₆. Accordingly, disability at this time point (DW₃₀₆) was assumed to remain constant after the 3-year study period. Each participant’s ongoing YLD was calculated by multiplying DW₃₀₆ by their estimated life years remaining, with the latter estimated by subtracting age at Tₙ from their life expectancy given in the Malawi life table (by sex and age). No adjustment was made for elevated mortality ratios of TB-survivors.

Total post-TB YLD for each participant was calculated by adding the data-derived 3-year YLD to the lifetime projection of YLD.

Years of life lost due to premature mortalities

While our study’s focus is on post-TB disability, for completeness, we estimated YLLs for our population of patients with TB. Cause of death was not available in our data, and we ran our analyses two times using two sets of assumptions. First, we assumed all deaths identified during the 3-year study period were TB related, and second, we assumed only the deaths of those known to be undergoing TB retreatment had been due to TB. In each case, YLL were calculated using aspirational life expectancy at the age of death, taken from the 2019 GBD reference life table. We took a conservative approach, assuming no additional TB-related deaths among those not completing follow-up and no incremental mortality risk after the follow-up period.

Comparison of active disease and post-TB disability

To understand the wider implications of our findings, we compared our estimates of post-TB YLD to those which might have been calculated for these patients during active disease only, using the GBD DWS of 0.408 HIV-positive and 0.333 HIV-negative provided for active drug-susceptible disease (online supplemental appendix table A1). We used mean durations of 1.1 years (HIV-negative) and 0.51 years (HIV-positive), taken from the duration assumptions used in the WHO’s TB burden estimations, and in line with those typically applied in TB cost-utility studies (online supplemental appendix table E1). Analyses were conducted in Stata V.14.0 (Stata Corp.2015, College Station, Texas) and RStudio V.1.2.5 (Boston, Massachusetts).

Data from the original cohort study have been shared with participants, patient advocacy groups, healthcare providers and the National TB programme in Malawi. These groups are involved in an ongoing programme of stakeholder engagement around strategies for post-TB care in Eastern Africa, which is being led by the study team (NIHR130307).

RESULTS

Study population

405 participants (275 men and 130 women) were recruited, with 299 completing full 3-year follow-up (the
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'three core sample'), including 292 participants interviewed at all six time points (T0→T36) (online supplemental appendix figure F1). At baseline, 60.5% (244/403) were HIV positive (2/405 unknown), and 77.3% (313/405) had microbiologically proven PTB. Mean age was 32.4 years for women (SD: 10.2), and 36.2 years for men (SD: 10.0). Cohort demographics and detailed respiratory parameters are published elsewhere.24

**HRQoL progression**

SGRQ scores at T0 ranged from 0 to 56.7 with median 8.8 (IQR 1.3–23.4). Data were moderately right-skewed, with 22.8% scoring 0 at T0. This proportion increased to 51.2% by T36, with data highly right-skewed (skewness 3.54). There were no statistically significant differences in EQVAS (p=0.188), EQ-5D (p=0.208) and SGRQ (p=0.064) scores by HIV status at T0. Across all HIV status/gender subgroups, the greatest improvement was seen in the 6-month post-treatment (online supplemental appendix figure F2 and table F1). When SGRQ progression was examined by baseline severity, improvements were seen across all severity quintiles (figure 1).

**DWs: 3-year period**

A total of 222 participants (55.1%) satisfied the criteria for at least one of the 12 identified cardiorespiratory DWs at TB treatment completion, with StateHF_MILD and StateCOPD_MILD satisfied by 52.6% and 52.4% of participants, respectively (online supplemental appendix figure F2). The most common (maximum) disability states at T0 were StateCOPD_MOD (23.3%) and StateHF_MOD (10.7%) (table 1). DWs demonstrated clear discrimination between SGRQ severity quintiles at each time point, with mean weights tracking SGRQ scores (figure 1). Consistent with SGRQ score, the proportion of participants fulfilling criteria for states fell with each visit until T30. The largest decrease was seen immediately post-treatment (44% decrease T0→T6), and by T30, a nadir had been reached with 14.6% (45/308) of participants meeting a DW description (figure 2).

**YLD: 3-year period**

The 3-year YLD across the core sample was 28.171, with mean 0.094 YLD (SD: 0.131) per participant, equivalent to 0.031 YLD per-year (table 2). Sensitivity analysis using the full data set and averages across time points calculated a similar 3-year mean disability of 0.096 YLD (+2%) per participant (online supplemental appendix table F4 and figure F4). At treatment completion, YLD were split proportionately by gender; however, by T30→T36 two-thirds of YLD were among women (table 3). The mean YLD of HIV-positive participants was lower than HIV-negative participants at baseline, with the relative difference growing over time. The 3-year DWs calculated for HIV-negative and positive participants were 0.041 (SD: 0.054) and 0.025 (SD: 0.033), respectively (table 2).

**YLD: lifetime**

By T30, 47/299 (15.7%) of the core sample satisfied a DW description with mean 0.104. Among core participants, mean life years left from T36, as given by the Malawi life table, were 31.0 years (men) and 38.9 years (women). The estimated post-3-year YLD for the core sample was 164.5 YLD.
| Health state name (Health state ID) | Health state lay description | Number for whom this disease state is their worst state at each time point (n, %) | GBD disability weight (uncertainty interval) | \(T_0\)  (n=403) | \(T_6\)  (n=376) | \(T_{12}\) (n=368) | \(T_{24}\) (n=319) | \(T_{30}\) (n=308) | \(T_{36}\) (n=301) |
|-----------------------------------|-------------------------------|----------------------------------------------------------------------------------|---------------------------------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Acute myocardial infarction, days 3–28 (State\textsubscript{ACUTE_MI}) | Gets short of breath after heavy physical activity, and tires easily, but has no problems when at rest. The person has to take medication every day and has some anxiety. | | | 0.074 (0.049–0.105) | 1 (0.2%) | 1 (0.3%) | 1 (0.3%) | | |
| Anaemia, moderate (State\textsubscript{ANEMIA_MOD}) | Feels moderate fatigue, weakness, and shortness of breath after exercise, making daily activities more difficult. | | | 0.052 (0.034–0.076) | | |
| Anaemia, severe (State\textsubscript{ANEMIA_SEV}) | Feels very weak, tired and short of breath, and has problems with activities that require physical effort or deep concentration. | | | 0.149 (0.101–0.209) | 37 (9.2%) | 4 (1.1%) | 11 (3.0%) | 2 (0.6%) | 1 (0.3%) | 2 (0.7%) |
| Asthma, controlled (State\textsubscript{ASTHMA_CON}) | Has wheezing and cough once a month, which does not cause difficulty with daily activities. | | | 0.015 (0.007–0.026) | 1 (0.2%) | 1 (0.3%) | 4 (1.3%) | 3 (1.0%) | 1 (0.3%) |
| Asthma, partially controlled (State\textsubscript{ASTHMA_PAR_CON}) | Has wheezing and cough once a week, which causes some difficulty with daily activities. | | | 0.036 (0.022–0.055) | | |
| Asthma, uncontrolled (State\textsubscript{ASTHMA_UNCON}) | Has wheezing, cough and shortness of breath more than twice a week, which causes difficulty with daily activities and sometimes wakes the person at night. | | | 0.133 (0.086–0.192) | | |
| COPD and other chronic respiratory problems, mild (State\textsubscript{COPD_MILD}) | Has cough and shortness of breath after heavy physical activity, but is able to walk long distances and climb stairs. | | | 0.019 [0.011–0.033] | 4 (1.0%) | 1 (0.3%) | 2 (0.6%) | 1 (0.3%) |
| COPD and other chronic respiratory problems, moderate (State\textsubscript{COPD_MOD}) | Has cough, wheezing and shortness of breath, even after light physical activity. The person feels tired and can walk only short distances or climb only a few stairs. | | | 0.225 (0.153–0.310) | 94 (23.3%) | 52 (13.8%) | 47 (12.8%) | 20 (6.3%) | 14 (4.5%) | 14 (4.7%) |
| COPD and other chronic respiratory problems, severe (State\textsubscript{COPD_SEV}) | Has cough, wheezing and shortness of breath all the time. The person has great difficulty walking even short distances or climbing any stairs, feels tired when at rest, and is anxious. | | | 0.408 (0.273–0.556) | | 1 (0.3%) |
| Heart failure, mild (State\textsubscript{HF_MILD}) | Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort. | | | 0.041 (0.026–0.062) | 42 (10.4%) | 40 (10.6%) | 29 (7.9%) | 23 (7.2%) | 21 (6.8%) | 21 (7.0%) |

Continued
There were 192.7 YLD over the full post-treatment period, giving a mean of 0.644 (SD: 1.87) lifetime YLD per participant, equivalent to 0.02 (SD: 0.053) YLD per life year remaining. Sensitivity analyses demonstrated that relaxing our stringent requirements for mapping states would have resulted in many more participants assigned disease states, and subsequently considerably larger disability estimates (online supplemental appendix table F5).

At a population level, 85.4% (164.5/192.7) of all YLD were incurred in the post-3-year period. Across all subgroups (men, women, HIV negative, HIV positive), 94% of full lifetime YLD were concentrated within the most severe 20% of participants.

Years of life lost due to premature mortality

Eight-two participants did not complete follow-up and were not known to have died, and baseline SCRO was therefore inferred for these participants from the core sample, using those subgroup means and the core sample size (n=403). Post-TB disability was, therefore, inferred from the core sample. The reduced to 862.4 DALYs per participant. This reduced to 812.8 DALYs by the more conservative estimate of YLLs estimated for active disease only, while lifetime projections of 54% and 39%, respectively, were calculated for active disease and post-TB.

When assuming all 22 deaths were TB related, we calculated 1016.7 YLL for HIV-negative participants (n=244) and 108.5 YLL for the HIV-negative participants (n=159).

When assuming only deaths of those undergoing retreatment were due to TB, we calculated 187.6 YLL and 54.3 YLL for HIV-positive and HIV-negative participants.

Total DALYS

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### Table 1 Continued

| Health state name (Health state ID) | Health state lay description | Number for whom this disease state is their worst state at each time point (n, %) | GBD disability weight (uncertainty interval) | T_0 (n=403) | T_6 (n=376) | T_12 (n=368) | T_24 (n=319) | T_30 (n=308) | T_36 (n=301) |
|------------------------------------|-----------------------------|-------------------------------------------------------------------|---------------------------------------------|--------------|--------------|--------------|--------------|--------------|--------------|
| Heart failure, moderate (State_{HF,MOD}) | Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. | - | 0.072 (0.047–0.103) | 43 (10.7%) | 16 (4.3%) | 9 (2.4%) | 4 (1.3%) | 6 (1.9%) | 6 (2.0%) |
| Heart failure, severe (State_{HF,SEV}) | Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. | - | 0.179 (0.122–0.251) | 222 (55.1%) | 116 (30.9%) | 99 (26.9%) | 57 (17.9%) | 45 (14.6%) | 47 (15.6%) |

COPD, Chronic obstructive pulmonary disease; GBD, Global Burden of Disease.

For our core sample of 119 HIV-negative and 179 HIV-positive participants, inclusion of YLD in the 3-year post-treatment period increased TB disability estimates by 34% and 36%, respectively, compared with those estimated for active disease only, while lifetime projections of 54% and 39%, respectively, were calculated for active disease and post-TB.

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DISCUSSION
Most adults successfully treated for PTB in urban Malawi have disability meeting the descriptions of GBD cardiorespiratory health states at treatment completion. While recovery is observed over time, 16% continue to satisfy at least one GBD disability state 3 years later. Our findings suggest that health plateaus after this 3-year time point, and assuming this level of disability then persists over the life course, we estimate a mean of 0.94 YLD per HIV-negative patient and 0.45 YLD per HIV-positive patient in the post-TB period. These compare to 0.59 YLD (HIV-) and 0.78 (HIV+) during active disease (derived from GBD data), with the majority of post-TB disability concentrated in a minority of people. Our results suggest currently unaccounted for post-TB morbidity makes a marked contribution to the morbidity of TB disease, and may, on average, exceed that experienced during active disease.

The average burden of disability experienced across this post-TB population is high. The GBD allocates DWs of 0.408 and 0.333 to active TB disease among HIV-positive and HIV-negative adults.17 Our study calculated average DWs of 0.025 and 0.041 for the 3-year period following treatment and estimated weights of 0.010 (HIV-positive) and 0.025 (HIV-negative) to apply thereafter. Our finding that HRQoL remains reduced following successful TB treatment is consistent with previous studies7–9 and with the degree of underlying post-TB respiratory pathology identified in this cohort and elsewhere.4,33

The weights derived in this study were smaller than those modelled by Quaife et al (0.053 for the post-TB period),22 and those reported by Pasipanodya et al which ranged from 0.173 for ‘non-impaired’ to 0.377 for ‘severely impaired’ survivors.23 However, we note that these studies did not account for HIV status, and estimated DWs using cross-sectional prevalence estimates.
Table 2  Three-year study period and lifetime projections of YLD within core sample, disaggregated by the severity of HRQoL impairment at T₀, and presented for the total cohort, and stratified by gender and HIV status

|                     | Disability over the 3-year follow-up period | Projected lifetime disability (including 3-year post-treatment) | Disability weights |
|---------------------|--------------------------------------------|---------------------------------------------------------------|--------------------|
|                     | N   | Mean YLD | Total YLD | Burden | N   | Mean YLD | Total YLD | Burden | During 3 years | After 3 years |
| All participants    |     |          |           |        |     |          |           |        |               |               |
| in core sample (n=299) |     |          |           |        |     |          |           |        |               |               |
| *Least severe 20%  | 94  | 0.000    | 0.000     | 0%     | 94  | 0.000    | 0.000     | 0%     | 0.000          | 0.000          |
| –                   | 30  | 0.012    | 0.371     | 1%     | 29  | 0.012    | 0.360     | 0%     | 0.004          | 0.000          |
| –                   | 55  | 0.041    | 2.238     | 8%     | 57  | 0.042    | 2.419     | 1%     | 0.014          | 0.000          |
| –                   | 60  | 0.111    | 6.672     | 24%    | 60  | 0.154    | 9.253     | 5%     | 0.037          | 0.000          |
| *Most severe 20%   | 60  | 0.315    | 18.890    | 67%    | 59  | 3.062    | 180.629   | 94%    | 0.105          | 0.083          |
| All 3-year         | 299 | 0.094    | 28.171    | 100%   | 299 | 0.644    | 192.662   | 100%   | 0.031          | 0.016          |
| participants       |     |          |           |        |     |          |           |        |               |               |
| Men (n=198)         |     |          |           |        |     |          |           |        |               |               |
| Least severe 20%   | 70  | 0.000    | 0.000     | 0%     | 38  | 0.000    | 0.000     | 0%     | 0.000          | 0.000          |
| –                   | 11  | 0.009    | 0.102     | 1%     | 10  | 0.009    | 0.092     | 0%     | 0.003          | 0.000          |
| –                   | 38  | 0.038    | 1.427     | 8%     | 38  | 0.038    | 1.438     | 2%     | 0.013          | 0.000          |
| –                   | 41  | 0.107    | 4.390     | 25%    | 40  | 0.134    | 5.365     | 6%     | 0.036          | 0.000          |
| Most severe 20%    | 38  | 0.307    | 11.661    | 66%    | 40  | 2.096    | 83.845    | 92%    | 0.102          | 0.060          |
| All men            | 198 | 0.089    | 17.580    | 100%   | 198 | 0.458    | 90.739    | 100%   | 0.030          | 0.012          |
| Women (n=101)      |     |          |           |        |     |          |           |        |               |               |
| Least severe 20%   | 24  | 0.000    | 0.000     | 0%     | 24  | 0.000    | 0.000     | 0%     | 0.000          | 0.000          |
| –                   | 19  | 0.015    | 0.286     | 3%     | 19  | 0.015    | 0.286     | 0%     | 0.005          | 0.000          |
| –                   | 18  | 0.048    | 0.867     | 8%     | 18  | 0.050    | 0.901     | 1%     | 0.016          | 0.000          |
| –                   | 21  | 0.139    | 2.912     | 27%    | 20  | 0.224    | 4.484     | 4%     | 0.046          | 0.001          |
| Most severe 20%    | 19  | 0.343    | 6.525     | 62%    | 20  | 4.813    | 96.253    | 94%    | 0.114          | 0.125          |
| All women          | 101 | 0.105    | 10.591    | 100%   | 101 | 1.009    | 101.923   | 100%   | 0.035          | 0.025          |
| HIV-positive       |     |          |           |        |     |          |           |        |               |               |
| participants (n=179)|     |          |           |        |     |          |           |        |               |               |
| Least severe 20%   | 57  | 0.000    | 0.000     | 0%     | 57  | 0.000    | 0.000     | 0%     | 0.000          | 0.000          |
| –                   | 19  | 0.013    | 0.246     | 2%     | 19  | 0.013    | 0.246     | 0%     | 0.004          | 0.000          |
| –                   | 35  | 0.039    | 1.373     | 10%    | 33  | 0.038    | 1.268     | 2%     | 0.013          | 0.000          |
| –                   | 32  | 0.090    | 2.876     | 22%    | 34  | 0.108    | 3.663     | 5%     | 0.030          | 0.000          |
| Most severe 20%    | 36  | 0.243    | 8.759     | 66%    | 36  | 2.069    | 74.471    | 93%    | 0.081          | 0.052          |
| All HIV positive   | 179 | 0.074    | 13.254    | 100%   | 179 | 0.445    | 79.649    | 100%   | 0.025          | 0.010          |
| HIV-negative       |     |          |           |        |     |          |           |        |               |               |
| participants (n=119)|     |          |           |        |     |          |           |        |               |               |
| Least severe 20%   | 37  | 0.000    | 0.000     | 0%     | 37  | 0.000    | 0.000     | 0%     | 3.333          | 0.000          |
| –                   | 11  | 0.011    | 0.125     | 1%     | 10  | 0.011    | 0.115     | 0%     | 8.000          | 0.000          |
| –                   | 23  | 0.048    | 1.113     | 8%     | 24  | 0.055    | 1.317     | 1%     | 8.000          | 0.000          |
| –                   | 24  | 0.161    | 3.852     | 26%    | 24  | 0.269    | 6.451     | 6%     | 8.000          | 0.002          |
| Most severe 20%    | 24  | 0.400    | 9.593     | 65%    | 24  | 4.321    | 103.714   | 93%    | 39.667         | 0.122          |
| All HIV negative   | 119 | 0.123    | 14.683    | 100%   | 119 | 0.938    | 111.597   | 100%   | 0.041          | 0.025          |

Shaded cells show average DWs for each subgroup, appropriate for YLD calculations in an economic evaluation. They are calculated as the mean 3-year YLD divided by three. For HIV status within gender, see online supplemental appendix table F3.

*Note least severe groupings larger due to number of participants measuring no impairment at T0. Further note, grouping by HIV status does not include one participant who declined testing.

HRQoL, health-related quality of life; YLD, years of life lost due to disability.
of COPD in a post-TB HIV-negative population\textsuperscript{22} or calculated DWs at a single point 20 weeks post-therapy in a high-income country, with the exact methods used to scale from SGRQ responses to DWs not reported.\textsuperscript{23} We estimated 247.6 post-TB YLDs across our baseline population ($n$=405; 61\% HIV-positive). To contextualise this estimate, we compared this disability to what might have been assumed during active disease for the participants in our sample. Remarkably, our YLD estimates for post-TB disability increased the mean TB-related disability estimates by 256\% (HIV-negative) and 214\% (HIV-positive). These values are in line with those estimated by Menzies \textit{et al}, who—\textit{notably also taking conservative assumptions}—estimated a mean increase of 385\% (95\% CI 154 to 755) in TB-related YLD globally, once morbidity experienced in the post-TB period had been added to that experienced during active disease.\textsuperscript{35} While the degree of TB disability will vary between countries—particularly associated to their income\textsuperscript{13}—our results point towards a vast amount of post-TB disability being overlooked among the 155 million TB survivors worldwide.\textsuperscript{19}

Our data suggest that post-TB morbidity is borne by a minority, with 94\% of YLD faced by 20\% of participants. This finding is consistent with the skewed distribution of respiratory pathology observed within this sample and has implications for approaches to post-TB care.\textsuperscript{4,24} When communicating to TB-affected communities, there is a need not only to acknowledge post-TB morbidity but also to emphasise that most adults completing treatment do in fact recover. Our findings indicate that therapeutic interventions may be best targeted at the minority with severe or persistent disease, where they would likely be most cost-effective.

Our study demonstrated higher disability among HIV-negative, compared with HIV-positive adults. This was observed at treatment completion, with differences widening over time. This is surprising, given our understanding of the detrimental effect of HIV on well-being, and the low CD4 count observed among the HIV-positive patients with TB.\textsuperscript{36} This might reflect an attrition bias, as our primary analysis excluded those who dropped out or died during follow-up, of whom 91\% were HIV positive. However, sensitivity analysis including all patients at all time points provided a mean DW only 2.1\% larger (0.0314 vs 0.0321), suggesting this was not responsible (online supplemental appendix table F4). We have previously reported more severe residual respiratory pathology among HIV-negative PTB survivors in this cohort,\textsuperscript{7} and as our DWs mainly pertain to respiratory symptoms, this difference may

### Table 3: YLD across time points split first by gender and second by HIV status

| Time Period | Number of participants | Mean YLD | Number of participants | Mean YLD | Ratio of male to female mean disability | p-value for difference in disability between groups |
|-------------|------------------------|----------|------------------------|----------|----------------------------------------|--------------------------------------------------|
| $T_0-T_6$   | 255                    | 0.029    | 123                    | 0.030    | 49:51                                  | 0.803                                            |
| $T_6-T_{12}$| 249                    | 0.018    | 119                    | 0.021    | 47:53                                  | 0.542                                            |
| $T_{12}-T_{24}$ | 212                | 0.026    | 107                    | 0.033    | 44:56                                  | 0.301                                            |
| $T_{24}-T_{30}$ | 208                | 0.007    | 105                    | 0.013    | 36:64                                  | 0.028                                            |
| $T_{30}-T_{36}$ | 200                | 0.006    | 101                    | 0.012    | 34:66                                  | 0.013                                            |
| $T_{36}-T_{36}$ | 101                | 0.105    | 198                    | 0.089    | 46:54                                  | 0.316                                            |

| HIV Status   | Number of participants | Mean YLD | Number of participants | Mean YLD | Ratio of HIV positive to HIV negative disability | p-value* for difference in disability between groups |
|--------------|------------------------|----------|------------------------|----------|----------------------------------------|--------------------------------------------------|
| HIV positive | $T_0-T_6$              | 231      | 0.026                  | 145      | 43:57                                  | 0.022                                            |
| HIV negative | $T_6-T_{12}$           | 225      | 0.017                  | 142      | 42:58                                  | 0.063                                            |
| HIV positive | $T_{12}-T_{24}$        | 192      | 0.023                  | 126      | 39:61                                  | 0.031                                            |
| HIV negative | $T_{24}-T_{30}$        | 187      | 0.006                  | 125      | 34:66                                  | 0.016                                            |
| HIV positive | $T_{30}-T_{36}$        | 180      | 0.005                  | 120      | 30:70                                  | 0.003                                            |
| HIV negative | $T_{36}-T_{36}$        | 179      | 0.074                  | 119      | 38:62                                  | 0.001                                            |

*Significant with $\alpha=0.05$

YLD, years of life lost due to disability.
reflect the extent of underlying post-TB lung disease between groups. 37 38

Also consistent with previous studies was our finding that YLD showed increasing differences between genders over time, with women bearing disproportionately more disability and reporting lower improvements in HRQoL (online supplemental appendix figure F5). A study of a South-Indian population 1-year post-treatment had reported lower social and mental well-being scores among women. 9 Gender disparities in the diagnosis and management of TB disease are receiving increased attention, 39 and our findings suggest that this agenda should aim to include the experience of post-TB morbidity.

Mortality among the TB survivors in this cohort was higher than expected at a population level. WHO life tables indicate that over our study period, one would expect fewer than three deaths among this group. 40 Post-treatment mortality data, our YLL post-TB must be considered alongside YLD if the true burden of TB disease is to be described.

Our study has several limitations. We focused on the cardiorespiratory sequelae of TB disease and did not include broader morbidity from extrapulmonary disease, drug side effects and psychosocial challenges. Recent studies have highlighted the broad extent of TB disability, and additional work to quantify these further types of morbidity is needed. 33 Our approach also assumed constant disability beyond 3 years post-treatment, however, TB survivors may experience respiratory exacerbations, 4 40 41 cardiorespiratory decline, 24 and recurrent TB disease, 42 43 such that disability in a minority might worsen over time. Our analyses did not consider reduced life expectancy among TB survivors 44 45 and importantly focused on residual morbidity among adult survivors of drug-sensitive PTB disease only. These limitations mean that our estimates of post-TB DALYs are likely conservative. Further data are needed from children, and those with multidrug-resistant and extrapulmonary disease, in urban and rural settings elsewhere. In the absence of cause of death data, our YLL (and therefore DALY) estimates required several assumptions, and data on cause of death among TB survivors are urgently needed to narrow these estimates. Finally, without a control group, it cannot be guaranteed that a participant’s post-TB disability was exclusively due to their TB. Our assumption of a causal link, however, is strengthened by the clear recovery patterns observed across the cohort following treatment completion, which are in keeping with recovery after severe illness such as TB disease.

This study also has important strengths. To our knowledge, no previous study has combined both HRQoL data from a cohort of TB survivors and GBD disability states and weights to directly derive DWs, YLD and DALYs for the post-TB period. By using primary HRQoL and mortality data from a large prospective cohort study of post-TB morbidity in Africa with extended follow-up, our novel approach ensured that our derived DWs are directly comparable to those used in the construction of DALYs for active TB and other diseases. Furthermore, our sensitivity analyses included comparisons between SGRQ and DW trajectories over time, and comparisons of YLD calculations between our full and core sample, and showed good consistency. Together, these factors suggest validity in both our analytical approach and findings. Finally, this study describes long-term morbidity after TB treatment completion and highlights a neglected period in the TB-patient journey.

CONCLUSION

By excluding the post-TB period, existing GBD calculations substantially underestimate the true burden of TB-related morbidity. This has implications for resource allocation to TB services, and for cost-utility analyses of interventions aimed at TB prevention, early diagnosis, reducing transmission or addressing post-TB sequelae. The methodological approach introduced here, using HRQoL data to allocate GBD-comparable DWs, could be applied to data from other studies of post-TB morbidity, in order to further our understanding of the impact of the sequelae of TB disease.

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data analysis, with input from GFN, LGN, JMJ, EW and JM. EMT was the lead author with input from all co-authors. All authors approved the final manuscript for publication, and EMT accepts full responsibility of the overall content as the guarantor.

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Appendices

**Title:** TB morbidity estimates overlook the contribution of post-TB disability: evidence from urban Malawi

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Appendix A: Selection of relevant GBD Disease States

Since the first GBD report (1996), many studies have generated disability weights sets. Methods vary, but typically use ‘disease-specific’ descriptions of health states, a panel of ‘judgers’ (either medical experts, affected patients, or general population), and a non-preference based valuation method administered by either questionnaire, interview, or panel meeting. The 235 unique health states evaluated in the 2013 GBD ‘Disability Weights Measurement Study’ were calculated by presenting members of the public with short and simple (non-medical) descriptions of health states, and then eliciting their relative preferences through pairwise comparisons. A relative ranking was then formed, and each unique state assigned a weight, anchored using an additional valuation question. Despite being considered ‘disease specific’, those valuing did not see names, only lay-descriptions which ‘emphasised the major functional consequences and symptoms associated with each health state’, meaning one health state can be used to describe the experience of several diseases or conditions. Accordingly, a disability weight initially ‘intended’ to represent one condition, e.g. anaemia, could be used to value another seemingly unrelated health state, provided that the symptoms of this state aligned with the health state description.

Table A1: Disability weight allocations for TB disease states within GBD 2016 study

| HIV Coinfection          | Drug-susceptible TB | Multidrug-resistant TB | Extensively drug-resistant TB | Latent TB infection |
|--------------------------|---------------------|------------------------|-------------------------------|---------------------|
| Without HIV coinfection | 0.333 (0.224-0.454) | 0.333 (0.224-0.454)   | 0.333 (0.224-0.454)           | 0 - (asymptomatic)  |
| No anaemia               | 0.408 (0.274-0.549) | 0.408 (0.274-0.549)   | 0.408 (0.274-0.549)           |                     |
| With anaemia, mild       | 0.411 (0.278-0.551) | 0.411 (0.278-0.551)   | 0.411 (0.278-0.551)           |                     |
| With anaemia, moderate   | 0.439 (0.307-0.577) | 0.439 (0.307-0.577)   | 0.439 (0.307-0.577)           |                     |
| With anaemia, severe     | 0.495 (0.353-0.64)  | 0.495 (0.353-0.64)    | 0.495 (0.353-0.64)            |                     |

Brackets represent 95% uncertainty intervals (UIs) derived from 1000 draws from the posterior distribution of each step in the estimation process - see [26].

Before beginning the study, an initial search within the Sequela, health state name, and Health state lay description fields of the GBD disability weight tables was conducted, using several key terms of interest (Table A2). Subsequently, all 235 unique health states were reviewed, with no further states than those in Table A2 identified.

Table A2: Number of health state descriptions and Sequelae for each of the search terms

| Search term:          | Lung | Respiratory | Breast | Chest | Tuberculosis | TB | Cough* | Wheezing |
|-----------------------|------|-------------|--------|-------|--------------|----|--------|----------|
| Found in name of a specified sequela | 12   | 43          | 1      | 0     | 16           | 0  | 1      | 0        |
| Found in unique health state name   | 0    | 81          | 0      | 1     | 15           | 0  | 0      | 0        |
| Found in any sequela lay description| 0    | 0           | 142    | 4     | 0            | 2  | 38     | 19       |
| Unique description in which found   | 0    | 0           | 14     | 4     | 0            | 1  | 0      | 5        |

States with at least one search term in any of: sequela, state name, or unique description: 30

*Note: search terms are strings, e.g. ‘cough’ would also return coughing, coughs etc.

The thirty health state descriptions of interest from this search, along with the specific sequelae to which they refer are shown in Appendix Table A3. These 30 states were reduced down to 16, based upon the severity of the symptoms and the feasibility of matching these to our cohort data (Table 2). Each of the descriptions was matched as closely as possible to the TB-sequelae reported by study participants.
Table A3: The refined list of health states

| Number of specified sequelae covered by health state | Health state name                  | Health state lay description                                                                 | GBD Disability Weight (uncertainty interval) |
|-----------------------------------------------------|------------------------------------|------------------------------------------------------------------------------------------------|---------------------------------------------|
| 1                                                   | Acute myocardial infarction, days 3-28 | Gets short of breath after heavy physical activity, and tires easily, but has no problems when at rest. The person has to take medication every day and has some anxiety. | 0.074 (0.049-0.105)                         |
| 25                                                  | Anemia, moderate                    | Feels moderate fatigue, weakness, and shortness of breath after exercise, making daily activities more difficult. | 0.052 (0.034-0.076)                        |
| 25                                                  | Anemia, severe                      | Feels very weak, tired and short of breath, and has problems with activities that require physical effort or deep concentration. | 0.149 (0.101-0.209)                        |
| 1                                                   | Asthma, controlled                  | Has wheezing and cough once a month, which does not cause difficulty with daily activities. | 0.015 (0.007-0.026)                         |
| 1                                                   | Asthma, partially controlled        | Has wheezing and cough once a week, which causes some difficulty with daily activities. | 0.036 (0.022-0.055)                         |
| 1                                                   | Asthma, uncontrolled                | Has wheezing, cough and shortness of breath more than twice a week, which causes difficulty with daily activities and sometimes wakes the person at night. | 0.133 (0.086-0.192)                        |
| 11                                                  | COPD and other chronic respiratory problems, mild | Has cough and shortness of breath after heavy physical activity, but is able to walk long distances and climb stairs. | 0.019 (0.011-0.033)                         |
| 8                                                   | COPD and other chronic respiratory problems, moderate | Has cough, wheezing and shortness of breath, even after light physical activity. The person feels tired and can walk only short distances or climb only a few stairs. | 0.225 (0.153-0.310)                         |
| 8                                                   | COPD and other chronic respiratory problems, severe | Has cough, wheezing and shortness of breath all the time. The person has great difficulty walking even short distances or climbing any stairs, feels tired when at rest, and is anxious. | 0.408 (0.273-0.556)                         |
| 17                                                  | Heart failure, mild                 | Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort. | 0.041 (0.026-0.062)                         |
| 17                                                  | Heart failure, moderate             | Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. | 0.072 (0.047-0.103)                         |
| 17                                                  | Heart failure, severe               | Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. | 0.179 (0.122-0.251)                         |
Appendix B: Mapping study SGRQ data to GBD states

Each of the shortlisted health states were disaggregated into the distinct clauses they contained, mindful of words such as ‘and’ and ‘or’. Once split out, each clause was mapped to the respiratory symptoms of each patient using responses of the SGRQ.

Table B1: Mapping patients to health states from GBD using SGRQ responses

| State name | Health state lay description split into necessary conditions | Mapping procedure |
|------------|---------------------------------------------------------------|-------------------|
| Acute myocardial infarction, days 3-28 | Gets short of breath after heavy physical activity, and tires easily, but has no problems when at rest. The person has to take medication every day and has some anxiety. | Answered 'Yes' to [playing sports or games makes me feel breathless OR My breathing makes it difficult to do things such as very heavy manual work, run, cycle, swim fast or play competitive sports OR I get breathless when walking up mountains*] and answered ‘Yes’ to I get exhausted easily but has no problems when at rest. Answered 'No' to feeling breathless when sitting or lying still Derived variable 'some_anxiety' = 1 (see bottom of table for more details) |
| Anemia, moderate | Feels moderate fatigue, weakness, and shortness of breath after exercise, making daily activities more difficult. | Answered 'Yes' to I get exhausted easily AND I feel breathless playing sports or games AND My breathing makes it difficult to do things such as carry heavy loads, dig the garden or shovel snow, jog or walk at 5 miles per hour, play tennis or swim Derived variable 'inteference_with_activities' = 1 |
| Anemia, severe | Feels very weak, tired and short of breath, and has problems with activities that require physical effort or deep concentration. | Answered 'Yes' to [I take a long time to get washed or dressed OR I cannot take a bath or shower or I take a long time OR I walk slower than other people, or I stop for rests OR Jobs such as housework take a long time, or I have to stop for rests OR If I walk up one flight of stairs, I have to go slowly or stop OR I hurry or walk fast, I have to stop or slow down OR My breathing makes it difficult to do things such as walk up hills, carrying things up stairs, light gardening such as weeding, dance, play bowls or play golf OR My breathing makes it difficult to do things such as carry heavy loads, dig the garden or shovel snow, jog or walk at 5 miles per hour, play tennis or swim OR My breathing makes it difficult to do things such as very heavy manual work, run, cycle, swim fast or play competitive sports.] Unable to code (however is OR statement so if above satisfied irrelevant) |
| Asthma, controlled | Has wheezing and cough once a month, which does not cause difficulty with daily activities. | (Coughing most days a week OR several days a week OR a few days a month) AND (Wheezing most days a week OR several days a week OR a few days a month) (not coded as taking maximum disability weight – see below) |
| Asthma, partially controlled | Has wheezing and cough once a week, which causes some difficulty with daily activities. | (Coughing most days a week OR several days a week) AND (Wheezing most days a week OR several days a week) The derived variable 'inteference_with_activities' = 1 |
| Condition, uncontrolled | Description | Criteria |
|-------------------------|-------------|----------|
| Asthma, uncontrolled    | Has wheezing, cough and shortness of breath more than twice a week, which causes difficulty with daily activities and sometimes wakes the person at night. | Answered "My cough and breathing disturbs my sleep" |
| COPD and other chronic respiratory problems, mild | Has cough and shortness of breath after heavy physical activity, but is able to walk long distances and climb stairs. | Answered "No" to walking outside on the level makes me breathless |
| COPD and other chronic respiratory problems, moderate | Has cough, wheezing and shortness of breath, even after light physical activity. The person feels tired and can walk only short distances or climb only a few stairs. | Answered "Yes" to "Walking outside on the level makes me breathless" OR "I walk slower than other people, or have to stop for rests" |
| COPD and other chronic respiratory problems, severe | Has cough, wheezing and shortness of breath all the time. The person has great difficulty walking even short distances or climbing any stairs, and feels tired when at rest, and is anxious. | Over past 3 months has coughed most days a week OR had shortness of breath most days a week OR had wheezing most days a week |

| Condition, mild | Description | Criteria |
|----------------|-------------|----------|
| Heart failure, mild | Is short of breath and easily tires with moderate physical activity, such as walking uphill or more than a quarter-mile on level ground. The person feels comfortable at rest or during activities requiring less effort. | Answered "No" to all three of the following:
- I feel breathless when sitting or lying still
- I feel breathless when getting washed or dressed
- I feel breathless when walking around the home |
| Heart failure, moderate | Is short of breath and easily tires with minimal physical activity, such as walking only a short distance. The person feels comfortable at rest but avoids moderate activity. | Answers yes to any of the following:
- I cannot play sports or games
- I cannot go out for entertainment or recreation
- I cannot go out of the house to do the shopping |
| Heart failure, severe | Is short of breath and feels tired when at rest. The person avoids any physical activity, for fear of worsening the breathing problems. | Answers to the following two statements:
- My breathing makes it difficult to do things such as walk up hills, carrying things up stairs, light gardening such as weeding, dance, play bowls or play golf
- AND any one of: |
I cannot do housework OR
I cannot move far from my bed or chair OR
I cannot go out of the house to do the shopping

‘interference_with_activities’ = 1 if any two of the following questions were answered ‘Yes’:

My cough makes me tired, I am breathless when I talk, my cough or breathing disturbs my sleep, I get exhausted easily, My cough or breathing is embarrassing in public, My chest trouble is a nuisance to my family, friends or neighbours, I have become frail or an invalid because of my chest, Exercise is not safe for me, I cannot take a bath or shower, or I take a long time, Jobs such as housework take a long time, or I have to stop for rests, I cannot go out for entertainment or recreation, I cannot go out of the house to do the shopping, I cannot move far from my bed or chair, (My chest trouble made me stop work altogether OR my chest trouble interferes with my work OR made me change my work),

OR any of My chest condition is the most important problem I have, causes me quite a lot of problems, causes me a few problems, It stops me doing one or two things I would like to do, it stops me doing most of the things I would like to do, it stops me doing everything I would like to do.

‘some_anxiety’ = 1 if any of the following questions were answered ‘Yes’:

‘I get afraid or panic when I cannot get my breath’ OR ‘I do not expect my chest to get better’ OR ‘I feel that I am not in control of my chest problem’ OR ‘Exercise is not safe for me’.

Note: For Baseline, 6-months and 12-months we could have used patients who answered EQ-5D-3L for anxiety/depression as level 2 or 3, however since not available across the full study, the decision was made to only use SGRQ data. See Appendix Tables F6 and F7 for validation of derived variables against EQ-5D responses for T0-T12.

Note: SGRQ Questions about cough, breathlessness, chest trouble etc. ask about what ‘usually’ makes the respondent breathless/cough/‘these days’, while activities questions ask about how these activities might be affected by breathing.
Mapping GBD descriptions
Additional considerations of the mapping are detailed below:

Climbing Stairs
While adapting and translating the SGRQ questionnaire for Malawi, the statement ‘If I walk up one flight of stairs I have to go slowly or stop’ was deemed not applicable to the population. In the Chichewa version, this was adapted to ‘If I walk up a mountain, I have to go slowly or stop’, and was accounted for in our mappings.

Minimum Fulfilment Criteria
The aim of this mapping was to calculate DALY weights which represent the minimum amount of disability in the population as according to the GBD weights, and accordingly we took the maximum of any satisfied weights. It was therefore unnecessary to map the requirement ‘which does not cause difficulty with daily activities’, reasoning that regardless of this condition, the disability weight associated would be reached if the other criteria are met. That said, well-defined statements such as ‘has no problems when at rest’ were mapped (answered ‘No’ to ‘feeling breathless when sitting or lying still’), to increase the accuracy of our overall classifications.

Applicability of activities
It must be recognised that the activities listed in the SGRQ do not apply to all people, independent of their health (e.g. some people even if healthy would not do housework, and others may not play sports). Therefore, when coding that a patient ‘avoids any physical activity’ the condition that all of these criteria must be met was relaxed.

Specified Time intervals
Timeframes asked in the SGRQ were closely mapped to those of the GBD descriptions. A conservative approach was taken, with “a few days a month” not considered to satisfy the requirement of “once a week”.

Avoidance of activities
In cases that the GBD descriptions state that an individual ‘avoids’ an activity, we have not been able to map this based on the fact that the activity makes them breathless.

Usual activities
The binary variable ‘interference_with_activities’ was generated based upon responses in the SGRQ questionnaire and used in the mapping of conditions Stateii, Statevii, and Stateix. For T0, T6, T12, these derived variables have been validated against the responses to the EQ-5D-3L usual activities question. Appendix Table D7

Anxiety
A binary variable ‘some_anxiety’ was created, equal to 1 if any of the following questions were answered ‘Yes’: ‘I get afraid or panic when I cannot get my breath’, ‘I do not expect my chest to get better’, ‘I feel that I am not in control of my chest problem’ or ‘Exercise is not safe for me’. For individuals present at T0, T6, T12, this was checked against the EQ-5D-3L question on Anxiety/Depression, if this was a level 2 or level 3 (moderate or severe). Appendix Table D6.

Uncertainty intervals
We did not account for the uncertainty intervals of estimates, taking the point-estimate for each state.
Appendix C: Proceeding from health states to calculating DALYs

**Figure C1:** Example of 3-year disability calculated for an individual satisfying four different disability weights, using the ‘area under the curve’ approach by averaging across timepoints.

Note that no data were collected at the 18-month timepoint.
Appendix D: Modelling lifetime disability

Several models were fitted to the average (across individuals) SGRQ scores at different timepoints. These included: polynomial models (up to third degree) a log model and a quadratic plateau model. The log model provided an improved fit over polynomial models, both visually and in terms of pseudo $R^2$, though when used to generate out-of-sample long term predictions, it predicted implausible negative SGRQ values beyond 5 years.

Having observed a plateau in our data towards the end of the three years of data collection, we considered the assumption that HRQoL would stay constant from $T_{36}$ for the remainder of life. This assumption was supported by a quadratic plateau model, which provided the best fit for the data. The model generally fit well and pseudo $R^2$ was slightly improved compared to the log model. SGRQ was estimated to plateau 3-years post-treatment at an average SGRQ value of 3.066.

| Table D1: Wellness of fit of several models fit to SGRQ data across $T_0 - T_{36}$ |
|-----------------------------------------------|----------------|----------------|
| Model                                  | Functional form | Pseudo-$R^2$ |
| Linear model                       | $y = a + bx$    | 81.2%         |
| Quadratic model                    | $y = a + bx + cx^2$ | 91.6%         |
| Cubic model                        | $y = a + bx + cx^2 + dx^3$ | 91.1%         |
| Log model                          | $y = a + \log(x)$ | 95.2%         |
| Quadratic plateau model            | $y = \begin{cases} a + bx - \frac{b}{2x_{\text{crit}}} \cdot x^2 & \text{if } x < x_{\text{crit}} \\ a + bx_{\text{crit}} - \frac{b}{2x_{\text{crit}}} \cdot x_{\text{crit}}^2 & \text{if } x \geq x_{\text{crit}} \end{cases}$ | 95.5%         |
| Where $x_{\text{crit}}$ denotes a critical $x$ value.                                    |                |

| Table D2: Quadratic plateau model estimation |
|-----------------------------------------------|----------------|----------------|
| $y = \begin{cases} a + bx - \frac{b}{2x_{\text{crit}}} \cdot x^2 & \text{if } x < x_{\text{crit}} \\ a + bx_{\text{crit}} - \frac{b}{2x_{\text{crit}}} \cdot x_{\text{crit}}^2 & \text{if } x \geq x_{\text{crit}} \end{cases}$ |                |

| Parameters | Estimate | Standard error | t-value | Pr(>|t|) |
|------------|----------|----------------|---------|----------|
| $a$        | 17.006   | 2.239          | 7.594   | 0.00474  |
| $b$        | -4.646   | 1.525          | -3.047  | 0.05558  |
| $x_{\text{crit}}$ | 6.001   | 1.276          | 4.702   | 0.01820  |

Residual standard error: 1.175 on 3 degrees of freedom
**Figure D1:** Quadratic plateau model overlaid on mean SGRQ scores at six timepoints of study.
Appendix E: Comparison of active disease and post-TB disability

To frame our findings for post-TB disability, we estimated what disability would likely have been calculated for the population of our core sample during their active tuberculosis disease. Estimates of duration of disease were taken from the technical annex of the WHO 2021 TB report. [https://cdn.who.int/media/docs/default-source/hq-tuberculosis/tb-report-2021/technical_annex_methods_2021.pdf](https://cdn.who.int/media/docs/default-source/hq-tuberculosis/tb-report-2021/technical_annex_methods_2021.pdf) (Table 1 page 25). This report uses uniform distributions for duration of treated TB of (0.2−2) for HIV-negative TB patients and (0.01−1) for HIV-positive. We took the means of these distributions to obtain mean durations of 1.1 years (HIV-) and 0.51 years (HIV+).

The values in column B are GBD disability weights for drug-susceptible TB.

Based upon these values, Columns D and E provide estimates for the mean and total TB-related disability (YLD) of our core sample up to point of treatment. Note, unlike our post-TB estimates, these are not calculated from data collected in this sample but represent estimates similar to those which would be presented in a typical TB cost-utility paper utilising DALYs, wherein primary Health-related Quality of Life data had not been collected. Columns F-through-I are taken from Table 2 in the main manuscript, with Columns J and K showing the percentage increase of disability when our values for the post-TB period are incorporated.

| Column | A* | B† | C | D | E | F | G | H | I | J | K |
|--------|----|----|---|---|---|---|---|---|---|---|---|
| Mean duration of treated TB (years) | GBD disability weight of active disease | Number of patients (core sample) | YLD during active disease | YLD 3 years post-TB | Projected post-TB Disability (including 3 year post treatment) | % Increase of disability when including post-TB period |
| Mean | Total | Mean | Total | Mean | Total | 3-years only | Lifetime |
| Source | WHO Global TB database | GBD | Our sample | ColA * ColB | ColD * ColC | Our study | Our study | Our study | Our study | ColG / ColE | ColJ / ColE |
| HIV-negative: | 1.1 | 0.333 | 119 | 0.37 | 43.59 | 0.12 | 14.68 | 0.938 | 111.60 | 34% | 256% |
| HIV-positive: | 0.51 | 0.408 | 179 | 0.21 | 37.25 | 0.07 | 13.25 | 0.445 | 79.65 | 36% | 214% |

*Values in column A are estimates of the duration of TB disease taken from WHO data, which include the period prior to diagnosis and the time on treatment.
†Values in column B are the disability weights allocated to this TB disease period provided by GBD estimates.
Appendix F: Additional Tables and Figures

Figure F1: Cohort chart showing deaths known to have occurred between timepoints of study.
Figure F2: Changes in SGRQ score between time-points, disaggregated by HIV-status and gender

Table F1: Changes in St George's Respiratory Questionnaire Total scores between interviews, disaggregated by sex and HIV status

|        | T₀ to T₆ (n=372) | T₆ to T₁₂ (n=363) | T₁₂ to T₂₄ (n=318) | T₂₄ to T₃₀ (n=307) | T₃₀ to T₅₀ (n=295) |
|--------|------------------|-------------------|--------------------|--------------------|--------------------|
| HIV-positive men  |                   |                   |                    |                    |                    |
| Improved         | 51               | 26                | 23                 | 17                 | 7                  |
| 34.7%            | 18.1%            | 19.2%             | 14.8%              | 7.2%               |
| No change        | 74               | 100               | 82                 | 91                 | 98                 |
| 50.3%            | 69.4%            | 69.2%             | 79.1%              | 88.3%              |
| Deteriorated     | 22               | 18                | 14                 | 7                  | 6                  |
| 15.0%            | 12.5%            | 11.7%             | 6.1%               | 5.4%               |
| HIV-negative men |                   |                   |                    |                    |                    |
| Improved         | 48               | 19                | 25                 | 15                 | 11                 |
| 47.1%            | 19.0%            | 27.5%             | 16.7%              | 12.8%              |
| No change        | 43               | 62                | 59                 | 67                 | 68                 |
| 42.2%            | 62.0%            | 64.8%             | 74.4%              | 79.1%              |
| Deteriorated     | 11               | 19                | 7                  | 8                  | 7                  |
| 10.8%            | 19.0%            | 7.7%              | 8.9%               | 8.1%               |
| HIV-positive women |                  |                   |                    |                    |                    |
| Improved         | 43               | 18                | 12                 | 9                  | 8                  |
| 51.8%            | 22.5%            | 16.7%             | 13.0%              | 12.1%              |
| No change        | 29               | 48                | 50                 | 51                 | 51                 |
| 34.9%            | 60.0%            | 69.4%             | 73.9%              | 77.3%              |
| Deteriorated     | 11               | 14                | 10                 | 9                  | 7                  |
| 13.3%            | 17.5%            | 13.9%             | 13.0%              | 10.6%              |
| HIV-negative women |                |                   |                    |                    |                    |
| Improved         | 14               | 8                 | 12                 | 9                  | 5                  |
| 35.0%            | 20.5%            | 34.3%             | 27.3%              | 15.6%              |
| No change        | 18               | 19                | 19                 | 19                 | 19                 |
| 45.0%            | 48.7%            | 54.3%             | 57.6%              | 59.4%              |
| Deteriorated     | 8                | 12                | 4                  | 5                  | 8                  |
| 20.0%            | 30.8%            | 11.4%             | 15.2%              | 25.0%              |
Table F2: Allocated health states and maximal disability weights at each time point

| Health State ID     | Disability Weight | T0 (n=403) | T6 (n=376) | T12 (n=368) | T24 (n=319) | T30 (n=308) | T36 (n=301) |
|---------------------|-------------------|-------------|------------|-------------|-------------|-------------|-------------|
| State Asthma Con    | 0.015             | 20 (5.0%)   | 12 (3.2%)  | 8 (2.2%)    | 9 (2.8%)    | 4 (1.3%)    | 5 (1.7%)    |
| State COPD Mild     | 0.019             | 211 (52.4%) | 101 (26.9%)| 86 (23.4%)  | 50 (15.7%)  | 38 (12.3%)  | 44 (14.6%)  |
| State Asthma Far Con| 0.036             | 0           | 2 (0.5%)   | 0           | 1 (0.3%)    | 0           | 0           |
| State NSF Mild      | 0.041             | 212 (52.6%) | 110 (29.3%)| 96 (26.1%)  | 51 (16.0%)  | 42 (13.6%)  | 45 (15.0%)  |
| State Anemia Mod    | 0.052             | 91 (22.6%)  | 37 (9.8%)  | 45 (12.2%)  | 8 (2.5%)    | 5 (1.6%)    | 14 (4.7%)   |
| State NSF Mod       | 0.072             | 166 (41.2%) | 69 (18.4%) | 64 (17.4%)  | 26 (8.2%)   | 20 (6.5%)   | 22 (7.3%)   |
| State Acute MI      | 0.074             | 52 (12.9%)  | 13 (3.5%)  | 20 (5.4%)   | 11 (3.4%)   | 3 (1.0%)    | 4 (1.3%)    |
| State Asthma Uncon  | 0.133             | 0           | 0          | 0           | 0           | 0           | 0           |
| State Anemia Sev    | 0.149             | 112 (27.8%) | 43 (11.4%) | 49 (13.3%)  | 13 (4.1%)   | 5 (1.6%)    | 10 (3.3%)   |
| State NSF Sev       | 0.179             | 0           | 1 (0.3%)   | 1 (0.3%)    | 0           | 0           | 0           |
| State COPD Mod      | 0.225             | 94 (23.3%)  | 52 (13.8%) | 47 (12.8%)  | 20 (6.3%)   | 14 (4.5%)   | 14 (4.7%)   |
| State COPD Sev      | 0.408             | 0           | 0          | 0           | 1 (0.3%)    | 0           | 0           |

Any disability weight - 222 (55.1%) 116 (30.9%) 99 (26.9%) 57 (17.9%) 45 (14.6%) 47 (15.6%)

Figure F3: Changes in mean EQ-5D index score and mean VAS score over three-year study period by SGRQ severity quintile at TB treatment completion.
Table F3: Three-year study period and lifetime projections of YLD within core sample, disaggregated by severity within each YLD over the three-year follow-up period  Projected Lifetime YLD (including 3 year post treatment)  Disability Weights

|                      | n   | Mean YLD | Total YLD | Burden | n   | Mean YLD | Total YLD | Burden | During 3 years | After 3 years |
|----------------------|-----|----------|-----------|--------|-----|----------|-----------|--------|----------------|---------------|
| **HIV-positive Men (n=111)** |     |          |           |        |     |          |           |        |                |               |
| Least severe 20%      | 41  | 0.000    | 0.000     | 0%     | 41  | 0.000    | 0.000     | 0%     | 0.000          | 0.000         |
| -                    | 5   | 0.010    | 0.051     | 1%     | 5   | 0.010    | 0.051     | 0%     | 0.003          | 0.000         |
| -                    | 22  | 0.035    | 0.767     | 10%    | 22  | 0.035    | 0.767     | 2%     | 0.012          | 0.000         |
| Most severe 20%       | 21  | 0.239    | 5.024     | 64%    | 22  | 1.579    | 34.741    | 92%    | 0.080          | 0.045         |
| **All HIV positive men** | 111 | 0.071    | 7.868     | 100%   | 111 | 0.340    | 37.775    | 100%   | 0.024          | 0.009         |
|                      |     |          |           |        |     |          |           |        |                |               |
| **HIV-negative Men (n=86)** |     |          |           |        |     |          |           |        |                |               |
| Least severe 20%      | 29  | 0.000    | 0.000     | 0%     | 29  | 0.000    | 0.000     | 0%     | 0.000          | 0.000         |
| -                    | 6   | 0.008    | 0.051     | 1%     | 5   | 0.008    | 0.040     | 0%     | 0.003          | 0.000         |
| -                    | 17  | 0.043    | 0.727     | 8%     | 18  | 0.047    | 0.840     | 2%     | 0.014          | 0.000         |
| Most severe 20%       | 17  | 0.136    | 2.313     | 24%    | 17  | 0.195    | 3.319     | 6%     | 0.045          | 0.000         |
| **All HIV negative Men** | 86  | 0.110    | 9.479     | 100%   | 86  | 0.599    | 51.548    | 100%   | 0.037          | 0.016         |
|                      |     |          |           |        |     |          |           |        |                |               |
| **HIV-positive Women (n=68)** |     |          |           |        |     |          |           |        |                |               |
| Least severe 20%      | 16  | 0.000    | 0.000     | 0%     | 16  | 0.000    | 0.000     | 0%     | 0.000          | 0.000         |
| -                    | 15  | 0.015    | 0.229     | 4%     | 15  | 0.015    | 0.229     | 1%     | 0.005          | 0.000         |
| -                    | 12  | 0.048    | 0.572     | 11%    | 10  | 0.047    | 0.467     | 1%     | 0.016          | 0.000         |
| Most severe 20%       | 12  | 0.095    | 1.145     | 21%    | 14  | 0.127    | 1.780     | 4%     | 0.032          | 0.000         |
| **All HIV positive women** | 68  | 0.079    | 5.387     | 100%   | 68  | 0.616    | 41.874    | 100%   | 0.026          | 0.013         |
|                      |     |          |           |        |     |          |           |        |                |               |
| **HIV-negative Women (n=33)** |     |          |           |        |     |          |           |        |                |               |
| Least severe 20%      | 8   | 0.000    | 0.000     | 0%     | 8   | 0.000    | 0.000     | 0%     | 0.000          | 0.000         |
| -                    | 6   | 0.021    | 0.123     | 2%     | 6   | 0.021    | 0.123     | 0%     | 0.007          | 0.000         |
| -                    | 6   | 0.099    | 0.595     | 11%    | 6   | 0.141    | 0.846     | 1%     | 0.033          | 0.000         |
| Most severe 20%       | 7   | 0.245    | 1.718     | 33%    | 7   | 1.535    | 10.745    | 18%    | 0.082          | 0.060         |
| **All HIV negative women** | 33  | 0.158    | 5.204     | 100%   | 33  | 1.820    | 60.049    | 100%   | 0.053          | 0.049         |

Mean disability weights for each grouping shaded in grey. Disability Weight quintiles are based on total disability. Two patients who did not provide HIV status are removed from these calculations.
Table F4 – Sensitivity analysis: three-year YLD using Baseline dataset and averages across timepoints

| Time period | $T_0$ | $T_6$ | $T_{12}$ | $T_{24}$ | $T_{30}$ | $T_{36}$ |
|-------------|-------|-------|---------|---------|---------|---------|
| Number of people at timepoint | 403   | 374   | 366     | 317     | 306     | 299     |
| Sum of individual disability weights at instant | 31.646 | 15.148 | 14.159  | 6.609   | 4.637   | 4.879   |
| Average individual disability | 0.0785 | 0.0405 | 0.0387  | 0.0208  | 0.0152  | 0.0163  |
| Averaged disability for interval | 0.0595 | 0.0396 | 0.0298  | 0.0180  | 0.0157  |
| Length of interval (years) | 0.5 | 0.5 | 1.0 | 0.5 | 0.5 |
| Length of interval * interval average disability | 0.0298 | 0.0198 | 0.0298  | 0.0090  | 0.0079  |

Average 3 year disability (summing row above) = 0.09619

Average 1-year disability (above row / 3) = 0.03206

Alternative method of disability weight calculation using averages across timepoints. This method includes all patients, who were LTFU during data collection.

Figure F4 – Graphical representation of YLD calculation following method which uses all patients.
| State lay description | Coding variation | Frequency | Additional coding |
|-----------------------|------------------|-----------|------------------|
| **Controlled Asthma**  |                 |           |                  |
| (State: ASTHMA_CON)   |                  |           |                  |
| Has wheezing and cough once a month, which does not cause difficulty with daily activities. | Coughing AND Wheeze | most days a week | 20 |
|                       |                   | OR several days a week | 12 |
|                       |                   | OR a few days a month | 8  |
|                       |                   |                  | 9  |
|                       |                   |                  | 4  |
|                       |                   |                  | 5  |
|                       | Coughing without Wheeze |                  | 146 |
|                       |                   |                  | 61 |
|                       |                   |                  | 69 |
|                       |                   |                  | 47 |
|                       |                   |                  | 45 |
|                       | Coughing OR Wheeze |                  | 159 |
|                       |                   |                  | 113 |
|                       |                   |                  | 86 |
|                       |                   |                  | 73 |
|                       |                   |                  | 48 |
|                       |                   |                  | 45 |
| **Partially Controlled Asthma**  |                  |           |                  |
| (State: ASTHMA_PAR_CON) |                  |           |                  |
| Has wheezing and cough once a week, which causes some difficulty with daily activities. | Coughing AND Wheeze | most days a week | 0  |
|                       |                   | OR several days a week | 2  |
|                       |                   | AND some difficulty daily activities | 0  |
|                       | Coughing without Wheeze |                  | 11 |
|                       |                   |                  | 16 |
|                       |                   |                  | 7  |
|                       |                   |                  | 7  |
|                       |                   |                  | 2  |
|                       |                   |                  | 2  |
|                       | Coughing OR Wheeze |                  | 15 |
|                       |                   |                  | 16 |
|                       |                   |                  | 7  |
|                       |                   |                  | 7  |
|                       |                   |                  | 2  |
|                       |                   |                  | 2  |
| **Uncontrolled Asthma**  |                  |           |                  |
| (State: ASTHMA_UNCON)  |                  |           |                  |
| Has wheezing, cough and shortness of breath [SOB] more than twice a week, which causes difficulty with daily activities and sometimes wakes the person at night. | Coughing AND Wheeze AND SOB | most days a week | 0  |
|                       | (Coughing AND Wheeze) without SOB |                  | 0  |
|                       | (Coughing OR Wheeze) AND SOB |                  | 3  |
|                       | (Coughing OR Wheeze) without SOB |                  | 2  |
|                       | (Coughing AND SOB) without Wheeze |                  | 11 |
|                       | (Coughing OR SOB) without Wheeze |                  | 3  |
|                       | (Coughing OR SOB) AND Wheeze |                  | 9  |
|                       | Cough or Wheeze or SOB |                  | 0  |
|                       |                  |                  | 2  |
|                       |                  |                  | 0  |
|                       |                  |                  | 0  |

Shaded cells show the stringent coding requirements used in our analyses, clearly leading to conservative estimates. The frequency requirements applied to coding/wheezing/SOB, and 'additional coding' details requirements of all.
Male and female participants were separately ranked by their improvement in SGRQ total score. While 50% of both men and women improved by 5 or more points, this 50% of highest improving men all saw larger improvements than the 50% of most improved women.

**Figure F5**

**Improvement in SGRQ between Baseline and 3 years split by gender**

|               | EQ-5D-3L anxiety = 1 | EQ-5D-3L anxiety = 2 or 3 | Total | Sensitivity | Specificity |
|---------------|----------------------|---------------------------|-------|-------------|-------------|
| **Baseline**  | some_anxiety == 0    | 244                       | 100   | 344         |             |
|               | some_anxiety == 1    | 38                        | 21    | 59          |             |
|               | **Total**            | **282**                   | **121** | **403**     |             |
| **6-month**   | some_anxiety == 0    | 264                       | 94    | 358         |             |
|               | some_anxiety == 1    | 3                         | 14    | 17          |             |
|               | **Total**            | **267**                   | **108** | **375**     |             |
| **12-month**  | some_anxiety == 0    | 286                       | 59    | 345         |             |
|               | some_anxiety == 1    | 14                        | 7     | 21          |             |
|               | **Total**            | **300**                   | **66**  | **366**     |             |

**Table F6: Cross checking the derived variable for anxiety against EQ-5D-3L responses in first three timepoints**

- some_anxiety = 1 if any of the following questions answered as ‘yes’:
  - I get nervous when I struggle breathing
  - I feel that I am not in control of my chest problem
  - Physical exercises can’t do me any good
  - I have no hope that my chest will get better

Note: it would not be expected for this variable to be entirely ‘sensitive’ when using the EQ-5D-3L responses as this question asks about ‘anxiety and depression’, whereas our derived variable was aiming to capture ‘anxiety’ only.
Table F7: Validation of derived variable for Interference with Activities against EQ-5D-3L responses T₀-T₁₂

|                | EQ-5D-3L usual activities = 1 | EQ-5D-3L usual activities = 2 or 3 | Total | Sensitivity | Specificity |
|----------------|-------------------------------|-------------------------------------|-------|-------------|-------------|
| **Baseline**   | Interference with Activities == 0 | 111                                 | 4     | 115         |             |
|                | Interference with Activities == 1 | 228                                 | 60    | 288         | 94%         | 33%         |
| **Total**      |                                | 339                                 | 64    | 403         |             |
| **6-month**    | Interference with Activities == 0 | 211                                 | 4     | 215         |             |
|                | Interference with Activities == 1 | 127                                 | 33    | 160         | 89%         | 62%         |
| **Total**      |                                | 338                                 | 37    | 375         |             |
| **12-month**   | Interference with Activities == 0 | 231                                 | 5     | 236         |             |
|                | Interference with Activities == 1 | 105                                 | 25    | 130         | 83%         | 69%         |
| **Total**      |                                | 336                                 | 30    | 366         |             |

*‘Interference with Activities’ = 1 if at least two of the following are met:*
  - I get short of breath sitting down or laying down
  - I get short of breath getting washed or dressed
  - I get short of breath walking around in the house
  - I get short of breath walking around outside
  - I get short of breath walking up stairs
  - I get short of breath walking up hills
  - I get short of breath playing sports
  - My cough makes me tired
  - My cough or breathing is embarrassing in public
  - My chest trouble is a nuisance to my family, friends, or neighbours
  - My chest condition is the most important problem I have, causes me lots of problems, or causes me a few problems
  - My chest stops me doing one or two things I would like to do, most of the things I would like to do, or everything I would like to do
  - My chest trouble made me stop work altogether, my chest trouble interferes with my work or made me change my work