TB mortality estimates for the End TB Strategy 2025 milestone and 2030 target assessment: data sources, analytical methods and process

Background document 2,
for meeting of
WHO Global Task Force on
TB Impact Measurement,
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Final version (23 September 2024) used to inform meeting discussions

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Questions to inform review & discussion

1. **Section 3** of this document sets out **five new or updated options** that could be used in the production of TB mortality estimates, along with the categories of country to which they are relevant.

   a) Expanded efforts by WHO to compile and use more recent data from national or sample vital registration (VR) systems

   Do you think this option should be implemented?

   Yes/No

   b) Updated literature review(s) to inform estimates of case fatality ratios for people with TB (treated for TB vs not treated for TB, disaggregated by HIV status and, for people living with HIV, ART status)

   How would you categorize an updated literature review of CFRs?

   Essential/Desirable but not essential/Not required

   c) Updated estimates for mortality hazards, for use in countries with model-based estimates

   Do you think updated estimates for mortality hazards should be used for model-based estimates?

   Yes, as described/Possibly suitable for use, but requires further work first (e.g. more scrutiny/analytical work/refinement)/No)

   d) New mortality studies that include data on TB

   How would you categorize new mortality studies that include data on TB?

   Essential/Desirable but not essential, may be feasible in a few countries only/Not required

   e) Wider and/or less restrictive use of available VR data on causes of death

   Do you think this option merits further exploration?

   Yes/No/Not sure

   Please give reasons for your answers.

2. Do you think there are any other options (new or updated) that should be considered?

3. Do you have any other comments or suggestions related to the production of TB mortality estimates required for the 2025 milestone and 2030 target assessment?

Contents

Introduction

A core function of the World Health Organization (WHO) is monitoring and reporting on the health situation and health trends. This is done in the context of global strategies and targets endorsed by Member States. In the period 2015–2030, there is particular attention to assessment of progress towards the health targets included in the United Nations (UN) Sustainable Development Goals (SDGs) *(1, 2)*, as well as other targets that are part of global strategies adopted by all WHO Member States in World Health Assembly (WHA) resolutions, WHO's General Programme of Work (GPW) and UN political declarations related to health.

For tuberculosis (TB), work on monitoring and reporting is led by WHO's Global TB Programme (GTB). This is done in the context of the SDGs (2016–2030), which include a target to end the global TB epidemic by 2030; the WHO End TB Strategy (2016–2035); and commitments made in political declarations at the first (in 2018) and second (in 2023) UN high-level meetings on TB *(1, 3-5)*. Each year, GTB implements an annual round of data collection from 215 countries and areas; the main findings and messages, as well as detailed data and disease burden estimates for all countries and areas, are published in WHO's annual Global TB Report *(6, 7)*.

The Global TB Report includes estimates of TB incidence and mortality at global, regional and country level, up to the latest complete calendar year. For the 2023 edition, the start year of the time series was changed to 2010 (from 2000), to give greater emphasis to the period for which milestones (for 2020 and 2025) and targets (for 2030 and 2035) have been set in the WHO End TB Strategy (**Table 1**) and the period covered by the SDGs. Particular attention was given to the status of progress towards the 2025 milestones. Within the SDG framework, the indicator for the target of ending the global TB epidemic is TB incidence per 100 000 population per year.[1]

Table 1 The WHO End TB Strategy milestones and targets

Indicator	Milestones		Targets	
	2020	2025	2030	2035
Reduction in annual number of TB deaths (compared with baseline of 2015)	35%	75%	90%	95%
Reduction in TB incidence rate (compared with baseline of 2015)	20%	50%	80%	90%
Percentage of TB patients and their households facing catastrophic costs due to TB disease	0%	0%	0%	0%

Since 2006, estimates of TB disease burden published in WHO global TB reports have been produced using data sources and analytical methods that are periodically reviewed by the WHO Global Task Force on TB Impact Measurement (hereafter, the Task Force) *(8, 9)*.

The Task Force was established in 2006, convened by GTB's TB monitoring, evaluation and strategic information (TME). Its initial purpose was to ensure a robust, rigorous and consensus-based assessment of whether 2015 targets for reductions in TB disease burden set in the UN Millennium Development Goals (MDGs, 2000–2015) and WHO Stop TB Strategy (2006–2015) were achieved at global, regional and country levels.[2] Its current purpose is to ensure robust, rigorous and consensus-based assessment of progress towards the milestones and targets for reductions in TB disease burden set in the WHO End TB Strategy (**Table 1**) and UN SDGs and, ultimately, assessment of whether or not these are achieved.[3]

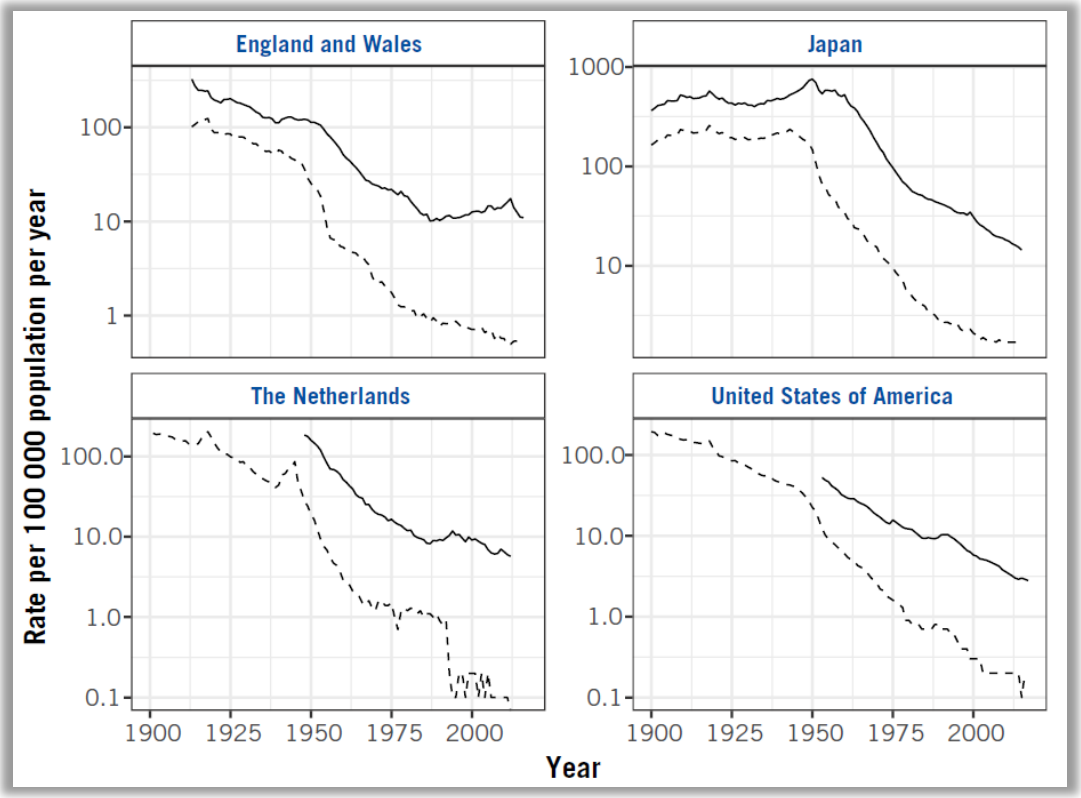
[1] This is part of SDG Target 3.3.
[2] The indicators for which targets were set were TB incidence, prevalence and mortality.
[3] The Task Force also aims to guide, promote and support analysis and use of TB surveillance and survey data for policy, planning and programmatic action.

To fulfil this purpose, the Task Force currently has four major strategic areas of work *(8)*. These are:

- Strengthening surveillance. This includes strengthening of national disease notification systems, for direct measurement of TB incidence; and strengthening of national vital registration (VR) systems that include coding of causes of death based on international standards,[4] for direct measurement of the number of deaths caused by TB.
- Priority studies to periodically measure TB disease burden. These include national TB prevalence surveys, national surveys of drug resistance among TB patients, national surveys of costs faced by TB patients and their households, and mortality surveys.
- Periodic review of methods used by WHO to produce estimates of the burden of TB disease.
- Analysis and use of TB surveillance and survey data.

The first two strategic areas of work focus on direct measurement of TB disease burden (epidemiological and, in the case of cost surveys, economic). The underlying principle for the Task Force's work since 2006 has been that estimates of the level of and trends in disease burden should be based on direct measurements from routine national surveillance systems and surveys as much as possible. The ultimate goal is that in all countries, TB incidence and mortality can be reliably tracked using surveillance data from national disease notification and VR systems (**Fig. 1**).

Fig. 1 Trends in TB incidence (solid line) and TB mortality (dashed line) based on data from national notification and national VR systems, four countries with reliable data over a lengthy time period



VR: vital registration.
Sources: Public Health England (2017) *(10)*, The Research Institute of Tuberculosis/JATA (2018) *(11)*, National Institute for Public Health and the Environment, Ministry of Health, Welfare and Sport (2016) *(12)* and Centers for Disease Control and Prevention *(13)*.

The first comprehensive reviews of methods used by WHO to produce estimates of TB disease burden under the umbrella of the Task Force were completed in 2006 (at the first Task Force meeting) and in 2008–2009. The methods used to produce WHO's assessment of whether the 2015 targets (for incidence, prevalence and mortality) were achieved (published in the 2015 WHO Global TB Report) followed a thorough review at a Task Force meeting held in March 2015 *(14)*. During the period of the

[4] i.e. based on the International Classification of Diseases (ICD).

End TB Strategy, methods used to produce estimates of TB incidence and mortality have been discussed at Task Force meetings held in 2016, 2018 and 2022 *(15-17)*. The meeting in 2022 focused on methods for estimating TB incidence and mortality during the COVID-19 pandemic.[5]

The 2030 targets of the End TB Strategy and SDGs are only six years away, and an assessment of the status of progress with respect to the 2025 milestones of the End TB Strategy will be required in 2026. In this context, and post-pandemic, a thorough review of the data sources, analytical methods and process to be used by WHO to produce estimates of TB incidence and mortality for the periods 2015–2025 and 2015–2030 is needed.[6]

This background document provides the basis for the required review of the data sources, analytical methods and process to be used for estimates of TB mortality. It has five major sections:

1. **Current data sources, analytical methods and process – an overview.** This provides a short description of the two major approaches that are used to produce estimates of the number of deaths caused by TB, and the processes used for country review of and input to these estimates in advance of their publication. The dynamic models used for a subset of countries for the specific period of the COVID-19 pandemic and its aftermath are also described.
2. **Current data sources and analytical methods: strengths, limitations, country concerns.** This summarizes the main strengths and limitations of the current data sources and analytical methods as well as the main current or recent concerns about estimates of TB mortality that have been expressed to WHO by countries.
3. **New or updated options that could be considered.** Five new or updated options that could enhance or replace current data sources and analytical methods are discussed. These are: expanded efforts to compile and use more recent data from national or sample vital registration (VR) systems; updated literature review(s) to inform estimates of case fatality ratios (CFRs); updated estimates for mortality hazards, for use in countries with model-based estimates; new mortality studies that include data on TB; and wider and/or less restrictive use of available VR data on causes of death.
4. **2025 milestone and 2030 target assessment – an initial mapping of options**. Suggestions for the options that could be used are provided. Particular attention is given to an initial mapping of options for the 30 high TB burden countries and 3 global TB watchlist countries that account for about 85% of the global number of TB deaths each year. Options for other countries are discussed with reference to major country groupings.
5. **Process for finalization and implementation of options**. This is discussed for two time periods: May–September 2024; and the period after the Task Force meeting to be held 25–27 September 2024.

Five questions for an initial round of feedback are listed on the inner cover page. Following feedback, the document will be updated. At least one round of feedback is envisaged in advance of the Task Force meeting scheduled for 25–27 September 2024.

[5] New methods to produce time series of estimates of the incidence of drug-resistant TB were also discussed.

[6] For assessment of the status of progress towards the target that no TB patients and their households face catastrophic costs as a result of TB disease, national facility-based surveys are recommended. In 2023, results from national surveys were used to produce model-based estimates for other low and middle-income countries. WHO guidance on national TB patient cost surveys is being updated in 2024, based on experience from surveys implemented between 2015 and 2023, but these updates are relatively light.

1. Current data sources, analytical methods and process: an overview

Following the first Task Force review of data sources and analytical methods used by WHO to produce estimates of TB disease burden in 2008–2009 and up to the COVID-19 pandemic, two main approaches were used to produce time series of TB mortality estimates[7] for publication in the annual WHO Global TB Report (**Fig. 2**).[8] These were:

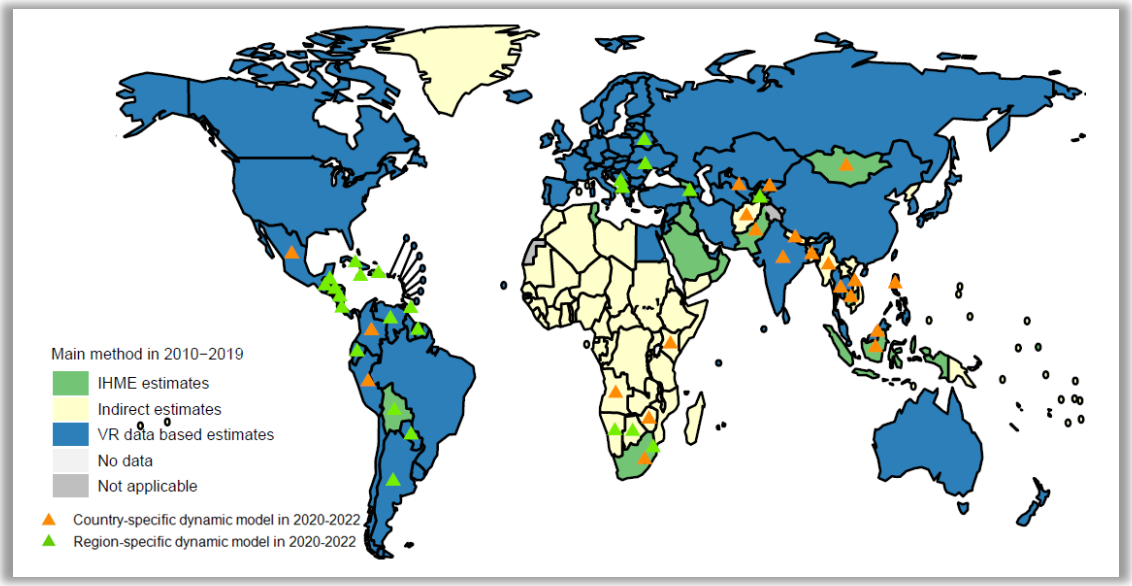
- **Method 1:** use of cause-of death data from national or sample VR systems officially reported to WHO, with adjustments to account for incomplete coverage (i.e. deaths for which no cause was documented) and ill-defined causes of death (in the International Classification of Diseases (ICD), code B46 in ICD-9 and codes R00–R99 in ICD-10);
- **Method 2:** estimation of the number of TB deaths based on the product of estimates of TB incidence and CFRs derived from literature reviews, with CFRs estimated separately according to TB treatment status (yes, no) and, for people with HIV, HIV treatment status (on antiretroviral treatment (ART) yes or no, and the duration of ART).

In addition, for some countries, estimates produced by the Institute for Health Metrics and Evaluation (IHME) were used. This was done when IHME estimates were known to be based on access to a wider range of VR and mortality survey data, compared with those available to WHO.

In line with ICD-10, estimates of TB mortality published by WHO make a clear distinction between deaths among HIV-negative people (officially classified as deaths caused by TB) and deaths among people with HIV (officially classified as deaths caused by HIV/AIDS, with TB as a contributory cause).

During the COVID-19 pandemic, there were 50 countries in which TB case notification data suggested considerable disruption to TB diagnostic and treatment services in 2020, 2021 or both years. For estimates of the number of TB deaths in the 3 years 2020–2022, country or region-specific dynamic models were used for 46 of these countries[9] (indicated by symbols in **Fig. 2**), calibrated to previously-published estimates for 2019. For one of these 46 countries (India), the country-specific dynamic model was also used in combination with data from a national TB prevalence survey and case notification data to produce estimates for the pre-COVID period (specifically, 2010–2019).

Fig. 2 Main data sources and analytical methods used to produce the estimates of TB mortality that were published in the Global TB report 2023, which covered the period 2010–2022



[7] Published time series have covered the period between a baseline year (initially 1990 for the period of the MDGs and Stop TB Strategy, most recently reset to 2010) and the most recent complete calendar year.
[8] As explained in the Introduction, methods were rereviewed in 2015, 2016, 2018 and 2022; the most substantive reviews of estimates of TB mortality were in 2015 and 2022.
[9] The exceptions were Azerbaijan, Brazil, Kazakhstan, and Ukraine. Up-to-date cause-of-death data were used instead of model-based estimates.

The methods adhere to global guidelines (GATHER) used by WHO for accurate and transparent reporting of health estimates *(18)*.

Table 2 provides a summary of the number of countries for which different combinations of methods were used, distinguishing between the time periods of 2010–2019 and 2020–2022.

Table 2 Comparison of the methods used in 2010–2019 and in 2020–2022 to estimate TB mortality

Methods used in 2010–2019	Methods used in 2020–2022					
	VR data with no available VR data for 2020–2022	Available VR data for 2020–2022	CFR-based	Country-specific model	Region-specific model	Total
VR data	68	9	2	9	18	106
IHME	8	1	0	4	3	16
CFR-based	0	0	81	9	3	93
Total	76	10	83	22	24	215

The rest of this section provides a short description of the data sources and analytical methods that were used to produce the estimates of TB mortality that were published in the Global TB Report 2023, as shown in **Fig. 2** *(6, 19)*, and of the processes commonly used by WHO to discuss and review estimates with Member States, prior to their publication. Details are available in a technical appendix *(20)*.

1.1 National or sample vital registration data officially reported to WHO by Member States

For the 10 years 2010–2019, national or sample VR data officially reported to WHO by Member States were the main data source used to inform TB mortality estimates for 121 countries (**Fig. 2**, blue). For India, officially published data from the sample registration system (SRS) were used *(6)*; detailed data from the SRS have not been officially reported to WHO. These 122 countries accounted for 60% of estimated global number of TB deaths in 2019.

VR data officially reported to WHO were only used if VR data quality was assessed as medium or high (as classified by the WHO data and analytics department) *(21)*.

National or sample VR data were also used for the three years 2020–2022 for 86 countries (**Table 2**):

- 82 countries in which no major disruptions to the provision of and access to TB diagnostic and treatment services were observed (based on TB case notification data) during the COVID-19 pandemic and its aftermath; and
- Four countries in which major disruptions were observed, but up-to-date VR data were available for the period 2020–2022 (Azerbaijan, Brazil, Kazakhstan and Ukraine).

1.2 Incidence estimates combined with CFR estimates

For 93 countries in the period 2010–2019 and in 83 countries in the period 2020–2022 (**Fig. 2**, yellow; **Table 2**), TB mortality among HIV-negative people was estimated as the product of incidence and literature-derived CFR estimates, with incidence and CFRs estimated separately according to TB treatment status (treated or untreated).

The incidence combined with CFR method was also used for all countries and all years (2010–2022) to estimate TB mortality among people with HIV. CFR estimates accounted for TB treatment (started or not started), ART (started or not started) and the duration of ART (< 1 year or ≥ 1 year).

The CFR estimates that were used (for both people with and without HIV) are shown in **Table 3**.

Table 3 Estimated CFRs for people with TB, disaggregated by TB treatment status, HIV status and HIV treatment status *(22, 23)*

HIV status	Category	CFR
HIV-negative	Not on TB treatment	0.43 (0.28–0.53)
HIV-negative	On TB treatment	0.03 (0–0.07)
People living with HIV	Not on TB treatment and not on ART	0.78 (0.65–0.94)
People living with HIV	On TB treatment and not ART	0.09 (0.03–0.15)
People living with HIV	Not on TB treatment and on ART <1 year	0.62 (0.39–0.86)
People living with HIV	On TB treatment and on ART <1 year	0.06 (0.01–0.13)
People living with HIV	Not on TB treatment and on ART ≥1 year	0.49 (0.31–0.70)
People living with HIV	On TB treatment and on ART ≥1 year	0.04 (0.00–0.10)

1.3 IHME estimates

For 16 countries,[10] estimates published by IHME were used, without any additional adjustments (**Fig. 2**, green). The 16 countries accounted for 16% of the estimated global number of TB deaths in 2019.

1.4 Country or region-specific dynamic models during COVID related disruptions and their aftermath (2020–2022)

Country-specific dynamic models were used to produce TB mortality estimates for the period 2020–2022 for 22 countries and region-specific models were used for 24 countries (Table 1, **Fig. 2**, **orange** and **green** triangles).

Models were used for countries in which TB case notification data suggested substantial disruptions to TB diagnostic and treatment services during the COVID-19 pandemic (>10% reduction in TB notifications in 2020 as compared with 2019). The 46 countries for which model-based estimates were produced accounted for 95% of the global reduction in TB notifications in 2020 (vs 2019). The 22 countries for which country-specific models were used accounted for 62% of the estimated global number of TB deaths in 2022 and the 24 countries for which region-specific models were used accounted for 1%.

The basic model framework is illustrated in **Fig. 3**. The modelling of disruptions associated with the COVID-19 pandemic focused on delays to diagnosis and treatment initiation. For data on the intensity and duration of disruptions, monthly national notification data (or quarterly if monthly data were not available) reported to WHO were used. It was assumed that reductions in notifications in 2020 and 2021, compared with an extrapolation of pre-2020 trends, were due to delays to diagnosis and treatment initiation, rather than shortfalls in reporting.

Countries were divided into two different categories, each with a dedicated model structure:

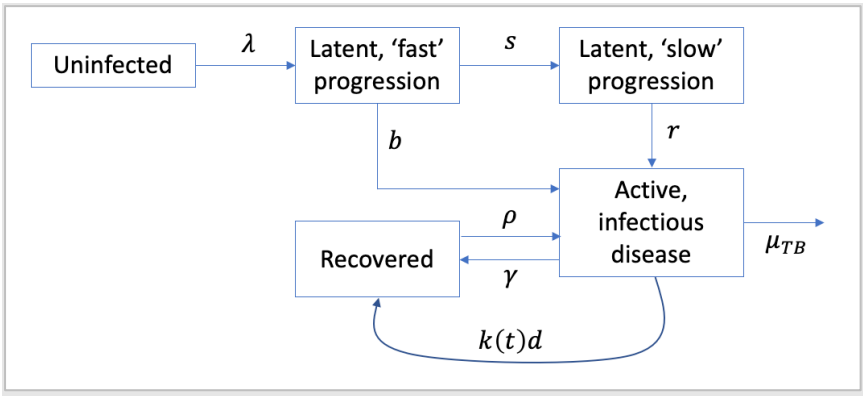
- countries where the private sector plays a strong role in the management of TB (countries belonging to the WHO PPM priority list, as well as countries from the WHO South-East Asia region having private sectors that are not part of this list); and
- countries with a high rate of HIV/TB coinfection (at least 10% of TB incidence, in 2019).

In some countries, to reconcile notification data with evidence provided by their national TB programmes (NTPs) that services had in fact returned to pre-pandemic levels in 2022, some of the

[10] These countries are Bolivia, Georgia, Honduras, Haiti, Indonesia, Iraq, Cambodia, Kiribati, Mongolia, Oman, Pakistan, Qatar, Saudi Arabia, Tajikistan, Tunisia and South Africa.

reduction in notifications was attributed to underreporting, rather than underdiagnosis. The extent of underreporting was determined such that model-inferred disruptions to TB services returned to zero by the end of 2022 and ranged from 10–20% for the countries for which this adjustment was applied.

Fig. 3 A Schematic illustration of the basic model structure



Rates shown in the diagram are as follows:
$\boldsymbol{\lambda}$, time-dependent force of infection;
$\boldsymbol{s}$, per-capita transition rate from latent, fast to latent, slow;
$\boldsymbol{b}$, per-capita hazard of breakdown to active disease in the first 2 years after infection;
$\boldsymbol{r}$, per-capita rate of reactivation thereafter;
$\boldsymbol{\gamma}$, per-capita rate of self-cure;
$\boldsymbol{\mu_{TB}}$, per-capita hazard of TB mortality;
$\boldsymbol{\rho}$, per-capita rate of relapse;
$\boldsymbol{d}$, per-capita rate of diagnosis and treatment initiation;
$\boldsymbol{k(t)}$, time-dependent reduction in diagnosis and treatment initiation due to disruptions.

1.5 Processes for discussion and review of estimates with WHO Member States

Every year, as part of the process for producing the WHO global TB report, country profiles are circulated to all 215 countries and areas (including all 194 WHO Member States) for review and feedback. These profiles are based on the data routinely reported to WHO in annual cycles of global TB data collection (e.g. notifications, treatment enrolment, treatment outcomes, diagnostic testing, financing, TB preventive treatment) as well as estimates of TB disease burden. Countries are requested to review their profiles and to provide feedback in case of any questions or concerns. At this stage, particular attention is given to the review of TB disease burden estimates. If there are questions or concerns, these are addressed (and usually resolved) through further written communications or online discussions.

In addition to this routine process for all countries, other processes are also used for more in-depth discussion and review of TB disease burden estimates. These include:

- **in-country workshops or missions** jointly organized by WHO and national counterparts. These are often held when results from a major new study become available to inform disease burden estimates (e.g. from a national TB prevalence survey or an inventory study). Sometimes, they are also organized in response to a specific request for a review, usually when there are concerns that it is difficult to resolve remotely.
- **multi-country workshops** convened by WHO to review and discuss TB disease burden estimates, and to update them if appropriate.
- **online bilateral discussions**. There has been growing use of such discussions since 2022. Particular attention has been given to countries for which additional inputs were needed to inform estimates in the context of COVID-related disruptions and recovery. Extensive online discussions were also held with India in 2022 and 2023, for joint review and discussion of methods for estimating TB disease burden, with particular attention to use of results from the 2019–2021 national TB prevalence survey as well as recently published cause-of-death data from the country's SRS.

2. Current data sources and analytical methods: strengths, limitations, country concerns

This section highlights the main strengths and limitations of the current methods as well as emerging issues identified by WHO. It also summarizes the main current or recent concerns about TB mortality estimates that have been expressed to WHO by countries.

2.1 Strengths and limitations

The main strengths and limitations of the current methods are described in **Table 4**.

Table 4 Current data sources and analytical methods – main strengths and limitations

Data source and analytical method	Strengths	Limitations
National or sample VR data	►Provide reliable direct measurement of the number of deaths caused by TB, if systems have high quality and coverage. ►Available for a large number of countries (124) that collectively account for about 60% of the estimated annual number of deaths from TB, globally.	►Data of sufficient quality and coverage not available for all countries, including most of the 30 high TB burden countries; no data for some countries, especially in the African Region. ►Data officially reported to WHO may not be available for all years, especially the most recent years. For this reason, staff in the WHO Regional Office for Europe requested that GTB include a request for recent VR data each year, as part of the annual round of global TB data collection from Member States that is managed by GTB. ►Number of available data points limited for some countries. ►For deaths with ill-defined causes, it is assumed that the proportion of deaths attributable to TB is the same as the observed proportion in recorded TB deaths.
Estimates of TB incidence combined with CFR estimates	►Provides a method for producing estimates in the absence of reliable national or sample VR data.	►CFR estimates are based on literature reviews dating from 2011 and 2012; these may require review/updating. CFRs stratified by treatment status (yes, no) are currently based on notification status (yes, no) and are the same for all countries. This assumes that treatment equates to notification and non-notification equates to untreated, even though some people who are notified may not be treated and some people who are not notified are nonetheless treated. It also does not account for country-specific differences in, for example, TB survival amongst those who are undiagnosed and untreated. ►Depend on estimates of TB incidence, which have their own limitations and associated uncertainty.
IHME based estimates	►Have access to more data than WHO ►Algorithm used for the reclassification of ill-defined cause of death	►Challenging to explain and reproduce *(24)*
Country or region-specific dynamic model combined with monthly or quarterly notification data (2020–2022 only)	►Allowed production of estimates that accounted for COVID-related disruptions to TB services, calibrated to pre-2020 WHO estimates. ►Extensively reviewed in 2021 and 2022.	►Assumption reductions in notifications reflected real reductions in TB diagnosis and treatment initiation, at least in 2020 and 2021. ►Uncertainty about key parameters e.g. reduction in TB transmission during lockdowns. ►Pandemic impact on broader TB determinants (e.g. undernutrition, poverty) not accounted for. ►Models may accumulate error with each year they are used, unless corrected/calibrated based on new direct measurements of TB disease burden.

In addition to the limitations identified in **Table 4**, there is also an emerging issue that requires attention. In a few countries (including high TB burden countries), case notifications are increasingly converging on the best estimates of TB incidence. If the number of deaths caused by TB is estimated as the product of incidence estimates and CFRs for the estimated proportion of cases that are treated and untreated, this convergence results in estimates of the number of TB deaths falling rapidly, which may not be plausible (the data also raise questions about whether increases in case notifications could in part be due to overdiagnosis or whether incidence estimates require review). The main examples are Uganda, Lao People's Democratic Republic and Zambia.

2.2 Country concerns

The main current or recent concerns about TB mortality estimates that countries have raised with WHO are shown in **Table 5**. The countries that have expressed each concern are listed.

Overall, there are fewer country concerns about TB mortality estimates, compared with TB incidence estimates (see accompanying background document 1).

Table 5 Current or recent concerns about TB mortality estimates raised with WHO by countries

Concern	Short description	Country examples	Comments
Estimates during period of COVID-19 pandemic and its aftermath too high	►This concern has been raised by some of the countries for which a country or region-specific dynamic model was used to produce estimates for 2020–2022.	Azerbaijan Brazil Georgia Kazakhstan Ukraine Cambodia, Indonesia, Philippines, Viet Nam	►For four of the listed countries, national VR data were provided to WHO and used in replacement of model-based estimates (the exception is Georgia). ►Briefings/webinars were held to discuss methods and data, in advance of publication of 2023 global TB report. ►Discussion of additional data that could be used under discussion with Philippines.
National VR data not of sufficient quality	►A few NTPs have expressed concern that the VR data being used by WHO are not of sufficient quality, and that the data from the NTP are more reliable because the NTP can diagnose TB, including post-mortem. In these instances, the number of deaths in NTP databases are higher than those in the national VR system.	Kyrgyzstan, Tajikistan	►WHO mission to Tajikistan in March 2024 included discussion of this issue; follow-up work is being done.
Estimates too high (pre and during COVID-19 pandemic)	►Estimates based on the indirect approach of using incidence estimates and CFR estimates can be considered to be too high. ►This can sometimes apply to VR-based estimates as well.	Ghana India	►Updates to mortality estimates require review of either incidence estimates (see accompanying background document) or the literature-based CFRs that are currently used. ►Mortality estimates for India were extensively reviewed in 2023. Updated estimates (with downward revisions for each year 2010-2022) were published in the Global TB Report 2023, based on new cause-of-death data from the country's SRS for the period 2013-2019 published between May 2022 and April 2023.

In addition to the concerns shown in **Table 5**, a question that is sometimes raised by NTPs is why the data on TB deaths from routinely reported TB patient cohort data are not used for TB mortality estimates. The reason why these data are not suitable then requires explanation.

3. New or updated options that could be considered

3.1 Expanded efforts by WHO to compile and use more recent data from national or sample VR systems

Cause-of-death data from national VR systems are officially reported by Member States to WHO. Within WHO, the process of data reporting, review, storage and use is managed by the Department of Data and Analytics (DNA). Every year, the WHO Global Tuberculosis Programme (GTB) obtains the latest cause-of-death dataset from DNA, for use in production of TB mortality estimates.

There can be delays in the reporting of national VR data, resulting in missed opportunities to use the most recent data for estimation of TB mortality in HIV-negative people. This means that trends in TB mortality in the period 2010–2022 sometimes rely on data for only a subset of years; in particular, data for the most recent years may be missing.

Some efforts have already been made by GTB to obtain data for more recent years, as part of the annual cycle of global TB data collection. These have focused primarily (although not exclusively) on countries that have expressed concerns about their TB mortality estimates. Expansion of these efforts to all countries could help to ensure that TB mortality estimates for a larger number of countries are informed by the most recent data.

If countries report data from their VR systems that have either not yet been evaluated against WHO's quality and coverage criteria, or the most recent evaluation is out of date, it will be necessary to discuss with WHO DNA about the appropriateness of using these data.

3.2 Updated literature review(s) to inform estimates of case fatality ratios

For the countries for which it is not possible to use cause-of-death data from national or sample VR systems, the CFRs that are used for estimation of TB mortality (**Table 3**) are based on two literature reviews conducted in 2011 and 2012.

Updating of these literature reviews could be helpful. For example, depending on the amount of new data available, it might be possible to stratify CFRs by WHO region (or other regional groupings). It might also be possible to make some adjustments to the estimated CFRs for notified and non-notified cases, to better account for underreporting (for example, in countries where a large share of people with TB are diagnosed and treated in the private sector).

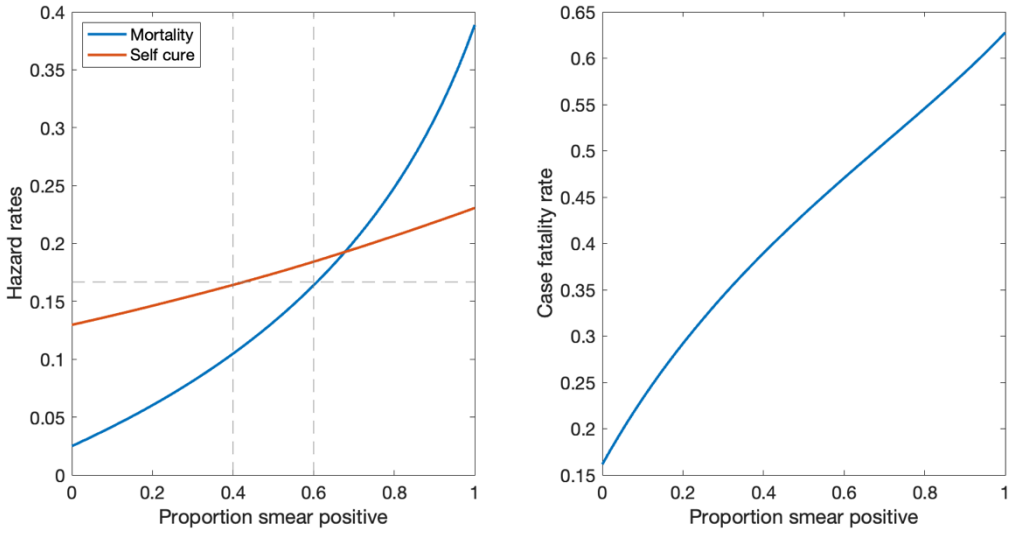
3.3 Updated estimates for mortality hazards, for use in countries with model-based estimates

For countries for which a country or region-specific model has been used to estimate the impact of COVID-related disruptions on TB incidence and mortality, two important parameters are the hazard rate of mortality, and of spontaneous cure, for HIV-negative people with untreated TB. Prior values for these parameters were drawn from a literature review in 2011, which synthesized survival data from the pre-chemotherapy era to estimate CFRs and durations of untreated TB, stratified by smear-negative and smear-positive status *(22)*. Based on the assumption that half of cases are smear positive, it was estimated that, overall, untreated TB (combining both smear positive and smear negative cases) has an average duration of three years, and a CFR close to 50%.

A more recent analysis revisited the same data to update these estimates, using a cohort model structure very similar to that used in the modelled burden estimates *(25)*. This study also stratified estimates by smear-positive and smear-negative status. However, for use in the modelled burden estimates, it is necessary to take a population average of these rates, depending on the proportion of people with TB who are smear positive at the point of diagnosis. Such data are not typically available in the routine programmatic data reported to WHO annually, that informs the burden estimates. Thus, as for the currently-used estimate, it is necessary to make assumptions about this proportion.

Fig. 4 illustrates the overall hazard rates of mortality and self-cure that would arise, under a range of scenarios for the proportion of people with smear-positive TB. The horizontal dashed line shows the prior estimates for both parameters, that have been employed in burden modelling so far: this figure illustrates that the updated estimates would tend to increase the self-cure hazard, and decrease the mortality hazard. Overall, therefore, we would expect a *decrease* in the CFR. In turn, when modelling the impact of COVID-related disruptions, this decrease would tend to mitigate the estimated increases in TB mortality that arise from these disruptions.

Fig. 4 Implications of recent re-estimations for case fatality rates, for modelled hazards of mortality and self-cure. The left-hand panel shows the estimated average hazard rates of mortality (in blue) and self-cure (in red), under a range of scenarios for the proportion of TB being smear-positive**.** This analysis draws from hazard rates specific to smear-negative and smear-positive TB, as published in recent work *(25)*. Vertical, dashed lines show an interval of +/-10 percentage points around 50% smear positive – a proportion typically assumed in the absence of data – while the horizontal dashed line at 1/6 on the y-axis shows values of mortality and self-cure hazards that would be assumed for overall TB (i.e. combining smear-negative and smear-positive forms), corresponding to a 50% case fatality rate, and an average duration of disease of three years. The right-hand panel shows how the implied case fatality rate would vary with the proportion smear positive.



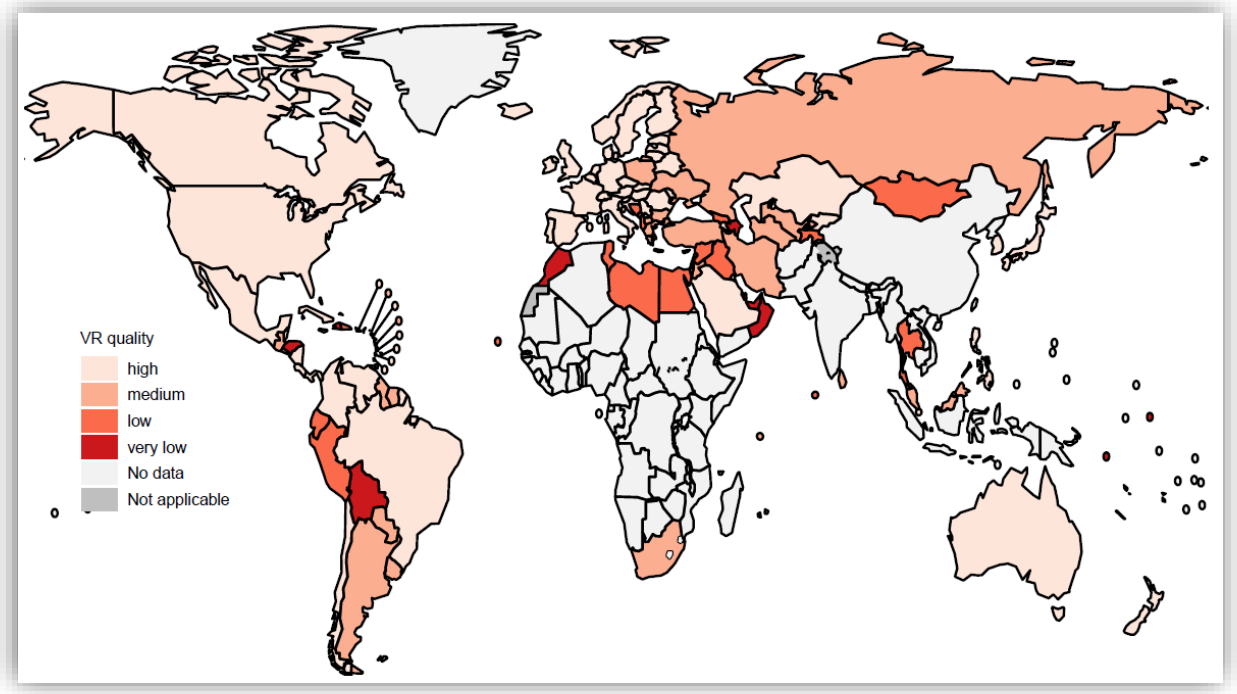
3.4 New mortality studies that include data on TB

The Public Health Foundation of India (PHFI) conducted a mortality survey (using verbal autopsy) in 2023, for the period 2019–2022. This has provided data that enable cross-checking/verification of existing estimates for 2010–2022 that are based on data for 2004–2019 from the country's SRS. Such surveys in other countries would also be helpful to inform or cross-check estimates of TB mortality.

3.5 Wider and/or less restrictive use of available VR data on causes of death

To assess whether the cause-of-death data from national VR systems that are officially reported to WHO can be used for TB mortality estimates, several criteria are used. These include the use of ICD-10 codes, the number of recent years for which data have been reported, and a measure for the overall quality of data *(21)*. **Fig. 5** shows countries categorized according to the overall quality of data.

Fig. 5 Quality of national VR data as assessed by the WHO data and analytics department



Note: VR data for China are reported directly to the WHO Global Tuberculosis Programme. For India, officially published data from the Sample Registration System are used.

The Data Division at WHO quantifies the 'usability' of VR data as a multiplication of completeness (i.e. the percentage of causes of death that are medical certified), and the percentage of deaths not assigned to a garbage code. Currently, VR data are used to directly estimate the number of deaths caused by TB in countries categorized as having data of "high" or "medium" quality (**Fig. 5**).

There are clear justifications for restricting the use of VR data to countries in the high or medium categories. Nonetheless, there may be value in somewhat more flexible approaches, which could accommodate countries that come close to the threshold for the "medium" category. As one illustrative example: for countries close to the threshold of "medium quality", VR data might still be used, but with expanded uncertainty intervals, in an estimation framework that incorporates both incidence and mortality (thus also ensuring consistency between these two outputs). Moreover, the assumed uncertainty intervals could be linked to usability, with wider uncertainty intervals for countries with lower usability.

Decisions would still need to be made about how precisely these uncertainty adjustments would work. It is possible for these relationships to be constructed systematically; for example, by statistical modelling of the error arising from incomplete coverage. However, these approaches would need to be carefully assessed, prior to application. Another limitation is that incomplete VR coverage may also introduce systematic biases in estimates of TB mortality. For example, TB mortality data might only be reported for specific population subgroups, which might not be representative of TB burden at the country level. Each country would need to be evaluated separately, for the risk of such systematic bias.

4. 2025 milestone and 2023 targets assessment – an initial mapping of options

4.1 30 high TB burden countries

Building on the existing options that are used to produce estimates of TB mortality explained in section 1 and the new options discussed in section 3, an initial mapping of options that could be used for the 30 high TB burden countries and three global TB watchlist countries is provided in Table 6. Countries are grouped according to WHO region. The mapping is intended to provide the basis for consultations with countries (see also section 5).

The mapping of options makes a clear distinction between the 2025 milestone assessment (for which estimates between 2015 and 2025 are required) and the 2030 target assessment (for which estimates between 2015 and 2030 are required), since there is more potential for new data generation and use of new analytical methods to inform the 2030 targets assessment. At the same time, as highlighted in the comments in the table, the availability of new data from 2025 onwards could subsequently also allow for refinement of the estimates for the period 2015–2025.

The main options considered in the table are:

- The use of direct measurements through VR data from a well-functioning CRVS (as described in **section 1.1**). This includes pro-active efforts made by GTB to obtain data for more recent years, as part of the annual cycle of global TB data collection (as described in **section 3.1**).
- The use of direct measurements through VR data from a CRVS (as described in **section 1.1**) with less restrictive quality and coverage criteria (as described in **section 3.5**).
- The combined use of incidence estimates with CFR estimates (as described in **section 1.2**). This may also include an updated literature review for estimates of CFRs (as described in **section 3.2**).
- The use of IHME estimates without any further refinement (as described in **section 1.3**).

4.2 Other countries

Beyond the 30 high TB burden countries and three global TB watchlist countries, the initial proposed mapping can be summarized as follows:

- Countries for which the current method relies on the use of direct measurements through VR data from a well-functioning CRVS. Continue to use this approach, based on as complete and up-to-date data as possible.
- Countries for which the current method relies on the use of IHME estimates. Continue this approach, preferably based on review of data sources and assumptions with IHME, or substitute this approach with the use of VR data that are officially reported to WHO and which meet WHO's CRVS quality and coverage criteria.
- Countries for which the current method relies on the combined used of incidence estimates with CFR estimates. Either continue this approach with updated CFR estimates, or substitute this approach with the use of VR data that are officially reported to WHO and which meet WHO's CRVS quality and coverage criteria.

Table 6 Data sources and methods for 2025 milestone and 2030 target assessment: initial mapping of options, 30 high TB burden countries and 3 global TB watchlist countries (organized by WHO region)

The 3 global TB watchlist countries are Cambodia, Russian Federation and Zimbabwe.

CN, case notifications; COD, cause of death; CS, country-specific; CRVS, civil registration and vital statistics; RS, region-specific; VR, vital registration

Country	Current data source(s), analytical method	2025 milestone assessment						2030 target assessment					
		VR data officially reported to WHO from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data reported to WHO, with less restrictive criteria	Other	Comments	VR data officially reported to WHO from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data reported to WHO, with less restrictive criteria	Other	Comments
AFRICAN REGION													
Angola	CFR-based and CS model		∗				CS model still relevant for 2020-2022		∗		?		Limited prospect of usable VR data before 2030*
Central African Republic	CFR-based		∗				Well-functioning CRVS unlikely by 2025		∗		?		Limited prospect of usable VR data before 2030*
Congo	CFR-based		∗				Well-functioning CRVS unlikely by 2025		∗		?		Limited prospect of usable VR data before 2030*
DR Congo	CFR-based		∗				Well-functioning CRVS unlikely by 2025		∗		?		Limited prospect of usable VR data before 2030*
Ethiopia	CFR-based		∗				Well-functioning CRVS unlikely by 2025		∗		?		Limited prospect of usable VR data before 2030*
Gabon	CFR-based		∗				Well-functioning CRVS unlikely by 2025		∗		?		Limited prospect of usable VR data before 2030*

Country	Current data source(s), analytical method	2025 milestone assessment						2030 target assessment					
		VR data officially reported to WHO from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data officially reported to WHO, with less restrictive criteria	Other	Comments	VR data officially reported to WHO from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data officially reported to WHO, with /less restrictive criteria	Other	Comments
AFRICAN REGION (continued)													
Kenya	CFR-based and CS model		⁎				Well-functioning CRVS unlikely by 2025. CS model still relevant for 2020-2022				?		Limited prospect of usable VR data before 2030*
Lesotho	CFR-based and CS model		⁎				Well-functioning CRVS unlikely by 2025. CS model still relevant for 2020-2022				?		Limited prospect of usable VR data before 2030*
Liberia	CFR-based		⁎				Well-functioning CRVS unlikely by 2025.				?		Limited prospect of usable VR data before 2030*
Mozambique	CFR-based		⁎				Well-functioning CRVS unlikely by 2025.				?		Limited prospect of usable VR data before 2030*
Namibia	CFR-based and RS model		⁎				RS model still relevant for 2020-2022				?		Limited prospect of usable VR data before 2030*
Nigeria	CFR-based		⁎				Well-functioning CRVS unlikely by 2025.				?		Limited prospect of usable VR data before 2030*

Country	Current data source(s), analytical method	2025 milestone assessment						2030 target assessment					
		VR data from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data officially reported tow WHO, less restrictive criteria	Other	Comments	VR data from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data officially reported tow WHO, less restrictive criteria	Other	Comments
AFRICAN REGION (continued)													
Sierra Leone	CFR-based		⁎				Well-functioning CRVS unlikely by 2025.				?		Limited prospect of usable VR data before 2030*
South Africa	IHME and VR data			⁎			IHME estimates usually updated every 2 years			⁎			
Uganda	CFR-based		⁎				Well-functioning CRVS unlikely by 2025				?		Limited prospect of usable VR data before 2030*
UR Tanzania	CFR-based		⁎				Well-functioning CRVS unlikely by 2025				?		Limited prospect of usable VR data before 2030*
Zambia	CFR-based		⁎				Well-functioning CRVS unlikely by 2025				?		Limited prospect of usable VR data before 2030*
Zimbabwe	CFR-based and CS model		⁎				Well-functioning CRVS unlikely by 2025. CS model still relevant for 2020-2022				?		Limited prospect of usable VR data before 2030*
REGION OF THE AMERICAS													
Brazil	VR data	⁎						⁎					
EUROPEAN REGION													
Russian Federation	VR data	⁎						⁎					

Country	Current data source(s), analytical method	2025 milestone assessment						2030 target assessment					
		VR data officially reported to WHO from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data officially reported to WHO, less restrictive criteria	Other	Comments	VR data from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data officially reported to WHO, less restrictive criteria	Other	Comments
SOUTH-EAST ASIA REGION													
Bangladesh	CFR-based and CS model		⁎				Well-functioning CRVS unlikely by 2025. CS model still relevant for 2020-2022				?		Limited prospect of usable VR data before 2030*
DPR Korea	CFR-based		⁎				Well-functioning CRVS unlikely by 2025.		⁎		?		Limited prospect of usable VR data before 2030*
India	VR data and CS model					SRS data, CS model	Important that up-to-date SRS data are officially published and thus available for use	⁎					Important that up-to-date SRS data are officially published and thus available for use
Indonesia	IHME and CS model			⁎			CS model still relevant for 2020-2022			⁎	?		Limited prospect of usable VR data before 2030*
Myanmar	CFR-based and CS model		⁎				Well-functioning CRVS unlikely by 2025. CS model still relevant for 2020-2022		⁎		?		Limited prospect of usable VR data before 2030*
Thailand	VR data and CS model	⁎					CS model still relevant for 2020-2022	⁎					

Country	Current data source(s), analytical method	2025 milestone assessment						2030 target assessment					
		VR data officially reported to WHO from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data officially reported to WHO, less restrictive criteria	Other	Comments	VR data from well-functioning CRVS	CFR-based with updated CFRs	IHME estimates	Use of VR data officially reported to WHO, less restrictive criteria	Other	Comments
WESTERN PACIFIC REGION													
Cambodia	IHME and CS model			*			CS model remains relevant for 2020-2022			*	?		Limited prospect of usable VR data before 2030*
China	VR data	*						*					
Mongolia	IHME and CS model			*			CS model remains relevant for 2020-2022			*			Limited prospect of usable VR data before 2030*
Papua New Guinea	CFR-based		*				Well-functioning CRVS unlikely by 2025.				?		Limited prospect of usable VR data before 2030*
Philippines	VR data and CS model	*					CS model remains relevant for 2020-2022	*					
Viet Nam	CFR-based and CS model		*				CS model remains relevant for 2020-2022		*		?		Limited prospect of usable VR data before 2030*

* Source: WHO data division

5. Process for finalization and implementation of options

Based on the current data sources and analytical methods used by WHO to produce TB mortality estimates (**section 1**, **section 2**), possible new options that could either refine or replace them (**section 3**) and the initial mapping of options to use for the 2025 milestone and 2030 targets assessment, both for individual countries or country categories (**section 4**), a clear strategy and plan for the finalization and implementation of options is required.

This section sets out suggested key elements of the process to be used and timelines, first for the period up to the Task Force meeting in September 2024 and then for the period after the Task Force meeting.

5.1 May to September 2024

Key elements of the process include (or have already included):

- **Discussions with countries**. GTB staff (along with colleagues in regional and country offices) have embarked on discussions about the initial mapping of options to be used for the 2025 milestone and 2030 targets assessment (**section 4**) with NTPs, during regional meetings, country missions, multi-country workshops and online bilateral meetings.
- **Circulation of this document to all those attending the September 2024 Task Force meeting**. This will be done in advance of the meeting.
- **September 2024 Task Force meeting**. The new or updated options described in this document will be discussed, and next steps identified (see also the meeting concept note and accompanying agenda).

5.2 October 2024 onwards

Key elements of the process are likely to include (but are not necessarily be limited to):

- **Further work on new or updated options**. This may be required and will be done according to the outcomes of the Task Force meeting.
- **Periodic rounds of country consultations convened by WHO**. These will probably need to be held via a combination of online bilateral discussions, country missions and multi-country workshops, adapted to the regional and country context and needs. A clear planning cycle of consultations, to ensure that in-depth discussions with at least high TB burden countries are convened 2–3 times in the period 2025–2030, may be appropriate.
- **Inputs to wider efforts to strengthen the quantity and quality of cause-of-death data that are available from national or sample VR systems**. The strengthening of national or sample VR systems is part of the broader public health agenda. However, those working on specific diseases can help to advocate for the importance of strengthening these systems, and engage with those efforts when appropriate. In WHO, such efforts are led by the Department for Data and Analytics.
- **Reviews of progress in periodic Task Force meetings, with adjustments to plans as needed.** Task Force meetings that include an overall review of progress will be held approximately every 2 years. These will complement smaller Task Force meetings and workshops on specific topics (online and in-person), to be held more frequently.

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