TB incidence estimates for the Sustainable Development Goal and End TB Strategy 2025 milestone and 2030 targets assessment: data sources, analytical methods and process

Background document 1, for meeting of WHO Global Task Force on TB Impact Measurement, 25–27 September 2024

Final version (23 September 2024) used to inform meeting discussions

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Note: This document refers in several places to "subclinical TB". In mid-October 2024, 2 weeks after the Task Force meeting, WHO convened a consultation on the topic of subclinical TB. In this consultation, it was agreed to replace the term "subclinical TB" with "asymptomatic TB".

Questions to inform review & discussion

1. Section 3 of this document discusses five new options for the production of TB incidence estimates, along with the categories of country to which they could be relevant.

   These are:
   - A new approach to use of national TB prevalence survey data for estimation of incidence, which accounts for the latest literature on the natural history of TB (with particular attention to subclinical TB)
   - Systematic and more routine use of a wider range of programmatic data (e.g. laboratory testing data, coverage of TPT, ACF data), to inform assumptions about trends in the years following a national TB prevalence survey or inventory study (up to the next survey/study)
   - Use of data from mass active case finding (ACF) campaigns to estimate the national prevalence of TB disease in the population (and in turn incidence), as a substitute for a repeat national TB prevalence survey
   - Case notification data combined with an upward adjustment based on the Universal Health Coverage Service Coverage Index (UHC SCI)*, for two groups of countries: a) those for which current estimates rely on notification data and expert opinion about case detection gaps; b) those for which current estimates rely on notification data combined with a standard adjustment
   - Informing incidence estimate using TB mortality data, in countries with good national vital registration systems that include coding of causes of death according to international standards, or results from a TB mortality survey

   *the UHC SCI is one of two SDG indicators being used to monitor progress towards UHC

   For each of these options, do you think it is:

   a) Suitable for use, as described
   b) Suitable for use, and could be used more widely (in more countries) than currently proposed
   c) Possibly suitable for use, but requires further work first (e.g. more scrutiny/analytical work/refinement)
   d) Not suitable for use

   Please give reasons for your answers.

2. Do you think there are any other options that should be considered?

   For example, other options for assessment of trends in the years following a national TB prevalence survey or inventory study, until a repeat survey/study is done? (see pp18-19, section 3.2)

3. Section 5 sets out a proposed process for the finalization and implementation of options to be used for production of estimates for TB incidence. Do you think the process proposed is:

   a) Suitable as described
   b) Suitable with revisions (e.g. additions, refinements, deletions)

   If you answered b), please explain what revisions you would propose.

4. Do you have any other comments or suggestions related to the production of TB incidence 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]

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

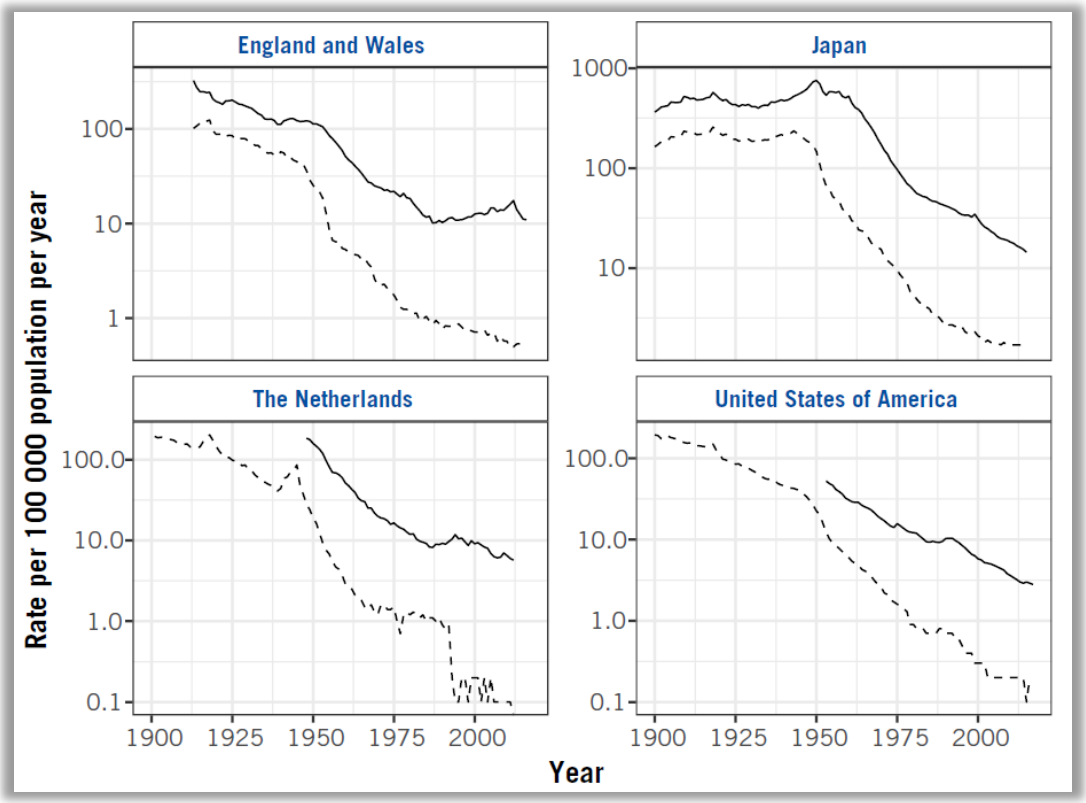
- Strengthening surveillance. This includes strengthening of national disease notification systems, for direct measurement of TB incidence; and strengthening of national vital registration (VR) systems that include coding of causes of death based on international standards,[4] for direct measurement of the number of deaths caused by TB.

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

- Priority studies to periodically measure TB disease burden. These include national TB prevalence surveys, national TB inventory studies, 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 periodic studies 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 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.[1]

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

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.[1]

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 incidence. It has five major sections:

1. **Current data sources, analytical methods and process: an overview.** This provides a short description of the five major sources of data and associated analytical methods that are used. These are results from a national TB prevalence survey, combined with either other data and assumptions to inform trends, or a dynamic model; case notification data and an inventory study (including capture-recapture analysis if justified and feasible); case notification data with a standard upward adjustment to allow for underreporting and underdiagnosis; case notification data combined with expert opinion about underreporting and underdiagnosis; and, for the specific period of the COVID-19 pandemic and its aftermath, dynamic models for a subset of countries. The processes used for country review of and input to estimates, in advance of their publication, are also described.
2. **Current data sources and analytical methods: strengths, limitations, emerging issues and country concerns.** This summarizes the main strengths and limitations of the current data sources and analytical methods, emerging issues, and the main current or recent concerns about estimates of TB incidence that have been expressed to WHO by countries.
3. **New options that could be considered.** Five options that could enhance or replace current data sources and analytical methods are discussed. These include an updated approach to use of prevalence survey data for estimation of TB incidence; systematic and more routine use of a wider range of programmatic data to inform assumptions about trends; use of data from mass active case finding (ACF) campaigns to estimate the national prevalence of TB disease in the population (and in turn incidence), as a substitute for repeat national TB prevalence surveys; use of case notification data combined with an upward adjustment based on the Universal Health Coverage Service Coverage Index (UHC SCI, which is one of two indicators in the SDGs that are being used to monitor progress towards UHC), as a substitute for case notification data combined with either a standard adjustment or expert opinion; and use of mortality data from national VR systems or TB mortality studies to cross-check estimates of TB incidence.
4. **2025 milestone and 2030 targets 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 88% of global TB incidence. 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.

Four questions are listed on the inner cover page. These will be used for an initial round of feedback in advance of the Task Force meeting, and subsequently during the meeting itself.

[1] 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.

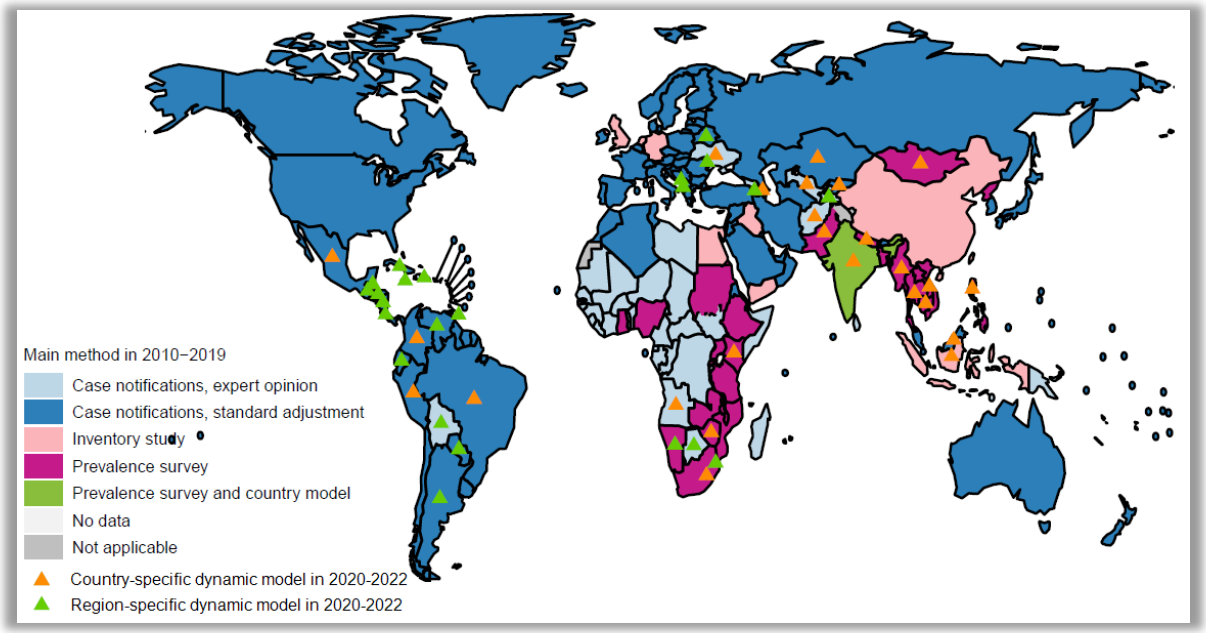
1. Current data sources, analytical methods and process: an overview

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, four main data sources and analytical methods were used to produce time series of TB incidence estimates[1] for publication in the annual WHO Global TB Report (**Fig. 2**).[2] These were:

- **Method 1:** national TB prevalence survey and assumptions about the duration of TB disease, as well as use of other data or assumptions to inform trends (especially in the absence of repeat survey data);
- **Method 2:** case notification data combined with a measurement of the level of underreporting from an inventory study and, if justified and feasible, capture-recapture analysis;
- **Method 3:** case notification data combined with a standard adjustment; and
- **Method 4:** case notification data combined with expert opinion.

During the COVID-19 pandemic, there were 49 countries in which TB case notification data suggested considerable disruption to TB diagnostic and treatment services in 2020, 2021 or both years. For incidence estimates in the 3 years 2020–2022, country or region-specific dynamic models were used for 48 of these countries[3] (indicated in **Fig. 2**), calibrated to pre-2020 burden estimates. For one of these 48 countries (India), the country-specific dynamic model was also used in combination with data from a national TB prevalence survey, TB mortality data and programmatic 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 incidence that were published in the Global TB report 2023, which covered the period 2010–2022



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

This section provides a short description of the data sources and analytical methods that were used to produce the estimates of TB incidence that were published in the Global TB Report 2023, as shown in

[1] The time series covered the period between a baseline year (initially 1990 for the period of the MDGs and Stop TB Strategy, subsequently updated to 2000 for the period of the SDGs and End TB Strategy) and the most recent complete calendar year.
[2] As explained in the Introduction, methods were rereviewed in 2015, 2016, 2018 and 2022; the most substantive reviews of estimates of TB incidence were in 2015 and 2022.
[3] The exception was Bangladesh. A country-specific model was used for TB mortality estimates, but not for TB incidence estimates. This was to avoid an odd discontinuity and given the absence of evidence about trends in the period 2010–2019. See also **section 2** and **section 4**.

Fig. 2 *(6, 19)*. Details are available in a technical appendix *(20)*. It also describes the processes commonly used by WHO to discuss and review estimates with Member States, prior to their publication.

1.1 National TB prevalence surveys

For the 10 years 2010–2019, national TB prevalence surveys were the main data source used to inform TB incidence estimates for 29 countries. These countries accounted for 66% of estimated global TB incidence in 2019. Survey results were used in combination with either a country-specific dynamic model (one country, India) or other data or assumptions to inform trends. For 14/29 of these countries, a country-specific or region-specific model was used to estimate TB incidence for the three years 2020–2022, during the COVID-19 pandemic and its aftermath (see **section 1.5** for further details). For the other 15 countries, it was assumed that pre-2020 trends were sustained.

1.1.1 Combined with other data or assumptions to inform trends

The 28 countries for which estimates for 2010–2019 were based on prevalence survey data combined with other data or assumptions to inform trends (**Fig. 2**, purple) accounted for 39% of estimated global TB incidence in 2019.

To estimate TB incidence in the year of a national TB prevalence survey, estimates of the prevalence of bacteriologically confirmed TB (≥15 years of age) from the survey are first adjusted to account for all ages as well as extrapulmonary TB, using TB notification data. Estimates of incidence are then produced based on combined use of prevalence estimates (for all forms and all ages) and estimates of the duration of disease. Estimates of disease duration are either: a) derived from the literature, with disaggregations according to TB treatment status and HIV status; b) derived from a mathematical model with three compartments (susceptible, untreated TB and treated TB) that uses both data from the prevalence survey and assumptions about how people with untreated TB transition to treatment, self-cure or death to find equilibrium solutions; or c) derived from combined use of both approaches.

Trends before and after the year of the survey were based on either additional data (e.g. previous national TB prevalence surveys, time series of TB case notifications, repeat surveys of TB infection) or assumptions that were informed by country consultations (either remotely or in-country, with the latter often done shortly after the finalization of survey results).

1.1.2 Combined with a country-specific dynamic model

For India, estimates for the period 2010–2019 were based on results from the first-ever national TB prevalence survey in combination other sources of data (e.g. annual notification data, mortality data from the country's sample registration system, drug sales data, estimates of the prevalence of TB infection) and a country-specific dynamic model. India accounted for 27% of estimated global TB incidence in 2019.

The model was developed and finalized through joint work involving WHO (at HQ and country levels), the Ministry of Health and Family Welfare and the Indian Council for Medical Research, and also benefited from the input of external modelling experts. More details about the model are available in the Global TB report 2023 *(6)*.

For estimates for the 3 years 2020–2022, the country-specific model was also used. The modelling to account for disruptions evident in TB notification data during the COVID-19 pandemic used the same methods as those developed by WHO (**section 1.5**), with an additional refinement (use of Google mobility data to inform assumptions about transmission).

1.2 Case notification data combined with a measurement of the level of underreporting from an inventory study and, if justified and feasible, capture-recapture analysis

For the 10 years 2010–2019, case notification data combined with results from an inventory study *(21)* that quantified the level of underreporting of people diagnosed with TB were used to produce TB incidence estimates for ten countries (**Fig. 2**, light pink). For seven of these countries, capture-recapture analysis was also done (Egypt, Germany, Indonesia, Iraq, the Netherlands, the United Kingdom,

Yemen); the other countries are China, France and the Republic of Korea. These ten countries accounted for 17% of global TB incidence in 2019 (of which China and Indonesia accounted for 16.5%).

In an inventory study, the level of underreporting of people diagnosed with TB is estimated by comparing independent databases that hold data about people diagnosed with TB. One of these databases must be a database that includes case-based data for people who have been notified as a TB case (either nationally or for a representative sample of geographic areas); other examples include databases managed by a national health insurance system and databases managed by a national laboratory system. If national databases already exist, then an inventory study can be done by analysing data that have already been collected, using record linkage. If not, then data on people diagnosed with TB need to be compiled prospectively, from a sample of public and private health facilities, and then compared with data about notified TB cases, through record-linkage.

Results from an inventory study can provide an estimate of the level of underreporting of people diagnosed with TB (i.e. the gap between the number of people notified as a TB case and the actual total number of people diagnosed with TB). If justified (certain assumptions must be met) and feasible, capture-recapture analysis through record-linkage of different lists of people diagnosed with TB originating from different providers can be used to produce an estimate of the total number of incident cases.

For capture-recapture analysis to be justified and feasible, six main assumptions need to be met *(21)*. These are:

- If S represents the number of case lists or data sources available, then at least three data sources are available (S≥3) and their dependencies can be accounted for in the model design;
- Every case has a chance of inclusion (whether they are actually included or not) in at least one of the lists described in bullet point 1;
- The proportion of mismatches and matching failures in record-linkage is low, which typically requires a large sampling fraction;
- There is a closed population during the study period (typically 3–6 months);
- There is homogeneity of within-source observation probabilities across subpopulation groups, such as those defined by socioeconomic and demographic characteristics; and
- The case definitions used across data sources are consistent.

For China, France and the Republic of Korea, estimates of TB incidence in the period 2010–2019 were based only on an upward adjustment of case notification data, based on the measured level of underreporting.

For one of the 10 countries (Indonesia), a country-specific dynamic model was used to estimate TB incidence for the three years 2020–2022, during the COVID-19 pandemic and its aftermath (see **section 1.5** for further details). For the other nine countries, it was assumed that pre-2020 trends were sustained.

1.3 Case notifications combined with a standard adjustment

For the 10 years 2010–2019, case notification data combined with a standard upward adjustment, to allow for some underreporting of people diagnosed with TB as well as some underdiagnosis or overdiagnosis, were used to produce estimates of TB incidence for 137 countries (**Fig. 1**, dark blue), which collectively accounted for 6.0% of estimated global TB incidence in 2019. The 137 countries include almost all high-income countries (the only exceptions being those for which results from an inventory study are available) and 61 middle-income countries and areas (mostly in the Americas and the Western Pacific and including many small island states).

The standard adjustment is based on a best estimate that notifications of people newly diagnosed with TB in any given year are equivalent to 85% (with a lower bound of 75% and an upper bound of 100%) of the actual number of incident cases.

For 26 of the 137 countries (Albania, Argentina, Armenia, Azerbaijan, Belarus, Belize, Brazil, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Grenada, Guatemala, Honduras, Jamaica, Kazakhstan, Kyrgyzstan, Republic of Moldavia, Malaysia, Mexico, Montenegro, Nicaragua, Peru, Paraguay and Venezuela), a country or region-specific dynamic model was used to estimate TB

incidence for the three years 2020–2022, during the COVID-19 pandemic and its aftermath (see **section 1.5** for further details). For the other 111 countries, estimates continued to be based on notification data with the same standard adjustment.

1.4 Case notifications combined with expert opinion about case detection gaps

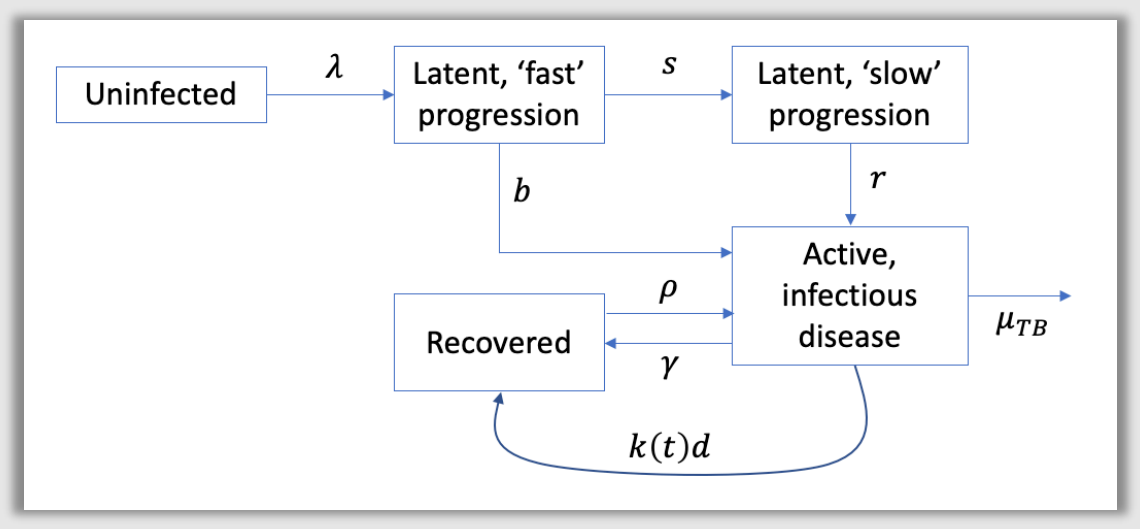
For 39 countries, TB incidence estimates for the 10 years 2010–2019 were estimated using TB case notification data, upward adjusted by a factor to account for underreporting, overdiagnosis and underdiagnosis based on expert opinion that was elicited in regional workshops, national consensus workshops or country missions. These 39 countries (**Fig. 2**, light blue) accounted for 11% of estimated global TB incidence in 2019. Most of these countries (n=25) are in the WHO African Region. Of the methods currently used, this one is the least preferred.

For seven of the 39 countries (Afghanistan, Angola, Bolivia, Botswana, Tajikistan, Ukraine and Uzbekistan), a country or region-specific dynamic model was used to estimate TB incidence for the three years 2020–2022, during the COVID-19 pandemic and its aftermath (see **section 1.5** for further details). For the other 32 countries, it was assumed that pre-2020 trends were sustained.

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

Country-specific dynamic models were used to produce TB incidence estimates for the period 2020–2022 for 25 countries and region-specific models were used for 23 countries (**Fig. 2**, orange and green triangles). Models were used for countries in which 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 48 countries for which model-based estimates were produced accounted for 95% of the global reduction in TB notifications in 2020 (vs 2019). The 25 countries for which country-specific models were used accounted for 62% of estimated global TB incidence in 2022 and the 23 countries for which region-specific models were used accounted for 1%. The basic model framework is illustrated in **Fig. 3**.

Fig. 3 A Schematic illustration of the basic model structure



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

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 (or reductions in incidence due to reduced transmission).

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 public-private/public-public mix (PPM) priority list and additional countries in the WHO South-East Asia Region with large private sectors); 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 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.

1.6 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 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. To date, such workshops have mostly been used for countries for which method 4 (notifications combined with expert opinion about case detection gaps) is relied upon.
- **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 based on results from the 2019–2021 national TB prevalence survey as well as other data (e.g. notifications, drug sales, TB infection survey, newly available mortality data from the sample registration system).

2. Current data sources and analytical methods: strengths, limitations, emerging issues, 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 very recent concerns about TB incidence 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 2**.

Table 2 Current data sources and analytical methods – main strengths and limitations

Data source and analytical method	Strengths	Limitations
National TB prevalence survey combined with *either*	Direct measurement of TB disease burden in a nationally representative sample of the population. Finds cases of TB among people who have not accessed health care (including those with subclinical TB i.e. those not reporting or recognizing symptoms), or who had previously sought care but were not diagnosed.	Special studies that add to ongoing costs of routine TB surveillance. Time consuming, logistically challenging. Participation tends to fall as countries become wealthier and more urbanized. Not applicable once TB burden falls below a certain threshold (required sample sizes become too large). Surveys measure bacteriologically confirmed pulmonary TB in adults; results have to be adjusted to cover all ages and extrapulmonary TB; assumptions or modelling then required to convert estimates of prevalence to estimates of incidence.
a) Literature or compartmental model-based estimates of disease duration; + other data or assumptions to inform trends *or*	All 28 countries implemented a survey in or around 2015, providing direct measurement that can be used as a baseline for assessing progress towards 2025 and 2030 milestones and targets.	Uncertainty about duration of disease and estimate of prevalence; if only one survey has been done, other data (less direct) and expert opinion used to estimate trends; flat trend in absence of any data. Last surveys ≥5 years ago; need for repeat surveys, especially if there were major COVID-related disruptions to TB notifications.
b) country-specific dynamic model + other data (India only)	Multiple sources of data used at the same time; calibration to prevalence survey and TB mortality data.	Uncertainty about TB mortality; no age stratification, uncertainty related to private sector drug sales. Potentially time-consuming process to review and validate the model and associated data.
Case notification data combined with measurement of underreporting from an inventory study, plus capture-recapture analysis if this is justified and feasible	Direct measurement of underreporting is better than reliance on a standard adjustment (method 3) or expert opinion about reporting gaps (method 4).	Inventory studies on their own measure the level of underreporting of people diagnosed with TB, but not the level of under (or over) diagnosis. Few high TB burden countries expected to be able to implement inventory studies that will meet the six assumptions required to estimate TB incidence using capture-recapture analysis. Most countries have done only one inventory study (most now several years old), with results assumed to apply to other years. Indonesia is the first country to implement a repeat study (in 2023–2024, after a first study in 2017). Cases of subclinical TB (people with TB disease who do not have/do not recognize TB symptoms) that never progress to symptomatic disease could be missing from notification data
Case notification data combined with standard upward adjustment (to account for a relatively limited level of underreporting, underdiagnosis and overdiagnosis)	Relies only on routine reporting of case notification data. Simple and straightforward, easy to explain. Used for almost all high-income countries since 2009.	Standard upward adjustment has not been reviewed since 2015; may be too high for some countries and potentially too low for some others. Only justified for countries with strong disease surveillance systems and high level of health system coverage. Cases of subclinical TB (people with TB disease who do not have/do not recognize TB symptoms) that never progress to symptomatic disease could be missing from notification data (one reason why an adjustment to account for underdiagnosis as well as underreporting is needed).
Case notification data combined with expert opinion about case detection gaps	Allows production of estimates in the absence of reliable survey and notification data.	Relies on expert opinion, which is increasingly outdated for many countries in this category.
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.

2.2 Emerging issues

2.2.1 Natural history of TB and subclinical TB

The clinical spectrum of TB disease, and "subclinical TB" in particular, has been the subject of several recent publications*(22-35)*. These publications include a recent systematic review of the natural history of pulmonary TB in adults, using data from the pre-chemotherapy era; analyses of data from national TB prevalence surveys; analysis of progression and regression between different states of pulmonary TB in adults; and discussion of how to classify and define states of TB infection and disease.

The reason why national TB prevalence surveys have been a major driver of this recent attention to disease states, including subclinical TB, is that they have consistently shown that a substantial proportion (a pooled average of around 50% *(36-38)*) of the people found to have bacteriologically confirmed pulmonary TB did not report symptoms suggestive of TB, when screened for symptoms as part of the survey. Instead, individuals were only identified as having bacteriologically confirmed pulmonary TB because they were eligible for diagnostic testing based on having an abnormal chest X-ray.

Although a variety of terminology and definitions for disease states have been used *(22)*, a 2024 publication provides a suggested classification of disease states that distinguishes three major categories: no disease (MTB infection); subclinical TB disease; and symptomatic/clinical TB disease *(34)*. In this conceptual framework, the essential difference between subclinical TB and symptomatic TB is that people with subclinical TB do not report or recognize symptoms or signs of TB disease, while those with symptomatic TB do. People with subclinical TB and symptomatic TB both have "macroscopic pathology" (observable directly on anatomical samples, by clinical examination or imaging e.g. via digital chest X-ray or more advanced imaging methods) and both can be either "infectious" or "noninfectious".[10]

For countries for which national TB prevalence surveys are currently the main data source used by WHO to produce estimates of TB incidence, the starting point is the measured prevalence of bacteriologically confirmed pulmonary TB in the adult population (**section 1.1**; **Table 2**). This includes people with "subclinical" infectious TB (according to the classification described above) and people with "clinical TB" (subsequently referred to in this document as "symptomatic" TB, to avoid confusion with clinically diagnosed TB). As explained in **section 1.1** and **Table 2**, estimates of the prevalence of bacteriologically confirmed pulmonary TB are then adjusted to include all ages and extrapulmonary TB, using notification data, following which TB incidence is estimated as the product of estimated prevalence (all ages, all forms) and the duration of TB disease. In this sense, for countries for which the main data source is a national TB prevalence survey, existing WHO estimates of TB incidence include people with subclinical infectious TB disease as well as symptomatic infectious TB disease.

At the same time, results from the recent systematic literature review of the natural history of TB *(28)* and the model-based analysis of progression and regression between states of pulmonary TB disease, using findings from this review *(29)* as well as other data, have potential implications for the existing approaches to estimation of disease duration, and the resulting estimates of incidence. Consequently, they raise the question of whether approaches using prevalence survey data for estimation of incidence should be updated to account for the latest literature on the natural history of TB and subclinical TB. This is discussed further in **section 3**.

2.2.2 Convergence of case notifications on best estimates of TB incidence

In addition to subclinical TB, a second emerging issue that requires attention is that in some high TB burden countries, case notifications are increasingly converging on the best estimates of TB incidence. This raises questions about whether increases in notifications could in part be due to overdiagnosis or whether incidence estimates require review. The main examples are Mozambique, Uganda, the United Republic of Tanzania and Zambia.

[10] The proposed classification divides both people with subclinical TB and those with clinical TB into two subcategories: "infectious" and "noninfectious". This results in five conceptual states in the proposed classification: TB infection; subclinical TB, infectious; subclinical TB, noninfectious; clinical TB, infectious; clinical TB, noninfectious.

2.3 Country concerns

The main current or recent concerns about TB incidence estimates that countries have raised with WHO are shown in **Table 3**. The countries that have expressed each concern are listed.

Table 3 Current or recent concerns about TB incidence 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. It is a particular concern among a few countries in which notifications had not returned to pre-pandemic levels by the end of 2022, but in which the NTP considers that case-finding efforts have "returned to normal" (e.g. according to diagnostic testing data from laboratories).	Georgia, Indonesia, Kazakhstan, Kyrgyzstan, Peru, Tajikistan, Uzbekistan	Estimates have been extensively discussed via bilateral meetings (mostly online); country missions to Tajikistan and Uzbekistan in March 2024; for Indonesia, awaiting results from 2024 inventory study; mission to Kazakhstan under discussion.
Estimates too high (pre, during, post-COVID)	This concern has been expressed by two of the countries for which incidence estimates during the COVID-19 pandemic were estimated based on the assumption that the pre-COVID level and trend was sustained. This is a particular concern among countries in which the NTP has made concerted efforts to improve case finding, treatment success and provision of TB preventive treatment.	Ghana, Lesotho	Estimates have been discussed with the NTP on several occasions (most recently with Lesotho during the 2023 Union conference). Key data source for both countries is a national TB prevalence survey (Ghana, 2013 and Lesotho, 2019).
	It has also been expressed by two countries that did experience major disruptions (based on TB case notification data) during the COVID-19 pandemic. In Bangladesh, the concern is linked to flat trend for 2010-2019 despite increasing notifications, linked with intensive programmatic initiatives to promote case-finding.	Bangladesh, Cambodia	Estimates for Cambodia will be reviewed and updated following completion of the 2023–2024 national TB prevalence survey. Main data source for Bangladesh is 2015 prevalence survey.
Estimates too low	A few countries are concerned that incidence estimates are too low, which may discourage further investments in efforts to improve TB services. This includes one country where recent increases in case notifications means that at face value, treatment coverage is approaching 100%.	Ethiopia, Equatorial Guinea, Uganda	An adjustment to estimates for Ethiopia was made in 2023 (aligned with the increase in notifications from 2022 to 2023, which reversed years of decline).
Estimates based on standard adjustment of notification data too high	A few countries are concerned that the upward adjustment is too large (and somewhat "arbitrary").	A few high-income countries including Saudi Arabia	WHO has suggested that an inventory study could enable use of a more accurate/precise adjustment.
Estimates based on standard adjustment of notification data too low	Two countries are concerned that the standard adjustment is no longer appropriate. This is also affecting eligibility for Global Fund grants.	Lebanon, Syria	This requires further discussion between the countries and WHO.
Population estimates do not reflect current realities	Two countries are concerned that the population estimates used by WHO do not reflect current realities.	Moldova, Somalia (also applies to e.g. Ethiopia, Myanmar, Sudan, Syria, Ukraine)	WHO is required by policy to use UN Population Division estimates *(39)*.

Of note, some of the concerns expressed by countries are closely linked to Global Fund eligibility and targets established as part of grants. Two of the countries that have expressed concerns that incidence estimates are too low have estimates that affected their eligibility to apply for grants. Other countries are concerned that they cannot achieve notification and treatment targets that have been derived from a combination of incidence estimates and coverage targets.[11] This is contrary to WHO guidance on national strategic planning, which recommends that targets should be based on recent notification and other programmatic data, and not derived from incidence estimates. For a small number of countries that can apply for grants for specific parts of the country only, a further problem with the approach of setting targets directly linked to incidence estimates is that it prompts requests for subnational incidence estimates, which are difficult to produce with a useful degree of precision in most countries.

3. New options that could be considered

Given the recognized limitations of the current methods that are used to produce TB incidence estimates (**Table 2**), periodic consideration of options that could improve or replace them is important.

Desirable (or necessary) characteristics of new options include:

- They will be a clear improvement on current methods by addressing at least one of their main limitations while not compromising their main strengths.
- They can be easily explained and understood, at least at a conceptual level. It is particularly important that data sources and analytical methods are understandable for national authorities in WHO Member States, including NTPs as well as other entities responsible for disease surveillance. This is essential for consultations and constructive discussions about estimates, including to facilitate inputs that can improve them (e.g. via provision of new or updated data, insights about factors that might influence trends).
- Data sources can be made available in the public domain and analyses can be reproduced by others, as recommended in the GATHER guidelines *(18)* used by WHO for health estimates. This is important to ensure transparency, and includes publishing the code used for analyses. It is also important for understanding what sources of data and assumptions have the most influence on published estimates, and in what direction.

This section sets out an **initial** set of new options that warrant consideration. They are designed to prompt further thinking, constructive critique and other ideas and suggestions. **It is expected that this initial set of options will be added to, refined or narrowed down during the process of review and discussion of this document**.

3.1 Option 1: New approach to use of national TB prevalence survey data for estimation of incidence that accounts for the latest literature on the natural history of TB (with particular attention to subclinical TB)

Potential application/relevance:
Countries for which a national TB prevalence survey is the main data source used to estimate the absolute level of TB incidence

As described in **section 2.2.1**, the last five years or so (and especially the last two) have seen renewed interest in the clinical spectrum of TB, including how people progress and revert between different states of disease in the absence of treatment *(28, 29)* and the concepts of "early TB" and "subclinical TB".

[11] Although not directly relevant to the focus of this document, which is estimates of TB incidence as a whole, a particular challenge in the context of Global Fund grants has been the setting of targets derived from estimates of the incidence of rifampicin-resistant TB (RR-TB). This is particularly problematic because with current diagnostics, detection of RR-TB is only possible among people with bacteriologically confirmed TB (not those clinically diagnosed), which needs to be accounted for to ensure that targets are realistic. In addition, estimates of RR-TB incidence are more uncertain than those for TB overall. RR-TB incidence estimates have been a recent concern for a few countries in eastern Europe and Central Asia that have a high burden of RR-TB and for which a country or region-specific dynamic model was used to produce overall estimates of TB incidence in the period 2020–2022.

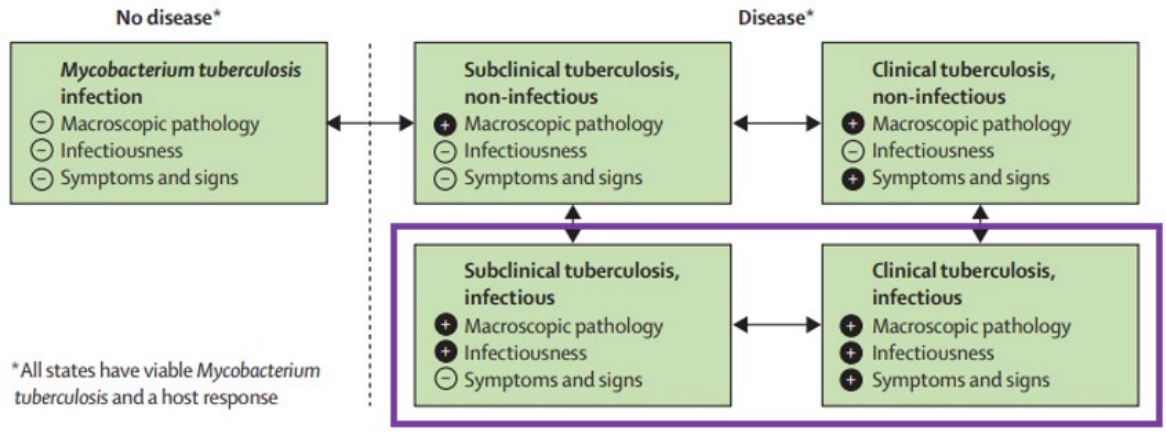
3.1.1 Conceptual framework for states of TB infection and disease, and what is counted in a national TB prevalence survey

The conceptual framework for classification of different states of TB infection and disease proposed by the International Consensus for Early TB (ICE-TB) group *(34)* is shown in **Fig. 4**. This includes five states, two of which are 1) subclinical TB (infectious) and 2) subclinical TB (non-infectious).

National TB prevalence surveys measure the number of prevalent cases of bacteriologically positive pulmonary TB among people aged ≥15 years i.e. the number of prevalent cases of pulmonary TB among people aged ≥15 years in the two states that are defined in the bottom-left and bottom-right green boxes in **Fig. 4** (subclinical TB, infectious; clinical TB, infectious).

Of note, although surveys screen all eligible participants (i.e. people aged ≥15 years who meet residency criteria) for symptoms, the list of symptoms that are asked about varies among countries and is not exhaustive (typically, it consists of the criteria used within routine health services); also, people may have symptoms but not recognize or report them. The counts of cases in prevalence surveys "not meeting symptom screening criteria" may therefore vary across countries for which prevalence survey data are available.

Fig. 4 Classification of five states of TB infection and disease proposed by the ICE-TB group
Prevalence surveys count the number of cases of bacteriologically positive (infectious) pulmonary TB in the two states within the **purple** box (not in the original, added here for emphasis), *restricted to people aged ≥15 years*



3.1.2 WHO model used in estimation of TB incidence based on prevalence survey data

For countries with prevalence survey data, one of the two current methods used by WHO for incidence estimation uses a model in which untreated TB (all prevalent cases, including both those reporting symptoms and those not reporting symptoms) is subject to a constant hazard of cure (whether spontaneously or through treatment) or death (see **section 1.1.1**). Assuming equilibrium conditions, this model is fitted to the following data from a prevalence survey:

(i) The overall prevalence of bacteriologically positive, pulmonary TB among adults (i.e. those aged ≥15 years);

(ii) Out of the treatment-inclusive prevalence (i.e. the sum of (i) and the number of adults with bacteriologically negative pulmonary TB who were on TB treatment at the time of the survey), the proportion that were on TB treatment, regardless of bacteriological status.

The contribution of (ii) is to inform the duration of untreated, pulmonary TB in adults. Generally, the higher the proportion, the shorter the delay. Combining this estimate of duration with prevalence estimates from (i) allows estimation of the incidence of bacteriologically positive pulmonary TB among people aged ≥15 years. Estimates for all ages and all forms of TB (i.e. including extrapulmonary TB) are then produced using adjustments based on TB case notification data.

3.1.2 Results from recent modelling analyses of the natural history of TB and associated questions

Results from two closely-related modelling analyses published in 2023 *(29, 31)*, which both use findings from a recent systematic review of the natural history of pulmonary TB *(28)* as well as other data, have raised new questions about how incidence should be conceptualised and quantified. These questions can be summarised under three topics, as follows.

1. ***Proportion of people with subclinical TB who develop symptoms***

Estimates from the recent modelling studies suggest that about 50% of people who develop subclinical infectious TB (defined as bacteriologically positive pulmonary TB and X-rays suggestive of active TB, but no TB-related symptoms or signs) *never develop symptoms*. This is a much higher proportion than that assumed to date and has potentially major implications for estimates of TB incidence derived from national TB prevalence surveys.[12] It raises the question of whether the incidence of pulmonary TB disease (when derived from prevalence surveys, in people aged ≥15 years) should be conceptualized as the onset of bacteriologically positive status ("infectious TB", and including subclinical as well as symptomatic TB), or as the onset of symptoms ("symptomatic TB").

2. ***Progression and regression between disease states***

Recent studies highlight the potential for progression and regression between different disease states. If an individual experiences multiple, distinct episodes of bacteriologically positive pulmonary TB disease, this raises the question of whether incidence should be conceptualized as the sum of such *episodes* at the population level in a given year, or rather as the number of *individuals* experiencing one or more such episodes in a given year. Even if incidence is counted at the level of individuals, not episodes, an individual experiencing two episodes several years apart could arguably represent two separate incident events. Thus the appropriate time interval between episodes, to count as separate incident events, is also a relevant question.

3. ***Adjustments for extrapulmonary TB and children***

Prevalence surveys provide data about the prevalence of bacteriologically positive, pulmonary TB among adults, while WHO incidence estimates need to capture all forms of TB in all age groups. Currently, WHO uses notification data to make the necessary adjustments (for example, using the proportion of total notifications among people aged <15 years).

However, as recent studies focused on pulmonary TB in adults *(31)*, it is unclear how their findings would extend to extrapulmonary TB and younger age groups. In particular, given that the vast majority of notifications are of people with symptomatic TB, it is unclear how adjustments of the incidence of *adult, infectious, pulmonary* TB would need to be modified to accommodate people in younger age groups and extrapulmonary TB.[13]

As one illustrative example: if the proportion of children with subclinical TB who develop symptoms is much higher compared with adults, then (other things being equal) a higher proportion of children with subclinical disease might ultimately develop sufficient symptoms to be diagnosed and notified, relative to adults with subclinical disease. In this scenario, adjustments to incorporate children aged <15 years, notifications among children would need to be down-weighted relative to adults.

3.1.3 Exploratory analyses

In relation to the first two points above, preliminary work suggests that the distinction between "infectious" and "symptomatic" TB has stronger implications for incidence estimates than "episodes" versus "individuals". Moreover, in feedback from a first round of review of an earlier draft of this document, there was emerging consensus that incidence estimates should focus on individuals rather than episodes.

[12] The other method currently used by WHO to estimate incidence from prevalence survey results relies on literature-derived estimates of disease duration. It does not make any explicit assumption about what proportion of people progress from subclinical to clinical TB (and the disease durations make no distinction between these two states).

[13] Currently, adjustments are not made for adults with bacteriologically negative pulmonary TB. This is also something that may warrant discussion.

The importance of the third point above, on adjustments for all forms of TB, depends on the outcomes of discussions related to estimates of the incidence of "infectious" and "symptomatic" TB, and in particular a proposed option for WHO incidence estimates and complementary burden estimates that could be produced and published in future (**Table 4** below).

On this basis, **Fig. 5** shows results from **an exploratory analysis of incidence estimates for adults with pulmonary TB**, using data from a recent national TB prevalence survey and two different definitions of incidence among individuals: "infectious" and "symptomatic". Estimates from the survey were: (i) overall prevalence per 100 000 population, (ii) the proportion of people with pulmonary TB who were on TB treatment at the time of the survey, and (iii) the proportion of people with bacteriologically positive TB at the time of the survey (prevalent cases) who did not report symptoms (i.e. were infectious, but subclinical).

As explained below the title of **Fig. 5**:

- The horizontal, dashed line shows incidence estimates for adult, pulmonary TB that are based on those published in the 2023 Global TB Report *(6)*. The published estimates (for all ages and all forms of TB) were adjusted using standard approaches, to restrict them to estimates for pulmonary TB among adults.
- Estimates shown in blue are derived from an exploratory "alternative model" that uses parameter values for rates of progression and reversion across the disease spectrum, including for the specific transition between subclinical and symptomatic pulmonary TB, from the recent literature on the natural history of pulmonary TB in adults *(28, 29, 31)*.
- Parameters provided in the most recent publication *(31)* were used as priors in a Bayesian calibration, against data derived from the national TB prevalence survey.

Fig 5. Estimates of the incidence of pulmonary TB in adults, for two different definitions of incidence. The horizontal, red dashed line shows estimates based on current WHO methods (and associated parameter values), adjusted so that they refer only to adult, pulmonary TB. The other incidence estimates (in blue) are based on recent model-derived estimates of rates of progression and regression across the spectrum of pulmonary TB disease among adults, in the absence of treatment (including the estimate that only about 50% of people with subclinical infectious TB go on to develop symptoms). "Infectious TB" means conversion from bacteriologically negative to positive status (i.e. including all new episodes of subclinical, as well as symptomatic, TB).

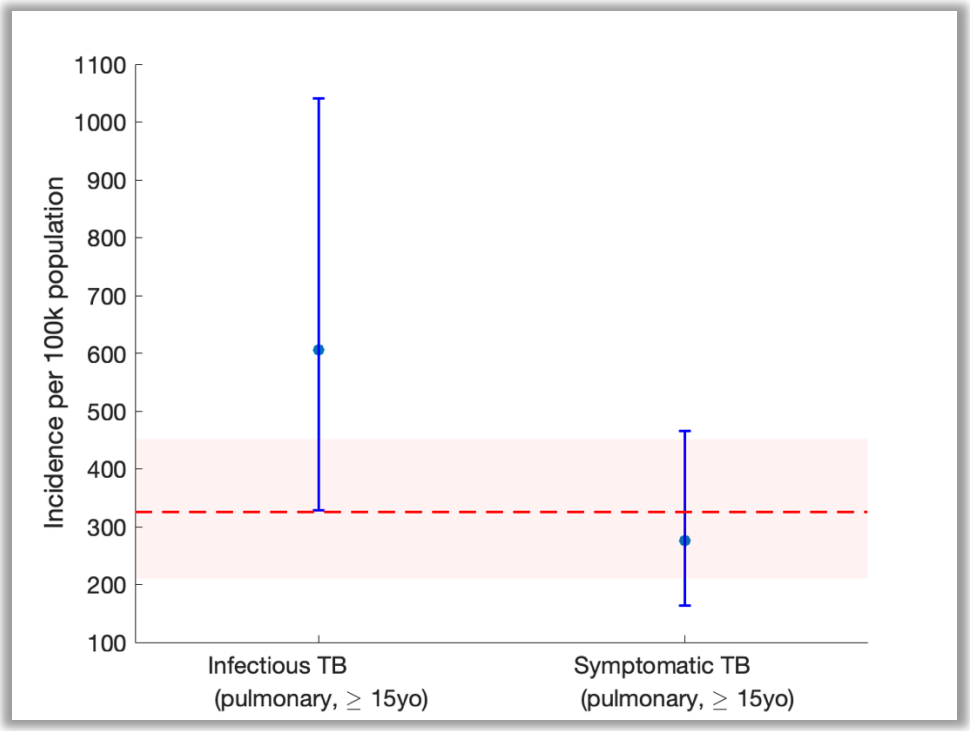


Fig. 5 shows how widely estimates could vary, depending on whether incidence is regarded as that of *infectious*, or *symptomatic* TB. In particular, the "alternative model" results in:

- An estimated annual incidence of *infectious*, pulmonary TB in adults of 606 per 100 000 population (95% uncertainty interval, 328–1040);
- An estimated annual incidence of *symptomatic*, pulmonary TB in adults of 276 per 100 000 population (95% uncertainty interval, 163–465).

In terms of the recent modelling analyses related to progression and reversion of pulmonary TB disease in adults in the absence of treatment, the following points are also worth highlighting:

- The evidence for rates of progression and regression between different disease states in the absence of treatment comes from historical cohorts from the pre-chemotherapy era. The extent to which these rates apply to populations in high TB burden countries today cannot be studied, for ethical reasons.
- The models use estimated rates of bidirectional transition between "minimal and subclinical disease" and "subclinical and clinical disease" in the absence of treatment. However, as noted in these studies, there is no direct evidence about transitions between subclinical and symptomatic/clinical pulmonary disease. The recent review of the literature *(28)* commented that "*historical studies did not capture information about symptoms effectively, especially over follow-up*" and that "*studies reported symptoms poorly, precluding direct estimation of transitions from subclinical (asymptomatic, culture-positive) disease*".
- The model parameters that could be directly informed by historical, longitudinal studies were the probability of progressing from microbiologically negative to microbiologically positive pulmonary TB disease (based on smear or culture tests) among a) people with baseline radiographic evidence of active TB and b) those with chest X-rays suggestive of inactive TB; and the probability of reversion from microbiologically positive pulmonary TB to undetectable disease.
- The two preceding points mean that it is important to clarify to what extent transition rates between subclinical and symptomatic pulmonary disease are informed by the available data, versus (for example) the assumed model structure. Updates from ongoing, collaborative work to address this key question will be presented at the Task Force meeting.

If further work results in consensus that there is a significant disparity between the incidence of infectious (bacteriologically positive) pulmonary TB (with or without symptoms) and the incidence of infectious symptomatic pulmonary TB, this will have implications for how WHO estimates of TB incidence derived from prevalence surveys are produced; how they are characterized/named; and what complementary estimates of TB disease burden might be relevant. For the purposes of assessing trends between 2015 and the milestone and target years of 2025 and 2030, the important thing is to use a consistent concept/definition of incidence.

Some possible options were proposed in an earlier version of this document. Based on feedback from several Task Force members with specific expertise in this area, a proposed approach that could be used by WHO in future is presented in **Table 4**.

Table 4 Proposed option for TB incidence and complimentary burden estimates to be produced and published by WHO in future

Incidence estimates, all countries	Complementary burden estimates	Comments
Incidence estimates that are considered equivalent to symptomatic/clinical TB	Estimates of the globally aggregated prevalence of subclinical and symptomatic/clinical infectious TB As part of country specific case studies to be featured in the Global TB Report, country-specific estimates of the prevalence of infectious TB (with subclinical and clinical TB disaggregated) for countries that have recently completed a national TB prevalence survey. Country-specific estimates of the incidence of infectious TB, to be produced** if requested by NTPs, and if appropriate data are available (e.g. from a recent prevalence survey).	***Incidence estimates*** • Likely to be consistent with time series of estimates previously published by WHO.* • Maintains consistency* between estimates derived from prevalence surveys and estimates for all other countries that are derived directly from TB case notification data (with the vast majority of notifications being people with "symptomatic/clinical" TB). • Corresponds well with the TB case notification data that are currently used to adjust prevalence survey results for pulmonary TB among people aged ≥15 years to cover all ages and all forms of TB (with the vast majority of notifications being people with "symptomatic/clinical" TB, while the relationship between notification data and subclinical TB has substantially more uncertainty). ***Complementary estimates*** • Complementing country-specific incidence estimates with a global prevalence estimate recognises the importance of infectious (symptomatic/clinical and non-symptomatic/subclinical) TB for transmission and associated actions to accelerate progress towards the targets for reduction of TB incidence. • Because the burden of infectious TB is expressed as prevalence, rather than incidence, it is directly driven by prevalence survey findings, and thus avoids the uncertainties described above (e.g. for the proportion of people with subclinical TB who develop symptoms). • Restricting an estimate of the burden of infectious TB to the global level avoids potential concerns about country-specific assumptions, especially for countries without recent prevalence survey data. • Country-specific estimates of the incidence of infectious TB (including symptomatic and subclinical) could be useful for countries considering programmatic activities to target subclinical TB. • To produce a global estimate of the prevalence of infectious TB will require development of suitable methods and associated analytical work.

* Estimates of TB incidence that include infectious cases that never progress to symptoms (non-symptomatic TB) could result in substantial upward revisions compared with time series of estimates published by WHO to date; communication/explanation would be challenging and acceptability by countries might be problematic; estimates may be of less programmatic relevance in many countries.
** These would not necessarily be published in global TB reports.

3.2 Option 2: Systematic and more routine use of a wider range of programmatic data to inform assumptions about trends

Potential application/relevance:
Countries for which a prevalence survey or inventory study is the main data source used to estimate the absolute level of TB incidence, to inform estimates for the years following the last prevalence survey or inventory study, at least until a repeat survey/study is done (i.e. complementary to current method 1 and current method 2)

Incidence estimates for which the main data source is a national TB prevalence survey (**section 1.1**), or that use case notification data in combination with expert opinion about case detection gaps (**section 1.4**), or for which the main data source is a single inventory study combined with capture-recapture analysis (**section 1.2**), require the use of additional data or assumptions to inform trends. In the time interval up to the next (repeat) prevalence survey or inventory study, or the next in-depth country consultation about case detection gaps, estimates of trends may become progressively more inaccurate. For countries for which country or region-specific models have been used to produce TB incidence estimates for 2020–2022, errors may accumulate with each year of use (**Table 1**).

More systematic, standardized and routine (e.g. annual) use of readily and widely available programmatic data to inform assumptions about trends could improve on the current approach (in which assumptions about trends are reviewed only periodically). Possible examples are routinely collected laboratory testing data and data that provide evidence of programmatic improvements.

3.2.1 Laboratory testing data alongside case notification data

There has been very limited use of routinely collected laboratory testing data in combination with case notification data. Data on the number of people with presumptive TB who are tested for TB may be particularly informative.

Given two countries with the same case notification rate, if one country has a very high testing rate (i.e. a substantial proportion of its population being tested for TB per year) and the other has a very low rate, then TB incidence in the first country is likely to be lower. Notifications in the second country may increase if programmatic improvements are put in place that result in the testing of more people with presumptive TB.

Use of data about the average number of people with presumptive TB who are tested per person notified as a TB case (number needed to test, NNT) could provide information about trends in TB incidence. For example, if the NNT is increasing over time, then other things being equal, this may be a good indication that TB incidence is decreasing (and vice versa).

Similar logic can be applied to notifications that are achieved through active case-finding (ACF), as opposed to routine TB services. As one example, recent work in Uganda has shown a clear decrease in the yield of ACF *(40)*, equivalent to a statistically significant increase in NNT from 106 to 192, and suggesting a decrease in TB disease burden during this time. While this Kampala-based study may not reflect national trends, it does suggest ways in which future ACF efforts could be useful for monitoring trends. Ideally, ACF interventions would be deployed at country level (such as CAST-TB; see **Box 1**), and performed in a consistent way over time, especially with respect to the screening and diagnostic algorithms being used, to allow comparison across years. On the former point, a factor that needs careful consideration is the scale at which ACF is sufficiently large to be informative of national trends.

Overall, monitoring NNTs would be most meaningful if it is applied to testing and notification data that is properly disaggregated, between these two sources (ACF vs routine services). Otherwise, for example, according to aggregated data, a country's NNT could increase substantially through the implementation of ACF alone: not because of any real decrease in TB incidence, but because the prevalence of TB in the population being tested is much lower than in health care settings.

3.2.2 Programmatic data on TPT and ACF coverage

3.2.1.1 TPT

Scaling up the coverage of preventive therapy (TPT) - particularly in adult and adolescent household contacts of notified TB patients – could have effects on TB incidence that would ideally be incorporated in burden estimates. For example, modelling of the impact of TPT in countries in the WHO South-East Asia Region suggests that its provision to all-age household contacts of index TB patients could reduce cumulative incidence by 10–15% over 17 years: a meaningful - if not dramatic – impact *(41)*. In countries where HIV infection is a major driver of the TB epidemic, increased uptake of TPT among people living with HIV could have a bigger impact.

Such modelling studies arguably show *upper limits* on the potential impact of TPT, since they assumed idealised implementation that is more typical of trial than programmatic conditions, including (for example) optimal uptake and completion of TPT. To account for these important factors in burden estimation, programmatic TPT data would need to include: (i) stratification by age and the HIV status of contacts initiating TPT, even if only to distinguish children from adults/adolescents (the latter being likely to have a stronger impact on TB transmission at the population level); and (ii) rates of regimen completion. Assumptions about the implications of non-completion of treatment would be needed, for the risk of developing TB. Ideally, these assumptions would be informed by programmatic evidence from the longitudinal follow-up of patients initiating TPT.

3.2.2.2 ACF

ACF can have substantial effects on TB incidence, by reducing opportunities for transmission. As described above for TPT, to capture these effects in a systematic way, it is likely that mathematical modelling would be required. The model would have to strike the right balance between simplicity (so that it can be understood) and complexity (to allow meaningful use and interpretation of available intervention data). For any modelling approach to be useful, it would also be necessary to validate the reported performance, or yield, of any given intervention. For example, ACF might show an apparently sizeable yield, but would have very limited effect on incidence if a substantial proportion of detected "cases" were in fact the result of false-positive diagnoses. Intervention data would need to be evaluated on a country-by-country basis, in close consultation with the NTP about the nature of the interventions, for example on the algorithm used to test for TB.

Using modelling to estimate the impact of interventions on TB incidence has other limitations as well. For example, modelling the impact of ACF requires assumptions about the infectiousness of people diagnosed with TB, and their contribution to transmission in the counterfactual situation of not being diagnosed through ACF. At the very least, modelled approaches should allow for uncertainty in these parameters, and be validated using empirical evidence about intervention impact (e.g. trial data from Viet Nam and any other settings with empirical estimates of epidemiological impact) *(42)*.

3.2.3 Additional considerations for assessing trends in incidence

In countries where notifications or VR data do not provide reliable measures of disease burden, prevalence surveys remain the most direct, unbiased way of measuring burden. However, a key limitation of prevalence surveys is that they cannot be performed frequently, owing to the time required to plan and execute them: indeed, current WHO guidelines recommend an interval of approximately 10 between surveys. In the years following any prevalence survey, therefore, other methods are needed to assess robustly how incidence and mortality are changing over time. This need is especially pressing in the context of the End TB Strategy and SDG milestones and targets: for countries not already preparing for prevalence surveys, it is already too late for any new survey results to be available in time for the 2025 milestone assessment.[14] Moreover, even for the 2030 targets, a prevalence survey would need to be completed in 2030 at the latest.

Current methods for estimating changes in incidence and mortality over time have scope for improvement. For example, Bangladesh and Nigeria are two prominent examples of countries that have seen substantial expansion of programmatic efforts in recent years, including systematic screening, but

[14] As noted in **section 4** (**Table 6**), estimates for 2015–2025 could be revised in the period 2026–2030 if new data from a periodic study become available in this time period.

their estimates of incidence and mortality remain unchanged. Even for countries without such strong programmatic efforts, the potential for secular trends in TB burden means that the need for robust methods to assess these trends is also important.

Annex 1 provides a summary of selected feedback from an initial round of review by people attending the Task Force meeting, including for Option 2. This feedback has raised important and valid issues, but leaves open the question, **"In countries that are unable to perform a repeat prevalence survey or inventory study in time for the 2025 milestones or 2030 targets assessment, how should changes in TB burden be assessed, in the years leading up to these time points?"**. During the Task Force meeting, ideas related to this important question will be welcomed (see also **question 2** on the inner cover page).

3.3 Option 3: Use of data from mass ACF campaigns to estimate the national prevalence of TB disease in the population (and in turn incidence)

Potential application/relevance:
Countries for which national TB prevalence surveys are currently the main data source used to estimate the absolute level of TB incidence, as a substitute for a repeat national TB prevalence survey

In the last 1–2 years or so, the question of whether there are easier and lower cost alternatives to national TB prevalence surveys has been raised, including by international agencies that have funded (or co-funded) these surveys in recent years. There has been particular interest in whether data from mass ACF campaigns in the community could be used as a substitute for a national TB prevalence survey.

ACF that includes use of chest X-ray (CXR) as well as questions about TB symptoms, followed by diagnostic testing for those who screen positive, is in some respects similar to what is done in a national TB prevalence survey *(36, 43)*. However, the use of ACF data to inform burden estimates can introduce additional layers of uncertainty, namely:

- The representativeness of the population covered by ACF, of the TB disease burden in the country as a whole;
- If ACF relies on symptom screening alone (i.e. without X-ray screening), assumptions are needed to extrapolate ACF findings to include people with TB who do not have symptoms; and
- The implications of false-positive diagnosis, for ACF approaches using a single diagnostic test.

Characteristics of national TB prevalence surveys and ACF campaigns that are relevant to the viability of mass ACF replacing national TB prevalence surveys are described in **Table 5**.

Box 1 provides an illustrative example, using data from a recent mass ACF initiative in Uganda called CAST-TB (Community Awareness, Screening, Testing, Prevention and Treatment to End TB and Leprosy). The findings show that incidence estimates derived from CAST-TB data have substantially wider uncertainty, and also substantially lower central estimates, than those derived from Uganda's prevalence survey in 2015. The implication is that ACF data are not necessarily a reliable substitute for data from national TB prevalence surveys. Nonetheless, as discussed in **section 3.2.1**, systematic ACF data over several years could be helpful in informing *trends* in TB incidence over time.

Table 5 National TB prevalence surveys and ACF campaigns: comparison of key characteristics

Characteristic	National TB prevalence surveys	ACF campaigns	Comments
Population screened	Adults aged ≥15 years meeting residency criteria, in randomly selected survey clusters (to ensure data are nationally representative)	Usually target subpopulations at relatively high risk of having TB and/or geographical areas with relatively high TB disease burden	If ACF targets populations at high risk of TB, or areas with an elevated level of TB disease burden, an adjustment would be required to estimate TB prevalence in the general population. Uncertainty in this adjustment introduces additional uncertainty to the estimate of prevalence.
Number of people screened	Sample size varies, but typically around 30 000–70 000, accounting for clustering and the desired precision of the prevalence estimate	Variable: most typically, thousands; but there are examples of more than 1 million	Recent mass ACF campaign in Uganda (CAST-TB) screened 1.3 million people in its first round (March 2022) and 5.1 million in its second round (September 2022), with the latter equivalent to over 10% of the population (47 million). Mass population screening has been done in the Russian Federation for decades.
Screening algorithm	Interview about symptoms, and chest X-ray	Typically relies on symptom screening, although some recent ACF initiatives are also involving X-ray and ACF in Russian Federation has included X-ray for decades	Prevalence surveys show that relying on symptom screening will miss a large proportion (typically 30 – 70%) of people with bacteriologically positive TB. If screening relies on symptom screening, an upward adjustment would be required to estimate the overall prevalence of bacteriologically positive pulmonary TB in the screened population. This adjustment introduces additional uncertainty to the estimate of prevalence.
Diagnostic algorithm	Two Xpert Ultra tests (to maximize sensitivity) followed by confirmatory testing using liquid culture (MGIT) for all those with a positive rapid test result (to maximise specificity)	Recently, typically relies on single tests with rapid molecular diagnostics	The diagnostic algorithm described for prevalence surveys is the one recommended in the latest (2024) WHO guidance on national TB prevalence surveys. It was defined following extensive discussions, consultations and data analysis *(44)*. Such a high sensitivity, high-specificity algorithm is typically not feasible in ACF; when estimating prevalence, adjustments would be needed, introducing additional uncertainty into prevalence estimates.
Cost	Median of around US$ 3 million; usually in range US$ 1–5 million; more if larger sample size for subnational estimates	Limited data on ACF costs; major cost drivers are likely to be diagnostic testing, X-ray screening (if applied) and staff time required for screening	A large ACF campaign that covers the general population and that uses both chest-Xay for screening and rapid tests for diagnosis will likely cost more than a national TB prevalence survey. It would be more like a national TB prevalence survey (which effectively does ACF in the general population, but at a small scale determined by sample size requirements) at a very large scale.
Standardization of procedures	Survey methods are standardized and need to be adhered to in practice, with strong oversight, training and supervision	ACF can be based on standardized procedures; the extent to which training, oversight and supervision are provided may vary	Prevalence surveys are based on clearly defined standard operating procedures (SOPs), which are set out in the survey protocol and associated documentation, and which should be closely supervised and monitored throughout. If procedures vary in ACF campaigns, this makes them less useful for burden estimation. In future, systematic guidance on making ACF useful for burden estimation may be helpful in addressing these challenges.
Data collection and data management	Specific database used for survey data collection, with a data management plan/protocol involving systematic data quality checks and regular data cleaning throughout the survey	ACF can also use a specific database although no systematic data management plan is currently available	In the absence of a systematic framework, overall data quality in ACF campaigns may vary depending on the context, potentially posing challenges in using these data for burden estimation. As above, incorporating new frameworks for database setup and management could be a useful component in future guidance on making ACF useful for burden estimation
Frequency	Every 10 years (approximately)	Variable, but could be annually or even more frequently	If ACF is repeated, it offers the clear benefit of providing data much more frequently than a prevalence survey. Such data could be used to inform trends; however, the trend might be different in targeted populations, compared with the general population.

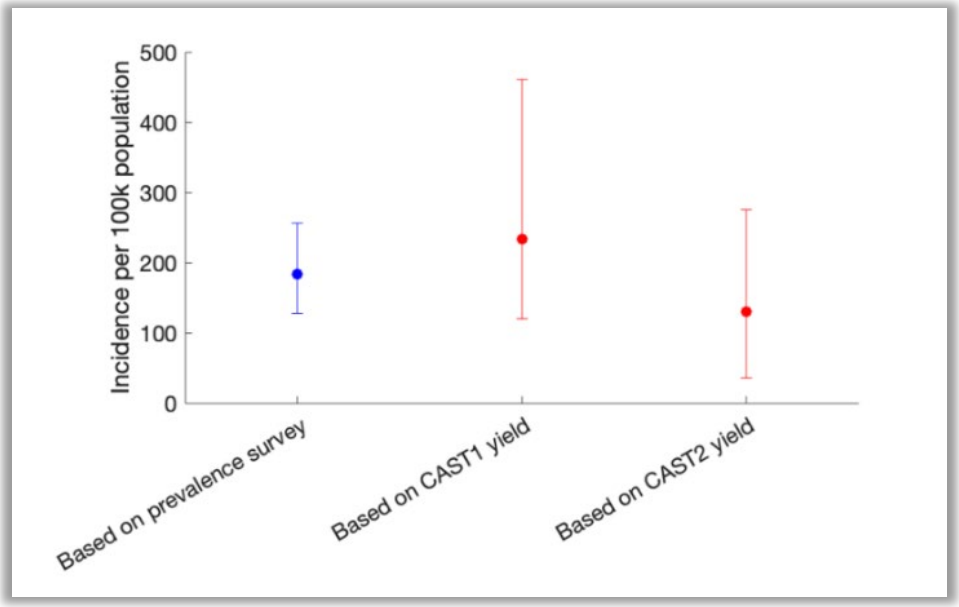
Box 1 'Dual purpose' interventions: could data from active case-finding be useful for estimating TB incidence?

In Uganda, the "Community Awareness, Screening, Testing, Prevention and Treatment to End TB and Leprosy" (CAST-TB) initiative began in 2022, to screen and test for TB in the community *(45, 46)*. Involving over 70 000 community healthcare workers, this initiative placed emphasis on raising community awareness of TB and case finding as well as strengthening links between communities and facilities, to improve treatment outcomes. Individuals were screened for symptoms, and those with symptoms suggestive of TB offered sputum sample for testing with Xpert Ultra.

In the first round of CAST-TB in March 2022, 1.29 million people were screened (out of a population of 44 million [2022]), of whom 179 144 screened positive, 117 975 were tested and 4043 were positive for TB. However, this round involved a strong component of addressing the backlog of close contacts of previously notified cases, as well as focusing efforts in high-prevalence settings such as prisons. In the second round of CAST-TB in September 2022, 5.13 million people were screened, of whom 428 444 screened positive, 225 813 were tested and 8121 were positive for TB. Although this round employed more door-to-door screening, given that it was implemented as an intervention, not as a study or survey, it is unclear how representative the screened population may have been, of TB burden in the country as a whole. Finally, unlike in a prevalence survey, due to the scale of the intervention and available resources, it was not possible to include culture confirmation of Xpert positive results. Overall, therefore, any burden estimates based on data from this intervention would need to make three corrections: one for the proportion of cases that report symptoms; another for the relative risk of TB in the screened population, relative to the general population, and another for the specificity and sensitivity of the confirmatory algorithm being used.

Fig. B1.1 shows incidence estimates incorporating, for illustration, the first two of these adjustments (red lines).

Fig. B1.1 Model-based estimates of incidence in Uganda, based on data from the 2015 national prevalence survey (in blue), and from recent rounds of ACF in the country.
A simple model of TB transmission dynamics was applied, simulating this model to equilibrium and calibrating separately to these different sources of data. For ACF-derived estimates, if Y is ACF yield, p is the proportion of TB that is symptomatic and R is the relative risk of TB in the screened population relative to the general population, the overall country-level prevalence is estimated simply as $Y/(pR)$. As described in the text, we assumed p to be uniformly distributed between 0.4 and 0.7. For the first round of CAST-TB, we assumed R to be to be uniformly distributed between 1 and 6; for the second round, we assumed R to follow a truncated exponential distribution, with boundaries at 1 and 6 (i.e. one more heavily weighted towards 1).



In **Fig. B1.1**, it is assumed that the screened population has a 1–6-fold relative risk of TB, compared with the general population. For the first round of CAST-TB this relative risk is modelled as a uniform distribution. As noted above, the second round involved a stronger component of door-to-door screening. Following discussion with the Uganda NTP, the relative risk in this round was thus modelled using a truncated exponential distribution (i.e. one weighted towards 1), reflecting expectation that any preferential screening in high-risk areas, while plausible, was unlikely to be so strong as to involve a six-fold relative risk. It is further assumed that 40–70% of overall TB prevalence is symptomatic (again, uniformly distributed). For comparison, the figure also shows incidence estimates derived from Uganda's prevalence survey from 2015, using model-based

methods similar to those previously employed by WHO for countries with prevalence survey data (blue line). For simplicity, estimates shown by the red lines do not include adjustments of the specificity of the confirmatory algorithm: doing so in a systematic way will require careful consideration of appropriate assumptions for specificity of Xpert Ultra, in this screened population. Nonetheless, the results serve to illustrate some salient comparisons between these different approaches.

In particular, based on ACF data alone, incidence estimates have substantially wider uncertainty than those based on national TB prevalence survey data. Moreover, central estimates vary considerably from those derived from national TB prevalence survey data. Even though the second round of CAST-TB involved a stronger component of door-to-door screening, it yields a central incidence estimate of 113 per 100 000 population, compared to 183 per 100 000 population for prevalence survey-derived estimates. Overall, because ACF efforts are typically not conducted in nationally representative populations and rely on symptom screening, they introduce important uncertainties that render them less informative for incidence estimation than prevalence survey data.

It is nonetheless important to explore the use of ACF data in combination with national TB prevalence survey data, to inform estimation of trends (see **section 3.2.1**). Moreover, given the sheer scale of CAST-TB, with minor adjustments to its design, it may be possible for this initiative to exert public health impact at the same time as improving burden estimates. For example, there could be value in a 'nested' study, where selected villages (or clusters) see an implementation of CAST-TB that is specifically geared towards collecting data for burden estimation: for example, placing more emphasis on screening populations that are representative of burden at the country level, and inclusion of chest X-ray as well as symptom screening. Appropriately selected, such clusters may also be informative for subnational burden estimation, which is not possible with current survey approaches. In such a design, there are important questions around the size of this 'nested' component, site selection, etc. To address such questions, a costing of CAST-TB – including these 'nested' activities - would be very helpful. Such costing would help to judge the affordability and cost-effectiveness of these and other potential designs for CAST-TB.

3.4 Option 4: Case notification data combined with an upward adjustment based on the SDG UHC service coverage index

Potential application/relevance:

a) Countries for which incidence estimates currently rely on notification data combined with expert opinion about underreporting, underdiagnosis and overdiagnosis (to replace current method 4)

b) Countries for which incidence estimates currently rely on notification data combined with a standard upward adjustment (to replace current method 3)

3.4.1 Countries for which TB incidence estimates currently rely on use of notification data combined with expert opinion about the level of underreporting, under-diagnosis and overdiagnosis

For 39 countries that accounted for 11% of the estimated global number of incident TB cases in 2019, TB incidence estimates rely on the use of case notification data combined with expert opinion (elicited in regional workshops, national consensus workshops or country missions) about underreporting of detected TB cases, underdiagnosis and overdiagnosis,[15] with trends estimated using either mortality data, national repeat surveys of the annual risk of infection or exponential interpolation using estimates of case detection gaps for specific years (method 4 in **Section 1**). Of the methods currently used by WHO for estimation of TB incidence, this is the weakest (due to its heavy reliance on expert opinion) and a more robust, replicable and standardized alternative is highly desirable.

One possible approach is to use existing, routinely-reported health system indicators, to inform estimates of TB treatment coverage (defined as the estimated percentage of incident TB cases that are notified and treated). In particular, the SDGs include a target to achieve universal health coverage (UHC) by 2030.[16] UHC means that everyone can obtain the health services they need without suffering financial hardship *(48)*. Two indicators are used to monitor progress: a UHC service coverage index

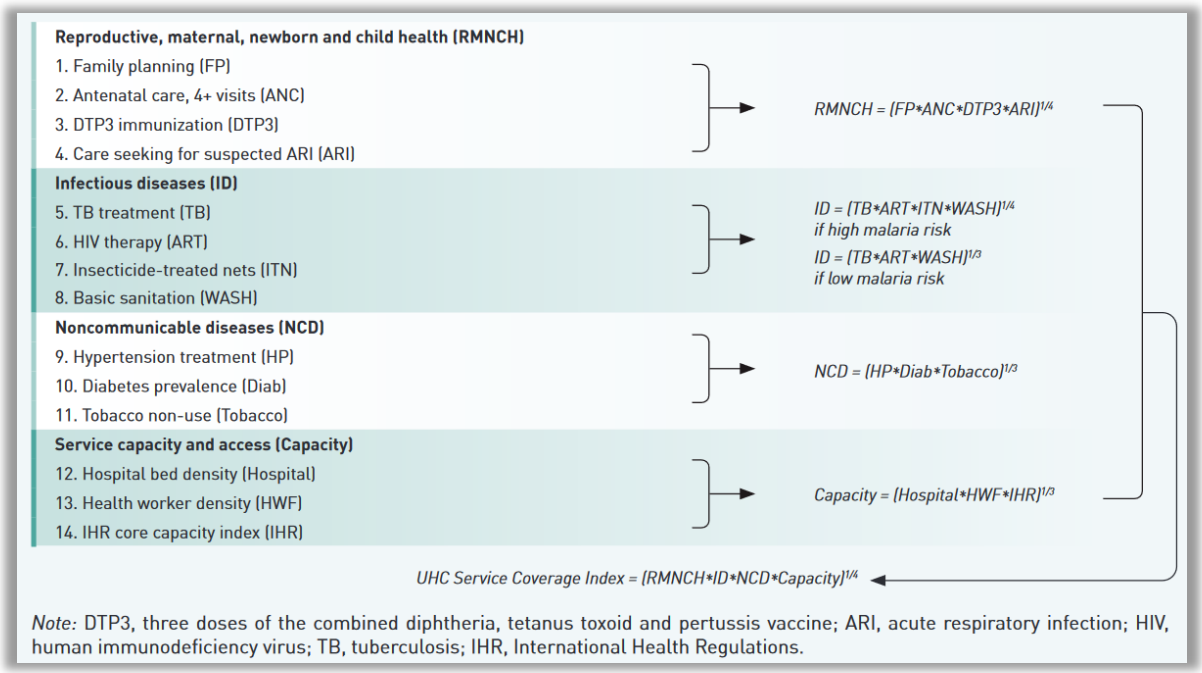
[15] For example, due to systematic screening in populations with a relatively low probability of TB disease.

[16] Target 3.8 is "Achieve universal health coverage, including financial risk protection, access to quality essential health-care services and access to safe, effective, quality and affordable essential medicines and vaccines for all" *(47)*.

(SCI) (Indicator 3.8.1), and the percentage of the population experiencing household expenditures on health care that are "large" in relation to household expenditures or income (Indicator 3.8.2).

The UHC SCI can take values from 0 (worst) to 100 (best). It is calculated as the geometric mean of 14 "tracer" indicators for the coverage of health care, one of which is TB treatment coverage (**Fig. 6**).

Fig. 6 Tracer indicators that are used to calculate the UHC SCI
This figure is reproduced from the 2023 WHO global monitoring report on progress towards UHC *(49)*.



Estimates of the UHC SCI were first published by WHO and the World Bank in a UHC monitoring report in 2017. The latest WHO report (published in September 2023) includes estimates for all WHO and UN Member States for 7 years: 2000, 2005, 2010, 2015, 2017, 2019 and 2021 *(50)*. To date, WHO has published reports that include UHC SCI estimates every 2 years; the latest year for which estimates are published in each report is the report year - 2 (for example, the 2023 report included estimates up to 2021). It is anticipated that reports with UHC SCI estimates for every WHO and UN Member State will continue to be published every 2 years until at least 2030; the next report is due for publication in 2025.

With estimates of the overall coverage of health care now available for all WHO and UN Member States for 2000–2021, which are calculated in a standardized way, which will continue to be produced every 2 years until at least 2030 and which are discussed with and reviewed by countries prior to their publication (a process managed by WHO's Data and Analytics department), the UHC SCI offers a potential proxy for TB treatment coverage in countries where no other data are systematically available for use. In other words, TB incidence could be estimated using TB case notification data that are upward adjusted using the UHC SCI (replacing an upward adjustment based on expert opinion).

This approach would be in two steps:

- Step 1: predict TB treatment coverage using the UHC SCI profile over time, using a statistical model;
- Step 2: estimate TB incidence using TB case notification data (routinely reported to WHO by all Member States every year) that are upward adjusted according to the predicted TB treatment coverage at Step 1 (replacing expert opinion).

Analysis for Step 1 was performed using data from 31 countries[17] *(6)* in which at least one national TB prevalence survey was implemented between 2000 and 2021 (since TB incidence estimates are derived

[17] Bangladesh, Cambodia, China, Democratic People's Republic of Korea, Eswatini, Ethiopia, Gambia, Ghana, India, Indonesia, Kenya, Lao People's Democratic Republic, Lesotho, Malawi, Mongolia, Mozambique, Myanmar, Namibia, Nepal, Nigeria, Pakistan, Philippines, Rwanda, South Africa, Sudan, Thailand, Uganda, United Republic of Tanzania, Viet Nam, Zambia and Zimbabwe.

from a direct, population-based measurement of TB disease burden in these countries). Using estimates of TB treatment coverage in these 31 countries (a total of 711 country-year data points), a linear mixed regression model with a random intercept to account for country variability was fitted with TB treatment coverage as the dependent variable and the UHC SCI, a 2-degree polynomial of time, WHO region and two-way interactions as independent variables (this model could evolve in the future depending on the fitting of the observed data, for example using another function of time):

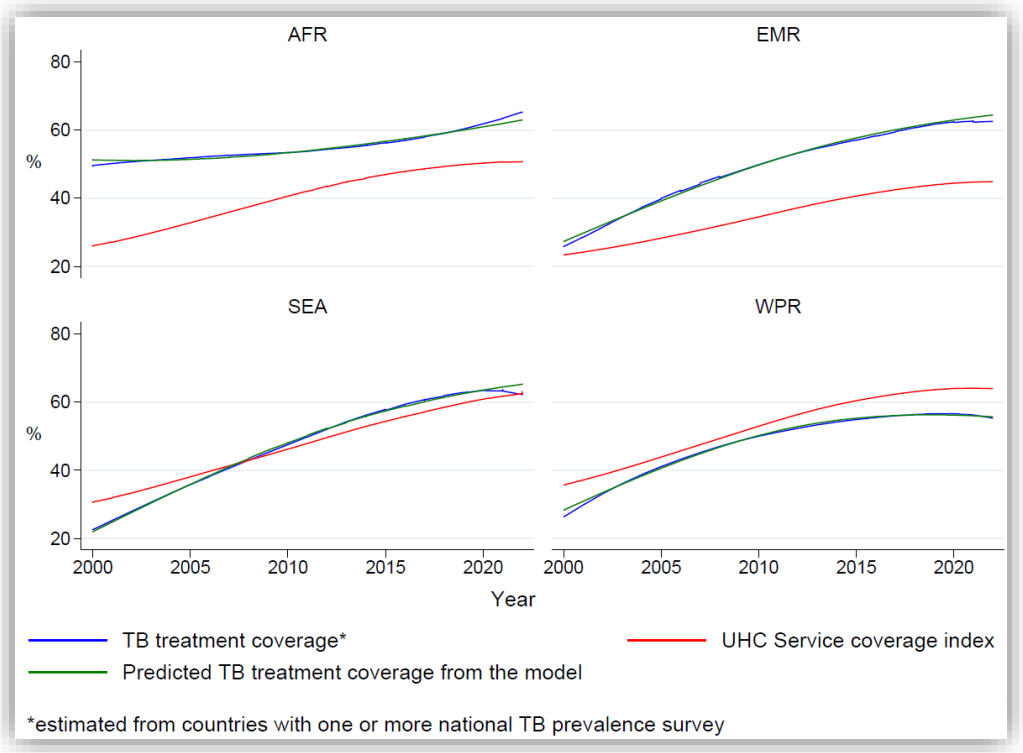
$$y_{i,j} = \beta_0 + \beta_1 t_{i,j} + \beta_2 t_{i,j}^2 + \beta_3 UHCSCI_{i,j} + \beta_4 UHCSCI_{i,j} * t_{i,j} + \beta_5 UHCSCI_{i,j} * t_{i,j}^2 + \beta_6 Region_{i,j} + \beta_7 Region_{i,j} * t_{i,j} + \beta_8 Region_{i,j} * t_{i,j}^2 + \alpha_i + \varepsilon_{i,j}$$

Where,

- $y_{i,j}$ is the treatment coverage of country *i* in year *j*
- $t_{i,j}$ and $t_{i,j}^2$ a 2-degree polynomial of time (year 2000–2022)
- $UHCSCI_{i,j}$ the Universal Health Coverage service coverage index for country *i* at year *j*
- $Region_{i,j}$ the WHO region for country *i*
- α_i the random intercept for country *i*
- $\varepsilon_{i,j}$ the residuals, normally distributed

Results from the goodness of fit of the model are shown in **Fig. 7**. There was a good fit of the data in all of the four WHO regions that include countries where national TB prevalence surveys have been implemented,[18] showing that a very good prediction of TB treatment coverage could be made in these countries based on the UHC SCI, time and WHO region. External validation of the model was not possible due to the current lack of a good candidate for validation. However, cross validation among the 31 countries is currently under consideration.

Fig. 7 Goodness of fit of the linear mixed model to predict TB treatment coverage, for the four WHO regions in which results from national TB prevalence surveys have been used for estimation of TB incidence, 2000–2022



AFR, African Region; EMR, Eastern Mediterranean Region; SEA, South-East Asia Region; WPR, Western Pacific Region.

[18] Surveys have *not* been implemented in the Region of the Americas or the European Region.

For Step 2, the estimated parameters of the model can then be used to estimate TB treatment coverage $\widehat{y_{i,j}}$ in the 39 countries i at year j where case notification data ($n_{i,j}$) combined with expert opinion about underreporting, underdiagnosis and overdiagnosis are currently used. TB incidence $I_{i,j}$ is then estimated as:

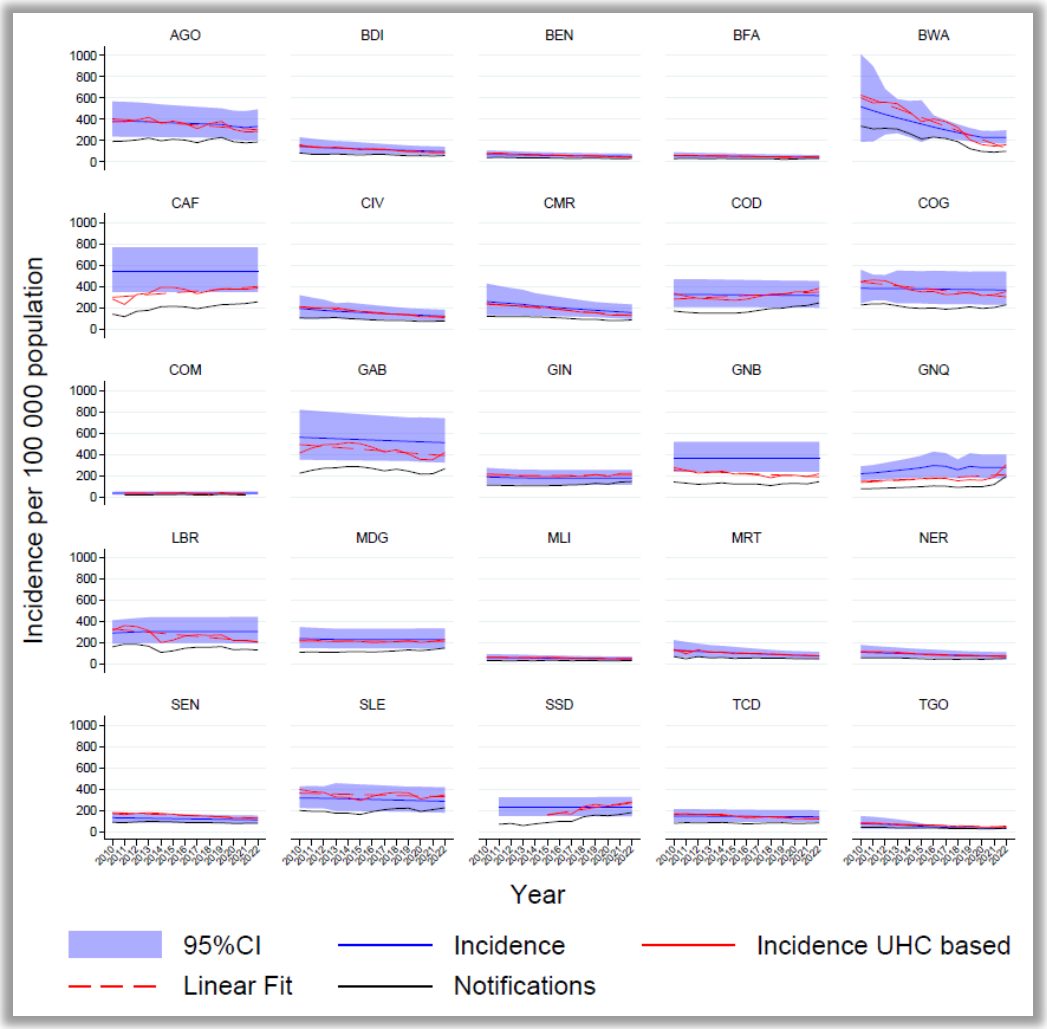
$$I_{i,j} = \frac{n_{i,j}}{\widehat{y_{i,j}}}$$

For illustration, **Fig. 8** shows the resulting estimates of TB incidence for the subset of 25 countries in the WHO African Region, compared with the currently published estimates that are based on expert opinion.

The estimates based on use of the UHC SCI (red lines) are close to the current best estimates in most countries; when there is more divergence, the UHC SCI estimates are still usually within the 95% uncertainty interval of the current estimates. The exceptions (estimates based on use of the UHC SCI outside the 95% uncertainty interval of the current estimates) are Guinea Bissau and Equatorial Guinea. Once uncertainty intervals are added to the UHC SCI-based estimates (see **section 3.4.3** below), the estimates may overlap. Where they do not, further discussion will be valuable in determining which estimate is likely to be more reliable.

If this approach is adopted, it would be necessary to re-analyse the UHC SCI estimates each time a new update is published, to explore the updated trends in countries for which it is used. If an update includes an unexpected change (e.g. a sudden increase or decrease in the UHC SCI), this change might not be well captured by the statistical model and updated country-specific customization might be required.

Fig. 8 Estimates of TB incidence based on TB case notification data and the UHC SCI (red line), compared with existing estimates based on TB case notification data and expert opinion (blue curves), 25 countries in the WHO African Region, 2010–2022



3.4.2 For high-income countries where a standard adjustment was used to assess under-reporting and under-diagnosis

Currently, TB case notification data combined with a standard upward adjustment (based on expert opinion informed by a limited number of inventory studies) that allows for a limited amount of underreporting of people diagnosed with TB as well as some underdiagnosis or overdiagnosis, are used to produce estimates of TB incidence for 137 countries (**section 1.3**).

It would be preferable to use an approach that remains standardized and grounded in routine TB case notification data, but also more customized if possible, based on other routinely available information. One possibility is to use the UHC SCI, without any further adjustment, as an approximation of TB treatment coverage (defined as the percentage of incident TB cases that are notified and treated).

TB incidence $I_{i,j}$ is then estimated as:

$$I_{i,j} = \frac{n_{i,j}}{UHC_{i,j}}$$

where $UHC_{i,j}$ is the UHC SCI of country i at year j, and $n_{i,j}$ the case notification of country i at year j.

Of note, UHC SCI values in the best-performing countries are around 85, which is consistent with the standard adjustment that has been used to date.

Fig. 9 and **Fig. 10** show estimates of TB incidence based on the current approach (notification data with standard adjustment) and this alternative approach (notification data adjusted based on the UHC SCI), for countries in the WHO European Region and the Region of the Americas.

Fig. 9 Estimated TB incidence using the UHC SCI as an approximation of TB treatment coverage in the WHO European Region, 2010–2022

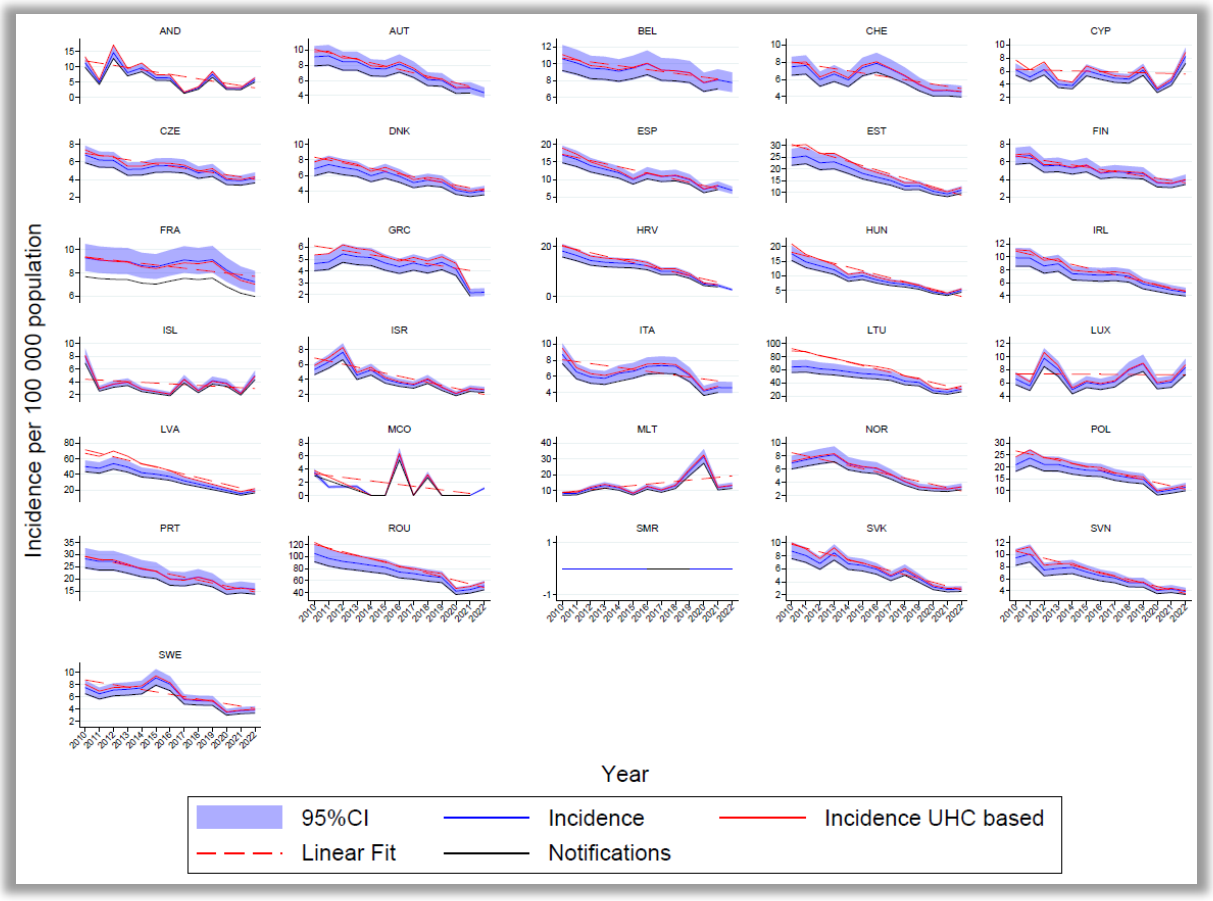
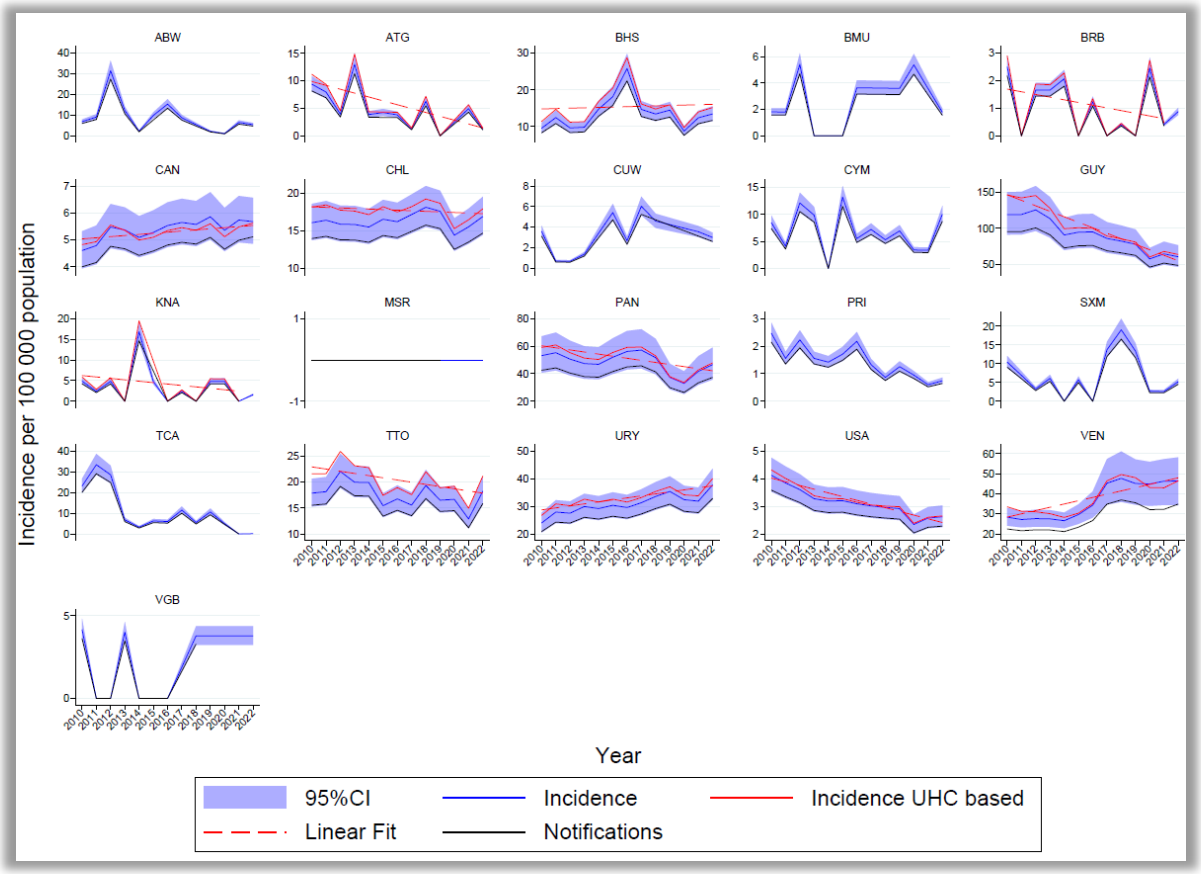


Fig. 10 Estimated TB incidence using the UHC SCI as an approximation of TB treatment coverage in the WHO Region of the Americas, 2010–2022



The estimates based on use of the UHC SCI (red lines) are close to the current best estimates in most countries; when there is more divergence, the UHC SCI estimates are still usually within the 95% uncertainty interval of the current estimates. The exceptions (estimates based on use of the UHC SCI outside or at the edge of the 95% uncertainty interval of the current estimates in several years) in the European Region are Andorra, Cyprus, Estonia, Latvia, Lithuania; and in the Region of the Americas, Argentina, the Bahamas and Trinidad and Tobago. However, once uncertainty intervals are added to the UHC SCI-based estimates (see **section 3.4.3** below), the estimates would probably overlap.

3.4.3 Strengths and limitations

The use of case notification data in combination with the UHC SCI results in estimates of incidence that are consistent with existing estimates for almost all countries, which is reassuring.

The main strength of using the UHC SCI approach, as a replacement for the existing approach of using case notification data combined with expert opinion, is that it does not rely on expert opinion but rather uses a range of indicators that provide information about health service coverage. For countries for which a standard adjustment is currently used, its main advantage is that it allows for more country specificity.

Other strengths are:

- It allows for both standardization and reproducibility, while allowing more country-specific customization.
- It is transparent and easy to explain.
- It relies only on routinely available estimates, which are available for almost all countries and areas.
- It is relatively quick and straightforward to implement.
- It is not resource-intensive - it is not time consuming, nor does it require considerable investment in country consultations during which expert opinion is elicited.

All of these strengths represent advantages over the two currently used approaches.

Limitations include:

- A rise in TB case notifications will imply a rise in TB incidence. However, this might be incorrect if an increase in TB case notifications reflects improvements in case finding, diagnosis and treatment.
- TB treatment coverage in the 31 countries where a prevalence survey was implemented may also rely on non-data driven assumptions about trends in TB incidence after the prevalence survey, including a flat trend (and an underlying flat treatment coverage).
- The UHC SCI is calculated using a geometric mean of sub-indexes of health coverage, including TB treatment coverage (using estimates provided by GTB). Therefore, the UHC SCI is not fully independent of the TB treatment coverage estimates used in the statistical model. However, 13 other indicators are also used to compute the UHC SCI. It was not possible to perform an analysis in which TB treatment coverage was excluded from the UHC SCI; however, this is not expected to make much difference to UHC SCI values.
- There are currently no estimates of the standard error of the UHC SCI. This means that no direct estimation of the standard error (and relative uncertainty intervals) for estimates of TB incidence is possible. To include uncertainty intervals for TB estimates using this approach, it would be necessary to make an assumption about the standard error.
- As for any statistical model, the linear model used in **section 3.4.1** relies on several assumptions (e.g., a linear relationship between independent variable and dependent variables, the independent variable is normally distributed, the independent variables are all linearly independent).
- The model would require validation every year and updates might be required to improve the goodness of fit.
- UHC SCI estimates are only available for specific years (2000, 2005, 2010, 2015, 2017, 2019, 2021); a linear interpolation was used to impute data for other years.
- The time period for which estimates of the UHC SHI are available lags behind the time period for which estimates are required for the WHO Global TB Report (e.g. the WHO Global TB Report for 2024 will include estimates of TB incidence up to 2023, but the latest year for which estimates of the UHC SCI will be available for this report are 2021). In the analyses above, estimates for 2022 were based on use of the last observation carried forward (LOCF) method, including in countries with important COVID-19 disruptions. For most countries this approach may be a reasonable approximation, given that the SCI does not typically show rapid changes from one period to the next.
- If there are sudden changes in TB case notifications (increase or decreases), the lag time for UHC SCI estimates could be problematic. Such cases would need specific, more customized attention.[19]
- Estimates of the UHC SCI are not available for some countries or areas (20 high income countries using standard adjustment, and one using expert opinion (Anguilla)) with small populations. For these countries, it would be necessary to use an alternative approach, such as a regional average of the UHC SCI or UHC SCI values from a similar neighboring country.
- In the WHO Region of the Americas and the European Region, no TB prevalence survey has been implemented and as such, there were no data available to fit the statistical model described in **section 3.4.1**. For the few countries in these regions for which incidence estimates are currently based on expert opinion (two in each region), specific customization may be required.

[19] If implemented, systematic data checking would be required for all countries for which this approach is used, to detect any significant change in TB notifications (e.g., +/- 20% as compared to previous year).

3.5 Option 5: Informing incidence estimates using TB mortality data

Potential application/relevance:
Countries with national or sample VR data of sufficient quality and coverage
Countries that have implemented a TB mortality survey

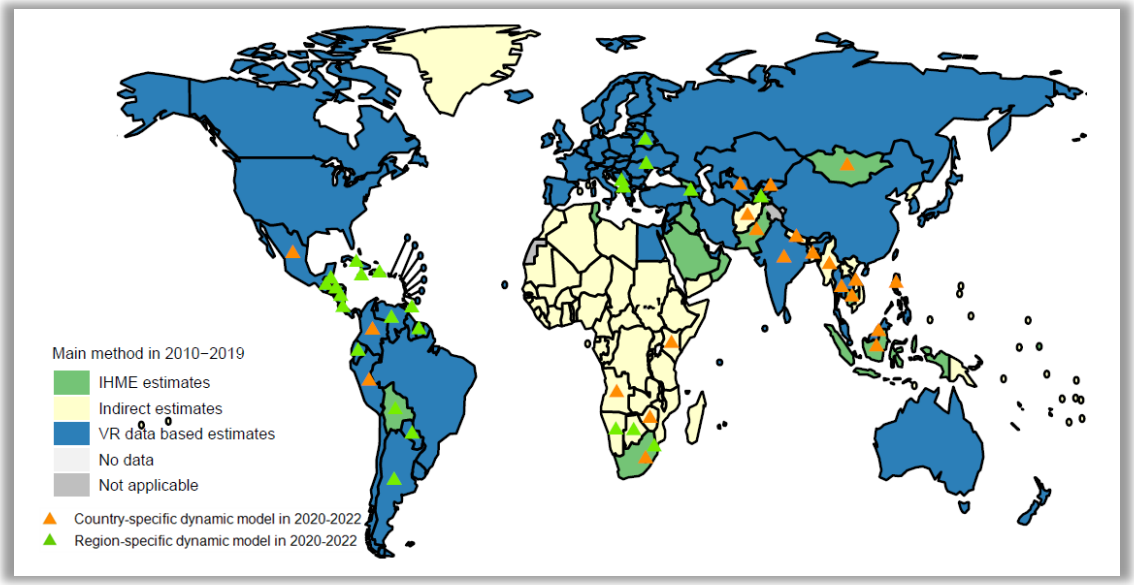
3.5.1 Informing incidence using TB mortality data, for countries with good VR systems

In countries with strong vital registration systems, data for TB mortality could offer valuable evidence for informing estimates of TB incidence. For example, recent modelling work in Brazil brought together different sources of data for TB burden to estimate incidence, with mortality data playing a critical role *(51)*. In essence, mortality data substantially narrows the range of possible incidence that could have led to that mortality.

A limitation of 'back-calculation' of incidence from mortality data is that it is generally only appropriate in countries with robust VR data. Crucially, TB mortality data should include not only those who died while on TB treatment (information that is routinely available in TB programmatic data), but also data about TB deaths among those who had not been diagnosed and notified with TB before death.

The countries for which national or sample VR data are currently used to produce estimates of TB mortality are shown in **Fig. 11**.

Fig. 11 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



3.5.2 Data from TB mortality studies to inform estimates of underdiagnosis

Even in countries without strong VR systems, there is valuable information to be obtained from mortality surveys, especially to provide evidence about the extent to which there is underdiagnosis of people with TB. Prevalence surveys cannot provide such information, because they produce only a cross-sectional view of TB burden.

A recent example is a TB mortality survey conducted by the Public Health Foundation of India, in the context of updating their post-pandemic TB burden estimates (R. Rao, *personal communication*, November 2023). This survey highlighted a substantial proportion of TB that had gone undiagnosed (including by the private sector), and played an important role in validating model-based estimates (see **section 1**). One point of discussion is whether such surveys should be encouraged in other settings as well.

To be applicable across settings, ideally surveys should follow a standard approach in identifying a history of TB. Even then, surveys only provide indirect evidence about TB incidence; their key benefit is to help characterise the proportion of TB that does undiagnosed. They may represent underestimates, since mild TB symptoms, followed by death from other causes, would go unrecognised.

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 incidence 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 **for 2025** in the table are:

- A prevalence survey (as described in **section 1.1**) combined with other data to inform assessment of trends. New options for assessment of trends include use of both routinely available data and data from periodic or ongoing interventions (e.g. ACF), as discussed in **section 3.2**. The methods for converting estimates of prevalence into estimates of incidence may also need updating (as discussed in **section 3.1**).
- An inventory study (as described in **section 1.2**) combined with use of routinely available data to inform trends. Routinely available data refer primarily to notification data, which could also be used alongside findings from routine record-linkage exercises.
- Case notification data with an upward adjustment according to the UHC SCI (as discussed in **section 3.4**). In **Table 6**, the initial mapping suggests this method for all countries for which estimates currently rely on a combination of notification data and expert opinion (**section 1.4**).

As commented in **Table 6**, the use of country and region-specific models remains relevant for estimation of TB incidence in a subset of countries during the period 2020–2022 (to account for COVID-related disruptions and their aftermath). Cross-validation of incidence estimates using TB mortality data is likely to be relevant in some countries; the main example indicated in **Table 6** is Brazil.

The main options considered **for 2030** in the table are the same as those for 2025 for 14/33 countries. For the other countries, **the main difference is that a repeat national TB prevalence survey in the period 2025–2030 becomes an option** for 19 countries: 10 in the African Region (Ethiopia, Kenya, Lesotho, Mozambique, Namibia, Nigeria, Uganda, the United Republic of Tanzania, Zambia, Zimbabwe), one in the Eastern Mediterranean Region (Pakistan), five in the South-East Asia Region (Bangladesh, DPR Korea, India, Indonesia, Myanmar) and three in the Western Pacific Region (Mongolia, Philippines, Viet Nam). This is in contrast to the period up to the end of 2025, when it is recognized that there is insufficient time to allow for the planning and implementation of a repeat survey in time for results to inform an assessment of progress with respect to the 2025 milestone. As commented in the table, however, results from repeat national TB prevalence surveys in the period 2025–2030 could be used not only for the 2030 target assessment, but also to revise/refine estimates of the progress that was made up to 2025.

In several of the countries where a repeat national TB prevalence survey is indicated as an option, there is already country interest in undertaking a repeat survey. These include Ethiopia, Nigeria, Uganda and the United Republic of Tanzania in the African Region; Pakistan in the Eastern Mediterranean Region; Bangladesh and Indonesia in the South-East Asia Region; and Viet Nam in the Western Pacific Region.

As discussed in **section 3.3**, the option of a nested study within a mass community ACF campaign could be an alternative to a stand-alone national TB prevalence survey, in countries where mass ACF is expected to be done in the period 2025–2030.

For some countries that implemented a national TB prevalence survey in the period 2007–2021, alternative options for consideration are indicated in **Table 6**: these include Indonesia, Lesotho, Mongolia, Mozambique, Namibia, South Africa, Thailand and Zimbabwe.

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 case notification data and expert opinion. Substitute this approach with the new method that uses case notification data in combination with the UHC SCI.
- Countries for which the current method relies on case notification data with a standard adjustment. Substitute this approach with the new method that uses case notification data in combination with the UHC SCI.
- Countries for which the current method relies on a national TB prevalence survey combined with other data or assumptions to inform trends. Substitute this approach with one of the two options that includes use of prevalence survey data that is shown in **Table 6** i.e. use of data from an existing prevalence survey combined with either a) a new approach to inform assessment of trends before and after the survey, or b) a repeat survey. As highlighted for high TB burden and global TB watchlist countries, a revised approach to the method for transforming estimates of prevalence into estimates of incidence may also be relevant.
- Countries for which the current method relies on an inventory study. Continue to use this method, with trends informed by either a repeat study or routinely available data (i.e. notification data, possibly combined with routine record-linkage exercises).

Table 6 Data sources and methods for 2025 milestone and 2030 targets 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. Asterisks indicate proposed options; if in brackets, the option is mapped as a likely "second choice" option.
CN, case notifications; COD, cause of death; CS, country-specific; IS, inventory study; PS, prevalence survey; RS, region-specific; SA, standard adjustment; UHC SHI, Universal Health Coverage Service Coverage Index

Country	Current data source(s), analytical method	2025 milestone assessment					2030 target assessment				
		PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments	Repeat PS(s) in period 2025–2030, or existing PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments
AFRICAN REGION											
Angola	CN, CS model			∗	?	CS model remains relevant for 2020–2022.			∗	?	Use same method as for 2025.
Central African Republic	CN, expert opinion			∗	?	PS unlikely to be feasible (e.g. security concerns).			∗	?	Use same method as for 2025.
Congo	CN, expert opinion			∗	?	PS unlikely to be feasible (e.g. security, geographic inaccessibility).			∗	?	Use same method as for 2025.
DR Congo	CN, expert opinion			∗	?	PS unlikely to be feasible (e.g. security, geographic inaccessibility).			∗	?	Use same method as for 2025.
Ethiopia	PS (2011), CN inform trends	∗				Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030. Consistent decline in N up to 2022.	∗ (repeat PS under discussion in country)				Repeat PS feasible in period 2025-2030, would allow direct measurement of change vs 2015.
Gabon	CN, expert opinion			∗	?	PS may not be feasible.			∗	?	Use same method as for 2025.
Kenya	PS (2015–2016), CS model, CN to inform trends	∗				Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030. CS model still relevant for 2020–2022.	∗ (there is interest in repeat PS at country level)				Repeat PS feasible in period 2025-2030, would allow direct measurement of change vs 2015.
Lesotho	PS (2019), CS model, CN to inform trends	∗				Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated based later, if a repeat survey in period 2025-2030.	(∗)		∗		Repeat PS feasible in period 2025-2030. However, high cost relative to total TB spending.

Country	Current data source(s), analytical method	2025 milestone assessment					2030 target assessment				
		PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments	Repeat PS(s) in period 2025–2030, or existing PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments
AFRICAN REGION (continued)											
Liberia	CN, expert opinion			∗	?	PS may not be feasible.			∗	?	Use same method as for 2025.
Mozambique	PS (2018–2019), assumption of flat trend	∗				Need for better use of data to inform trend. Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030.	∗		∗		Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2018.
Namibia	PS (2018), CN inform trends, RS model	∗				Trend for years prior to PS and up to 2019 based on CN (consistent decline driven by HIV epidemic, ART coverage). RS model remains relevant for 2020–2022.	(∗)		∗		Repeat survey may not be best option (challenges with lab testing in 2018).
Nigeria	PS (2012), assumption of flat trend	∗				Need for better use of data to inform trend (e.g. doubling in TB notification rates, 2019–2022). Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030.	∗ (there is interest in repeat PS at country level)		∗		Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2012.
Sierra Leone	CN, expert opinion			∗	?	PS may not be feasible.			∗	?	Use same method as for 2025.
South Africa	PS (2017-2019), CN inform trends	∗				PS not feasible before 2025. Trend based on CN (decline driven by HIV epidemic, ART coverage).	∗		∗		Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2017-2019.
Uganda	PS (2014-2015)	∗				Almost flat trend, needs review. CN approaching estimated incidence. Current discussions about CAST-TB data. Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030.	∗ (there is interest in repeat PS at country level, combined with CAST-TB)				Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2015.

Country	Current data source(s), analytical method	2025 milestone assessment					2030 target assessment				
		PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments	Repeat PS(s) in period 2025–2030, or existing PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments
AFRICAN REGION (continued)											
UR Tanzania	PS (2012), CN to inform trend	∗				Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030. Trend based on CN (consistent decline driven by HIV epidemic, ART coverage).	∗				Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2012. US CDC working with NTP on developing protocol for repeat PS in next 1-2 years.
Zambia	PS (2013-2014), CN to inform trend	∗				Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030. Trend based on CN (consistent decline driven by HIV epidemic, ART coverage).	∗ (there is interest in repeat PS at country level)				Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2013-2014.
Zimbabwe	PS (2014), CN to inform trend, CS model	∗				Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030. Trend based on CN (consistent decline driven by HIV epidemic, ART coverage). CS model remains relevant for 2020–2022.	∗		∗		Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2013-2014. Feasibility of repeat survey needs to be assessed.
REGION OF THE AMERICAS											
Brazil	CN with SA, CS model			∗		UHC SCI could replace SA. Epi review in 2024 opportunity to explore options. Crosscheck using VR data.			∗		Use same method as for 2025.
EASTERN MEDITERRANEAN REGION											
Pakistan	PS (2011), CS model	∗				Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030.	∗ (country discussing repeat PS)				Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2011.
EUROPEAN REGION											
Russian Federation	CN with SA			∗					∗		

Country	Current data source(s), analytical method	2025 milestone assessment					2030 target assessment				
		PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments	Repeat PS(s) in period 2025–2030, or existing PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments
SOUTH-EAST ASIA REGION											
Bangladesh	PS (2015-2016), assumption of flat trend	∗				Need for better use of data to inform trend. Repeat PS not feasible before 2025 but 2015-2025 estimates could be updated later if repeat PS in period 2025-2030.	∗				Repeat PS feasible in period 2025-2030, would allow direct assessment of change vs 2015.
DPR Korea	PS (2016), assumption of flat trend	∗		∗		Need for better use of data to inform trend. Repeat PS not feasible by 2025.	(∗)		∗		Repeat PS may not be feasible.
India	CN, PS (2019-2021), CS model	∗			∗	Existing CS model to be further developed to include use of laboratory data and potentially subnational certification data, mortality survey results, expansion of TPT and ACF.	∗				CS model further expanded to include additional data sources (e.g., ACF yield, up to date SRS COD data).
Indonesia	CN, IS (2015-2016), CS model		∗ (repeat study in 2024)			Utility of 2024 inventory study results to be assessed mid-2024. Considerable efforts have been made to reduce underreporting through record linkage with national health insurance system (NHIS). CS model remains relevant for 2020–2022.	? (there is country interest but it may not be necessary)	∗			Depending on utility of 2024 IS, repeat study or routine record-linkage (e.g. with NHIS) required.
Myanmar	PSs (2009–2010, 2017–2018), CS model	∗				Third PS not feasible before 2025. CS model remains relevant for 2020–2022.	∗		∗		Unclear if third PS possible in period 2025-2030. Existing PS could be used alongside other data, possibly combined with use of CN adjusted for UHC SHI for some years?
Thailand	PS (2012), CS model	∗	∗	∗		IS would be useful to directly assess underreporting. Thailand is only HBC that has high level of UHC SCI (80) and financial protection. VR data could help for cross-checking. CS model remains relevant for 2020–2022.		∗	∗		There is country interest in a repeat PS, but low participation in last survey (data from Bangkok clusters could not be used). IS could be more informative. Use of UHC SCI also an option.

Country	Current data source(s), analytical method	2025 milestone assessment					2030 target assessment				
		PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments	Repeat PS(s) in period 2025–2030, or existing PS(s) PLUS other data to inform trends	IS PLUS routinely available data to inform trends	CN adjusted using UHC SCI	Other	Comments
WESTERN PACIFIC REGION											
Cambodia	Repeat PSs (2002, 2011), CS model	⁎				Repeat PS due to be completed in July 2024, with results available by around end September 2024. CS model remains relevant for 2020–2022.	⁎				Results from repeat PS expected around September 2024.
China	CN data and inventory study (IS)		⁎			Would be helpful for WHO to have access to more detailed IS results. Updated S&B assessment would also be useful. Worth exploring if record-linkage could be done annually.		⁎			Use same method as for 2025.
Mongolia	PS (2013-2014), CS model	⁎	⁎			IS recommended in most recent TB epidemiological review (2022). CS model remains relevant for 2020–2022.	(⁎)	⁎			IS recommended in most recent TB epidemiological review (2022).
Papua New Guinea	CN, expert opinion			⁎	?				⁎	?	PS unlikely to be feasible for reasons of security, costs, and geographic inaccessibility.
Philippines	PS (2007, 2016), CS model	⁎	⁎		?	IS under discussion within country. Data available to inform trends include data from screening of emigrants to the United States of America. CS model remains relevant for 2020–2022.	⁎	⁎		?	PS could be done but may not be needed (e.g. if IS done). Data available to inform trends include data from screening of emigrants to the United States of America.
Viet Nam	PS (2006–2007, 2017–2018), CS model	⁎	⁎			IS under discussion within country. CS model remains relevant for 2020–2022.	⁎	⁎			PS could be done but may not be needed (e.g. if IS done).

DPR Korea, Democratic People's Republic of Korea; DR Congo, Democratic Republic of the Congo; UR Tanzania, United Republic of Tanzania.

5. Process for finalization and implementation of options

Based on the current data sources and analytical methods used by WHO to produce TB incidence 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):

- **Expert review of new options to be considered – first round**. This discussion document was circulated to a subset of the people who participated in the most recent (May 2022) Task Force meeting that focused on methods used to produce estimates of TB disease burden, to request their initial feedback on the possible new options that are described in **section 3**, as well as to invite suggestions for additional options. This was done between May and early July.
- **Discussion at June 2024 meeting of WHO's Strategy and Technical Advisory Group for TB (STAG-TB)**. A preview of three of the options described in **section 3** was presented and feedback elicited.
- **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.
- **Revisions based on first round of review and other discussions**. This document was revised in August, based on the first round of feedback as well as ongoing discussions with NTPs and ongoing discussions related to the specific topic of subclinical TB (see **section 3.1**).
- **Circulation of an updated draft 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 options set out in this document as well as existing options 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 options as well as further work on the mapping of existing and new options to countries, according to the outcomes of the Task Force meeting in September**. Further work may be required on new options proposed for consideration and further discussions with countries about the mapping of existing and new options will be necessary.
- **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.
- **Guidance and support for the design, implementation, analysis and reporting of any priority studies needed for periodic, direct measurements of TB disease burden**. The two major types of study (**section 1**) are national TB prevalence surveys in a priority set of countries (unless suitable alternatives can be identified, see **section 3**) and inventory studies to measure the level of underreporting of people diagnosed with TB (possibly combined with capture-recapture analysis to estimate incidence).
- **Concerted efforts to strengthen routine TB surveillance.** Building on progress made since around 2013, intensified efforts to strengthen the quality and coverage of TB case notification systems are important. Ideally, by 2030, a first set of high TB burden countries should have TB surveillance systems that meet all the standards and associated benchmarks in the WHO TB

surveillance checklist that are within the remit of the surveillance system (i.e. 9/10, all those except the standard related to UHC).

- **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.

In terms of priority studies to periodically measure TB disease burden, it is worth highlighting that in the period 2007–2015, intensive and concerted efforts at national, regional and global levels were made to ensure the implementation of national TB prevalence surveys in 22 "global focus" countries. These included national and multi-country workshops (from the development of survey protocols through to analysis of results and dissemination of findings); provision of "end-to-end" expert technical support (through a mix of "Asia-Asia", "Asia-Africa" and "Africa-Africa" collaboration as well as support from international technical agencies), particularly for countries implementing their first-ever surveys; and mobilization of the required funding from domestic and international sources (primarily the Global Fund, but also USAID and JICA). A comparable level of effort may be required in the period 2025–2030, for prevalence surveys and inventory studies.

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Annex 1 Selected feedback on approaches discussed in Section 3, with specific focus on methods for assessing changes in TB incidence over time

As described in section 3.2.3, there is a need for methods to assess how TB incidence is changing over time, for example in the years following a prevalence survey. Among new methods discussed in section 3, some have potential for informing such trend estimates. However, as noted in feedback from an initial round of review by some attending the Task Force meeting, each of these proposed methods has limitations that need to be considered. A sample of such comments is summarised in the table below, for those methods that may have relevance for informing trends. During the Task Force meeting, one key topic of discussion will be on the appropriate way forward for estimating trends in incidence, in light of this collective feedback.

Proposed approach	Sample feedback
Systematic and more routine use of a wider range of programmatic data to inform assumptions **1. Laboratory testing data alongside case notification data (i.e. tracking the 'number needed to test' to identify 1 person with TB)**	***Feasibility:*** Probably needs much more empirical testing first. In particular, is it feasible to have these data reported? ***Cautions in interpretation:*** Even if reported, changes in programme strategy could potentially cause fluctuations in the time series that have nothing to do with true incidence changes. How to keep everything else (e.g. access to care, diagnostic algorithm, population screened) consistent so that changes in the NNT reflect trends or burden? Assuming tests can be disaggregated by passive vs. active case finding, […] these data could improve estimates in a way that is easily explained to national programmes. Laboratory and notification data […] would need to be accompanied by detailed information from the NTP about any changes in programmatic approaches or policy over the time period. ***We don't yet know the specific formula to use:*** Requires further work because a specific quantitative formula has not been proposed. Challenge is how to link those to trends. Even in models there is an assumption of how such changes would impact overall burden?
Systematic and more routine use of a wider range of programmatic data to inform assumptions **2. Modelling the impact of ACF and TPT on incidence and mortality**	***Modelled estimates of impact may not be reliable:*** Generally disfavor the approach of using programmatic data on ACF and TPT through a model to estimate TB incidence - feels too indirect TPT coverage approach needs further work on assumptions of reduction in transmission following TPT, reduction in TB incidence following (non-)completion of TPT, and the coverage of ACF certainly needs more data (from other countries than Uganda, Vietnam), on e.g. methods used for case finding, area, type of population included in ACF, etc. Variability in quality and methods used for ACF interventions within and across countries will challenge this approach. Many countries have ACF implemented in multiple smaller geographic areas by different partners and protocols. Getting reliable, accurate input on fidelity of implementation and standardization of approaches across partners would be challenging, but WHO guidance could help moving forward. Assumptions about the infectiousness of people diagnosed with TB, and their contribution to transmission without ACF would need to be evaluated for each campaign.

Using data from mass ACF as a replacement of prevalence survey data to estimate incidence	***Challenges in using mass ACF data to estimate absolute level of prevalence*** Results from ACF are more uncertain than from prevalence surveys. This method is not a clear improvement over prevalence studies. ***Use of mass ACF data*** Better used as an indicator of trends (where a time trend can be established from ACF data) rather than absolute level (i.e., ACF data and prevalence survey data considered comparable). It is also possible that the success of ACF in targeted groups will mean ACF-derived measures of trend will show faster reductions than is truly the case at the population level. Also, if it is to be used as a measure of trend it may need to be done in a way that differs from the way ACF would otherwise be done (i.e., more attention to a having a standardized approach, and population representativeness) ***Can ACF be implemented systematically enough to be useful for burden estimation?*** Concerned about how well we will ever understand the implementation of ACF interventions and think there are likely too many variables and too much variation between settings and over time to use these data for these types of estimates. It would be useful to provide an example of how to go about defining the relative risk of TB in the screened population, relative to the general population for ACF in a standardized way. ***Potential for addressing biases*** There are parallels here with using ANC for HIV testing. There was good work done by the HIV community looking at real biases of using ANC clinics data, and bias existed, but was quantifiable and therefore the data were useful in the end.
Use of UHC SCI to adjust case notifications	***Improvement on expert opinion*** It is (much) better than the currently used method of expert opinion or standard adjustment. However, it is not fully clear to me how the different tracer indicators are collected/estimated, and when and where proxy tracer indicators were used. ***Do increasing notifications always mean increasing incidence?*** Need further work, especially on the formula, to solve the problem of increase of notification will make the estimation incidence increase Rising case notifications in those countries reflects better diagnosis and treatment, not rising incidence. So the use of any CN-based method will make it exceptionally difficult to achieve global targets. ***Face validity*** The bigger question is whether countries believe these results are more reflective of their actual incidence than the previous estimates. I would put face validity over statistical validity!
Back-calculating incidence from mortality (only in countries with good VR data)	***Potential usefulness*** I believe that this approach has already been quite useful in a limited number of settings with robust VR systems. For settings where the mortality data are good enough, this represents a high-value strategy. ***Understanding limitations of VR data*** …Interested in a comment or discussion around the extent to which any limitations in the diagnosis in TB among the living are 'inherited' (shared) by VR systems. ***Importance of assumptions relating mortality to incidence*** Issue with direct estimation of incidence from mortality data is, I feel, that the incidence-to-mortality rates are not constant over time (see Fig 1) and may depend on many factors, such as implementation of ACF to find and treat TB early, implementation of TPT, new and more effective treatment regimens (esp. in high DR-TB burden countries), etc. This needs to be considered if using this method.