TIME Estimates (v. 6.01, Feb 21): user guide

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Target audience: National TB Programs and other health planners using OneHealth tool (https://avenirhealth.org/software-onehealth.php) for costing TB plans or sector wide plans.

Dissemination platforms: https://avenirhealth.org/software-onehealth.php and https://www.who.int/activities/tb-monitoring-and-evaluation

1 Contents

About this guidance

This guidance, developed by Avenir Health and WHO's Global TB Programme, is addressed to planners using OneHealth tool (OHT) for costing TB plans or sector wide plans. TIME Estimates is a TB burden and target population estimation tool that uses statistical methods to project TB service volumes, such as the number of patients eligible for TB preventive treatment (TPT) or for treatment of active TB. These projections can be used for multi-year planning and costing exercises, by a non-technical user. TIME Estimates is not an impact modelling tool and cannot be used for detailed impact modelling, although it does allow for the estimation of the reduction in TB mortality following the scale-up of TB notifications.

This guidance is organized in the following section:

- Section 1, **TIME Estimates:** Presents an overview of the TIME Estimates model and its uses and a summary of purposes for which it cannot and should not be used.
- Section 2, **Spectrum Software Suite:** Presents an overview of the Spectrum Software suite and the relationship between Time Estimates and the other modules in Spectrum, focussing on the OHT model. This section provides an overview of the configuration of OHT and explain the basic formulae behind the cost calculations of OHT. These formulae are fundamental to the OHT model and to the link between the OHT and the TIME Estimates model. This link is established through 'Target Populations'.
- Section 3, **Uses of TIME Estimates:** Presents an overview of the main uses of TIME Estimates, the first being to produce Target Populations. Other uses, such as producing estimates of TB burden and impact on TB mortality, are also explained.
- Section 4, **Using TIME Estimates to generate target populations for OneHealth:** This is the main section of this guidance document, describing in detail how the OHT user configures and uses TIME Estimates to produce target populations. This process involves a review of TB data published by the WHO and presented in the Program Statistics, with a focus on notification and its breakdown into different case types and RR/MBR burden. A new section in the current version of OneHealth for the describing and configuring the TB prevention program is described in detail. The user is guided to review the Target Population table produced by TIME Estimates and is guided to methods for editing the Target Population directly. The user is shown how to generate results other than Target Populations, such as projections of TB Incidence and TB mortality.
- Section 5, **Using target populations from TIME Estimates.** Presents two examples of the type of target populations the OHT user will use when costing TB programs. Example 1 shows how the number of smear positive cases is used to cost smear microscopy. Example 2 shows how the number of persons evaluated for TPT is performed and used to cost TB prevention programs.
- Section 6, **Technical annexes** to explain 1) The use of cubic spline method to fit TB indicators. 2) Estimating impact on TB mortality resulting from TB Notification scale-up. 3) Calculating populations eligible for TB preventive therapy.

1. TIME Estimates

This guidance focuses on the use of TIME Estimates available within OneHealth tool (OHT) as part of the TB planning modules[1] (https://avenirhealth.org/software-onehealth.php) and its use for:

1. Target population estimation for Tuberculosis (TB) costing using OHT TB module,
2. TB burden and mortality estimates for use in assessing projected notifications and its impact on TB mortality.
3. Input for TIME Impact, a TB impact model also available within OHT.

   The TIME Impact model is for technical use and it takes a significant time investment to use it correctly.

1.1 What TIME Estimates can do

- Produce statistical projections/trends for the next 3-5 years fitted to historical and current data that are preloaded into the system from WHO databases[2].
  - **Default projections are preloaded** into the system from WHO databases. These include:
    - Projections of expected notifications of different case types
    - The number of people eligible for TPT (a new feature in TIME Estimates since January 2021).
    - Projections of TB incidence and TB mortality.
  - **The user can create new projections and trends with the model to replace the default projections.**
- Produce target population numbers to link to the OHT for costing purposes.
- Can be used to estimate the short-term impact on TB mortality in a very basic way and results to be used with caution.
  - TIME Impact model is used for more sophisticated modelling of TB incidence and mortality.

1.2 What TIME Estimates cannot do

- Detailed modelling of TB interventions
  - The TIME Estimates model deals mainly with projection of TB notification, treatment and preventive therapy scale up. Underlying activities (for example, case finding methods) are not modelled in any detail. The usual activities of a TB program can however be costed with OHT and TIME Estimates used in tandem.
- Detailed modelling of the impact of TB interventions
  - TIME Estimates is a TB burden and target population estimation tool rather than an impact modelling tool.
- Produce long-term statistical projections.
  - Assumptions that ensure relative accuracy of statistical projections do no hold long term. For this reason it is advised that TIME Estimates is solely used for short term (up to 5 years) statistical projections.

[1] Available within OHT for TB planners are two impact modules: TIME Estimates, TIME Impact and one costing module.

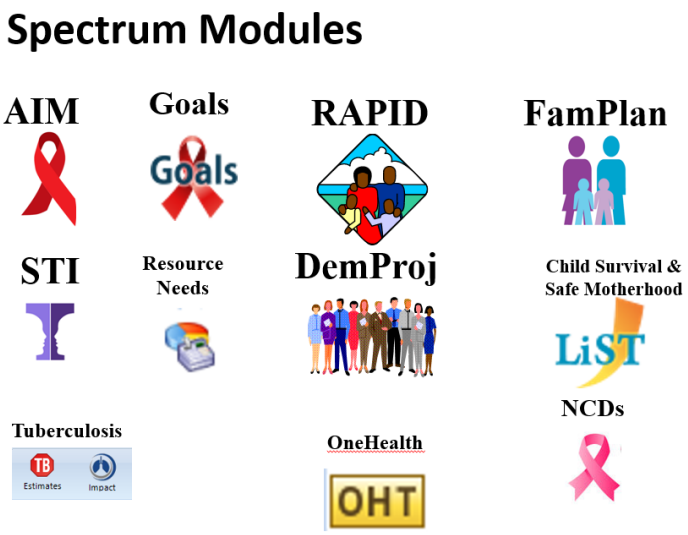
[2] https://www.who.int/teams/global-tuberculosis-programme/data

2 Spectrum Software Suite

Spectrum is a system of policy models that support analysis, planning and advocacy for health programs. It is used to project future needs and examine the effects of policy options. Each model (or Module) in Spectrum has a similarly functioning interface that is easy to learn and to use. The text in this document, which focusses on TIME Estimates, contain both the instructions for users, and methodology for those who want to know exactly how the underlying calculations of TIME Estimates work.

Figure 1 depicts the impact modules in Spectrum.

Figure 1: Spectrum modules



The modules within Spectrum that are linked to TIME Estimates are described below. The user should consult the Spectrum manual[3] for further details.

2.1 DemProj (Demography)

DemProj projects the population for an entire country or region by age and sex, based on assumptions about fertility, mortality, and migration. A full set of demographic indicators can be displayed for up to 100 years into the future. Urban and rural projections can also be prepared. Default data needed to make a population projection is provided from the estimates produced by the Population Division of the United Nations. DemProj is a required module for all projections created in Spectrum since its population projection is utilized by most of the other modules.

- The OHT/TIME Estimates user will generally use the demographical model data and outputs without adjustments.
- There are situations where the user may want to update the demographical model. For example, the user has access to the data from census or a survey not yet in the model. Or the

[3] https://avenirhealth.org/Download/Spectrum/Manuals/SpectrumManualE.pdf

user needs to, for consistency purposes, to update the model to produce estimates that match estimates produced by another process. For such the cases details can be found in the Spectrum manual (SpectrumManual\DemProj[3]). Such updates are usually done in consultation with in-country demographers of experts from population and statistical institutes, and involve the use of data such total fertility rate (TFR), age-specific distributions of TFR, lifetable details and international immigration inputs.

2.2 AIM (AIDS Impact Model)

AIM projects the consequences of the HIV epidemic, including the number of people living with HIV, new infections, and AIDS deaths by age and sex as well as AIDS orphans. AIM is used by UNAIDS to make the national and regional estimates it releases every two years. AIM interacts directly with DemProj as HIV often has substantial demographic impacts.

- The OHT/TIME Estimates user will generally use the HIV model's data and outputs without adjustments. The Demographical and HIV modules are reviewed and used annually by UNAIDS and country teams to produce HIV burden estimates.

2.3 TIME Impact

The TIME Impact module allows users to generate projections of TB incidence and notifications. The main difference with respect to TIME Estimates is that TIME Impact models TB transmission and other aspects of TB epidemics mechanistically (attributes them mechanisms that can be influenced in different ways) and opposed to statistically like TIME Estimates (underlying mechanisms of TB epidemics are not attributed to mechanisms that the user can influence). TIME Impact can therefore be used to assess the epidemiological impact of a variety of user-defined interventions. Results of TIME are used to generate cost-effectiveness estimates of interventions using One Health.

The TIME model (Impact or Estimates) does not influence the HIV or demographical models. The TIME Impact model is generally used separately from the TIME Estimates model with the only link being that the official burden estimates that TIME Impact is calibrated to reside in the TIME Estimates model.

The technical user can also use impose impact estimated from TIME Impact on statistical burden trends in TIME Estimates. This will only be done when there is a requirement to benchmark the burden projections on official estimates while reflecting the impact of TB programs.

- The OHT/TIME Estimates user will generally not use the TIME Impact model. This model is mostly used in close collaboration with a technical model consultant.

2.4 OneHealth

OneHealth (OHT) is a tool that can be used to inform the development of strategic plans for health sector planning. OHT is a unified framework to be used for supporting the planning, costing and budgeting of health sector priorities, including health system strengthening strategies. As such it represents a modular instrument for program-specific and sector-wide applications and helps to ensure a consistent costing methodology across different health programs. The tool illustrates the health system implications of scaling up intervention delivery, shows the capital investment gap and allows a comparison of costs with the estimated financial resources available.

The tool facilitates an assessment of costs related to the areas of maternal, new born and reproductive health, child health, vaccination, malaria, **tuberculosis**, HIV/AIDS, nutrition, and water sanitation and hygiene, to help assess progress in achieving health impact. It also contains modules for the areas of human resources, infrastructure, logistics, financial space, programme and channel analysis, intervention coverage and costing, bottleneck analysis, programme costing, summary outputs and budgeting.

OHT interacts directly with TIME Estimates in that intervention coverage settings are directly linked between TIME Estimates and OHT. OHT is also used in a way that influence demography and HIV and therefore the TIME Impact and Estimates models as well.

2.5 Key steps in configuring TB interventions and services for costing in OneHealth

Figure 2 shows TIME Estimates and other disease models active within OneHealth. The interactions between the TIME Estimates model and OneHealth is facilitated within the **Health Systems** area of OneHealth. Here the user will configure **interventions** and **programmatic activities** to cost, i.e. *the two main categories of cost that OHT uses in Health Systems modules*. The key steps of the process to be followed for costing interventions are listed below. These steps will be explored in detailed examples in Section 6.

- **Define the target population:**
    - The user links an intervention to a population meant to receive the interventions or health service. For example, diagnosis with microscopy can be linked to the bacteriologically positive notified cases which is an output from the TIME Estimates model.
- **Define the population in need (PIN):**
    - The user can specify that a proportion of the population is eligible for the intervention. For example, a proportion of all notified cases may need patient support.

      PIN can also be used to achieve other types of adjustments. In section 6.1 an example is shown where PIN for diagnosis with smear microscopy is set to 20 (which shows in the editor as 2000%) to account for the fact that about 20 suspects are tested to find and notify a case.
- **Set coverage targets:**
    - The user specified current and future targets. For example, diagnosis with Xpert may increase from, for example, 40% in the first year of the plan being costed to 80% by the end of the costing period.
- **Define the cost ingredients of the interventions (also called Treatment Inputs):**
    - The user specifies the costing ingredients of the interventions. This will typically comprise of:
        - commodities (e.g. all the commodities needed for a given diagnostic test)
        - staff time, e.g. staff time provided by technicians, doctors, community health workers and other staff types as configured in **Human Resources** section of OneHealth.
        - Outpatient and inpatient days (optionally)

Full explanations on OneHealth costing module described in the other sessions on the OneHealth Tool structure and its TB component.

- **Delivery channel:**
    - Finally, as each intervention can be provided through different channels at different costs and the user can configure under "Delivery channel", the proportion provided to each 'channel' which is used to make a distinction between services provided by each. This distinction can be driven by different between facilities, typically related to cost or health system planning.

      For example, a service can be provided, for example, by community health workers, by staff in a primary care facility, a TB unit or clinic/center and a district-level or regional hospital. Staff costs generally increase for services provided at the higher level 'channels' or 'facilities' (e.g. doctors may deliver the service as opposed to community health workers delivering the service) and the user can use the ability of OneHealth to change this distribution of delivery channels over time to study how costs may be cut by delivery at lower-level facilities, where appropriate.

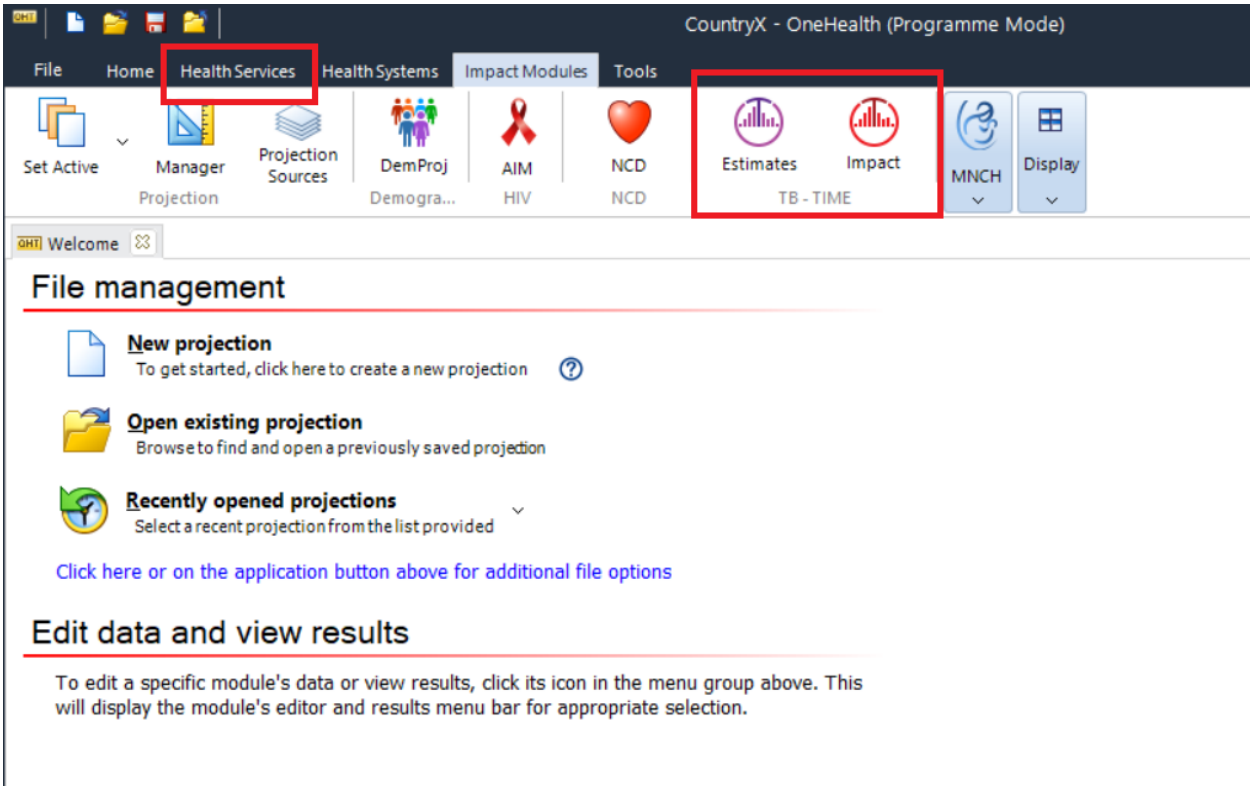
2.6 Formulae for costing interventions in OneHealth

As fully explained in OneHeath tool for TB costing training materials[4]. These elements combine to determine **intervention cost** according to the following formulae:

- Population in need of intervention = Population (demographic projection) x Proportion (%) of population identified as in need of the intervention
- Population receiving the intervention = Population in need of intervention x Coverage (%)
- Intervention cost = Population receiving the intervention x Units of resources needed per case x Price per unit
- Cost per delivery channel = Population receiving the intervention x Units needed per case x Price per unit x Delivery Channel (%). Channel analysis is not explored in this guidance and the user can refer to more detailed OneHealth documentation for this purpose[4].

[4] https://avenirhealth.org/software-onehealth.php and will also be uploaded by WHO https://openwho.org/

Figure 2: TIME Estimates and other disease models available to users within OneHealth.

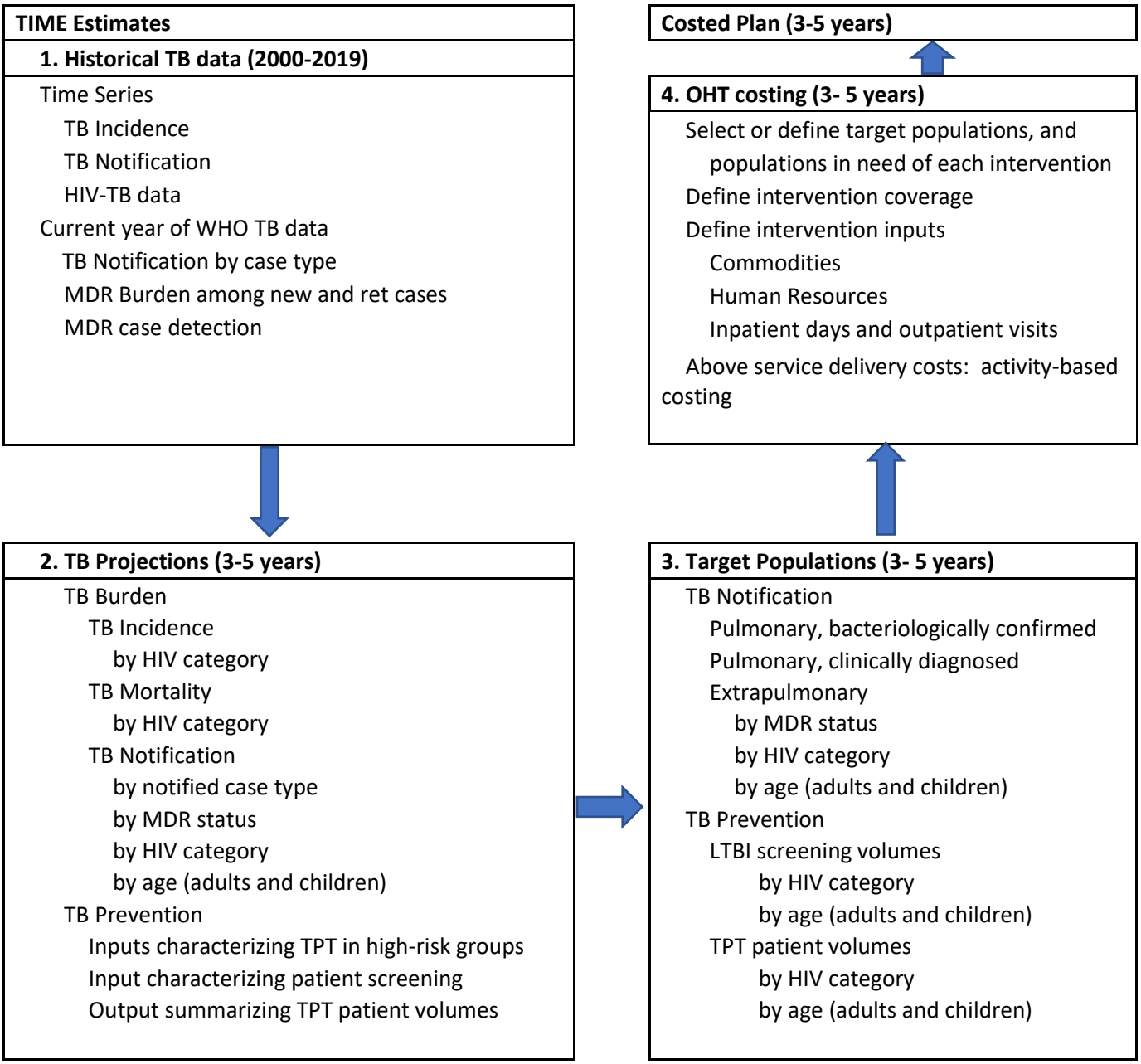


3 Uses of TIME Estimates

The key elements of the TIME model and process flows related to the main uses of TIME Estimates are shown in Figure 3.

1. The model stated data for key TB indicators. This data is loaded from WHO databases.
    a. User reviews and may edit this data
2. The model projects key TB burden indicators using cubic-spline methods.
    a. The user can accept the default projections or re-run them in the case where data changes were made or if the user wants to explore the possibility of getting a better fit than the default fit.
3. Target populations for OHT costing purposes are produced and evaluated.
    a. The user reviews and possibly edits the target population table in TIME Estimates
4. Target populations and other costing elements are used to produce a costed TB plan or strategy.
    a. The user utilizes target populations and other information to formulate a costed plan.

Figure 3: Key elements and process flows of the TIME Estimates model. Data from WHO refers to data currently available, for example 2019 data available in 2021. TPT refers to TB preventive therapy.



3.1 Projection of Target Populations

TIME Estimates is an OHT/Spectrum module for the estimation and projection, at country level, of Target Populations and other TB service estimates, that are the basis of costing in OHT.

For example, TIME Estimates projects the number of bacteriologically positive cases, which is an input to costing diagnostic tools. It projects the number of people that are eligible for TB Preventive Therapy (TPT), which is an input into TPT intervention costs.

Producing and using target populations will be discussed in more detail in the sections below.

3.2 Projection of TB burden

TIME Estimates also projects key TB burden indicators, with an emphasis on indicators relevant to HIV-TB and estimating the potential impact of HIV interventions (e.g. ART) on the burden of HIV-TB. (See Annex 1 and 2 for details)

An immediate application of the TIME Estimates module is to estimate the number of incident TB cases by CD4 category (data for the CD4 categories are produced by the Spectrum AIM model). Many countries are expanding ART coverage and the model can be used to estimate resource requirements above those that will result from current ART guidelines. Another important use is to estimate HIV+ TB mortality and the impact of ART expansion.

The model is essentially an incidence model, which is fit to incidence data from the WHO Global TB Programme (GTB) TB database and disaggregated according to CD4 category. To this end, a regression method is devised to estimate relative risk (RR) for TB incidence according to the CD4 categories used by Spectrum for national HIV projections. Spectrum data are based on the national projections prepared towards the UNAIDS Report on the Global AIDS Epidemic 2019.

TB mortality is calculated as product of incidence and case fatality ratios (CFR), and the model can be used to study the impact of increased notification on TB-related mortality, although this impact estimates comes with caveats.

3.3 Projecting the impact on TB mortality of scaling up TB Notifications

The mortality estimation method outline above responds to increases in TB notifications, since the CFR of notified (which usually implies treated) cases is lower than those of cases not notified. However, since the impact on TB incidence of the TB notification increase on TB mortality is not captured, in a dynamic way (as it is with the use of the TIME Impact model) the results are simply indicative and should be treated with caution.

4 Using TIME Estimates to generate target populations for OneHealth

4.1 Overview

There are four main steps to produce target populations for OHT.

1. Activate TIME Impact model and Estimates (TIME)
2. Review and update data in Program Statistics
3. Fit the model
4. Generate and edit results for target populations

4.2 Step 1. Activate TIME Estimates module in TIME Estimates in Project Manager

- **Location in OHT:** Impact Modules\Manager
- **Steps for OHT user:** Review file name, projection start and end year and default country data

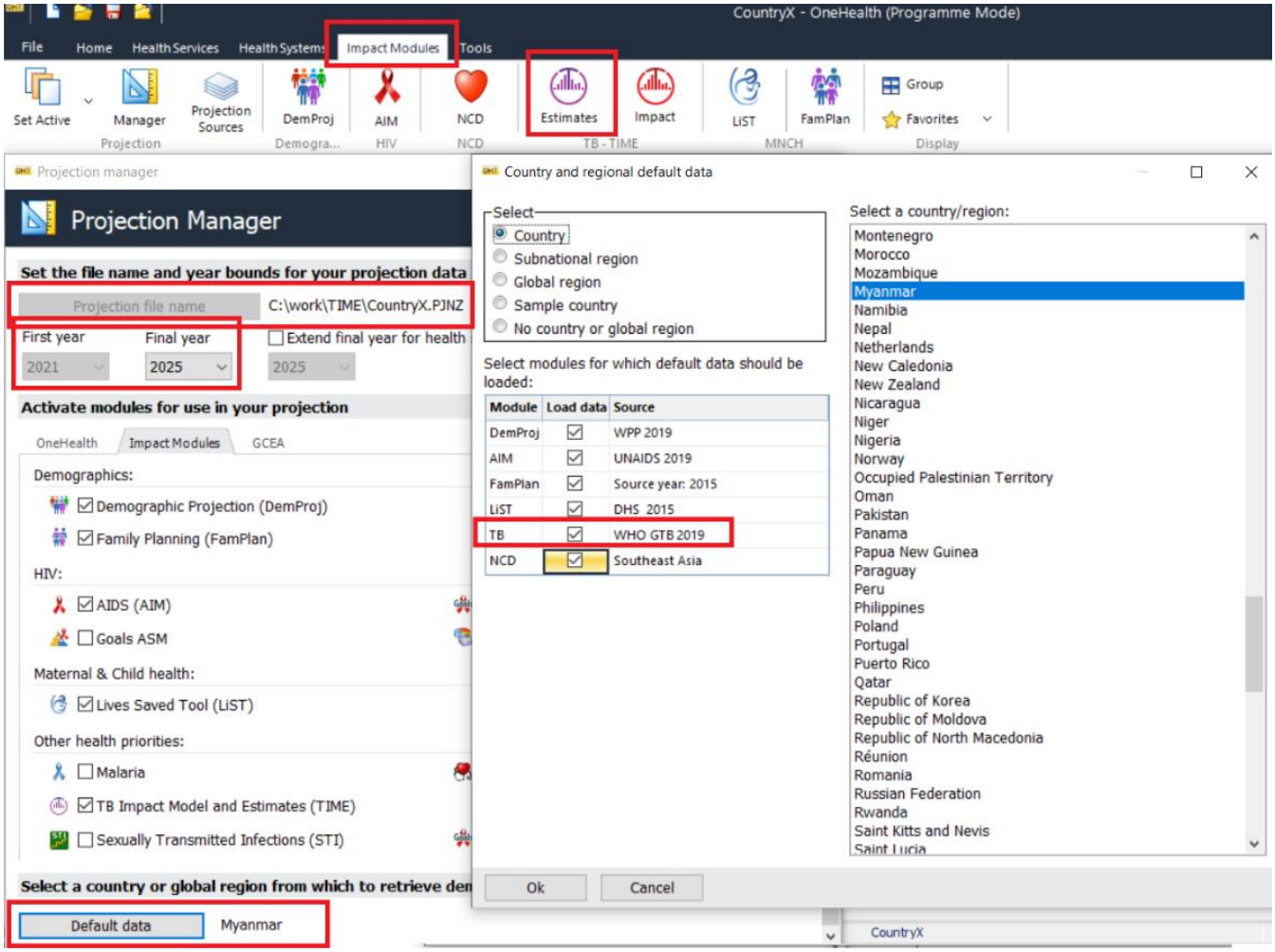
It is assumed that the user followed the Spectrum Manual and instructions to create a projection for a given country and that step is not described in detail here.

TIME Estimates is activated via the Program Manager, as shown in figure 4. When using OHT, TIME will automatically be active. TIME relies on information from the DemProj and AIM models, which must also be active when TIME is active. This dependency between TIME Estimates on AIM is forced by the software and the user needs simply to be aware of it.

The process of projection set-up and configuration is described in more detail in the OneHealth and Spectrum manuals. Figure 4 highlights the key elements:

- Each projection must be assigned a filename.
- Each projection is assigned a start and final year. For costing of national TB plans, the time horizon will generally span 3-5 years.
- Several disease modules can be active at the same time. However, each disease model has its own complexities and the user should consult their manuals when using them.
- Each projection is associated with the of a specified country. It is shown in figure 4 that the final year of WHO TB data, which provides the default data for TIME Estimates, is currently 2019.

Figure 4: The TIME Impact model and Estimates



4.3 Step 2. Review and update data in Program Statistics

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics
- **Steps for OHT user:** Review and update historical data for TB burden, TB Notifications and RR/MDR TB

4.3.1 Overview of Program Statistics window

- Default historical data for TB incidence, prevalence, notification, HIV+ TB burden, DR TB burden and testing are available in the Program Statistics window. In addition, Program Statistics also hosts "Active screening and TPT" a section that presents default assumptions to allow estimating baseline and projected volumes of clients for preventive testing and therapy. A short-term projection of the historical data is presented for the following indicators (these are projections the user can directly edit):
    - TB notification ("Notified cases types").

    - Historic WHO data is available for 2000-2019 for TB incidence and TB notifications in 2021. As WHO releases global report and data updates, AvenirHealth updates default data.
    - The notification split by case type is only available for the last year of WHO data (currently[5] 2019).
    - MDR related data is available only for recent years or in the case of burden estimates, only for the last year of MDR burden data in the WHO database.
- Six tabs are presented into the Program Statistics window (figure 5). These data should be reviewed and updated if needed before generating projections of target populations for OHT (or of TB burden), which is done in the section "Fit indicators", as explained in a next section.
    - **TB Incidence**: Historical data for TB incidence, by HIV status
    - **TB Prevalence**: Data for selected years the TB Prevalence survey results is featured. These data are not used at all by the OHT user. It is used by the TIME Impact model users for calibration purposes and the OHT user need simply be aware of it.
    - **TB Notifications**: TB case historic notifications are presented in "Total notified (historical)". Default projections of TB notifications, of different case types, that are used for TB costing in OHT, are presented by default in "Notified cases types" tabs either absolute numbers or as percentage. These indicators are explained in the next section.
    - **HIV+ TB burden**: Default WHO data collated from surveys, routine testing or sentinel HIV surveys is shown for selected years available for "Percentage of incident TB cases that are HIV+" and "Percentage of HIV+ TB cases receiving ART" Data used to estimate HIV-TB burden in the section "Fit Indicators".
    - **Drug resistant TB care**: Three tabs include "RR burden" among new and previously treated, showing the latest WHO estimate with hi and low bounds (representing a 95% confidence interval), "RR Case Detection" showing historical WHO data and default projections of the proportion of new and previously treated cases that are tested for RR and "MDR/RR Treatment".
    - **Active screening and TPT**: Preventive therapy in households, high-risk groups and ART cohorts is detailed in this section.

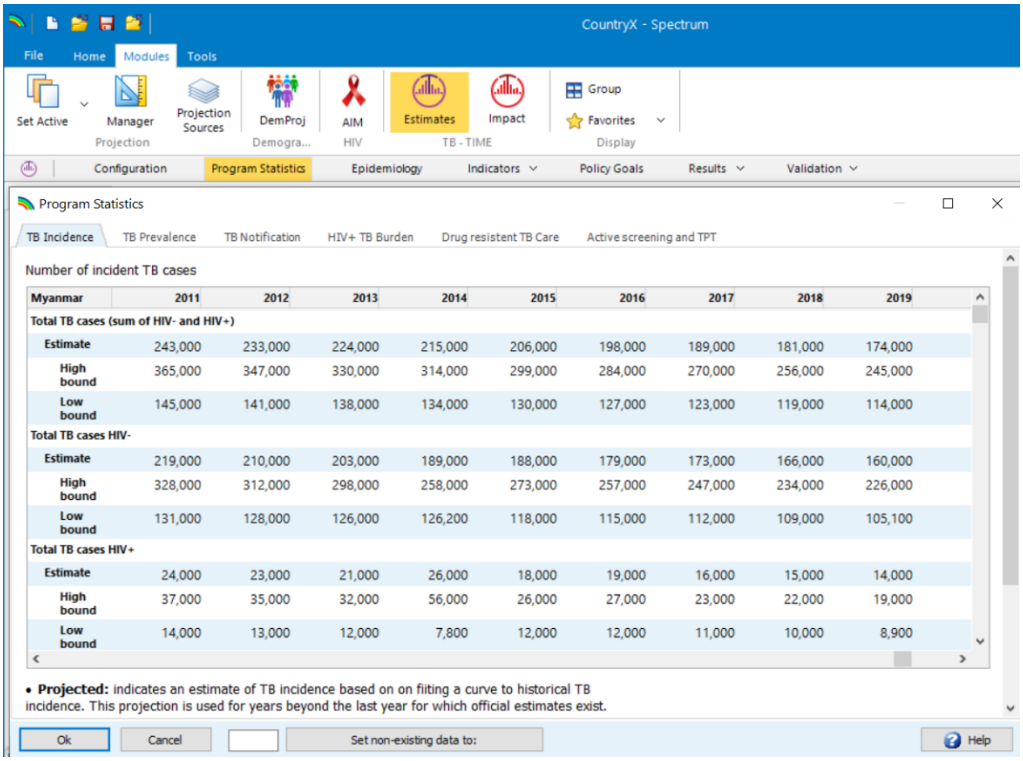
[5] As of February 2020.

4.3.2 Review and update of TB incidence data

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\TB Incidence.
- **Steps for OHT user:** Review WHO data for total TB Incidence, 2000-2019 (or final year of WHO data) and update if necessary.

Historical TB incidence data are presented in this tab. See figure 5.

Figure 5: TB Incidence data editors



4.3.3 Review and update of TB notification data

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\TB Notification
- **Steps for OHT user:** Review and update TB notification data

The key data related to TB costing in OHT reside in the TB Notification section of Program Statistics, is presented in three sub-tabs:

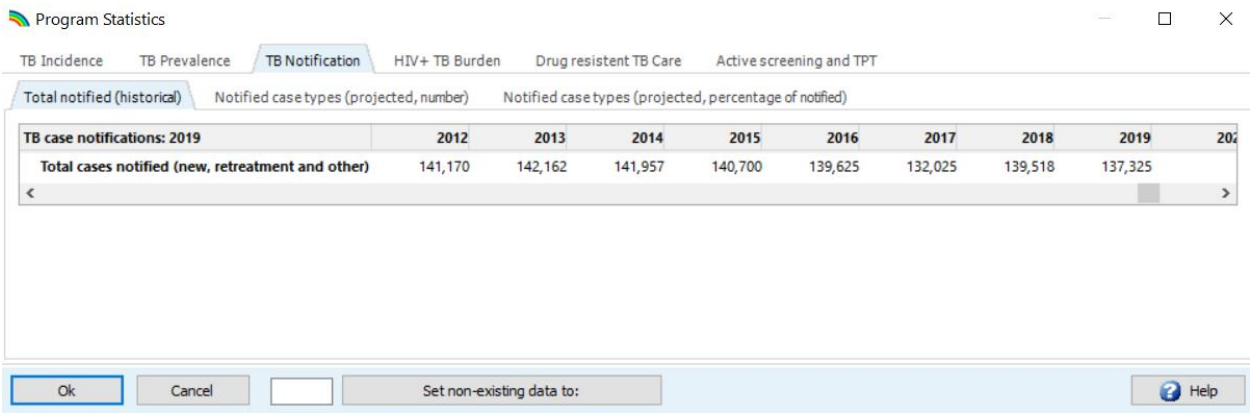
- *Total notified*: Historical data for total TB Notification (all case types)
- *Notified case types (projected, number)*: Projected notifications disaggregated by case type, based on the 2019 split. Values for the case types are displayed as absolute numbers.
- *Notified case type (projected, percentage of notified)*: Projected notifications disaggregated by case type, based on the 2019 split. Values for the case types are displayed as a percentage of total notifications.

4.3.3.1 *Total notified (historical)*

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\TB Notification\Total Notification (historical).
- **Steps for OHT user:** Review WHO data for total TB Notification, 2000-2019 (or final year of WHO data) and update if necessary.

The first tab "Total notified (historical)" shows the historical data for total notifications (as reported by the country to WHO Global TB Programme (GTB)), see figure 6. The data are available until the last year of data available from GTB (at the time of writing, it is 2019).

Figure 6: Total TB Notifications



4.3.3.2 *Notification case types (projected, number)*

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\TB Notification\Notification case types (projected, number).
- **Steps for OHT user:** Review and update split in TB Notification by case type in 2019 (or final year of WHO data). The user can set projections of TB notification, but this projection must be reviewed following the model fitting step.

This table shows notification projections data by case types, see figure 7.

The default projection of total notification shown in this table is prepared by Avenir Health and are used for various TB analyses projects. These defaults provide a good starting point for many applications. The process of replacing the default projections by updated model fits, which is the recommended procedure when, for example, as the user edits historical data in "Program statistics", is explained in Annex 1. **The refitting process is explained in a next section**.

Notifications are split into the following case types, based on the distribution of these case types reflected in the last available year of WHO data (e.g. 2019).

- Case types:
    - New cases (Pulmonary bacteriologically confirmed, Pulmonary clinically diagnosed, Extrapulmonary

    - Relapse (Pulmonary bacteriologically confirmed, Pulmonary clinically diagnosed Extrapulmonary)
    - Previously treated cases, including and excluding relapse cases
    - Cases in children < 15 years
- To edit values in this tab, the user must check the box 'Enable editing of absolute numbers'
    - Note that some indicators cannot be edited (shown in grey in figure 7 and in the tool once "enable editing of absolute numbers" is ticked by the user): these are calculated from other indicators.

Whenever the user changes the forward projection of total TB notification (by simply keying in the new value in the tap "Notified cases types (projected, number", the distribution of case types based on the last year of WHO data (e.g. 2019) is used to disaggregate the trend of total notifications according to case type for future years (i.e. the period between the last year of WHO data to the final year of the projection)

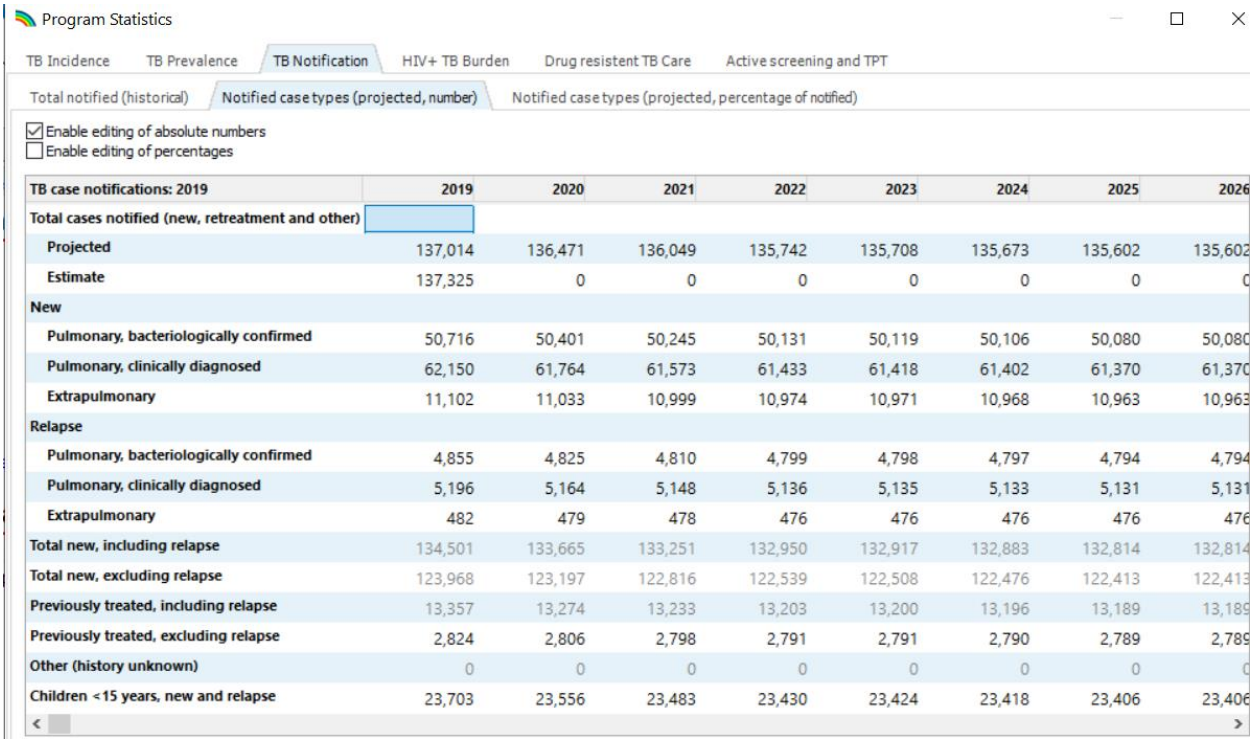
The list of case types is fixed and will be updated periodically by Avenir Health when WHO modifies the definition of case types or if they add new case types to the database.

These projected number of notifications by different case types form the basis of costing by serving as available target populations in OHT. This is explained in detail in the sessions on the OneHealth Tool structure and TB components. Here is a brief example:

- Bac+ cases serve as the Target Population for smear-microscopy and GeneXpert costs. (In OHT this target population number is adjusted for the number of cases that are tested to find an actual case)
- Cases in children are the basis of costs related to paediatric TB as opposed to cost linked to adult TB.
- The full list of target populations indicators and forecast of cases that can be used in OHT costing can be found by generating the results table that is found in **Results/OneHealth Target Populations.**

This topic is discussed in a next section.

Figure 7: TB notification by case type



TB case notifications: 2019	2019	2020	2021	2022	2023	2024	2025	2026
Total cases notified (new, retreatment and other)								
Projected	137,014	136,471	136,049	135,742	135,708	135,673	135,602	135,602
Estimate	137,325	0	0	0	0	0	0	0
New								
Pulmonary, bacteriologically confirmed	50,716	50,401	50,245	50,131	50,119	50,106	50,080	50,080
Pulmonary, clinically diagnosed	62,150	61,764	61,573	61,433	61,418	61,402	61,370	61,370
Extrapulmonary	11,102	11,033	10,999	10,974	10,971	10,968	10,963	10,963
Relapse								
Pulmonary, bacteriologically confirmed	4,855	4,825	4,810	4,799	4,798	4,797	4,794	4,794
Pulmonary, clinically diagnosed	5,196	5,164	5,148	5,136	5,135	5,133	5,131	5,131
Extrapulmonary	482	479	478	476	476	476	476	476
Total new, including relapse	134,501	133,665	133,251	132,950	132,917	132,883	132,814	132,814
Total new, excluding relapse	123,968	123,197	122,816	122,539	122,508	122,476	122,413	122,413
Previously treated, including relapse	13,357	13,274	13,233	13,203	13,200	13,196	13,189	13,189
Previously treated, excluding relapse	2,824	2,806	2,798	2,791	2,791	2,790	2,789	2,789
Other (history unknown)	0	0	0	0	0	0	0	0
Children <15 years, new and relapse	23,703	23,556	23,483	23,430	23,424	23,418	23,406	23,406

4.3.3.3 Notification case types (projected, percentage of notified), used alternatively to "Notified cases types (projected, percentage of notified)

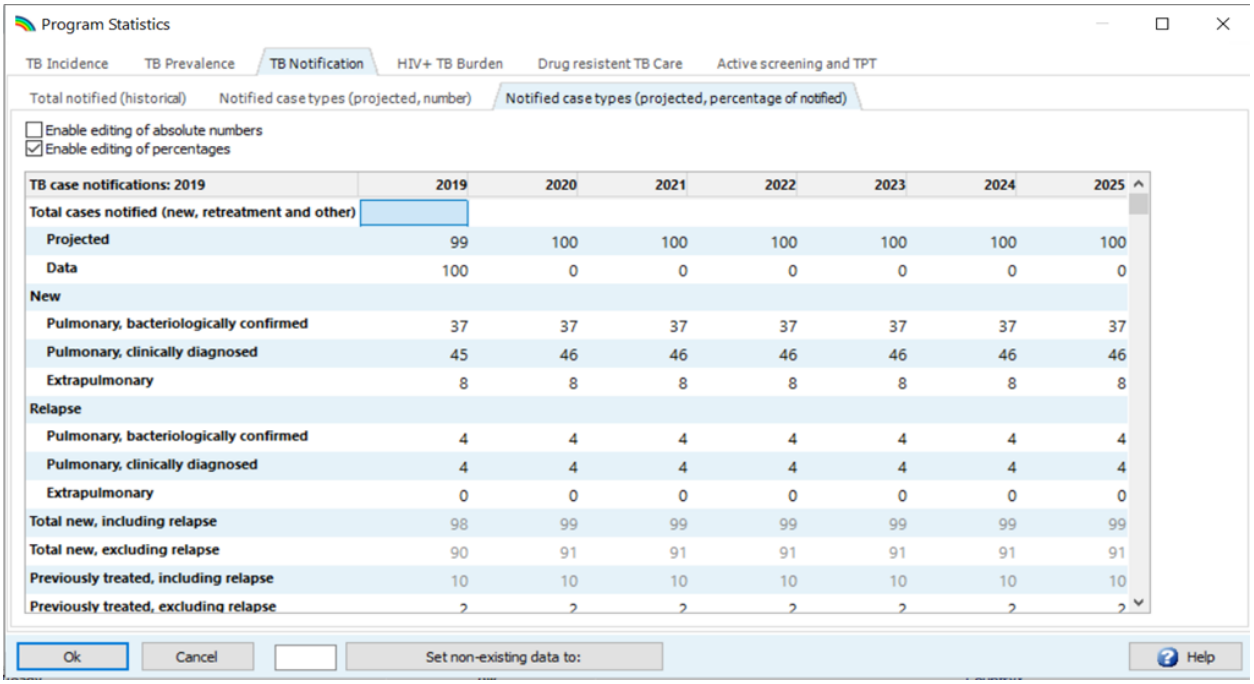
- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\TB Notification\Notification case types (projected, percentage of notified).
- **Steps for OHT user:** Review and update split in TB Notification by case type in 2019 (or final year of WHO data).

The table shows notifications data by case types, expressed as percentage of total TB notifications at the last year of WHO data (currently 2019), figure 8.

To edit values in this tab, the user must check the box 'Enable editing of percentages.' The user needs to prepare this data and express case types as percentage of the total. Note that the user must choose between editing the case type distribution as an absolute number, or as proportion of the total number of cases.

Whenever the user changes the forward projection of total TB notification, the distribution of case types based in 2019 (or whatever the last year of WHO data may be) is used to disaggregate the trend of total notifications according to case type.

Figure 8: TB notification by case type as percentage of total notifications



TB case notifications: 2019	2019	2020	2021	2022	2023	2024	2025
Total cases notified (new, retreatment and other)							
Projected	99	100	100	100	100	100	100
Data	100	0	0	0	0	0	0
New							
Pulmonary, bacteriologically confirmed	37	37	37	37	37	37	37
Pulmonary, clinically diagnosed	45	46	46	46	46	46	46
Extrapulmonary	8	8	8	8	8	8	8
Relapse							
Pulmonary, bacteriologically confirmed	4	4	4	4	4	4	4
Pulmonary, clinically diagnosed	4	4	4	4	4	4	4
Extrapulmonary	0	0	0	0	0	0	0
Total new, including relapse	98	99	99	99	99	99	99
Total new, excluding relapse	90	91	91	91	91	91	91
Previously treated, including relapse	10	10	10	10	10	10	10
Previously treated, excluding relapse	2	2	2	2	2	2	2

4.3.4 Review and update of DR-TB data

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\Drug resistant TB care
- **Steps for OHT user:** Review and update most recent estimate for RR/MDR TB burden. Review and RR case detection (DST coverage) among new and previously treated cases. Review and edit MDR/RR treatment volumes.

The **Drug resistant TB care** tab in Program Statistics shows WHO data for latest year (e.g. 2019) and projections. These provide the basis for projecting target populations related to MDR/RR case detection and treatment which are done in "RR Case Detection" and "MDR/RR Treatment" tabs respectively.

Within the drug resistant TB care tab, there are three sub-tabs:

1. *RR burden* (figure 9)- Estimate of Rifampicin resistance (RR) burden among new and previously treated cases. Proportion of cases that are XDR.
2. *RR Case Detection* (figure 10) – Proportion of new and previously treated cases tested for RR.
3. *MDR/RR Treatment* (figure 11)- Number of MDR/RR cases initiating second-line treatment.

The user must review and edit data in these three tabs if needed.

4.3.4.1 RR Burden

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\Drug resistant TB care\RR Burden
- **Steps for OHT user:** Review and update most recent estimate for RR/MDR TB burden in 2019.

This tool section shows rifampicin-resistance (RR-TB) burden in new or previously treated bacteriologically confirmed pulmonary cases. RR-TB burden is stated as a number or percent of these

pulmonary case types. The user should focus on entering the correct percentage of RR among new and previously treated cases in 2019. This is used to split total notifications by non-MDR and MDR for costing purposes.

Figure 9: RR Burden

Program Statistics

TB Incidence | TB Prevalence | TB Notification | HIV+ TB Burden | Drug resistent TB Care | Active screening and TPT

RR Burden | RR CaseDetection | MDR/RR Treatment

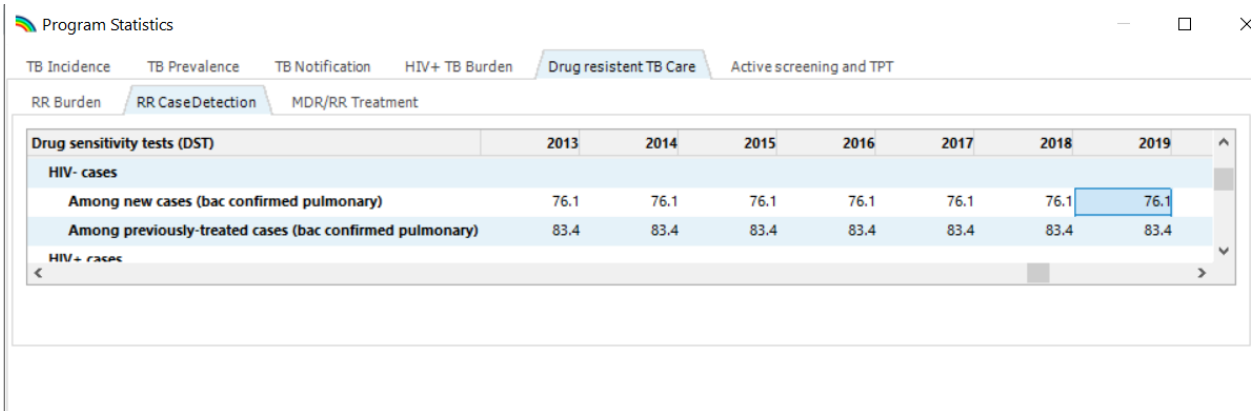
Rifampicin-resistant (RR-TB)	2019	2020	2021	2022	
RR among new pulmonary cases	Source: User Entered	Source: User Entered	Source: User Entered	Source: User Entered	Source: Us
Estimate	6,591	0	0	0	
High bound	6,860	0	0	0	
Low bound	6,322	0	0	0	
Percent(%)	4.90	0.00	0.00	0.00	
High bound	5.10	0.00	0.00	0.00	
Low bound	4.70	0.00	0.00	0.00	
RR among re-treated pulmonary cases					
Estimate	2,404	0	0	0	
High bound	2,538	0	0	0	
Low bound	2,271	0	0	0	
Percent(%)	18.00	0.00	0.00	0.00	
High bound	19.00	0.00	0.00	0.00	
Low bound	17.00	0.00	0.00	0.00	
XDR among MDR (%)	0.80	0.80	0.80	0.80	

4.3.4.2 RR case detection

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\Drug resistant TB care\RR Case Detection
- **Steps for OHT user:** Review and update DST data for the historic period (e.g. 2000-2019). Emphasis is on the last estimate (e.g. 2019). The projection of the DST target for the period following 2019, or whatever the base year is, is typically set in OHT but can be set in this editor too.

This tool section shows the proportion of new or previously treated bacteriologically confirmed pulmonary TB patients with test results for rifampicin: historical and default projections.

Figure 10: RR Case Detection

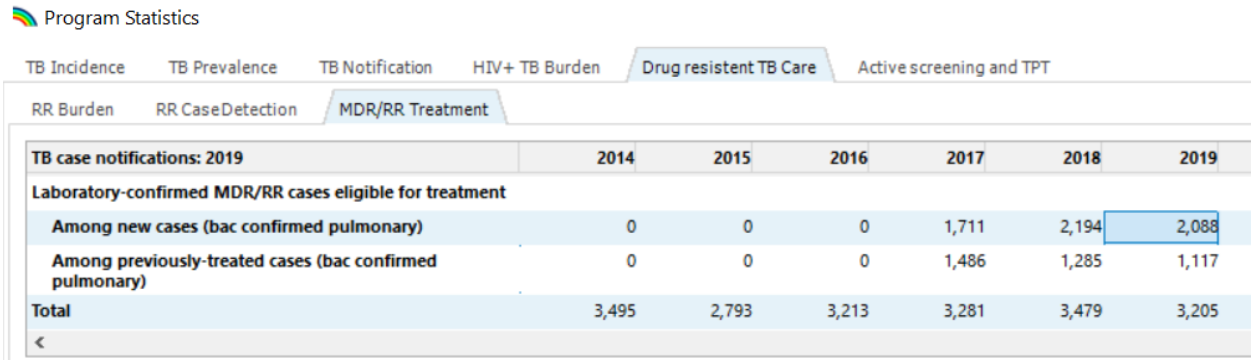


4.3.4.3 *MDR/RR treatment*

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\Drug resistant TB care\MDR/RR Treatment
- **Steps for OHT user:** Review and update most recent estimates for MDR/RR treatment volumes. Forward projections of treatment volumes are made by the TIME Estimates software by applying the ratio of MDR to all notifications in 2019 (or whatever final year of WHO data may be)

This section shows the new or re-treatment cases receiving MDR/RR treatment.

Figure 11: MDR/RR Treatment



TB case notifications: 2019	2014	2015	2016	2017	2018	2019
Laboratory-confirmed MDR/RR cases eligible for treatment						
Among new cases (bac confirmed pulmonary)	0	0	0	1,711	2,194	2,088
Among previously-treated cases (bac confirmed pulmonary)	0	0	0	1,486	1,285	1,117
Total	3,495	2,793	3,213	3,281	3,479	3,205

4.3.5 Review and update data and assumptions to estimate patient volumes for active LTBI and TB screening and TB preventive therapy

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\Active screening and TB
- **Steps for OHT user:** For the period of the costing exercise the user configures active screening for latent and active TB and configures linkage to TPT and active TB treatment for eligible cases. There is no historical data to configure. Configuration is done separately for households, high-risk groups and ART cohorts.

The **active screening and TPT** tab details screening for active TB disease and latent TB infection (LTBI) in high-risk groups, as well as the provision of TB preventive therapy TPT. These editors were incorporated into OHT software in January 2021 (OHT v.6.02 onwards).

Unlike the other TIME Estimates/Program Statistics editors that cater for historic WHO defaults (e.g. total notification) and projections, the editors/tab of “Active screening and TPT” collect the information needed to estimate the number eligible for TPT, which enable the user to estimate the population eligible for preventive therapy and active screening. These estimates are in turn used for costing in OHT TB module. The formulae used by TIME Estimates (not explicit/seen by user) for estimating the number eligible using the assumptions describe is described in Annex 3.

These editors are used to estimate the size of target population using the WHO’s approach for estimating TPT eligibility (see Annex 3). The purpose is to provide target populations for costing LTBI screening and Preventive Therapy (TPT) services in OHT, as well estimating target populations for costs related to actively screening high-risk groups for active TB infection.

The **active screening and TPT** editor/tab has three sub-tabs related to the screening three types of key populations prioritised for screening and prevention, see figure 12:

1. *"Screening and TPT in households" (Program statistics):* This tab represents the assumptions to estimate screening in household of index cases. The user may review this data if local and recent data to feed the assumptions is available, otherwise it can be left unchanged.
2. *"Screening and TPT in high-risk groups" (Program statistics)*: This tab represents the assumptions to estimate all high-risk groups not in household. These include diabetics, or miners exposed to silica, the elderly and other high-risk groups that are important from the perspective of TPT in a given country. The user may review this data if local and recent data to feed the assumptions is available, otherwise it can be left unchanged.
3. *"Screening and TPT settings" in ART cohorts Program Statistics)***:** This tab represents the assumptions to estimate screening in ART cohorts. The information on the number of HIV patients come from the ART module in Spectrum.

There are three types of data or assumptions used for each population that form three steps of TPT configuration towards producing target populations for TPT-related indicators. The user is expected to review and either accept the default values or update them with local data, where possible:

1. Setting the characteristics of the population (figure 12). The user can review and update the default assumptions which quantify the size of the population of interest (e.g. households, high-risk groups or PLHIV on ART) as well as the prevalence of latent and active TB infection in that population (e.g. households, high-risk groups or PLHIV on ART). There are considerations unique to each group:
    a. In the case of household contacts, the user must review and update if needed the average household size and the proportion in the household under five years of age. The household contact population size is estimated from the number of index cases which are defined to be all bacteriologically-confirmed cases (see Annex 3). The user can also specify the proportion of clinically diagnosed cases that are added to the index cases (default is 0).
    b. For high-risk groups estimates, the user will go to "Screening and TPT in high-risk groups" and will specify the size of all high-risk groups (combined into a single population) as a percentage of the total population.
    c. For ART cohorts, in "TB and LTBI characteristics in ART cohort" editor the user does not specify the size of the population as these numbers come directly from the official national AIM file.
2. The approach to providing TPT to the population (figure 13). In "Screening and TPT settings" the user must configure whether TPT is given presumptively or following screening for LTBI. For those screened the method used for testing, or mix of methods, must be defined in "Latent TB test mixture". The user must also state if active TB is screened among those not eligible for and proceeding to TPT. This is done by completing the "Proportion of evaluated and PT eligible cases linked to PT"
    a. "Active TB screening and treatment" ("Screening and TPT settings) indicators (Proportion screened for active TB among suspects not PT-eligible" and "Proportion of active TB cases found linked to treatment) show "0" by default. The user must specify a proportion of the suspects that entered the TPT cascade to be screened for active TB

(used for diagnostic costs for active TB) and the proportion of them linked to treatment for active TB (used to cost TB treatment).

   b. Active TB screening is not extended to ART cohorts in the current model. This is due to TB notification in ART cohorts being handled via routine notifications in the TB notifications tab.
   c. For those screened the prevalence of latent TB provided in step 1 is used.

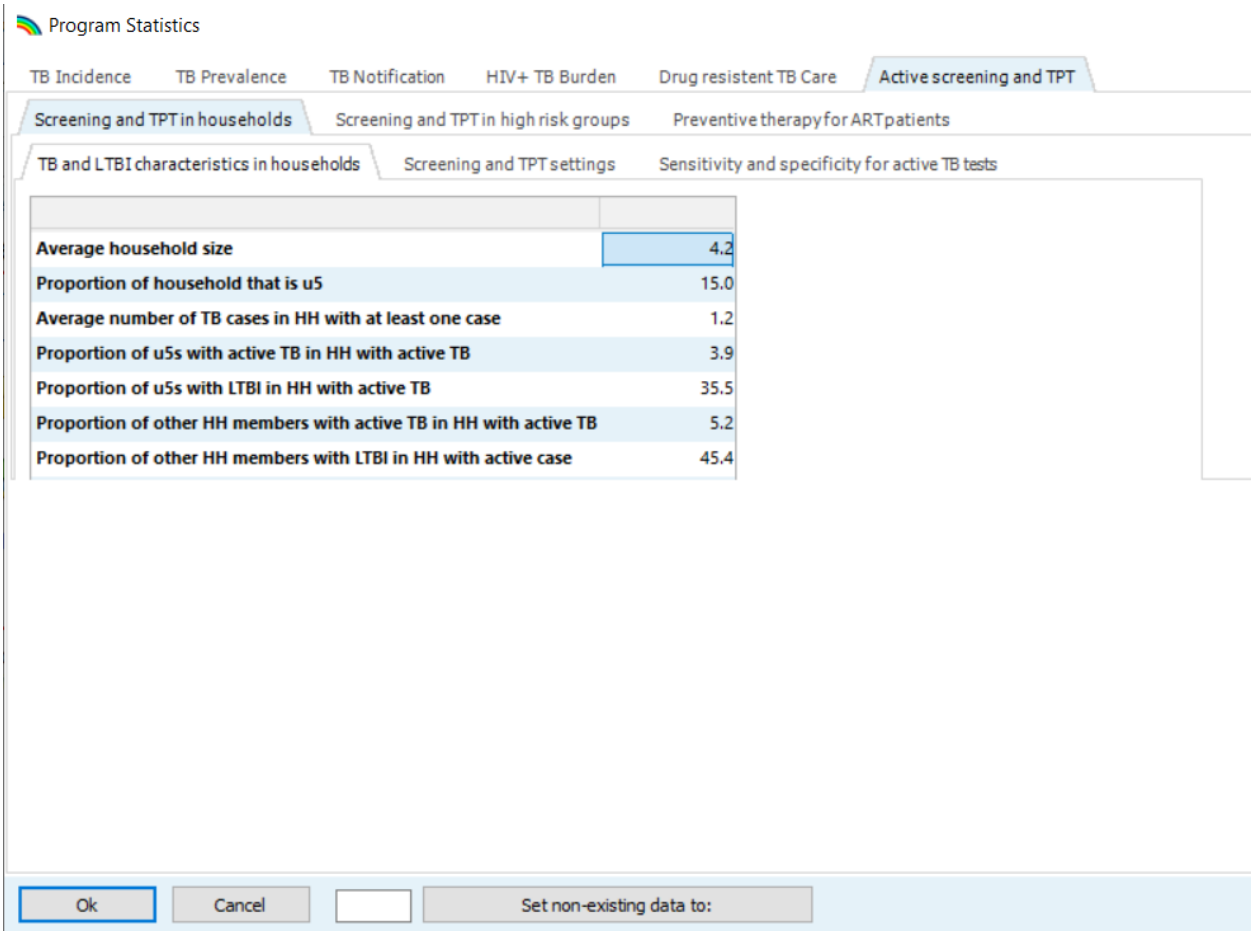
3. "Sensitivity and specificity for active TB tests" editor allows the user to specify the total sensitivity of the test(s) used to screen for active TB (figure 14).
   a. This is the reason why information is needed in step 1 on the prevalence of active TB. This sensitivity setting determines how many true positive TB case (sensitivity x TB prevalence x screening population size) will be found among the suspects screened. population size) will be found among the suspects screened. The specificity setting determines how many false positive cases will diagnosed by the algorithm (1-specificity) x (1- TB prevalence) x screening population size).

Default data are provided where available and are meant to allow for an assessment of population size for the key groups targeted by 2020 guidelines for TB[6]. For example, in household settings, TPT is generally given presumptively to children, but to adults mostly following screening of latent TB infection and ruling out active TB. In ART cohorts TPT is also generally given presumptively. In high-risk groups there will likely be screening involved – this TIME Estimates/Program statistics/Screening and TPT settings editor is for the user to reflect a national policy.

The three types of populations (households, high risk groups and ART patients) and the three sub-tabs for each population (TB and LTBI characteristics in …, screening and TPT settings and sensitivity and specificity for active TB tests) is shown in the headings of figure 12, a figure that focuses on "Screening and TPT in households".

[6] https://www.who.int/publications/i/item/who-consolidated-guidelines-on-tuberculosis-module-1-prevention-tuberculosis-preventive-treatment

Figure 12: Screening and TPT in households



4.3.5.1 TB and LTBI characteristics

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\Active screening and TPT\TB and LTBI characteristics
- **Steps for OHT user:** The user must define/configure the characteristics needed to define the size of the population and the prevalence of latent and active TB of the population in question. For each population, i.e. household, high-risk or ART patients, there is text at the bottom of the editor to explain the inputs needed for each population.

In the three tabs available for "TB and LTBI characteristics in households, high-risk groups and ART cohorts, the user will specify data related to TB disease and LTBI for the selected population (e.g. households, high-risk groups, ART cohorts) as explained below. See figure 13 for households as an example.

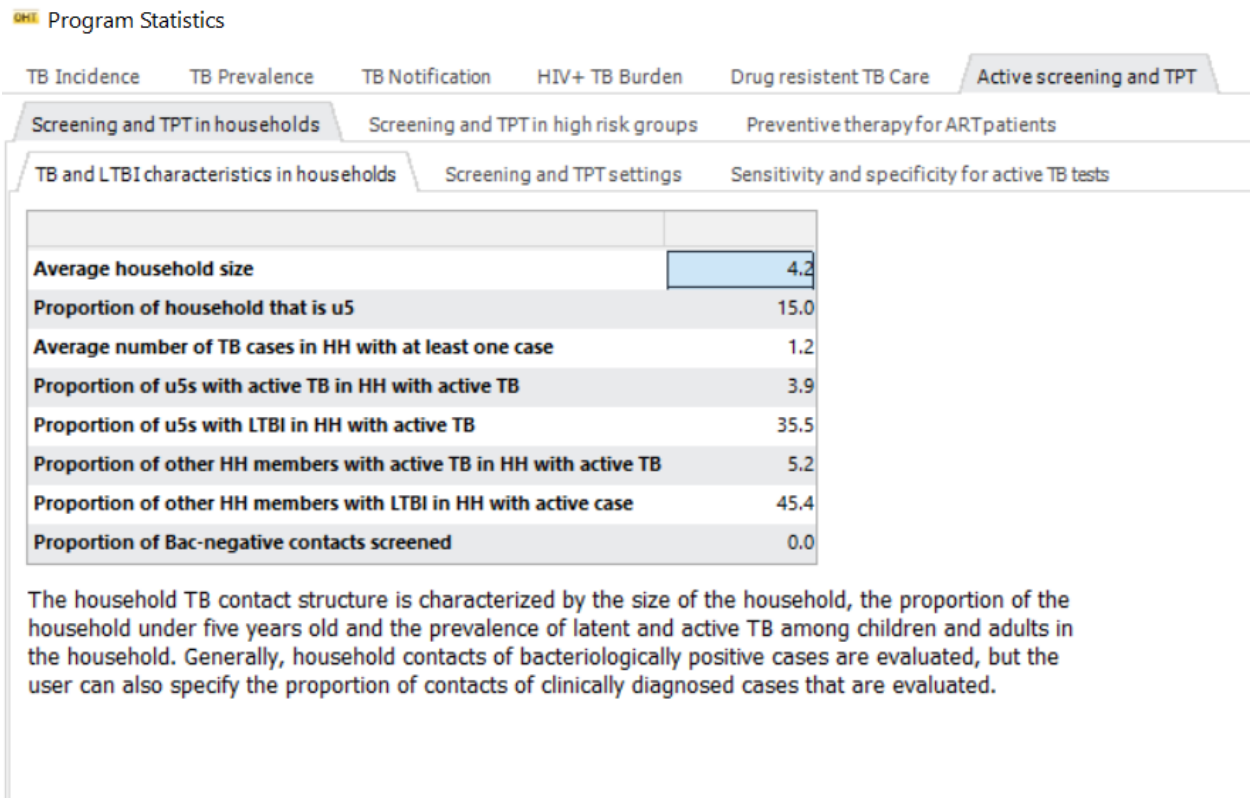
For *screening in households,* in "Screening and TPT in households/TB and LTBI characteristics in households" editor the user must review and if needed change the default data that define the households of index cases in term of the average size of households and the proportion of which is under five-year-olds (U5s), as well as the latent TB infection (LTBI) and TB disease prevalence in the

households of index cases. This information is needed to estimate the number of latent and active TB cases that will be found in the household. The default data have been informed by the literature[7] (see also Annex 3) and can be updated with country-specific data if available (see Annex 3). The user can also specify that a proportion of bacteriologically negative index cases that will also be included in the contact tracing approach.

Similarly, for *screening in high-risk groups*, in the "Screening and TPT in high-risk groups/TB and LTBI characteristics in high-risk groups" editor, the user must provide an estimate for the size of the population, which is expressed as a proportion of the total population (i.e. user populates the assumption for "Proportion of population in high risk groups"). Other assumptions are pre-populated by default and do not require changing unless local and recent evidence is available to inform the change.

In the case of *ART cohorts*, in the "Preventive therapy for ART patients/TB and LTBI characteristics in ART cohort" the editor deals separately with new ART patients and existing ART patients. The HIV model, which is updated annually in UNAIDS-coordinated process, provides information on the size of ART cohorts to the TIME Estimates model (for all years) and the user does not have to provide this information.

Figure 13: TPT population characteristics



[7] Fox et al. Contact investigation for tuberculosis: a systematic review and meta-analysis, Eur Respir J 2013; 41: 140–156, DOI: 10.1183/09031936.00070812 and currently under review for update.

4.3.5.2 "Screening and TPT settings in households, ART cohorts or high-risk groups"

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\Active screening and TPT\Screening and TPT settings
- **Steps for OHT user:** The user must define/configure all steps of the latent and active TB screening cascade: the proportion to be evaluated, the split between presumptive TPT and TPT following testing, the mix of LTBI tests and the proportion of the population screened for active TB and linked to TB care.

Here the user must do the following:

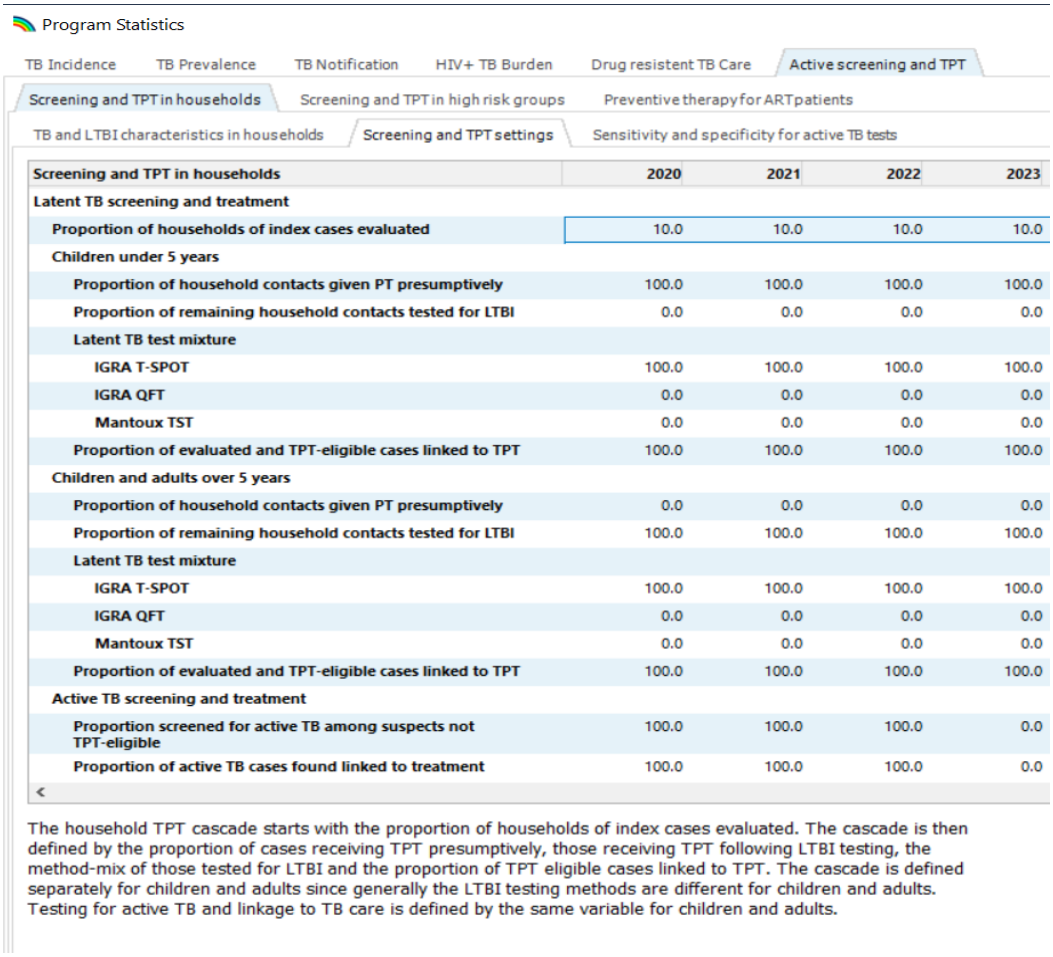
1) Define the coverage of the active screening approach by completing values for "Proportion of (either households of index cases evaluated/population in high-risk groups evaluated or proportion of new ART patients evaluated. Note that this coverage setting will be set in OneHealth. This links between coverage and other setting and OneHealth is explained in more detail in section 6.

2) Review and if needed change which proportion of people assessed is eligible for TPT presumptively or eligible following screening for latent TB

3) Review for those screened what is the mix of LTBI testing methods used. Default is screening for LTBI by TSPOT.

Note that inputs are separated for children under 5 and adults and children over 5. See figure 14. Note further that the same method mix should be specified in this editor as is specified in OHT where the user also describes the mix of methods used for LTBI screening.

Figure 14: Screening and TPT settings



Screening and TPT in households	2020	2021	2022	2023
Latent TB screening and treatment				
Proportion of households of index cases evaluated	10.0	10.0	10.0	10.0
Children under 5 years				
Proportion of household contacts given PT presumptively	100.0	100.0	100.0	100.0
Proportion of remaining household contacts tested for LTBI	0.0	0.0	0.0	0.0
Latent TB test mixture				
IGRA T-SPOT	100.0	100.0	100.0	100.0
IGRA QFT	0.0	0.0	0.0	0.0
Mantoux TST	0.0	0.0	0.0	0.0
Proportion of evaluated and TPT-eligible cases linked to TPT	100.0	100.0	100.0	100.0
Children and adults over 5 years				
Proportion of household contacts given PT presumptively	0.0	0.0	0.0	0.0
Proportion of remaining household contacts tested for LTBI	100.0	100.0	100.0	100.0
Latent TB test mixture				
IGRA T-SPOT	100.0	100.0	100.0	100.0
IGRA QFT	0.0	0.0	0.0	0.0
Mantoux TST	0.0	0.0	0.0	0.0
Proportion of evaluated and TPT-eligible cases linked to TPT	100.0	100.0	100.0	100.0
Active TB screening and treatment				
Proportion screened for active TB among suspects not TPT-eligible	100.0	100.0	100.0	0.0
Proportion of active TB cases found linked to treatment	100.0	100.0	100.0	0.0

The household TPT cascade starts with the proportion of households of index cases evaluated. The cascade is then defined by the proportion of cases receiving TPT presumptively, those receiving TPT following LTBI testing, the method-mix of those tested for LTBI and the proportion of TPT eligible cases linked to TPT. The cascade is defined separately for children and adults since generally the LTBI testing methods are different for children and adults. Testing for active TB and linkage to TB care is defined by the same variable for children and adults.

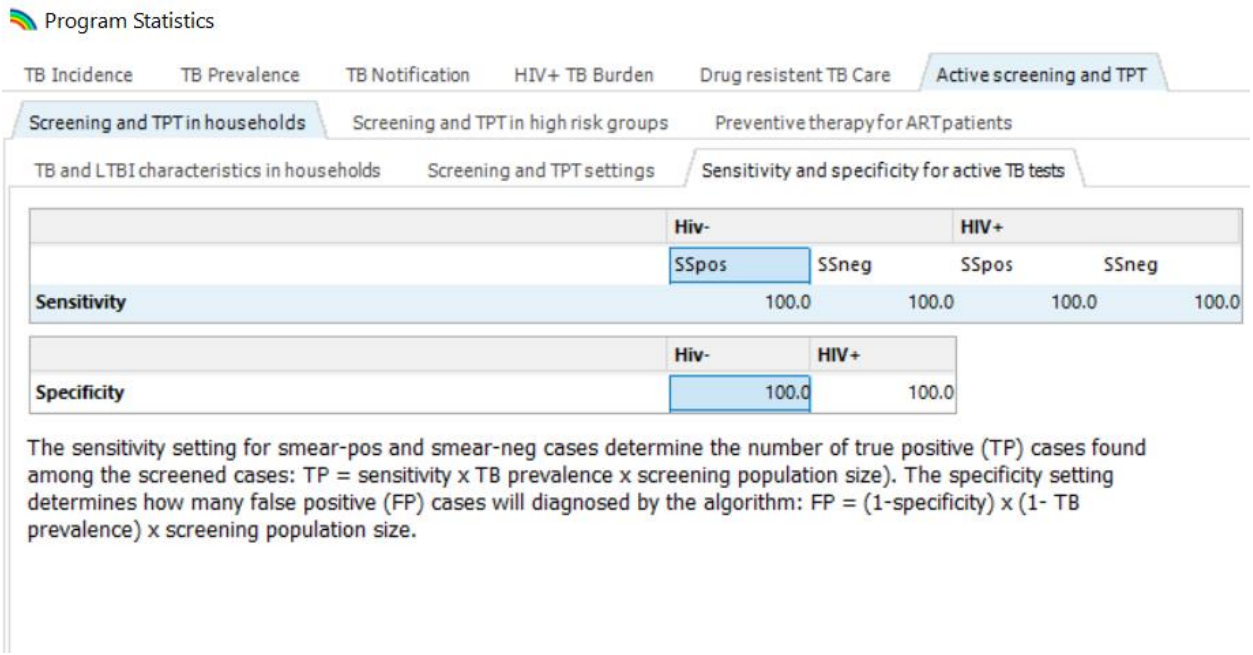
4.3.5.3 Sensitivity and specificity for active TB tests

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\Active screening and TPT\Sensitivity and specificity for active TB tests
- **Steps for OHT user:** The user must define/configure the average sensitivity and specificity of active TB screening algorithm used.

Here the user must state, for the proportion of screened cases also screened for active TB, the average sensitivity and specificity of the screening test . Note that for large screening programs the issue of non-perfect specificity and False Positives become relevant from a costing perspective and the costs associated with this will generally limit ACF in high-risk populations.

Further, the user should note that active TB screening is not an option in the module section that deals with ART cohorts – the reason is that this type of screening is handled as being part of routine testing in the TB Notifications section. See figure 15.

Figure 15: Sensitivity and specificity for active TB tests



4.4 Step 3. Fitting a TIME Estimates projection

- **Location in OHT:** Impact Modules\TIME Estimates\Indicators\Fit indicators and \Display indicators
- **Steps for OHT user:** In Fit indicators the user can use the Fit all option to produce all needed forward projections via cubic-spline projections.

The fitting process is described in detail in Annex 1. The user will see that default projections are provided for total TB notifications and TB for TB incidence. These default projections are reliable and serve many purposes.

However, the OHT user can generally get a better fit via the “Fit All” option since when focusing a single country, the fitting algorithm can use a large number of samples in the statistical method, this would be impractical when processing default projections for all countries.

For this reason, it is recommended that the user fits the model via the Fit All option, instead of working with the default forward projections.

4.5 Step 4. Generating and edititing results for TB target populations

- **Location in OHT:** Impact Modules\TIME Estimates\Results\OHT Target Populations and Impact Modules\TIME Estimates\Program Statistics\OHT Target Populations
- **Steps for OHT user:** Review the resulting OHT target populations table which contains all target populations that are available in OHT for costing TB interventions. The user can also directly edit the target population table in cases where more suitable target population numbers can be produced externally to the TIME Estimates model.

Once the data in Program Statistics have been reviewed, updated (if needed) and the model fit is accepted (Annex 1 explains how to fit the model), then the target populations can be generated by TIME Estimates.

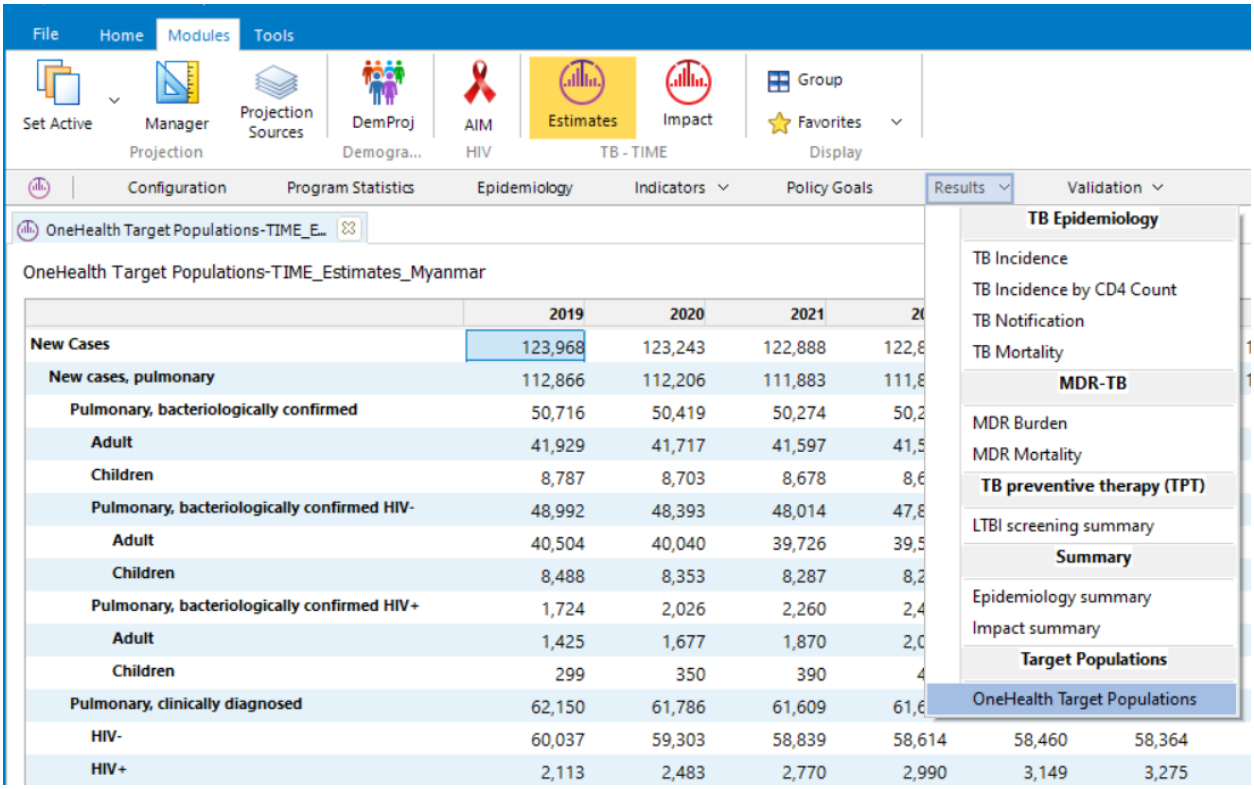
4.5.1 Generating results for target populations

- **Location in OHT:** Impact Modules\TIME Estimates\Results\OHT Target Populations and Impact Modules\TIME Estimates\Program Statistics\OHT Target Populations
- **Steps for OHT user:** Review the resulting OHT target populations table which contains all target populations that are available in OHT for costing TB interventions. To generate results and view the target populations click on **Results > OneHealth Target Populations**.

The Target Population table lists all the data generated by TIME Estimates that can be used as target populations in OHT. Based on the information in Program Statistics/TB Notifications, the table shows (see figure 16)

- Case types :
    - New cases
        - Pulmonary bacteriologically confirmed
        - Pulmonary clinically diagnosed
        - Extrapulmonary
    - Relapse
        - Pulmonary bacteriologically confirmed
        - Pulmonary clinically diagnosed
        - Extrapulmonary
    - Previously treated cases, including and excluding relapse.
- Each case type is disaggregated by drug resistance (MDR status), by HIV status and by age, as relevant for the indicator.
- Note that each indicator which has sub-indicators showing the disaggregation of the numbers. For example, **Pulmonary, bacteriologically confirmed** which has two sub-lines, showing the numbers disaggregated by **Adults** and **Children.** This indicator is also disaggregated by HIV status, figure 16.
- The table also lists the number eligible for TPT:
    - The number of people at risk that were assessed during the pre-TPT stage.
    - The number eligible for LTBI testing. This is the number that proceed past the pre-TBT evaluation stage but require testing to proceed to TPT eligibility. In generally high-risk cases are given TPT presumptively, i.e. without LTBI testing. However, it is assumed that the user is familiar with the WHO guidelines for TPT.
    - The number eligible for TPT either without (i.e. presumptively) or with LTBI testing.
    - Disaggregated by HIV-status and adult by children and adults – to account for differences in testing and treatment options for these types of cases.

Figure 16: OneHealth Target Populations



	2019	2020	2021	2022	2023	2024
New Cases	123,968	123,243	122,888	122,8		
New cases, pulmonary	112,866	112,206	111,883	111,8		
Pulmonary, bacteriologically confirmed	50,716	50,419	50,274	50,2		
Adult	41,929	41,717	41,597	41,5		
Children	8,787	8,703	8,678	8,6		
Pulmonary, bacteriologically confirmed HIV-	48,992	48,393	48,014	47,8		
Adult	40,504	40,040	39,726	39,5		
Children	8,488	8,353	8,287	8,2		
Pulmonary, bacteriologically confirmed HIV+	1,724	2,026	2,260	2,4		
Adult	1,425	1,677	1,870	2,0		
Children	299	350	390	4		
Pulmonary, clinically diagnosed	62,150	61,786	61,609	61,6		
HIV-	60,037	59,303	58,839	58,614	58,460	58,364
HIV+	2,113	2,483	2,770	2,990	3,149	3,275

4.5.2 Directly edit target populations

- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\TB Notifications and Impact Modules\TIME Estimates\Program Statistics\OHT Target Populations
- **Steps for OHT user:** Review the resulting OHT target populations table which contains all target populations that are available in OHT for costing TB interventions. To generate results and view the target populations click on **Results > OneHealth Target Populations**.

The user may choose to use the estimated numbers for target populations for costing which are derived externally from TIME Estimates. The user can always enter these directly in OHT-TB costing module as "custom target population".

However, the target population structure in TIME Estimates can also be changed or edited in different ways within the TIME Estimates software:

1. Editing the target populations by modifying the projection of notifications and recalculating the target population (by generating it under **Results/OneHealth Target Populations**)
2. Directly editing the target population table

4.5.2.1 Editing target populations by modifying projected notifications

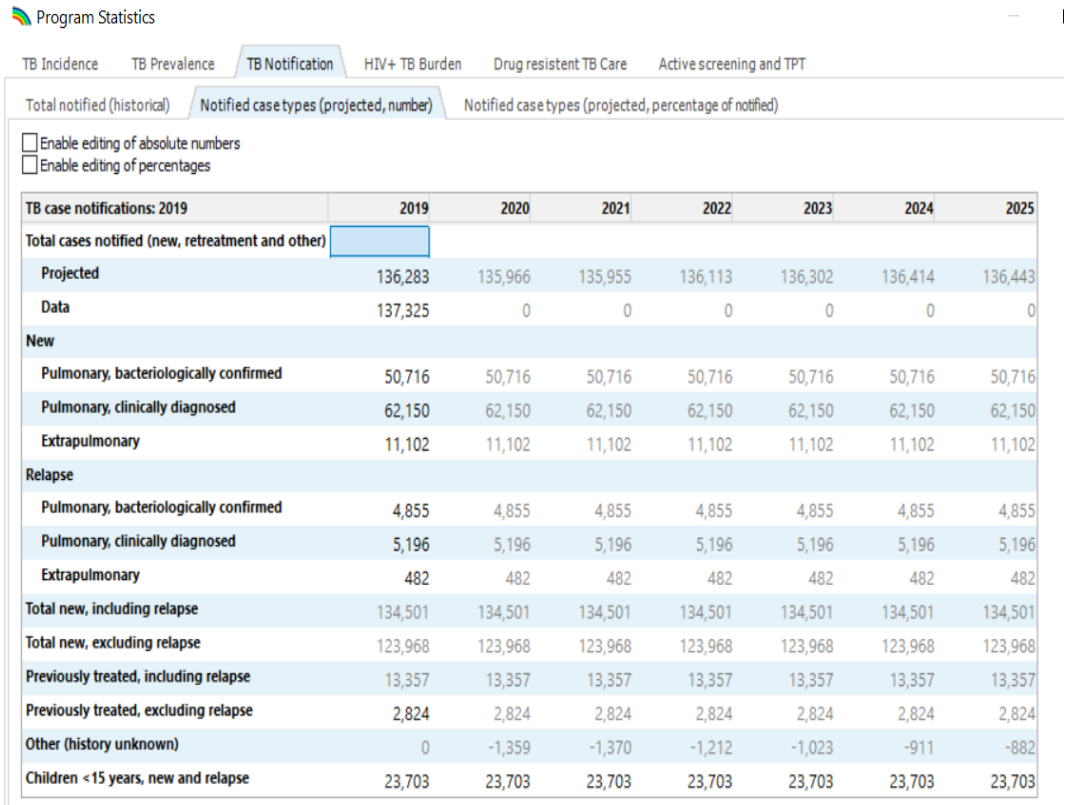
- **Location in OHT:** Impact Modules\TIME Estimates\Program Statistics\TB Notifications
- **Steps for OHT user:** The user can edit the projection of total TB notification. This projection will then be used with the split in TB case types, including the volume of MDR patients as specified

in the **Drug resistant TB care** section, to make forward projections of various target populitions needed for TB costing.

Returning to the **Program Statistics > TB Notifications > Notified case types (projected, number)**, the user can click "Enable the editing of absolute numbers" and then manually provide projected numbers of each case type. **Note the user must ensure that the different case types add up to the total**. For example, the user must ensure the three types of New and Previously treated case add to Total Notifications (excluding cases with unknown treatment history). See figure 17.

Note that the top lines show the projected TB notification, with data shown in the lines below. The Projected TB notification estimate will generally not fit the data point exactly. The reason for this is that the fitting method is designed to produce a best fit to all the historical data points. This fit to all data points can be better seen under **Indicators/Display Indicators/Notification** (figure 41) or **Results/TB Notification** (figure 22), where the user can use visual inspection to assess the quality of the overall fit. In general, fitted trends appearing under the indicator "projected" should provide reasonable input to costing results and the user should review the implications for costing before iterating the fitting process, as the costing results may be reasonable without further refinements of the fitted trends.

Figure 17: TB Notifications, projected numbers. Estimate refers to the estimate of total notifications for the years available as reported to WHO (ending in 2019 in this case). Projected refers to the projection/trend that is fitted through the estimates (the fitting process is described in Annex 1).

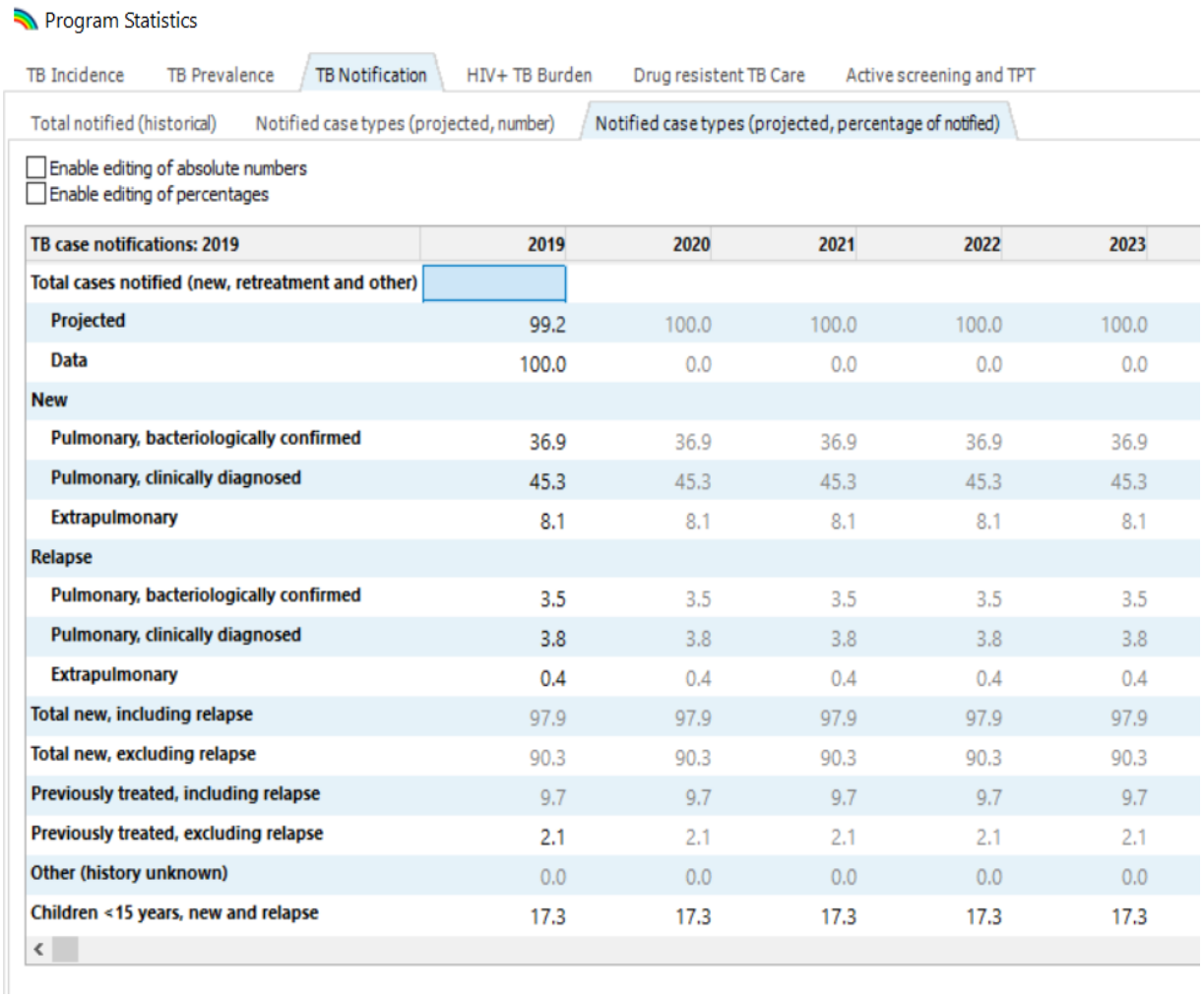


TB case notifications: 2019	2019	2020	2021	2022	2023	2024	2025
Total cases notified (new, retreatment and other)							
Projected	136,283	135,966	135,955	136,113	136,302	136,414	136,443
Data	137,325	0	0	0	0	0	0
New							
Pulmonary, bacteriologically confirmed	50,716	50,716	50,716	50,716	50,716	50,716	50,716
Pulmonary, clinically diagnosed	62,150	62,150	62,150	62,150	62,150	62,150	62,150
Extrapulmonary	11,102	11,102	11,102	11,102	11,102	11,102	11,102
Relapse							
Pulmonary, bacteriologically confirmed	4,855	4,855	4,855	4,855	4,855	4,855	4,855
Pulmonary, clinically diagnosed	5,196	5,196	5,196	5,196	5,196	5,196	5,196
Extrapulmonary	482	482	482	482	482	482	482
Total new, including relapse	134,501	134,501	134,501	134,501	134,501	134,501	134,501
Total new, excluding relapse	123,968	123,968	123,968	123,968	123,968	123,968	123,968
Previously treated, including relapse	13,357	13,357	13,357	13,357	13,357	13,357	13,357
Previously treated, excluding relapse	2,824	2,824	2,824	2,824	2,824	2,824	2,824
Other (history unknown)	0	-1,359	-1,370	-1,212	-1,023	-911	-882
Children <15 years, new and relapse	23,703	23,703	23,703	23,703	23,703	23,703	23,703

Similarly, returning to **Program Statistics > TB Notifications > Notified case types (projected, percentage of notified)**, the user can click “Enable the editing of percentage” and then provide the relative distribution of case types (i.e. relative to the total notification number). The relative percentages are then applied to the projected total notification, which is produced by cubic-spline projection as explained in the next section. **Note that the user must ensure that the relative percentages add up to 100%.** For example, the user must ensure the three types of New and Previously treated case add to 100% (excluding cases with unknown treatment history). See figure 18.

The two approaches, namely absolute or relative values for different notified case types, serve the same purpose, which is to project case types forward for costing purposes. The user must decide which approach works best in his/her situation. The implication of case type split is only seen when the user evaluated target population for costing, and when the user uses OneHealth to study the resource implication of diagnosis for each case type.

Figure 18: TB Notifications, percentage of total notifications



TB case notifications: 2019	2019	2020	2021	2022	2023
Total cases notified (new, retreatment and other)					
Projected	99.2	100.0	100.0	100.0	100.0
Data	100.0	0.0	0.0	0.0	0.0
New					
Pulmonary, bacteriologically confirmed	36.9	36.9	36.9	36.9	36.9
Pulmonary, clinically diagnosed	45.3	45.3	45.3	45.3	45.3
Extrapulmonary	8.1	8.1	8.1	8.1	8.1
Relapse					
Pulmonary, bacteriologically confirmed	3.5	3.5	3.5	3.5	3.5
Pulmonary, clinically diagnosed	3.8	3.8	3.8	3.8	3.8
Extrapulmonary	0.4	0.4	0.4	0.4	0.4
Total new, including relapse	97.9	97.9	97.9	97.9	97.9
Total new, excluding relapse	90.3	90.3	90.3	90.3	90.3
Previously treated, including relapse	9.7	9.7	9.7	9.7	9.7
Previously treated, excluding relapse	2.1	2.1	2.1	2.1	2.1
Other (history unknown)	0.0	0.0	0.0	0.0	0.0
Children <15 years, new and relapse	17.3	17.3	17.3	17.3	17.3

4.5.2.2 *Editing target populations directly*

- **Location in OHT:** Impact Modules\TIME Estimates\Configuration\OHT Target Populations and Impact Modules\TIME Estimates\Program Statistics\ OHT Target Populations
- **Steps for OHT user:** The user can activate the use of a table for the direct entry of OHT target populations. The table is first loaded with the current projections from the model. The user can then edit any part of the table.

The user can also directly edit target populations, as opposed to producing different ones by redoing indicator fitting) to provide their own estimates for use in the OHT TB module.

To activate this feature, go to the left most tab “Configuration” and click “allow user editing of OneHealth Target Population” as shown in figures 19 and 20. Note that this box is not checked by default, which means that target populations generated by TIME Estimates will be used by default in OHT costing. And that by default the target population is not visible for editing, but only after generating it via **Results/OneHealth Target Populations**.

Figure 19: Configuration to allow the direct editing of target populations

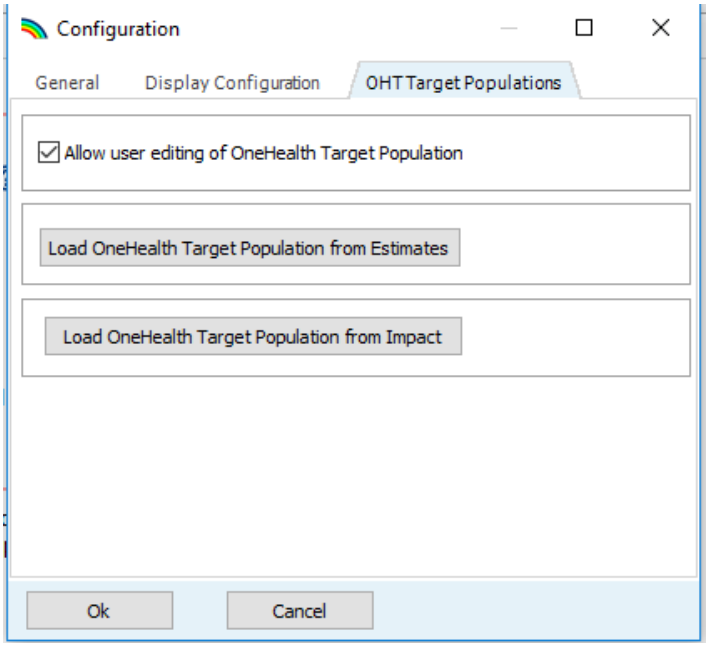
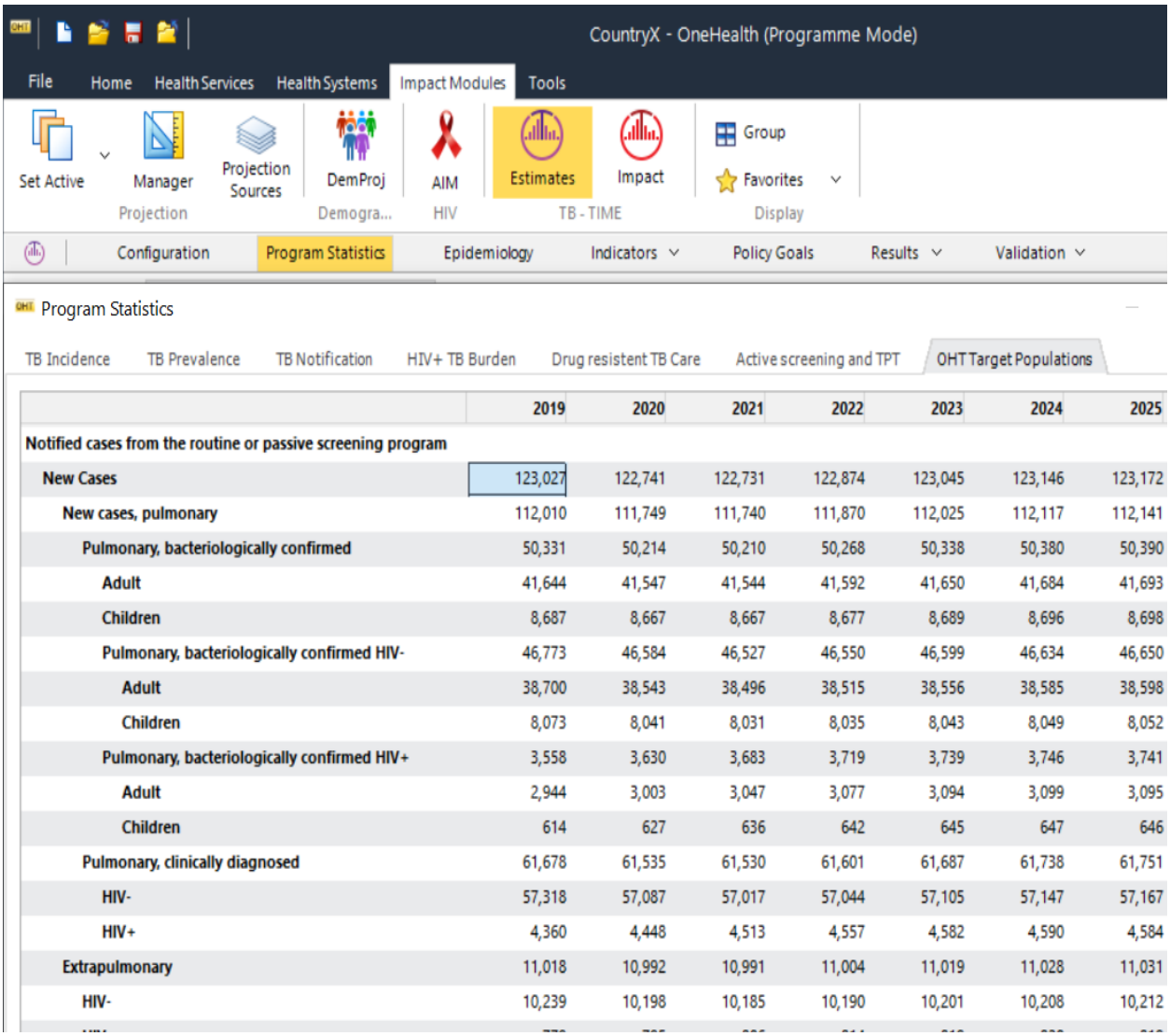


Figure 20: Target population table in the Program Statistics/OHT target population section.



	2019	2020	2021	2022	2023	2024	2025
Notified cases from the routine or passive screening program							
New Cases	123,027	122,741	122,731	122,874	123,045	123,146	123,172
New cases, pulmonary	112,010	111,749	111,740	111,870	112,025	112,117	112,141
Pulmonary, bacteriologically confirmed	50,331	50,214	50,210	50,268	50,338	50,380	50,390
Adult	41,644	41,547	41,544	41,592	41,650	41,684	41,693
Children	8,687	8,667	8,667	8,677	8,689	8,696	8,698
Pulmonary, bacteriologically confirmed HIV-	46,773	46,584	46,527	46,550	46,599	46,634	46,650
Adult	38,700	38,543	38,496	38,515	38,556	38,585	38,598
Children	8,073	8,041	8,031	8,035	8,043	8,049	8,052
Pulmonary, bacteriologically confirmed HIV+	3,558	3,630	3,683	3,719	3,739	3,746	3,741
Adult	2,944	3,003	3,047	3,077	3,094	3,099	3,095
Children	614	627	636	642	645	647	646
Pulmonary, clinically diagnosed	61,678	61,535	61,530	61,601	61,687	61,738	61,751
HIV-	57,318	57,087	57,017	57,044	57,105	57,147	57,167
HIV+	4,360	4,448	4,513	4,557	4,582	4,590	4,584
Extrapulmonary	11,018	10,992	10,991	11,004	11,019	11,028	11,031
HIV-	10,239	10,198	10,185	10,190	10,201	10,208	10,212

When “allow user editing of OneHealth Target Population” is ticked, a new tab becomes available under Program Statistics, called **OneHealth Target Populations** (figure 21). The table has many rows and the main structure of the table is:

- Notified cases from the routine or passive screening program
    - New cases
    - Previously treated cases
- First-line treatment
    - Children and adults
- Second-line TB treatment
    - MDR and XDR
- TB preventive therapy (TPT)
- Active TB screening in households and high-risk groups

If the user edits the OHT Target Populations, he/she is responsible for ensuring consistency of the target population stated in the table. For example, the disaggregation by age, HIV and drug resistance status add up to the relevant totals. **Note there are no automated checks in place, these checks are the responsibility of the user.**

The other two options in the **Configuration/OneHeath Target Population** tab are (see figure 19):

- **Load Target Populations from Estimates**: Target populations are loaded into the user-editable table from TIME Estimates. This option is the starting point for the OneHealth-TB user as it will create a target population table with estimates from the model which the user can edit. It can be used to re-instate the model’s values after they have been edited.
- **Load Target Populations from Impact**: This method is out of the scope of this guidance. The non-expert user of the Estimates model would never use this option. It requires a fully calibrated TIME Impact model so that target populations are loaded into the user-editable table from TIME Impact.

4.6 Step 4. Generating other results (incidence, mortality, notifications and epidemiology summary)

- **Location in OHT:** Impact Modules\TIME Estimates\Results\
- **Steps for OHT user:** View projections of TB burden, TB notifications, TB mortality, summary of LTBI results and summary of overall epidemiology.

The above sections focused on OneHealth Target Populations. Other results that are relevant to OHT costing users include:

1. Epidemiology results:
    a. TB Incidence: Figure 21
        i. Incidence is shown by HIV status. Confidence intervals are shown.
    b. TB Notifications: Figure 22
    c. TB Mortality: Figure 23
    d. Epidemiology summary: Figure 24
2. LTBI screening summary, (see figure 25: here the user can visualize results by population screened (households, high-risk groups or ART cohorts), by age (U5s or O5s) and HIV status (HIV-neg or HIV-positive). Note that results are calculated LTBI indicators for the start to end year of the projection. This is because LTBI and TPT results are used for costing. Some of the general results, like total notifications, are available for past years since there results are needed for evaluation as part of calibrating the model to past data.
3. Impact summary (figures 26)– impact on TB mortality of the notification increase specified in Policy Goals (figure 44)

4.6.1 A note of results visualization using different display formats

Most figures in Spectrum OHT have configuration options:

- The user can set the years of display.
- The user can display a table instead of a chart.
- The user can copy the contents of the chart or of a table for report writing purposes.

Whenever the user goes to the Result section (i.e. “Estimates/Results"), after editing any data in the data editors (i.e. in any of the tabs other than the Results section), the model is recalculated. For example, mortality is recalculated from incidence, notification and case-fatality inputs as detailed per Annex 1.

1. Epidemiology results

Figure 21: Epidemiology: TB Incidence

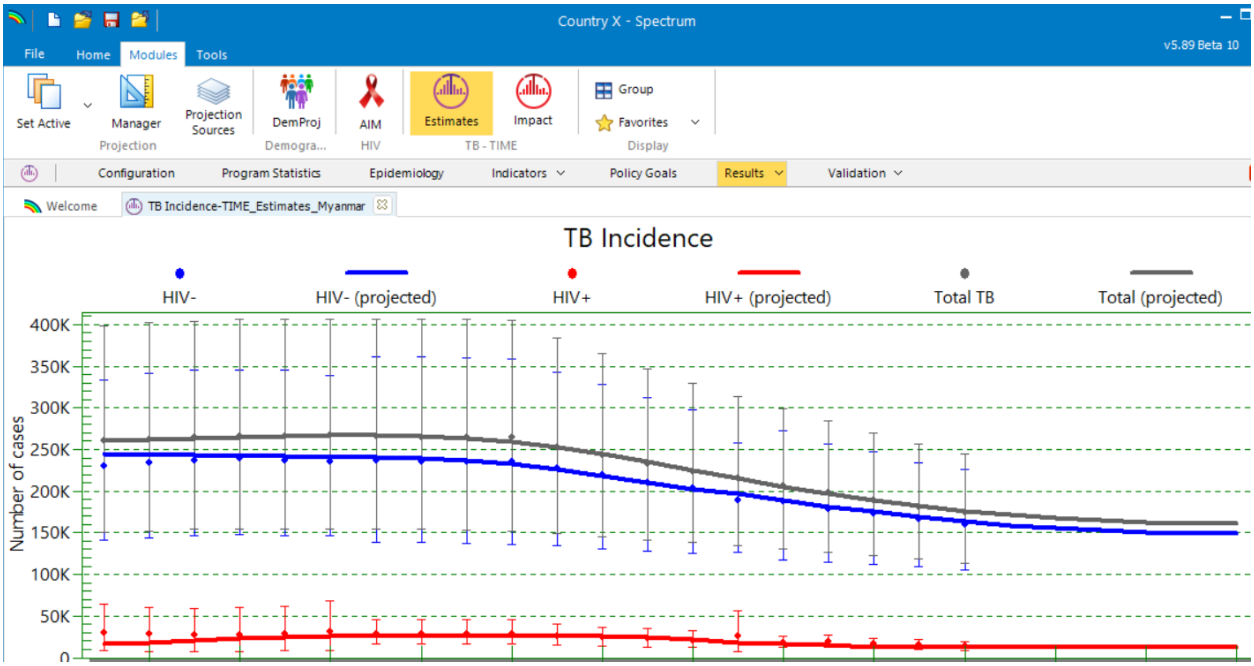


Figure 22: Epidemiology: TB Notification

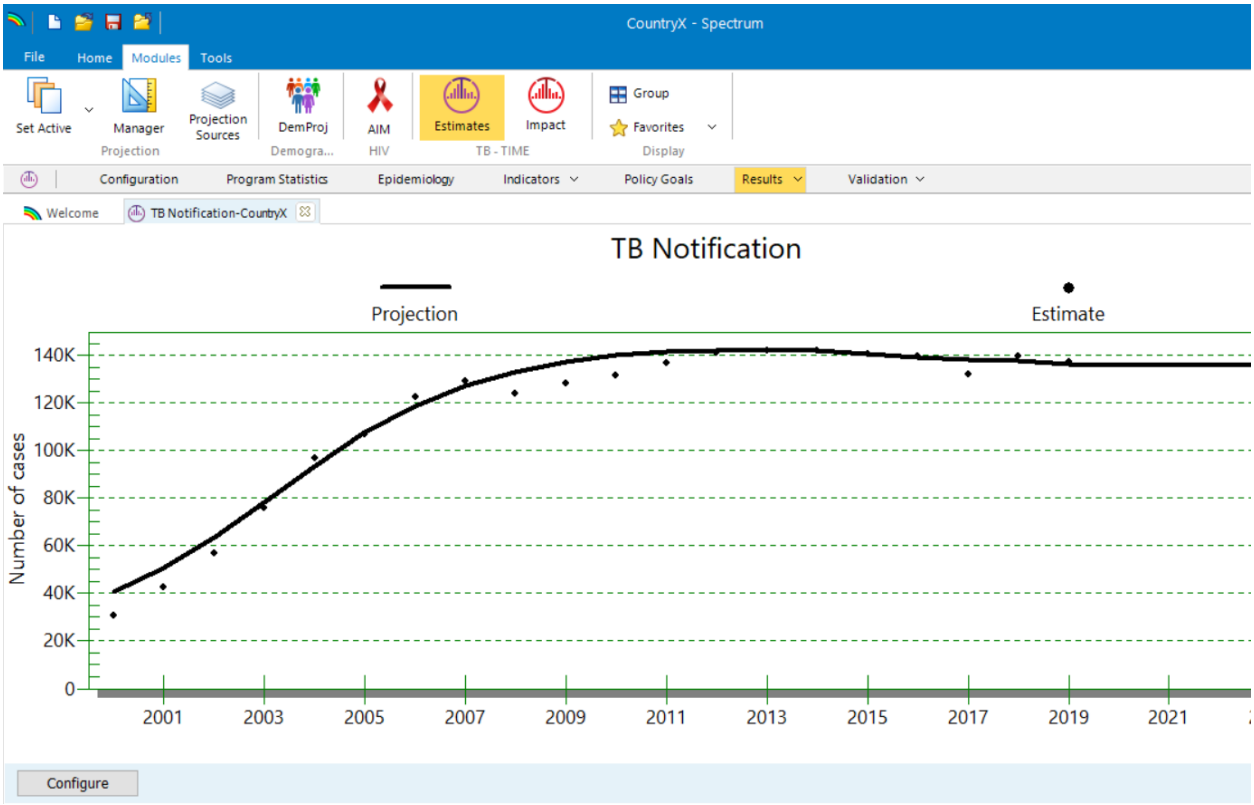
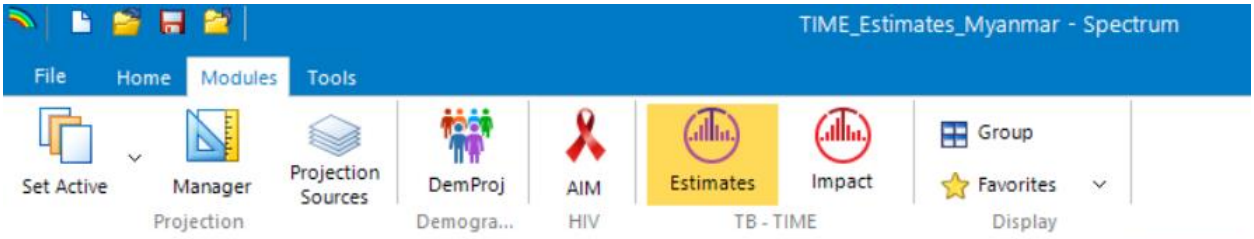


Figure 23: Epidemiology: TB Mortality

Figure 24: Epidemiology summary



Epidemiology summary-TIME_Estimates_Myanmar

	2019	2020	2021	2022	2023	2024	2025
TB Incidence							
Total incidence	176,335	171,620	167,895	165,037	163,033	161,675	160,836
HIV- TB incidence	170,341	164,723	160,346	157,027	154,701	153,085	151,973
HIV+ TB incidence	5,994	6,897	7,549	8,011	8,332	8,590	8,863
Receiving ART more than one year	0	0	0	0	0	0	0
Receiving ART less than one year (by CD4 count)	0	0	0	0	0	0	0
> 500	0	0	0	0	0	0	0
350 - 500	0	0	0	0	0	0	0
250 - 350	0	0	0	0	0	0	0
200 - 250	0	0	0	0	0	0	0
100 - 200	0	0	0	0	0	0	0
50 - 100	0	0	0	0	0	0	0
< 50	0	0	0	0	0	0	0
Not Receiving ART (by CD4 count)	5,994	6,897	7,549	8,011	8,332	8,590	8,863
> 500	583	541	507	478	457	442	436
350 - 500	845	799	759	724	695	676	669
250 - 350	1,098	1,079	1,049	1,015	982	959	950

2. LTBI screening summary

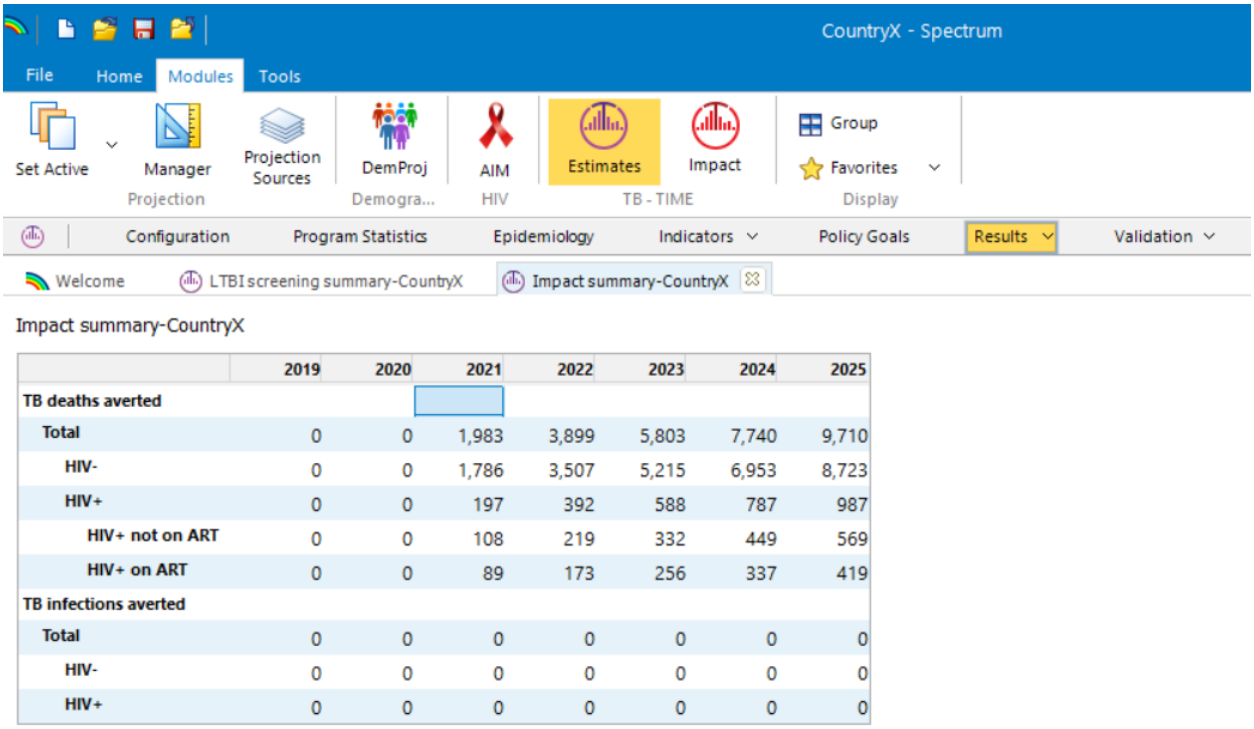
Figure 25: LTBI and TPT results

LTBI screening summary-CountryX

	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	20
Latent TB																						
Population enter TPT cascade	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2,760,530	2,782,965	212,1
Proportion suspects continue to latent TB tests	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	365,735	368,467	
Latent TB tests																						
IGRA T-SPOT	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	365,735	368,467	
IGRA QFT	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
Mantoux TST	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
All tests for LTBI	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	365,735	368,467	
TPT eligible, screened	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	166,044	167,284	
TPT eligible, presumptive	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	54,335	54,629	20,1
TPT eligible, screened and presumptive	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	220,379	221,913	20,1
Number linked to TPT	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	220,379	221,913	20,1
Active TB																						
Number to test for active TB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	834,692	840,790	21,2
Number tested for active TB	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	814,112	819,878	
Number linked to TB treatment	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	814,112	819,878	

3. Impact summary (figure 26)– impact on TB mortality of the notification increase specified in Policy Goals Policy Goals Results: Impact on TB mortality. Annex 2 details how to use Policy Goals to estimate impact on TB mortality.

Figure 26: Policy Goals Results: Impact on TB mortality



Impact summary-CountryX

	2019	2020	2021	2022	2023	2024	2025
TB deaths averted							
Total	0	0	1,983	3,899	5,803	7,740	9,710
HIV-	0	0	1,786	3,507	5,215	6,953	8,723
HIV+	0	0	197	392	588	787	987
HIV+ not on ART	0	0	108	219	332	449	569
HIV+ on ART	0	0	89	173	256	337	419
TB infections averted							
Total	0	0	0	0	0	0	0
HIV-	0	0	0	0	0	0	0
HIV+	0	0	0	0	0	0	0

5 Step 5: Using target populations from TIME Estimates to cost TB interventions

The purpose of this section is to provide concrete examples of how the user configures the cost elements for an intervention using the outputs from TIME Estimates. Complementary educational materials on using OHT TB module for costing are available in the training sessions on the OneHealth Tool structure and TB component and covers in detail what the OHT user needs to do to cost "Interventions" and "Program costs". The link between editors in OneHealth and editors and results in TIME Estimates will become clearer to the user.

5.1 Example 1: How to use TIME Estimates Target Populations to cost diagnosis with smear microscopy in OHT TB module for costing

- **Location of Target Populations in OHT**: OHT\Program or channel analysis and Impact Modules\TIME Estimates\Program Statistics\TB Notifications
- **Location of TIME Estimate outputs used in intervention costing in OHT**: OHT\Program or channel analysis and Impact Modules\OHT TB module\Intervention\Target population, Population in Need and Coverage
- **Location of other costing elements used in intervention costing in OHT**: OHT\Program or channel analysis and Impact Modules\OHT TB module\Intervention\Treatment inputs and Delivery Channels
-
-

- **Steps for OHT user to estimate patient volumes:** The user configures the target populations to cost smear microscopy in OHT and counterpart editors in TIME Estimates.
- **Steps for OHT user to estimate intervention costs and delivery channels:** The user configures
- "Treatment inputs" and "Delivery channels" in OHT TB costing module.

The main elements in OneHealth are accessed in the **Health Services/Programme or Channel analysis** section of OneHealth as per figure 27. Note that on the left-hand bar is a setting where the user can select **TB** as the health are to focus on.

The elements for this example:

- **Target Populations** (OHT in figure 28 and TIME Estimates in figure 29).
    - The default target population (which can be altered by the user by scrolling down the target population menu button) is the number of new, adult bacteriologically confirmed cases that are diagnosed. OHT TB module for costing features the indicator itself and the underlying indicator data is located in TIME Estimates/Results/Target Population (or else in TIME Impact if that is used instead) This is a row in the target population table produced by the TIME Estimates model, as per figure 28. The user can edit this target population table in TIME Estimates (sections 4.5.1 and 4.5.2).
- **Population in Need** (figure 30).
    - In this example population in need (PIN) is set to 2000. This a way of accounting for the fact that many suspects are tested to find one notified case. This is called the number needed to test. In this case, the default assumption is that number needed to test is 20 (to be replaced by the user based on local epidemiology knowledge). The user can make this number change over time. As TB screening algorithms adopt less strict entry conditions it may be that over time more suspects must be tested to find a case. On the other hand, testing may also become more focussed. It is up to the user to reflect the realities in their TB program and its policies.
- **Intervention Coverage** (figure 31)
    - In this example, coverage changes from 80% to 20%. This is a typical situation from programs that are coming less reliant on smear microscopy for diagnosis. This change is usually accompanied by more reliance on increased diagnosis with Xpert. And in the row for Xpert diagnosis the user may, as an example, set coverage from 20% to 80%.
    - Note that while in this example coverage with smear microscopy and Xpert adds to 100%. This does not always have to be the case, as some cases may receive diagnosis with multiple diagnostic methods.
    - Note that the lines in figure 31 are marked in red. Red indicates that these interventions do not correspond to a coverage variable in the TIME Estimates model. In this case, coverage serves only a purpose in costing which is to achieve the correct role of different diagnostic methods in the diagnostic algorithm. In the next example we will look at interventions that do link to coverage variables in TIME Estimates.

Up to this stage, TIME Estimates use in OHT costing module ends. The remaining steps for the user to complete the intervention costing, i.e. user documenting "Treatment inputs" and "Delivery channels"

involve use of editors in the OHT TB costing module alone. Further details available in complementary training materials "Budgeting for TB using OneHealth tool" available online[8].

- **Treatment Inputs** (figure 32)
    - "OHT TB module/Intervention/Treatment inputs" editor shows the cost elements that require documenting by the user.
    - Figure 30 shows the treatment inputs for the smear microscopy. This is obtained by clicking on a unit cost when the **Treatment Inputs** is first entered. The user should note in which currency the unit costs are reported. This can be configured between the national currency or USD, as per OneHealth manuals
    - The treatment inputs comprise three components:
        - **Drugs and supplies** – These are the commodities. In this example they include slides, chemicals and other components. The user can edit these or add to them. Defaults are available in a list of commodities and the prices provided in OneHealth.
        - **Medical personnel** – These represent staff time. In this example staff time will typically be a laboratory technician or another staff type as configure under Human Resources. Staff time costs can be costed as part of sector-wide human resources costs.
        - **Outpatients visits and inpatients days** – When OHT is used for disease specific costing and the user wishes to cost the use of health system by specific disease users, this can be done in this tab. This represents health system access costs associated with the intervention or service. In this example it may be that a case visited a clinic. In other diagnostic methods the case may have visited a hospital. This depends in detail on current and future set-up of health systems.
- **Delivery channels** (figures 33 and 34)
    - This OHT TB module/Intervention/Delivery channels editor allows the user to document the delivery channels (hospital, clinic, community etc or user-selected local context specific categories)
    - Figures 33 and 34 show an arbitrary example which illustrates the principle of a program shifting the delivery of a service from a higher (and presumably more costly) to a lower (and presumably less costly) delivery channel. It is not meant to be a detailed account of delivery analysis. It is included for the sake of completeness of the typical costing steps related to TB services.
    - Figure 33 shows that diagnosis with smear microscopy occurs predominantly at hospital level in the base year.
    - Figure 34 shows a shift so that diagnosis with smear microscopy occurs predominantly at the clinic level by the time the target year of a new strategic plan is reached.

[8] https://avenirhealth.org/software-onehealth.php and https://www.who.int/activities/tb-monitoring-and-evaluation

Figure 27: Cost configuration in OneHealth

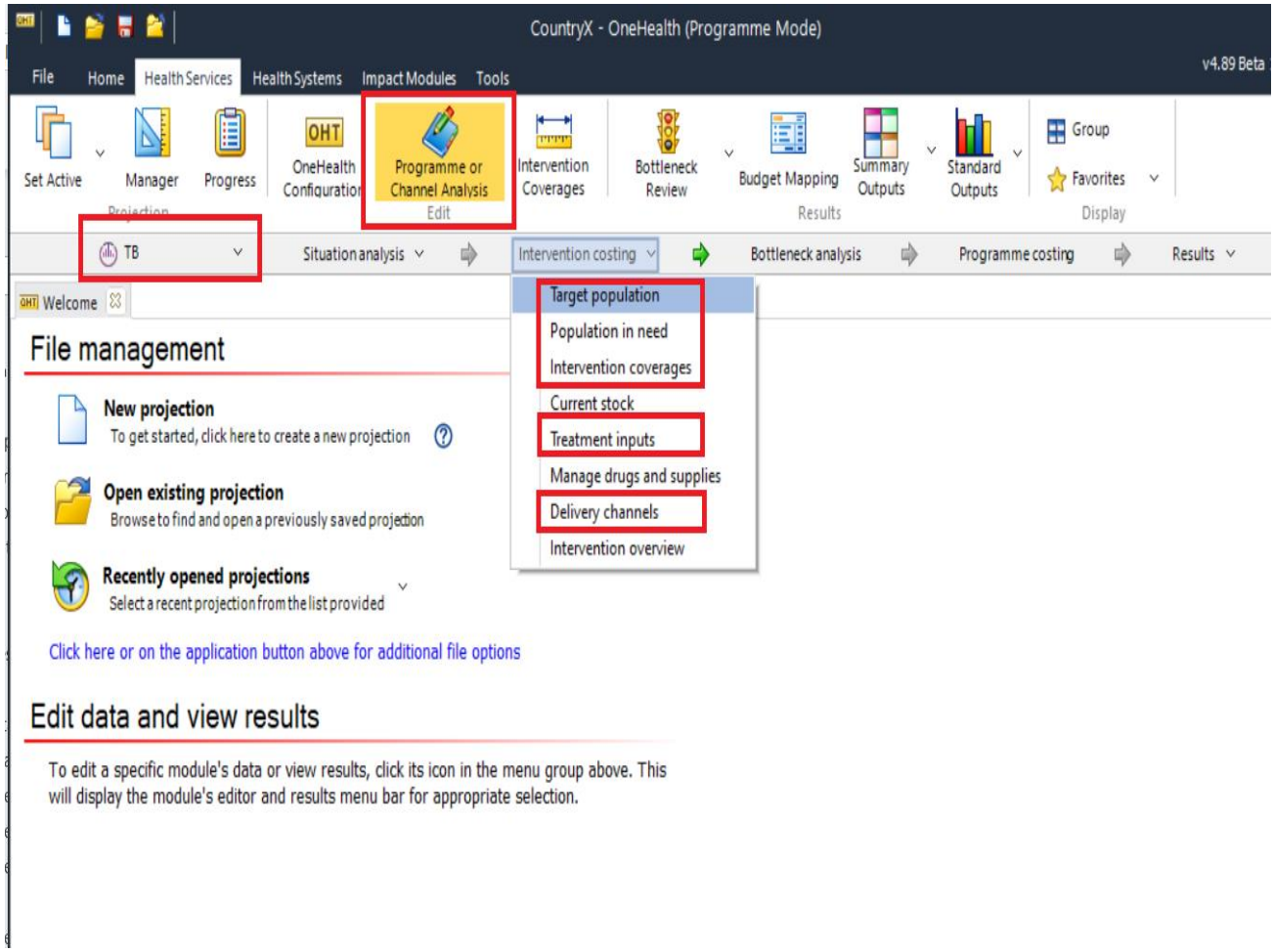


Figure 28: Selecting the target population for diagnosis with smear microscopy in OHT TB module/Intervention costing/Target population editor.

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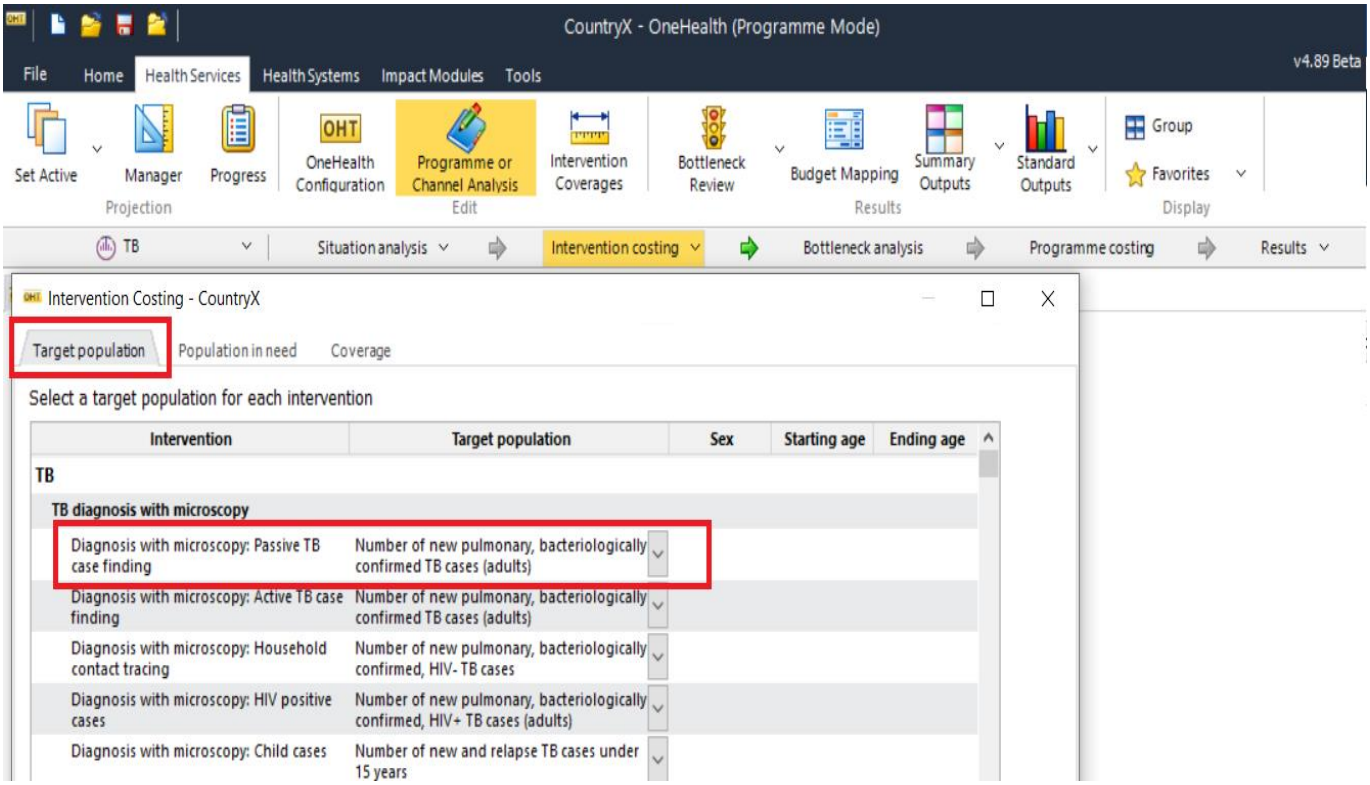
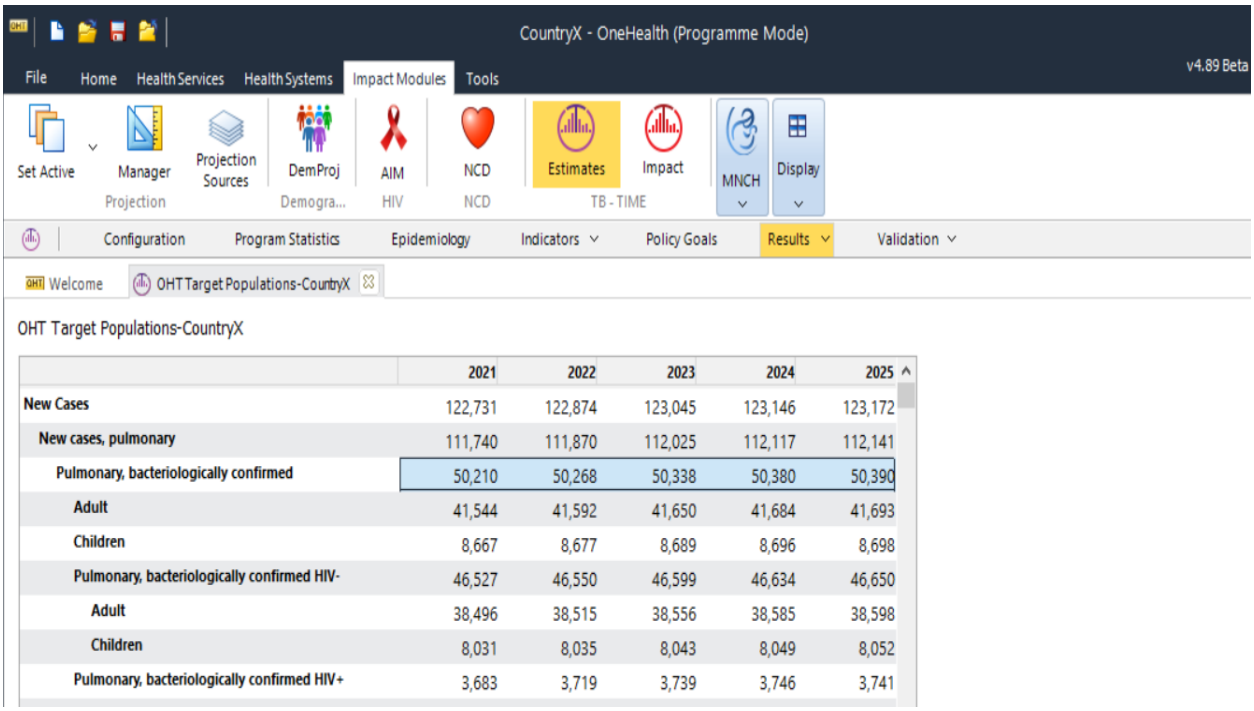


Figure 29: New adult pulmonary bacteriologically confirmed cases as target population for OneHealth costing



	2021	2022	2023	2024	2025
New Cases	122,731	122,874	123,045	123,146	123,172
New cases, pulmonary	111,740	111,870	112,025	112,117	112,141
Pulmonary, bacteriologically confirmed	50,210	50,268	50,338	50,380	50,390
Adult	41,544	41,592	41,650	41,684	41,693
Children	8,667	8,677	8,689	8,696	8,698
Pulmonary, bacteriologically confirmed HIV-	46,527	46,550	46,599	46,634	46,650
Adult	38,496	38,515	38,556	38,585	38,598
Children	8,031	8,035	8,043	8,049	8,052
Pulmonary, bacteriologically confirmed HIV+	3,683	3,719	3,739	3,746	3,741

Figure 30: Setting the population in need for diagnosis with smear microscopy in OHT TB module/Intervention costing/Population in need editor.

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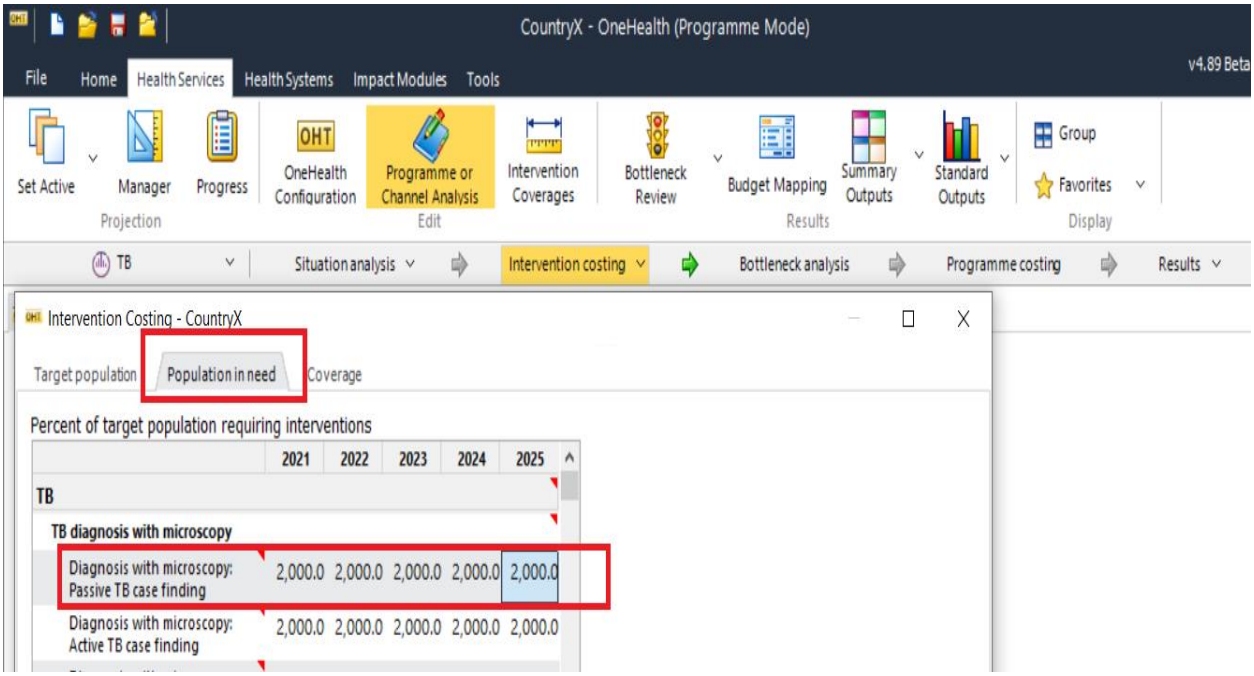


Figure 31: Setting the coverage for diagnosis with smear microscopy in OHT TB module/Intervention costing/Coverage editor.

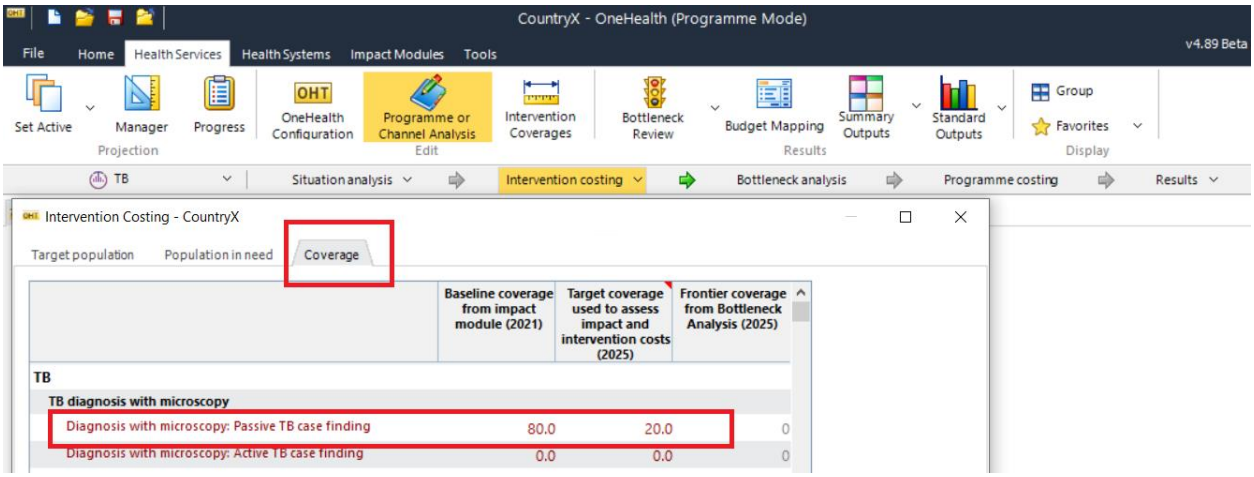


Figure 32: The treatment inputs for smear microscopy

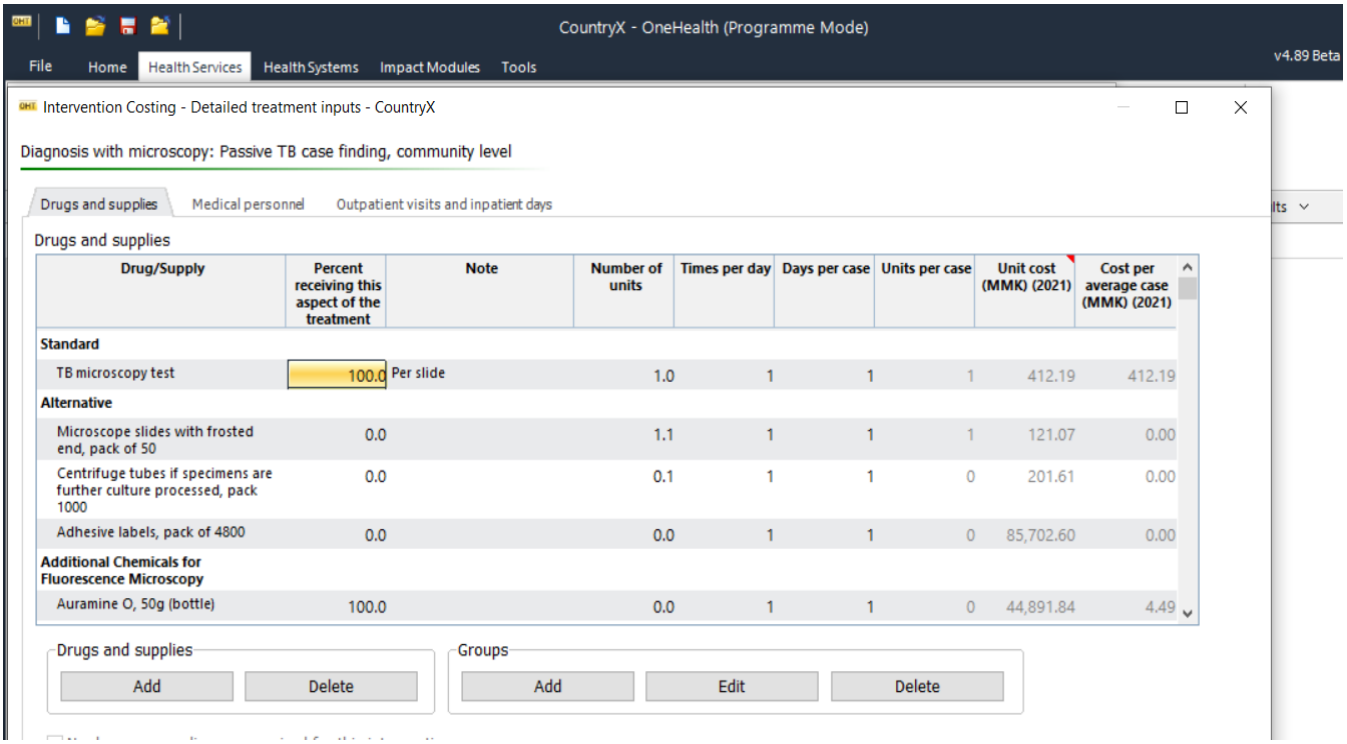


Figure 33: Setting delivery channels in the baseline year.

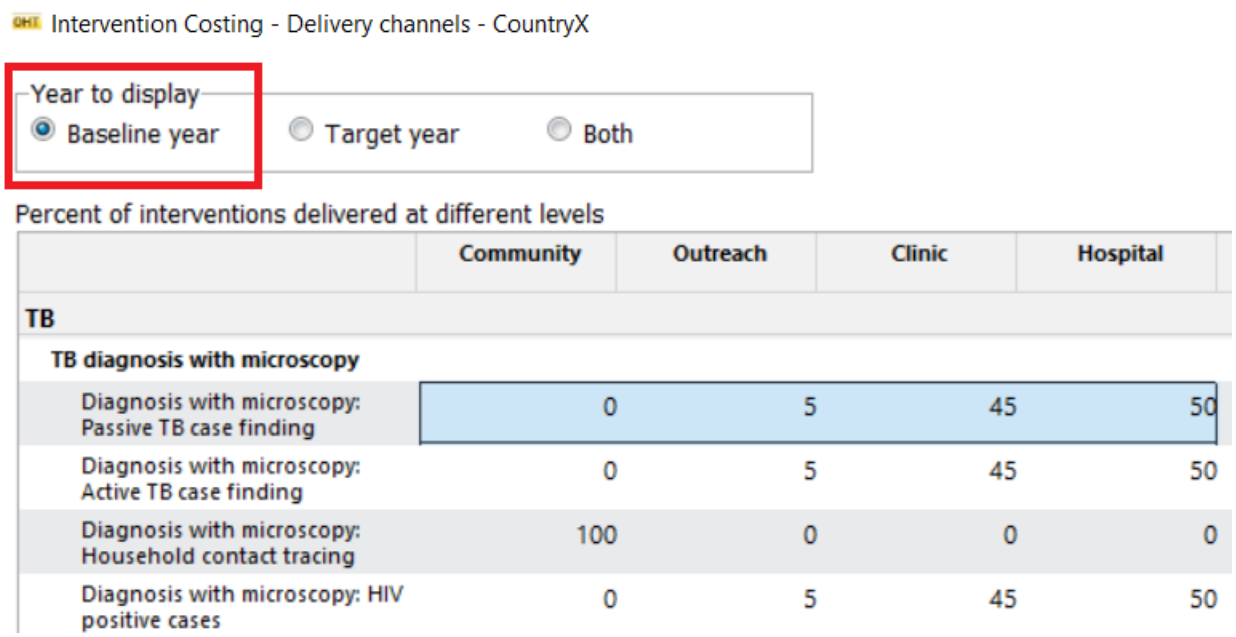


Figure 34: Setting delivery channels in the target year.

Intervention Costing - Delivery channels - CountryX

Year to display

○ Baseline year ◉ Target year ○ Both

Percent of interventions delivered at different levels

	Community	Outreach	Clinic	Hospital
TB				
TB diagnosis with microscopy				
Diagnosis with microscopy: Passive TB case finding	0	20	70	10
Diagnosis with microscopy: Active TB case finding	0	5	45	50
Diagnosis with microscopy: Household contact tracing	100	0	0	0

5.2 Example 2 : How to use TIME Estimates Target Populations to cost TB preventive therapy in OHT TB module for costing

- **Location of Target Populations in OHT**: OHT\Program or channel analysis and Impact Modules\TIME Estimates\Program Statistics\TB Notifications\Active screening and TPT
- **Location of TIME Estimate outputs used in intervention costing in OHT**: OHT\Program or channel analysis and Impact Modules\OHT TB module\Intervention\Target population, Population in Need and Coverage
- **Location of other costing elements used in intervention costing in OHT**: OHT\Program or channel analysis and Impact Modules\OHT TB module\Intervention\Treatment inputs and Delivery Channels
-
- **Steps for OHT user to estimate patient volumes:** The user configures the costing elements TPT in OHT and counterpart editors in TIME Estimates.
- **Steps for OHT user to estimate intervention costs and delivery channels:** The user configures
- "Treatment inputs" and "Delivery channels" in OHT TB costing module.

When costing a typical TPT the user must be aware of few elements of the analysis, depending on national guidelines and their implementation:

- Pre-TPT evaluation- Suspects are evaluated or assessed. This step generally involves a clinical evaluation or further methods to determine if a suspect may have active TB. Those who do not, continue in the TPT cascade[9].
- LTBI testing-Cases may proceed to TPT presumptively or without LTBU testing. This is often the case for suspects at very high risk of TB infection, such as children in households of index cases or ART patients. The remaining cases may be tested for LTBI before being eligible for TPT. The details of the cascade depend on in-country guidelines and policy.
- TPT- the final step in the cascade for presumptive or LTBI tested cases is the PT itself.

This cascade is depicted in OHT TB costing module and TIME Estimates as explained below:

- **Target populations** (OHT TB module in figure 35 and TIME Estimates in figure 36)
    - These figures show the default linking of the relevant target populations for the steps of the TPT cascade that is costed to target populations in TIME Estimates' target population table (figure 35). The target populations are calculated (behind the scenes, in TIME Estimates model) by processing the household, high-risk and ART TPT section of the TPP component of the TIME estimates model.
    - Target populations for TPT (in TIME Estimates/Results/OHT Target Population) are split by adults, children and ART status since the LTBI testing methods and TPT regimens may differ for these types of cases.

[9] WHO consolidated guidelines on tuberculosis: module 1: prevention: tuberculosis preventive treatment

- **Population in Need (PIN)**
    - Default assumption in PIN for TPT cascade: for simplicity that the PINS are set to 100% for all the elements of the TPT cascade. This simply means that the numbers provided by TIME estimates as target populations are all in need of the service implied by the step of the cascade, i.e. evaluation, testing or treatment[9].
- **Intervention Coverage** (figures 37 and 38)
    - The user documents in this tab the coverage of pre-TPT. In this example (figure 37), coverage of the pre-TPT step, i.e. suspect evaluation, increases from 10% to 100%. This may be the case if a country has low coverage of the TPT cascade at present and aspire to achieve new WHO guidelines for TPT.
    - Note that for existing or current ART patient coverage goes only to 30%. This is just an example for a target level. However, it puts focus on the fact that this target will generally not be 100%. This is due to an increasing proportion of ART patients that would have received TPT, say for 3 or 6 months depending on national policy and implied regimen, and these patients will not receive TPT again. While there will be some catch-up in ART cohorts, the focus is more on new ART patients to ensure that eventually the whole ART cohort would have received TPT.
    - In this example TPT coverage, which in practice implies linking to actual treatment for those proceeding in the cascade as eligible, goes from 70% to 100%. This could represent an effort to improve linking to care in a new NSP.
    - Note that the lines in figure 37 are marked in black. Black (as opposed to red in the previous example) indicates that these interventions do correspond to a coverage variable in the TIME Estimates model. When the user hits the option to transfer these coverages to TIME Estimate (called "Transfer coverages to impact modules" in the OneHealth coverage editor), he/she will see the coverages in the TPT editors. Figures 38 shows how the coverage of pre-TPT evaluation is now set to 10% in 2021 and increases to 100%, just as it does in the OneHealth coverage editor.

Again, as in previous example, up to this stage, TIME Estimates use in OHT costing module ends. The remaining steps for the user to complete the intervention costing involve use of editors in the OHT TB costing module alone. Further details available in complementary training materials "Budgeting for TB using OneHealth tool" available online[10].

- **Treatment Inputs**

    The inputs are not shown here. The commodities and personnel time may involve, depending on in country TPT program details:

    - The pre-TPT step of evaluating suspects may involve the cost of a clinical examination.

[10] https://avenirhealth.org/software-onehealth.php and https://www.who.int/activities/tb-monitoring-and-evaluation

- LTBI testing is based on distribution of testing method: IGRA TSPOT, IGRA QFT or Mantoux TSPOT). In “TIME Estimates/Program statistics/Active screening and TPT/Latent TB test mixture” editor, the user determined the test mix. In OHT TB costing module the fix is set as part of the Treatment Inputs of the intervention.
- TPT involves a regimen pertaining to a TPT target population such as Isoniazid (INH), Rifapentine (RPT) or Rifampin (RIF) or other.
- There are also staff time and patient visits to consider, as is the case with all interventions.

Figure 35: Selecting target populations for the TPT cascade in OHT TB module (for costing).

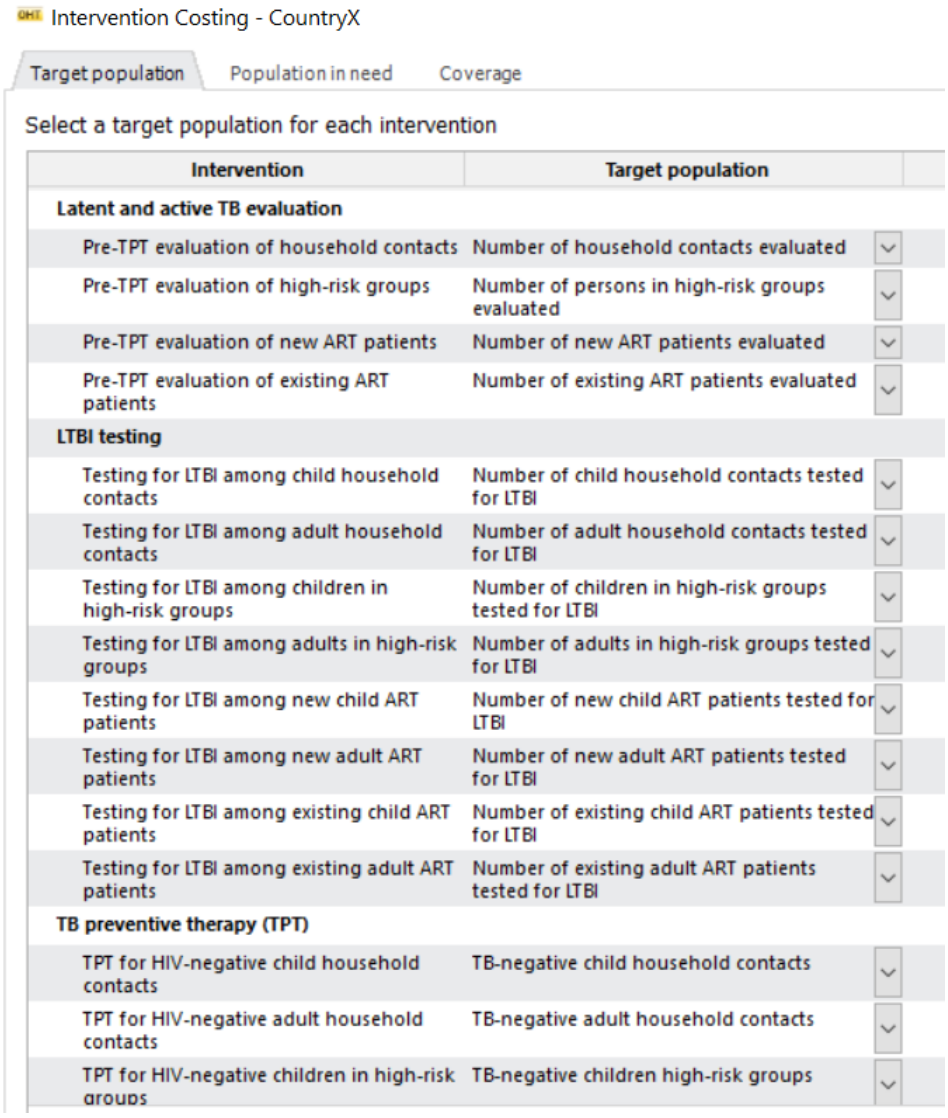


Figure 36: TPT target populations

OHT Target Populations-CountryX

OHT Target Populations-CountryX

	2021	2022	2023	2024	2025
Latent and active TB evaluation	444,252	447,720	450,991	453,812	456,162
Pre-TPT evaluation of household contacts	238,464	238,622	238,847	238,937	238,880
Pre-TPT evaluation of high-risk groups	0	0	0	0	0
Pre-TPT evaluation of new ART patients	1,923	1,886	1,847	1,813	1,787
Pre-TPT evaluation of existing ART patients	203,865	207,212	210,297	213,061	215,495
LTBI testing	5,841	13,355	20,881	52,814	61,709
Testing for LTBI among child household contacts	818	1,873	2,931	3,989	0
Testing for LTBI among adult household contacts	5,022	11,482	17,951	48,825	61,709
Testing for LTBI among children in high-risk groups	0	0	0	0	0
Testing for LTBI among adults in high-risk groups	0	0	0	0	0
Testing for LTBI among new child ART patients	0	0	0	0	0
Testing for LTBI among new adult ART patients	0	0	0	0	0
Testing for LTBI among existing child ART patients	0	0	0	0	0
Testing for LTBI among existing adult ART patients	0	0	0	0	0
TB preventive therapy (TPT)	27,920	64,542	101,898	126,513	164,641
TPT for HIV-negative child household contacts	7,273	16,627	25,993	22,075	27,900
TPT for HIV-negative adult household contacts	1,109	2,538	3,971	5,405	10,092

Figure 37: Coverage setting for typical TPT cascade using OHT TB module/Intervention/Coverage editor.

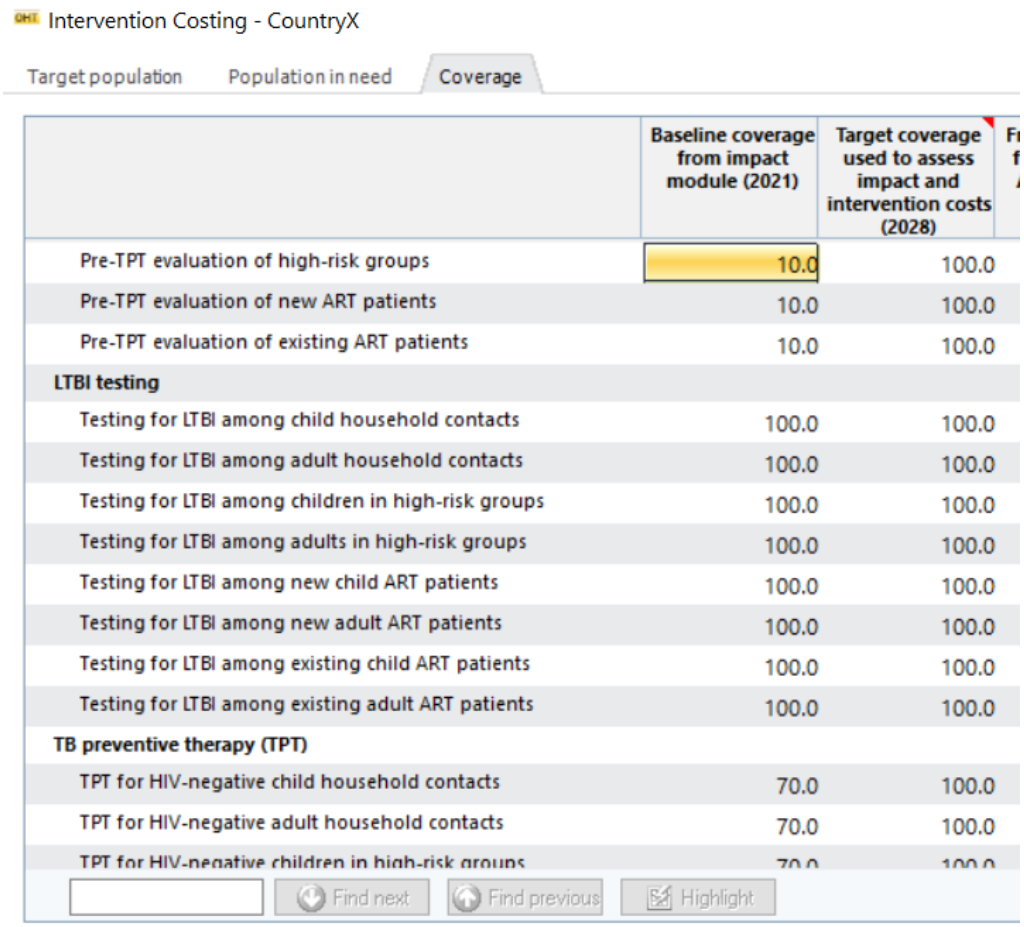
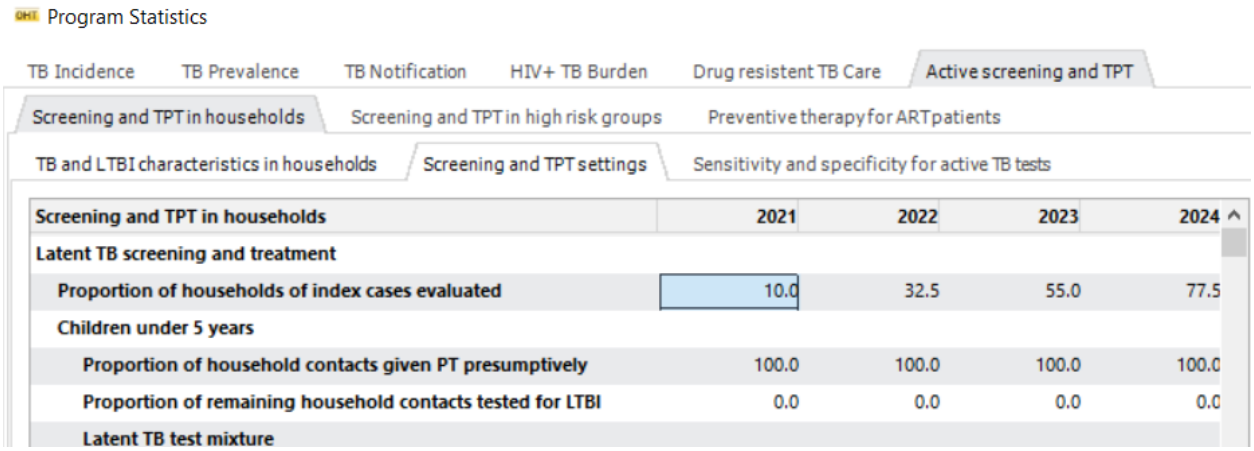


Figure 38: Intervention coverage defined by the user in OHT TB module/Intervention/Coverage editor (Figure 36) and linked with TIME Estimates/Program statistics/Active screening and TPT editor. This link is established in the OneHealth coverage editor when then user selects "Transfer coverages to impact modules".



6 Annexes

6.1 Annex 1: Statistical projections of TB indicators in TIME Estimates using cubic-spline methods

The purpose of this annex is to explain how the user fits epidemiology indicators reviewed in TIME Estimates using cubic spline methods. TIME Estimates uses a generic method and interface for curve fitting via cubic splines. This process is explained in detailed in the Spectrum Manual[11] in the TIME Estimates section.

If the user changes the historical epidemiology data in TIME Estimates/Program statistics and wants to replace the default projections (which are pre-loaded by Avenir Health periodically based on the default data), the key steps are:

1) The user should set the time horizon of the cubic spline projection.
2) Use the current fitting parameters and the "Fit All" option. This option will automatically fit trends to the all the indicators. It may take 30 seconds or so to run.
3) Evaluate the fit trends and if the user wants to replace then, then change the fitting parameter again and use the "Fit All" option again.

6.1.1 Time horizon of the forward projection

Location in OHT: OHT\ Impact Modules\TIME Estimates\Configuration

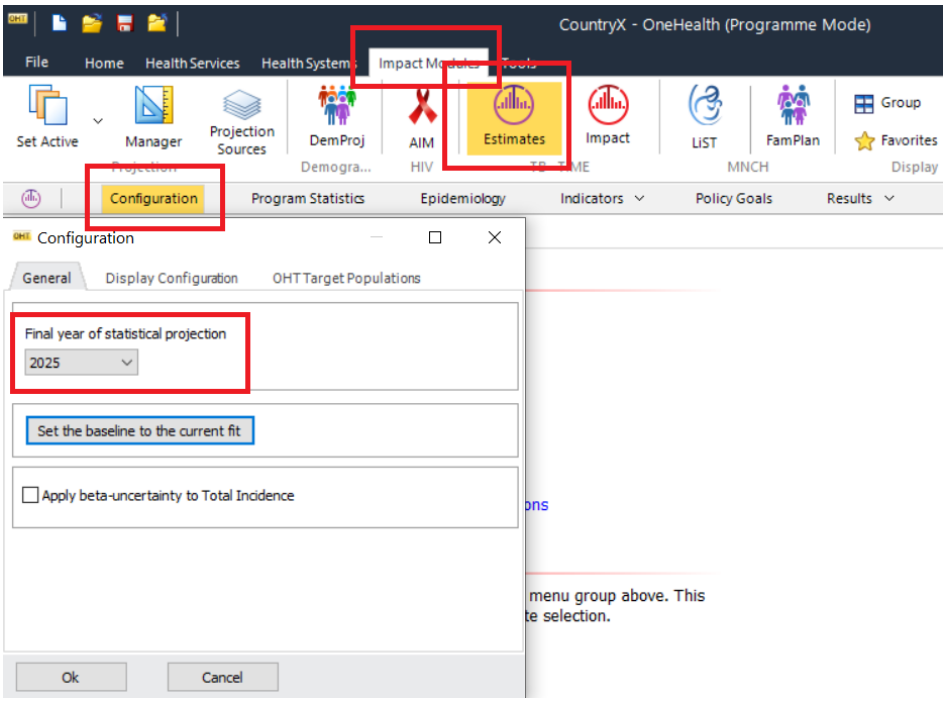
Steps for OHT user: The user configures final year of statistical projection. It is recommended that the final year of statistical projection is no more than 3-5 years after the start year of the OHT projection.

It is generally recommended that statistical projections of any trend be over the short term, unless it is plausible that regression parameters hold over long periods. Accordingly, for projections of TB burden indicators, such as for TB incidence and TB notification, the recommendation is to use statistical projections for no more than 3-5 years of forward projection. The end year will be configured at the start of planning and cannot be changed.

In TIME estimates there is a configuration where the final year of projection is set, as showed in Figure 39 below.

[11] Spectrum Manual (avenirhealth.org)

Figure 39: Setting the final year of projections in TIME Estimates



6.1.2 Cubic spline fitting parameters

Location in OHT: OHT\ Impact Modules\TIME Estimates\Indicators\Fit Indicators

Steps for OHT user: The user configures the fitting parameters first and second uses "Fit All" to perform all fits to indicators that TIME Estimates is designed to do. The user should use this option whenever any data were changed in the Program Statistic section.

TIME Estimates provides an interface for fitting and displaying indicators. Default projections for all indicators and most countries (around 150 countries) are read from an internal database into which pre-fitted projections are loaded and appear by default in TIME Estimates/Program statistics/Notified cases types (projected) even before the user reviews Program statistics and fits the model (TIME Estimates/Indicators/Fit indicators). While the default epidemiology projections generally fit available data well, there are projections for some countries which demand data adjustments and re-fitting so it is encouraged that the OHT user proceeds to this step of Indicators/Fit indicators especially if Program statistics have been modified.

TIME Estimates uses a generic interface for curve fitting (figure 40). The top-left panel provides a way of selecting a given indicator. Once selected, the user can set parameters that will influence the fitting of the curve to underlying data, based on cubic spline fitting.

6.1.2.1 General fitting parameters:

Number of splines: The more splines covering the projection interval the greater the ability of the cubic spline to respond to sharp changes in data. However, more parameters introduce the risk of over-fitting the data, producing unreliable projections beyond the years of available data. Tests with the TIME Estimates model suggest that 9-11 basis function are sufficient to fit most indicators.

Fitting method: Total incidence and notification is fit with a least-squares method. The user can use either a least-squares (default) or importance sampling method for HIV-TB incidence. The results produced by these two options are generally very similar.

Smoothness penalty: This setting allows the user to control the influence of the smoothness penalty. Reducing the penalty will allow greater flexibility in fitting data but will lead to uncontrolled projections beyond years of data. As with the number of basis functions (linear combinations of these allow for the construction of essentially all curve shapes relevant to TB indicators), a subjective judgment must be made regarding the compromise between fitting more data points versus producing smooth future projections.

'Order' of Smoothness penalty: This setting controls the type of penalty that is imposed on the projection. A 'first order' penalty favors a projection which is smooth. Mathematically it penalizes large difference between adjacent cubic spline coefficients. A 'second order' penalty favors a projection that follows recent trends in the data. Mathematically it penalizes large second-order differences between adjacent cubic spline coefficients.

Uncertainty interval: The checkbox "Estimate uncertainty intervals" is used to toggle between having uncertainty intervals or not. When selected, a specified "Number of bootstraps" is used to generate the uncertainty interval, which represents a 95% confidence interval for the indicator. The more bootstraps used, the more accurate the final uncertainty intervals, but the longer time requirements for the processing will be.

6.1.2.2 Parameters specific to fitting HIV+ TB incidence

When fitting HIV+ TB incidence, a second set of parameters must be specified:

RR for CD4 > 500 cells/uL (%): This setting sets the risk for TB infection at a specified level relative to the risk for HIV- cases, which is estimated by the algorithm.

Increase in RR per 100 uL CD4 decline (%): This setting controls the exponential increase in risk for TB infection for each 100 uL units of CD decline.

Reduction in RR for HIV patients on ART (%): This setting controls the reduction in risk of TB infections for HIV patients receiving ART.

Relative weight of survey, sentinel and routine HIV-TB testing data. The method simply replicates each dataset, if available, a specified number of times. More weight is typically given to population surveys, being the most unbiased assessment of HIV+ TB incidence. This is a subjective way of ensuring that the final HIV+ TB incidence estimates matches estimates from population surveys as closely as is possible given overall TB incidence and the properties of the HIV+ population (namely CD4 distribution and ART status).

Data inclusion threshold: HIV+ TB incidence estimates obtained from routine testing are typically biased when coverage is low, since under such conditions only the most severe cases are tested. This setting

specifies a coverage setting below which to reject routine testing data in the HIV+ TB incidence estimate.

6.1.2.3 Fit All

After setting the parameters for all curves or accepting the default values (which typically works well), the user must click the "Fit All" button which will process the fitting of all indicators. The Indicator at the right bottom are two progress bars to show how the bootstrap sampling method is progressing as it runs for each indicator.

The method will generally produce a good fit with current settings as they are designed to be highly flexible to typical TB data inputs.

Figure 40: General fitting parameters for cubic spline fitting

6.1.3 Evaluating goodness of TIME Estimates fit to data

The fitting method tries to minimize the distance between the projected indicator and the data points. The basic method for evaluating goodness-of-fit is to visually inspect how close the fitted curve lies with respect to the data. The data points from WHO are generally smooth and the first to these data points are very close to the data points, as can be seen in a typical example shown in figure 40 above.

If the data points do not follow a visually smooth trend, then the fitted curve will fall between the data points and may not fall on the last data point. This is demonstrated in figure 41 below: the fitted curve does not pass through the last data point, which the user may regard as the official estimate. Instead,

the curve an as attempt to minimize the distance between a fit/projection and **all** the data points. Such deviations are generally not critical when costing a TB program and are unavoidable when used model projections of target populations related to TB costing.

The user should also look at the continuation of the curve as this is what will be used for future costing. Generally, uncertainty in a projected curve grows as the curve moves past the years of available data. This concept is demonstrated in figure 42, which shows how the confidence bounds of the fitted TB incidence grows 'slowly' past the last year of WHO data.

If the user allows too much flexibility in the fitted curve, for example by increase the number of basis points and reducing the smoothness penalty (see fitting parameters in section 6.1.2), it will result in a better fit to a given data point, but also, generally to a drastic increase in uncertainty. This concept is demonstrated in figure 43. Here the smoothness penalty was relaxed from 0.05 to 0.001. The model has more flexibility now to fit data and the 2019 TB incidence estimate is almost matched. But the post 2019 curve is also less constrained with a drastic increase in uncertainty associated with the projection post 2019.

Ideally the post-data part of the curve will change smoothly over the years of the projection. Drastic changes, such as those demonstrated in figure 43, should be flagged as unrealistic and this type of projection is clearly less desirable than the initial model, which did not fit the 2019 data point as well. The user can adjust the fitting parameters to make the curve smoother and less responsive and less prone to drastic changes, but that may mean a non-perfect fit to recent data. The user must settle on reasonable compromise keeping in mind that the goals is TB costing and not TB burden estimation. The default fitting parameters generally achieves this compromise very well, and the user can simple use "Fit All" for a good first attempt at fitting the model.

Figure 41: Model fit to data that shows variation, with possible outliers

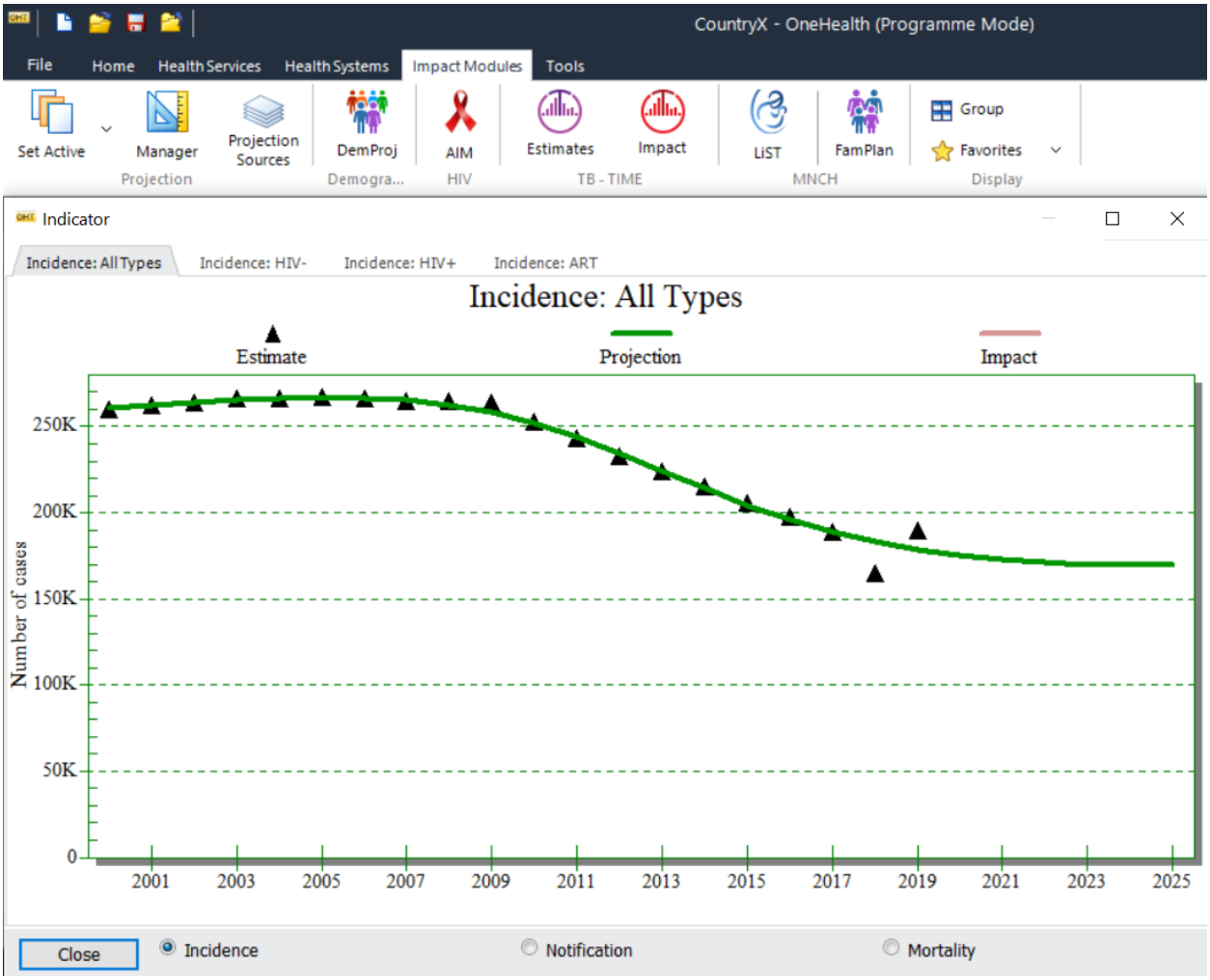


Figure 42: Demonstrating a modest increase in uncertainty for projected time points outside of available data.

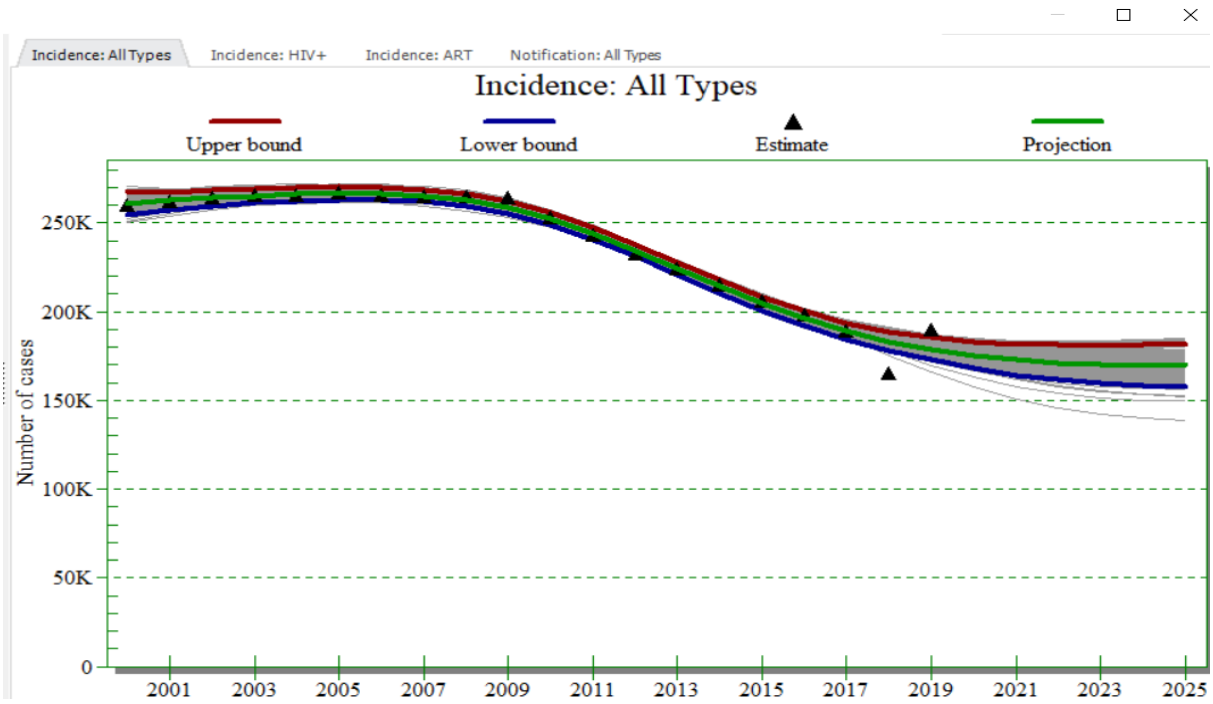
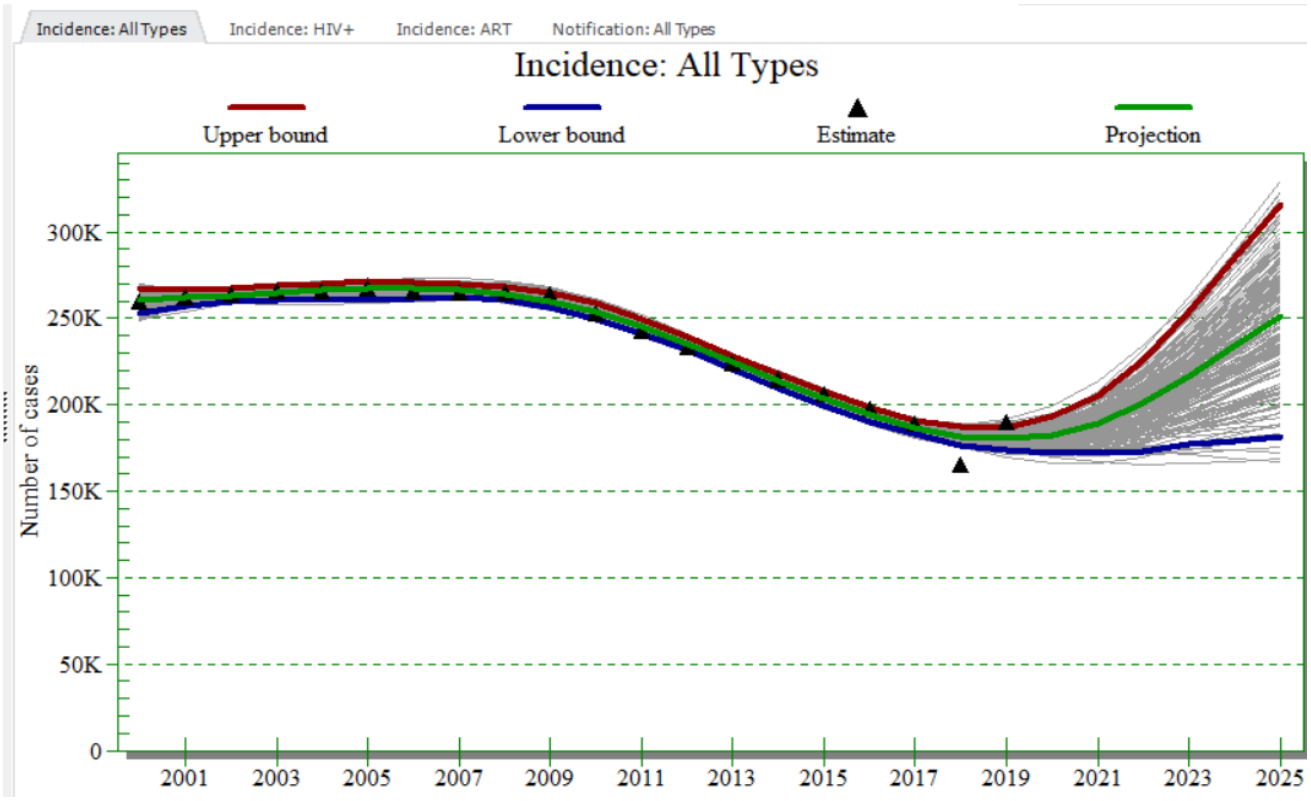


Figure 43: Demonstrating a drastic increase in uncertainty when the user allows the model to overfit the data.



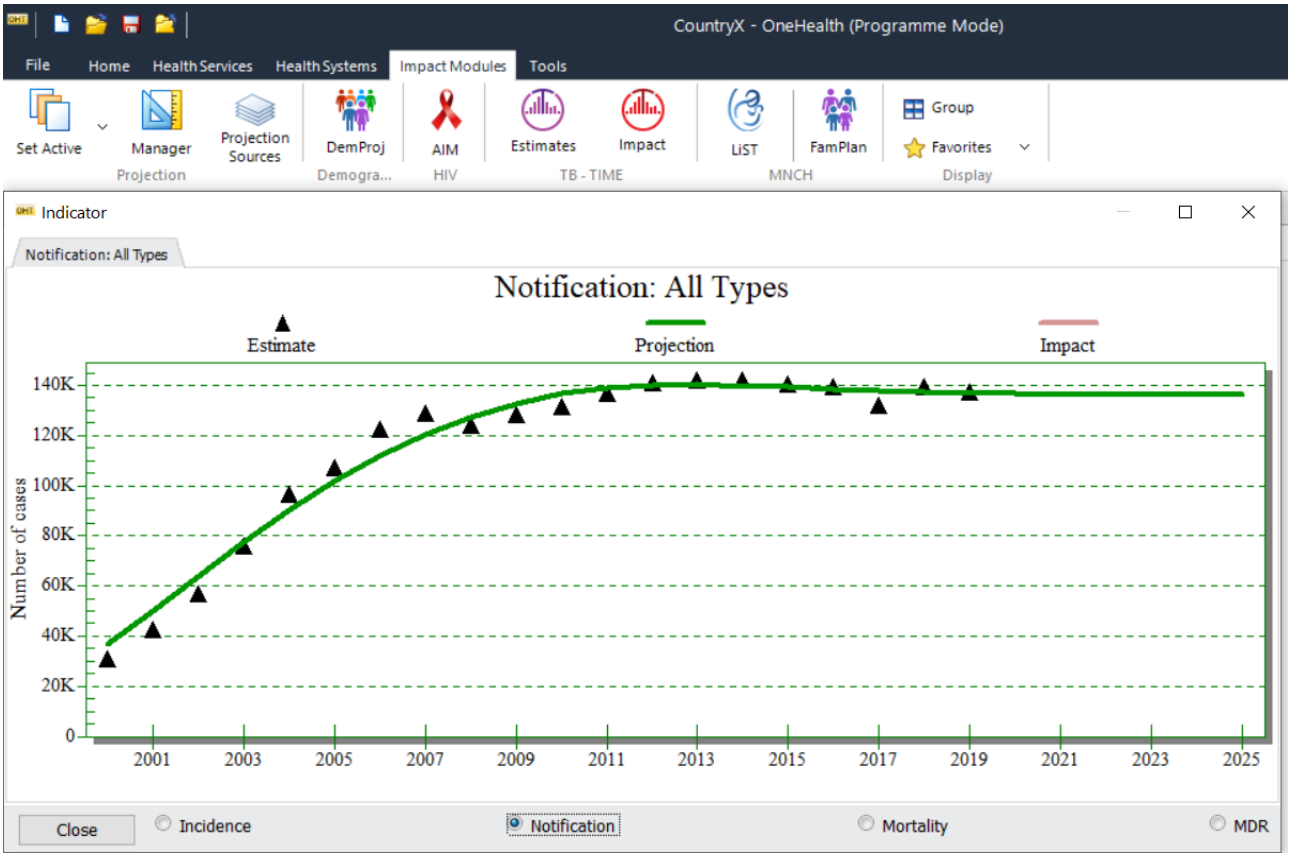
6.2 Annex 2: Estimating impact on TB mortality (with "Policy Goals") using TIME Estimates

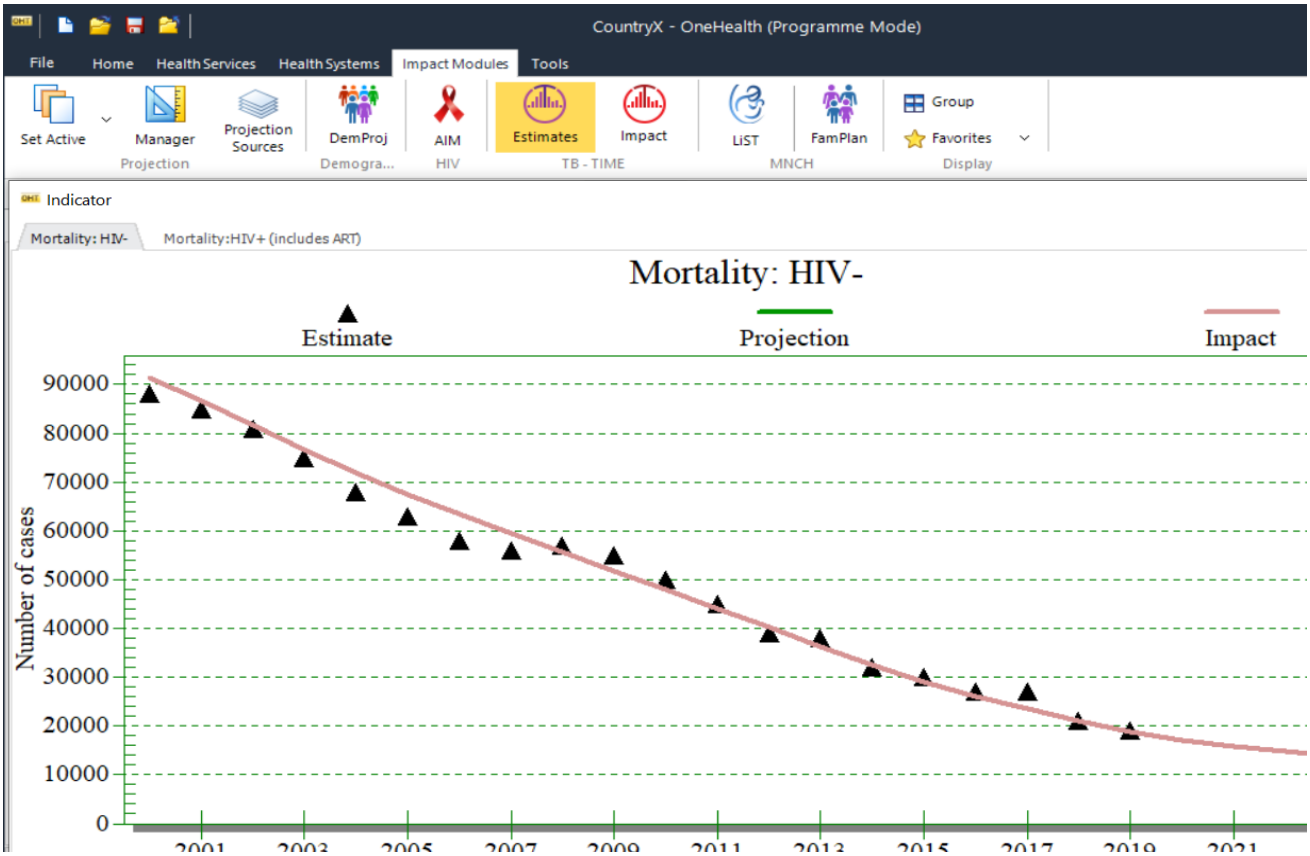
The section shows the trends of TB Notification, Incidence and Mortality is done via a the cubic-spline method described in Annex 1. The trends are used then used to estimate the reduction in TB mortality that is expected to follow an increase in TB notifications.

6.2.1 TB notification

The projection of TB notification is based on direct cubic-spline fitting to historical TB Notification data. Results can be viewed under **Indicators/Display Indicators**, see figure 44**. Note the radio button at the bottom of the chart is used to switch between displays.**

Figure 44: Viewing fitted results in "TIME Estimates/Indicators/Display indicators" tab: TB notification and mortality.




CountryX - OneHealth (Programme Mode)
File
Home
Health Services
Health Systems
Impact Modules
Tools
Set Active
Manager
Projection Sources
Projection
DemProj
Demogra...
AIM
HIV
Estimates
Impact
TB - TIME
LiST
FamPlan
MNCH
Group
Favorites
Display
Indicator
Mortality: HIV-
Mortality:HIV+ (includes ART)
Mortality: HIV-
Estimate
Projection
Impact
Number of cases
90000
80000
70000
60000
50000
40000
30000
20000
10000
0
2001
2003
2005
2007
2009
2011
2013
2015
2017
2019
2021

6.2.2 TB incidence and mortality

This section summarizes the method of estimating TB incidence and mortality in TIME Estimates . The calculation outlined in this section will be triggered every time the users generates results in the "Time Estimtates/Results" tab after any epidemiology data were changed in the Program Statistics data editors[12].

TIME Estimates also projects key TB burden indicators, with an emphasis on indicators related to HIV-TB (by CD4 category as produced by the Spectrum HIV model [13]) and with the aim of estimating the potential impact of HIV interventions (e.g. ART scale up) on the burden of HIV-TB. The model can also be used to study the impact of increased TB notification on the TB-related mortality.

The model estimates projected incidence by fitting to existing incidence data from the WHO Global TB Programme (GTB) TB database and disaggregated according to CD4 category. To this end, a regression method is devised to estimate relative risk (RR) for TB incidence according to the CD4 categories used by Spectrum for national HIV projections. Spectrum data used by TIME estimates (numbers of PLHIV in different CD4 categories) are based on the national projections prepared towards the UNAIDS Report on the Global AIDS Epidemic 2019.

The data which defines the HIV-split is stated in this tab. The information on HIV-burden is derived from HIV-TB surveys, testing for TB in sentinel HIV settings or testing for HIV as part of routine TB testing as shown in figure 45. Th user can edit any these estimated or provide new estimates if they are available but not in the tool. For example, the results of a new survey may be available in which case the user can add the estimate and its bounds to the row "Prevalence of HIV-TB" in the year/column represented by the survey results.

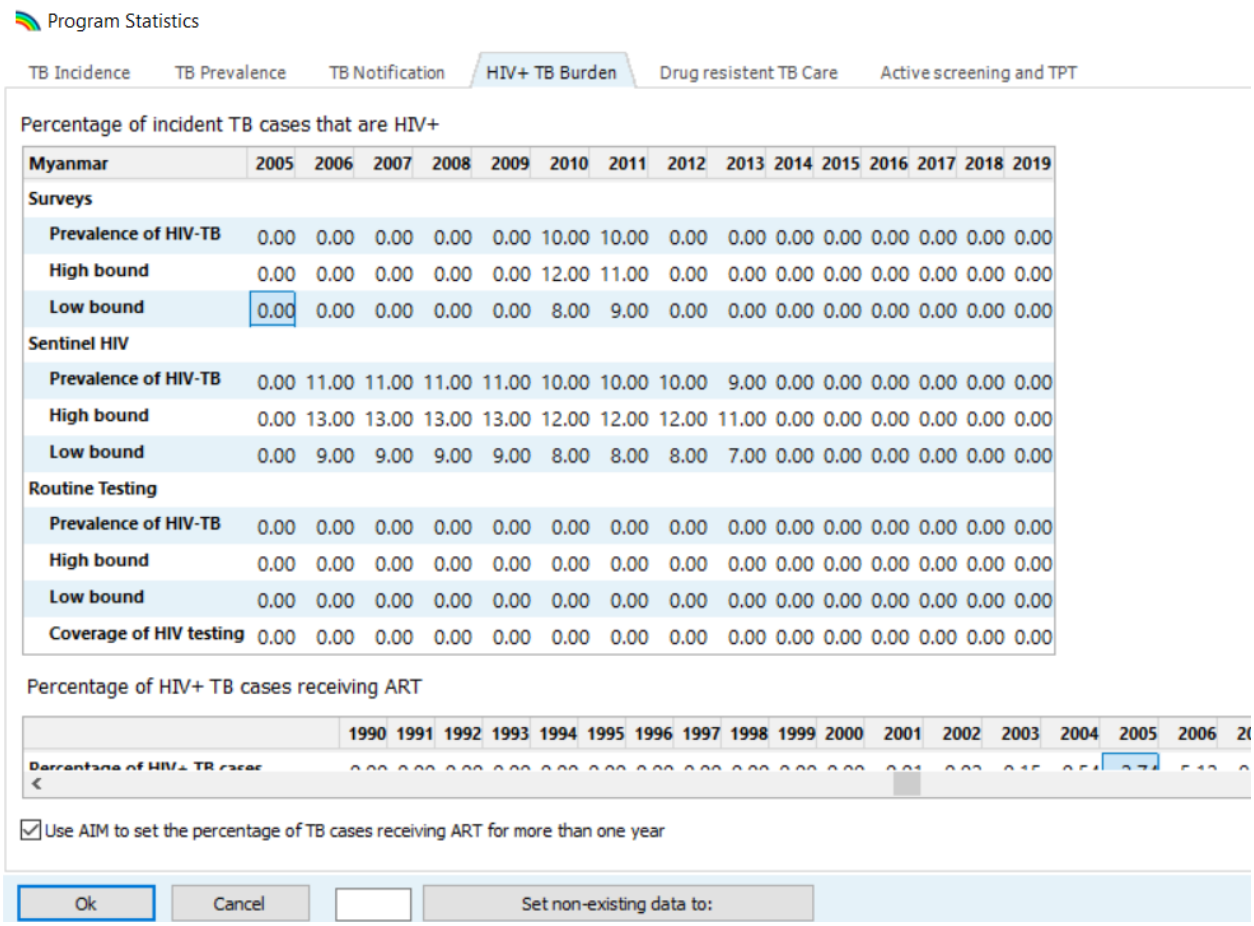
This information is used in the cubic-spline method for estimating the split of TB incidence by HIV status.

TIME Estimates calculates TB mortality as product of estimated incidence and case fatality ratios (CFR); therefore, the model can also easily be used to estimate the impact of increased notification on TB-related mortality. The case fatality ratios are shown in Epidemiology/Case fatality ratios, see figure 46. The user will generally not edit these case fatality ratios as they are the result of systematic review.

[12] Any data change by the user sets a flag in the software that a recalculation is needed the next time any results are requested by the user.

[13] Spectrum AIM at Avenir Health, Spectrum, http://www.AvenirHealth.org/software-spectrum.php

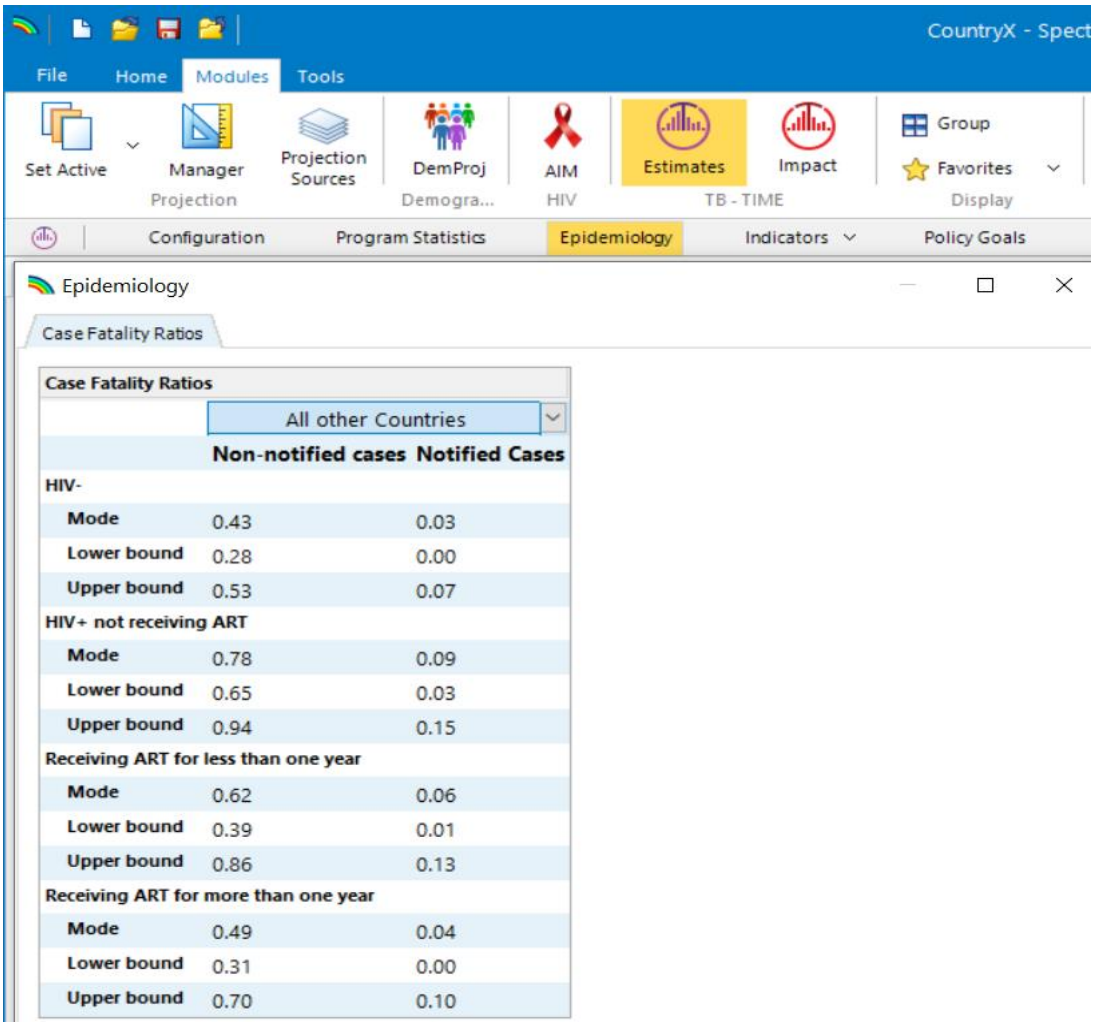
Figure 45: Data to estimate HIV-TB burden in "TIME Estimates/Program statistics/HIV+ TB burden" editor.



Myanmar	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
Surveys															
Prevalence of HIV-TB	0.00	0.00	0.00	0.00	0.00	10.00	10.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
High bound	0.00	0.00	0.00	0.00	0.00	12.00	11.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Low bound	0.00	0.00	0.00	0.00	0.00	8.00	9.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Sentinel HIV															
Prevalence of HIV-TB	0.00	11.00	11.00	11.00	11.00	10.00	10.00	10.00	9.00	0.00	0.00	0.00	0.00	0.00	0.00
High bound	0.00	13.00	13.00	13.00	13.00	12.00	12.00	12.00	11.00	0.00	0.00	0.00	0.00	0.00	0.00
Low bound	0.00	9.00	9.00	9.00	9.00	8.00	8.00	8.00	7.00	0.00	0.00	0.00	0.00	0.00	0.00
Routine Testing															
Prevalence of HIV-TB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
High bound	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Low bound	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Coverage of HIV testing	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00

	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
Percentage of HIV+ TB cases																	

Figure 46: Case fatality ratios documented in "TIME Estimates/Epidemiology/Case Fatality Ratios" tab.



Case Fatality Ratios

	All other Countries	
	Non-notified cases	**Notified Cases**
HIV-		
Mode	0.43	0.03
Lower bound	0.28	0.00
Upper bound	0.53	0.07
HIV+ not receiving ART		
Mode	0.78	0.09
Lower bound	0.65	0.03
Upper bound	0.94	0.15
Receiving ART for less than one year		
Mode	0.62	0.06
Lower bound	0.39	0.01
Upper bound	0.86	0.13
Receiving ART for more than one year		
Mode	0.49	0.04
Lower bound	0.31	0.00
Upper bound	0.70	0.10

6.2.3 Estimating reduction in mortality

Location in OHT: OHT\ Impact Modules\TIME Estimates\Policy Goals

Steps for OHT user: The user states a proposed increase in overall notification using XX. This increase is compared to the notification trends that results from "Fit All" to estimate impact on TB mortality

The only impact estimate produced by TIME Estimates (called Policy Goal here) is the reduction in mortality that is expected to follow notification increases. The user is shown the current incidence trend, with upper and lower bounds, see figure 47. The user can edit notifications in the years following baseline, to the final year with the constraint that notifications cannot exceed incidence. This is done in "TIME Estimates/Policy goals/Total cases" indicator.

6.2.3.1 Policy Goals Results

TB mortality is re-calculated and compared to the previous result, prior to the scale-up. The results are shown in Figure 48, which is located under **Results/Impact Summary**

The mortality estimation method outline above responds to increases in TB Notification, since the CFR of notified (which usually implies treated) cases is lower than those of cases not notified. However, since the impact of the TB notification increase on TB incidence is not captured (as it is with the use of the TIME Impact model) the results are simply indicative and should be treated with caution.

Note that the notification changes made in the Policy Goals editor is automatically transferred to the Program Statistics/TB Notification editor (see figure 49). The user can also alternatively directly edit TB notifications in that editor.

Figure 47: User increases TB Notifications under Policy Goals (or in Program Statistics) to obtain impact on TB mortality.

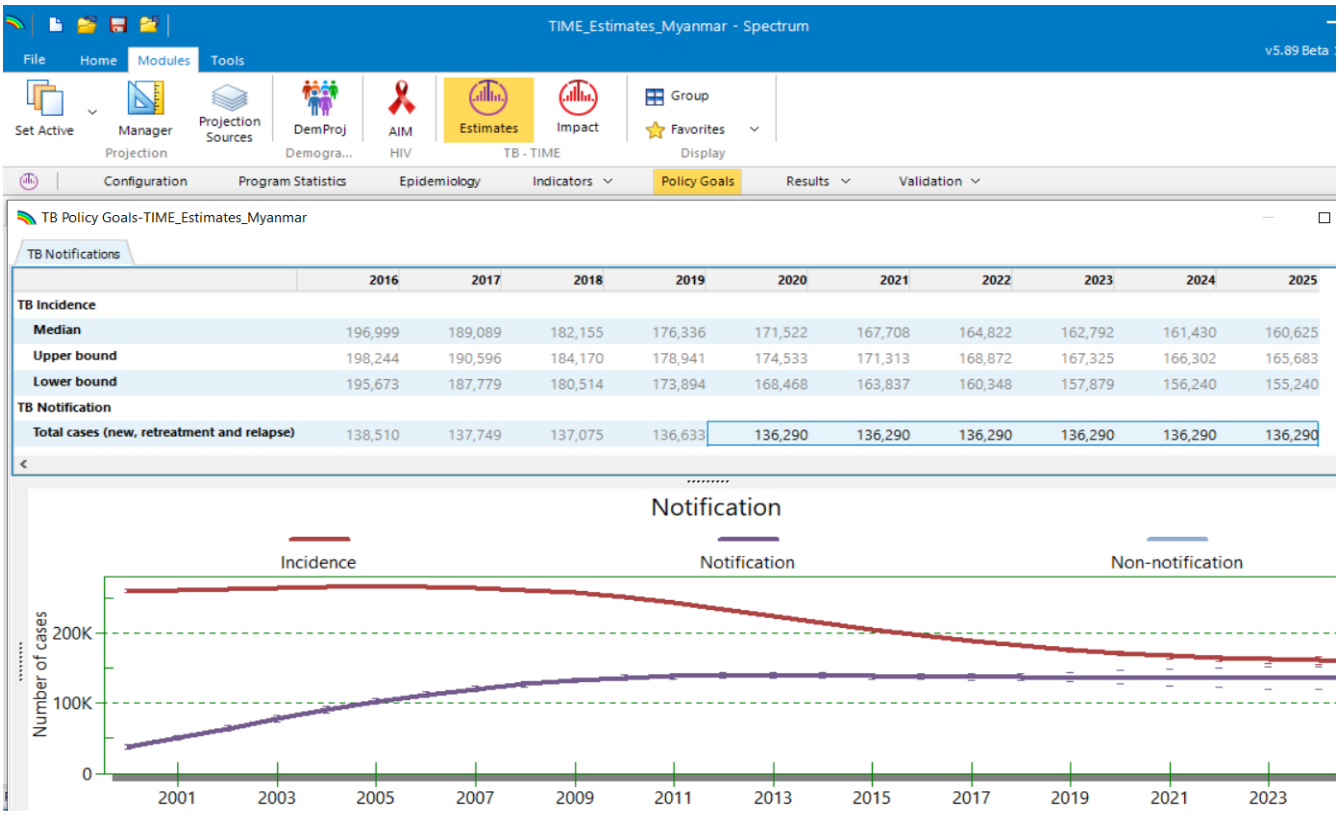
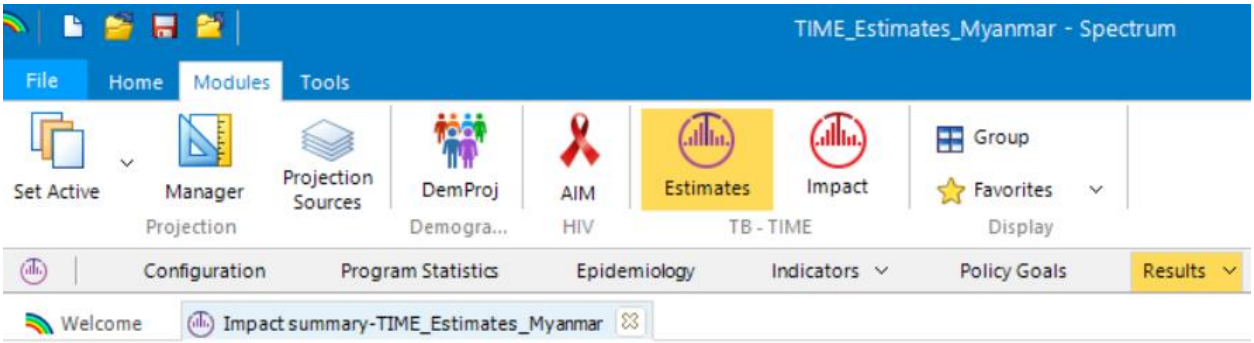


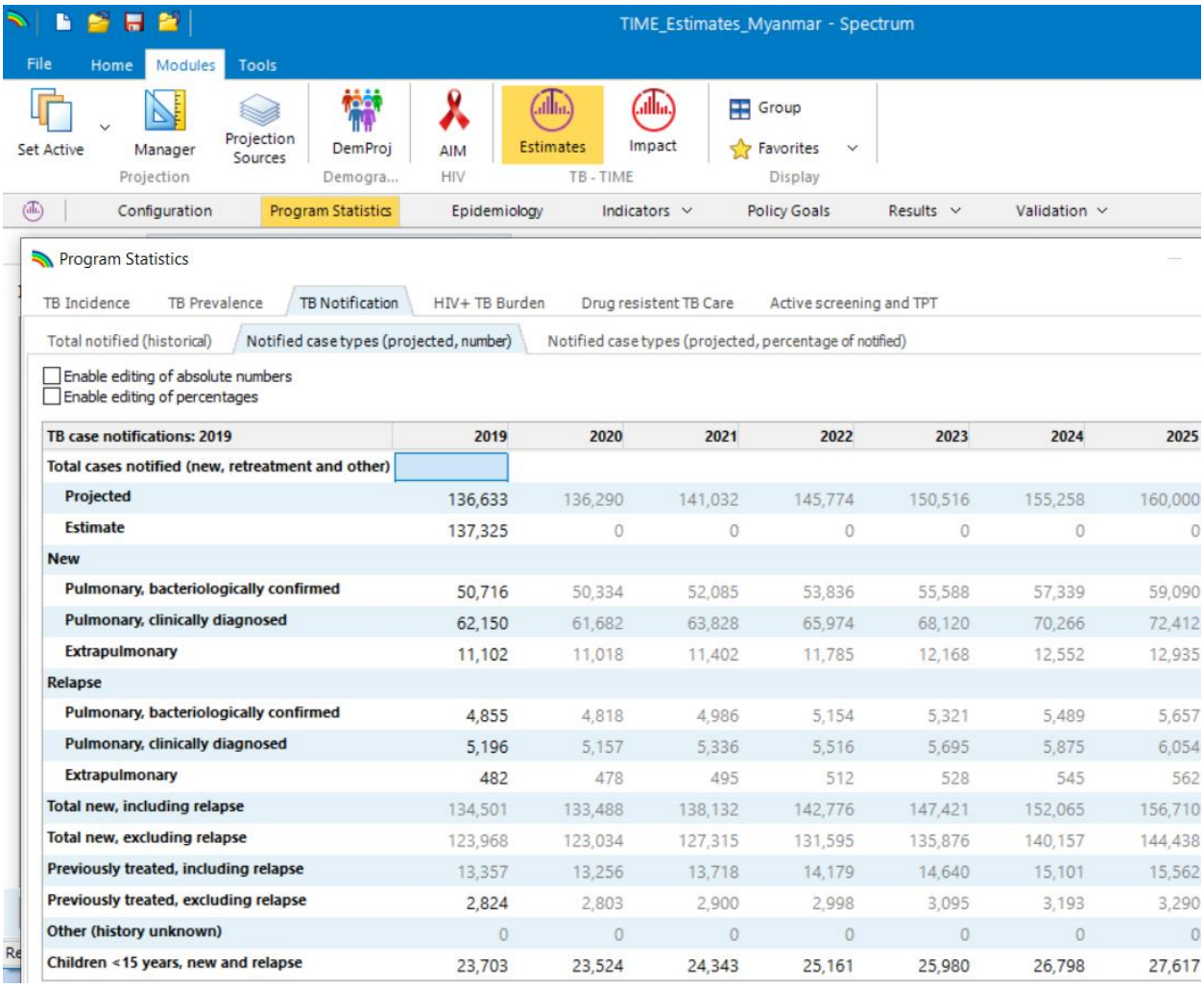
Figure 48: User views policy Goals Results: Impact of TB notification changes on TB mortality



Impact summary-TIME_Estimates_Myanmar

	2018	2019	2020	2021	2022	2023	2024	2025
TB deaths averted								
Total	0	0.00	0.00	2,041.72	4,167.76	6,171.13	8,120.62	10,023.30
HIV-	0	0.00	0.00	1,889.12	3,832.36	5,649.19	7,407.66	9,112.09
HIV+	0	0.00	0.00	152.59	335.39	521.94	712.96	911.21
HIV+ not on ART	0	0.00	0.00	152.59	335.39	521.94	712.96	911.21
HIV+ on ART	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
TB infections averted								
Total	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
HIV-	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
HIV+	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00

Figure 49: Notification increases under Policy Goals is also reflected in Program Statistics/ TB Notifications



TB case notifications: 2019	2019	2020	2021	2022	2023	2024	2025
Total cases notified (new, retreatment and other)							
Projected	136,633	136,290	141,032	145,774	150,516	155,258	160,000
Estimate	137,325	0	0	0	0	0	0
New							
Pulmonary, bacteriologically confirmed	50,716	50,334	52,085	53,836	55,588	57,339	59,090
Pulmonary, clinically diagnosed	62,150	61,682	63,828	65,974	68,120	70,266	72,412
Extrapulmonary	11,102	11,018	11,402	11,785	12,168	12,552	12,935
Relapse							
Pulmonary, bacteriologically confirmed	4,855	4,818	4,986	5,154	5,321	5,489	5,657
Pulmonary, clinically diagnosed	5,196	5,157	5,336	5,516	5,695	5,875	6,054
Extrapulmonary	482	478	495	512	528	545	562
Total new, including relapse	134,501	133,488	138,132	142,776	147,421	152,065	156,710
Total new, excluding relapse	123,968	123,034	127,315	131,595	135,876	140,157	144,438
Previously treated, including relapse	13,357	13,256	13,718	14,179	14,640	15,101	15,562
Previously treated, excluding relapse	2,824	2,803	2,900	2,998	3,095	3,193	3,290
Other (history unknown)	0	0	0	0	0	0	0
Children <15 years, new and relapse	23,703	23,524	24,343	25,161	25,980	26,798	27,617

6.3 Annex 3: Formulae for estimating the number of people requiring TB preventive therapy.

The methods for estimating TPT eligibility is specified in this section. They are based on the methods used by WHO which are published in a technical annex of the Global TB report[14].

6.3.1 Household contacts

Formula for estimating the number of household contacts eligible for LTBI treatment, **n**:

n=b / c * H * p * L * (1-t)

where

- **n**-is the number of people eligible
- **b**- is the number of notified bacteriologically confirmed pulmonary TB. Note that in TIME estimates a proportion of bacteriologically negative pulmonary TB cases may also be included as index cases.
- **c**- is the average number of TB cases per household
- **H**- is the average household size. For children a further correction **p** is made for proportion of the household that is under 5 years old. For adults (H-1) is used as the index case in the household is genrally an adult.
- **t**- is proportion of household contacts with active TB, which is generally established at pre-TPT evaluation.
- **L**- indicates testing for LTBI. In high TB burden countries, L is set to 1 (testing for LTBI is not required according to current guidelines).

6.3.2 High-risk groups

The number of persons at risk is directly specified by the user as opposed to being estimated based on exposure to index cases. Factors **L** and **t** are also used to control for the prevalence of latent and active TB infection and the role of testing for both.

6.3.3 ART patients

The number of ART patients at risk is directly specified by the HIV model (AIM) in Spectrum. For this reason, the AIM model is always active when the TIME Estimate model is active. Factors **L** and **t** are also used to control for the prevalence of latent and active TB infection. However, testing for active TB is not provided as an option for the user to control. This is due to an assumption the testing of HIV+ cases, on or not on ART, is done in the routine TB program, and not as part of active case finding.

[14] TB20_Technical_Appendix_20201014.pdf (who.int)