Projections of notified cases

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There has been growing demand for guidance and tools related to development of epidemiological projections that can also be linked to costing of interventions and assessments of cost-effectiveness, notably in the last 2–3 years in the context of Global Fund concept notes development.

The End TB Strategy has reinforced this development by generating demand for projections of how post-2015 targets for reductions in TB incidence and TB mortality can be achieved at country level, and the potential contribution of different strategy components. These include not only traditional interventions focused on finding and treating cases, but also the role of progress towards UHC, social and economic determinants, new tools and risk reduction strategies (for example, prevention of HIV infection, AIDS, diabetes, smoking, or prevention of catastrophic expenditures for health).

Examples of tools developed to facilitate the development of projections include:

1. An online programme ([http://tbprojections.herokuapp.com/](http://tbprojections.herokuapp.com/)) generating projected scenarios of case notifications by country or subnational area based on recent trends and anticipated changes in determinants of case notifications such as under-reporting or active case finding. Attached to this background document is a description of the methods based on a very simple time-series approach implemented in the online programme;

2. The impact module of “TIME”, which implements a complex dynamic model of TB transmission with more advanced features than the above online programme and is being developed by Avenir Health and the London School of Hygiene and Tropical Medicine for use within the OneHealth tool, described in more detail in *background documents 5f*.
Projections of TB notifications

Technical Description

In the following we introduce the notations and models used for computing projections for TB notifications.

Historical data used by the model

We denote with $I$ the set of years from which data is used for projection. $I$ is a continuous set, i.e., no year in between two years in $I$ is missing. The first year in $I$ is given by the user as a starting year. If a data point for a year after the starting year is missing or if it is considered an outlier by the user, it is linearly interpolated based on the data points immediately before and immediately after the missing one. If the most recent years in $I$ (one or more data points) are classified as outliers, they cannot be linearly interpolated and end up being in the projection domain.

A minimum of data points is required to have a meaningful projection. The default for this threshold is set to 10 points. If not enough data for the projection is available an error page is displayed.

The data used for projections are rates per population of size $10^5$.

Exponential smoothing

The selected historical data is fed to an exponential smoothing algorithm that tries different parameters for single and double exponential smoothing and returns the level and trend obtained optimizing the Mean Absolute Scaled Error [1]. The level $\lambda$ and the trend $\tau$ are then used to compute the history-based forecast for the $\ell$ following years according to the usual formula for exponential forecast:

$$f(h) = \lambda + h \cdot \tau$$

for $1 \leq h \leq \ell$.

Example. If the more recent year in $I$ is 2013 and $\ell = 5$ the forecast is computed for years 2014, 2015, ..., 2018 and $f(1)$ is the estimated notification rate per population of size $10^5$ in year 2014.

Adjusting for interventions

The application uses the exponential smoothing forecast described above as a starting point to produce forecasts that are adjusted for the following (possible) interventions.
• **Better reporting.** The user is asked to quantify under-reporting as a percent rate, to give an estimation of how much under-reporting will have improved at the end of the projection period and to give a time frame in which they are going to implement measures to reduce under-reporting. Since we model data as rates per population of size $10^5$, an estimated under-reporting percent rate $u$ is converted in a rate per population of size $10^5$ according to the following formula:

$$U_0 = \frac{N \cdot u}{(1 - u)}.$$

where $N$ is the last data point available the notification rate.

• **Active case finding.** The user is asked if active-case finding is planned in the country, for which years and with which estimated impact. To estimate the impact we redirect them to an available application[2].

• **Better access to health care.** The user is asked if the country is going to dramatically improve access to health-care during the projection period and by how much (in %).

**Compartmental model**

The adjusted forecasts are computed according to a simple compartmental model for the detected TB cases. The model has two compartments: detected reported cases and detected not-reported cases. The system is not closed: in case of active case finding and health care system improve new individuals enter the detection system. However, we make the hypothesis that in both cases they are reported, i.e., they all end up in the detected reported compartment.

Let $N_i$ denote the rate of notifications at year $i$ and $U_i$ denote the rate of detected but not reported cases at year $i$ ($i \in \{1, \ldots, \ell\}$). Also, $U_0$ is the rate of detected but not reported cases at the beginning of the projection as inputed by the user.

We model under-reporting as exponentially decreasing with constant rate $p$ during the intervention years.

The rate $p$ can be easily inferred from the number of years it will take to implement better reporting. In fact, under-reporting gets to a rate smaller than $T$ in $k$ years if

$$U_0(1 - p)^k < T.$$

The time window in which under-reporting is improved is denoted by $R$ ($R$ is a list of years).

The final under-reporting rate $T$ can be inputed from the user. If, according to the user, under-reporting will be completely fixed, then it is fixed to $T = 0.1$ (1 case per population of size 1 million).
The patients that did not previously have access to the health system are believed
to enter the detection and notification system uniformly over the projection
years: for each year the amount of additional notification coming from this class
of patients is denoted by $H_i$. $H_i$ is estimated according to the most recent WHO
estimates for the prevalence rate $\pi$ in a population of size $10^5$. If the access to
health care is believed to increase by $x\%$ in $\ell$ years,

$$H_i = \left(\frac{1}{\ell}\right) \cdot \left(\frac{x}{100}\right) \cdot \pi.$$ 

At year $i$ the total number of notifications is computed as the sum of $H_i$, the
newly reported cases $pU_{i-1}$ and the notification number at year $i$ decreased by
an year-dependent rate $c_i$. In particular, $c_0$ is derived from the exponential
smoothing forecast according to $c_0 = \tau/(\lambda + \tau)$ and at the end of the projection
$c_i$ is equal to a value $c_f$ inputed by the user. The progression from $c_0$ to $c_f$ is
obtained through linear interpolation. Note that $c_0$, as well as the rates $c_i$ for
the first years, may be positive (i.e., correspond to a growth) if the estimated
trend $\tau$ is positive.

To sum up, the update equations can be written as:

$$N_0 = \lambda + \tau$$

$$N_i = N_{i-1}(1 + c_i) + pU_{i-1}\|i\in R + H_i, \quad i \in \{1, \ldots, \ell\}$$

$$U_i = U_{i-1} - pU_{i-1}\|i\in R, \quad i \in \{1, \ldots, \ell\}.$$ 

The cases found through active case finding are also believed to be uniformly
spread over the years in which the intervention is performed: if $D$ is the set
of years in which active case finding is performed and $F$ is the total impact
of active case finding on the notification rate, for each year $i \in D$, an amount
$F_i = F/D$ is added to the above computed value $N_i$. Note that $F_i$ is added on
top of the previously computed value $N_i$ because the impact of this intervention
is in a defined time window and does not propagate further.

For some inputs for which there may be significant uncertainty (e.g., for the
final yearly decline $c_f$) the user is allowed to give a minimum and a maximum
value. Those are used to generate a best-scenario and worst-scenario projection.

**Projections of notifications for MDR cases**

Based on the best- and worst-scenario estimates for notifications we also compute
projections for the number of notified patients that are diagnosed with MDR TB.
To do this, we estimate the detection rate using the ratio between detected MDR
cases and estimated MDR cases (according to the latest WHO estimates). The user is asked to forecast an improved detection rate at the end of the projection window. The detection rate is believed to improve linearly starting from the present rate. The projection is computed disaggregating for retreat-relapse and new cases in order to account for a different MDR risk.

Remark: this method assumes the ratio of retreat-relapse and new cases to be constant over time, as well as the probability for a TB patient to be infected with MDR TB.

Projections at regional level and with higher time frequency

The application can compute projections at sub-national level or with higher time frequency (monthly or quarterly). To this end, the user is required to input the relevant data with a satisfactory level of completeness. The data is then processed as described in the above part of this document.

Open questions

- Should other factors like HIV prevalence and average income be included in the picture, for example to slow-down or accelerate the speed at which changes happen (fix of under-reporting, incidence decline, etc)?

- In the same direction of the question above: some choices have been made arbitrarily (exponential / linear progression, uniform distribution of newly detected cases). Is there a rational we can apply? Should those choices be country-dependent?

Future directions

- It may be useful to consider also triple exponential smoothing as well as dumping trends for the history based prediction. Triple exponential smoothing may be particularly relevant for monthly or quarterly prediction in countries where notifications have a clear seasonal behavior.

- It would be valuable to establish a validation framework for the model.

References
