This report is an annex of the Global Fund Board Strategy Committee report
*2017-2022 Strategic KPI Framework:*
*Proposed performance targets for KPIs 1, 2 & 8*

# 01 Annex 1: Overview of models and methods for KPIs 1, 2 and 8

## 1. Overview of Approach and Indicators

The aim of the target setting exercise was to establish targets for KPI 1, KPI 2 and KPI 8 that represent 'ambitious yet realistic' program outcomes and impact consistent with good stewardship of available funding from all sources including the allocation from the Global Fund.

Table 2 shows the KPI framework approved by the Global Fund Board at its 35th Board meeting (GF/B35/EDP05). Targets have been developed either directly through the application of disease transmission models or through a benchmarking approach as explained below.

**Table 2: Board Approved KPIs 1, 2 and 8**

| **Key Performance Indicators** | | |
|---|---|---|
| **KPI 1** | **Performance against impact targets** | |
| | i. | Estimated number of lives saved |
| | ii. | % Reduction in new infections/cases |
| **KPI 2** | **Performance against service delivery targets** | |
| **HIV** | i. | # of adults and children currently receiving ART |
| | ii. | # males circumcised-* |
| | iii. | % HIV+ pregnant women receiving ART for PMTCT* |
| | iv. | % of adults and children currently receiving ART among all adults and children living with HIV* |
| | v. | % of people living with HIV who know their status* |
| | vi. | % of adults and children with HIV known to be on treatment 12 months after initiation of ART* |
| | vii. | % of PLHIV newly enrolled in care that started preventative therapy for TB, after excluding active TB* |
| **TB** | i. | # of notified cases of all forms of TB - bacteriologically confirmed plus clinically diagnosed, new and relapses |
| | ii. | % of notified cases of all forms of TB - bacteriologically confirmed plus clinically diagnosed, new and relapses among all estimated cases (all forms) |
| | iii. | # of case with drug-resistant TB (RR-TB and/or MDR-TB) that began second-line treatment |
| | iv. | # of HIV-positive registered TB patients (new and relapse) given anti-retroviral therapy during TB treatment |
| | v. | % of TB cases, all forms, bacteriologically confirmed plus clinically diagnosed, successfully treated |
| | vi. | % of bacteriologically-confirmed RR and/or MDR-TB cases successfully treated* |
| **Malaria** | i. | # of LLINs distributed to at-risk-populations |
| | ii. | # of households in targeted areas that received IRS |
| | iii. | % of suspected malaria cases that receive a parasitological test [public sector] |
| | iv. | % of women who received at least 3 doses of IPTp for malaria during ANC visits during their last pregnancy in selected countries* |
| **KPI 8** | **% Reduction in HIV incidence in women aged 15-24*** | |
| **Notes** | * Indicator to be tracked in a specific set of countries. See Annex 3 for list. | |

Mathematical models of resource allocation and transmission dynamics provide a formalized framework according to which such targets can be generated in a transparent manner, with an internal consistency between all the targets and exogenous constraints and integrating the variety of data that bear on these outcomes.

Thus, for KPI 1, KPI 8 and several components of KPI 2 a modelling framework was developed (Figure 2). In this framework, the 'total envelope' of available resources for each disease for each country over the period of the strategy is the main input to the models. No distinction is made as to the origin of the monies (domestic or external, the Global Fund or other). The models then determine allocation of the money across program elements, and then project the impact that such a program would have on the epidemic. The overarching strategic direction for the allocation is set by the published guidance of the corresponding disease specific technical agency. The models used are the same as those agencies have used in their most recent 'Global Plans'.[27]

Within each disease two financing scenarios were considered, one in which the domestic resources available increase only at a rate consistent with economic growth ("base" scenario), and an "ambitious" scenario in which domestic financing in a country increases to reach benchmarked levels of spending according to disease burden and size of government budget (see Annex 2 for more details).

The exercise was repeated using multiple sets of assumptions so that targets are expressed as ranges that reflect uncertainty arising from possible projections of finance as well as uncertain burden levels and intervention efficacies.

However, it is important to acknowledge that several important features of the real-world process of program design and implementation are not included in any of the models. Principal among these are:

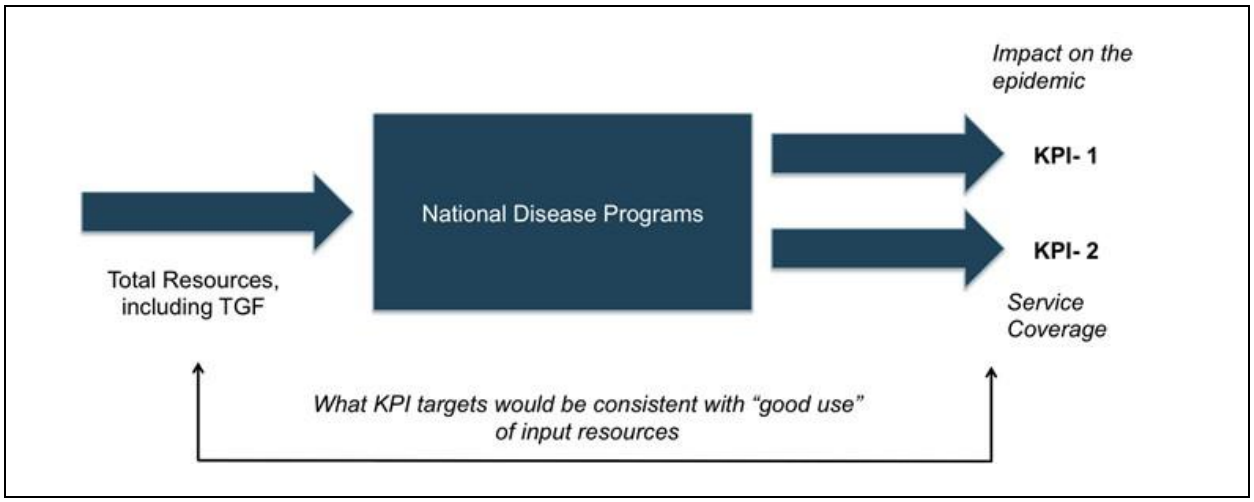
- Uncertainty around financing projections
- Constraints on programming of monies within countries (e.g. models assume full fungibility between programs, geographies, donors' funding priorities)
- Limited demand for programs
- Under-estimated costs of implementation
- Greater than expected non-direct costs
- Limitations to absorptive capacity.

Therefore, these targets may be considered a kind of "null hypothesis" for what could happen, and can trigger constructive discussions about program impact in the case if targets are apparently exceeded or not fully met. With time and new data, some of these uncertainties will resolve and it is recommended that the projections be updated to reflect that, in a regular and predictable manner. The uncertainties in the process are such that targets should not be used in any prescriptive manner at the country level.

The projections have been developed for each disease by a separate model under a common analysis plan. In the case of HIV and TB, certain assumptions and data are shared to ensure compatibility, and TB outcomes for deaths are limited to those occurring among HIV-negative persons, to avoid double-counting of impact from interventions.

[7] For KPI 8 the relevant guidance is the UNAIDS 2016 guidance "HIV Prevention Among Adolescent Girls and Young Women". A particular challenge is that current models do not include all interventions recommended to reduce HIV incidence for adolescent girls and young women in high burden settings.

**Figure 2**: **Overall model for target setting process**




Targets are formed either for all countries or for the subset of relevant countries for the portfolio of Global Fund eligible countries (see Annex 3). Aggregations of country-level projections are made on the basis that drivers of uncertainty in the ranges are independent in the case of HIV and TB and correlated in the case of Malaria. In the case of HIV and TB, variance is largely driven by uncertainty in epidemic level of behaviors in response to intervention, which are likely to vary independently between countries. In the case of Malaria, where variance is dominated by the underlying universal assumptions on epidemiology, vector bionomics and immunological dynamics. Furthermore, the alternative funding scenarios are combined in the overall summary targets with the assumption that the two are equally likely and that the financing outcomes of independent between countries. Overall targets are defined as the median and 90% interval of that mixture distribution

**Lives Saved (KPI 1 i)**

The methodology used to estimate the number of lives saved is aligned with the recommendations of an independent expert group that the Global Fund has convened in 2014.[8] The Global Fund Strategic Review 2015, produced by a group of independent technical experts, confirmed the credibility of this approach and the derived estimates.

Specifically, the calculation of lives saved is based on the difference in the number of deaths occurring in two model projections for 2017-2022, one in which the projected amounts of resources are available and used, and an alternative 'counterfactual', in which it is assumed that, after 2015, there is no intervention.

In the case of HIV this counterfactual assumes that any sexual behavior changes established by 2015 would persist but no ART would be available after 2017. In the case of TB, the counterfactual treatment is immediately withdrawn from those currently receiving it, which is modelled as TB-related deaths being equal to the trajectory of incidence multiplied by the Case Fatality Rate for persons untreated.[9] In the case of malaria, vector control is reduced to the extent that disease patterns come to reflect conditions observed around the year 2000.

[8] Expert Panel on Health Impact of Global Fund Investments Geneva, 10–11 July 2014
[9] (0.43 (0.28-0.53)

**Reduction in Incidence (KPI 1 ii)**

The calculation of the reduction in incidence is given as the average of the reduction in the incidence rate (number of infections or cases per population at risk per time) – pooled across all Global Fund eligible countries - across three diseases, and relative to the incidence rate occurring in the year 2015. In the averaging, equal weighting is given to the incidence rate reduction in each disease. The denominators of incidence (of new infections for HIV and of cases for TB and malaria) rates were defined as follows: per person-time of the uninfected population (for HIV), per person-time of the whole population (for TB) and per person-time of the population at risk (for malaria).

**Targets derived from benchmarking**

Some of the KPI 2 indicators (highlighted with an asterisk in Table 2) are not amenable to the same disease transmission model-based analysis because the data available are not sufficient to define a functional relationship between those indicators, costs and effects. Here, instead of using disease transmission models, targets are derived from a benchmarking exercise and using the Global Plan targets as the upper bound of the range. The lower bound is derived by analyzing the distribution of performance against each indicator among the set of Global Fund eligible countries, and setting the lower bound to correspond, generally, to the 75th percentile value of that distribution. This lower bound represents the coverage or outcome that countries with better performance have managed to reach. Progress towards targets is monitored as the number of countries of the set that are progressing into this defined interval with the expectation that all countries in the set are within the interval. Table 3 provides more details on each of the indicators in this group.

**Table 3**: **KPI 2 Methods for setting targets for non-modelled indicators**

| Indicator | Method for target setting |
|---|---|
| **HIV** | |
| % of people living with HIV who know their status | **Target:** mean of 75th percentile value across Global Fund eligible countries and Fast Track target<br>• **Lower bound**: 75th percentile value across Global Fund eligible countries<br>• **Upper bound**: Fast Track target |
| % of adults and children with HIV [who have started ART] known to be on treatment 12 months after initiation of ART | **Target**: mean of the 2012-2016 Strategy target and Fast Track target<br>• **Lower bound**: 2012-2016 Strategy target<br>• **Upper bound:** Fast Track target |
| % of PLHIV newly enrolled in care that started preventative therapy for TB, after excluding active TB | **Target**: mean of 80th percentile value across Global Fund eligible countries and Fast Track target<br>• **Lower bound**: 80th percentile value across Global Fund eligible countries<br>• **Upper bound**: Fast Track target |
| **TB** | |
| % of TB cases, all forms, bacteriologically confirmed plus clinically diagnosed, successfully treated | **Target**: the TB 2016-2020 Global Plan and the 2012-2016 Global Fund target<br>• **Lower bound**: 75th percentile value across Global Fund eligible countries<br>• **Upper bound:** Global Plan and the 2012-2016 Global Fund target |
| % of bacteriologically-confirmed RR and/or MDR-TB cases successfully treated | **Target**: mean of 75th percentile value across Global Fund eligible countries and the TB 2016-2020 Global Plan target<br>• **Lowe bound**: 75th percentile value across Global Fund eligible countries<br>• **Upper bound**: the TB 2016-2020 Global Plan target |
| **Malaria** | |
| % of suspected malaria cases that receive a parasitological test (public sector) | **Target:** mean of 50th percentile value across Global Fund eligible countries in Sub-Saharan Africa and the WHO global target. The 50th percentile value is applied to account for potential over estimation of measure due to reliability of reporting data.<br>• **Lower bound**: 50th percentile value across Global Fund eligible countries in Sub-Saharan Africa<br>• **Upper bound:** WHO Global target |
| % of women who received at least 3 doses of IPTp for malaria during ANC visits during their last pregnancy in selected countries* | **Target:** mean of 75th percentile value across Global Fund eligible countries using WHO estimate of IPTp2 (2 doses) coverage and global target<br>• **Lower bound:** 75th percentile value across Global Fund eligible countries using WHO estimate of IPTp2 (2 doses) coverage<br>• **Upper bound:** WHO global target |

## 2. Disease-Specific Model Details

### HIV

Modelling of the impacts for HIV was carried out by *Avenir Health* using the Goals model with some aspects of the design, assumptions and interpretation supported by the Imperial HIV model.[10] This model has been set up for 46[11] countries, either as part of the UNAIDS Fast-Track[12] target-setting exercise, or in the development of National Strategic Plans or development of Investment Cases. These countries collectively include almost 90 percent of all people living with HIV.

The models were calibrated in close collaboration with respective countries through a series of regional or in-country workshops from 2013-2016. It was assumed that the scale-up of interventions followed the Fast-Track trajectory between the time of last-available data and the beginning of the projection period. For the 59 other countries, a country-specific model was not developed and instead results are generated through extrapolation from one of the other directly modelled countries, selected according to similarity of epidemiological characteristics. The width of the ranges of model results is increased for countries that are not directly modelled. Direct modelling or extrapolation was not possible for 22 of the 122 eligible countries (mostly small island economies) due to non-availability of necessary data.

To determine the allocation of resources to program components within a country, the cost-effectiveness of each of a repertoire of potential interventions was ranked for each intervention with an objective of maximizing DALYs averted, subject to the constraint that ART coverage must not be reduced. Then, funds were allocated in order from the most cost-effective intervention to the least cost-effective. Maximal coverage targets are the same as used in Fast-Track.

Following the UNAIDS Fast-Track methodology, the interventions available for selection in programs were: ARV therapy, voluntary medical male circumcision, programs to prevent mother-to-child transmission (PMTCT), condom promotion and distribution, outreach services to key populations (sex workers, men who have sex with men, people who inject drugs), opioid substitution therapy, pre-exposure prophylaxis (for adolescents, sero-discordant couples and key populations in selected countries), and behavior change communication. Additional program elements - management, surveillance and enabling activities - were always included in the program, and the cost of these was represented as a fixed mark-up on the direct costs. In all cases, it was confirmed that Global Fund assumed cost for commodities were in broad alignment with model assumptions. We note that as most persons considered to have reached the latest stage of disease are already on treatment, the requirement to prioritise those in greatest need of treatment is implicit within the model calibration and the constraint that no one is removed from treatment.

Projections do not incorporate the extent to which experts anticipate any rises in resistance will affect overall outcomes and impact. But, other analyses[13] show that the potential to use new regimens (either among initiations or all on first-line) could substantially reduce the loss of impact from resistance, irrespective of levels of circulating resistance.

[10] Stover J, Hallett TB, Wu Z, Warren M, Gopalappa C, Pretorius, et al. How Can We Get Close to Zero? The Potential Contribution of Biomedical Prevention and the Investment Framework towards an Effective Response to HIV PLoS One 9(11):e111956. doi:10.1371/journal.pone.0111956.
[11] List of countries with full models: Bangladesh, Bolivia, Botswana, Brazil, Burkina Faso, Cambodia, Cameroon, China, Costa Rica, Democratic Republic of the Congo, Dominican Republic, Egypt, El Salvador, Ethiopia, Ghana, Guatemala, Haiti, India, Indonesia, Jamaica, Kenya, Lesotho, Liberia, Malawi, Mexico, Morocco, Mozambique, Namibia, Nicaragua, Nigeria, Pakistan, Panama, Russian Federation, Rwanda, Saint Lucia, Sierra Leone, South Africa, Swaziland, Thailand, Uganda, Ukraine, United Republic of Tanzania, Viet Nam, Zambia, Zimbabwe.
[12] Stover J, Bollinger L, Izazola JA, Loures L, DeLay P, Ghys PD What is Required to End the AIDS Epidemic as a Public Health Threat by 2030? The Cost and Impact of the Fast-Track Approach PLOS ONE 11(5):e0154893: doi:10.1371/journal.pone.0154893.
[13] Phillips, Stover, Cambiano, et al, Impact on mortality, new infections and ART program costs of ART drug resistance in low income settings in sub-Saharan Africa, Forthcoming, 2016

**Figure 3**: **The HIV Modelling process**


^Ordering scale-up of resources (with respect to intervention and target population) by univariate ICER until funds exhausted. This approach is found to give similar outcomes of optimal allocation and uncertainty as other methods.
*To generate uncertainty distributions.

The uncertainty ranges produced for the KPI target for each financing scenario represent:

- Uncertainty in epidemic fit and level: 10 sets of epidemiological parameters were used to capture the uncertain and historic trajectory of HIV epidemics. These were the best from among 1000 models fits to the official UNAIDS estimates, with variation induced in transmission probabilities and efficacy of condoms, VMMC and ART in reducing transmission risk (Table 4)
- The efficacy of interventions, PrEP, 'behaviour change communication' (+/- 10% of baseline estimates, which are derived through synthesis of the literature), circumcision and condoms (induced through fitting as described above)
- Unit costs of interventions (for SW, MSM, PWID and VMMC) used post-optimization to determine uncertainty in achievable coverage levels (Table 5)
- Uncertainty in assigning impact estimates to countries not directly modelled.

**Table 4: Parameter Ranges for Factors Affecting the Probability of Transmission of HIV**

| Parameter | Value | Source |
|---|---|---|
| Probability of transmission per act (Female to Male) | 0.001 (0.0008-0.0016) | Baggaley *et al.,*[14]<br>Baggaley RF, White RG, Hollingsworth TD, Boily M-C et al[15]<br>Gray et al [16] |
| Multiplier on per act transmission<br>• Male to female<br>• Presence of STI | <br>1-1.5<br>2-11<br>2-4 | Baggaley *et al.,*[14]<br>Galvin and Cohen[17], Powers et al[18],Baggaley RF, White RG, Hollingsworth TD, Boily M-C et al[15]<br>Vittinghoff *et al.* |

[14] Heterosexual risk of HIV-1 infection per sexual act: a systematic review and meta-analysis of observational studies Marie-Claude Boily, Rebecca F Baggaley, Lei Wang, Benoit Masse, Richard G White, Richard Hayes, and Michel Alary, Lancet Infect Dis. 2009 Feb; 9(2): 118–129.
[15] Baggaley RF, White RG, Hollingsworth TD, Boily M-C et al., 2013, Heterosexual HIV-1 Infectiousness and Antiretroviral Use Systematic Review of Prospective Studies of Discordant Couples, EPIDEMIOLOGY, Vol: 24, Pages: 110-121, ISSN: 1044-3983.
[16] Probability of HIV-1 transmission per coital act in monogamous, heterosexual, HIV-1-discordant couples in Rakai, Uganda Ronald H Gray et al The Lancet • Vol 357 • April 14, 2001.
[17] The role of sexually transmitted diseases in HIV transmission, Galvin SR1, Cohen MS. Nat Rev Microbiol. 2004 Jan;2(1):33-42.
[18] Rethinking the heterosexual infectivity of HIV-1: a systematic review and meta analysis. Powers KA, Poole C, Pettifor AE, Cohen MS. Lancet Infect Dis. 2008 Sep;8(9):553-63. doi: 10.1016/S1473-3099(08)70156-7. Epub 2008 Aug 4.

| Parameter | Value | Source |
|---|---|---|
| • MSM contact | | |
| Relative infections by stage<br>• Primary infection<br>• Asymptomatic<br>• Symptomatic | 0.8-44<br>1<br>4-12 | Boily et al.[13]<br>Pinkerton[19]<br>Bellan et al[20]<br>Boily M-C et al[14] |
| Historical intervention effectiveness<br>• Condom use<br>• Male circumcision<br>• ART | 0.8 (0.6 – 0.9)<br>0.6 (0.22 – 0.77)<br>0.8 (0.73 -0.99) | Weller and Davis[21]<br>Avert; Gray; Bailey[22]<br>Cohen HPTN[23] |

**Table 5: Ranges on Unit Costs for HIV intervention (Ratio to median cost)**

| Intervention | Lower Bound | Upper Bound |
|---|---|---|
| Outreach to Sex workers | 0.42 | 1.63 |
| Outreach to MSM | 0.29 | 1.87 |
| Outreach to PWID | 0.41 | 1.62 |
| Outreach to PMTCT | 0.28 | 2.33 |
| VMMC (per man circumcised) | 0.58 | 1.34 |
| ART (pppy) | 0.51 | 1.65 |
| The lower and upper bounds were estimated from the unit costs by country used in the HIV/AIDS country investment case analyses. Data were available for 28 to 50 countries (except VMMC which had 13 countries). The lower bound is the ratio of the lower quartile to the median and the upper bound is the ratio of the upper quartile to the median. Quartiles were used rather than 2.5 and 97.5 percentiles to eliminate extreme outliers in these small samples. | | |

For KPI 8 "the reduction in HIV incidence in women aged 15-24" the model being used to generate the results is based on the assumption that the incidence trajectory among 15-24s is equal to that for all adults. This assumption

[19] Probability of HIV Transmission During Acute Infection in Rakai, Uganda, Steven D. Pinkerton, AIDS Behav. 2008 Sep; 12(5): 677–684.
[20] Reassessment of HIV-1 Acute Phase Infectivity: Accounting for Heterogeneity and Study Design with Simulated Cohorts, Steve E. Bellan , Jonathan Dushoff, Alison P. Galvani, Lauren Ancel Meyers.
[21] Condom effectiveness in reducing heterosexual HIV transmission.Avert; Gray; Bailey, Weller S, Davis K, Cochrane Database Syst Rev. 2002;(1):CD003255.
[22] Male circumcision for HIV prevention: from evidence to action? Weiss, H. A., Halperin, D., Bailey, R. C., Hayes, R. J., Schmid, G., & Hankins, C. A. (2008). AIDS (London, England), 22(5), 567–574. http://doi.org/10.1097/QAD.0b013e3282f3f406.
[23] Prevention of HIV-1 Infection with Early Antiretroviral Therapy, Myron S. Cohen, M.D., Ying Q. Chen, Ph.D., Marybeth McCauley, M.P.H., Theresa Gamble, Ph.D., Mina C. Hosseinipour, M.D., Nagalingeswaran Kumarasamy, M.B., B.S., James G. Hakim, M.D., Johnstone Kumwenda, F.R.C.P., Beatriz Grinsztejn, M.D., Jose H.S. Pilotto, M.D., Sheela V. Godbole, M.D., Sanjay Mehendale, M.D., Suwat Chariyalertsak, M.D., Breno R. Santos, M.D., Kenneth H. Mayer, M.D., Irving F. Hoffman, P.A., Susan H. Eshleman, M.D., Estelle Piwowar-Manning, M.T., Lei Wang, Ph.D., Joseph Makhema, F.R.C.P., Lisa A. Mills, M.D., Guy de Bruyn, M.B., B.Ch., Ian Sanne, M.B., B.Ch., Joseph Eron, M.D., Joel Gallant, M.D., Diane Havlir, M.D., Susan Swindells, M.B., B.S., Heather Ribaudo, Ph.D., Vanessa Elharrar, M.D., David Burns, M.D., Taha E. Taha, M.B., B.S., Karin Nielsen-Saines, M.D., David Celentano, Sc.D., Max Essex, D.V.M., and Thomas R. Fleming, Ph.D., for the HPTN 052 Study Team* N Engl J Med 2011; 365:493-505, August 11, 2011,DOI: 10.1056/NEJMoa1105243

could lead to over-estimation of potential impact in this age-group due to those in the age-group having, in recent years, been less readily reached by programs (e.g. circumcision programs tending to have lower coverage among men of this age, which would indirectly benefit women), and these women tending to benefit less than older women from the coverage of ART increasing among their male partners, since fewer of their potential HIV-positive partners (who are younger than the average HIV-positive man) will have initiated ART. PEPFAR's target of a 40% reduction in incidence over a shorter-time period of 3 years was conditional on very rapid scale-up of an opt-out intervention package being implemented and measured in only the highest HIV incidence (15-24) districts. Furthermore, another assumption is that comprehensive, quality programs to address HIV incidence amongst adolescent girls and young women will be taken to scale at a level that impacts on national incidence rates. Given these considerations, the placement of the lower bound from the model results was determined from 40% to 50% with a median target of 45%.

**TB**

The TB Impact Model and Estimates (TIME) model[24] was used by Avenir Health to produce the TB modelling estimates (Figure 4). The TIME model was also used to quantify the potential impact achieved by implementing the Global Plan to End TB.[25]

Allocation of resources within a country takes the National Strategic Plan as the template. For 13 countries, such plans had been created through consultation with epidemiologists and program managers, convened by Stop TB and the Global Fund. With the projected allocation of resources, the available spending is then scaled-back in equal proportion across program elements such that the total costs is equal to the projected funding available. With that program configuration, the TIME model is used to project the service coverage and impact that would result from such a program. A final adjustment is made to ensure that, in no country does the year-on-year reduction in TB case incidence exceed an upper rate limit, which starts at 0% in 2015 and increases steadily to a maximum value of 10% in 2025. This upper limit is based on historical evidence for achievable impact.

As noted above, 13 countries are modelled directly[26], whilst the others are modelled indirectly through a mapping system whereby they are assigned the best fitting model in the country group into which they had been classified in the Global Plan analysis (based on epidemiology, health system resources and other variables). Directly modelled countries represent 72% of the burden in Global Fund eligible countries. The width of model ranges was increased for countries not explicitly modelled, by adding the variance of the impact estimates of countries not assigned to a given country.

In the TIME model, calibrations are based directly on the country-specific WHO estimates (published in the WHO 2016 Global TB Report). The projections from 2015 to the start of 2017 are based on extrapolation using cubic-splines in order to determine baseline trends. Assumptions about the natural history of TB are given in Table 6. Parameters related to progression to TB disease among those HIV positive are multiplied by a Relative Risk. There is an increase in risk associated with HIV when the CD4 cell count is high (>500 per microlitre) and an additional risk for each 100 cell drop of CD4 cells below 500. The sensitivity and specificity of diagnostics are based on international literature, but it is noted that in reality each country tends to have a unique combination of tools and thus a unique profile of diagnostic performance, which introduces uncertainty into these results.

Assumptions about the sensitivities and specificities of different diagnostic tool are described in TIME documentation. Average sensitivities, which depend on country-specific diagnostic algorithm details (e.g. combination of tools, smear and HIV status of cases, and other factors), were estimated and applied for each country. Scale-up patterns were 'S-shaped' reaching target levels in 2025, as described in the TB Global Plan 2016-2022. Final screening rate levels were specific to each country and were set to a level that would ensure detection of at least 90%

[24] TIME Impact – a new user-friendly tuberculosis (TB) model to inform TB policy decisions, Hoeben et al, BMC Medicine 2016 14:56
[25] The Global Plan to End TB 2016-2020
[26] List of countries with full models: Afghanistan, Bangladesh, Democratic Republic of Congo, India, Indonesia, Mozambique, Nigeria, Pakistan, Philippines, Tanzania, Thailand, Ukraine and Zimbabwe.

of active cases before they would die of untreated TB. The annual decline in incidence was capped at 10% to align with End-TB Strategy and TB Global Plan 2016-2020.

The uncertainty bounds thus represent:

- Epidemic fit and level variations (in the 2015 WHO estimates)
- Uncertainty in assigning impact estimates to countries not directly modelled.

**Figure 4: The TB Modelling Process**

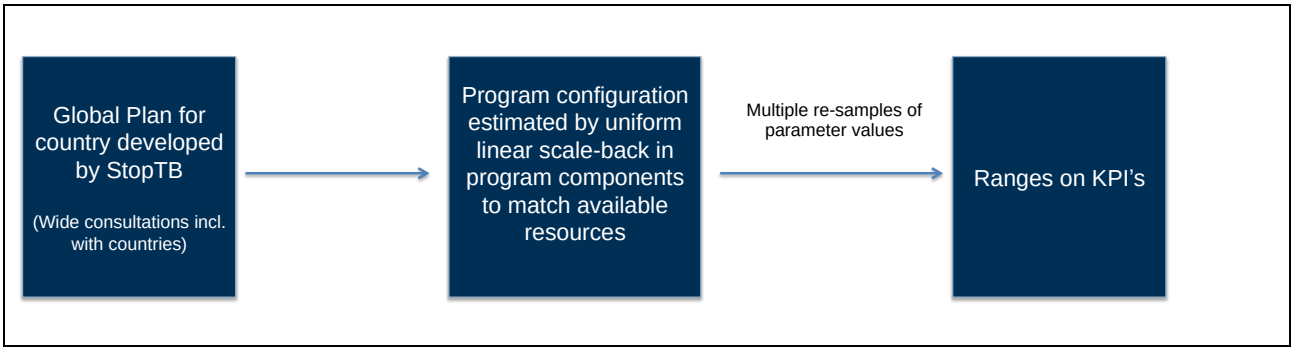



**Table 6: Natural History Parameters in TB Model**

| | HIV negative persons | Relative risk of HIV positive persons (CD4>500) | Compounded Relative Risk for each 100 CD4 cell (per microlitre) below 500. |
|---|---|---|---|
| *Progression to TB*[27] | | | |
| Develop primary TB | 11.5<br>(8 , 15) | 2.6<br>(2.11 , 3.2) | 1.36<br>(1.3 , 1.42) |
| Reactivation rate | 0.1<br>(0.01 , 0.25) | 2.6<br>(2.11 , 3.2) | 1.36<br>(1.3 , 1.42) |
| Protection provided by prior infection | 65<br>(37 , 90) | 0.8<br>(0.6 , 1) | -1.3<br>(-2 , -1) |
| *Smear status* | | | |
| Cases developing Smear positive TB | 45<br>(40 , 50) | 32.7<br>(21.9 , 42.5) | |
| Relative infectiousness of smear negative TB | 22<br>(10 , 37) | 22<br>(10 , 37) | |
| Smear conversion rate | 1.5<br>(0.7 , 3) | 2.25<br>(1.5 , 3) | |
| *Recovery* | | | |

[27] Espinal, M.A., et al., *Standard short-course chemotherapy for drug-resistant tuberculosis: treatment outcomes in 6 countries*. Jama, 2000. **283**(19): p. 2537-2545.; Menzies, N.A., et al., *Population health impact and cost-effectiveness of tuberculosis diagnosis with Xpert MTB/RIF: a dynamic simulation and economic evaluation*. PLoS Med, 2012. **9**(11): p. e1001347; Dowdy, D.W. and R.E. Chaisson, *The persistence of tuberculosis in the age of DOTS: reassessing the effect of case detection*. Bull World Health Organ, 2009. **87**(4): p. 296-304.; Dye, C., et al., *Prospects for worldwide tuberculosis control under the WHO DOTS strategy. Directly observed short-course therapy*. Lancet, 1998. **352**(9144): p. 1886-91; Sonnenberg, P., et al., *How soon after infection with HIV does the risk of tuberculosis start to increase? A retrospective cohort study in South African gold miners*. J Infect Dis, 2005. **191**(2): p. 150-8; Williams, B.G., et al., *Antiretroviral therapy for tuberculosis control in nine African countries*. Proc Natl Acad Sci U S A, 2010. **107**(45): p. 19485-9; Murray, C.J. and J.A. Salomon, *Modelling the impact of global tuberculosis control strategies*. Proc Natl Acad Sci U S A, 1998. **95**(23): p. 13881-6; Lew, W., et al., *Initial drug resistance and tuberculosis treatment outcomes: systematic review and meta-analysis*. Ann Intern Med, 2008. **149**(2): p. 123-34.

| | HIV negative persons | Relative risk of HIV positive persons (CD4>500) | Compounded Relative Risk for each 100 CD4 cell (per microlitre) below 500. |
|---|---|---|---|
| Self-cure rate | 20 (10 , 25) | 10 (6 , 16) | - |
| *TB Mortality* | | | |
| TB mortality rate (Smear positive) | 30 (20 , 41) | 60 (40 , 82) | - |
| TB mortality rate (Smear negative) | 21 (18 , 25) | 42 (36 , 50) | - |
| *MDR* | | | |
| Relative fitness of MDR strains | 73 (58 , 85) | 73 (58 , 85) | - |
| Rate of acquiring MDR | 1.4 (1 , 1.7) | 1.4 (1 , 1.7) | - |
| Treatment success when using FL for MDR treatment naive | 61 (53 , 70) | 61 (53 , 70) | - |
| Treatment success when using FL for MDR previously treated | 45 (35 , 58) | 45 (35 , 58) | - |

**Malaria**

The modelling of potential malaria impacts was carried out using the malaria transmission model developed at Imperial College.[28] [29] This model contributed to the development of the WHO Global Technical Strategy for Malaria.[30] (Figure 5). The model represents malaria transmission and interventions at the sub-national level (first-level administrative unit) in all 66 of the Global Fund eligible countries that have stable *Plasmodium falciparum* transmission.

Allocation of resources within a country was determined algorithmically with the objective of maximizing the reduction in cases and deaths, giving equal weighting to each. Program configuration is specified down to the first administrative level. Possible interventions include: vector control (long-lasting insecticidal nets, indoor residual spraying), seasonal malaria chemoprevention (in eligible countries) and treatment. Two constraints were placed on intervention package selection. Firstly, countries were classified according to their historic use of IRS or LLIN for vector control (categories of IRS or LLIN or either) so that the model selected the continued scale-up of the already preferred method. Secondly, to account for operational feasibility, the scale up of vector control distribution was capped at an access level of 85 percent, which translates to a usage of approximately 75 percent (assuming a three-year net distribution cycle). Other program elements were included as fixed costs - program management, surveillance and other interventions (IPTp and RDT use for non-malaria fever).

Costs were closely aligned to those used in the Malaria Global Technical Strategy. Those countries with unstable *P. falciparum, P. vivax* or that were in 'prevention of reintroduction' stages were not modelled. Costs for countries not-modelled, taken from the Global Technical Strategy, were accounted for when budgeting for the modelled countries.

Calibration was made to the 2015 WHO estimates of cases and deaths. The latest data available for all countries in a consistent manner is reported in the World Malaria Report 2015. It was assumed that the coverage of all services is

[28] Griffin, J. T. et al. Reducing Plasmodium falciparum malaria transmission in Africa: a model-based evaluation of intervention strategies. PLoS Med. 7, e1000324 (2010).
[29] Griffin, J. T. et al. Potential for reduction of burden and local elimination of malaria by reducing Plasmodium falciparum malaria transmission: a mathematical modelling study. Lancet Infect. Dis. 3099, 1–8 (2016).
[30] World Health Organization. Global technical strategy for malaria 2016-2030 (2015).

held constant between 2015 and the start of 2017. Whilst this is likely conservative on the impact in the intervening period, it is not thought to have a large effect on the projected dynamics from 2017 onwards since the expected response to scaling up coverage is very rapid.

Uncertainty intervals represent the uncertainty in current endemicity levels, bionomics and so the potential efficacy of interventions and unit costs of interventions (Table 7).

Resistance is not included in the model as insufficient data are available to form meaningful projections. It is suggested that this issue is monitored and as new data emerge, projections can be updated accordingly.

**Figure 5: The Malaria Modelling Process**


^Allowing for fixed costs * Minimises case incidence and mortality rates, giving equal weighting to each

**Table 7: Key Parameters for Malaria model**

| Factor | Parameterization Strategy[31] |
|---|---|
| Endemicity | Baseline transmission estimated from MAP prevalence (Africa) & WHO reported cases (outside Africa) scaled to be consistent with WHO cases 2015;<br>Variation in model parameters leads to differences in estimated baseline transmission (cases in 2000). |
| Costs | 50 sets of costs agreed as part of Malaria GTS included as part of full uncertainty analysis. |
| Intervention Efficacies | Variation in model parameters leads to differences in efficacy of vector control (through different vector bionomics) and treatment (through different immunity parameters) |
| Maximum Feasible Coverage | Uncertainty in the scenario with full internal optimisation captures uncertainty in coverage levels; scenarios with different "maximum" bounds for vector control & treatment are also included. |
| Within-country allocation decisions | Two sets of runs were performed with: (i) geographically-uniform package of interventions and (ii) optimal geographic allocation (SNU1). This incorporates uncertainties in the ability of a country to use information rationally and to efficiently allocate resources within its borders. Summaries were taken across the combined output distribution of both runs. |

[31] Griffin et al. PLoS Med 2010; Griffin et al. Nat Comms 2014, Griffin et al. Proc R Soc B 2015; White et al. Parasites & Vectors 2011; Okell et al. PLoS Med 2008.

# 02 Annex 2: Projection of available resources

**Forecast of available resources** To estimate the amount of funding available in Global Fund-eligible countries over 2017-2022, a forecast was developed for financing from domestic, Global Fund and other external sources. The methodology to project financing was similar to that of the financing forecast for the Investment Case for the Global Fund Replenishment 2017 to 2019, which was published in December 2015. As countries and regions will report against achievement of the Strategy targets, it is critical that the setting of these targets is based on financing projections as per national plans and the latest economic outlook for each country. Therefore, while remaining broadly aligned with the Investment Case methodology, some key updates were made to the data inputs and the methodology so that the financing projections best reflect each country's context. The forecast was carried out for all countries eligible for Global Fund support according to the 2017 eligibility list.

### 1. Domestic financing

As governments increasingly finance the national response to HIV, TB and malaria, a key input to the exercise was the forecast of domestic resources available for the three disease programs. The projections for domestic financing applied the same methodology and data sources as for the Investment Case for the Global Fund Replenishment 2017 to 2019.

The basis for domestic financing forecast were government commitments for the three disease programs, submitted in Concept Notes as part of the Global Fund's co-financing policy requirements. When the Investment Case forecast was developed, commitments data were available for 89 countries for each of TB and HIV and for 60 countries for malaria. By the time of the Strategy target setting exercise, commitments were available for 101 countries for HIV, 94 countries for TB, and 70 countries for malaria. Therefore, the domestic financing baseline was updated to incorporate the new commitments data, as well revised commitments from a few countries. For most countries, the commitments spanned the 2015 to 2017 period.

As domestic financing is such an important determinant of total available financing, two scenarios were modelled for domestic financing over 2017-2022:

1) A *"base" scenario*, where domestic commitments are projected in line with forecasted economic growth, measured by the IMF's forecast of general government expenditure per capita from the World Economic Outlook database.
2) An *"ambitious" scenario*, where a) domestic commitments are projected in line with forecasted economic growth as in the base scenario and, in addition, b) financing from the "underspending countries" reaches by 2030 benchmark levels of spending according to disease burden and size of government budget.

The economic growth projections used in the Investment Case were updated with latest data from the IMF (April 2016), which for many countries was revised downwards.

For the ambitious scenario, the approach is the same as for the Investment Case in that benchmark levels of spending are defined by a Domestic Investment Priority Index (DIPI), using indicators agreed upon with technical partners. The DIPI value is calculated for each country as follows:

$$\left[\frac{\left(\frac{disease\ specific\ spending}{disease\ burden\ indicator}\right)}{per-capita\ government\ expenditure\ budget}\right]$$

Countries are ranked by their DIPI value. For countries with a DIPI value below the 75$^{th}$ percentile, their domestic spending is projected so that by 2030 it reaches the 75$^{th}$ percentile value. The underlying rationale for this approach is that countries that spend less on the disease program relative to their

peers with similar disease burden and ability to pay are the countries with the greatest potential to increase their spending.

### 2. Non-Global Fund external financing

A key difference from the Investment Case methodology is the approach to forecast external financing. For the Investment Case, non-Global Fund external financing was estimated using latest data from the IHME's Development Assistance for Health (DAH)[32], and the aggregate amount per disease was assumed to remain constant over 2017-2019. For the Strategy target setting forecast, external financing data was taken directly from projections provided by countries in their Concept Notes, and refined based on projections provided directly to the Global Fund by some donors to inform the external financing adjustment part of the 2017-2019 allocation methodology. Country-specific levels of external financing from 2015-2017 were assumed to remain constant over 2017-2022.

For an ambitious scenario, a fixed amount of external financing was added separately by disease, based on the IHME estimate of unallocated external funding. This refers to an amount of development assistance that IHME has identified as being provided, but where it was not possible to directly allocate it to a country. The modellers were asked to optimally allocate these funds to countries, at a maximum of 10% per country, in line with the principles of the Global Fund's allocation methodology. The rationale for this assumption is that external financing reported in Concept Notes is likely to be underestimated for a number of countries, and that allocating those funds according to impact would be an approximate approach to overcome this underestimation.

### 3. Global Fund financing

The forecast of Global Fund financing assumes available funds from the Global Fund allocation in line with the Audit and Finance Committee's recommendation to the Board regarding the Sources of Funds for Allocation for the 2017-2019 allocation period[33]. These funds are distributed according to the approved allocation methodology, incorporating latest estimates of disease burden, GNI per capita and external financing projections. It is important to note that at this stage, the allocations do not reflect adjustments for qualitative factors. To cover the 2017-2022 period, the allocation methodology is run over two funding cycles, assuming the same amount of funding available for the 2020 to 2022 replenishment period. Forecasted disbursements for 2017 and 2018 based on from the 2014-2016 allocation period are added to the relevant country amounts.

### 4. Financing assumptions in the impact modelling

For each country, the total financing (domestic, Global Fund and other external) forecasted over 2017-2022 was provided to modellers as a share of the NSP funding need. Shares were provided instead of absolute amounts so that the funding can be aligned with total costs assumed in the models.

For most countries the NSP funding need reported in Concept Notes was available only until 2017, so beyond this timeframe the NSP need for each country was projected to 2022 in line with the annual growth rates of the Global Plan resource need. For malaria, given the cyclical changes in NSP costs due to LLIN mass campaigns, an average of 2015-17 was taken to estimate the NSP need in 2018 and the NSP funding need thereafter was projected from 2018.

Two scenarios were provided to incorporate the base and ambitious scenarios of domestic financing, with the aim of providing lower- and upper-bound estimates for the service coverage and impact targets.

[32] Institute for Health Metrics and Evaluation (IHME). Development Assistance for Health Database 1990-2015. Seattle, United States: Institute for Health Metrics and Evaluation (IHME), 2016.
[33] GF/SC02/DP04 and GF/AFC02/DP04

The impact modelling exercise made the following assumptions regarding the forecast of available funds:

- Funding shares are fixed per country. This differs from the Investment Case where external financing was allowed to be reallocated across countries to achieve maximum impact globally, under the assumption that all donors would target financing accordingly.
- For the ambitious scenario, as already mentioned above, the unallocated funds were optimally allocated to countries, at a maximum of 10% per country, in line with the principles of the Global Fund's allocation methodology.

Table 8 provides the resulting projections in terms of percentage of Global Plan need covered during the period 2017-2022.

**Table 8: Percentage of need funded over 2017-2022 by disease (overall and by income group) for base scenario ("B") and ambitious scenario ("A")**

| | **All Global Fund eligible countries** | | **Low-income countries*** | | **Lower-middle-income countries*** | | **Upper-middle-income countries*** | |
|---|---|---|---|---|---|---|---|---|
| | **B** | **A** | **B** | **A** | **B** | **A** | **B** | **A** |
| **HIV** | **68%** | **83%** | 64% | 77% | 64% | 83% | 79% | 89% |
| **TB** | **63%** | **76%** | 47% | 65% | 62% | 79% | 73% | 77% |
| **Malaria** | **70%** | **79%** | 73% | 85% | 68% | 75% | 67% | 98% |
| **Total** | **67%** | **81%** | **64%** | **78%** | **64%** | **80%** | **77%** | **86%** |

*amongst Global Fund eligible countries

# 03 Annex 3: Agreed subset of countries for KPI 2 and KPI 8

As stated out in the Board-approved KPI Framework (GF/B35/EDP05), a number of indicators are applied only to a subset of Global Fund eligible countries. Following the Board decision these subsets were defined and agreed with technical partners. They are specified in Table 9 below.

**Table 9: Countries contributing to Strategy targets**

| KPI 2 - HIV | Subset of countries for indicator |
|---|---|
| ii. # males circumcised | **14**<br><br>Botswana, Ethiopia, Kenya, Lesotho, Malawi, Mozambique, Namibia, Rwanda, South Africa, Swaziland, UR Tanzania, Uganda, Zambia, Zimbabwe |
| iii. % HIV+ pregnant women receiving ART for PMTCT | **26**<br><br>Angola, Botswana, Cameroon, Chad, Côte d'Ivoire, DR Congo, Ethiopia, Ghana, Guinea, India, Indonesia, Kenya, Lesotho, Malawi, Mali, Mozambique, Namibia, Nigeria, Rwanda, South Africa, South Sudan, Swaziland, UR Tanzania, Uganda, Zambia, Zimbabwe |
| iv. % of adults and children currently receiving ART among all adults and children living with HIV | **33**<br><br>Angola, Bangladesh, Botswana, Cambodia, Cameroon, Chad, Cote d'Ivoire, DR Congo, Ethiopia, Ghana, India, Indonesia, Kenya, Lesotho, Malawi, Mozambique, Myanmar, Namibia, Nigeria, Pakistan, Philippines, Rwanda, South Africa, South Sudan, Sudan, Swaziland, Thailand, Uganda, Ukraine, UR Tanzania, Viet Nam, Zambia, Zimbabwe |
| v. % of people living with HIV who know their status | |
| vi. % of adults and children with HIV known to be on treatment 12 months after initiation of ART | |
| vii. % of PLHIV newly enrolled in care that started preventative therapy for TB, after excluding active TB | **35**<br><br>Angola, Bangladesh, Botswana, Cambodia, Cameroon, Central African Republic, Chad, Congo, DR Congo, Côte d'Ivoire, Ethiopia, Ghana, Guinea-Bissau, India, Indonesia, Kenya, Lesotho, Liberia, Malawi, Mozambique, Myanmar, Namibia, Nigeria, Pakistan, Papua New Guinea, Philippines, South Africa, Sudan, Swaziland, UR Tanzania, Thailand, Uganda, Viet Nam, Zambia, Zimbabwe |
| **KPI 2 – Tuberculosis** | **Subset of countries for indicator** |

| | | |
|---|---|---|
| vi. | % of bacteriologically-confirmed RR and/or MDR-TB cases successfully treated (cured plus completed treatment) among those enrolled on second-line anti TB treatment | **33**<br><br>Bangladesh, Belarus, Côte d'Ivoire, DPR Korea, DR Congo, Ethiopia, Ghana, India, Indonesia, Kazakhstan, Kenya, Kyrgyzstan, Mozambique, Myanmar, Nigeria, Pakistan, Philippines, South Africa, Ukraine, Uzbekistan, Viet Nam, Angola, Azerbaijan, Papua New Guinea, Peru, Moldova, Somalia, Tajikistan, Sudan, UR Tanzania, Uganda, Zambia, Zimbabwe |

| **KPI 2 – Malaria** | | **Subset of countries for indicator** |
|---|---|---|
| v. | % of women who received at least 3 doses of IPTp for malaria during ANC visits during their last pregnancy in selected countries | **36**<br><br>Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Comoros, Congo, DR Congo, Côte d'Ivoire, Equatorial Guinea, Gabon, Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Niger, Nigeria, Papua New Guinea, Senegal, Sierra Leone, South Sudan, Sudan, UR Tanzania, Togo, Uganda, Zambia |

| **KPI 8 – HIV incidence in women aged 15-24** | | **Subset of countries for indicator** |
|---|---|---|
| KPI 8 | % reduction HIV incidence in women aged 15-24 | **13**<br><br>Botswana, Cameroon, Kenya, Lesotho, Malawi, Mozambique, Namibia, South Africa, Swaziland, UR Tanzania, Uganda, Zambia, Zimbabwe |