# Technical updates and method development for the UNAIDS Estimates

September 2018

Report and recommendations from a meeting of the UNAIDS Reference Group on Estimates, Modelling and Projections

Bern, Switzerland, 18-19 September 2018

## REPORT & RECOMMENDATIONS

UNAIDS
JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS
UNHCR UNICEF WFP UNDP UNFPA UNODC ILO UNESCO WHO WORLD BANK

The meeting of the UNAIDS Reference Group on Estimates, Modelling and Projections was organised for UNAIDS by the Secretariat of the Reference Group (www.epidem.org), managed at Imperial College London and the University of Cape Town. Participants of the meeting are listed at the end of this document.

Kelsey Case, October 2018

## Abbreviations

| | |
|---|---|
| AIM | AIDS Impact Model |
| ART | Antiretroviral therapy |
| CSAVR | Case Surveillance and Vital Registration tool |
| EPP | Estimation and Projection Package |
| MTCT | Mother-to-child transmission of HIV |
| PEPFAR | The U.S. President's Emergency Plan for AIDS Relief |
| PHIA | Population-based HIV Impact Assessment |
| PMTCT | Prevention of mother-to-child transmission of HIV |
| UNAIDS | Joint United Nations Programme on HIV/AIDS |
| WHO | World Health Organization |

# Background

## UNAIDS Reference Group

The Joint United Nations Programme on HIV/AIDS (UNAIDS) relies on impartial scientific advice from international experts in relevant subject areas to provide guidance on how to best calculate estimates and projections of the prevalence, incidence, and impact of HIV/AIDS globally. The UNAIDS Reference Group on Estimates, Modelling and Projections acts as an 'open cohort' of epidemiologists, demographers, statisticians, and public health experts to provide scientific guidance to UNAIDS and partner organisations on the development and use of the tools used by countries to generate annual HIV estimates. The group is coordinated by a Secretariat managed at Imperial College London and the University of Cape Town.

The work of the UNAIDS Reference Group has been organised into two tracks:

- 'Technical update' work streams: These work streams are oriented around conducting research and providing technical feedback and guidance on specific updates for the suite of tools used for annual UNAIDS estimates, i.e. Spectrum, which includes the AIDS Impact Module (AIM), the Estimation and Projection Package (EPP), and the Case Surveillance and Vital Registration tool (CSAVR).
- 'Thematic' meetings: These meetings are focused on convening new research to catalyze innovation on specific aspects of HIV estimates that require substantial conceptual or methodological development.

## Meeting objectives and outline

The meeting of the UNAIDS Reference Group was held at the Institute for Social and Preventive Medicine, University of Bern in Bern, Switzerland, 18-19 September 2018. The purpose of this meeting was to provide technical recommendations for updates to Spectrum and accompanying estimation tools. Specific objectives included reviewing new methods for estimating the first '90' of the UNAIDS '90-90-90' goals, planned implementation of the HIVE model and key updates and method development for the Spectrum and EPP models.

The meeting featured presentations and group discussion to generate consensus recommendations. The programme was divided into the following sessions:

1. Review of model development
2. EPP updates
3. Spectrum updates

This report presents a summary of the meeting presentations and discussions. The presentations are available to UNAIDS Reference Group members at www.epidem.org (non-members, please contact the Secretariat). The final recommendations can be found at the end of this report.

The recommendations drafted at these meetings provides UNAIDS with guidance on generating HIV estimates, provides an opportunity to review current approaches, and helps to identify the data needed to further improve the estimates. Previous meeting reports are available at www.epidem.org. This transparent process aims to allow the statistics and reports published by UNAIDS and partners to be informed by impartial, scientific peer-review.

The list of participants and meeting agenda are included in Appendix I and Appendix II, respectively.

## Session 1: Review of model development

The work to refine the models and tools used to produce the UNAIDS Estimates is ongoing and occurs in accordance with the timelines for the country estimation process. The current timeline for software development is as follows:

- Final software for generalized epidemics: **1 November 2018** (distribution 1 December 2018)
- Final software for concentrated epidemics: **1 January 2019** (distribution 1 February 2019)

All modifications to be incorporated for the 2019 Estimates round will need to be completed and tested in advance of these deadlines. It was suggested the group should be cautious in implementing changes that substantially affect the estimates if these modifications have not been fully tested and should be mindful of making minor interim changes where there are substantial changes on the near-term horizon.

The U.S. President's Emergency Plan for AIDS Relief (PEPFAR) indicated they would like to strengthen their support this round in many concentrated epidemic income settings in the Caribbean, Asia Pacific and Eastern European and Central Asia regions.

**Estimating the first '90'**

A central aim for 2019 is to provide countries with a tool to estimate the first '90' (proportion diagnosed) of the UNAIDS 90-90-90 targets. Mathieu Maheu-Giroux is leading the development of a new modelling approach to support this aim. The modelling framework developed, and incorporated as an extension to completed Spectrum estimates, uses national survey and programmatic to data estimate the proportion diagnosed. Key areas for further development include additional testing and analysis of the modelling approach, improved representation of uncertainty, model validation and finalisation of the web interface.

**HIVE model implementation**

The HIVE model is a geospatial HIV estimation method developed by Samir Bhatt and Pete Gething to produce district-level estimates of prevalence, people living with HIV (PLHIV) and ART coverage. This approach will be implemented in a web-based interface, with the aim for use in the 2019 Estimates. Countries will prepare all required datasets, submit these over the web. The model is computationally intensive and anticipated to require several hours to up to three days to produce results. Countries will receive automated notification when results are completed and ready to review. Feedback on the HIVE model indicated that countries wanted greater input into the modelling process (covariates, for example), and model outputs, and training on how the model works. Technical experts highlighted it will be important for geospatial estimates to appropriately represent uncertainty.

## Session 2: EPP

This session focussed on review of the age structured model development and implementation. EPP is also being implemented in the cloud for access from Spectrum in the cloud, this work is ongoing.

**R-hybrid**

The R-hybrid model is the newly re-named logistic random walk model. In data-rich settings, R-hybrid provides an improved model fit and results in patterns of incidence and prevalence that are better aligned with programme (notably ART scale-up) and survey (notably age-structured prevalence) data. However, use of R-hybrid will increase fitting time and requires additional memory. Formal guidance for countries regarding model selection is needed, particularly for countries in west and central Africa where use of R-hybrid may substantially alter estimates compared to other approaches (R-spline). Review of the transmission probability, the r(t) parameter, may help guide model selection. R-hybrid is not yet well tested in concentrated epidemic settings with sparse data.

Implementation of the R-hybrid model in EPP is ongoing. At present, the R-hybrid model is fitting to aggregate data (15-49 years) but the aim is to fit to age- and sex-specific data. It was agreed fitting to age-specific prevalence data with fixed incidence rate ratios is the only potential option for implementation of an age- and sex-structured approach prior to the Nov 1 software deadline. Key priorities for implementation of this approach include ensuring EPP estimation results are consistent with R implementation and developing a structure to pass information from EPP to Spectrum.

## Session 3: Spectrum

The case surveillance and vital registration (CSAVR) tool in Spectrum is undergoing substantial development for the 2019 Estimates round. Modifications in AIM are more minor and focus predominantly on providing diagnostic tools and enhanced visualisation of outputs to help users understand the model results and flag potential inconsistencies arising from the data or modelled estimates. Work is ongoing to fully implement Spectrum on the web.

**CSAVR**

The CSAVR tool in Spectrum has undergone several modifications. Sex and age have been added to the model, and it has been reimplemented using the EPP-ASM model code base for improved efficiency. While countries previously entered all new reported cases (adults and children) the model now represents adults only (15+ years).

An extension of the model that stratifies incidence by key populations is under development. Populations represented include men who have sex with men, people who inject drugs (male vs female) and female sex workers. Inputs are currently required for all key population groups to use this model. Default values are provided for the size of each key population and for turnover assumptions within each population for use in the absence of country data. Default starting parameters will likely also be required.

Questions arose from the initial results, notably the CD4 inputs (and model fitting to CD4 data) and the patterns of incidence which sometimes illustrate very high early spikes. Further model testing and comparison is required. Relaxing the requirements for all key populations to be represented and assumptions about the relationship in HIV transmission and incidence across population groups were identified as important areas for further development.

**AIM**

Several updates have been incorporated into Spectrum. These include updated fertility rate ratios, implementation of a visualization for cascade for testing in antenatal care (ANC) and PMTCT, an updated editor for child ART inputs, and new editors to reflect the treatment cascade.

The fertility rate ratio editor has been updated and now includes regional default patterns, age-specific reduction in fertility on ART, and a local adjustment factor used to specify national or subnational fertility effects. A “fit local adjustment factor” option is now also included which fits fertility rate ratios to data on HIV prevalence among pregnant women (read from EPP or entered directly) and includes the option to restrict PMTCT coverage below 100%. Note this option is intended for use as a diagnostic tool as opposed to a “quick fix”. It was recommended to move the location of this tool to after the estimation of incidence.

A new viewer has been added which reflects the cascade through ANC testing and PMTCT, intended to help identify potential issues (arising from programme data and/or modelled estimates) which contribute to unrealistic estimates of PMTCT coverage. It was suggested to differentiate model estimates vs data and to consider creating a checklist for the inputs recommended to further scrutinise to help guide users through an analysis of this cascade.

New charts have been added to visualise modes of MTCT. These includes stacked bar charts for the type of PMTCT prophylaxis received, the resultant number of new child infections by type of prophylaxis, and the resultant contribution to the rate of MTCT. These viewers are intended to help countries better understand what is accounting for the estimated rate of MTCT.

Finally, the input editor for children receiving ART has been updated to allow children on ART as an aggregate (0-14) value, or by 5-yr age group. Countries can now switch between use of these different inputs over time.

Two new input editors have been added to the Program Statistics tab to reflect the treatment cascade. *Knowledge of status* (the first '90') has been added and can be read-in directly from different sources or input directly. *Viral suppression* (the third '90') has also been added, including the number on ART, the number tested, and the number virally suppressed for adults and children. These inputs are linked to charts which provide visualization across the entire treatment cascade.

Spectrum is being fully implemented on the web and users will soon be able to choose whether to use the downloaded software or the web-based version. Different levels of permissions will be given to web users to control those who are able to edit country projections. It was recommended that an automatic log or audit trail captures all changes made to the files. UNAIDS requested they are able to review country files on the web-based application.

# Recommendations

UNAIDS Reference Group on Estimates, Modelling and Projections

**Technical Updates Meeting**

18-19 September 2018, Bern, Switzerland

| Recommendation/Action Item | Lead Person(s) | Proposed timeline |
|---|---|---|
| **Session 1: Model development**<br>• Recommendations for modelling the first 90 estimates<br>• Updates on HIVE model implementation | | |
| **Modelling the first 90**<br><u>Model updates and areas for further investigation:</u> | | |
| • Model outputs: Add proportion of those testing positive who are new diagnoses | Mathieu Maheu-Giroux | 09-10/2018 |
| • Review transition to awareness:<br>✓ Explore sensitivity of estimates to alternative specifications for relative HIV testing rates, including allowing higher HIV testing rate for HIV+ persons.<br>✓ Consider potential for over-reported numbers on ART in programmatic data or under-reporting of HIV testing history e.g. West Africa (but note also potential for over-reporting in less-stigmatised settings) or awareness of status. | Mathieu M-G, Jeff Eaton; review results w: Leigh Johnson, Josh Salomon | 09-10/2018 |
| • Sensitivity analysis: Review results with higher testing amongst HIV+ | 1st 90 modelling team | 09-10/2018 |
| • Uncertainty: Explore options for more appropriate representation | 1st 90 modelling team | 12/2018 |
| • Web interface: Finalise | 1st 90 team | 11/2018 |
| • Review final model specifications and validation results with interested Reference Group Members | Coordinated by Secretariat | 10/2018 |
| • Develop model documentation for country use/application | 1st 90 modelling team, Kim Marsh | 11/2018 |
| <u>Model validation</u>: | | |
| • Comparison of PHIA estimates to model estimates (correcting year of PHIA survey) Produce a summary ppt or one pager explaining differences | Kim Marsh | 10/2018 |
| • Use at subnational level: Test with Zimbabwe and Kenya country teams | 1st 90 modelling team, country teams | 11/2018 |
| • Comparison model results with ALPHA Network cohort data (Kisesa, Rakai) | Mathieu M-G, Emma Slaymaker | 2019 |
| **HIVE model implementation** | | |
| • Model implementation finalised for 2019 estimates | HIVE team | 01/2019 |
| • Preparation of geo-masked PHIA data (CDC focal point should receive files), example country provided to John Stover | Irum Zaidi, Sasi J | ASAP & by end Dec |
| • Review HIVE model workflow: Can prevalence estimation model be prepared and run prior to producing revised Spectrum estimates? | John Stover, HIVE team | 01/2019 |
| • Implement functionality to download output files | HIVE team | 01/2019 |
| • Meeting/workshop to provide countries with training and detailed explanation of HIVE<br>• Allow a function to review and determine which covariates are included | UNAIDS | Q1 2019 |

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| **Session 2: EPP**<br>• Review of the age-structured model and implementation in EPP | | |
| **Age-structured model implementation** | | |
| • Aim to implement age-specific HIV prevalence data in calibration, but lower priority; if not possible, revert to previous survey input page.<br>  ○ Consider fitting to age-specific prevalence data with fixed incidence rate ratios method for implementation. | Tim Brown, Jeff Eaton | 09-10/2018 |
| • Review EPP performance with IMIS optimization step and ensure EPP estimation results are consistent with R implementation. | Tim Brown, Jeff Eaton | 09-10/2018 |
| • Review survey database compared to values input to Spectrum 2018 files | UNAIDS | 11/2018 |
| • Continue to recommend use of decision tree to guide choice of model structures in data-sparse settings. Update data tree to include R-hybrid | UNAIDS | 2019 |
| • Define model comparison metric to validate use of R-hybrid model in data-rich settings. | Jeff Eaton | 09-11/2018 |
| ○ Demonstrate in workshops rationale for R-hybrid and model performance | Jeff Eaton, UNAIDS | 2019 |
| ○ Consider whether it is possible to consider model selection metrics for each individual EPP region without tending to overfit data | Jeff Eaton | 2018 |
| • Follow up with Le regarding sample sizes (1900) – need to balance memory issues and speed with statistically sound methods | Tim Brown, Le Bao | 10/2018 |
| • Display ANC prevalence data compared to pregnant women prevalence | Tim Brown | 09-10/2018 |
| • Remove ANC validation from EPP in favour of new ANC testing cascade input in Spectrum | Tim Brown, John Stover | 09-10/2018 |
| • Make final recommendation on which JAVA to use before January | Tim Brown | 12/2018 |
| **Age-structured model** | | |
| • Retain ART incidence reduction parameter 0.7<br>  ○ Note this parameter is less influential in data-rich settings with more flexible r-hybrid model. | | |
| • Review prior distribution choice for R-hybrid model | Jeff Eaton | 09-10/2018 |
| • Short-term: change date of switch to RW in Uganda (to 2000). | Jeff Eaton/Tim Brown | 09-10/2018 |
| ○ Longer term: Consider phase-in change in random walk variance. | Jeff Eaton | 2019 |
| • Re-run out-of-sample validation with different amounts of flexibility and compare results | Jeff Eaton | 10/2018 |
| • Concentrated epidemics: Test weaker equilibrium prior to see if more realistic results with R-spline. | Tim Brown | 2018/2019 |
| **Session 3: Spectrum**<br>• New methods for fitting to case surveillance and vital registration data<br>• New methods and model features in AIM | | |
| **CSAVR** | | |
| • Implement updated CSAVR model using EPP-ASM code base for improved efficiency and confirm that results match the old CSAVR model. | Guy Mahiane | 09-10/2018 |
| • Review data inputs and re-examine model fits with r-logistic model option.<br>  • Areas for concern: CD4 at diagnosis, high incidence in 1970 | Kim Marsh, Guy Mahiane | 09-10/2018 |
| • Replace default key pop sizes with those from reviews; decide whether to adopt key population structure this year | Kim Marsh, Guy Mahiane | 10/2018 |
| • Update data input sheets to reflect all inputs are now for ages 15+ | UNAIDS | 2018 |

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| **AIM**<br>• Consider use of the same fertility adjustment for 40-49 as for 35-39<br>• Amend ANC testing cascade visualization: all pregnancies and HIV+ pregnancies on different scales.<br>• Include check boxes/warning messages to highlight data anomalies.<br>• Add age-sex disaggregation when showing rates of viral suppression. | Avenir Health (ALL) | 10/2018 (ALL) |
| **Spectrum on the web**<br>• Allow administrator to submit final file using Spectrum on the web.<br>• Allow administrator to authorize UNAIDS to access their files (read only).<br>• Add audit trail feature – who changed what when.<br>• Include Spectrum version and file name with model outputs | Avenir Health (ALL) | 10-11/2018 (ALL) |

## Appendix I: List of Participants

| Name | Affiliation |
|---|---|
| Leigh Johnson | University of Cape Town |
| Jeff Eaton | Imperial College London |
| Kelsey Case | Imperial College London |
| Josh Salomon | Stanford University |
| Mary Mahy | UNAIDS |
| Kim Marsh | UNAIDS |
| Peter Ghys | UNAIDS |
| Ian Wanyeki | UNAIDS |
| John Stover | Avenir Health |
| Guy Mahiane | Avenir Health |
| Robert Glaubius | Avenir Health |
| Tim Brown | East-West Center |
| Irum Zaidi | OGAC |
| Ray Shiraishi | CDC |
| Tim Fowler | US Census Bureau |
| Adam Trickey | Bristol University |
| Matthias Egger | ISPM, Bern |
| Nina Anderegg | ISPM, Bern |
| Chantal Quinten | ECDC |
| Ard van Sighem | Stitching HIV Monitoring |
| Andreas Jahn | I-Tech / Malawi DHA |
| Ana Roberta Pascom | Brazil MOH |
| Sasi Jonnalagadda | CDC |
| Michelle Morrison | BMGF |
| Daniel Low-Beer | WHO |
| Michel Beusenberg | WHO |

**Remote participants:**

| | |
|---|---|
| *Mathieu Maheu-Giroux* | *McGill University* |
| *Hmwe Kyu* | *IHME* |
| *Le Bao* | *Penn State* |
| *Roma Bhatkoti* | *CDC* |

## Appendix II: Agenda

UNAIDS Reference Group on Estimates, Modelling and Projections

**Technical Updates Meeting**

18-19 September 2018, Bern, Switzerland

AGENDA

**Tuesday, 18 September 2018**

| Time | Duration (min) | Topic | Presenter(s)/ Lead Discussant |
|---|---|---|---|
| 1400 | 30 | Meeting opening<br>• Welcome and introductions<br>• Meeting objectives and overview<br><br>UNAIDS 2019 estimates overview and key dates | <br>Mary Mahy, UNAIDS<br>Leigh Johnson, Univ of CT<br><br>Mary Mahy, UNAIDS |
| **Session 1: Review of model development**<br>(Chaired by Leigh Johnson)<br>Objectives<br>• Recommendations for modelling the first 90 estimates<br>• Updates on HIVE model implementation | | | |
| 1430 | 75 | Model proposal for estimating the first 90<br><br>Discussion | Mathieu Maheu-Giroux, McGill University |
| 1545 | 30 | Coffee break | |
| 1615 | 30 | HIVE Model implementation<br><br>Discussion | John Stover, Avenir Health |
| 16:45 | 15 | Day 1 wrap-up | Leigh Johnson, Univ of CT |
| 17:00 | – | Close of Day 1 | |

**Wednesday, 19 September 2018**

| Time | Duration (min) | Topic | Presenter(s)/ Lead Discussant |
|---|---|---|---|
| 0900 | 15 | Introduction to Day 2 | Leigh Johnson, Univ of CT |
| **Session 2: EPP**<br>(chaired by Leigh Johnson)<br>Objectives<br>• Review of the age-structured model and implementation in EPP<br>• Review of demographic inputs and implications | | | |
| 0915 | 45 | Feedback from Kenya software testing workshop<br>Discussion | Mary Mahy, UNAIDS |
| 1000 | 60 | Implementation of age-structured model in EPP<br>Group discussion | Tim Brown, East-West Center |
| 1100 | 30 | Coffee break | |
| 1130 | 60 | Methods used for the age-structured model<br>Demographics<br>Group discussion | Jeff Eaton, Imperial |
| 1230 | 60 | Lunch | |
| **Session 3: Spectrum**<br>(chaired by Leigh Johnson)<br>Objectives<br>• Review new methods for fitting to case surveillance and vital registration data<br>• Review of new methods and model features in AIM | | | |
| | | | |
| 1330 | 75 | CSAVR updates<br>Group discussion | Guy Mahiane, Avenir Health |
| 1445 | 75 | Updates in AIM<br>- FRR updates and fitting<br>- Sources of MTCT<br>- ANC testing cascade<br>- Treatment cascade<br>- Recommendations from mortality meeting<br>Group discussion | John Stover and Robert Glaubius, Avenir Health |
| 1515 | 30 | Coffee | |
| 1545 | | Updates in AIM (continued) | |
| 1630 | 30 | Wrap-up, review of recommendations and close | Leigh Johnson, Univ of CT<br>Jeff Eaton, Imperial |
| 1700 | - | Meeting close | |