Method Development for the UNAIDS Estimates: October 2017

Report and Recommendations from the Fall Meeting of UNAIDS Reference Group on Estimates, Modelling and Projections

London, United Kingdom, 16-18 October 2017

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) based at Imperial College London. Participants of the meeting are listed at the end of this document.

December 2017, Sabrina Lamour, Reference Group Project Manager, s.lamour@imperial.ac.uk

Introduction

The Joint United Nations Programme on HIV/AIDS (UNAIDS) Reference Group on Estimates, Modelling and Projections exists to provide impartial scientific advice to UNAIDS and other partner organisations on global estimates and projections of the prevalence, incidence and impact of HIV/AIDS. The Reference Group acts as an 'open cohort' of epidemiologists, demographers, statisticians, and public health experts. It is able to provide timely advice and address ongoing concerns through both *ad hoc* and regular meetings. The group is co-ordinated by a secretariat based in the Department of Infectious Disease Epidemiology at Imperial College London. The work of the Reference Group occurs in coordination with other groups including the United States Centers for Disease Control and Prevention (US CDC), the Analysing Longitudinal Population-based HIV/AIDS data on Africa (ALPHA) Network, the International epidemiology Databases to Evaluate AIDS (IeDEA) Network, European Centre for Disease for Disease Prevention and Control (ECDC), the Measurement and Surveillance of HIV Epidemics (MeSH) Consortium, and the Institute for Health Metrics and Evaluation (IHME), among others.

Aim of the meeting

The general purpose of each Reference Group meeting is to support the further development and refinement of the current methods used to generate UNAIDS Global Estimates of HIV (i.e. Spectrum modelling software package, used by countries to produce their national and subnational estimates), as well as address other research and development issues that are relevant to the Reference Group. For this meeting, the objectives were as follows:

1. To provide technical recommendations for updates for Spectrum 2018, following reported results from UNAIDS 2017 Estimates
2. To review and discuss method development surrounding the Reference Group core theme areas, namely:
    - Continuous Update and Improvement
    - Age-structured models
    - Use of case-report and mortality data
    - Use of program service data
    - Spatially-specific estimates
    - Catalyse focused research and data collection

Outline

The UNAIDS Reference Group Fall Meeting 2017 was held at the Rydges Kensington Hotel in London, United Kingdom, on the 16th, 17th and 18th October 2017. The meeting featured presentations combined with group discussion, to generate consensus recommendations. The programme was divided into the following sessions:

1. Country Estimates and Software Updates
2. Incidence Estimation using EPP
3. Modelling Age- and Sex-specific HIV Estimates
4. Use of Routine and Program Data
5. Use of Population Survey Data
6. Estimating Key Populations
7. Incidence Estimation using Case Reports
8. Spatial-specific Estimates
9. Estimating Mortality on ART
10. Comparison between UNAIDS and GBD Estimates

This report includes summaries of the presentations and discussions for each session. Links to the presentations are available to UNAIDS Reference Group members on the October 2017 Meeting page, on the Reference Group website (for non-members, please contact the Secretariat). The final recommendations and

action items can be found towards the end of this report, which have been categorised according to the five core themes, mentioned above.

The recommendations drafted at Reference Group meetings give UNAIDS guidance on how best to calculate estimates of the HIV epidemic in populations, provide an opportunity to review current approaches, as well as help to identify which data are needed to inform those estimates. Earlier reports are published on the Reference Group website (www.epidem.org), which include additional information on the different modelling tools described in this report. Such transparent processes aim 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. Country Estimates and Software Updates (Spectrum and EPP)

UNAIDS Estimates 2017

Results reported for the 2017 UNAIDS country estimates were presented by Mary Mahy. She highlighted that declines in prevalence and incidence were observed in most regions, especially for children, largely owing to global expansions of programmes to prevent mother-to-child HIV transmission (PMTCT), yet flagged the apparent rise of new infections observed in central Europe and Asia. Mary highlighted UNAIDS' plans to improve the quality of antenatal clinic (ANC) data for 2018 estimates, including increased contact with country teams, webinars, and through UNAIDS strategic information (SI) advisors.

Spectrum/AIM Updates

John Stover described the recent changes implemented in Spectrum 2017 and plans for Spectrum 2018, including the incorporation of the 2017 update for the demographic data (World Population Prospects, WPP 2017), which have led to improved estimates of PMTCT coverage for a number of countries that had been previously overestimated. New treatment cascade inputs (e.g. knowledge of status and viral suppression) and a dashboard showing the county's status relating to HIV targets (such as the 90-90-90 cascade), have been introduced. Additionally, options for allocation of CD4 distribution for new individuals on antiretroviral treatment (ART) were modified to improve AIDS-related mortality estimates. John described the reconfiguration of Spectrum's uncertainty calculations, aimed to improve model efficiency and reduce Spectrum file sizes, where numbers of draws have been reduced from 1000 to 300, and the uncertainty has been aggregated (saving only upper and lower confidence bounds of model indicators and using the bounds from the most recent year to inform historical bounds). The Reference Group approved of these implementations in Spectrum.

Robert Glaubius described a tool in Spectrum to adjust fertility rate ratios (FRR's) to better fit HIV prevalence among pregnant women, and thus more accurately estimate the number of HIV-positive pregnant women and PMTCT coverage. This has been tested in 8 countries so far. Further guidance as to which data source the tool should be calibrating to was needed, i.e. prevalence from antenatal clinic (ANC) sentinel surveillance sites (ANC-SS), from routine testing antenatal program data (ANC-RT) or demographic health surveys (DHS). It was agreed that this was be addressed in the subsequent "Modelling Paediatric HIV and need for ART" meeting (19-20 October 2017, London), where the group concluded that the aggregated ANC -RT data should be used for this calculation.

Tobi Saidel presented results from a literature review and extended analysis on ECDC analysis for central and western Europe, to investigate whether the current default age and sex patterns of incidence for concentrated epidemics in Spectrum required updating. It was concluded that as yet, there was not sufficient evidence to justify altering parameters. The data outside of Europe primarily were from key population potentially skewing the incidence ratios. The Reference Group encouraged further pursuit of this investigation looking for data from the general population (such as data from antenatal clinics, etc.) and to be made aware of any new studies arise that may alter current assumptions.

Estimation and Projection Package (EPP) Updates

The latest updates in the EPP were presented by Tim Brown, which included the introduction of an ANC validation page, to better assess quality of ANC-RT data. For EPP 2018, an addition of an external HIV infections page (for HIV infections acquired from e.g. hospitals, migrant/overseas workers) will be made available for concentrated epidemics. Approaches for generic methods to improve incorporation of direct incidence estimates and associated uncertainty into EPP were discussed (e.g. from Population-based HIV Impact Assessment's/PHIA's and other data sources). The Reference Group agreed on the changes and plans for EPP, and anticipates the roll-out of the web-based Spectrum/EPP for the 2019 round of estimates.

Session 2. Incidence Estimation using EPP

Recent investigations on the impact of the equilibrium prior in the modelling of incidence curves in EPP were presented by Tim Brown and Jeff Eaton. Results by Tim Brown showed that without the prior, the r-spline model was more responsive to the data, which often resulted in decreased incidence trends for recent years in data-rich scenarios. In contrast, for data sparse scenarios, notably for concentrated epidemics or subnational files, the exclusion of the equilibrium prior gave highly variable results and should not be recommended.

Jeff Eaton presented alternative methods for modelling r(t) in the absence/presence of equilibrium prior. He presented the historical development of different modelling techniques over the course of the global HIV epidemic and proposed that a newer model may be more suitable as more countries enter the "control phase" of the epidemic, with more flexibility to capture recent data-driven trends (e.g. decreases in incidence following scale-up of intervention programmes). He recommended to use a parametric model (e.g. logistic function) for the earlier years of the epidemic, combined with a stochastic random walk (instead of equilibrium prior), for the most recent and projected years — named the "rlogRW" model. Haidong Wang explained that IHME have also investigated modelling in the presence or absence of equilibrium prior and random walk, and had agreed to collaborate with Jeff and Tim Brown for further research. It was also recommended that Jeff should investigate the impact of rlogRW model in countries with relatively sparse data sets, including concentrated epidemics, and present model comparisons with other models, e.g. r-flex, a random walk model, and refine the transition between the parametric and stochastic parts of the model.

The Reference Group thus agreed that for the immediate term, the default should be to continue using the equilibrium prior in EPP, but that EPP should include a functionality to disable the prior for selected users (e.g. model developers and UNAIDS). The group recognises that this is a temporary solution until improved models are fully developed.

Session 3. Modelling Age- and Sex-specific HIV Estimates

Jeff Eaton described the new developments for the incorporation of the age- and sex-specific model (ASM) into EPP, to better capture transmission dynamics into the model, including sex-specific transmission rates, sexual activity/contact rates by CD4 category and age categories, etc. He presented ASM updates (e.g. changes in transmission parameters for people on ART) and latest results for 25 countries across sub-Saharan Africa, using the previously described 'rlogRW' model. Generally, a reduced saturation peak, followed by a smoother and more gradual decline in prevalence and incidence curves was observed in the results when using the ASM model, compared with other models.

Concerns were raised whether the increasing sex ratio of incidence between females and males may have been due to low response rate, and it was suggested that non-responders for DHS and PHIA's should be queried, by different age categories. The group also suggested considering behavioural aspects, e.g. partner acquisition rates, agree at first sex, etc. from ALPHA network data and national household survey data, and unsafe sex as an additional covariate, as used by IHME. The Reference Group agreed that the presented results show improved model fits with the ASM model, yet request that further comparisons with the other epidemic settings currently using EPP that do not use ASM (e.g. concentrated epidemic settings) should be shown. Collaboration with IHME and ALPHA network for model development was encouraged and design specification for an updated ASM for implementation into Spectrum should be presented at the next Reference Group meeting.

Session 4. Use of Routine and Program Data

The importance of scrutinising the ANC-RT data was reiterated at the meeting, considering that the data are used to inform incidence trends within a population in EPP, and in Spectrum, for estimates of HIV prevalence in pregnant women and PMTCT coverage. Ben Sheng presented analyses on comparing different modelling methods using data from either ANC-SS or ANC-RT sites in overlapping years for Uganda, to more accurately

estimate the ANC-RT bias calibration parameter currently used in EPP. The Reference Group agreed that this analysis should continue and should be expanded to more countries.

Mathieu Maheu-Giroux and Peter Young presented results which demonstrated that HIV prevalence estimates are affected by differing levels of ANC coverage and completeness of reporting, respectively. Mathieu illustrated that lower HIV testing coverage was associated with higher HIV prevalence, and that not accounting for this relationship results in overstating the HIV prevalence decline among pregnant women in Malawi. Discussions followed as to the potential reasons for differences in ANC coverage (e.g. stock outs of diagnostic kits, refusal rates, issues with data collection/recording, variances in reporting times, etc.) which countries continue to address, and that facilities which typically reach 90% coverage often represent large district hospitals in high prevalence areas. The Reference Group recommended that Mathieu should extend his analyses to additional countries and investigate the application of simpler heuristic approaches, such minimal testing coverage thresholds of 80-90% to account for the demonstrated biases, and share the results with the Reference Group.

Peter Young explained the range of different sources and real-life constraints that contribute towards incomplete data documentation in Kenya, and presented analyses indicating positive correlations between facilities with more complete data reporting and higher HIV prevalence. He also highlighted a limitation of existing DHIS2 data extracts, which are not able to differentiate between true zero values from missing values that are also marked as zero in the data.

John Stover provided an update on a tool they have developed to automatically extract DHIS2 data into Spectrum (which is currently pending approval for use in Kenya) that may improve the data collection process. It was also recommended that an additional indicator on reporting status for each facility should be added to the tool. Further investigation of missingness and errors in data from systems using electronic medical records (EMR) was also suggested as a useful source for validation. The Reference Group acknowledged that the high burden areas are often supported by PEPFAR that will be pushing for high coverage and data completion, which may inadvertently further increase disparities in data coverage and completeness in the future, and encourages continued research to improve handling of ANC data.

Whether labour and delivery data among women who did not attend ANC should be included in the ANC-RT data was queried, yet concerns were raised about ensuring the women were already tested earlier within their pregnancy. By excluding women who skip ANC and only show up at delivery may also potentially bias the results if those women have different prevalence levels. Whilst research suggests the application of model-based adjustments to estimate true prevalence trends among pregnant women, it was recommended that countries should continue to input ANC-RT data as observed, and that any subsequent adjustments should be clearly visualised in EPP.

Session 5. Use of Population Survey Data

Mathieu Maheu-Giroux presented an assessment of the impact of potential misclassification of HIV status on HIV prevalence estimates from earlier demographic health surveys (DHS) which used testing algorithms subsequently found to have suboptimal specificity (see https://dhsprogram.com/pubs/pdf/MR22/MR22.pdf for more information). He showed results for a number of African countries where original prevalence estimates were compared with those adjusted for such potential errors, using a Bayesian latent class model. It was agreed that in general, the adjusted prevalence estimates were similar to the unadjusted estimates, with the exception of Zambia and Uganda, which showed large discrepancies. Based on these results, the Reference Group recommended the continued use of unadjusted DHS data, yet that the adjusted results should be used for Zambia estimates (the appropriate communication with justification towards the country team was also advised).

Jessica Justman gave an overview of the ongoing Population-based HIV Impact Assessment (PHIA) project and recent results, which included data for Zimbabwe, Malawi and Zambia. In addition to prevalence and incidence, Jessica showed results on the HIV care cascade (90-90-90), which indicated that further effort was particularly needed to raise the awareness of HIV status (i.e. the first 90). A comparison between PHIA and DHS results for 6 African countries showed comparable results between the surveys. The Reference Group

also noted the suggestion that the prevalence of viral load suppression (VLS) among all HIV positive persons may be useful as a composite indicator of the uptake and effectiveness of national HIV services.

Session 6. Estimating Key Populations

Key populations typically have different HIV transmission dynamics and risks associated with them than the general population, and estimation of their sizes and their impact on prevalence and incidence in the general population has been limited. New approaches for extrapolating and combining key population size estimates were presented in this session by Le Bao, Abhirup Datta and Jess Edwards. Le described methods using Bayesian hierarchical modelling to allow simultaneous analysis of multiple data sources with information pooling to improve size estimation, showing results from Bangladesh and Ukraine. Abhirup presented work in Cote d'Ivoire using Bayesian estimation with spatial structure to use known indicators for MSM (men who have sex with men) populations from certain regions to inform other regions where data were missing. Jess Edwards (in collaboration with MESH), presented results for the Dominican Republic, where results were extrapolated from specific regions to generate national level estimates combining various data sources (e.g. national socio-demographic data, DHS prevalence, etc.

Additionally, Keith Sabin presented MSM size estimates derived from non-conventional data sources (e.g. from dating apps), which may suggest that UNAIDS could be currently underestimating the number of MSM. He demonstrated that that inaccuracies in size estimates of certain key populations affects the distribution of all the different risk groups, which may also result in errors in the shape of the epidemic curve.

The need for key populations to be specifically included in the modelling process for estimates in generalised epidemics was discussed and what the potential impact of such groups on HIV transmission dynamics in generalised epidemics may be. This led to further discussions about whether key populations are sufficiently captured in household survey data, where various participants expressed differing views. The Reference Group agreed that this would be an open-research question. Marie-Claude stated that her group is currently investigating the contribution of MSM and FSW to overall HIV prevalence in Cameroon and Senegal and that they could present their findings at the next meeting. The Reference Group also acknowledged that key populations require further scrutiny and that current models do not capture transmission dynamics for these populations sufficiently, stating that new models may need to be developed to specifically address this area.

Session 7. Incidence Estimation using Case Reports

Guy Mahiane described the recent developments in the case reporting and vital registration tool in Spectrum (CSAVR), which included a reconfiguration for estimating the number of new diagnoses, based on fitting the observed values to the predicted values (the previous proposal for estimation of time lag between infection and diagnoses had since been dropped), the addition of a second order segmented polynomial curves as another option for modelling the incidence curve, and using automatic AIC model selection to make the fitting process less dependent on the user. Queries were made regarding the model's assumption that the diagnosis rate was proportional to the mortality rate and that further investigation may be needed for validation. It was also acknowledged that further investigation for improved fitting to the number of deaths and the number of people living with HIV (PLHIV) was in progress. The Reference Group encouraged closer work with between the CSAVR and EPP incidence tools, particularly for key populations, and recommended exploration of using more efficient EPP-ASM code base to accelerate CSAVR estimation.

Kim Marsh explained that Spectrum typically overestimates mortality for countries that use the CSAVR tool (currently at 54), yet presented that a large proportion of these also have suboptimal vital registration data. Discussions followed on approaches to improve data quality by providing countries with further guidance on the data requirements. Questions arose as to whether Spectrum should be validated against raw WHO mortality data or WHO cause-specific adjusted mortality data. Further clarification as to how the adjustments were made was also sought. The Reference Group proposed that the unadjusted mortality data should be used, yet advised that further consultation may be required to agree on a more informed final decision.

Brazil was presented as a case study, to compare estimates from CSAVR/Spectrum results with those of the Imperial College Brazil Model, developed by Tara Mangal. Kim Marsh highlighted that Brazil represented a unique case where Spectrum was calibrated to estimates of incidence and mortality reported by Brazil, rather than being independently modelled and validated. Results for prevalence were found to be similar across the two approaches, yet there were large differences in their incidence estimates.

Haidong Wang followed by presenting the methods for calculating incidence at IHME for the Global Burden of Disease (GBD) estimates, where countries were modelled according to two approaches, namely an ensemble model for generalised epidemics (largely based on EPP/Spectrum model with additional adjustments for mortality), or they applied a Cohort Incidence Bias Adjustment (CIBA), used for concentrated epidemics with vital registration data. The results for Brazil were also shown for comparison, which were different to both the Spectrum and Brazil model estimates. The reasons behind the stark differences between the three modelling approaches were unclear and it was noted that this could cause confusion when communicating contrasting results to countries. The Reference Group thus recommended that a thorough model comparison exercise be undertaken, using Brazil as a case study to compare CSAVR-Spectrum, the Imperial College Brazil model, and IHME's methods, to better understand the differences between the approaches and provide improved guidance to countries. It was agreed that a model comparison between EPP/Spectrum, IHME and the Thembisa model should also be performed for South Africa, as an example of a generalised epidemic.

Session 8. Spatially-specific Estimates of HIV

Pete Gething informed the Reference Group of the geospatial HIVE-MAP workshop hosted by UNAIDS (July 2017, Johannesburg — see minutes report), where preliminary reports were generated and they received feedback from 4 countries. Since the workshop, HIVE-Map results have been generated for 10 countries in total (South Africa, Malawi, Zambia, Zimbabwe, Mozambique, Kenya, Uganda, Tanzania, Lesotho and Swaziland), which include estimates for HIV prevalence, PLHIV, ART coverage and numbers of new infections by relative incidence risk, at the district level for each country. Pete also explained the work that was planned for early 2018, including the incorporation of the PHIA survey data.

Sam Bhatt further described the developmental updates that occurred in the geospatial HIVE-MAP model, and explained that future work included the propagation of Spectrum uncertainty around the estimates, and investigating different weighting schemes for data fitting. Sam highlighted the need for obtaining country-approved demographic and geographic information, as the discrepancies initially observed in their results were largely due to use of different/out-dated shape files and population sizes from countries. The assumption that people are seeking healthcare only within their own residential district was also explained as a current model limitation, and that further work on the ART catchment model is planned, to better capture the migration dynamics of people seeking care (e.g. using data from IeDEA and ALPHA Network).

Steve Gutreuter presented comparisons of estimates between HIVE-MAP model, the Small Area Estimates (SAE) model, and Spectrum disaggregated worksheets, showing high concordance between approaches for HIV prevalence. However, it was noted that there were larger mismatches in PLHIV and incidence estimates between the methods, which were partly due to the use of different data sources by models, e.g. differences in allocated district population sizes.

Jeff Eaton demonstrated the need for better incorporation of uncertainty when estimating coverage for antiretroviral treatment (for both the numerator, i.e. number of people on ART, and the denominator, PLHIV, which itself is estimated on prevalence and population size). The heterogeneity associated with estimates of ART numbers and PLHIV are currently propagated to large uncertainty ranges for ART coverage in Spectrum (and thus also in the HIVE model, which is calibrated to Spectrum results), and proposed an alternative approach for jointly modelling ART coverage, numbers on ART and PLHIV, using auxiliary data. The Reference Group acknowledged that further investigation was needed in this area and proposed that PHIA data may provide useful information on the relationship between ART coverage and numbers of ART, and to consider investigating temporal ART coverage patterns in the data (e.g. to determine whether certain districts are becoming truly "saturated").

The Reference Group recommended the preferred use of the HIVE-Map model for subnational estimates, where available. A common data repository with shared access to country-approved data files (e.g. demographic information and shape files) was currently being set up by UNAIDS, in collaboration with the HIVE-team, to ensure that all relevant parties (HIVE team, UNAIDS, PEPFAR) use the same data source for reported estimates. The Reference Group also recommended that a joint communication for the HIVE-Map alongside Spectrum was needed, in the form of webinars and a summary guidance document. The latter should explain the role of the HIVE-Map model as an extension to Spectrum results for countries at a granular subnational level, and should include a short summary of Spectrum assumptions and outputs versus those of the HIVE-Map model. Similar branding for use of Spectrum and the HIVE-Map was advised, to improve the continuity from Spectrum to the HIVE-model. Additionally, future correspondence regarding HIVE results should jointly copy the HIVE team, UNAIDS and relevant partners.

Session 9. Estimating Mortality on ART

In lead up to the Reference Group meeting, the Secretariat has collaborated with research groups to collate recent estimates for mortality for individuals on ART. Kate Wilson presented Spectrum estimates for life expectancy, crude mortality, and mortality rates by CD4 count for individuals on ART, compared with latest results from Europe (by Antiretroviral Therapy Cohort Collaboration – ART-CC), Brazil (Tara Mangal, Imperial College), South Africa (Leigh Johnson, UCT), and Zambia (Charles Holmes, CDC). Results showed that Spectrum may be overestimating mortality on ART, particularly for Brazil and Europe. It was also noted that unlike most other data imply, the Spectrum default mortality rates for Latin America and Caribbean (LAC) region (based on data from IeDEA) were higher for females than males. It was thus recommended that IeDEA would re-examine their data to determine an explanation for this. IeDEA and ALPHA network also agreed that they would compare results between their overlapping sites.

The Reference Group recommended that a task force should be established to specifically address current assumptions for mortality estimates for individuals on ART, review recent data for trends in ART-related mortality, and agree on recommended changes to ART mortality rates in Spectrum for Brazil, the LAC region, Europe, etc. This working group would include members of the UNAIDS, IeDEA, ALPHA network, UNAIDS, the Secretariat, and the aforementioned research groups who provided the mortality data used for the comparisons.

Constantin Yiannoutsos presented developments in their disengagement and mortality Markhov model, which include assumptions on duration for re-entry of previously disengagement people back into care, and mortality associated with being out of care, derived from recent field research in East African IeDEA cohorts. The Reference Group requested that the model includes CD4 progression among those on ART, where individuals are stratified on their CD4 counts (e.g. at the point of disengagement from care). It was recommended that by the next Reference Group meeting, IeDEA would present validation of their model with data from East Africa, with plans to pilot in Spectrum for other regions thereafter.

Session 10. Comparison between UNAIDS and GBD Estimates

Haidong Wang presented the latest results produced for GBD 2016 estimates, including comparisons with earlier GBD 2015 estimates and with UNAIDS 2017 estimates, showing strong similarities between latest GBD and UNAIDS estimates on a global scale. He noted that IHME used an old version of Spectrum for their comparisons for individual countries. Their assumption that income was proportional to initiation on ART was also queried. The Reference Group encouraged regular collaboration with IHME (e.g. teleconference meetings every 2 months) to investigate linkage between income and ART initiation (e.g. by examining PHIA data), perform a systematic review the modelling approaches for GBD and UNAIDS estimates, and ensure that IHME GBD estimates are able to maximally benefit from the most current research and recommendations of the UNAIDS Reference Group.

Key Recommendations

Recommendation/Action Item	Lead Person(s)	Proposed timeline
1. Continuous Update and Improvement		
Spectrum AIDS Impact Model (AIM) Output Customisation: The Reference Group agrees that the additional display outputs for Spectrum, including the HIV dashboard and treatment cascade plots (e.g. 90-90-90, etc.) are implemented	Avenir Health	Immediate
Uncertainty Analysis: The newly reconfigured uncertainty analyses (based on 300 draws for year of estimate, only saving the upper/lower bounds for indicators, and applying current year variation to earlier years) to be implemented in Spectrum	Avenir Health	Immediate
CD4 Cell Count at ART Initiation: The Reference Group approves offering the choice to users of the two approaches for allocation of CD4 distribution for new individuals on ART (i.e. entering median CD4 count upon initiation or, if data unavailable, by defining the default allocation, with the added parameter to balance between expected mortality and distribution of eligible population)	Avenir Health	Immediate
Age Distribution for New Infections: Further consultation is planned to agree on new age distributions for new infections specific for Europe	Avenir Health, UNAIDS, Tobi Saidel	Immediate
HIV-related Fertility Rate Reduction: Incorporation of subfertility effects in Spectrum were further addressed in the "Modelling Paediatric HIV and need for ART" meeting (19-20 October 2017, London). Recommendations were as follows:		
• Fertility rate ratios (FRR's) to be adjusted in women not on ART, to incorporate subfertility results presented by Alpha Network (Milly Marston) and Jeff Eaton	Avenir Health, Milly Marston, Jeff Eaton	Immediate
• Implement parameter in Spectrum to allow changes to the FRR of women on ART. Default value for parameter will remain at 1.0 pending further analysis and investigation	Avenir Health	Immediate
• ANC routine data is recommended for fitting FRR's in Spectrum if data meet completeness and reporting standards. ANC sentinel surveillance data are not recommended for fitting FRR's	Avenir Health	Immediate
Spectrum on the Web: Current efforts to be continued, to make Spectrum (including EPP) available online alongside the desktop version, ready for countries to use in 2019	Avenir Health, East-West Center	Ongoing
Estimation and Projection Package (EPP) Incidence Curve r(t) Fitting: • The continued use of the equilibrium prior for modelling incidence curves is recommended as default for the immediate	East-West Center	Immediate

term, though the option to remove the equilibrium prior should be available, yet restricted to specific users (e.g. modellers and UNAIDS), for cases where use of the prior causes questionable results		
• Alternative model designs to be further investigated that balance model structure and flexibility, and that consider the following: i) concentrated epidemics and data spare scenarios; ii) optimised fitting time and; iii) comparisons to r-flex (random walk) model	Jeff Eaton, East-West Center, IHME	May 2018
<u>Incorporation of Direct Incidence Estimates</u>: Further investigation for generic methods to improve direct incorporation of incidence estimates (e.g. from PHIA's, and other sources) into EPP/Spectrum is recommended, e.g. exploring correlations between incidence and prevalence data	Jeff Eaton, East-West Center, Avenir Health	Immediate
Overall <u>Use of Demographic Household survey (DHS) Data</u>: The continued use of 'unadjusted' DHS data for HIV estimates has been agreed, with the exception of Zambia, where the use of adjusted estimates should be recommended and communicated to the country estimates team	UNAIDS, Mathieu Maheu-Giroux, ICT Intl	Immediate
• For the Uganda 2011 AIS, the Reference Group recommends using confirmed HIV testing results. This recommendation should be communicated to the country estimates team and confirmed estimates provided by CDC	UNAIDS OGAC/CDC	Immediate
<u>Size Estimates of Key Populations</u>: • The Reference Group encourages more countries to investigate their key population sizes, and recognises the need for validation of current size estimations for key populations from independent approaches	UNAIDS, Le Bao, Abhi Datta, Stefan Baral, Jess Edwards	Ongoing
• Methods to include key population size estimates with uncertainty estimates into Spectrum/EPP model fitting process for concentrated epidemics (and potentially also generalised epidemics) to be investigated. This should include further research into estimating default uncertainty values based on either global, regional or type of epidemic	UNAIDS, East-West Center, Avenir Health	Ongoing
• Novel data sources, such as social media data, are encouraged, but utilization of these data requires further epidemiological analysis and scrutiny (e.g. checking for double counting for estimates based on numbers of app downloads)	UNAIDS	Ongoing
• The Reference Group recognises that current models do not aim to capture the contribution of transmission in/by key populations, and that alternative models would need to be used (and, in some cases, developed) to better reflect transmission dynamics	Unassigned	Ongoing

• Further research to determine whether key populations (e.g. MSM and FSW) are sufficiently captured and adequately represented in current household survey data is required	Leigh Johnson, ALPHA Network (TBC)	May 2018
Collaboration with IHME (GBD Estimates): The Reference Group encourages continued collaboration and regular correspondence with IHME, in particular for: (i) comparisons for Brazil and South Africa, investigations on ART mortality; (ii) testing linkage between income and earliness of initiating ART with PHIA data; and, (iii) understanding and communicating differences/similarities between GBD and UNAIDS estimates on overall burden estimates and '90-90-90' statistics. • Reference Group Secretariat to organise teleconferences with IHME and relevant parties, every 2 months	Secretariat, IHME, UNAIDS, Avenir Health, Leigh Johnson	Ongoing
2. Age-structured models		
ASM Development and Implementation: Development for the age/sex-specific model (ASM) and incorporation of age/sex-specific adult mortality to be continued. The design specification should be agreed by the Spring Reference Group meeting, to be ready for testing by countries at the next 2019 UNAIDS estimates regional workshops. Method development should consider the following: • Ensure capability to incorporate additional PHIA survey indicators into model inference • Approaches for ASM to be used for generalised epidemics with sparse data sets and concentrated epidemics to be pursued	Jeff Eaton, East-West Center, Avenir Health	May 2018
3. Use of case-report and mortality data		
Case Surveillance and Vital Registration (CSAVR) Tool Incidence Estimation in CSAVR: • The Reference Group agrees to the implementation of the newly reconfigured incidence estimation in CSAVR (estimating new diagnoses and fitting the observed values to those predicted, dropping the time-lag estimation, adding second order segmented polynomial curves and AIC model selection)	Avenir Health, UNAIDS	Immediate
• Further consultation to agree on whether raw or adjusted WHO vital registration mortality data and/or IHME mortality estimates should be used for model fitting	Avenir Health, UNAIDS, IHME, Secretariat	Immediate
• Investigate use of more efficient EPP-ASM code base for CSAVR estimation	Avenir Health, Secretariat	Ongoing
Comparison of model estimates using case-reports Brazil and South Africa to be used as case studies to undertake an in-depth model comparison between different modelling tools using case-reporting data for HIV estimates (for Brazil: CSAVR/Spectrum, Imperial College Brazil Model, and IHME models; for South Africa: Spectrum, Thembisa and IHME models), to understand differences and improve guidance for countries on these different approaches	Tara Mangal, Leigh Johnson, Avenir Health, UNAIDS, IHME	May 2018

Mortality on ART Assumptions
ART Mortality Task Force:
• A working group dedicated to investigating mortality on ART to be immediately established, with a teleconference to be organised in November 2017 (by the Secretariat) to address:
  ○ Review whether Brazil data can be recommended for use in Brazil; and European data in Europe
  ○ Review female and male mortality rates for Latin America Region currently in Spectrum from IeDEA
  ○ Review current assumptions for Europe and recommend how they should be adjusted to better match data by the ART Cohort Collaboration (e.g. recent temporal trends)
• By the next Reference Group meeting, the working group should propose new schedules for on-ART mortality and provide possible explanations for trends in mortality rates. Results from other data sources (e.g. China mortality analyses) are welcomed
	ART Mortality Working Group (Secretariat, Avenir Health, UNAIDS, IeDEA, Alpha Network, IHME) & ART-CC
	
	Alpha Network, IeDEA, IHME, Avenir Health, Le Bao/Guo Wei
		Immediate
		
		May 2018

Mortality and Disengagement from Care Model Development: Model development to be extended to include CD4 progression/regression. Model to be tested with upcoming data from IeDEA-East Africa cohorts and presented at the next Reference Group meeting, to review incorporation into Spectrum • The revised model should be able to accommodate potential novel data sources and, subject to review and testing, should be piloted in Spectrum in 2018, before roll-out for country estimates	IeDEA	May 2018
4. Use of programme service data		
Incorporation of ANC-RT Data in EPP: • Newly implemented validation screen for routine ANC data (ANC1, number of known HIV positives, number of people tested/ANC visits, number of tested positives, etc.) with coverage diagnostic plots is agreed for current implementation • Investigation on approaches to compare antenatal routine data (ANC-RT) and sentinel surveillance data (ANC-SS) to be extended to more regions, to improve ANC-RT calibration parameter Exploration studies on ANC-RT Data: • Investigation of the effect of testing coverage on prevalence to be extended to more countries (e.g. Kenya, Zimbabwe, Cote d'Ivoire, and potentially PEPFAR data) and to be tested at 80% and 85% coverage. Development of simple heuristic adjustment to be explored to improve model efficiency • The Reference Group encourages the continuation of studies exploring the impact of facility reporting • The Reference Group recognises the need for monthly facility data for robust inference of trends from routine health facility	East-West Center Ben Sheng, Le Bao Mathieu Maheu-Giroux, Jeff Eaton Peter Young UNAIDS, WHO, PEPFAR, Global	Immediate May 2018 May 2018 May 2018 Ongoing

data. Standard DHIS extraction tool should additionally include whether facility filed a report in a given reporting period	Fund Technical Assistance & partners	
5. Spatially-specific estimates		
Geospatial (HIVE-Map) Model HIVE-Map Model Implementation: • The Reference Group recommends the use of the HIVE-Map as the preferred model for subnational HIV estimates, to be used in those countries for which it is available	HIVE Team (Pete Gething, Sam Bhatt), UNAIDS	Immediate
• The Reference Group encourages collaboration of the PHIA survey team and the HIVE team, to facilitate inclusion of PHIA survey data in HIVE estimates, used in the PEPFAR Country Operational Plans (COP) 2018	CDC, ICAP, HIVE team, UNAIDS, Secretariat	Immediate
HIVE-Map Dissemination and Communication: • HIVE-Map to be communicated as providing an extension to Spectrum results to countries, to provide estimates at a granular subnational level	UNAIDS	Immediate
• A joint guidance document for HIVE-MAP use alongside Spectrum should be generated and future joint copying of HIVE team, UNAIDS and partners to be coordinated for future correspondence	HIVE team, UNAIDS, PEPFAR, Avenir Health	Immediate
HIVE vs SAE Comparison: Model comparisons between HIVE-Map and small area estimates (SAE) model to be extended to more countries and include further indicators, to better understand differences and aid method development	HIVE team, Steve Gutreuter	May 2018
HIVE-Map Data Collection and Curation: • The Reference Group recommends systematic work with Central Statistical Offices to assemble and curate standardised shape files and population data, which may include intelligence gathering from other disease fields	OGAC, UNAIDS	Sept 2018
• UNAIDS are working to plan the next steps to establish a central repository for HIV-related data inputs to the Spectrum model and HIVE-Map model	UNAIDS, HIVE team	Sept 2018
HIVE-Map Method Development: • HIVE-Map ART catchment modelling to be further developed using currently available program/cohort study data (e.g. IeDEA, Manicaland, ALPHA network, PHIA, other home information collected at clinics, etc.), and to include learning and incorporation of types of health facility	HIVE team, IeDEA, Simon Gregson, ALPHA network, ICAP	Ongoing
• HIVE-Map to have the capability of including 'incidence assay information' from new diagnoses among pregnant women from forthcoming data sources	HIVE team	Ongoing

• The Reference Group encourages the sustainability of the HIVE-Map model to be used by countries for routine use. Continued collaboration between the HIVE-team and Spectrum modellers is agreed with the future aim to establish direct links between Spectrum-on-the-web and an online interface of the HIVE-Map, for improved cohesion between the models	HIVE team, Avenir Health, UNAIDS	Ongoing
6. Catalyse focused research and data collection		
<u>Exploratory Studies on HIV-related subfertility</u>: The Reference Group encourages further exploratory studies to determine potential differences in fertility between women on or off ART, relative to HIV negative women	Alpha Network, IeDEA	May 2018

Appendix I: List of Participants

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Appendix II: Agenda

UNAIDS Reference Group on Estimates, Modelling and Projections

Method Development for the UNAIDS Estimates: October 2017, London, UK

MEETING AGENDA

Day 1: Monday, 16th October 2017

Time	Duration (mins)	Topic	Presenter(s)
Session 1: Country Estimates and Software Updates (chaired by Peter Ghys) Objectives ● Feedback from UNAIDS 2017 estimates improve 2018 estimates ● Discuss latest Spectrum and EPP software updates			
09:00	10	Meeting overview	Peter Ghys, Tim Hallett
09:10	20	Progress since last Reference Group meeting and overview of final report for 2017 estimates	Mary Mahy
09:30	30	Review of Spectrum updates & development plans ● Treatment cascade, PMTCT coverage validation, uncertainty analysis, ART mortality, software update ● Fitting the fertility rate reduction pattern ● Incidence rate ratio patterns in concentrated epidemics	 John Stover Rob Glaubius Tobi Saidel
10:00	30	Review of EPP updates and development plans	Tim Brown
10:30	30	Coffee break	
11:00	60	Discussion on 2017 estimates and software updates ● Review country results, issues and improvements for 2018 ● Discussion on Spectrum & EPP, and agree next steps	All
12:00	60	Lunch break	
Session 2: Incidence Estimation using EPP (chaired by Tim Hallett) Objectives ● Review current assumptions for modelling r(t) curve ● Agree on recommended procedures for incidence estimation in EPP			
13:00	15	Current assumptions and impacts of using the equilibrium prior	Tim Brown
13:15	30	Alternative approaches for modelling r(t)	Jeff Eaton
13:45	45	Discussion on incidence curve fitting in EPP	All
14:30	30	Coffee break	
Session 3: Modelling Age- and Sex-specific HIV Estimates (chaired by Simon Gregson) Objectives ● Review age-sex model (ASM) and discuss updates ● Agree on precision and use of age and sex disaggregated data from Spectrum ● Determine next steps for ASM method development and implementation			
15:00	30	Age-sex model update	Jeff Eaton
15:30	45	Discussion on age-sex model development and use	All
16:15	15	Wrap-up of Day 1	Tim Hallett
16:30	–	End of Day 1	

Day 2: Tuesday, 17th October 2017

Time	Duration (mins)	Topic	Presenter(s)
Session 4: Use of Routine and Program data (chaired by Jeff Eaton) Objectives ● Review incorporation of routine ANC (ANC-RT) in EPP/Spectrum ● Agree on recommended procedures for use of routine data			
09:00	15	Comparison of Prevalence between ANC-SS and ANC-RT	Ben Sheng
09:15	15	Effect of testing coverage on prevalence	M. Maheu-Giroux
09:30	15	Effect of facility reporting on prevalence	Peter Young
09:45	45	Discussion on and modelling ANC-RT data and modelling/evaluating current trends	All
10:30	30	Coffee break	
Session 5: Use of Population Survey Data (chaired by Simon Gregson) Objectives ● Assess misclassification errors across DHS data ● Review results of recent PHIA surveys ● Agree on guidance on recommended procedures for modelling survey data			
11:00	15	Assessing the impact of immunoassay misclassifications for DHS using Bayesian Latent Class analysis	Mathieu Maheu-Giroux
11:15	15	PHIA Results & comparison with other surveys	Jessica Justman
11:30	45	Discussion on strategies to incorporate survey data	All
12:15	60	Lunch break	
Session 6: Estimating Key Populations (chaired by Tim Brown) Objectives ● Description of biases built around the effects of differing size estimates in different contexts ● Determine next steps towards recommended approaches for extrapolation of size estimates that can be shared with countries			
13:15	05	Current tools and problem statement	Keith Sabin
13:20	45	New methods for size estimation of key populations ● Bayesian Estimation of MSM population size in Cote d'Ivoire ● Bayesian Hierarchical Model for Size Estimation ● Key population size estimation as a missing data problem	 Abhi Datta Le Bao Jess Edwards
14:05	10	Impact of different size estimation methods on HIV estimates	Keith Sabin
14:15	45	Discussion on size estimation and key populations	All
15:00	30	Coffee Break	
Session 7: Incidence Estimation using Case Reports (chaired by Kim Marsh) Objectives ● Discuss latest CSAVR tool updates ● Review alternative incidence modelling tools for case report data ● Determine next steps towards guidance on use of incidence tools for concentrated epidemics			
15:30	15	Review of CSAVR updates	Guy Mahiane
15:45	15	● Use of CSAVR: Brazil Case Study ● Mortality data included in CSAVR	Kim Marsh
16:00	15	Modelling incidence in Latin America: Brazil Model	Tara Mangal
16:15	15	Incidence Estimates by GBD	Haidong Wang
16:30	45	Discussion on case-reporting tools & mortality in CSAVR	All
17:15	15	Wrap-up of Day 2	Tim Hallett
17:30	–	End of Day 2	

Day 3: Wednesday, 18th October 2017

Time	Duration (mins)	Topic	Presenter(s)
Session 8: Spatial-specific Estimates (chaired by Mary Mahy) Objectives ● Review 2017 results from Geospatial HIVE-Map Model ● Determine next steps for HIVE-Map Model and provide recommendations for spatial-specific estimates for 2018+			
09:00	60	Geospatial Model Developments and Results	Pete Gething, Sam Bhatt
10:00	15	Comparison of HIVE-Map with Small Area Estimates and Spectrum	Steve Gutreuter
10:10	15	Estimating ART Coverage	Jeff Eaton
10:30	30	Coffee break	
11:00	30	Discussion on HIVE-Map method development, use, and strategies for spatial-specific estimation	All
11:30	30	Discussion on HIVE-Map for DREAMS evaluation	All
12:00	60	Lunch break	
Session 9: Estimating Mortality on ART (chaired by Tim Hallett) Objectives ● Review current assumptions and novel data on mortality on ART ● Agree of recommended procedures for modelling mortality			
13:00	15	Comparisons of mortality on ART	Kate Wilson
13:15	15	Feedback from Research groups on Mortality on ART estimates ● Alpha Network, ART Cohort Collaboration, Brazil, South Africa, and Zambia	Emma Slaymaker, Adam Trickey, Tara Mangal, Leigh Johnson, Charles Holmes
13:30	30	Discussion on estimating mortality on ART	All
14:00	30	Coffee break	
Session 10: Comparison between UNAIDS and GBD Estimates (chaired by Tim Hallett)			
15:30	30	GBD HIV Estimates and comparison with UNAIDS	Haidong Wang
16:00	30	Final meeting discussions	All
16:30	30	Meeting wrap-up and recommendations	Tim Hallett
17:00	–	Meeting close	