Method Development for the UNAIDS Estimates: November 2016

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

New York, USA, 7-8 November 2016

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.

Sabrina Lamour, January 2017

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 also 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 European Centre for Disease for Disease Prevention and Control (ECDC), the Measurement and Surveillance of HIV Epidemics (MESH) Consortium, the United States Center for Disease Control and Prevention (US CDC) and the Institute for Health Metrics and Evaluation (IHME), among others.

Aim of the meeting

The general purpose of the Reference Group meetings 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 packages, used by countries to generate 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 2017
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 2016 was held in Scandinavia House, Manhattan, New York, USA on the 7th and 8th November 2016. The meeting featured presentations combined with group discussion to generate consensus recommendations. The program was divided into the following sessions:

I. Software Updates
II. Mortality and Age-structure Developments
III. Comparison between UNAIDS Estimates and other Modelling Groups
IV. Spatially-specific Estimates of HIV
V. Modelling HIV Incidence
VI. Incorporating New Data Sources and Updates from our Partners

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 November 2016 Meeting page on Reference Group website (for non-members, please contact the project manager). The final recommendations and action items can be found end of this report and have been categorised into the five the core themes, mentioned above.

The recommendations drafted at Reference Group meetings give UNAIDS guidance on how best to calculate estimates of the HIV epidemic on 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 further 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 I. Software Updates

Spectrum Updates

John Stover presented a summary of the latest implementations in the AIDS Impact Module (AIM) of Spectrum, including the updates to the Fit (incidence) to program data tool (FTP), and adjustments addressing the historical changes of mortality among those on antiretroviral therapy (ART), including discontinuities in mortality following changes in ART guidelines, as well as recent progress in the development of the web-based Spectrum software. With regard to the FTP tool, he suggested that Spectrum parameters obtained from the previous year's results would be used to inform current estimates, on a country by country basis, to speed the fitting process. The Reference Group agreed that a database of parameter values from earlier years should be created. Values from the previous year should be set as default in the fitting process, with the added capability to incorporate future data to improve parameterisation.

He additionally presented plans to track paediatric infections into adulthood in Spectrum. This work is on the agenda for the paediatrics working group. Please refer to the report for the "Estimating the Future of Paediatric HIV and the need for ART 2016" meeting, co-organised by UNAIDS, World Health Organisation (WHO) and the Reference Group, for further information (available at www.epidem.org).

Anna Radin discussed research on exploring the causes of obtaining implausibly high estimates of coverage for prevention of mother-to-child transmission of HIV (PMTCT) programs. The underestimation of HIV prevalence among women at ages of high fertility was an important contributing factor towards the overestimation of PMTCT coverage. She also pointed out that the coverage of the first visit to antenatal care (i.e. percent of pregnant women attending at least one antenatal care visit (ANC1)) should be checked against the PMTCT coverage (among HIV positive pregnant women).

Robert Glaubius presented the latest progress by Avenir Health to improve Spectrum estimates of age-specific HIV prevalence by improving the age- and sex-specific incidence rate ratios (IRR's) in Spectrum through an additional fitting step, where Spectrum projections were fitted to national-survey based prevalence. Such IRR adjustments have been tested with several country files using both a static or time-variant dynamic form, both of which have been shown to improve the accuracy of age-specific HIV prevalence with results better aligned to survey patterns than Spectrum estimates without the modified IRR's. Furthermore, application of the fitted IRR's resulted in a reduction in the PMTCT coverage in 20 of the 25 countries tested thus far, addressing the issue of PMTCT overestimation, as discussed previously. It was agreed that this revised method should be implemented, yet Robert should continue testing the IRR adjustments on the remaining Spectrum country files, relay the results with the Reference Group, and provide further recommendation of the use of either static or dynamic time-variant IRR's, on a country-by-country basis, for the Reference Group to review.

EPP Updates

Tim Brown presented the multiple newly added features in the Estimation and Projection Package, which were well received by Reference Group. Such features included the incorporation of additional variance in ANC sentinel surveillance (ANC-SS) prevalence to capture non-sampling error and improve the EPP model fit, an auxiliary data approach to approximate a Bayesian hierarchical modelling at a subnational/subpopulation level (further discussed in the geospatial section of report), and the ability to include cohort-based incidence. Latest implementations also included the capability of incorporating routine HIV testing data from antenatal clinics (ANC-RT) for PMTCT screening, in addition to ANC-SS, and the implementation of age- and sex-specific demographic structures for generalized epidemics into EPP, to improve consistency and aid continuous integration with AIM (please refer to meeting presentations from Jeff Eaton and Robert Glaubius for further information on implementation). Additional minor adjustments, bug-fixes and final testing remain to be completed for some of the features before the final software release for country roll-out in 2017.

Tim reminded the Reference Group of the license issues with the use of the Bayesian hierarchical model, which uses generalised linear mixed-effects models (GLMM) that operate under a GNU General public licence. He raised his concerns on fulfilling terms to operate EPP and Spectrum with a GNU license and instead, suggested that alternative approaches should be sought, which would still meet the Guidelines for

Accurate and Transparent Health Estimates Reporting (GATHER). The Reference Group agreed and have recommended that further legal advice on holding an alternative public licence should be undertaken, e.g. through consultation between UNAIDS and the WHO legal department.

Tim Brown also highlighted the various technical and design issues in software user-interface and proposed that the Reference Group convenes a specific working group on user-interface, to address such issues, as well as agree on clear terminology (e.g. PMTCT versus ANC-RT), to which the Reference strongly agreed.

Session II. Mortality and Age-structure Developments

Multi-state Markov models for Mortality and Disengagement from Care (IeDEA)

Constantin Yiannoutsos and Giorgos Bakoyannis presented their latest work on modelling estimates of mortality and disengagement from care, in the presence of outcome misclassification, highlighting the current challenges in reporting/classifications that may result in underestimating mortality whilst in HIV care and the potential for overestimating disengagement if people who transfer facilities are misclassified as having disengaged from care instead. Constantin and colleagues have generated a probability matrix for transition in and out of care (further described in May 2016 meeting report), yet currently lack sufficient data on the dynamics of people moving in and out of care. Constantin proposed two solutions to help inform the models: using a sentinel surveillance (double-sampling) as an internal validation approach (their preferred solution), or an external validation approach, using misclassification probabilities from other studies. The Reference Group recognises current challenges in ascertaining the true proportions of disengagement, reengagement, transfer and death, and additionally suggested that if such sentinel programs were to be undertaken, they should be implemented in southern and central African regions as a priority.

The importance of ensuring continuity of high quality recording and reporting of routine patient data was emphasised, especially as the care and treatment programmes are transitioning from international organisations (e.g. PEPFAR and CDC) to country management. Lastly, Constantin proposed either a relaxation in the current Markov processes or the addition of more Markov stages in Spectrum, for the model to consider the time spent in HIV care and incorporate re-engagement into care. The Reference Group appreciated these suggestions yet given the considerable implications on changes to current modelling structures, have recommended that sensitivity analyses should be undertaken first in order to assess the impact of re-engagement into care on current estimates. UNAIDS also agreed that countries require additional support and guidance to report on disengagement of care, to improve estimates.

Comparison of empirical data and UNAIDS estimates of adult mortality

Latest comparisons between UNAIDS 2016 estimates from Spectrum and empirical estimates of adult all-cause mortality (45q15), obtained from DHS sibling histories and recent household death data, were presented by Bruno Masquelier. Orphan rates derived from census and household surveys among children aged 5-9 were also compared with Spectrum outputs. In addition, a Bayesian B-spline model initially developed for child mortality by the UN Inter-Agency Group for Child Mortality Estimation was applied to the empirical measurements from surveys and censuses to obtain smooth trends in sex-specific adult mortality. His results highlighted that Spectrum consistently generated higher estimates of adult all-cause mortality and orphanhood and displayed strong discrepancies in sex ratios and age patterns of adult mortality, when compared with empirical data sources. A noticeable exception was adult mortality among males and paternal orphanhood in countries with very high HIV prevalence in Southern Africa. Findings related to age patterns of mortality are in agreement with the results observed by Avenir Health, who are tackling these issues through the aforementioned IRR adjustments (Robert Glaubius). Discrepancies observed in levels and sex ratios could potentially be reduced by the work pursued by Jeff Eaton (further outlined in the age-structure section).

Consequently, the Reference Group has recommended that Bruno Masquelier should repeat his analyses using the forthcoming Spectrum version that includes the adjusted IRR's and relay the updated results at the

next Reference Group meeting. In addition, survey and census estimates of the probability 45q15 will be incorporated into the next version of Spectrum in the validation section of AIM, to compare the AIM output with empirical measurements. The future aim is to additionally include mortality estimates as part of AIM calibration.

Age-structured Models

Jeff Eaton described the methodology behind the incorporation of age- and sex-specific demographic structures into EPP in more depth, highlighting that phase I of age-structure in EPP has been completed and implemented into the EPP software (further detail of age-structure model development can be found in the May 2016 meeting report). Recent developments have included significant improvements in model structure and efficiency through Incremental Mixture Importance Sampling (IMIS) with optimisation. Concurrent to Robert Glaubius's work, Jeff presented an alternative method for estimating age and sex-specific HIV incidence rate ratios from age-specific prevalence data using a second order random walk (RW2) model for age-specific IRRs.

Jeff summarised future work plans for age-structured modelling, which included the combination of age-specific prevalence with incidence assays and ANC-RT data, and the incorporation of adjusted IRR's into Spectrum. The Reference Group were in favour of the implementation of age-structure in EPP, and have recommended continued collaboration between Avenir Health and Jeff Eaton to optimise IRR modifications. The current challenges in generating demographic inputs required for the age-structured EPP model were also highlighted, which involved a labour-intensive raking to multiple data sources.

Session III. Comparison between UNAIDS Estimates and other Modelling Groups

ECDC Tool

The European Centre for Disease Prevention and Control (ECDC) have a HIV modelling tool, available online, that supports two methods that use case-report data to estimate HIV incidence (the London method, developed by Andrew Phillips and the incidence method - see June 2015 meeting report). Ard van Sighem presented the latest updates to the model, including corrections and improvements to the Bootstrap replications for confidence intervals calculations and smoothing of incidence cases, and amending distribution time from infection to diagnosis. The approach used by ECDC benefits from the fact that little historical data are required to generate incidence estimates.

Kim Marsh subsequently provided feedback from the ECDC-UNAIDS workshop that was held in February earlier this year, where both Spectrum software and the ECDC modelling tool were discussed and applied in six countries. The workshop demonstrated the current limitations of Spectrum's FTP tool in reproducing incidence estimates similar to those from the ECDC tool. John Stover added that further improvements to the FTP tool are currently underway, including methods to allow the option of simplified (non-peak) parameterisation of incidence function in AIM Program Data Reporting Tool. It was recommended that a working collaboration between UNAIDS, Avenir Health and ECDC should be continued, to plan the integration of using incidence estimates from ECDC tool as an alternative input into Spectrum than FTP or EPP, for high-income countries. The Reference Group also recommended that UNAIDS should organise further workshops with European countries and ECDC, as to encourage country involvement and data sharing to improve their estimates for countries within the European region (and other high-income settings).

Comparison of UNAIDS and IHME/GBD Estimates

Comparisons between 2016 HIV estimates and methodologies used by UNAIDS and the Institute for Health Metrics and Evaluation (IHME) group in their Global Burden of Disease study (GBD2016), are currently underway and are highly anticipated. Kim Marsh and Haidong Wang, who are co-ordinating this work, have agreed to disseminate the preliminary results to interested parties as soon as they are available.

Reflecting uncertainty in numbers on ART

Kim Marsh raised the current problems faced in data quality evaluation, quantification and measurement of uncertainty for numbers of people on ART and for other program statistics in Spectrum. She pointed out the need for developing a consistent approach to model ART coverage and estimate the 90-90-90 cascade measures. Preliminary results were presented from a subjective assessment by countries on ART numbers, performed at the Global HIV Cascade Workshop convened by the WHO in Dubrovnik in October 2016, which showed clear inconsistencies between data quality judgement and confidence. Kim presented efforts made using Imperial College's Cascade tool, towards evaluating data based on a simplified weighting scheme, yet concerns were raised as to the over-simplification of this proposed method. The Reference Group agreed a working group on quantifying uncertainty program data should be established by December 2016 (lead by UNAIDS), to agree on best approaches for the inclusion of uncertainty around ART numbers and other statistics, e.g. people living with HIV (PLHIV), numbers of diagnoses, numbers in HIV care, etc. into EPP/Spectrum.

Session IV. Spatially-specific Estimates of HIV

Geospatial Modelling

Pete Gething and Samir Bhatt have developed a Bayesian geospatial model which incorporates a range of data sources with predictor data (covariates) that are informed by existing UNAIDS parameters, to generate spatially-specific HIV estimates at the most granular level (see May 2016 meeting report for further detail). These can be aggregated to any geographic level of interest with rigorous representation of uncertainty. Pete and Sam provided an update on their geospatial modelling estimates, including improvements in their method development for their models on HIV prevalence (using either the facility or survey geospatial models which have now been tethered to Spectrum), ART coverage, and incidence. The latest results for Mozambique, South Africa and Kenya were presented yet remain to be completed (work on Swaziland was also currently underway). Further method development plans included the combination of the facility and survey geospatial models (Sam Bhatt) and testing, adjusting and validating their catchment modelling parameters with actual behavioural data, and improving their incidence estimates.

The Reference Group agreed with these plans and proposed that program/cohort study data, e.g. from IeDEA, Manicaland, ALPHA network and PHIA's, would be able to inform the model with further behavioural and demographic data, particularly for the catchment modelling. The Reference Group encouraged the geospatial team to extend their work to other countries, notably those part of the DREAMS (Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe women) initiative. Questions also arose regarding the most optimal form of communicating and presenting the uncertainty in their estimates (e.g. as confidence intervals on maps), particularly for incidence. Additionally, further work would be needed to be able to differentiate the covariates in Spectrum that would benefit from disaggregation at the subnational level, from those that should remain nationally homogenous (this point will be explored at the 2017 country workshops). Pete emphasised that whilst currently the geospatial model is still in the developmental phase, progress is being made to move towards allowing the tool to generate information that would be useful to program managers in the evaluation and development of program plans.

Bayesian Hierarchical Modelling at Sub-national and Subpopulation Level

The auxiliary data approach to approximating the hierarchical subnational/subpopulation model has been successfully implemented into EPP and has been subject to vigorous testing by Le Bao's group in countries with generalised epidemics with no major concerns. The hierarchical model aims to improve the reliability of EPP estimates through the generation of auxiliary data (pseudo sites) that take information from neighbouring areas, and is thus aimed to be more of use to data-poor countries. This model uses GLMM which operates under a GPL license (see licensing issues in the previous EPP section of report; further information on the use of GLMM also detailed in October 2015 meeting report).

Le Bao demonstrated three versions of the hierarchical GLMM model with varying degrees of heterogeneity among areas and sub-population: the second version, Model B (heterogeneous but similar trends), produced the best results for both model fit and complexity and was thus recommended to be selected as default. A range of extensions for this model were presented by Le and Amy Zhang, namely the spatial model (extension A), the multiple groups model (extension B), incorporation of predictors/covariates (extension C), the factor model (extension D, which has long term forecasting capability) and modelling missing data (extension D, to account for the fact that missing data may not be missing at random but be subjected to bias).

The Reference Group recommended the implementation of the hierarchical model for use (with 'default' samples sizes and pseudo-sites) for countries with generalised epidemics. They also encouraged the work on modelling of key subpopulations and expressed further interest in the missing data extension, which was agreed to be a timely and relevant issue, given the recent expansion of data sources such as routine testing (ANC-RT) data and case-reporting data. Further modifications that are also required in the current model included the incorporation and generation of auxiliary sites for both ANC-SS and ANC-RT (PMTCT) data into the hierarchical model in EPP.

Vision for success for spatially-specific-estimates

Given many of the complementary information provided by the geospatial and hierarchical models, it was agreed that continued collaboration and discussions between the modelling teams were required to determine the approach to best combine the two approaches in Spectrum. Furthermore, several questions were raised about the future plans for spatial modelling in general, including the following:

- How to best use spatially-specific estimates?
- What is the most appropriate spatial scale for decision-making that yields estimates of reliable quality and certainty? (Currently, this is thought to be the District level in most cases)
- What are specific 'use cases', apportioning prevention efforts at macro-scale, siting of services, management/evaluation of services?
- What is the goal for software and process integration, and within what timeframe?

Consequently, it was recommended that by next Reference Group meeting, the geospatial modelling team should demonstrate district level estimates, examples of uncertainty and use cases, and present agreed timelines for action for working on 7-10 (DREAMS) countries planned for roll-out. Country representatives anticipated to benefit from this work should also be included at this meeting.

Session V. Modelling HIV Incidence

Measuring incidence among key populations

Keith Sabin emphasised the high demand by donors, research communities and program teams for incidence estimates in key populations, including for people who inject drugs (PWID), men who have sex with men (MSM), sex workers (SW) and transgenders (TG). He presented his approach, which combined multiple data sources (e.g. Spectrum estimates, Models of Transmission (MoT), new case reports from ECDC reports), explaining that rate ratios were calculated as incidence in a population over global incidence (from Spectrum). Keith raised concerns on the heterogeneity of data quality and confidence, particularly for national estimates, and proposed that the average of aggregated country results could potentially be used as representative of global trends. He also highlighted the challenges in data sourcing, especially with the increasingly more common transition from survey data to case-reporting.

The proposal for providing global incidence trends was agreed as particularly useful for advocacy towards policy makers and decision-makers, yet further method development was recommended, especially regarding improvements on the quantification of uncertainty for incidence estimates. It was also agreed that UNAIDS would further advocate for data collection on key populations from countries, for estimates to be continued effectively using case-report data. Additionally, Keith was encouraged to consult and collaborate

with external partners e.g. Hopkins key population transmission group, and to seek other data sources (e.g. Integrated HIV Bio-behavioral Surveillance /IBBS program data, IHME, etc.), to improve estimate accuracy.

Incidence Assay

Jeff Eaton presented a proposal for the reformulation of likelihood for assay-based incidence measurements to account for sampling frame and survey design, to incorporate incidence estimates from complex household-based surveys, including forthcoming PHIA surveys. Jeff highlighted the current complications in incorporating incidence data such as the lack of consensus on ways to estimate the design effect for incidence estimates. Following consultation with other Reference Group members and survey statisticians, he recommended methods for incorporating surveys which handle incidence as EPP currently handles prevalence, using a normal distribution to approximate likelihood for transformed incidence and account for uncertainty.

Preliminary results demonstrate better matched estimates with survey incidence data and improved capture of uncertainty ranges. Further guidance for country teams to calculate incidence, prevalence, standard error and correlation (between incidence and prevalence) in multiple statistical programs (R, STATA, SAS) are currently underway by Jeff Eaton, Le Bao, and Tim Brown. It was recommended that this feature should be implemented into next year's version of EPP, following further data analyses from forthcoming PHIA's, to be able to provide incidence data at a national level.

Questions were raised about the potential future utilization of incidence assays among pregnant women and considerations about incorporating such estimates in epidemic trend estimates. The group discussed that biases associated with using pregnant women as a sentinel population for prevalence are likely to be exacerbated for incidence estimation. The Reference Group strongly recommended new research consisting of detailed modelling, analysis, and validation of assay-based incidence measurement among pregnant women in preparation for future applications, and collaboration with the WHO HIV Incidence Assay Working Group.

Since this Reference Group meeting, the linkage between Jeff Eaton and the WHO HIV Incidence Assay Working group has been made, and he will present his work at the upcoming WHO meeting at pre-CROI (February 2017).

Session VI. Incorporating New Data Sources and Updates from our Partners

Incorporation of ANC-RT data into EPP

Countries have been transitioning from HIV surveillance using unlinked anonymous testing in selected sentinel antenatal clinics (ANC-SS) to routine testing of pregnant women for screening for PMTCT programs (ANC-RT). Le Bao and Ben Sheng have been investigating how to accommodate this transition in EPP, which has been implemented into EPP at both a site-level and census level (i.e. aggregate data from all or most ANC-RT ANC's in the country) into the current model version. Ben Sheng described the model and showed simulated results as well as preliminary results using routine data from Malawi, followed by Jeff Eaton, who presented preliminary results using routine data from Kenya. In general, it appeared that at the site level, ANC-RT data provided a continuation of HIV prevalence trends observed with earlier ANC-SS data, in many cases narrowing the uncertainty ranges, though further investigation with country data was encouraged to confirm this finding. However, data from Kenya illustrated that crude ANC-RT prevalence trends can sometimes represent changes in programme coverage or reporting, and emphasised that careful review and examination of ANC-RT data is required before incorporating into EPP estimation.

Discussions arose as to whether the site- or census-level data from all or most ANC-RT ANCs in the country should be used by countries, with the final agreement being that during this early transitionary phase, analyses for both levels should be encouraged. Specific recommendations were generated with regards to data manipulation and handling, to be informed from forthcoming analysis that would provide information

on “thresholds” of data quality (e.g. ANC-SS/PMTCT coverage). Such work would be included in guidance to countries on handling and interpreting ANC-RT data alongside ANC-SS (at country workshops). Additional support on the expected changes in estimates from the transition from ANC-SS to ANC-RT estimates should be provided to countries at the upcoming 2017 estimates workshops, organised by UNAIDS.

Update from Partners: PHIA

Jessica Justman provided an update from the Population-based HIV Impact Assessment (PHIA) Project, consisting of household-based HIV-focused national surveys in the general population of 13 PEPFAR-selected African (and Caribbean) countries led by ICAP at Columbia University and the US CDC. The aim is to both describe the epidemic and build capacity for study design and support data collection and analyses in those countries. Data collection from multiple countries are already underway, and preliminary data analyses from the countries in 2015 (Zimbabwe, Malawi and Zambia) has been published on 1st December 2016. Further details and progress will be made available on their website (http://phia.icap.columbia.edu). The Reference Group eagerly anticipates the data; further collaboration and discussions with PHIA team are planned to discuss comparability of PHIA data with other data sources, and methods to incorporate PHIA data into UNAIDS estimates 2017.

Update from Partners: ALPHA Network and MESH Consortium

Georges Reniers presented a description of ALPHA Network activities and MESH, on behalf of Basia Zaba and James Hargreaves, respectively. Latest ALPHA Network results indicated a rapid population-wide decline in mortality since the introduction of ART, though mortality rates among PLHIV remained at least twice as high as that of HIV negatives, with strong gender disparities.

Since the last reference group meeting, the MESH Consortium have continued to support activities to optimise the use of routine HIV data, including contributing towards the development of CBS situational analysis tool for WHO and Global Fund, providing technical support and consultations for policy makers, assessing the utility of recency tests, and performing various study analyses. Multiple activities are ongoing, including supporting WHO/UNAIDS in guideline development / implementation for measuring the HIV care and prevention cascades, estimating HIV attributable mortality and mortality among people commencing ART, characterising metrics of stigma, etc. Continued collaboration between the Reference Group and all research partners are ongoing.

Data Repository

Mary Mahy explained that a proposal for the establishment of a data repository and associated management structures, to securely store and handle large amounts of structured data for model analyses, is currently underway. Some expressed their concerns with data handling and further usage by third parties, to which the Reference Group clarified that the use of repository would not imply that data would be shared nor that any control of those data is lost, and is unrelated to issues of sharing of those data to third parties beyond UNAIDS and its partners. It was clarified that the purpose is to provide a data handling tool to assist countries with using increasing complex data and sophisticated modelling software in the future. A more detailed updated will be provided at the next Reference Group meeting.

Key Recommendations

Recommendation/Action Item	Tasked Person(s)	Proposed timeline
1. Continuous Update and Improvement		
Spectrum ART eligibility: Further encouragement for countries to report CD4 count upon ART initiation, as part of data preparation for country team workshops in 2017. Country users to enter data into Spectrum, which will automatically smooth the curve for AIDS deaths.	UNAIDS	Jan 2017
PMTCT coverage: Built-in checks to be incorporated in model for user-led validation of PMTCT coverage, including comparisons between survey based ANC1 attendance, PMTCT coverage and HIV prevalence among pregnant women.	Avenir Health	Dec 2016
PMTCT coverage: Adjustments in HIV prevalence are required to reduce Spectrum overestimation in PMTCT coverage; addressed by adjusting age-specific incidence rate ratios (IRR's - see age-structures)	Avenir Health	Dec 2016
Estimation and Projection Package (EPP) GLMM in EPP: The Reference Group actively encourages the GATHER statement and open-source software, yet the use of a GPL for the entire Spectrum and EPP software is not currently recommended owing to considerable technical, legal and ownership issues.	UNAIDS, Tim Brown	Mid 2017
User-interface working group: a working group on user-interface to be convened to consider design issues in EPP and Spectrum, and ensure consistent and clear terminology.	UNAIDS, Tim Brown, Avenir Health, Le Bao, Secretariat, John Stover	Establish Jan 2017
Key population incidence: The Reference group encourages the generation of incidence estimates for key populations on a global level and recommends further improvements in method calculations, particularly with calculating uncertainty bounds. Further consultation with external partners (e.g. Hopkins key population group) and use of additional data (IBBS, program data, IHME) to be undertaken to improve estimates	Keith Sabin	Mid 2017
Uncertainty on numbers on ART: Further discussions between the UNAIDS and partners to be held to consider issues with evaluating data quality, measuring uncertainty on numbers on ART and other program statistics in Spectrum, and communicating uncertainty with countries. In particular, to explore how adding a range to ART programme data in Spectrum might impact our uncertainty around incidence at the country level. This agenda item to be addressed at a January teleconference	Secretariat, UNAIDS, Avenir Health, Tim Brown, Le Bao	Jan 2017

2. Age-structured models		
Age-structure incorporation in EPP Demographic Projections: UNAIDS Reference group understands the need for subnational demographic projections which are reliant on USG funding for Census Bureau	Census Bureau	Jan 2017
Guidance on age-structure: Guidance and consultations with countries are required to ensure that the changes in country estimates that will result are (i) understood, (ii) reasonable and (iii) appropriate. The Reference Group recommends that checks are defined a priori and that a working group be formed to define a battery of tests	Secretariat, Josh Salomon, UNAIDS	Dec 2016
Age-specific Incidence Rate Ratio (IRR) Adjustments IRR adjustments: Improvements to age-specific IRR's through an additional fitting step in Spectrum has been implemented by Avenir Health (Robert Glaubius) to better match to prevalence data. Avenir Health to complete method evaluation with all country files and recommend application of either static or dynamic time-variant IRR's, on a country-by-country basis. Additional post-hoc minor corrections for IRR adjustments also remain to be completed (expected to be minimal).	Avenir Health	Jan 2017
IRR adjustments: Avenir Health to disseminate results from their trial usage of IRR adjustments on data to the working group for a recommendation of implementation to be given in January 2017	Avenir Health, Reference Group	Jan 2017
IRR methodical comparisons: Further investigation and comparisons between Robert Glaubius's method and other methodical approaches for age-specific IRR adjustments to be performed to optimize method development	Avenir Health, Jeff Eaton	Jan 2017
Phase II: Incorporate age-structured data into epidemic estimation: Implementation of age/sex-specific IRR's in progress. Incorporation of age/sex-specific adult mortality, pattern of HIV incidence due to implemented in Spectrum 2018 (work on HIV care cascade estimation still in progress)	Avenir Health, Tim Brown, Jeff Eaton	Dec 2017
3. Use of case-report and mortality data		
Overall Recommendations PHIA Surveys: Strong interest to incorporate results from current PHIA surveys from first tranche of countries. Further discussions on the comparability of HIV data between PHIA and other surveys (DHS, etc.) due to testing/procedural factors to be held (January teleconferences to be held).	John Stover, Mary Mahy, Jeff Eaton, PHIA team	Jan 2017 and onwards
GBD & UNAIDS HIV Estimates: Comparison of results and methods are currently underway and will be presented at the next agenda meeting. Secretariat to convene virtual meeting of interested parties in the reference group during 2017	Kim Marsh, Haidong Wang, Reference Group Secretariat	2017

Incidence Fit to Program Data Tool (FTP) FTP Tool: The option of simplified (non-peak) parameterisation of incidence function in AIM Program Data Reporting Tool should be to be added	Avenir Health	Jan 2017
FTP Tool: A database with final parameter values from previous years from each country should be created to inform new estimates to speed the fitting process. Parameter values should be set as default, with the added capability to incorporate forthcoming data to improve parameterisation	Avenir Health	Jan 2017
High-income Country Estimates ECDC Tool: UNAIDS to organise further workshops with European countries and ECDC to encourage country involvement and data sharing, to improve their high-income country estimates	UNAIDS, ECDC	April 2017
ECDC Tool: Further liaison between ECDC, UNAIDS and Avenir Health to plan integration of incidence estimates from ECDC tool as an alternative input to the Spectrum files for high-income countries	UNAIDS, ECDC, Avenir	Dec 2017
Use of Mortality Data Mortality comparison: Bruno Masquelier to repeat comparisons between UNAIDS estimates (using revised Spectrum software with IRR adjustments) and estimates from surveys and censuses compiled into a database. Results to be fed data back to Reference Group for final recommendation (at the next Reference Group meeting)	Bruno Masquelier	May 2017
Mortality Database and Model validation: 45q15 should be incorporated as a validation screen in Spectrum to appear automatically. Bruno Masquelier will send his estimates to Avenir Health (John Stover)	Bruno Masquelier, Avenir Health	Dec 2017
4. Use of programme service data		
ANC-RT (PMTCT) data in EPP: functionality exists in the current release of EPP, is expected to be widely used. Both anonymous testing at ANC sentinel sites (ANC-UAT) and routine testing (ANC-RT) can be included (with/without overlapping sites), without significant statistical issues	Le Bao, Tim Brown, Jeff Eaton	Jan 2017
ANC-RT (PMTCT) data in EPP: Avenir Health to explore the development of a tool that would expedite the extraction of data from DHIS into Spectrum. The tool should be ready for demonstration by the next country workshop (to be implemented 2018 estimates)	Avenir Health, UNAIDS	Demonstration by Feb 2017
Guidance on ANC-RT data: Specific recommendations were made about data manipulation and handling and gaining further insight from analysis will be forthcoming, that can inform “thresholds” of data quality. Such work will then be included in guidance to countries on handling and interpreting ANC-RT data alongside ANC-UAT (at country workshops)	UNAIDS, WHO, CDC, Secretariat, Le Bao, Tim Brown	Feb 2017 by ToT

5. Spatially-specific estimates		
Geospatial Model Geospatial model validation: Validations of modelling catchment areas and covariate parameters to be performed, using currently available program/cohort study data, e.g. IeDEA, Manicaland, ALPHA network, PHIA	Sam Bhatt, Pete Gething	2017
Geospatial model roll-out: By next reference group meeting, geospatial modelling team should demonstrate district level estimates, examples of uncertainty and use cases, and agreed timelines for action for working on 7-10 countries planned for roll-out (country representatives should be included at the meeting)	Pete Gething, Sam Bhatt	May 2017
Within-country Hierarchical Model Hierarchical model in EPP: Auxiliary data approximation to hierarchical model has been implemented in EPP and can be recommended for use (with 'default' samples sizes and pseudo-sites). Guidance to be developed by UNAIDS/WHO	UNAIDS, WHO	Jan 2017
Hierarchical model in EPP: Further modifications are required to be able to incorporate both ANC surveillance and routine (PMTCT/ANC-RT) into the hierarchical model in EPP	Le Bao, Tim Brown	Dec 2016
6. Catalyse focused research and data collection		
Modelling mortality and disengagement from care (IeDEA) Reengagement on ART: A clear and persistent question is how to best use routine data for estimating patterns of engagement with the ART program (disengagement, re-engagement) "care cascade". Estimates should be developed using IeDEA (and other) data that estimate directly the parameters needed by the models. Funding opportunities for that should be pursued	UNAIDS, IeDEA, MESH	2017-2018
Data Repository Develop proposal for data repository and review with country teams, UNAIDS and stakeholders	UNAIDS, Secretariat	Q1 2017

Appendix I: List of Participants

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* Remote participation

Appendix II: Meeting Agenda

Day 1: Monday, November 7th 2016

Time	Duration (mins)	Topic	Presenter(s)
Session I: Software Updates - chaired by Peter Ghys			
09:00	15	Welcome and Meeting Overview	Peter Ghys, Tim Hallett
09:15	75	Review of Spectrum Updates	John Stover, Anna Radin, Robert Glaubius
10:30	15	Coffee break	
10:45	75	Review of EPP Updates	Tim Brown
12:00	60	Lunch break	
Session II: Mortality and Age-structure Developments - chaired by Mary Mahy			
13:00	45	IeDEA Estimation of Mortality and Disengagement from Care	Constantin Yiannoutsos, Giorgos Bakoyannis
13:45	45	Mortality Comparisons	Bruno Masquelier
14:30	45	Age-structured Model Development	Jeff Eaton
15:15	15	Coffee break	
Session III: Comparison between UNAIDS Estimates and other Modelling Groups - chaired by Jeff Eaton			
15:30	20	Measures of Uncertainty for ART in Spectrum	Kim Marsh
15:50	70	Modelling High-Income Countries	Ard van Sighem, Kim Marsh, John Stover
17:00		End of Day 1	

Day 2: Tuesday, November 8th 2016

Time	Duration (mins)	Topic	Presenter(s)
Session IV: Spatially-specific Estimates of HIV - chaired by Simon Gregson			
09:00	60	Geospatial Model Update	Pete Gething, Samir Bhatt
10:00	45	Modelling using a Hierarchical Approach	Le Bao
10:45	15	Coffee break	
Session V: Modelling HIV Incidence - chaired by Mary Mahy			
11:00	45	Estimating Incidence Amongst Key Populations	Keith Sabin
11:45	45	Incidence Assay Update	Jeff Eaton, Le Bao, Tim Brown
12:30	60	Lunch break	
Session VI: Incorporating New Data Sources and Updates from our Partners - chaired by Tim Hallett			
13:30	45	Incorporating Routine Testing Data from Antenatal Clinics into EPP	Ben Sheng, Jeff Eaton
14:15	20	PHIA Project Update	Jessica Justman
14:35	25	ALPHA Network and MeSH Consortium Updates	Georges Reniers
15:00	15	Coffee break	
15:15	45	Demographic Projections Update	Peter Johnson, Tim Fowler
16:00	30	Data Repository Update	Mary Mahy
16:30	30	Final Discussions and Recommendations	Tim Hallett
17:00		Meeting Close	