Method Development for the UNAIDS Estimates:
June 2015

Report and recommendations from a meeting of the

UNAIDS Reference Group on Estimates, Modelling and Projections

Boston, USA, 2-4 June 2015

REPORT & RECOMMENDATIONS

UNAIDS
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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.

Aim of the meeting

This meeting had three key aims:

1. To support the current methods used to generate global estimates of HIV and address key issues that arose during the recent round of country estimates.
2. To review and discuss method development surrounding the four main theme areas:
   - Age-structured models
   - Use of case report and mortality data
   - Use of programme service data
   - Spatially-specific estimates of HIV
3. To review and discuss estimates of HIV and all-cause mortality in southern Africa

Approach

The meeting featured presentations combined with group discussion to generate consensus recommendations. The list of participants is included in Appendix I and the meeting agenda is included in Appendix II.

The recommendations drafted at Reference Group meetings give UNAIDS guidance on how best to produce estimates of HIV/AIDS, provides an opportunity to review current approaches and also helps to identify information needs (earlier reports are published on the Reference Group website www.epidem.org). This transparent process aims to allow the statistics and reports published by UNAIDS and WHO to be informed by impartial, scientific peer review.

Report and Recommendations

The UNAIDS Reference Group on Estimates, Modelling and Projections provides guidance and recommendations to UNAIDS and other partners on estimates and projections of the prevalence, incidence and impact of HIV/AIDS. This includes ongoing updates and improvements to the tools currently used – the Estimation and Projection Package (EPP) and the AIDS Impact Module (AIM) in Spectrum – and new method development which can be categorised into four main theme areas:

- Age-structured models
- Use of programme service data
- Use of case report and mortality data
- Spatially-specific estimates of HIV

An additional meeting was held to discuss estimates of all-cause mortality and AIDS mortality in southern Africa.

I. Spectrum Updates

The software changes in the current round of HIV estimates presented many challenges – both in the provision of fully tested software and in understanding the effect of these changes on estimates, and disentangling these effects from those resulting from the incorporation of new data. Key differences in the 2014 estimates compared to 2013 estimates: trends in incidence decline less steeply, reduction in estimates of HIV+ pregnant women in need of PMTCT, fewer children living with HIV, higher treatment coverage in children and discontinuities in incidence trends. The new adjustments to ANC data to reflect general population trends largely contributed to the slightly flatter incidence trends. In many countries this has then resulted in a decline in the estimated number of HIV+ pregnant women and the corresponding numbers of women in need for PMTCT, which then results in lower estimates of children living with HIV and increased coverage of ART among children.

Child estimates in AIM

The estimates of HIV among children rely upon many other estimates and assumptions – estimates of adult incidence from EPP are fed into AIM and distributed by age and sex (sex ratio of incidence and age and sex-specific incidence rate ratios). These new infections are tracked by CD4 resulting in a pattern of HIV prevalence that is subject to age-specific fertility rates (reduced for HIV+ women not on ART) to determine the number of pregnant women in need of PMTCT. HIV outcomes of children born to HIV+ mothers are largely dependent on timing of infection, treatment and prophylaxis strategies.

In the recent estimation round, a compartmental CD4 model for children was implemented in AIM (similar to the adult CD4 model), which required detailed data for parameterisation with limited data available for validation. The child CD4 progression parameters are fit to match estimated survival curves by timing of infection (Marston, et al) and the CD4 distribution of HIV+ children from the Paediatric Prognostic Markers Collaborative Study (Dunn, et al). The assumptions for child mortality on treatment are informed by data from the IeDEA Consortium for each region. These data are more limited outside East Africa (and variable), thus for southern Africa smoothed patterns of mortality were used which require further consideration. The age-distribution of children on ART is unknown, thus ART in AIM is distributed based on need; however, it was discussed that data on median age of starting ART should be available (~4-5 years). The limited data on HIV prevalence amongst children

makes validation of these estimates difficult. Analyses that follow mother-child pairs are needed in order to better understand child outcomes. In addition, an updated analysis of the probability of MTCT is needed to reflect the increased uptake of ART among women with CD4 counts >350.

Very high estimates of PMTCT coverage in many countries are still a concern but it is difficult to disentangle why this occurs – due to underestimation of prevalence in females, assumptions for the sex ratio and age-pattern of incidence, not capturing fertility appropriately or double-counting in PMTCT. The adjustment of trends in ANC to reflect general population trends is likely contributing and warrants further consideration given that the numbers of pregnant HIV+ women are calculated from the adjusted prevalence trend.

Recommendations:

- ✓ **UNAIDS to commission an updated analysis of probabilities of MTCT.** *Follow-up: UNAIDS*
- ✓ **UNAIDS/Avenir Health to follow-up with Mary-Anne Davies regard median age of ART in children.** *Follow-up: Avenir Health*
- ✓ **Further investigation into fertility in the ART era – regional differences, fertility rebound on ART.** *Simon Gregson, Basia Zaba, UNAIDS*
- ✓ **IeDEA to provide age distribution of children starting ART, UNAIDS to also request these data from countries.** *Follow-up: UNAIDS*
- ✓ **Assemble technical group to review PMTCT data for a selection of countries with coverage >100%.** *Follow-up: Avenir Health, UNAIDS*
- ✓ **Further review of child mortality patterns on ART for southern Africa.** *Follow-up: Avenir Health, IeDEA (southern Africa)*
- ✓ **Review updated Marston analysis of child survival and modified hypothetical curves.** *Follow-up: Avenir Health*

Discontinuities in incidence – "the bumps"

The EPP model in Spectrum is a non-age structured model fitting to HIV prevalence data amongst adults age 15-49 to produce a historical trajectory and short-term projection of HIV prevalence. HIV incidence is estimated from prevalence and this incidence curve is passed to AIM. AIM is a fully age-structured model, includes mother-to-child transmission (MTCT) and a child model. Both EPP and AIM are built on the same CD4 model but do not produce identical results, largely due to age-effects including different rates of CD4 progression and mortality by age. Ageing-out (of EPP at age 50) is also an issue particularly as ART coverage expands. AIM also allows certain populations to be eligible for ART regardless of CD4 count (e.g. pregnant women, co-infection with TB) which is currently not captured in EPP. Given these differences, an adjustment factor in AIM makes small adjustments to incidence each year to match EPP prevalence. An arbitrary cap on this adjustment was implemented to prevent sudden "bumps" or discontinuities in incidence, but in some instances this resulted in an inability to match prevalence. Relaxing the cap on this adjustment resulted in additional "bumps".

Further investigation into these differences uncovered discrepancies between EPP and AIM for progression through the CD4 model and for the timing of changes to treatment eligibility criteria. These corrections appear to solve many of the discontinuities in incidence. However, this will not solve all "bumps" as some are due to scale-up of ART particularly when there is a switch from reporting numbers on treatment to projecting future treatment coverage (%). Other bumps are due to differences amongst the 50+ population ageing out which become more important as an epidemic

ages. Over time, there are more 50+ exits in AIM than EPP exits which drives 15-49 prevalence down relative to EPP and results in incidence "bumps" in AIM to maintain the same level of prevalence. In concentrated epidemics, incidence bumps are often due to underlying epidemic patterns amongst key populations (different timings of prevalence trends).

Recommended next steps:

- ✓ **Reconcile differences between EPP and Spectrum, including testing the change in one-year of advancement of ART eligibility in EPP,** *Follow-up: John Stover, Tim Brown, review Aug 2015*
- ✓ **Define mechanism for Spectrum to pass information on specially-eligible pops,** *Follow-up: John Stover, Tim Brown, review Aug 2015*
- ✓ **For the immediate term, consider AIM passing the number of 50+ HIV+ exits each year to EPP (currently only passing 50+ on ART),** *Follow-up: John Stover, Tim Brown, review Aug 2015*

Joint estimation of CD4 progression and survival

The aim of this work, led by Tara Mangal, is to jointly estimate progression of CD4 decline and survival by age, sex and region to inform revised parameters in Spectrum. A Hidden Markov model was developed which describes the probability of the "true" state depending on the data observed. This approach allows estimation of progression through stages and is efficient when dealing with highly censored data. Key updates include the addition of: extra transitions onto ART from every CD4 stage (due to early ART access); augmented data to improve transitions through age-group boundaries; age and gender effects on the initial state probabilities; and age and CD4 compartments that match those in Spectrum.

Compared to the parameters currently in Spectrum, results from this work illustrate:
- Time in CD4 category shorter than Spectrum parameters
- Estimated net mortality higher than Spectrum parameters
- Survival in Asia is different (shorter) than Spectrum parameters

The transition rates between CD4 compartments were not significantly affected by age and there was only a small effect of gender. Importantly, in Asian cohorts CD4 decline and mortality after HIV infection (in the absence of ART) was significantly faster compared with European and African cohorts. The next step is to investigate set-point viral load which is a strong predictor of progression.

Recommendation:

- ✓ **TM to provide final estimates to JS to test in Spectrum to investigate the effect on estimates,** *Follow-up: Tara Mangal and John Stover, review Nov 2015*

Heckman selection models to adjust for missing data

Heckman selection models adjust for missing data without having to assume these data are missing at random. Applied to estimates of HIV prevalence from nationally representative surveys, the models require a valid selection variable which predicts participation in HIV testing but not HIV status. Mark McGovern provided an update on advances to these methods, empirical validation of the interviewer selection variable (Africa Centre using gift intervention), the incorporation of spatial dependence which provides an efficient method to calculate point estimates at the subnational level, and demonstrated software publicly available for use of these methods. A series of training workshops are underway with the next workshop at Harvard, 8 September 2015.

Future work includes the incorporation of multiple survey years into the same model, modelling non-contact alongside non-consent and broader application (all countries). In addition, a sub-group analysis (age, education, wealth, etc) and a randomised controlled trial among a high-risk group in Tanzania (fall 2015) with participation incentives.

It was discussed that large adjustments will likely only be expected in high HIV prevalence, and low participation situations; however, the confidence intervals will increase across a wider range of scenarios. While more prescriptive cut-off thresholds would be useful for guidance on when to use these methods, countries should not be required to use these models as there will be situations where the assumptions are violated. Ideally, participation rates would increase and adjustments would not be needed. It was also discussed that outputs that facilitate interpretation of the results would be beneficial for users such as illustrative graphs of response rates by interviewer team.

Recommendations:

- ✓ **Demonstrate magnitude of effect incorporating all forms of non-response (non-contact and non-consent),** *Follow-up: Mark McGovern, Nov 2015*
- ✓ **Demonstrate magnitude of effect amongst all data sets,** *Follow-up: Mark McGovern, Nov 2015*
- ✓ **Present methods and results to DHS,** *Follow-up: Mark McGovern, Nov 2015*

Key outcomes from WHO/UNAIDS HIV surveillance meeting in Bangkok

The overall aim for future HIV surveillance is for better quality data, available at the local level (including the facility level) and disaggregated by age, sex and key population. For a more sustainable future, a shift to the use of routinely collected data is needed (case-based surveillance). The priority agenda is for more granular data, metrics for key populations and the use of facility-based data and HIV case-based data to support the health services cascade and monitoring of these services.

II. Age-structured models

Jeff Eaton presented a proposal for incorporating age-structure into EPP. The key motivations for this are to provide age-specific estimates, to remove the need for the prevalence adjustment and for improved consistency between EPP and AIM, and to account for selection biases in ANC data.

Implementation is proposed as follows:

1. **Add demographic structure to EPP**
   - Use existing assumptions and parameters from Spectrum in EPP which will result in internally consistent results and remove the need for the prevalence adjustment
   - Key caveat is the resulting computational time (estimated 5x longer)

2. **Account for selection biases in ANC data**
   - <u>Biases in ANC</u>: Potential biases in ANC data compared to general population – only women, attendance at ANC at sentinel sites, age-distribution of ANC, relationship between HIV and fertility – which may change over time and as epidemics age.
   - <u>Fertility in HIV+:</u> A preliminary analysis conducted by Milly Marston for fertility in HIV+ women by years since seroconversion from ALPHA data found that crude fertility rates decline over time (in part due to age), but after adjusting for age-specific fertility a significant decline in fertility of HIV+ women remained.
   - <u>Implementation</u>: To incorporate age and stage of infection on fertility, HIV fertility rate ratios (FRR) were calculated by CD4 stage and age to match sub-fertility observed in ALPHA data. Those on ART >1 year assumed to have a FRR=0.6 (equal to those with CD4 350-500). *Note that moving to no effect on ART (FRR=1, current Spectrum assumption) can change estimates substantially with high ART coverage.*
   - <u>Results</u>: When incorporated into the age-structured model, the results (adjusting for age-specific fertility rates and stage of infection) do not suggest major differences, with minor reductions in prevalence, incidence and AIDS deaths (slightly later peak).
   - <u>Predictive performance</u>: Out-of-sample prediction (to national surveys) compared with regular EPP (log posterior density of withheld survey calculated) indicates the adjustment model slightly improves the fit.

3. **Estimate age/sex-specific IRRs using age-specific prevalence data**:
   - Preliminary investigation illustrated the AIM default values fit well in many instances compared to survey data, but discrepancies remain, particularly at subnational level. *Proposal for further investigation: Impose smoothness; use existing IRRs from ALPHA as informative priors; use hierarchical model)*

4. **Estimate changes in age-specific incidence over time**
   - Model should have the flexibility to be sensitive to changes in age-specific prevalence over time, but enough structure to constrain historical trends. *Proposal: Analysis in countries where data are available to generate informative priors for other settings and quantify uncertainty for historical period.*

The proposed approach was implemented using the spline model (but applicable for both trend and classic models) using 5-year age groups (to simplify and reduce computational time). The results illustrate that incorporating age-structure into EPP resulted in small differences to 15-49 prevalence and incidence. While there are currently many simplifications, the complexity of Spectrum can be added. The next steps are to add demographic detail (and migration) MTCT and the child model. The differences were perhaps smaller than anticipated, but this method would importantly provide the

platform for the inclusion of increased complexity in the data when available, removes the need for adjustments between EPP/AIM and improves consistency.

Key concerns include the complexity of implementation (testing and de-bugging), computational burden (large barrier at present). For implementation in concentrated epidemic settings, it should be considered whether demographic assumptions for key populations could be improved compared to the current assumptions made by Spectrum. Major model changes should occur in years with regional workshops thus inclusion of these methods for the 2017 regional workshops would require a faster, fully specified and robustly tested model by the end of 2016.

Incidence-rate ratios in AIM

Spectrum takes the incidence curve from EPP (adults age 15-49) and distributes this by sex and age. In generalised epidemics the incidence-rate ratios (IRR) are based on ALPHA Network data. In concentrated epidemics heavily affected by injecting drug use (IDU), the IRRs are based on data from eastern European and Australia cohorts. The default pattern in AIM can be altered (and can change over time) but very few countries make any changes. Avenir Health has built a database of country data for age-specific prevalence extracted from national household surveys to allow countries to easily compare the outputs from AIM to their survey data. A formal comparison for all countries with surveys found that many countries fit well using the default parameters (even under the default assumption of a constant IRR pattern from 1970 to present). In countries where there were discrepancies, these generally fell into two categories:

1. National survey data exhibited very odd patterns of age-specific prevalence (which often occurred in low prevalence areas)
   Recommendation: Not advisable to attempt to match to very odd patterns
2. Outputs of age-specific prevalence from AIM, when using the default pattern of IRRs, simply did not fit the patterns observed in national surveys. Here, post-hoc adjustments to IRRs resulted in a good match to survey data (Zambia, Swaziland).

In summary, the current approach works well in most generalised epidemics. It is relatively easy to adjust the pattern of IRRs when necessary in order to improve the fit to national survey data.

Recommendations for age-structured models:

- ✓ **Adding age-structure into EPP:**
    - – **Continue development, test functionality and performance of proposed specification with agreement on model specification by Jan 2016**
    - – **Plan for inclusion in the models by Jan 2017,** *Follow-up: Jeff Eaton, UNAIDS, East West Centre, Avenir Health*
- ✓ **Adjusting incidence rate ratios in AIM: Provide countries with guidance on how to use the IRR adjustments and how to calibrate when there are multiple national surveys.** *Follow-up: Avenir Health and UNAIDS to incorporate guidance into Spectrum manual and workshop documents.*
- ✓ **Data collection: UNAIDS should routinely request data disaggregated by age and sex (ANC, PMTCT, ART).** *Follow-up: UNAIDS*

III. Use of case report and mortality data to inform HIV estimates

Concentrated epidemic countries are often in the situation of not having enough data for estimating HIV prevalence using methods based on prevalence surveys (DHS, AIS) but do have other information – case report and mortality data – that can be utilised to inform other estimation approaches. There are many ongoing streams of work to generate HIV estimates using these data sources, including the development of new methods and approaches and further refinement of the tools currently available.

Tools available in AIM to fit incidence to programme data

Two new features for fitting incidence are available in AIM. The *fit mortality* tool allows countries to rescale incidence estimated from surveillance and survey data to fit mortality data, while the *fit incidence to programme data* tool fits an incidence curve to case-reports (adjusted for reporting lag), AIDS deaths and estimates of PLHIV (adjusted for undiagnosed). While no countries used the *fit mortality tool,* three countries that have not previously produced a Spectrum file used the *fit incidence to programme data* tool to derive national estimates, and at least six countries switched from EPP fits to use of this tool (Bahamas, Barbados, Brazil, Venezuela, Costa Rica, and Oman).

Advantages of this approach are that countries with strong case-based and vital registration (VR) data want this information incorporated in the fitting and have more confidence in estimates using this approach as opposed to use of prevalence data from surveys which may be of variable quality, occur infrequently, and are not representative at the national level. The key caveats of this approach are that a single incidence curve is produced that is not disaggregated by key population, and without appropriate adjustments (for the % undiagnosed and estimated undercount of AIDS-related deaths) fitting directly to case-report data may result in estimates that are too low.

It was observed that the mortality data in recent years from VR data did not exhibit the strong decline observed in modelled estimates attributed to ART expansion – Brazil, Costa Rica and Oman all have flat mortality trends from the VR data. For Brazil, ART allocation was modified to reflect high ART coverage at low CD4 count (i.e. restricting the expansion to higher CD4 counts) in order to constrain mortality. This approach worked well in matching to mortality data, but did not match programme data on median CD4 at ART initiation which was much higher.

The key next step for improving this tool is to better capture uncertainty which was somewhat arbitrary in the current round applying the bounds from the EPP fits (dispersion) to the results generated from the incidence tool. It was discussed that plotting both the raw case-report data and the adjusted data may help the user understand the effect of the time lag between infection and diagnosis and changes over time. Spectrum could also calculate the lag if users enter median CD4 at diagnosis. It may also be possible to calculate deaths amongst undiagnosed, learning from other methods and the ALPHA Network data.

UNSW pilot for the use of case-reporting data to estimate HIV incidence

David Wilson and his team piloted two approaches during the Middle East and North Africa (MENA) regional workshop with the aim to estimate HIV incidence based on case-reporting surveillance. Two back-calculation methods were attempted:

1. **Aggregate-level model:** Use of HIV diagnoses (+AIDS diagnoses when available) and markers for recent infection to develop a time-dependent distribution of time from infection to diagnosis. Aggregate country data are entered into a spread sheet for each year and

incidence estimates are calculated by back-projection using the number of diagnoses for each year based on the user-specified distributions.

2. **Individual-level, CD4-based model:** The method uses date of HIV diagnosis and CD4 count around diagnosis to simulate individual CD4 decline. Date of infection is estimated by matching actual CD4 count to a simulated distribution and back-projecting to a likely CD4 count at infection. Incidence estimates are calculated by back-projection from time of diagnosis to likely time of infection. This method requires detailed individual-level data for date of diagnosis, CD4 around diagnosis (and optionally: age, sex, mode of exposure, dates of previous negative HIV tests).

These methods were piloted in the MENA region workshop; however, countries did not have data on testing patterns and limited data were available at the individual level. In Tunisia, the available CD4 data from case-reporting illustrated very low CD4 counts which suggests testing rates have not changed over time and the proportion diagnosed is low. This will result in mortality being a competing risk with people dying without diagnosis (which is not captured in these methods). In Morocco, there was some evidence of a shift in mean CD4 in recent years, suggesting a change in testing patterns over time. Overall, without an understanding of changes in testing rates over time, the availability of case-report data alone was not sufficient for estimating incidence thus these back projection methods are likely inadequate for the majority of LMICs. However, case-report data can be an added component to other estimation methods.

It was discussed that de-duplication of case-report data is an important but difficult task that needs to be approached on a country-by-country basis and requires local expertise and knowledge of the surveillance system.

Update on the use of case-report data to estimate HIV incidence in the ECDC region

The European Centre for Disease for Disease Prevention and Control (ECDC) supports two methods that use case-report data to estimate HIV incidence. These include:

1. **Incidence method:** Reconstructs the incidence curve for the entire epidemic. HIV cases are calculated from observed AIDS cases until the introduction of ART (1996). HIV diagnosis is used as an alternative marker with adjustments made for how recent a newly diagnosed infection is (CD4 count or simultaneous HIV/AIDS diagnosis).
   - Data required (over time):
     - Annual total number of AIDS cases (up to 1996)
     - Annual number of HIV diagnoses
     - Annual number of HIV/AIDS cases
     - CD4 count at time of diagnosis (if available)
     - Demographic data: Mode of transmission, sex, country of birth
     - Estimates of the undiagnosed population
   - Limitations: Under/delayed/incomplete reporting, double counting, mortality before diagnosis and large proportions of migrant populations can substantially affect estimates

2. **London method** (A Phillips): Utilises the relationship between CD4 counts and AIDS to capture those who present for testing due to AIDS symptoms.
   - Data required (for at least one year – high quality)
     - Annual number of HIV/AIDS cases
     - CD4 count at diagnosis
     - Mode of infection
     - HIV-related symptoms (if available)

[11]

- Estimates of the undiagnosed population in need of immediate treatment
- Key benefit: Estimates can be generated with only one year of surveillance data.
- Key limitation: People may be testing earlier thus the relationship between pre-AIDS diagnosis and time to AIDS is less straightforward.

The **incidence method** was piloted in the Netherlands, Denmark, Bulgaria (IDU), Estonia (no CD4 counts, did not work) and Germany (only ½ of all cases reported to ECDC). Limitations of the incidence method include death before diagnosis which will underestimate HIV incidence (assumed to be small), death after diagnosis (not always available in surveillance data) and migration out of the country after diagnosis which will have a similar effect on estimates as death. This method assumes that CD4 data are missing at random. If this is not true and a high proportion of those missing have low CD4, it becomes a key issue. For countries with incomplete historical data, this method still predicted recent incidence well but performed poorly for historical estimation.

ECDC has developed a tool which houses both of these approaches. Countries enter their data into a wizard that decides which method is appropriate for use. Incidence is estimated from pre-populated data (reported to ECDC) and the user is able to modify the results. Countries can also input their own datasets. Upcoming workshops are scheduled on the use of these tools. A longer term aim aim is to integrate the country datasets with WHO-Europe.

Incorporation of multiple data sources to estimate HIV incidence

Tara Mangal is leading this stream of work which expands on previous methods that use case-report data but with the key aim to incorporate multiple data sources to inform estimation. This will expand on earlier work conducted by Juan Vesga which fit to HIV cases, AIDS cases and AIDS deaths in Colombia. Further expansion will include the addition of ART (with rate of uptake and effect of mortality changing over time), inclusion of age-structure, risk groups, and will consider mis-reporting of mortality data and death before diagnosis.

The model will be applied to data from Brazil where ethical approval has been granted to access data for: notification of AIDS cases; reported AIDS deaths; number receiving ART; CD4 count at notification. Key challenges anticipated include the misreporting of AIDS deaths (and changes over time), trends in mortality that are not consistent with ART scale-up, missing data (missing at random/non-random), and private diagnoses which are not recorded and only picked up when on ART. A post-hoc validation to prevalence data will occur if access to prevalence data is obtained.

Use of case-based surveillance in China

Le Bao and John Stover worked with China to help provinces produce their own estimates in Spectrum, but with modifications to the advanced parameters in Spectrum in order to reflect country data. China has a patient database of over 500,000 PLHIV. Standard protocol for enrolled patients is to receive CD4 tests twice a year. A simple analysis of this database was conducted to derive new parameters for CD4 progression and mortality on/off ART. Compared to ALPHA Network patterns, the survival parameters from the Chinese data were similar at younger ages (15-24 years) but much longer at older ages. Overall, the results using the modified parameters compared to the default Spectrum parameters were similar for the HIV+ population and AIDS deaths but the CD4 distributions of those not on treatment were very different. China is very interested in receiving feedback and assistance, particularly for refining the progression and mortality patterns.

Tara Mangal highlighted that censoring is a key issue for estimating CD4 progression and mortality which can artificially extend survival (by 5 years in European/African cohort) and thus she had to

explicitly model transition to ART to overcome this bias. Tara's model is computationally intense (currently takes 3 weeks to run) but she can provide training on the methods. Christophe Fraser also has a less computationally intense method that may be useful as a more immediate solution. It was discussed that identifying median CD4 count at diagnosis would be the necessary initial step.

Case surveillance data in generalised epidemic settings

HIV case-reporting may be able to more appropriately and accurately capture and provide key information. In LMIC, case-based surveillance in increasingly a future possibility which would provide additional data and information that is routinely collected but not currently routinely used, to better inform strategic decision making and estimation processes. This includes data from testing and treatment facilities collected with electronic record systems.

Case surveillance tracks the full continuum of HIV disease and thus may be an efficient and more granular way to routinely provide key data and strategic information. It is expected that with international support, countries with generalised epidemics will invest in this surveillance.

It was discussed that in generalised epidemic countries the lack of a unique identifier makes case-based surveillance an enormous challenge due to different reporting systems, the inability to de-duplicate case-reports across systems and many facilities still using paper-based reporting. While case surveillance in generalised epidemic settings is more of an ideal scenario at the moment, there is a longer-term vision for this to occur with pilot projects set to roll out in the near future.

Recommendations for use of case report and mortality data to generate estimates:

- ✓ **Incidence fitting tool in AIM: Investigate incorporating mean CD4 at diagnosis and having Spectrum convert lag between infection and diagnosis; investigate methods to better capture uncertainty.** *Follow-up: Avenir Health, review Nov 2015*
- ✓ **Model development: Imperial and UNSW to develop working collaborations, in consultation with Ard van Sighem with aim for testing in workshop Latin America workshop (Q4 2015),** *Follow-up: UNAIDS, Ref Group, TM, DW, AvS, review end 2015*
- ✓ **ECDC: Review process and outcomes of ECDC estimation workshop, how the issues mentioned above are addressed and future plans for estimation in coordination with UNAIDS estimates.** *Follow-up: Chantal Quinten, July 2015*
- ✓ **Case-based surveillance in generalised epidemics: Continue to follow CDC-led pilot projects (Ethiopia, Kenya, Senegal) for routine collection of case-based surveillance in generalised epidemic settings.** *Follow-up: Jacob Dee to keep Group informed*
- ✓ **China case-based surveillance: A better understanding of the data collected (including median CD4 at diagnosis) in the first instance.** *Follow-up: John Stover to link Tara Mangal to China CDC.*
- ✓ **Case-report data: Request case-report data by age and sex where available (Argentina, others?)** *Follow-up: Txema Calleja, UNAIDS*
- ✓ **Case-report data: Important to have better understanding of who is starting treatment (median CD4 at initiation).** *Follow-up: Imperial collaboration with Brazil*

IV. Use of PMTCT programme service data

In generalised epidemics, countries are transitioning from surveillance in ANC to surveillance in PMTCT. The World Health Organization, US Centers for Disease Control and Protection (CDC) and partners are working to develop guidance for this switch. It is important to understand differences in data obtained from these two sources which will have implications for estimates of HIV and related indicators. The sensitivity of diagnostic testing in PMTCT programmes compared to ANC surveillance is variable and often low and it is not immediately clear if this is due to diagnostic false negatives or surveillance false positives. While specificity is improved, results are still variable which is important given the large number of women tested in PMTCT programmes. Most PEPFAR countries are implementing PMTCT assessments which illustrate suboptimal sensitivity and specificity of PMTCT testing compared to surveillance testing. The cause of the discrepant results is unclear and may be due to problems with routine diagnostic testing, with EIA oversensitivity, or data recording errors.

In sub-Saharan Africa, only Rwanda has transitioned to use of programme data, but many countries will soon follow. The WHO Guidelines are in the final development stage and describe two design approaches for surveillance:

1. **Census** (preferred approach): All women attending ANC sites
   - Census based on individual-level data (preferred): Requires electronic medical records, most countries are not currently in position to implement
   - Census based on aggregate data (from health management information system, HMIS): Requires routine reporting system, generally unable to provide disaggregated data (age, etc)

2. **Sentinel surveillance:** Convenience sample, i.e. the historical approach
   - Real time: ANC staff collect routine programme data in real time as pregnant women visit ANC during the surveillance period → resource intensive but provides support to ensure quality of routine data and testing
   - Retrospective: Data collection occurs after the surveillance period →less resource intensive, but does not allow support to site to ensure quality of data and testing

It was discussed that a third approach, the probabilistic design that aimed to be representative at the sub-national level, has been dropped in favour of these simpler approaches. It is expected that some countries will continue with the sentinel design, while others may transition to census based on aggregate data (HMIS). The latter will likely mean that detailed data (disaggregated by age and available at lower levels) will not be feasible.

The issue of known positives was queried and it was discussed that patients receive the routine standard of care for the clinic thus known positives may not receive an HIV test if this is not the routine standard of care, but this should not affect the data that are captured (known positive women not should be recorded). It was discussed that with the move towards age-structured models and a more granular level of detail in the future it will be somewhat essential to have programme data disaggregated by age.

Incorporating PMTCT data into EPP fitting

As countries transition from ANC surveillance to PMTCT surveillance, EPP will need to be able to accommodate this new data source. Le Bao is leading this work which aims to:

- Understand the required level of data quality and the impact of wrong assumptions
- Validate the model assumptions

Incorporating PMTCT data results in an unbalanced longitudinal design, whereby ANC data are used for the historical period and PMTCT data are used for the current period. Some continuity across these data sources is needed to accurately estimate the trend which could be ANC/PMTCT data available at the same sites and surveys available before and after the transition. If there is no continuity, it is difficult to distinguish the trend at the transition and whether it is due to real differences or due to the calibration parameters (calibration on ANC prevalence and calibration on PMTCT prevalence, with respect to survey prevalence).

There are several ways to improve continuity:

- Sample more PMTCT sites from historical ANC sites and adjust the PMTCT census by down-weighting the over-sampled sites
- Obtain a longer time series of PMTCT data
- Use an informative prior distribution for the ANC and PMTCT calibration constants
- Obtain PMTCT data from earlier years (pre-transition) and input these alongside the existing ANC surveillance data (not feasible for most countries)

Assuming the ANC and PMTCT calibration parameters were the same did not work in the preliminary implementation, thus it was assumed they were independent. New Suggestion: *Assume ANC and PMTCT are dependent, derive an informative joint prior distribution.* Assume the random effect is constant over time and that PMTCT and ANC share the same random effect (correlated, when from the same site) which helps to achieve some continuity, then investigate how to integrate this into the likelihood using data from Mozambique, Kenya, South Africa and Zimbabwe where PMTCT and ANC data are available at the same sites and overlap for a few years.

The additional challenge is that the large sample size of PMTCT data (with small variance) will dominate the trend. An additional variance component may be needed to ensure the trend from survey data is not ignored if inconsistent with the trend from PMTCT. It may be realistic to assume that lower quality data (i.e. PMTCT) would have additional variance compared to high quality data. A new error term (non-sampling error) could be added. But should the variance be estimated, or fixed? Will it vary across sites or years? Should a similar term be added for ANC? Le will use synthetic data to better understand to contribution of PMTCT data in the estimation and the consequence of making wrong assumptions which will provide insight into the properties of the data required to generate robust estimates.

It was discussed that surveillance from PMTCT will have more sites – some will overlap with ANC some will not. It will be important to explore the overlap, effect of different number of surveillance locations, number of years of PMTCT data and the sample size within each location. The issue of know positives not being tested in PMTCT will be incorporated in the different error term for PMTCT. The transition years are a key concern with incomplete PMTCT coverage and expanding PMTCT which may cause issues.

Incorporating PMTCT data into an age-structured EPP

In the near-term future, a key aim is to add age-structure into EPP which will require age-structured surveillance data feeding into EPP. These data are currently not routinely reported in most settings in SSA. Drawing on work conducted in Tanzania by Annabelle Gourlay, Basia Zaba described how age-specific data from clinics with electronic medical registrars (EMR) could be applied to aggregate data from PMTCT to adjust the aggregate data for missed tests (by age) and the pattern of prevalence by age. The main limitation of this approach is that when availability of electronic

registrars is very low, it may only be at "centres of excellence" or urban areas, which may not be representative of the general population. As EMR use increases this may be a useful approach.

Recommendations for PMTCT Guidelines:

- ✓ **The UNAIDS Reference Group recommends additional information on age be a priority in the PMTCT guidelines (and essential to include full age-structure if the records are electronic), ideally 5-year age groups. If this is not possible, it will be important to have under 20 years separate from >20 years.** *Follow-up: Jacob Dee to keep Reference Group informed of outcomes*
- ✓ **In addition to PMTCT prevalence by age, it is essential to collect ART status at first ANC visit.** *Follow-up: Jacob Dee*

Recommendations for incorporating PMTCT data into EPP fitting:

- ✓ **A better understanding of the level of continuity required is needed. Continue to work with synthetic data to understand the necessary overlap (also data quality requirements), and provide quantitative assessment of effect.** *Follow-up: Le Bao, review Nov 2015*

V. Spatially-specific estimates

There is an increasing aim to produce detailed estimates at more local levels in order to obtain programme-relevant information to support more strategic planning, decision making and resource allocation. However, data may be sparse in some areas, or for key populations, at these lower levels. Le Bao has developed a hierarchical model which borrows information from data-rich areas to inform data-poor areas with similar epidemiological patterns. Samir Bhatt and Pete Gething are developing methods that are able to incorporate different data sources, including programme data at the site-level, to produce estimates of HIV incidence, prevalence and ART coverage which can be aggregated to any administrative level of interest and provide an appropriate representation of uncertainty.

Hierarchical approach for generating sub-national estimates

Le Bao has further developed his hierarchical model and methods for its use in concentrated epidemics. For generalised epidemics, it was last suggested (Oct 2014 meeting) to explore the inclusion of data from all ANC sites (to help inform trends at sub-national level) but to down-weight these data in order to give importance to the local ANC data. This simplified approach will work for data-sparse areas and can be applied using any EPP model (spline, trend, classic) Computing time will increase due to the inclusion of all sites and the weighting factor needs to be determined.

A similar approach can be considered for concentrated epidemics, relating trends in HIV prevalence across subnational areas and sub-populations. The hierarchical model applied in concentrated epidemics fits a time trend for each high risk groups across all areas using all data with the predictive distribution used as a prior distribution on the EPP output. Alternatively, the predictive distribution can be used as imputed observations from a new clinic. Here, a new site is added with imputed data from 1998-2011, using a total sample size across all years comparable to the "real" sites but smaller. This appears to result in improved fitting by removing very early, unrealistic curve fits. The next steps include model validation, exploring alternative parameters and fine tuning the parameters.

It was discussed that while the theory is rational, for concentrated epidemics, the data that go into the model may be questionable which can give rise to rather questionable trends; however, the variation will give rise to different levels of uncertainty and thus the variance should indicate whether to trust the data.

Geospatial analyses at the sub-national level

Samir Bhatt and Pete Gething from University of Oxford have developed a Bayesian geospatial model which aims to be able to incorporate a range of data sources (currently survey and programme data) and predictor data (covariates) and combines this information with a sophisticated regression model to generate spatially-specific estimates of HIV that can be aggregated to any geographic level of interest and also provide a rigorous estimate of uncertainty. Model validation illustrates very good out-of-sample predictive performance, which further improves when a joint model (inclusion of neighbouring countries) is built which removes the boundary effects. The next steps are to incorporate PMTCT data (site level), replicate for ART to get maps of coverage, constrain ART and prevalence to match to incidence, and then to include migration effects.

It was discussed that it would be helpful to understand the important covariates (key predictors). It was also discussed that right now, this is just a spatial model, mapping the anomaly (why some places are high and why some places are low) and not mapping the raw prevalence data. Catchment

areas for the PMTCT data will need to be defined so that HIV prevalence corresponds with a particular area.

Recommendations for hierarchical model:

- ✓ **Test on multiple countries with long time series and in countries where there are divergent trends in different areas.** *Follow-up: Le Bao, Nov 2015*
- ✓ **Test concentrated epidemic approach using Vietnam.** *Follow-up: Le Bao, Nov 2015*
- ✓ **Investigate and provide guidance on weighting factor.** *Follow-up: Le Bao, Nov 2015*

Recommendations for geo-spatial analyses:

- ✓ **Share maps with Mozambique for feedback,** *Follow-up: Samir Bhatt, UNAIDS, June 2015*
- ✓ **Explanation of key covariates,** *Follow-up: Samir Bhatt, review Nov 2015*
- ✓ **Estimation of incidence,** *Follow-up: Samir Bhatt, review early 2016*
- ✓ **Adapt modelling of PMTCT and incorporate ART data, pilot for South Africa,** *Follow-up: Samir Bhatt, (South Africa geospatial meeting), continue to collate data (2015) and review 2016*
- ✓ **Improved understanding of patterns of catchment (patient mobility for services) in PMTCT data from empirical data,** *Follow-up: Simon Gregson, Basia Zaba*
- ✓ **Incorporate migration data (longer term),** *Follow-up: Samir Bhatt, 2016*

VI. Adult Mortality

A half day meeting was held to review and discuss all-cause and HIV mortality estimates in southern and eastern Africa and considerations for incorporating all-cause mortality data into HIV epidemic inference. In Spectrum, the current approach for generalised epidemics is to estimate historical epidemic trends based on ANC and survey prevalence. The estimates of adult mortality in these settings are not directly informed by mortality data and are dependent on the estimates of HIV prevalence and incidence, assumptions for CD4 progression, survival and ART uptake.

Generating non-AIDS life tables in high HIV-burden countries

The World Population Prospects (WPP) 2012 provided country-specific life tables. Spectrum requires non-AIDS projections for high HIV burden countries; therefore, for these countries, Avenir Health converted each country life table into the relevant model life table, ran Spectrum to add the HIV mortality and then adjusted the all-cause mortality (by adjusting life-expectancy at birth) in an iterative approach to match the WPP 2012 projection. The resulting age distributions of WPP 2012 vs Spectrum populations are not perfect but match fairly well.

It was discussed that the UN Population Division did end up estimating non-AIDS projections for 39 high HIV burden countries, and will do so in 2015 for 27 key countries affected by AIDS, but these projections are not published. Because Spectrum and the UN Population Division are on different estimation cycles, HIV mortality will differ and ideally the no-AIDS counterfactual should be in-sync, re-estimated dynamically, year by year.

For the non-AIDS projections produced by the UN Population Division, most of the parameters from Spectrum are used to estimate AIDS mortality, with some simplifications, and some modifications to match empirical data where available. The F:M sex ratio of incidence is taken from Spectrum which has an important impact on the levels and trends of mortality that warrants greater consideration – resulting in an overestimate of female mortality and an underestimate of male mortality for many countries. The assumed sex ratio of incidence in Spectrum (which rises to 1.4 fairly early in the epidemic) is often inconsistent with adult mortality patterns from country data.

The WPP 2012 estimates of HIV prevalence are comparable to Spectrum estimates of HIV prevalence in recent years, but often vary greatly in the historical period which results in very different mortality. It was queried whether there were any efforts to match the output population from Spectrum to UNPD and discussed that while comparisons and validations are conducted there is not a systematic attempt to match outputs.

It was discussed that for the non-AIDS projection, the use of a single model over several decades is often inadequate. Moving forward the UN Population Division will consider the use of an alternative approach for estimating mortality in countries highly affected by AIDS (relational models).

Comparison of empirical data and UNAIDS estimates of adult mortality

In sub-Saharan Africa, the lack of VR data results in estimation of adult mortality rates occurring in two stages: Estimates of non-AIDS mortality are derived from model schedules of mortality combined with child mortality and then modelled estimates of AIDS-related deaths are incorporated. Bruno Masquelier compared empirical estimates of adult all-cause mortality (from DHS sibling histories and recent household death data) and orphan rates (from census and household surveys) to Spectrum estimates.

The results illustrate that Spectrum estimates of orphans are higher than observed in DHS/MICS/census, particularly for maternal orphans. Adult all-cause mortality estimates are higher

in Spectrum than in DHS, especially for female mortality. However, in some countries in southern Africa with very high HIV prevalence (Lesotho, South Africa), the modelled estimates (Spectrum) are lower than the empirical data. For countries in eastern Africa, the sibling estimates are much lower that Spectrum model estimates, but get closer over time.

The sex differences (sex ratios) from VR/census data do not see female mortality going higher than male mortality. The underestimate of adult male mortality rates from Spectrum are either due to the assumed sex ratio of incidence, or because mortality of the uninfected population is too low. Overall, the agreement between model-based and survey/census-based estimates of mortality, and the age patterns of mortality, varies greatly. The systematic differences between Spectrum and DHS indicate that further investigation is needed.

AIDS and all-cause mortality from vital registration data in South Africa

There have been many past efforts to estimate AIDS deaths from VR data in South Africa (Groenewald et al, 2005, Chapman et al 2006, Birnbaum et al 2011). The National Burden of Disease (NBD) study in South Africa extends the approach developed by Groenewald et al, but uses empirically-based estimates of the completeness of death registration.

Estimates of adult all-cause mortality from the NBD study in South Africa were compared with those from Spectrum. The discrepancies between these estimates can mostly be attributed to differences in estimates of AIDS deaths. In general, the Spectrum estimates of AIDS mortality (males and females), are higher than estimates from the NBD study (2010, in particular). When compared over time to an expanded array of mortality estimates, the Spectrum estimates are still much higher in the historical period (2000-2010), but do decline in the more recent period, in better agreement with other estimates. South Africa may not be the only country with this issue, Spectrum all-cause mortality estimates for Zimbabwe and Botswana are much higher at the peak (and after) than empirical data, which also does not support more deaths in females than males in Spectrum all-cause mortality estimates. These discrepancies also appear to be mainly due to an overestimate of AIDS mortality.

Lessons learned from this work include: Concerted effort required to derive the best estimates of all-cause mortality. Great care is needed in using country published estimates (i.e. census) if the data are not of good quality. Completeness may not be constant by age (disintegration of households on old age deaths), which is controlled for by assuming limited changing in non-AIDS deaths (penalising). The level of household disintegration (death of household before they can report on the death of one of the partners) with AIDS deaths is unclear.

It was discussed that there was a meeting in South Africa last year to better understand the differences in estimates for mortality from different models (in particular, Leigh Johnson's Thembisa model) and that the published Spectrum results do not reflect changes made to the estimates as a result of this meeting. It was discussed that a better understanding is needed for the discrepancy in Spectrum results compared to other model results.

Trends in HIV- and HIV+ mortality from ALPHA Network:

Data from the Alpha Network sites indicate that for HIV- mortality, male mortality is approximately 1.2x female mortality, with the exception of the South Africa site where male mortality is twice female mortality. For HIV+ mortality, there is little difference in mortality by sex in the pre-ART period, but females have a survival advantage in the later period largely due to ART.

Adult mortality estimates for high HIV-burden countries in GBD

Completeness of adult vital registration process (death distribution methods and spatial-temporal regression): Vital registration systems may not capture all adult deaths. In the GBD study, the completeness (or quality) of adult VR data is predicted based on child completeness – completeness in child VR (under 5 mortality reporting) informs the completeness in adult VR, then a spatial-temporal regression is used (borrowing information over space and time) to obtain final estimate.

Estimates of 45q15: Sibling survival data are used extensively for estimates of the probability of dying between age 15-60. There are for key sources of bias in these data:

1. <u>Selection bias:</u> Under-representation of high mortality sibships in the sample population, which results in mortality estimates biased downward without adjustments.
   →*GBD study: Gakidou-King weights to weight sibships, the missing sibships are added back into the survey, reiterative process.*

2. <u>Zero reporter bias</u>: Sampled population excludes those sibships where no siblings are eligible to report on mortality of their sibling (>bias in high mortality populations)
   →*GBD study: Direct estimation of missing sibling deaths by age and sibship size, add back into observed sample before calculating mortality*

3. <u>Sparse data:</u> Often limited data for certain age groups (i.e. DHS often only 15-49, but for 45q15 estimates, also need respondents age 50-59).
   →*GBD study: Logistic regression model with the (strong) assumption that the mortality pattern is same for those at older ages.*

4. Recall bias: Omission bias, respondents omitting siblings, omitting deaths.
   →*GBD study: Quantify amount of bias, adjust 45q15 estimates upward*

The different 45q15 estimates are synthesised using spatial-temporal regression (Gaussian process regression). For countries affected by HIV/AIDS, the all-cause mortality estimation process is split into two steps: first, the HIV counterfactual age pattern of mortality (5q0 and 45q15) is obtained and applied to a new relational model life table system, and then the excess mortality due to HIV is added to the HIV-free age pattern of mortality.

Relational model life table: For each country-year, an HIV-free life table standard is created. A set of empirical life tables with closest 5q0 and 45q15 (using Mahalonobis distance) is identified, with preference given by space and time with an automated weighting scheme across different life tables. The next step is to allocate excess mortality due to HIV by age (increase in age-specific death rates), which is calculated in reference to the risk of death at age 40.

Matching to resolve inconsistency (GBD 2013, generalised epidemic countries): Spectrum AIDS deaths for some age/sex groups were larger than all-cause mortality thus the GBD methods used modified Spectrum (IHME modified version) to produces 10,000 sets of estimates, then randomly pair each Spectrum set with an all-cause mortality set, calculate pair-specific HIV/AIDS deaths in excess of all-cause deaths, then identify 250 pairs with the fewest excess deaths, and resample both Spectrum and all-cause mortality estimates to obtain final estimates.

It was discussed that the all-cause mortality data being used for SSA estimates are predominantly from South Africa. It was also discussed that treatment is not explicitly accounted for in the GBD methods.

Relational life tables

Sam Clark has developed a singular value decomposition model for age-specific mortality patterns with ideas for extending the model to include HIV prevalence and ART coverage into models of age-
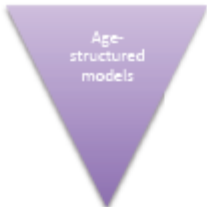
specific mortality. The overall aim of this work is to use empirical data to produce a model of full age schedules of demographic consequences, which could potentially also include covariate parameters (HIV prevalence, ART coverage). The output is a predicted age schedule of mortality by sex. This model could be used to:

1. Summarise Spectrum mortality outputs as a simple function of HIV prevalence and ART coverage (which does not require running Spectrum)
2. Create empirically calibrated HIV/ART parameterised model life tables from ALPHA Network data

Recommendations for estimates of mortality:

- ✓ **For the next round of UNAIDS estimates, use the unpublished no-AIDS projections from UNPD.** *Follow-up: UNAIDS, UN Population Division, Avenir Health*
- ✓ **UNAIDS to follow-up with UNPD regarding estimation cycles and possibilities for improved synchronisation of these cycles,** *Follow-up: UNAIDS, UN Population Division*
- ✓ **Further investigation into the assumption of early F:M prevalence/incidence ratio; investigate the sex ratio pattern required that would bring the estimates of mortality into sync with other estimates and empirical data.** *Follow-up: John Stover, UNAIDS*
- ✓ **Create comprehensive database of age/sex-specific adult mortality estimates from high HIV prevalence countries and analyse comparison of estimates from different survey types to better understand biases in mortality estimates** *Follow-up: Bruno Masquelier, Patrick Gerland, Jeff Eaton*
- ✓ **Develop statistical model for including mortality data into likelihood function for age-specific estimates model.** *Follow-up: Jeff Eaton*
- ✓ **Circulate draft paper about methods for analysing sibling history mortality data used for GBD 2014,** *Follow-up: Haidong Wang*
- ✓ **Continue development of relational life tables,** *Follow-up: Sam Clark*

Proposed timeline for the scope of work identified:

	Age-structured models	Use of programme service data	Spatially-specific estimates	Use of case-report and mortality data	Continuous Update and Improvement
June meeting	Review proposals for age-structure in EPP (w/o inference); and ideas for inference on epidemic.	Review guidelines, and research needs	Presentation of methods including 'straw man' illustration	Review performance (any mods) of UNSW methods. Examine other methods and discuss new directions.	
End of Year Meeting	Finalize specification of age-structure model	Patterns of attendance (& how to incorporate into spatial modelling);	Methods finalized & published; including production of incidence estimates. Hierarchical models spec finalized and tested	Review of trials of next generation of case-report models from Latin America	Test CD4 model integration; Review of Heckman model effects Breakthrough in PMTCT issue.
2016	Integration of age-structure into EPP	...	Production of estimates for ++ countries	Deployment of methods in next generation of tools.	
2017	*Major set of method updates launched*				

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Appendix I: List of Participants

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Appendix II: Meeting Agenda

Method Development for the UNAIDS Estimates: June 2015

2-4 June 2015

DAY 1: Tuesday, June 2nd

Session 1: Opening session and age-structured models (Chair: Tim Hallett)			
900	15	**Meeting opening - Meeting aims, key issues, introductions**	Peter Ghys, UNAIDS Tim Hallett, Imperial College London
915	20	**Issues arising from current round of country estimation** *- The "new bumps" and resolution* *- Comparison of HIV prevalence amongst pregnant women in Spectrum vs national surveys* *- Fertility in HIV+ compared to HIV- women* *- MTCT rates in the ART era*	Mary Mahy, UNAIDS
935	25	**Investigation into discrepancies between EPP & Spectrum with changing ART eligibility criteria**	Tim Brown
1000	25	**Incorporating age-structure into EPP**	Jeff Eaton, Imperial College London
1025	20	**Comparison of Spectrum patterns of prevalence by age to survey data and changes required to the incidence rate ratios to improve this match**	John Stover, Avenir Health
1045	*20*	*Coffee break*	-
1105	55	**Group discussion and recommendations**	ALL
Session 2: Child Estimates in AIM (Chair: Tim Hallett)			
1200	20	**Methods for obtaining estimates amongst children** *- Review of child CD4 model and expected update from IeDEA data* *- Review of methods for calculating pregnant women in need of PMTCT* *- Review of MTCT rates and updates to these rates* *- Comparison of child HIV prevalence estimates from Spectrum to estimates from national surveys*	John Stover, Avenir Health
1220	40	**Discussion and potential decisions required** *- Plan and timeline for CD4 model updates* *- Reconsideration of methods for calculating pregnant women in need of PMTCT needed?* *- Updated meta-analysis for MTCT rates?* *- Further research into fertility differences HIV+/- and regional differences for the potential impact of ART on fertility (i.e. western vs southern Africa).* *- Key unresolved issues from implementation of child CD4 model (Peter Johnson)*	ALL

DAY 1 (cntd)

1300	*45*	*Lunch*	-
Session 3 - Updates (Chair: Tim Hallett)			
1345	20	**Update on Heckman methods - method development and software**	Mark McGovern, Harvard
1405	15	*Questions and discussion*	ALL
1420	20	**Update on joint estimation of HIV progression and survival**	Tara Mangal, Imperial College London
1440	15	*Questions and discussion*	ALL
1455	10	**Update on key recommendations from the Bangkok HIV Surveillance meeting**	Txema Calleja, WHO
1505	*25*	*Coffee break*	-
Session 4 - Fitting incidence to programme data in AIM (Chair: Tim Hallett)			
1530	20	**Fit to programme data tool in the country estimation process** *- Use (which countries and how used)* *- Results, comparison to previous estimates using EPP, adjustments made (to time lags, to % undercount)* *- Comparison of declines in AIDS mortality from programme data compared to Spectrum estimates*	Kim Marsh, UNAIDS
1550	25	**Overview of fitting incidence to programme data tool and updates** *- Review of tool* *- Incorporating ART coverage by CD4 to fit to mortality data*	John Stover, Avenir Health
1615	45	**Discussion & Recommendations** *- Further improvements, guidance for use*	ALL
1700		**Close**	-

Day 2: Wednesday, June 3rd

Start	Duration	Subject	Speaker
900	5	Opening and introduction	Tim Hallett, Imperial College London
Session 5 - Use of case reports and other routinely collected data sources to generate estimates of HIV incidence (Chair: Peter Ghys)			
905	25	**Methods for using case-report data to estimate HIV incidence**	David Wilson, UNSW
930	25	**ECDC approach to generate estimates of HIV incidence - update and key challenges**	Ard van Sighem, Stichting HIV Monitoring
955	10	**Future plans for estimation in ECDC countries**	Chantal Quinten, ECDC
1005	25	*Clarifying questions*	-
1030	*30*	*Coffee*	-

DAY 2 (cntd)

1100	10	**Future plans for method development on the use of case-report and other routinely collected data to generate estimates of HIV incidence**	Tara Mangal, Imperial College London
1110	10	**Use of case reports and other routinely collected data sources to generate estimates in generalised epidemics**	Jacob Dee, CDC
1120	30	**Use of case report data to inform model parameters** *- Estimating incidence rate ratios by age and sex in Argentina and China* *- Results from Argentina and China* *- Estimates of AID-related mortality and progression rates in China from HIV case reports*	John Stover, Avenir Health
1150	70	**Group discussion & recommendations**	ALL
1300	*60*	*Lunch*	
Session 6 - Use of programme data to inform estimates (Chair: Simon Gregson)			
1400	40	**New guidelines for PMTCT-based surveillance** *- Options available, key issues (including availability of age-specific data & testing in known positives), system requirements* *- Country plans for adoption and implementation*	Jacob Dee, CDC/Txema Calleja, WHO
1440	10	Questions	ALL
1450	25	**Incorporating PMTCT data into EPP fitting** **-** *Proposals for validating model assumptions and understanding the impact of making wrong assumptions*	Le Bao, Penn State
1515	15	Questions	ALL
1530	30	*Coffee*	-
1600	15	**Incorporating PMTCT data into age-structured EPP** *- Use of standardisation to produce age-specific prevalence estimates from aggregate data*	Basia Zaba, LSHTM
1615	15	**Future research agenda** **-** *Preliminary suggestions*	Simon Gregson, Imperial College London
1630	60	**Group discussion**	ALL
1730		Close	

DAY 3: Thursday, June 4th

		Session 7 - Spatially-specific estimates (Chair: Tim Hallett)	
830	20	**Hierarchical model - Revisions, improved efficiency, use with key populations**	Le Bao, Penn State
850	30	Questions & Discussion	ALL
920	30	**Spatially-specific estimates of HIV - method development, initial results**	Samir Bhatt, University of Oxford
950	40	Group discussion	ALL
1030	*30*	*Coffee*	
		Session 8 - Mortality (Chair: Josh Salomon)	
1100	20	**Considerations for incorporating all-cause mortality for HIV epidemic inference**	Jeff Eaton, Imperial College London
1120	15	**Current methods for non-HIV life tables for SSA in Spectrum**	John Stover, Avenir Health
1135	30	**Comparison of empirical data and UNAIDS estimates of adult mortality in high-prevalence countries**	Bruno Masquelier
1205	40	Group discussion	ALL
1245	*45*	*Lunch*	-
1330	30	**Data, methods, and estimates of adult mortality in high-prevalence countries from UNPD and future directions**	Francois Pelletier/Patrick Gerland UN Population Division
1400	15	*Questions*	ALL
1415	30	**Data, methods and estimates for GBD adult mortality in high-prevalence countries**	Haidong Wang, IHME
1445	15	*Questions*	ALL
1500	20	**Time and age trends in all-cause and cause-specific adult mortality in southern Africa**	Rob Dorrington, University of Cape Town
1500	15	**Mortality trends among HIV- and HIV+**	Basia Zaba, LSHTM
1520	15	**Simple, Parameterized Model of Age Patterns of Mortality - Ideas for Incorporating HIV Prevalence and ART Coverage**	Sam Clark, Univ of WA
1535	60	Group discussion & recommendations	
		Closing session	
1635	10	Closure	Peter Ghys, Tim Hallett
1645			