Spectrum 2013

Report of a meeting of the UNAIDS Reference Group on
Estimates, Modelling and Projections held in London, England
24-26 September 2012

TECHNICAL REPORT AND RECOMMENDATIONS

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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, the World Health Organization (WHO) 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, Imperial College London.

Aim of the meeting

To finalise the changes needed in Spectrum in advance of the start of the new estimation cycle for the UNAIDS 2013 Global Estimates.

The specific objectives of this meeting were:

1) To review the results of model fitting in concentrated and generalised epidemics using two revised approaches to curve fitting – r trend and spline – which will replace the variable r method currently in the Estimation and Projection Package (EPP) component of Spectrum.

2) To review new data and analyses available and make recommendations for methods and parameters to use for Spectrum 2013.

Approach

The meeting featured presentations of model simulations, recent data and analyses and presentations and discussions of ongoing work, combined with group discussion. The meeting agenda is included in Appendix I. The meeting was attended by 28 experts; each contributed, not only data, simulations, insights, experience and analyses, but worked to produce a set of recommendations drafted at the meeting. The list of participants is included in Appendix II.

The recommendations drafted at Reference Group meetings give UNAIDS and WHO 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.

1. New models *r trend* and *spline* to replace *r-flex* in EPP

The r-flex model (aka variable r) in the EPP component of Spectrum was used by the majority of countries with generalised epidemics for generating 2011 Global Estimates. This method was adopted in order to have less structure on curve fitting (compared to using the EPP classic model) and provided greater flexibility that could better capture the changes in prevalence (increase/decrease) after the decline period or stabilisation which has been observed in some countries, for example Uganda and Kenya. While r-flex performed fairly well when used for generalised epidemics, the main caveat was that it was extremely flexible which often resulted in unrealistic incidence curves. As a result, two modified approaches have been proposed to replace r-flex. These models offer the flexibility to capture long time series of data and changing trends post-decline/stabilisation, but have more structure to produce more realistic incidence curves.

1. **Spline model:** Hybrid force of infection model which uses B-splines with a difference penalty to obtain the in-sample fit and a random walk out-of-sample (projections).

2. **R trend:** A refined r-flex model which imposes some common structure on r(t), the simple random walk, and uses more informative prior distributions.

Spline model, Dan Hogan
The spline model in is a hybrid force of infection model that combines the strengths of the spline (in-sample) and the random walk (out-of-sample projection). The spline approach produces smooth, well-behaved curves and the difference penalty provides structure which allows the model to perform well in sparse data settings. The random walk approach stabilizes incidence trajectories beyond the data. This approach has been tested in 31 countries with generalised epidemics and 14 countries with concentrated epidemics.

R trend model, Le Bao
The r trend model imputes a systematic mean structure on the change in r(t), the driving factor of the epidemic, r(t), which is a function of the initial infection rate and HIV prevalence. In generalised epidemics, the common structure of r(t) begins with a high value to initiate the epidemic and then declines over time when prevalence levels off or increases after the decline period. The higher the initial prevalence the more likely the infection rate will decrease, thus r(t) and current HIV prevalence determine future prevalence levels. The benefits of this approach are that the parameters are easy to identify and interpret, and information can be shared across sub-regions.

There are currently two versions of the r trend model, a 6-parameter model and a 7-parameter model. The latter is a modified version of the former which offers the additional flexibility to change the epidemic start time and the equilibrium condition. The 7-parameter model relies on past prevalence, the past infection rate and the equilibrium condition to model the annual change in the infection rate. This model has roughly the same performance as the 6-parameter model but with slightly longer fitting times.

Hierarchical model, Le Bao
For generalised epidemics in sub-Saharan Africa, common patterns of r(t) across countries can be used in a hierarchical model. The main assumption is that urban and rural error parameters are more or less similar which allows information to be borrowed from parameter estimates in the urban fit to inform the rural fit in situations when there is sparse data. The main caveat of this approach is the complicated spatial structure which makes it difficult to identify how to characterise all of sub-Saharan Africa.

The initial results indicate that the projections improve when one area has very good data (e.g. urban areas) and the other area has few data (e.g. rural areas). If both areas have few data, the projection is poor. The hierarchical model for concentrated epidemics is more complicated. This will require a large database of "trends" in each of the at-risk sub-populations in order to assign an informative prior distribution to each sub-population. This is something that can be done but as a longer term aim.

Questions that arose included whether to specify a peak parameter later for rural areas than urban and whether to put less structure on rural parameters than the urban parameters. A key concern is whether too much information is being borrowed from the urban fitting and thus creating a rural epidemic in some instances. Results for some countries shifted the rural peak earlier when borrowing information from the urban fit, which in the absence of data, may be viewed as either more plausible or as creating an epidemic.

Discussion on spline, r trend and the hierarchical model

There is a need for a better understanding of where and how the spline model and r trend diverge thus it is essential to explore model performance in specific, defined situations. Objective criteria are needed to identify important differences in these approaches. Standard testing scenarios and metrics should be generated to evaluate performance across a range of different epidemics such as rapid ART scale-up, rapid decline epidemics, rapid rise epidemics, countries with poor datasets, countries with great datasets and estimates and projections for incidence. The models should be tested with both concentrated and generalised epidemics. Criteria are needed to identify how well the models describe an epidemic in-sample and also evaluate how they perform out-of-sample in the projection. If multiple methods are made available, countries will need clear guidance for which model to use and when to use it.

It is likely that the main difference between the two approaches, r trend and spline, is how they perform for estimating incidence; there also appears to be more variability around incidence in the projection. While the incidence curve is taken from EPP and passed to Spectrum, the models do not fit to incidence; incidence is obtained from prevalence thus one step removed from the data. With both models, there appears a tendency to get a decline in incidence based on obtaining incidence from prevalence.

Recommendations for models in EPP:

- ✓ **Replace r-flex (aka variable r)**
- ✓ **Keep EPP classic as a separate model**
- ✓ **Conduct a systematic evaluation of the two new models, r trend and spline, to identify one approach (if possible) to use moving forward**
- ✓ **Develop recommendations for how countries will decide which model to use and the conditions for using each model.**
  Reference Group, review Dec 2012

Recommendations for decision on new models in EPP – spline and r trend:

Objective evaluation of r trend and spline in three stages:

1. **Define objective criteria for metrics of differences**
   Working group: Tim Hallett, Josh Salomon, Dan Hogan, Le Bao, Jeff Eaton, Basia Zaba, UNAIDS, Oct 2012
2. **Test the models in concentrated and generalised epidemics**
   UNAIDS, Nov 2012
3. **Identify the important differences in these two approaches**
   Working group, Reference Group, UNAIDS, Dec 2012

Recommendation for model uncertainty and estimates of incidence:

- ✓ **Recommendation for Dan Hogan, Le Bao, Adrian Raftery and Josh Salomon to write a paper on these two key topics**
  Dan Hogan, Josh Salomon, Le Bao, Adrian Raftery

Recommendations for hierarchical model:

- ✓ **Continue work on developing the hierarchical model for the ongoing, longer-term agenda.**
- ✓ **Cross validation testing in data-rich countries -- remove data to simulate the situation in many of the rural epidemics, compare the resultant estimates to evaluate performance.**
  Le Bao, review progress in spring 2012

2. EPP

The following details the current issues identified and under review which pertain to the EPP component of Spectrum, and the consensus recommendations derived at this meeting.

2.1 Validation of results in EPP

Experience from comparing Spectrum results to the Global Burden of Disease study results highlighted inconsistencies from one round of estimates to the next and wide variations in the best fit compared to the median of the posterior distribution which exposed the urgent need for countries to validate the fits obtained and to be more critical of their results in EPP. Countries need to be encouraged to review fits in the EPP stage as opposed to getting to the final stage in Spectrum before realising that there are inconsistencies. In order to encourage this review, validation checks should be incorporated into EPP.

Recommendations:

- ✓ **Include previous SPT files in the EPP software.** Add a screen after the fitted results that compares the previous SPT file with the current SPT file for prevalence and incidence, overall and by sub-population. Allow the user to read the SPT file but do not make these files publicly available.

- ✓ **Add a validation page in EPP.** Include a table where validation data or pre-loaded checks, such as mortality or AIDS case report data, can be manually entered.

- ✓ **Provide guidance on the use of validation checks.** Include specific guidance in the EPP help pages and incorporate this guidance into the country workshops. Note that Spectrum also has a comprehensive validation page thus countries will need formal guidance and recommendations for the specific validation checks in EPP and in Spectrum.
  EPP team, November 2012

2.2 ART apportionment

ART apportionment in EPP is currently imperfect; ideally there should be a breakdown by sub-population. Proposed improvements are expected to double the fitting time, thus will need to be carefully considered.

Recommendation:

- ✓ **Continue to work on methods to improve the apportionment of ART in EPP.**
  EPP team, medium-term agenda, review progress spring 2013

2.3 Single site fitting in EPP

The new models have problems fitting single site trends (e.g. prisoners in Iran). Ideally, the variation from the same sub-population in a country with a similar epidemic could be used to obtain inter-site variability (multiplier in the variation). This method has been previously used in sub-Saharan Africa (Grassly) and should be considered for use in concentrated epidemics with limited data.

Recommendation:

- ✓ **Contact Ard van Sighem to identify whether data are available by sub-population to inform and whether this might be possible.**
  Geoff Garnett to contact Ard van Sighem, October 2012

2.4 End dates in EPP

Spectrum allows users to change the end dates of the projections and thus it would be helpful if EPP is also able to do this. Note that this will invalidate fitting in EPP.

Recommendation:

- ✓ **Identify if this can be easily incorporated into EPP.**
  EPP team, November 2012

3. Spectrum

The following details the current issues identified and under review which pertain to Spectrum, and the consensus recommendations derived at this meeting.

3.1 Non-AIDS mortality

The UN Population Division is no longer producing 'no AIDS' life expectancy estimates and thus Spectrum will instead receive all-cause mortality estimates (May 2013) and will need to iterate in order to define the non-AIDS mortality. In order to prevent Spectrum from being an extremely large file, the country information will need to be stored in an appropriate application, such as a web-based host.

Recommendation:
- ✓ **Test the iteration method in advance in order to facilitate a smooth transition when UNPOP estimates are available.**
  Futures Institute, ongoing, review implementation in early summer, 2013
- ✓ **Use non-AIDS life tables from ALPHA Network to validate the Spectrum iteration approach**
  Basia Zaba and Futures Institute, review early summer, 2013

3.2 Tuberculosis modelling

Countries are increasingly asking for indicators and estimates of TB to report with their HIV/AIDS estimates. Countries also need to identify the effect of increasing ART coverage on TB, thus a greater integration of TB modelling in AIM is desired. Carel Pretorius is working on integrating the TB model into AIM in Spectrum. This model uses the WHO's STOP TB database and country AIM files to generate projections of TB incidence by HIV status and notification by case type and different CD4 categories. The main caveat of this approach is that the model fits are a two-part process with currently no easy simplification thus would require Carel to do the fitting for each country. This is not a sustainable method.

Recommendation:
- ✓ **Present this work at the TB Consortium meeting in South Africa to obtain expert comments, feedback and recommendations.**
  Carel Pretorius, September 2012

3.3 Child mortality pattern in Spectrum from IeDEA

Currently, Spectrum has a single mortality parameter for children >6 months which is applied to the entire world. It is also not known whether the method that Spectrum is using for allocating ART is in balance with what is happening in the countries. It is possible that Spectrum is over-estimating treatment allocation in younger age groups and underestimating treatment allocation in older ages. The IeDEA consortium has data for the distribution of kids starting on ART and by age. It may be relevant to use the IeDEA data to inform the paediatric age profiles of treatment initiation but it is also important to remember that the patterns are rapidly changing.

Recommendation:
- ✓ **Review the data available and consider incorporating to inform patterns in sub-Saharan Africa.**
  Constantin Yiannoutsos and John Stover, October 2012

3.4 Effect of adult cotrimoxazole on mortality

An analysis of IeDEA data found that adult cotrimoxazole does not significantly affect mortality among patients on ART. The trend is in the right direction, but the difference is not large enough to need to consider for inclusion in Spectrum.

4. Heckman methods

Previous results from the use of Heckman-type selection models[1] suggested that selective non-participation in HIV testing in nationally representative household surveys may significantly change prevalence estimates in some surveys. Further efforts expanding this work identified that HIV prevalence in males may be underestimated in a small number of surveys.[2] One key concern with using the prevalence correction from Heckman methods was that the resulting F:M ratios of prevalence post-adjustment did not seem realistic. As a result, additional work continues to refine the methods used. Further analysis and triangulation of data was done in the countries where HIV prevalence was thought to have been underestimated in order to validate the proposed Heckman adjustments.

4.1 Heckman methods – Random effects model

Previous Heckman models have adjusted HIV prevalence for non-response using a fixed effects approach to identify the interviewer effect. There are three key caveats of this approach: 1) If an interviewer conducts only a few interviews, it may not be possible to identify the effect, and if the interviewer is very good or very poor, it will be impossible to identify the interviewer effect (either 0 or 100). As a result, all of these observations will have to be dropped. 2) Bootstrapping is not possible thus the regression parameter uncertainty is not accounted for. 3) The fixed effects maximum likelihood estimators (MLE) are consistent but can be biased in small samples (they do not incorporate what is happening in the tails). The first two problems can be solved using a random effects approach. For the third, Bayesian Model Averaging (BMA) can provide unbiased estimates in small samples. Results for Zambia illustrate that the random effects BMA and MLE are quite similar, thus the MLE approach is fine for Zambia. But in Ghana where there is low prevalence and a small sample size the BMA and MLE are quite different.

Overall, while point estimates from household surveys may be biased as they assume non-response is random, the difference is not as large as observed using the fixed effects model (Barnighausen, et al[1]). These findings signify that selective non-participation does not appear to be a major concern for estimates of HIV prevalence from national household surveys. However, the additional uncertainty from the use of the Heckman methods is something that should be included in EPP. In the short term, it might be applicable to do this by increasing the bounds around DHS surveys.

4.2 Further investigation into sex ratios in Zambia Ghana, Mali and Côte d'Ivoire

These four countries had significant differences in prevalence when using Heckman methods to account for the effect of selective non-participation. Further investigation of sex ratios in available data – prevalence, mortality, case report and treatment data – in these four countries found that there is no evidence to support the sex ratios of prevalence that result from the Heckman adjustment in Ghana and Zambia. In Côte d'Ivoire, there is some data to support the Heckman-adjusted sex ratio of prevalence and in Mali the two ratios are very similar.

Recommendations for Heckman methods:

- ✓ **Investigate additional countries using the random effects model and run full simulations in order to allow for full confidence in the methods and results and to identify how the confidence intervals change in the full simulations (smaller or larger).**
  Mark McGovern, spring 2013

- ✓ **Generate age- and sex-specific results for Zambia using the random effects model to compare with mortality data from SAVVY.**
  Mark McGovern to generate age- and sex-specific results for Zambia, spring 2013
  Mary Mahy to provide mortality data from national SAVVY survey

- ✓ **Increase the bounds around DHS surveys by a certain % dependent on 'missingness' for urban and rural.**
  Dan Hogan, Tim Brown, Josh Salomon, review at Reference Group meeting Dec 2012

- ✓ **Further investigation into including DHS in the likelihood.**

5. Sex ratios of prevalence, incidence and AIDS mortality

During initial discussions of the Heckman results, it was identified that more information is needed on sex ratios of prevalence across different settings. Following the Global Burden of Disease (GBD) study and the comparison of estimates of AIDS mortality in the GBD study to Spectrum[3], it was noted that the sex ratios of mortality were different in the two sets of estimates. Spectrum incorporates a pattern for the sex ratio of incidence and thus it was agreed that further investigation was needed into sex ratios of prevalence, incidence, AIDS mortality and treatment.

5.1 Sex ratios of prevalence from Demographic and Health Surveys (DHS)

Spectrum takes incidence from EPP and then in generalised epidemics, divides HIV among males and females based on the sex ratio of incidence. Currently, the incidence ratio stabilises after 10 yrs in a default pattern. In sub-Saharan Africa (SSA), the median F:M ratio of incidence at stabilisation is 1.38, while outside SSA, the median is 0.84. In IDU-driven epidemics in Eastern Europe it is 0.42.

A PhD dissertation from Sara Hertog[4] investigated sex ratios of prevalence from DHS in generalised epidemics. A detailed analysis for two countries found that in Tanzania, the key factors explaining the difference were that women were exposed to sexual activity for longer periods of time and were more likely encounter an infected partner (the latter explains the majority of the difference). In Kenya, these two factors did not explain the difference; instead it was found that women had the same risk as uncircumcised men, while circumcised men had a lower risk. A cross-sectional analysis of datasets from 15 countries identified five statistically significant factors related to sex ratio of prevalence including: percent urban, sex ratio of professional occupation, sex ratio of premarital sexual activity and the mean age difference between partners. However, taken together, these factors only explained ~16% of the variation. Note that there was no observed correlation with the maturity of the epidemic (women surviving longer). Even within the same country, sex ratios of prevalence vary across survey and it is likely that this variation is real.

Various options to implement in Spectrum were discussed including reverting back to using country-specific ratios from the most recent survey or the mean value across all surveys or whether the guidance should be to use a ratio of 1.5 if the confidence intervals overlap this value. It was also suggested that regional values could be used as the default. Spectrum previously used prevalence from EPP as the input, and calculated sex ratios of prevalence thus the question was posed as to whether this method should be reinstated.

5.2 Sex ratios of prevalence and incidence from ALPHA sites, 1990-2010

Data from the ALPHA Network cohorts have been pooled into a single dataset which allows the investigation of the patterns of prevalence and incidence ratios over time. As an initial step, identifying the proportion of the population with HIV status unknown provides insight into possible biases that may affect the sex ratios. In the pooled dataset, HIV status unknown is nearly always higher amongst males than females over time, but with no generaliseable trend (different by study). The highest unknown status is in older ages, largely due to testing criteria (age restrictions).

In order to fully probe the pooled dataset, specific criteria are used to maximise the use of the demographic surveillance data and minimise the unknown status. Results illustrate that HIV prevalence is higher in females than males and by age, prevalence is higher in females at younger ages and in males at older ages. For sex ratios, the F:M sex ratios of prevalence and incidence decrease with age, increase over time, and are much higher when ART is available. The finding that the sex ratio becomes higher in women when ART is available (above all other factors), suggests that because more women are on ART, incidence is dropping faster in males.

5.3 Sex ratios in South Africa compared to Spectrum outputs

Rob Dorrington from the University of Cape Town compiled data available for sex ratios of all-cause mortality, AIDS mortality, prevalence, incidence, ART and ART by CD4 in South Africa and compared these to the corresponding sex ratios from the Spectrum file for South Africa.

In South Africa, the all-cause mortality data illustrates an increases in the F:M mortality ratio that then decreases over time, presumably due to the effect of ART. Compared to the vital registry (VR) data, the all-cause mortality ratios (F:M) from Spectrum seem too high in the pre-AIDS period. By age, the all-cause mortality ratios are similar except for the second increase (spike) that occurs in older age groups in Spectrum while the VR data plateaus. For AIDS mortality, the F:M ratio in Spectrum continually increases over time with no observed effect of ART. By age, the AIDS mortality ratio in Spectrum peaks at a lower level with the peak in earlier years (15-19 yrs), and has a second peak in later years (45-49 yrs) that is not observed in VR data which plateaus.

The sex ratios for prevalence in Spectrum ratios are fairly stable over time and are not allowing for higher F:M on ART. By age, the first peak in Spectrum is at 15-19 years compared to 20-24 in HSRC data and the second peak in Spectrum appears too high. The sex ratios of incidence in Spectrum appear fine for the early age groups, but not the later age groups – there is no strong evidence of the increase in incidence in the 45-49 year age group that occurs in Spectrum.

The sex ratio of the number on treatment over time in Spectrum appears too low (compared to HSRC, Cornell et al and Johnson model), but note that the surveys may have bias (more women participating). Looking at the sex ratio of ART by CD4, Cornell et al illustrates that women at higher CD4 counts are being put on ART. It is likely that in South Africa, the sex ratio on treatment gets larger because of pregnant women and maybe also as a result of more testing and identification. This is not being observed in the results from Spectrum where there is currently no sex differential for treatment.

Looking at the total numbers, the all-cause mortality over time (15-59 years) and the total numbers of AIDS death over time in Spectrum are too high (compared to ASSA, IHME, VR). This may be a result of incidence in Spectrum being too high at times, or a result of the progression pattern from infection to AIDS death not being long enough.

Recommendations:

- ✓ **Include numbers on treatment by sex as a Spectrum input as an initial step to improving sex ratios. This will affect mortality, which will then affect the prevalence ratio then incidence ratio.**
  Futures Institute, review December 2012

- ✓ **Review and compare mortality estimates after including the sex ratio on treatment**
  Futures Institute, Reference Group, review Dec 2012

- ✓ **Additional testing to identify if the default pattern for sex ratios of incidence should change over time including testing the use of country-specific values from surveys, using 1.5 in generalized epidemics if the CIs overlap 1.5 and considering the use of regional defaults.**
  Futures Institute, review progress Dec 2012

- ✓ **UNAIDS to liaise with PEPFAR and WHO to identify if there is differential treatment access by sex in children.**
  UNAIDS, Rob Lyerla, Txema Calleja, Dec 2012

- ✓ **Include available national-level mortality data from US Census Bureau and UNPOP as a validation.**
  Futures Institute, Peter Johnson

6. Incidence in older age groups

In Spectrum, incidence is extrapolated from prevalence in 15-49 yr olds using Tim Hallett's method[5] with an extrapolation for those 50+. However, a recent unpublished review by Boerma and Ghys found higher prevalence in older age groups compared to Spectrum estimates, suggesting that Spectrum may be underestimating incidence in older age groups. As a result, the current age-specific incidence pattern in Spectrum has been updated to reflect this finding which results in a second peak in incidence that appears somewhat questionable. As follow-up, an analysis of non-response in older age groups was conducted to identify if the estimates from population-based surveys with HIV testing might be biased and found that non-response rates in those 50+ were similar or lower than the overall non-response rate.

An analysis of the pooled ALPHA dataset illustrated that while there might be some suggestion for a "hump" in older ages (with very large confidence intervals), it is probably more reasonable to interpret this as a levelling off/plateau as opposed to a continued decline with an upward spike. It was also discussed age is an imperfect measure – people often inaccurately self-report age or year of birth; there may also be preference for a specific birth year or digit.

Recommendations for a revised age pattern of incidence:
- ✓ **Tim Hallett to re-conduct his previous analysis estimating incidence from prevalence using updated survey data for review and comparison and will also look into methods to capture the uncertainty (bootstrap).**
  Tim Hallett, Ian Timaeus, Basia Zaba, John Stover – November 2012
- ✓ **Implement the updated incidence pattern (from Hallett method) as an interim step and compare results with the mortality data from South Africa.**
  Futures Institute, Dec 2012
- ✓ **Test the use of incidence rates in Spectrum and compare the results with mortality data from South Africa.**
  Tim Hallett to provide incidence rates, Futures Institute to test and compare, Rob Dorrington to aid with South Africa comparison, review in spring 2013
- ✓ **Test the use of an incidence pattern that plateaus instead of declining sharply and increasing in older ages.**
  Futures Institute, review Dec 2012

Recommendation for surveillance:
- ✓ **Future data collection efforts should not be age-capped and organisations should encourage surveillance systems to collect more information on older age groups**
- ✓ **Consider including older age groups in national population-based surveys that measure HIV prevalence**

Recommendation for longer-term agenda:
- ✓ **Identify if it is possible to keep track of those 50+ in EPP**
  EPP team, review progress spring 2013

7. Longitudinal analysis of CD4 progression

Work is ongoing to conduct a pooled statistical analysis of longitudinal CD4 cell decline data to estimate age and sex-specific CD4 progression rates (expanding upon the CASCADE analysis) in order to revise and validate CD4 model parameters in Spectrum. The progression parameters currently used in Spectrum were obtained from fitting and are not based upon real data, but a cross-sectional comparison of the CD4 distributions in Spectrum for people not on treatment in Kenya and Uganda suggests fairly good agreement with the Kenya and Uganda AIS data.

It was discussed that for Spectrum, regional progression patterns are needed and additional datasets should be sought out in order to further inform regional trends. Analyses should be done by sub-type and risk group to inform regional trends. Of note, the seroconverter data is age at infection as opposed to current age which is used for the age-specific progression parameters in Spectrum. Also, the cohort data for recent years gets censored with CD4 counts <200 due to treatment initiation thus an extrapolation method may be needed for progression below CD4 200. It was also raised that the unequal CD4 bins in Spectrum make it difficult to compare transition rates.

Recommendations:

- ✓ **Identify if other data may be available to inform regional trends – Thailand, China, Brazil, India, Africa Centre**
  John Stover (India), Peter Ghys (Thailand & China), Jeff Eaton (Africa Centre, Brazil), Oct 2012

- ✓ **Further consideration into age at seroconversion (data available from the cohorts) vs current age (Spectrum)**
  John Stover, Nikos Pantazis, Oct/Nov 2012

- ✓ **Define minimum required covariates (e.g. age, sex, geographical location, risk group)**
  John Stover, Nikos Pantazis, Peter Ghys, Jeff Eaton, Nov 2012

- ✓ **Changes to the current sizes of the CD4 boxes will need to be for a later version of Spectrum. Once all the data are available this is something that could then be considered.**
  Reference Group, John Stover, Jeff Eaton, discuss spring 2013

8. PMTCT and ART estimates of coverage and need

Coverage estimates for PMTCT and ART for countries producing Spectrum files were reviewed. For the few developing countries where coverage levels >100% were seen, the reported numbers on ART might be unadjusted figures or the progression patterns might be too slow, or more people are starting ART at low CD4 counts. For PMTCT coverage in developing countries, the fertility reduction may need adjustment or the F:M ratios of incidence might be too low. An investigation into country programme data for ART and PMTCT highlighted that facilities often have difficulty accounting for patients leaving care and may often be capturing initiates as opposed to those currently on care. More routine information is needed on treatment re-initiation, transferring, loss-to-follow-up and mortality.

Recommendations:
- ✓ **Advocate for biomarkers to be included in national testing surveys (CD4 or viral load)**
- ✓ **Validation studies in a few countries using pill count for comparison**
- ✓ **Validation studies in a few countries collecting biomarkers (Uganda)**
- ✓ **Mobility reporting as routine surveillance – identifying if those receiving treatment were previously receiving care elsewhere as part of routine data collection**

  PEPFAR, UNAIDS, longer-term research aim

9. Incident HIV infections in pregnancy

While some studies have found an increased risk of incident HIV infection in pregnancy,[6, 7] the study populations – serodiscordant couples or sexually active women – might not be representative of the entire population and thus the results might not be generalisable at the population level. The ALPHA Network pooled dataset was used to explore this in more detail and found that at the general population level there is no evidence for an increased risk of HIV transmission during pregnancy. There may possibly be an increased risk in 15-19 year-olds (not statistically significant), but younger people may be more likely to be in a discordant relationship.

Recommendation:
- ✓ **A higher rate of incidence among pregnant women should not be implemented in Spectrum.**

Appendix I: Meeting Agenda

UNAIDS Reference Group on Estimates, Modelling and Projections			
Spectrum 2013			
Venue: Novotel Hotel, Paddington			
DAY 1, Monday, Sept 24, 2012			
Start	**Duration**	**Subject**	**Speaker**
830	*30*	*Tea and coffee available*	*-*
900	5	Opening remarks and introductions	Peter Ghys
Session 1 -Spectrum: R-flex and r-spline (Chair: Geoff Garnett)			
905	45	Results from application of mean-shift model in concentrated epidemics; results from hierarchichal model; revised model following reviewer feedback	Le Bao
950	10	Questions	-
1000	10	Review and comparison of results from both models in concentrated epidemics	Dan Hogan
1010	20	Results from implemenention of the models in EPP	Tim Brown
1030	10	Questions	-
1040	*20*	*Coffee break*	
1100	15	Results from model testing	UNAIDS
1115	10	Questions	-
1125	20	Additional considerations -- use of DHS trends and uncertainty for incidence projections	Dan Hogan/Le Bao
1145	45	Group discussion: Recommendation for method to adopt, considering: *- How do the model fits compare between methods? Model fits for generalised vs concentrated epidemics? - Are we able to generate recommendations? Additional testing and comparison needed?*	
1230	*60*	*Lunch*	-
Session 2 - Spectrum & EPP: Progress reports, new features (Chair: Josh Salomon)			
1330	35	EPP Team: Updates, ongoing progress, new features, outstanding issues	Tim Brown
1405	15	Discussion	
1420	35	Futures Institute Team: Updates, new features, outstanding issues	John Stover
1455	25	Discussion	
1520	*25*	*Coffee break*	-
1545	20	Futures Institute Team: Update on integration between AIM and TB model in Spectrum	Carel Pretorius
1605	15	Discussion	
Session 3 - IeDEA Consortium (Chair: Basia Zaba)			
1620	35	New data and analyses from IeDEA Consortium data: - Longitudinal outcomes adjusting for loss to follow-up - Update on new data avail (including Western Europe and USA) - New data on survival of children on ART - Impact of adult cotrimoxazole on mortality	Constantin Yiannoutsos
1655	30	Questions, discussion and recommendations	
1725		Close	
DAY 2, Tuesday, Sept 25, 2012			
830	*30*	*Tea and coffee available*	-
Session 4 - Heckman methods and sex ratios of prevalence, incidence and AIDS mortality (Chair: Tim Hallett)			
900	20	Heckman methods - Bayesian approach	Jeff Eaton/Dan Hogan
920	20	Heckman methods - Random effects model	Mark McGovern
940	20	Heckman methods - Further work, alternative approaches and research agenda when considering how to extrapolate for countries with no DHS, methods for >1 DHS, use at the urban/rural/provincial level	Josh Salomon/Till Barnighausen
1000	30	Discussion	
1030	*20*	*Coffee break*	-
1050	20	Sex ratios of prevalence: Analysis of DHS data	Futures Institute
1110	20	Sex ratios of prevalence: Results from further investigation into Zambia, Mali, Cote d'Ivoire, Ghana	UNAIDS
1130	20	ALPHA Network: Age-specific sex ratios of prevalence and incidence from ALPHA sites	Basia Zaba/Milly Marston
1150	20	South Africa: Age-specific sex ratios of AIDS mortality and prevalence over time	Rob Dorrington
1210	35	Discussion	-
1245	*60*	*Lunch*	-
Session 5 - Validating Spectrum estimates of AIDS mortality (Chair: Tim Hallett)			
1345	20	Comparison of Spectrum AIDS mortality estimates to ALPHA mortality	Futures Institute/ALPHA Network
1405	20	Discussion	-
Session 6 - CD4 progression parameters in Spectrum (Chair: Peter Ghys)			
1425	15	Spectrum CD4 model - Initial investigation into the effects of transition rates on AIDS mortality	Peter Johnson
1440	15	Overview of CD4 project, participating groups, proposed analyses	Jeff Eaton
1455	10	Questions	
1505	*25*	*Coffee break*	
1530	20	Initial results from replicated analysis using pooled dataset	Nikos Pantazis

		DAY 3, Wednesday, Sept 26, 2012	
845	*30*	*Tea and coffee available*	-
Session 7 - Incidence in older age groups (Chair: Tim Brown)			
915	15	Comparison of estimates of prevalence in 50+ from Spectrum vs surveys	Futures Institute
930	15	UNAIDS analysis of non-response in 50+	UNAIDS
945	20	Alpha network results from analyses of age-specific incidence and prevalence in 50+	Basia Zaba/Milly Marston
1005	25	Group discussion	-
1030	*20*	*Coffee break*	-
Session 8 - PMTCT and ART estimates of need and coverage (Chair: Simon Gregson)			
1050	15	Analysis of Spectrum need estimates and country estimates for ART/PMTCT including estimates of need for Pregnant women, TB patients and discordant couples	Futures institute
1105	10	Discussion	-
1115	15	Zambia analysis of reconciling reported numbers on treatment	Jeff Eaton
1130	10	Discussion	
1140	10	Country examples for review/discussion: Ziimbabwe	Simon Gregson
1150	40	Group discussion	
1230	*60*	*Lunch*	-
Session 9 -Pregnancy & child bearing (Chair: Simon Gregson)			
1330	15	ALPHA network: Incident HIV infection during pregnancy	Milly Marston
1345	25	Group discussion	
Session 10 - Model testing, timeline (Chair: Peter Ghys)			
1410	25	Additional population and demographic issues identified during model testing	Peter Johnson
1435	20	Discussion	
1455	35	Timeline; plan for future model testing; preparations in advance of training of trainers and country workshops	Group
1530		Close	

Appendix II: List of Participants

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