Technical Meeting to Review Spectrum 2011

and

Considering potential bias in DHS and ANC data

Report of a meeting of the UNAIDS Reference Group on
Estimates, Modelling and Projections held in Seattle, WA, USA,
20-21 October 2011

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

The aim of this meeting was twofold:

1) To review the performance of the new version of Spectrum 4.0, the integrated software which combines the Estimates and Projection Package (EPP) and Spectrum into a single user interface. In particular, to review the new methods adopted in response to the changing treatment criteria and prevention of mother-to-child transmission

2) To review the potential biases in survey and surveillance data, specifically Demographic and Health Survey (DHS) and antenatal clinic (ANC) data, and to discuss the results from recent trials on risks of transmission during pregnancy and as a result of hormonal contraception use.

Approach

The meeting featured presentations of recent data and analyses, presentations and discussions of ongoing work, presentations of trial result and reviews of published data, and group discussion. The meeting agenda is included in Appendix I.

The meeting was attended by 33 experts; each contributed, not only data, insights, experience and analyses, but also worked to produce a set of recommendations, drafted at the meeting.

The recommendations drafted at Reference Group meetings give UNAIDS and WHO guidance on how best to produce estimates of HIV/AIDS, an opportunity to review current approaches and also help 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. Technical Review of Spectrum 2011

In the last year the Reference Group has provided technical support for the integration of the Estimation and Projection Package (EPP) and Spectrum, the tools used to generate national estimates of HIV, into a single user interface. In response to the changing sources of data, improved understanding of HIV epidemiology and new expectations, for example, estimation of incidence, estimation of the number of people needing ART and PMTCT services, and changing treatment criteria, the models have been further developed in order to accommodate these requirements. In early 2011, Spectrum 4.0 was launched at the regional workshops for use in the 2011 estimates process. Following the workshops, a technical meeting was held in Seattle, on October 20th, 2011 to review the integration process, discuss issues that arose during the workshops, identify the remaining issues and generate recommendations for improvement.

1.1 Summary from Regional Workshops

Overall, there was positive feedback from the regional workshops, and countries appreciate the new software, which is simpler and easy to follow. The estimates and projections are important for countries and are used for programme reporting and evaluation (impact), target setting, resource allocation, ART costing, to generate incidence estimates, to obtain denominators and to calculate coverage levels. From the county perspective, it is important to have confidence in the models and in the results and to be able to explain and justify the reasons why any estimates change. Communication is a key area for improvement. This includes how to interpret and communicate the results, particularly when they had changed as a result of new software or changes made to the software which alter the interpretation of data rather than changes observed in data themselves. Communication of exactly what has changed, how it has changed, and the consequences for the results will help to empower model users to be able to explain any differences in estimates in their countries.

In Asian countries there was positive feedback about the additional two days allocated to address data issues. In other regions, model users requested guidance on issues surrounding data quality and availability, precise definitions for the data inputs and a prioritisation list for key inputs which have the greatest effect on the model outputs. Additional specific issues identified during the workshops and suggestions for improvement are identified below.

Issues identified during the regional workshops:
- Software was not fully tested
- Countries did not have all programme data at the workshop (especially problematic for PMTCT data on postnatal prophylaxis and breastfeeding)
- Not all facilitators were fully versed in the software; no training on Workbook method
- Working papers not up-to-date and did not include all aspects of the models
- Users need simple guidance document, similar to previous Spectrum manual
- Users need guidance on how to change the population
- UNAIDS timeline is very tight and countries also have their data validation process which takes time, thus, extremely tight timelines

Suggestions for improvement (from workshop facilitators and participants):
- Consider having more facilitators present topics in future workshops in order to build rapport
- Enhanced guidance on data quality issues
- Enhanced communication:
  - Software version updates
  - Software modifications/bugs

CC = current change in methods, FR= further research

- Model changes based on new data/analyses
- Explanations for advanced options used
- More detailed explanation to explain: *What has changed? Why? What effect will this have on the results?*

– More emphasis in the workshops on impact
– De-bugged and pilot-tested software before the workshops begin
– Cut-off time point for model software changes
– Incorporate costing into the workshops
– Consider a separate workshop for countries that use Workbook

During the workshops, it was agreed that no changes would be made to Spectrum after a June cut-off date and thus there is currently a "frozen" version of Spectrum available on the internet for countries to use to prepare their files. However, it was identified that there are essential modifications that need to be implemented into the frozen version.

Recommendations:
– **Include only the <u>essential</u> modifications in a (slightly) updated version of Spectrum for the 2011 round of estimates.** CC: Futures Institute, December 2011
– **Enhanced model training for CDC facilitators. US Government will help to support this recommendation.** CC: Anindya De and Rob Lyerla

1.2 Software Information

Countries need better manuals which are up-to-date and simple (similar to the previous Spectrum manual). Specifically, they need guidance on how to change the demographic data, recommendations for how to handle missing programme data, in particular, PMTCT data for postnatal prophylaxis and breastfeeding, and separate information specifically for dealing with data issues in concentrated epidemics. Additionally, it would be useful to have all the necessary, up-to-date information, background documents and model software contained in one place.

Recommendations:
– **Write up the issues identified in the training into formal documentation materials.** CC: EPP team and Futures Institute.
– **Develop a manual on data adjustment for low level and concentrated epidemics.** CC: EPP team
– **Develop a checklist of essential data for countries to bring to the regional workshops.** CC: UNAIDS
– **Create a webpage on UNAIDS site where all information is contained including a quick start guide, working papers, model software, data needed, etc.** CC: UNAIDS

1.3 Model Structure

1.31   <u>Flexible models for force of infection (r)</u>

Model fitting in Spectrum is done through EPP. The EPP 'classic' method obtains a model fit using four parameters. This method puts strong constraints on the structure and results in an inflexible shape which can have difficulties capturing complicated prevalence data, for example, a second uptick of prevalence. As a result new methods were previously considered and the flexible r method ("r-flex") was implemented in Spectrum 4.0. However, during the regional workshops, some issues were identified which led to a review of the

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method currently used, a review of an alternative method and the discussion and consideration of proposed modifications for improvement.

R-flex

For complicated prevalence data, r-flex is able to provide better estimates compared to EPP classic, but the uncertainty increases when making projections. For many countries, the current version of r-flex is too slow to fit (12-20 hours to run for countries with many surveillance sites). It is often too flexible (highly sensitive to prevalence estimates and thus generating incidence patterns deemed unrealistic despite being statistically supported by the data) and it is difficult to explain the advanced options and provide guidance on how to constrain the variance. For concentrated epidemics, it does not work well for very low prevalence or when there are very few data points. There were also country examples where the bounds cross and where the 'best fit' crosses outside the confidence bounds.

Benefits of random walk: parameters are actual values of r (as opposed to spline coefficients), easier to explain to end-users, prediction beyond last year with data can be separated from the model fitting.

R spline

Modelling the force of infection parameter with B-splines. Time-varying force of infection parameter (r) allows fitting of a more diverse set of epidemic trajectories. Use splines to generate curves for r as opposed to a random walk (currently implemented). Spline is a linear combination of base functions; it has the ability to generate a flexible curve from relatively few parameters. B-splines with a second degree difference penalty enforces smoothness in changes in the slope of r. Compared to r-flex, the spline method is conceptually similar, produces similar results for most countries but yields smoother curves for incidence; however, incidence estimates can be extreme in the projections.

Benefits of spline: smoother curves (particularly for the "best fit" curve), penalty offers more structure, fewer parameters to estimate.

Two proposed modifications to the current method employed:
1. Impose some common structure on r(t) (the simple random walk), reduce the variance with a hierarchical model with a hierarchical structure and use more informative prior distributions.
2. Employ Dan Hogan's spline method to obtain the in-sample fit but use Le Bao's random walk method for the projections.

Recommendations

Short term solution for 2011 estimates: Heavily constrain and validate the estimates with the data available.

Longer term solution:
– **Le Bao to develop his proposed modifications and test on appx 30 different countries (including all countries which used r-flex for their estimates).**
– **Dan Hogan to employ his spline method for the fitting and Le Bao's random walk method for the projections and test this method on the same 30 different countries for comparison (fit, projections, speed) with Le Bao's method.**
– **For projections, investigate whether we should consider taking the median value as opposed to the best fit (based on random walk thus best fit might be too random).** FR: Reference Group

Timeline: Reference Group to review results in early February technical meeting

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1.32 Calibration/prevalence adjustment in Spectrum

Spectrum and EPP do not produce the same prevalence for a given incidence curve. When this was investigated in further detail, it was identified that there is agreement for new infections in those 15-49 years and for the 15+ population but that it is the rate of exit of HIV+ individuals at age 50 that is producing the difference in the 15-49 prevalence. EPP currently assumes that this exit occurs with the same turnover as everyone else but it will actually change over time. Note that if you are using the concentrated-IDU epidemic pattern, the number of 15+ will be substantially larger.

Recommendations:

- **Maintain the prevalence calibration in Spectrum for now.**
- **Explore ways of changing over time the rate of HIV+ individuals exiting at age 50 in EPP.** FR: EPP team and Reference Group

1.4 Model Fitting

1.41 "Define Pops"

For concentrated epidemics, users need to define the size/proportion of each sub-population without an HIV epidemic. But countries generally do not have these data and instead enter the total number of IDUs, for example. This will then lead to an underestimate of the IDU population size and thus and underestimate of incidence in concentrated epidemic. For most low level and concentrated epidemics, the additional mortality impacts on the population size are small.

Recommendations: For the longer term, consider alternative options such as a different population model for concentrated epidemics or use of an "adjust fits" function. FR: Reference Group, EPP team

1.42 Regional trends to inform estimates

In concentrated and low prevalence epidemics there can be very limited data for some countries thus it would be useful to have recommendations for regional trends which give some indication of what is occurring such as peak prevalence is specific groups and the timing of increases, decreases and stabilisation of prevalence. More detailed information on specific sub-populations would also be helpful.

Recommendations:

- **Further research on regional trends for specific populations, for example MSM, and summarise these data with the possibility of using this information to constrain prevalence.** FR: UNAIDS, Reference Group
- **Further research to identify heterogeneity in behaviour within populations, for example, the proportion of MSM with higher risk behaviour in different regions, is recommended.** FR: UNAIDS, Reference Group

1.5 Model Parameters and Programme Data

1.51 CD4 Progression Parameters

In order to accommodate different treatment criteria over time and changing guidelines for PMTCT, Spectrum has been modified to incorporate a CD4 "bin structure" with progression through these CD4 count bins once infected. The current progression parameters used in Spectrum were obtained by fitting, done to match the Alpha network progression from new infection to AIDS deaths and to match data for those defined as "in need" of ART. Compared

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to the CD4 progression data currently available, the parameters used in Spectrum progress more slowly which would imply that Spectrum has the potential to underestimate treatment need. Conversely, the complaint from many countries is that Spectrum is overstating need for treatment.

Recommendation: More data are needed to better understand CD4 progression. Request further data from Africa Centre, IeDEA consortium, Connie Celum group and await Uganda AIS data and review when available (cross-sectional comparisons). FR: Reference Group, Futures Institute

1.52   Fertility rates of HIV+ women

Age specific fertility rate ratios of HIV+ and HIV- women were derived from a meta analysis of DHS surveys that tested for HIV. However, the 15-19 year old age group requires adjustment due to likely differences in sexual activity. A linear function was previously used for adjustment but this resulted in lower rate ratios (compared to 20-24 yr olds) in some countries where a high proportion of 15-19 year olds were sexually active.

Recommendation: Neff Walker to provide Futures Institute with the updated log fit model for the 15-19 year age group to replace the linear fit method. CC: Neff Walker, Futures Institute

1.53   Mortality parameters in Spectrum

The IeDEA consortium has routinely collected clinical data from sub-Saharan Africa and the Asia Pacific region with additional data expected from South America, Mexico and EuroSIDA. These data will be used to inform adult and paediatric survival on ART, paediatric ART and CD4 distributions with the potential of generating regional patterns. Data for 2nd line treatment will also become available.

Recommendation: Reference Group to review all results when available; discuss patterns and how to use them to inform the parameters in Spectrum.

Timeline: C Yiannoutsos to complete analyses completed by end of December, Ref Group to review and make decision Jan/Feb.

1.54   Programme Data

Many countries do not have data for the PMTCT section, in particular, the postnatal prophylaxis and breastfeeding section. Additionally, ART for pregnant women input is not linked to adults on ART (at request of the countries) which can be confusing.

Recommendations:
-   **Consider default values or dropout rates for the postnatal section as many countries did not fill these sections in.** CC: Futures Institute
-   **Incorporate a link or a reminder note to flag ART for pregnant women to ensure countries fill these values in.** CC: Futures Institute

1.6 Model Outputs

1.61   Sub-national estimates

Countries are increasingly interested in generating sub-national estimates, to better inform programme planning and resource allocation. For many countries, the urban/rural dichotomy is not useful, as it is not well defined and does not follow the epidemic distribution. However, in order to generate individual Spectrum files for each district/region, countries will need detailed demographic data which are often not currently available.

Recommendations:

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- **Countries should be encouraged to analyse their ANC trends and see if they cluster (by province, some other factor). If so, they may want to not consider using a single national file but instead breaking down by districts/region.**
- **US Census Bureau, with the support of OGAC, should work on sub-national demographic estimates, creating a tool kit with recommendations for methods to use.**

1.62   Mortality Outputs

Countries in Latin America have articulated that Spectrum is over-estimating mortality (note that alternatively, prevalence may be overestimated). Brazil and Argentina have done a reconciliation process, analysing mortality reports to generate a revised mortality estimate which resulted in general agreement with Spectrum estimates.

Recommendations:

- **Continue with this work as something to check against and look at as comparison.**
- **Adjusted mortality could be added into Spectrum, solely to allow for comparison with estimated mortality, thus any discrepancies would be identified at an earlier stage.**

1.63   Estimates of treatment need

The new model structure results in different estimates of need (for PMTCT for ART) for 2009 compared to the estimates obtained using the previous version of Spectrum. Therefore, ART coverage values already published in the Universal Access report are not the same as the estimates obtained from Spectrum 4.0. This creates difficulties for countries as they strive to reach Universal Access targets and have different estimates for the same year as a result of the different models. Further, if there is disagreement with the estimates obtained for treatment need, then this can result in disagreement with the level of treatment coverage calculated. Because the models have changed, countries are unable to compare trends over time and this can lead to distrust of coverage figures.

Recommendation: Conduct further research into countries that have large discrepancies – check the plausibility of all estimates (births, prevalence, ANC coverage). FR: UNAIDS

1.64   Need for PMTCT and PMTCT coverage estimates

Countries with high coverage of PMTCT often have more women receiving PMTCT (taken from programme statistics) than the model estimates of those in need of PMTCT, which results in coverage greater than 100%. Are we underestimating HIV+ pregnant women? Are the numbers from programmes too high? Should there be a higher female:male ratio? It was discussed that Spectrum is no longer using DHS data for the sex ratio of incidence and is instead using 1.4 as standard which could be the problem.

Recommendation:

- **Compare results when using the country-specific prevalence ratio and when using data from DHS.** FR: UNAIDS, Futures Institute
- **In Spectrum, add a warning flag for countries with national survey data to remind them to update the sex ratio.** CC: Futures Institute

1.65   Standardised metrics of change

In interpreting model outputs, it would be helpful to have something for countries to latch on to as opposed to comparison of a previous report to a new report, thus standardised metrics of change with an uncertainty interval around the change that has occurred may be very useful. This would require the identification of metrics to focus on as standard. One suggestion was the absolute change-in prevalence in 2 years and the uncertainty around this change.

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Recommendation: Working group to discuss standardised metrics of change and identify specific metrics and to consider including this in the 2013 round of estimates. FR: Reference Group and UNAIDS to follow-up.

1.7 Model Testing

A key element to improve the estimation process is to have the model fully tested and de-bugged before the regional workshops begin. The use of Unfuddle to organise issues that arose with the software was useful for the first two months but was less useful during the workshops when you need urgent answers and have multiple issues.

Recommendations:

– **Review of code is essential; repeat this process with Peter Johnson and Leigh Johnson.**
– **OGAC will help to support model testing by identifying the Census Bureau as an instrumental component of code review.** CC: OGAC
– **Generate a model testing schedule, working backward from June deadline.** CC: Reference Group, UNAIDS
– **Define a standard set of tests that need to be run each time there are updates.** CC: Futures Institute and EPP team
– **Conduct analyses on new software to determine if results are similar to previous years, if results match expectations for MTCT rates, deaths averted, changes in prevalence, etc.** CC: UNAIDS, Futures Institute and EPP team
– **Model reviewers to allocate a priority list of modifications/fixes to be made.** CC: Peter Johnson and Leigh Johnson
– **Named and contracted model testers for greater accountability.** CC: UNAIDS

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2. Indentifying sources of bias in population-based household survey data

New methods and analyses [1] suggest that there is the potential for selection bias to have an effect on HIV prevalence estimates obtained in population-based surveys if unobserved factors are associated with both participation and HIV status. This is an important consideration for national estimates of HIV as the current methods often calibrate to the prevalence levels obtained from Demographic and Health Surveys (DHS).

2.1   HIV testing in the DHS
        DHS data are nationally representative sample surveys. Since 2001, certain surveys have included HIV testing with sample sizes ranging from 8,000 – 15,000. In 2003, MEASURE DHS launched the AIDS Indicator Survey (AIS), an independent survey dealing only with HIV/AIDS issues. The blood collection for HIV testing in these surveys may be carried out by interviewers, nurses or health technicians. Consent for biomarker collection occurs after the individual interview has been completed. This consent may be obtained by the interviewer who conducted the individual interview, another interviewer who did not conduct the individual interview, or by a nurse or health technician whose only responsibility is biomarker collection. Therefore, there are two categories of non-response – non-response to the individual interview and non-response to HIV testing.

        Note that MEASURE DHS does not adjust any results in the country reports; these adjustments happen later. For HIV prevalence estimates, DHS look at potential bias due to non-response and statistical models are used to predict gender-specific prevalence for those who complete an interview but do not consent to HIV testing and those who do not have an interview or HIV testing.

2.2   Heckman-type selection models to account for selective non-participation in HIV testing surveys
        The conventional approach to correct for selection bias in HIV prevalence estimates generally suggests non-participation is not a major cause for concern. However, it is possible that unobserved factors influence the decision to participate in HIV testing surveys. Initial work conducted by Barnighausen et al [1] corrected for selection on unobserved factors in the Zambia 2007 DHS data using Heckman-type models and found a significant effect for male prevalence. This work was then replicated for other countries in sub-Saharan Africa to identify:
          – If the findings are consistent across surveys
          – If the selection model suggests there is cause for concern for potential effect of selection bias
          – The 95% confidence intervals for uncertainty in selection model parameter estimation
        While this work is ongoing, preliminary results suggest that HIV prevalence could be underestimated in some countries, which could affect estimates of HIV incidence and treatment coverage. However, the findings are not consistent across surveys and the models indicate the relationship between HIV status and participation in HIV testing varies (and can go in either direction). The use of conventional imputation methods may also underestimate uncertainty around HIV prevalence in many countries (because they do not take into account parameter uncertainty).

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The main limitation of this method is that the model is sensitive to violations of its assumptions – the selection variables must be relevant predictors of selection, but not predictors of HIV status.

Replication work is also ongoing by another research group and includes the following aims:
1) Conduct a simulation study to characterise:
    a) How well the model estimates prevalence when selection criteria are met
    b) Evaluate how poorly the model estimates prevalence when the selection criteria requirements are not met
    c) Explore the performance of the model in more detail
2) Replicate the Barnighausen et al [1] analysis using the 2007 Zambian DHS and then expand to analyse other DHS data.

Discussion

Further work is needed to validate the findings of this initial work. However, it is clear there is additional uncertainty that we are currently not capturing in Spectrum. Before makng any changes this is something that we first need to validate and better characterize. Heckman methods likely provide a better estimate of this uncertainty, but there is concern over whether the assumptions of the Heckman model are maintained in the analyses. We need to ensure that the adjusted prevalence from DHS data are used when fitting models. We should also reconsider driving the likelihood through the point estimate obtained from nationally representative household surveys, but will need more work here in order to make this decision.

Immediate recommendation:
– **For now, maintain current methods**

Short-term recommendation:
– **Identify why there are differences in results between the two groups using Heckman methods.**
– **More work to identify the best selection variables and to obtain a better understanding of the variance and how to adjust the variance in DHS results and how this can be incorporated into Spectrum. Continue with this work for implementation in the 2013 round of estimates.**
– **Identify the differences in the confidence interval of the DHS estimate when using the increased variance in the estimate from DHS. Identify whether we should change the confidence intervals around DHS or include the increased variance.**

Timeline: Meeting in WA DC, convened by OGAC to review the results from Sam Clark's team and Dan Hogan's group. Meeting in February to discuss the implementation issues (based on Jan meeting)

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3. ANC prevalence trends compared to DHS data

In many countries, HIV prevalence in men is different from HIV prevalence in women, which may suggest the epidemic is happening differently by sex and thus there may be differences in trends in ANC compared to DHS data. This would then imply that ANC data might not be a good marker for trends occurring in men. To date, there is no population based survey with a significant decline in both men and women; there are also inconsistent changes in behaviour when disaggregated by sex.

The current methods used to generate national estimates of HIV, combine DHS data together (male and female) which is essential due to the scarcity of representative datasets for men. Therefore, the fitting of epidemics is heavily dominated by the female trend. If ANC trends are significantly different from trends observed in population-based surveys, we may need to consider giving more weight to the latter when generating national estimates of HIV. It was agreed that it is still unknown whether there actually are different trends between males and females. In order to compare, countries will need 3-4 nationally representative surveys, and then we can start to think about fitting epidemic curves for men and women separately, if warranted. It was discussed that a potential future improvement would be to restrict on age the ANC data that is used in the models. This would handle the evolving biases, but would not capture the sex difference. At this time, it is unlikely that we can extract this information for most countries. We would also then need to change the entire fitting process and weighting, and reconfigure EPP.

The Alpha Network is uniquely poised to be able to assist with many of the necessary questions for investigation and further research, thus a specific list of research questions was produced for this group to consider in order to inform the methods used to generate national estimates of HIV. These questions include:

- What happens to fertility of HIV+ women when on treatment?
- Is there a shift in fertility observed in ANC in the ART era - especially if policy is adopted that all pregnant women should be on ART regardless of CD4 count?
- What is the desire for children when HIV+ in different settings? And are there shifts in trends (potentially as a result of country recommendations)?
- What is the relationship between PMTCT coverage and biases in who is attending ANC?
- What proportion of women use oral and injectable contraception across different settings?

Recommendations
- **This is an important surveillance question, but we need more DHS data and should also look at the Alpha Network data.** FR: Reference Group
- **Consider recommending regular national population surveys if countries have high prevalence.**

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4. HIV risk surrounding contraception and pregnancy

There is additional evidence, recently published, of increased risk of both acquisition and transmission of HIV when pregnant [2]and also as a result of hormonal contraception use, importantly, injectable contraception.[3]

The data from a prospective cohort study of 3790 HIV-1 discordant couples from East and southern Africa was used to compare, among women using and not using hormonal contraceptives, the incidence rates of HIV-1 acquisition in women and HIV-1 transmission from women to men. Hormonal contraception was associated with a 2-fold increase in risk of HIV-1 acquisition by women, and HIV-1 transmission from women to men. Increased HIV-1 risk was found among the subgroup using injectable contraceptive methods. Risk was also elevated among oral contraceptive users but the sample size of oral contraceptive users was small.

It is also possible that physiological changes that occur during pregnancy (such as high levels of progesterone), may increase the risk for women to acquire HIV-1 during pregnancy and pregnant HIV-1-infected women to transmit the virus to their sexual partners. Sexual behavioural factors of women who become pregnant may also predispose to HIV-1. To investigate these hypotheses, data obtained from the Partners in Prevention HSV/HIV Transmission study, a prospective study of HIV-1 serodiscordant couples (N=3321), were analysed to assess the relationship between pregnancy and HIV-1 incidence, for both acquisition among women and transmission from women to men. An approximately 2-fold increased HIV-1 risk during pregnancy was found for both uninfected pregnant woman and for the uninfected male partners of infected pregnant woman. For HIV-1 acquisition in women, adjustment for sexual behaviour reduced the risk estimate (unadjusted HR 2.3, adjusted HR 1.7), which suggests sexual behaviour may play a role. For transmission to men, the risk estimate remained statistically significant (and increased slightly) with adjustment for sexual behaviour (unadjusted HR 2.3, adjusted HR 2.5)

Recommendation: Incorporate increased risk during pregnancy into the incident infection parameter for HIV acquisition among pregnant women in the table of MTCT rates in Spectrum. CC: Futures Institute

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REFERENCES

1.   Barnighausen T, Bor J, Wandira-Kazibwe S, Canning D. Correcting HIV prevalence estimates for survey nonparticipation using Heckman-type selection models. *Epidemiology* 2011; **22**(1): 27-35.

2.   Mugo NR, Heffron R, Donnell D, et al. Increased risk of HIV-1 transmission in pregnancy: a prospective study among African HIV-1-serodiscordant couples. *Aids* 2011; **25**(15): 1887-95.

3.   Heffron R, Donnell D, Rees H, et al. Use of hormonal contraceptives and risk of HIV-1 transmission: a prospective cohort study. *The Lancet infectious diseases* 2012; **12**(1): 19-26.

Appendix I: List of Participants

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Appendix II: Meeting Agenda

UNAIDS Reference Group on Estimates, Modelling and Projections
Technical Review of Spectrum 2011

Thursday, October 20th, 2011

Start	Duration	Subject	Speaker
830	*30*	*Coffee/tea available*	-
900	15	Opening remarks and introductions	Peter Ghys
Session 1 - Spectrum 2011: Summary from workshops and discussion on the implementation process (Chair: Peter Ghys)			
915	20	Summary from regional workshops	Karen Stanecki
935	10	Discussion	-
945	15	Workshop experiences: Feedback from CDC facilitators	Anindya De
1000	15	Workshop interviews: Feedback on use of the model and model results from the sub-Saharan Africa workshop	Kelsey Case
1015	*20*	*Coffee break and light refreshments*	-

1035	20	Group discussion: The implementation process
		   - *What worked well?*
		   - *What did not work?*
		   - *If we were to do this all over again, what would we do differently?*	

Session 2 - Spectrum 2011: Technical Issues, (A) Review of R-flex, (B) CD4 progression, (C) IeDEA Consortium (Chair: Adrian Raftery)			
1055	20	Review of R-flex: Country-specific examples from workshops	Karen Stanecki
1115	30	Review of R-flex: Update and ongoing work, recommendations for how to constrain incidence	Le Bao
1145	20	Review of spline method and results from application with countries that had r-flex challenges	Dan Hogan
1205	20	Discussion	-
1225	15	CD4 progression: Progression parameters currently used in Spectrum and review of methods used	John Stover
1240	15	CD4 progression: Review of data available, CASCADE analysis and further considerations	Jeff Eaton
1255	15	Discussion	-
1310	20	IeDEA Consortium: New analyses and data available and implications for model parameters	Constantin Yiannoutsos
1330	10	Discussion	-
1340	*35*	*Lunch*	-
Session 2 - Spectrum 2011: Technical Issue cntd, (D) Generating estimates, (E) Mortality, (F) Estimates of MTCT & validating PMTCT data (Chair: John Stover)			
1415	15	Generating estimates: Review of results from countries generating sub-national estimates	Karen Stanecki/Mary Mahy
1430	15	Discussion: *Is the urban/rural division for generating estimates still relevant? Should there be a move to provincial estimates?*	-

1445	15	Mortality: Country comparisons of demographic data and modelled estimates	Child	Karen Stanecki
		Estimates: Issues related to estimates of children in Spectrum		
1500	10	Discussion		-
1510	10	TFR discount: Review of methods and update from DHS data		Neff Walker
1520	15	Validation of PMTCT/ART need estimates; country expamples of issues identified and implications		Txema Calleja
1535	10	Discussion		
1545	*20*	*Coffee break*		-
Session 4 - Update from EPP and Spectrum teams: Outstanding issues, work in progress, new developments (Chair: Josh Salomon)				
1605	20	EPP team		Tim Brown
1625	10	Discussion		-
1635	20	Futures Institute Team		John Stover/Carel Pretorius
1655	10	Discussion		-
Session 5 - Model testing (Chair: Josh Salomon)				
1705	20	Group discussion: Model Testing *- How do we do testing?* *- What worked well?* *- What do we still need to address?* *- Was Unfuddle useful?*		
1725	20	Model Testing: Review of ouststanding issues identified		Peter Johnson
1745	10	Discussion		-
1755	5	Wrap-up and close		Geoff Garnett

UNAIDS Reference Group on Estimates, Modelling and Projections

Quantifying sources of bias and new insights on risk of HIV infection

Friday, October 21st, 2011

Start	Duration	Subject	Speaker
800	*30*	*Coffee/tea available*	-
830	10	Opening remarks and introductions	Geoff Garnett
Session 1 - Quantifying souces of bias (Chair: Geoff Garnett)			
840	20	Methods used to prevent, and correct for, bias in DHS data	Noah Bartlett
900	10	Discussion	
910	20	Heckman-type selection models: Overview and rationale for use, results from sub-Saharan Africa	Dan Hogan
930	10	Discussion	
940	20	Heckman-type selection models: Rationale for replication of T Barnighausen work, methods used, project plan	Sam Clark /Brian Houle
1000	10	Discussion	
1010	*20*	*Coffee break and light refreshments*	-
1030	30	Discussion of this work, implications for estimates, recommendations	
Session 2 - Trends in ANC prevalence and data from cohorts (Chair: Txema Calleja)			
1100	20	Review of ANC prevalence trends	Mary Mahy
1120	10	Discussion	
1130	25	Trends in ANC prevalence atttendees compared to DHS; mathematical modelling to assess the validity of ANC prevalence trends historically (pre-ART) and in the ART era	Kim Marsh/Tim Hallett
1155	10	Discussion	
1205	25	ALPHA network data -- HIV prevalence in pregnant women compared to women in the general population; fertility in the ART era	Milly Marston
1230	10	Discussion	
1240	20	Discussion of this work, implications for estimates, recommendations	
1300	*60*	*Lunch*	-
Session 3 - HIV risk surrounding contraception and pregnancy (Chair: Neff Walker)			
1400	20	Hormonal contraception and risk of acquisition and transmission of HIV	Renee Heffron
1420	10	Discussion	
1430	20	Pregnancy and risk of acquisition and transmission of HIV	Jared Baeten
1450	10	Discussion	
1500	25	Discussion of this work, implications for estimates, recommendations	
1525	*20*	*Coffee break*	-
Session 4 - Final discussion and consensus recommendations (Chair: Geoff Garnett & Peter Ghys)			
1545	35	Further analyses needed, recommendations for how to proceed, proposed timeline	
1620	10	Final comments	
1630		Close	