Improving the EPP and Spectrum estimation tools for the 2008-9 round of national estimates with specific attention to prevalence fits and their uncertainty, changes in the urban:rural population ratio, bias in HIV prevalence measured in national surveys, incidence estimates, orphanhood estimates, effects of ART; and a discussion on concurrent partnerships

Report of a meeting of the UNAIDS Reference Group on Estimates, Modelling and Projections held in London, 28th and 29th of February 2008.

TECHNICAL REPORT AND RECOMMENDATIONS

Joint United Nations Programme on HIV/AIDS

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The meeting of the UNAIDS Reference Group on Estimates, Modelling and Projections (the 'Epidemiology Reference Group') was organised for UNAIDS by the UK secretariat of the Reference Group (www.epidem.org) based at Imperial College London. Participants of the meeting are listed at the end of this document. The recommendations in this document were arrived at through discussion and review by meeting participants and drafted at the meeting.

Annick Borquez, London, May 2008.

Introduction

The Reference Group on Estimates, Modelling and Projections
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 United Nations and 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 (www.epidem.org).

Aim of the meeting
The aim of this meeting was to bring together experts to produce recommendations on how to improve the accuracy of prevalence as well as incidence estimates, focussing on specific issues which have emerged in past estimation processes and to refine the methods regarding the inclusion of ART in the models. Another priority was to review orphanhood estimates as well as the current knowledge on the relationship between concurrency and HIV.

Approach
The meeting featured both presentations of recent data and group discussions, which focused on specific technical issues. Presentations and discussion topics are listed in Appendix I.

The meeting was attended by 48 experts (see Appendix II for a list of participants). Each contributed, not only data, insights and analysis, but also worked hard to produce a set of recommendations, drafted at the meeting. We would like to thank them for their hard work and attendance 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.

Improving EPP

EPP prevalence trends for some countries (e.g. Kenya, Cambodia) imply zero incidence in Spectrum which is not realistic. Also, unusual trends where the epidemic is levelling off such as in Uganda or South Africa are not being picked up by the model. The assumption is that EPP captures the full range of dynamics of the epidemic, however it can not reproduce the impact of behaviour change taking place over its course.

1. Improving the efficiency of parameter search in Bayesian melding

Possible solutions to improve EPP model fits have been proposed in previous meetings, including allowing increased flexibility in the EPP parameters (R jump, R drift, R drift + Phi jump or unconstrained) which would increase the number of parameters and thus the computational demand. In response to this, Incremental Mixture Importance Sampling (IMIS) was proposed as an alternative to sample parameters with much better efficiency. This method also allows a better representation of the possible trajectories of prevalence curves than Sampling-Importance-Resampling (SIR), the method used currently, which sometimes produces few unique curves. The newly proposed algorithm is as follows:

-Start with SIR as in the current EPP but sampling fewer parameter vectors θ from the prior (500 often enough; 5,000 almost always enough).

-Find the input parameter vector with the highest weight, θ^{high}.

-Draw B new points from a multivariate normal distribution centred on θ^{high}. (for instance B= 500). Combine them with the previous set of points.

-Form new weights = prior density*likelihood / importance sampling function (a weighted average of the previous prior distribution and the new multivariate normal distribution).

-Repeat until there are no large weights.

-Resample from all the parameter vectors sampled, with the weights.

The method was tested for Ghana with very encouraging results, the number of unique points increased by over 300 fold, the maximum weight decreased considerably and the efficiency improved dramatically. Importantly, the method allowed for the median to be different from the lower bound which was not the case when using the current methodology.

Recommendations:

- Test IMIS for a few countries for which there are known concerns about multiple local maxima to make sure this sampling approach works.
- Generate and test the code and if successful implement in EPP.

2. Improving the fit of the EPP model to country data:

a. Application of the r-jump model

The r-jump model, which involves changing the value of r at a certain point in time, was explored for urban Kenya, urban Uganda, urban Rwanda and South Africa. The models were fit using Bayesian melding with the new IMIS method and compared to the standard EPP models via Bayes' factors (Bayes factor= Prob(Data|Model2) /Prob(Data|Model1) where Prob(Data|Model1) can be estimated from the Bayesian melding output as the average of Likelihood(θi)* Prior(θi) / Importance Sampling Function (θi)). The results indicated that the r-jump model offered a better approximation to the data for all modelled epidemics, and especially for Uganda and South Africa. Model combination via Bayesian Model Averaging (BMA) was proposed as a solution if there was uncertainty about the choice of the model, this gives a

weighted average of the posterior distributions from the models. However, although the method provides a solution to the problems encountered by some countries, it is not ideal. Firstly because it gives an odd irregular aspect to the curve at the r-changing point and secondly because similar curves can be obtained by either increasing or decreasing r, suggesting caution must be used when modifying this parameter.

Recommendations:

- Implement "r-jump" in EPP for use during the upcoming estimation round (2008-2009) as a short term solution.
- Explore constraints of r-jump to avoid nonsensical fits.

b. Relaxing the structural assumptions

In the long term, the plan might be to relax the structural assumption which currently divides the population into a low and a high risk group and where the resupply is determined by the parameter phi. Since most infections and deaths occur in the high risk group and there is no migration from the low to the high risk group, phi needs to be modified to increase the number susceptible in this group and obtain the expected number of new infections. This is not an accurate representation of the distribution of risk behaviours in generalised epidemics and it imposes constraints on the estimation process. An alternative solution is to have one group only and to allow for differences and changes in sexual behaviours by increasing the flexibility in parameters (r in particular).

Recommendations:

- Relaxing of the structural assumptions to be explored/developed by Josh Salomon
- Convene a special meeting to revisit the modelling (including models with relaxed structural assumptions as above) in time for the 2010 round.

c. Inferring parameter values from behavioural data

As part of exploring this issue, it was investigated whether behavioural data could serve to infer parameter changes in EPP. General declining trends in behavioural indicators such as age at first sex and fraction of young people reporting premarital sex are not consistent with positive values of phi in many EPP country models suggesting that these have a limited use in this context. Although trends in indicators such as percentage of men and women reporting high risk sex without a condom are consistent with prevalence trends this can not be used to quantify a particular parameter in the model.

d. Grouping sites according to their prevalence trends

Still in the context of addressing and preventing zero incidence curves, the EPP model assumes that one curve shape defines the overall epidemic, meaning that each site is fit using a multiplier applied to this one shape and the likelihoods for fitting use this. This is misleading as different prevalence trends are observed at different sites, and assuming a common trend forces the model to choose the sites that have more weight, which in some cases results in unrealistic or atypical prevalence and hence incidence trends. Grouping sites according to their trend and fitting these separately in EPP corrects for this problem. It is not clear yet how populations will be applied to the groupings and there are concerns about having a replicable algorithm for defining groupings.

Recommendation:

- The possibility of grouping sites according to their prevalence trends needs to be further explored, to address the above issues and concerns.

3. Incorporating demographic changes: urban/rural population ratio

In the same way that EPP does not incorporate behaviour change, neither does it account for temporal demographic changes such as urbanization. As urban and rural regions exhibit differences in prevalence, changes in the urban:rural population ratio, which is used to combine the prevalence of both populations, may have an impact on the value of the total prevalence, but especially on the trend over time.

Recommendations:

- Allowing a changing urban-rural population ratio should be a user defined property of EPP. This should make it possible to specify the population distribution across sub-populations for as many time points as the user wants.
- The changing ratio should not be used in EPP fits, but should be incorporated when combining rural and urban prevalence to give the final prevalence.

4. Biases in HIV surveillance data

The identification of biases and of their magnitude in prevalence estimates from ANC data and from national population surveys is a dynamic process as data collection methods, prevention programmes and treatment coverage evolve over time. Discrepancies between the two sources of data need to be constantly revisited. The availability of ART and the expansion of VCT programmes are two important factors that could affect attendance at ANC clinics. This has been explored but it is too early to make conclusions as both ART and VCT are still in their early phases in many countries, this issue was addressed during the session on Spectrum.

In the same context, another potential bias in HIV prevalence estimates is the non-response bias due to the mobility of absentees in national population-based surveys. A study by Mishra and colleagues carried out in 2006 found that adjusting for non-response made little difference to estimated national prevalence. However, higher prevalence of HIV in mobile groups has been frequently reported. To address this issue, analyses looking at the association between mobility and HIV risk in DHS and AIS data from Côte d'Ivoire, Ethiopia, Ghana, Haiti, Kenya, Lesotho, Malawi, Rwanda and Zimbabwe were carried out by Milly Marston, Kaveri Harriss and Emma Slaymaker. HIV status of non-responders was predicted using various logistic regression models depending on the information available. Using the predicted HIV status of non-responders, adjustments were made to national prevalence estimates. A non-significant but positive trend was found for mobile men and women in most countries but this did not generate significant differences between observed and predicted HIV prevalence estimates. There is then no solid evidence that non-response is an important bias in household surveys.

Recommendations:

- National surveys should explore bias in the HIV prevalence estimate and include the analysis and result in the report.
- When producing national estimates, HIV prevalence should be corrected for known bias (as per above methods). The corrections should be discussed in the UNAIDS estimation training workshops and in the country consensus meetings.

Estimating incidence and changes in incidence

Incidence should be the key indicator to assess the course of an epidemic. However, it is difficult to obtain this value for HIV due to its long asymptomatic period. The gold standard to measure HIV incidence is still the prospective cohort study where individuals are tested for HIV at relatively short intervals. However, this is a very expensive and difficult process, hampered by loss to follow up and other difficulties. An alternative has been to infer incidence from new AIDS cases, however this does not provide information on recent infections and data on AIDS cases notification is scarce in many countries. Prevalence measures are much more readily available and although they incorporate old as well as new infections, and are intrinsically dependent on current AIDS mortality rates, they are a function of incidence. It is then possible to infer incidence from prevalence data. Currently incidence is derived in Spectrum from prevalence which is calculated in EPP. New methods for estimating incidence from prevalence as well as the current status of incidence assays were addressed in this meeting.

1. Estimating incidence from prevalence

The expansion of demographic health surveys with HIV testing and other population based surveys represents a novel source of data to calculate incidence estimates. Analytic methods have been developed that make use of this data with the intention to bypass the biases associated with ANC data such as sub-fertility due to HIV, or selection bias of ANC sites. Two types of methods were presented, one that infers incidence from a single survey, developed by Meade Morgan and colleagues and one that infers incidence from two surveys, developed by Tim Hallett and colleagues. The first method is based on the following equation: $I_a = \frac{P_a - P_{a-1}}{1 - P_{a-1}/100}$ where I_a and P_a are the

incidence and the prevalence per 100 at age *a* respectively and P_{a-1} is the prevalence at age *a-1*. Prevalence as well as population size are adjusted for cumulative deaths assuming steady incidence. The advantage of this method over the method used in EPP and Spectrum is that it provides confidence intervals. To provide a measure of uncertainty of incidence estimates in Spectrum, plausibility bounds are obtained from Monte Carlo simulations varying prevalence trends from EPP as well as progression times of treatment eligibility and of AIDS death, age pattern and ART survival but this is not ideal. The method was applied to PBS data from Kenya, Uganda and Malawi and the results obtained were comparable to those from EPP and Spectrum, suggesting that it could be used as an alternative method. It is however important to keep in mind the limitations inherent in this method, firstly the influence of the assumptions increase with age, also it assumes constant incidence which is not valid in many epidemics, it is very dependent on the smoothing methods and does not correct for the changes in mortality caused by the effect of ART.

The second method described in Hallett et al 2008 (PLoS Medicine, April 2008) uses two consecutive surveys and infers incidence from prevalence in an “age-cohort” observed at two time points using demographic accounting. Although the same individuals are not followed through time, they are sampled from the same population and are assumed representative. To estimate the number of new infections it is necessary to account for mortality in both infected and uninfected individuals. This can be done either by using locally-collected cohort mortality rates among those infected or by using the distribution of survival after infection which might be more generalisable but harder to accomplish. The method has been tested with simulated

data and with data from the Manicaland, Masaka, and Kisesa cohorts giving good estimates and capturing incidence level and pattern well. As for the previous model, the estimates differ more from observed rates at older age groups. The method has been implemented in a Workbook and both ways of estimating mortality rates were incorporated as these retrieved similar results.

Recommendations

- One of the above methods should be applied routinely to national survey data; however no preference for either of the two was expressed as it was pointed out that the choice will depend on the data available. Few countries have completed more than one population based survey; but this is likely to change in the following years. The Morgan et al method can be used when only one survey is available but makes many assumptions about trends in incidence.
- Further tests need to be carried out to check whether the methods are generalisable as they have only been applied to African settings.
- For countries with generalised epidemics, the age-specific incidence in Spectrum should be distributed on the basis of age-specific incidence rate estimates derived from applying the Hallett et al method to the country-specific data (in the case of countries that have one or more national surveys) or to the data of all countries with a national survey (in the case of countries that do not have a national survey).

2. BED assay update

Incidence-assays that could differentiate recent HIV infections from older seroconversions represent an ideal method to measure incidence as they would spare the numerous difficulties characteristic of prospective cohort studies as well as the uncertainty intrinsic to modelling estimates. Several assays have been developed in the past years; however, calibration, misclassification and validation problems have hampered their implementation on a large scale. These three basic concepts of incidence assays have been explored in a literature review carried out by Rebecca Guy and John Kaldor from the NCHECR which will available soon. Calibration consists in determining the cut-off of the lab assay to define the window period that will be detected as recent infection (e.g. for the BED assay the window period goes from seroconversion to an antibody proportion cut-off resulting in a duration of approximately 155 days). Misclassification, better described as performance characteristics is the sensitivity and the specificity of the test which are tested by applying the assay to samples for which the duration of infection is already known. Validation is the comparison of incidence rates measured in a population with the assay and with a different method believed to be reliable. The main issues which emerged from this review were that uncertainty around window periods was often large, that few assessments concerning the effect of long lasting infections and of ART on performance characteristics had been done and that there was a great variation in the way the comparisons had been undertaken to validate the assays, with limited reporting of the virus subtype and sample numbers. Validation of incidence assays should ideally be done through longitudinal cohort studies with continued follow-up for incident seroconverters and follow-up of persons already HIV-infected at screening for at least 1 year. Suitable studies include HIV vaccine preparedness cohorts and HIV prevention intervention trials (e.g., Thai BMA; VaxGen trials; ZVITAMBO, IAVI). There is then scope for further work before incidence assays can be considered for gold standard for incidence estimation. However their reliability has certainly improved and some have started to be used routinely.

Recently, application of the BED assay for HIV incidence surveillance has been put in place in China, Thailand, Cambodia, Zimbabwe, South Africa, Ethiopia, Cote d'Ivoire, Botswana, Kenya, Uganda, Zambia, and Honduras. The BED assay detects recent infections; however, it also detects late stage infections as it relies on the weak antibody response occurring at the beginning of the infection which is also observed at late HIV stages due to the deterioration of the immune system. Two adjustment formulas developed by McDougal et al. (2006) and Hargrove et al. (2008) to correct for misclassification have been recommended by OGAC. The first adjusts for false long-term infections and for false recent infections in the one year window period and over one year. The Hargrove adjustment factor only adjusts for false recent infections which occurred over one year earlier. Adjustments have only been validated for HIV-1 subtypes B (Zimbabwean females) and C (MSM in Amsterdam); therefore interpretation in other subtypes, countries and populations remains unclear. Other assays such as the avidity enzyme immunoassay and the rapid HIV-ID test are under development and could be used in an algorithm along with the BED assay.

Recommendations:

- Incidence estimates derived on the basis of laboratory assays for recent infections should not yet be used to calibrate incidence in Spectrum, as they do not yet offer the required level of validity,
- Incidence estimates obtained from mathematical models could be used to invalidate lab-based estimates but not yet to validate them.

Spectrum: effects of ART and uncertainty

ART causes changes at different levels of the epidemic, one of them is that it increases life expectancy of HIV positive individuals resulting in an increase in prevalence, however this does not happen homogeneously across ages and sexes making it harder to interpret the consequences. ART's impact on life expectancy is known, from ART-LINC studies, to be dependent on the CD4 cell count at the start of treatment (other study: *ART CC, JAIDS 2007)*. Additionally time to ART eligibility is dependent on the age at infection: people infected younger have a slower progression to AIDS (Collaborative Group on AIDS Incubation and HIV Survival and including the CASCADE EU Concerted Action, *The Lancet,* 2000). These dynamics are currently not taken into account in Spectrum.

1. Estimating number of people in need of treatment

Currently ART is incorporated in Spectrum by assuming that eligibility for ART occurs 3 years prior to death. As median survival time is estimated to be of 11 years in both developed and developing countries, ART eligibility is assumed to start at a median of 8 years post infection. To calculate the number of people in need of treatment, the distribution of the time since infection is inferred from the incidence curve. The distribution of progression to ART eligibility and the survival distribution are applied to this curve and the overlap between those eligible for treatment and those still alive are considered to be in need of treatment. This includes both the people on treatment and the people in need of treatment, but who have not yet receive it. The proportion of people on treatment is estimated from in country data so it is then possible to infer the proportion of those in need of treatment who have not received it. Eligibility for ART, however, is not a simple function of time since infection. As said previously, it is also dependent on the age at infection. There is no evidence that sex has an effect on progression to AIDS, but as women generally become infected at a younger age, they progress to ART eligibility slower, but this is actually an effect of age at infection rather than an effect of sex.

Recommendations

- Investigate whether using age-specific patterns for progression from infection to need for treatment introduces big differences between EPP and Spectrum

2. Estimating death rate post ART

Currently, death rate post ART is only dependent on the time from start of ART, i.e. 20% mortality is assumed for those who started treatment under one year ago and 10% mortality for subsequent years. As ART coverage expands, patients will be treated earlier and this will have important effects on the AIDS associated death rate, it is thus necessary to incorporate the effect on death rate of CD4 cell count at treatment initiation to make sure the estimates are representative.

Recommendations

To estimate survival on ART:

- Develop two values for first year survival on ART by CD4 counts at treatment initiation. A suggested boundary would be initiating treatment with a CD4 count above or below 100.
- Develop a relationship between average CD4 count at the time of starting ART and coverage (as coverage expands patients will be treated earlier)

- Allow first year survival to vary between the two patterns depending on number of people on ART (converted into coverage)
- Do not use age- and sex-specific patterns for survival on ART

3. Effects of ART on ANC Prevalence Measurement

Another concern related to the expansion of ART is the effect it will have on ANC prevalence measurements. Different biases could emerge from the availability of treatment, it is important to understand these effects in order to develop accurate means to measure them and to correct for them. It is currently assumed that women with HIV have a lower fertility due to biological effects of the virus but also due to a reduction in the reproductive lifespan, to the potential rupture of the relationship with their partner or simply to the decision of not having children. This means ANC data underestimates the prevalence in women, however other factors interfere such as the fact that ANC sites are mostly urban where prevalence is higher leading to an overestimation of prevalence.

ART availability could modify the fertility of women living with HIV though different paths: firstly, treatment counteracts the negative effects of HIV on natural fertility; it also increases lifespan and thus reproductive lifespan. On the behavioural side, an improved health associated to treatment could contribute to having a more active sexual life and could encourage women to have more children. Regular access to health care to receive treatment should be accompanied with better treatment of STIs also improving fertility. ART could possibly reverse the sub-fertility associated with HIV. Conversely, increased access to health care could also mean higher access to contraception leading to a decrease in fertility.

Biases could also arise from inequalities in access to treatment; it has been observed that more women than men have access to ART in low resource settings, additionally these start treatment younger and healthier meaning that they will have longer survival leading to a higher HIV prevalence in women than men. Estimates of prevalence from ANC clinics will then overestimate the HIV prevalence in men; corrections of the female to male ratio will be needed. There could also be geographical inequalities in access to treatment, ANCs with ART services are more likely to be located or initially rolled-out in urban settings where HIV prevalence is high, exacerbating the tendency of ANC data to over-estimate prevalence. Additionally, uneven availability may lead HIV+ rural women to preferentially access facilities that offer these services.

Another problem is posed by the discrepancy that will emerge between incidence estimated derived from EPP and from Spectrum. ART is not incorporated in EPP but it is in Spectrum, and eventually when ART programs expand in countries and when enough time elapses the effects on prevalence will be important and incidence derived from Spectrum will diverge from incidence derived from EPP. Several possibilities were discussed such as incorporating ART in EPP or combining EPP and Spectrum. It was questioned whether more sophisticated models should be used but it was pointed out that many countries do not have the data required for these. This remains an issue that needs to be addressed carefully.

Recommendations

- Follow on-going studies (eg. Mwanza and Manicaland) to better understand these biases
- ART clinics should collect information on pregnancy and ANC attendance that could inform the magnitude of this effect
- Revisit the surveillance guidelines on how to collect information on residence of attendee to explore how representative ANC clinic samples are of geographic areas and whether this changes with the introduction of treatment.
- Develop methods for determining the ART use of women attending surveillance sites
    - If available from records, collect from records
    - Consider possibility of testing blood for ART use
- Elaborate the disease model in EPP to represent progress to treatment eligibility and offer separate survival curves for those who are on treatment. The user will specify the number of people on ART for each sub-population.

Pending issues

Other issues to be considered in a future meeting are the failure rate of 1st line ART and the effect of treatment interruption. Findings from the SMART cohort study (Strategies for Management of Antiretroviral Therapy) presented at CROI 2008 showed that interrupting therapy and resuming it had an important effect on the CD4 count and thus on survival probabilities. Patients who interrupt treatment experience a rapid decline in CD4 cells which increase very slowly once treatment is re-started. As this might be quite a common problem in resource poor settings in Africa, there could be an overestimation of the number of years gained if this feature is ignored.

Update on estimation of orphanhood due to AIDS and non-AIDS causes

Discrepancies between the UNAIDS (Spectrum) and the DHS estimates of maternal orphans is a problem that has been addressed previously. In the last meeting in Baltimore, it was suggested that new model life tables should be used by the UN Population Division for several countries in sub-Saharan Africa to lower non-AIDS mortality and thus the estimates of the number of non-AIDS orphans. This recommendation has been implemented and although it did result in smaller discrepancies between modelled and survey-based estimates of both maternal and paternal orphans, Spectrum estimates of maternal orphans remain consistently higher than those observed in surveys.

1. Exploring the discrepancies between modeled and DHS data estimates of orphans

The issue has been explored in depth by analyzing the data from recent sub-Saharan African DHS surveys and three other DHS surveys in order to detect missing or "hidden" orphans and/or misreporting of non-orphaned children as orphans. Two approaches have been used; the first one compared the relationship of both the child and the mother with the household head using information from the DHS surveys. If these were inconsistent or if the child was reported as adopted or fostered then the child was considered as a potential orphan. The percentage of potential hidden orphans obtained from this analysis ranged from 0.2% in Lesotho to 9% in Côte d'Ivoire. The second method used to estimate "hidden orphans" was to compare children declared as having a mother in the household schedule with the birth history of that mother taken during the mother's interview. Each child that was not found in the mother's birth history was then considered as a potential "hidden orphan". In the majority of the surveys, no hidden orphans were found using this method. Only 0.8% of children of interviewed mothers were potential hidden orphans. Miss-declared orphans (non-orphaned orphans) were estimated using both methods, the average number was quite low. The maximum number of orphans was estimated by adding declared and hidden orphans and subtracting miss-declared orphans, 7.3% of children were estimated to be orphans.

Adult mortality rates as well as number of children of dead mothers were inferred from sibling history data to be used in Spectrum. The percentage of orphans was estimated from these values, using a simple model and assumptions about fertility and children mortality. The percentage of children who are orphans varied from 5.4% to 7.1% which is considerably higher than the calculated 3.9% from direct reporting and quite close to the 7.3% estimated in Spectrum, indicating that there may be a substantial number of "hidden" orphans.

In conclusion, the model has improved and we are now approaching consistency with estimates of orphanhood from surveys, taking into account the "hidden" orphan phenomenon.

Recommendations

- Uncertainty bounds should be emphasised and sensitivity analysis performed.
- For countries where DHS estimates and Spectrum model estimates disagree, an in-depth study should be conducted.
- While orphanhood estimates from surveys should be interpreted as conservative, it is not recommended that household surveys routinely correct

orphanhood estimates. A note on the survey results should indicate that these are probably lower bounds.
- Shea Rutstein's paper should be reviewed, available and referenced in the survey reports.
- Survey questions as well as training should be improved to try and minimise misreporting of orphanhood status.

2. Estimation and Projection of Dual Orphans:

Until 2002, only estimates of maternal orphans were produced, since then paternal orphans are also estimated. The overlap between maternal and paternal orphans, namely dual or double orphans, is predicted by a regression model developed by Ian Timæus and fitted to empirical data on orphans aged 0-14 collected in national DHS household surveys. In the model, the number of dual orphans is a function of the number of expected dual orphans (number of maternal orphans*number of paternal orphans) and of several covariates which include the age of children, the HIV prevalence lagged by 5 years, the percentage of women remaining single at ages 15-19 and the percentage of women in polygynous unions.

Recommendations:

- The proposed method should be reviewed by some peers and if no major faults or drawbacks are identified it should be implemented in Spectrum.
- This change in the models (as well as other changes) should be proactively communicated to users as soon as the change is in place.

3. Estimating orphans due to AIDS in concentrated epidemics:

Estimates of the number of orphans are inferred in Spectrum from adult fertility and mortality rates. In generalized epidemics, background fertility is assumed to be the same in AIDS infected populations and non-infected populations (with adjustments for AIDS). In concentrated epidemics, this assumption is probably invalid as IDUs, sex workers, MSM and clients of sex workers may well have a different fertility than the general population. Estimates of the number of orphans have only been produced for countries with generalized epidemics. However, there is a strong pressure from organizations such UNICEF and OGAC and from the countries themselves to produce estimates of orphans due to AIDS for all countries. A literature review on the fertility of Most at Risk Populations (MARPs) was carried out by Neff Walker and colleagues, and although there is little direct information on the birth history of these populations, most regions have proxy data on fertility such as marriage rates.

Recommendations:

- A facility should be added to Spectrum that allows either to enter country-specific information about fertility of the major groups constituting the local epidemic, or to use default values based on regional data from the above review by Walker et al. Spectrum should use that fertility data to adjust the estimated number of orphans due to AIDS, although the resulting estimates carry important uncertainty.

Concurrent partnerships and the spread of HIV

Concurrency has been the focus of attention for several years now as it has been suggested that this partnership pattern could be fuelling the HIV epidemic in some countries. This question is relevant to the Reference Group work as it is has to do with modes of transmission and a better understanding of the issue would influence the way behavioural surveillance is done (what should we be measuring) as well as prevention strategies.

1. How strong is the evidence?

Modelling work provides evidence of the plausibility that concurrency can increase the speed and magnitude of HIV spread. Surveys offer evidence that concurrency exits. However there is no conclusive observational evidence that concurrency increases the risk of HIV at the individual or at the partner level. Ecological studies suggest an association between HIV prevalence and concurrency but it is hard to control for confounding. The Rakai study, for instance, indicates that concurrency is a risk factor for HIV infection but it is not possible to differentiate the effect of multiple partnerships from concurrent partnerships as all the reported multiple partnerships are concurrent. In addition there are discrepancies between the number of women and men reporting having concurrent partnerships. An analysis of available DHS data from few countries is underway and may further inform the relationship between the prevalence of concurrent partnerships and the HIV prevalence in populations.

2. Definition and measurement of concurrency

Definitions of concurrency vary between studies hampering the comparison and joint analysis of their findings. It was highlighted that the term “partnership” is often confusing and that it means different things to different people. In particular the concept of a casual partnership can be misleading and it can be interpreted differently by those modelling, those working in the field and those interviewed. An initiative aiming to create a typology describing these different types of partnerships including concurrency would be of great use. It was emphasised that it is the length of the overlap that matters and an in depth discussion on the achievability of measuring it in DHS questionnaires as well as on the formulation of the actual question(s) is needed.

Appendix I:

Meeting's agenda

DAY 1			
Start	**Duration**	**Subject**	**Speaker**
900	10	Opening remarks and meeting objectives	Peter Ghys and Geoff Garnett
Session 1: Feedback on 2007 estimates and regional training			
910	10	Summary of level and trends in new 2007 estimates	Peter Ghys
920	10	Feedback from 14-15 November 2007 UNAIDS consultation on Estimation	Ron Brookmeyer
930	10	Feedback from 2007 training workshops: main gaps, and needs for next round	Rob Lyerla
940	30	Discussion	
1010	20	*Coffee break*	
Session 2: Improving EPP			
1030	15	Examples of need for constraining minimal incidence: Cambodia and Kenya	Tim Brown, Boaz Cheluget, Vonthanak Saphonn
1045	15	Constraining future prevalence trends	Adrian Raftery
1100	15	Using behavioural data to infer parameter values in EPP	Joshua Salomon
1115	25	Improving efficiency of parameter search in Bayesian melding	Adrian Raftery
1140	15	Comparison of declines in prevalence among ANC versus community	Milly Marston
1155	15	Incorporating changing Urban:Rural population ratio in EPP	Patrick Gerland
1210	10	Bias due to mobility in the measurement of HIV prevalence in surveys	Milly Marston
1220	10	Discussion	
1230	30	*Working Lunch*	
1300	10	Developing Uncertainty around national prevalence trends in concentrated epidemics: how to quantify uncertainty in size of populations?	Rob Heimer
1310	20	Discussion	
Global Fund's proposed methods for Evaluating Impact of prevention programmes			
1330	15	Proposed methods	Tim Hallett
1345	15	Discussion	
Session 3: Estimating incidence and changes in incidence			
1400	10	Current Spectrum methods for estimating incidence and the uncertainty around it	John Stover
1410	15	Estimating incidence for a single population survey	Ray Shiraishi
1425	15	Estimating incidence for consecutive surveys	Tim Hallett
1440	20	Detecting recent changes in incidence from prevalence data over time: is it possible?	Rob Dorrington
1500	30	*Coffee Break*	
1530	15	Summary of WHO end-January consultation on incidence assays	Txema Calleja
1545	15	Update on BED	Keith Sabin
1600	45	Working Groups	
1645	15	*Coffee Break*	
1700	45	Working groups continued	
1745	15	Reports of the working groups	
1800		*Closure*	

DAY 2			
Start	**Duration**	**Subject**	**Speaker**
Session 4: Spectrum: effects of ART and uncertainty			
900	15	When should ART be started and how does survival depend on this?	Tim Hallett
915	10	Time from ART eligibility to death in lower income countries: evidence from cohort studies	Marcel Zwahlen
925	15	Modelling ART	Andy Phillips
940	20	Potential impact of ART availability on biases in ANC attendance and surveillance data	Kim Marsh
1000	30	Discussion	
1030	20	*Coffee Break*	
Session 5: Update on estimation of orphanhood due to AIDS and non-AIDS causes			
1050	5	Latest comparison of orphanhood estimates from Spectrum vs. surveys	Neff Walker
1055	20	1) Comparison of DHS individual orphan reports with data from the DHS birth history question and sibling data to validate the former 2) Female vs. male mortality: age gaps in couples	Shea Rutstein
1115	5	Update on orphanhood estimation in Zimbabwe	Laura Robertson
1120	10	Regression analysis for dual orphanhood	Ian Timaeus
1130	10	Fertility of groups with high risk behaviours and implications for orphanhood estimation in concentrated epidemics	Neff Walker
1140	25	Discussion	
Session 6: Concurrent partnerships and the spread of HIV			
1205	15	Definition of concurrency	Sevgi Aral
1220	15	Measuring and interpreting concurrency: quality, validity and importance of behavioral data	Daniel Halperin
1235	10	Association of HIV incidence with concurrent partnerships in the Rakai study	Tom Lutalo
1245	10	DHS analyses of the association of HIV prevalence with concurrent partnerships	Vinod Mishra
1255	15	Modelling Concurrency	Mirjam Kretzschmar
1310	15	How solid is the evidence of the impact of concurrency on the HIV epidemic?	Geoff Garnett
1325	35	*Working Lunch*	
1400	60	Discussion Concurrency	
1500	45	Working groups	
1545	15	*Coffee break*	
1600	45	Working groups continued	
1645	15	Reports of the working groups and final recommendations	
1700	30	Final comments	
1730		*Closure*	

Appendix II:

List of Participants

Name	Title and Affiliation	Email	Telephone
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