# Report of the meeting of
# The Reference Group on HIV/AIDS Estimates, Modelling and Projections.
# Geneva, 10-11 June 1999

## Introduction

The function of the workshop was to review available data on the extent of the HIV pandemic, the nature of biases in that data and methods of using such data for estimates of the current and future burden of disease. Included in this was the outcome of disease, mortality, empirical evidence of which provides additional information on the impact of HIV and AIDS.

The topics covered have immediate relevance, in that estimates are regularly required by policy makers and UNAIDS/WHO need to update figures. Our deliberations were aimed both at long term recommendations of the scope of research that would be beneficial, and short term recommendations for upcoming rounds of estimation. The timetable for estimates is such that some short term recommendations will not be possible for the current round where figures are required by August 1999 for consultation with a view to release at the end of the year. In revising figures either up or down there is a cost in terms of credibility and misinterpretation. Therefore, it is important that revisions are carefully assessed and the methods used rigorously assessed to prevent the need for unnecessary further alterations.

## HIV surveillance and data imputation

Estimates of the number of people living with HIV and the burden of HIV-related sickness and death rely heavily on data generated by sentinel surveillance systems.

These data are generally gathered by national AIDS programmes, and collated and distributed in the public domain by UNAIDS and WHO in country-specific Epi Fact Sheets, and by the US Bureau of the Census in the HIV/AIDS surveillance database. The group recognises the value of these efforts, and urges that they be continued and expanded.

Of course the value of surveillance data is limited by the quality of that data. The WHO's Global Programme on AIDS developed guidelines for sentinel HIV surveillance in the late 1980s. Designed largely to meet the needs of countries facing generalised, heterosexually-driven epidemics, notably those in sub-Saharan Africa, these guidelines are less appropriate for other epidemic types. In addition, they do not reflect the current state of knowledge about the course of the epidemic.

The group sited the clear need for additional data and recognises the need for population based sero-surveys to better interpret the information collected at HIV sentinel surveillance sites.

## Existing initiatives to improve surveillance systems

The group recognises the efforts of UNAIDS and WHO to develop guidelines for "second generation surveillance" of HIV and STDs that incorporate the use of behavioural data and better reflect the diversity of epidemics around the world. The group encourages the finalisation and publication of these guidelines, including operational guidelines to help guide those responsible for surveillance systems at the country level.

In guidelines for surveillance in **concentrated epidemics**, the group urges that the following issues be addressed:

- The estimation of the size of sub-populations at higher risk of infection.
- Achieving sample sizes in hard to access sub-populations. Specifically, we would recommend that point prevalence be reconsidered in favour of period prevalence where access to the sub-populations is limited or numbers are small.

- Appropriate proxies for the general population, particularly where poor service utilisation and low fertility reduce the representativeness of pregnant women at antenatal clinics.

In guidelines for surveillance in **generalised epidemics**, the group urges that the following issues be addressed:

- The relationship between HIV prevalence in urban and non-urban areas
- Samples sizes that allow for disaggregation of prevalence by age. The group recommends that sample sizes at ANC be increased across the entire reproductive age range at sites where this is feasible.
- The appropriateness of collecting sero-prevalence in groups acting as proxies of populations with high risk behaviour. The group believes that in high-prevalence generalised epidemics, data from STD clinic attenders are difficult to interpret; resources may be better used elsewhere. Surveillance among sex workers should, however, continue in all epidemic states.

The group also notes the potential for increasing bias in sentinel surveillance among pregnant women in countries providing effective interventions to reduce transmission of HIV from mother to child.

Even where sites and samples are appropriately chosen to minimise bias, data quality depends upon the quality and reliability of the testing procedure itself. The group urges that greater efforts be made to regularise quality control of laboratory practices, for example by retesting random sub-samples of stored sera at reference laboratories.

***Recommendations for immediate action***

Urban-rural differentials

- The group urges UNAIDS/WHO and the US Bureau of the Census to put together in one site all the information and the assumptions used in determining levels of prevalence in urban and rural areas of each country acknowledging that this information is already available on various publicly accessible web sites.
- The group recommends that more systematic efforts are made at a country level to document the characteristics of individual sentinel sites and the catchment populations they are assumed to represent. This should include information about the overall client volume at each site.
- The group requests that a background paper be prepared, reviewing existing knowledge about differentials in infection between areas with different levels of urban infrastructure and geographic integration with other areas. The paper should provide countries with guidance in adjusting data from sentinel surveillance sites to reflect gradients of infection between urban and non-urban areas.

Alternative surveillance populations

- The group recognises that there are biases associated with traditional sentinel populations and, further, that there are severe limitations in using these populations in many of the emerging and concentrated epidemics of Asia. Population-based surveys undertaken for other purposes may provide samples that can be used in unlinked anonymous surveillance for HIV. The group recommends that an inventory of such surveys be compiled, and that it be circulated to countries which may have unrecognised sources of samples for potential HIV surveillance.

**Increased capacity for using surveillance data within countries**

The group strongly supports greater use of surveillance data for making estimates of HIV prevalence and associated sickness and death at country level. It urges UNAIDS and WHO to contribute to building capacity for creating estimates within countries, for example through

training, adequate guidelines, and the provision of international technical support for national estimation exercises.

The group also recommends that a checklist be prepared to guide countries in documentation of key assumptions used in preparing estimates. Existing systems for exchange of information between country and international data collection institutions (for example through the Epi Fact Sheet mechanism) should be strengthened.

The group recognises that creating sustainable capacity for better surveillance data collection and use at country level demands more resources than are currently available. The group strongly urges greater allocation of resources for this purpose.

**The problem of missing data**

The group recognises that efforts to strengthen surveillance systems are unlikely to bear fruit overnight. The persistent problem of erratic data collection or reporting, and the missing values it results in, will face those making national level estimates of HIV prevalence and mortality for some time. Where missing data differ from observed data in systematic ways, this has the potential to jeopardise the reliability of estimates made.

The group urges that the issue of missing data be carefully considered in making estimates. It may be possible to use imputation methods to correct for missing data. However, more work is needed to define parameters correlated with HIV prevalence that could be used to allow imputation methods to be applicable. It is also recognised that, to reflect the heterogeneity of national epidemics, these parameters may vary by country or epidemic state.

The group recommends a detailed statistical study of the possible biases introduced by ignoring the problem of missing data in producing estimates.

The group recommends a rigorous investigation into the use of imputation methods and their performance ability.

Whether "expert opinion" or any other method is used to correct for missing data, the assumptions used in making the corrections should be explicitly stated and published together with estimates.

The group also recognises that there are situations in which data quality or availability are so poor that imputation or other correction methods are likely to fail. It recommends that no attempts should be made to use these methods in these situations.

**Biases in antenatal surveillance data**

- The only data currently widely available for the assessment of trends in HIV prevalence in 'generalised' epidemics is ANC surveillance.
- There are three sources of difference between prevalence in ANC surveillance and in the general female population: only pregnant women are tested; only pregnant women who attend ANCs are tested; and the clinics selected for surveillance may not be representative. Demographic adjustment techniques available so far only address the first problem, the other two can only be addressed by widening the surveillance systems and by better characterising surveillance sites.
- How representative pregnant women are of all women of the same age varies by age, pattern of sexual activity, stage of the epidemic and the extent of contraceptive use. For each age ANC based HIV prevalence data underestimate the prevalence of HIV among the general female population, with the exception of younger pregnant women where estimates are often biased upwards.
- The downward biases are strongest in mature epidemics, non-contracepting populations with young fertility patterns and in populations with a high prevalence of fertility-reducing STDs.

- There is currently no consensus on the best methods to adjust for the biases in ANC data. There is a need for more community sero-surveys that also include fertility data and data on ANC use carried out in conjunction with ANC surveillance. In particular, there is a lack of information from regions other than Sub-Saharan Africa.
- A detailed review of existing data will be carried out to develop adjustment factors taking into account the scale and the age of the epidemic.
- Methods are needed to characterise surveillance sites and the communities they serve to assess the generalizability of surveillance data and adjust for biases. To assist the analysis of ANC data the collection of additional information such as parity and birth interval may be helpful.

**Incidence**

- The estimation of incidence has two functions (1) For advocacy – a point estimate of incidence can be made using models based on prevalence data. (2) Identification of trends over time to inform evaluation of interventions.
- The use of ANC data is unavoidable because it is the only widely available data. However, trends in antenatal prevalence do not reflect current changes in incidence. Increasing incidence suggested by an increased rate of increase in prevalence is easier to interpret than a decline in incidence which may be a natural part of the progression of the epidemic or could be a product in biases in the age and fertility of those infected as the epidemic ages.
- At younger ages that are less affected (although not unaffected) by mortality and fertility change serial age prevalence curves can reflect changes in incidence but have to be interpreted with great caution.

**Female – Male HIV prevalence ratio**

- Current UNAIDS/WHO estimates of adult (15-49) HIV prevalence assume equal prevalence among men and women in sub-Saharan African countries.
- Current evidence suggests that prevalence is higher in women than in men. There is a dearth of population based data from which to assess the ratio elsewhere in the world.
- Skewness of the sex ratio is maintained by factors such as:

1) Earlier ages at infection among women than in men.
2) Differential transmission probabilities through heterosexual sex from infected men to women and from infected women to men.
3) Contrasting patterns of sexual behaviour between men and women.

- The sex ratio in HIV prevalence varies by scale and stage of epidemic.
- Migrant labour associated mobility is liable to have a significant impact on observed sex ratios of HIV prevalence. The influence of this relationship needs to be investigated further.
- Data from as many existing population based studies as possible should be reviewed and analysed to asses the level of the ratio of female to male HIV prevalence by type and stage of epidemic and provide a basis for deriving adjustment factors.
- Further surveys are needed to measure the ratio of female-to-male HIV prevalences in a wider range of populations at different stages of epidemics. The possibilities of differential participation bias for males and females should be addressed in the design and interpretation of such surveys.

**Recommendations for action:**

**Short term action**

- A detailed review of existing data will be carried out to develop adjustment factors for all adult women 15 to 49 from ANC data taking into account the scale and the age of the epidemic.
- For advocacy – a point estimate of incidence can be made using models based on prevalence data.
- Data from as many existing population based studies as possible should be reviewed and analysed to asses the level of the ratio of female to male HIV prevalence by type and stage of epidemic and provide a basis for deriving adjustment factors.

**Long term research**

- There is a requirement for more community sero-surveys that also include fertility data and data on ANC use carried out in conjunction with ANC surveillance.
- Methods are needed to characterise surveillance sites and the communities they serve to assess the generalizability of surveillance data and adjust for biases. To assist the analysis of ANC data the collection of additional information such as parity and birth interval may be helpful.
- Further surveys are needed to measure the ratio of female-to-male HIV prevalences in a wider range of populations at different stages of epidemics. The possibilities of differential participation bias for males and females should be addressed in the design and interpretation of such surveys.
- Studies of the relationship between HIV incidence and prevalence over time will help inform the interpretation of prevalence data to infer patterns of incidence.

**Conclusions and recommendations regarding the estimation of adult mortality in the context of the HIV epidemic**

- These conclusions and recommendations are divided into two parts: the first refers to the availability of data relevant for the estimation of adult mortality and the second on the approach to take in making the best use of data available in order to assess general mortality levels and estimate the excess mortality due to HIV/AIDS.
- With respect the availability of data, the group stressed the need to take steps to improve the data base for mortality estimation by making an effort to compile and put in the public domain data emanating from data collection systems that are already in operation in the different countries, especially data from civil registration systems. In particular, the WHO representative noted that WHO had been making an effort to collect data on registered deaths from African countries and would collaborate with the group in making those data available for others in the group to analyse. It was suggested that both UNAIDS and WHO might undertake a concerted effort to ensure that in countries where civil registration exists (even if incomplete) or where censuses have gathered information on deaths in the past year, the relevant data on deaths by age and sex be tabulated and put in the public domain.
- Regarding the future gathering of information, it was noted that the United Nations recommendations for the 2000 round of censuses already included the recommendation that censuses gather information on deaths in the household during the preceding year and of the sex and age at death of the deceased. However, it was judged necessary that UNAIDS or WHO, through their representatives at the country-level, try to make patent vis-à-vis the relevant authorities the importance of gathering such information.
- Surveys were recognized as another key means of obtaining information relevant for the estimation of mortality. Because of their versatility, it was thought that surveys should include a variety of questions to obtain data allowing the application of different estimation approaches. High priority should be given to the inclusion of questions on the survival of siblings (in the

form of sibling survival history) and to the survival of parents. If sample size were large enough, information on deaths in the household over a year could also be obtained. Given that the Measure programme continued to carry out DHS type surveys, it was suggested that UNAIDS contact Macro to make the case for continuing to include the sibling and orphanhood questions in those types of surveys given their proved utility in the estimation of adult mortality even if not so useful for the estimation of maternal mortality.

- It was suggested that African countries that had a tradition of including questions on orphanhood in censuses be encouraged to continue including those questions in the 2000 round of censuses.
- With respect to the estimation of adult mortality in countries with limited or deficient data, the importance of using a battery of methods to derive estimates from a variety of sources was emphasized. However, it was recognized that the estimates obtained were unlikely to be perfectly consistent and that it was necessary to continue working in the following areas:

- The assessment of the performance of the different methods in contexts where mortality has been rising because of HIV/AIDS.

- The application of existing methods to a variety of cases so as to have a better basis for assessing their performance under different circumstances.

- The development of methodology to derive estimates of excess mortality due to HIV/AIDS on the basis of adjusted estimates of adult mortality.

- Because these activities implied further research and it was not yet clear how successful existing methods would be in producing acceptably accurate measures of mortality for the most affected countries, the group judged that it was premature to use estimates of adult mortality as a basis for the adjustment of estimates of the prevalence of HIV. However, the group urged that more work be done in comparing selective indicators of mortality or of excess mortality due to AIDS as derived from mortality data with those obtained from models of the HIV epidemic. Three models should be considered: the IWG, that of the Oxford Group, and that of the Rotterdamn Group (STDSim). It was also suggested that it might be useful for demographers to analyse the data emanating from longitudinal cohort studies.
- The relationship between the incidence and prevalence of HIV and consequent mortality is dependent upon survivorship amongst those infected. There is little data available from developing countries with which to assess the duration from HIV infection to death. Currently, a small sample of incident cases from Masaka in rural Uganda have been followed and the mortality rate observed to date would suggest that the median survival time will be around nine years. This figure should be used for the least developed countries, whereas for most countries a median survival of 11 years observed in industrial countries in the absence of antiretroviral therapy should be used. Where it is used, the impact of effective therapy should be noted and included in figures. Observations from industrialised countries also suggests that age at infection determines the survival time this may be influential if some epidemics are predominantly amongst young people. In the short term the Masaka data by age and sex should be analysed to the extent possible.

**Curve Fitting Recommendations**

- The group discussed procedures to be used by UNAIDS/WHO to arrive at country-specific estimates. A primary issue was whether to continue with the procedure used in the past, which utilizes epimodel in conjunction with expert judgment and assumes the new infection curve to be described by a gamma density, or to adopt a new procedure.
- It was agreed that there would be a short term decision on what might be practical to implement in time to use for the 1999 country-specific estimates and a research agenda directed toward a longer term improvement in approach. It was also agreed that whatever procedure was decided on for the 1999 estimates should be regarded as one step in an evolutionary improvement.The use of new methods should be dependent on a rigorous process of testing the methods, through experimental use, comparison of results from different methods (where the explanation of differences indicates which methods are most appropriate) and statistical review.
- It was pointed out that the current approach does not make use of the age- and sex-specific prevalence information in the US Census Bureau data base. It was agreed that while this information can and should be utilized in the longer term, it would not be practical to implement such an approach in time for the 1999 estimates.
- It was recommended that UNAIDS/WHO attempt to implement a back calculation approach along the general lines of epimodel, but utilizing a function form for the new infection curve that captures more appropriately the shape of the post peak curve. An essential consideration in arriving at this recommendation was the statement by Tim Brown that his new browser-based implementation would be ready by August of this year and could accommodate this innovation.
- It was agreed that the functional form adopted should have epidemiologically interpretable parameters, including in particular the post peak asymptotic endemic level. Several suggestions for functional forms were made. It was agreed that further suggestions could be communicated to the Reference Group Secretariat by email by July 1. The Secretariat would forward these suggestions to the Reference Group members, who would have two weeks to comment on and state preference for the suggested alternatives. The Secretariat will arrive at a final decision and communicate this recommendation to members and to UNAIDS/WHO by July 15.
- The previous exercise of country specific models was based on fitting a prevalence curve in epimodel through a time series of adjusted national HIV/AIDS prevalence estimates. It was discussed, whether statistical curve fitting procedures using all surveillance site data for major urban areas and outside major urban areas could simplify this process. Procedures would then also need to be identified on how to adjust the data from outside major urban areas. The group agreed that further work should be done to explore the usefulness of such procedures. Another suggestion was to only fit a curve through prevalence points in urban areas and use a country specific correction factor for rural areas. The group agreed that such a process may be appropriate in countries with no or extremely limited data for rural areas, separate consideration of the data from urban and rural areas is preferable as epidemics often evolve following different trends.
- The group agreed that, with two exceptions, estimates should not be made for countries lacking necessary data. The exceptional countries are India and China, which figure so prominently in global AIDS statistics that to exclude them would result in severely misleading statistics. Concurrently it was strongly recommended that the UNAIDS/WHO publication presenting the estimates explain this exception, the reason for it, the way in which estimates for the exceptional countries were arrived at, and state appropriate qualifications regarding the accuracy of the estimates.
- The group recognized that various national and international organizations need to generate future scenarios for the epidemic. The group recommended that approaches adopted by new UNAIDS/WHO should facilitate this work insofar as possible without compromising the immediate UNAIDS/WHO objective of preparing the best possible near term estimates.

- Two recommendations for the longer term research agenda were made. The first was to explore the robustness of forecasts of different statistics. Numbers of AIDS deaths, for example, can be forecast more reliably than new infections. The second was to develop models which are, on the one hand, simple enough to be usable by UNAIDS/WHO in producing estimates, but which also allow utilization of available data on age- and sex-specific prevalence.