Evidence and causes of declines in HIV prevalence and incidence in countries with generalised epidemics

Report based on a meeting held in
Harare, Zimbabwe, 15-17th November 2004

Sponsored by UNAIDS, WHO, CDC & UNICEF
Organised by the UNAIDS Reference Group on Estimates, Modelling and Projections (www.epidem.org)

UNAIDS

This meeting was organised for UNAIDS by the secretariat of the Reference Group on Estimates, Modelling and Projections (http://www.epidem.org) based at Imperial College London, UK. 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.

Nicholas Grassly, London, February 2005

Introduction

Aims of meeting

A recent overview of trends in HIV prevalence estimates from antenatal clinic surveys in sub-Saharan Africa (SSA) revealed some evidence of declines in eastern Africa but stagnation in central, southern and western Africa (*1*). However, a lot of geographic variation in trends occurs within this overall picture, and consistent downward trends in prevalence have been observed for some antenatal clinics scattered across SSA. To assess whether significant declines in HIV prevalence are occurring at the national and sub-national level in countries with mature generalised epidemics a meeting of national programme staff, researchers and public health experts was convened by UNAIDS in Harare in November 2004. This meeting was sponsored by UNAIDS, WHO, CDC and UNICEF, and organised by the UNAIDS Reference Group on Estimates, Modelling and Projections (www.epidem.org). This meeting aimed not only to determine whether declines in HIV prevalence are occurring, but to also attempt to distinguish mortality from behaviour change as causes of declines in the number of people living with HIV/AIDS.

Meeting Overview

The meeting was divided into two parts. The first included an overview of trends in HIV prevalence, knowledge about HIV/AIDS and sexual behaviour in countries with mature generalised epidemics, together with an exploration of the links between HIV incidence, AIDS mortality and sexual behaviour in this context. Presentations on these cross-cutting themes led to working group discussions that resulted in recommendations on 3 issues:

1) Interpreting trends in HIV prevalence and incidence
2) Interpreting trends in HIV/AIDS knowledge, skills and behaviour
3) Modelling the sexual transmission of HIV

In the second part of the meeting national programme staff presented country reviews, using national HIV and other STI surveillance data, cohort studies and behavioural surveys. A key strength of these analyses was the integrated analysis of behavioural and sero-prevalence data. Comparison between countries was facilitated through the use of a broadly standardised presentation format, a template for which is included in Appendix B. Nine countries with mature generalised epidemics were invited to present at the meeting: Uganda, Ethiopia, Zambia, Côte D'Ivoire, Kenya, Malawi, Rwanda, Haiti and Zimbabwe. Papers based on these presentations are to appear in a special issue of the peer-reviewed scientific journal *Sexually Transmitted Infections* in 2005.

Working Group Recommendations

1. Interpreting trends in HIV prevalence and incidence

Available Data Sources

1. Sentinel surveillance among antenatal clinics (ANC)
2. National population-based surveys
3. Small area population-based surveys
4. Sentinel surveillance among high risk populations, e.g. sex workers
5. PMTCT
6. VCT
7. Blood Donors
8. Military Recruits

Monitoring trends in ANC

Before assessing trend consider changes in:

1. data quality
2. methodologies
3. number and characteristics of surveillance sites
4. population at individual ANC sites
5. HIV testing strategies
6. age structure
7. Urban/Rural site and urban/rural status of the clients

Monitoring trends in population based surveys

Before assessing trend consider changes in participation rate, the timing (e.g. every 5 years for DHS) and comparability of surveys. Trends can be derived at national level and usually at provincial level; but not at district-level

Laboratory quality

Prevalence results from earlier years (with less or no quality assurance) are likely to be less valid than results from recent years). Therefore consider a wider confidence interval for data points from earlier years, give more weight to data points from years in which quality has improved and focus on more recent data with documented laboratory quality improvements.

Results from stored samples are likely to be less valid compared to fresh samples (therefore recommend that these samples are dealt with as above for samples from earlier years).

Analysis of trends in prevalence

Analyses of trends should be restricted to those sites with consistent reporting over time. Three data points showing a consistent trend in prevalence are needed to conclude there is a trend. Any analysis of trend should consider the magnitude and power of the change over a period of consistent data collection. Time spanning the data points should be 3-6 years. In general, the period of most interest for evaluation of a decline in prevalence will be some years after prevalence has peaked, since the decline in prevalence immediately following the peak prevalence is part of the natural epidemic due to mortality of those most at risk of infection who were infected early on in the epidemic

Confidence intervals about prevalence estimates should be presented and statistical tests should be used to assess significance of trends. Test for trend analyses should attempt stratification by site and by other confounders (e.g. standardized by age).

Trends should be measured for national and sub-national levels, since measuring trends only at the national level may obscure significant changes at sub-national level, if sub-national epidemics occur with different timing. However, this is balanced by less data being available at sub-national level.

Currently very few countries have more than one population prevalence survey and therefore survey-based trends in prevalence have not been assessed.

As a caveat, it was noted that statistical significance does not necessarily mean importance or relevance; the latter require judgment.

Analysis of trends in incidence

'Detuned' assays such as BED (*2, 3*) are promising but these methods need further validation.

Trends identified from cohort studies are not necessarily representative for the country and require sufficiently long period of observation to confirm trends.

The Estimation and Projection Package (EPP) tends not to be very sensitive to changes in incidence and mortality, but has the advantage of considering mortality and incidence at the same time.

Trends in ANC prevalence among 15-19 or 15-24 year olds can be used as proxy for incidence. However, this method is subject to bias. For 15-19 year olds changes in fertility and age at sexual debut may confound changes in incidence. Furthermore, for countries with late sexual debut this age group may be poorly representative. For 15-24 year olds there is clearly some effect of mortality among the older ages.

It is therefore recommended that the age distribution of those attending ANC is monitored over time, and that HIV prevalence among young women at ANC is presented by single years of age in national reports (with appropriate confidence intervals). The potential of using a slightly younger age group to monitor trends in incidence (e.g. 15-22 yrs) should also be explored. It is recommended that trends in HIV prevalence for women with a first pregnancy at ANC is also analyzed, especially in countries with low levels of contraceptive use.

In general, whenever possible, compare trends in incidence using above methods (incidence assays, cohort studies, EPP, prevalence in narrow age bands of young women and in primigravidae)

How can natural history changes be distinguished from changes due to programmatic effort?

We need more data on programmatic effort and behaviour change, and also on the relationship between prevalence and the balancing effects of mortality and incidence of new infections. A more convincing analysis can be presented when changes in prevalence, incidence, behaviour and mortality are juxtaposed.

In the absence of modelling, changes due to programmatic effort may be evidenced as a deviation from the prevalence-incidence trend. The use of models allows prevalence, incidence, behaviour and mortality to be examined at the same time.

How to interpret small area changes?

Community-based research studies in small areas are not necessarily representative of the country as a whole, but have potential to gain a better understanding of HIV transmission and may be linkable to local programmatic information.

National datasets (either ANC or population-based survey) can be used to analyse changes in one or some geographic areas only, to explore differences between these areas and rest of country in duration of epidemic and local programmatic efforts

Further research that can help address the evaluation of trends HIV prevalence and incidence

The BED assay needs further validation with regard to laboratory methods (subtypes) and the development of appropriate epidemiologic and statistical methods.

More epidemiological studies are needed on how to interpret measured incidence data (e.g. from BED testing) and relationship with incidence in the general population.

Mortality data collection and analysis needs to be expanded and improved using sample vital registry (e.g. SAVVY), DHS sibling survival and in-depth demographic surveillance sites.

Refine EPP and Spectrum to allow direct input of measured incidence (e.g. by BED) and mortality data (e.g. from SAVVY, or sibling history and, orphanhood questions from household surveys).

Quantify the effect of mortality in the 20-24 year olds on prevalence in the 15-24 age band, in the 20-24 age band, and in single year age bands. Following this analysis, explore suitability of using prevalence in slightly younger group than currently recommended 15-24 year age band, e.g. 15-22, as proxy for incidence.

2. Interpreting trends in HIV/AIDS knowledge, skills and behaviour

It was recommended that, in general, the emphasis should be on behavioural indicators rather than knowledge and skills.

Which criteria should be used to evaluate trends?

Difficult to decide general criteria to establish trends in behaviour since it depends on the indicator (e.g. age at first sex vs. number of casual partners), consistency of methods and sampling over time. A conservative approach would be to determine trends from only four points or more of data, when the behavioural survey is linked to changes in HIV incidence, and five points otherwise. On the other hand if there is sufficiently clear change then it might be possible to find a significant effect with only three points. A general recommendation is that all trend analyses report and take due account of all identified sources of error and bias in behavioural indicators.

We stress the importance of reporting sample sizes, confidence intervals. A problem is that many sources of error, resulting from sample frames, non-response, phrasing of questions in multiple languages etc., are not possible to quantify statistically meaning that confidence intervals have little meaning. A major aid to the interpretation of data is transparency: it is important to report non-response error, sample sizes, provide an accurate definition of the study population, etc.

How can natural history changes be distinguished from changes due to programmatic efforts?

There are two key issues:

1) Are people changing their behaviour?
2) Are behavioural changes due to programmatic effects?

In answer to (1) we recommend a set of slides to be published by UNAIDS be produced that illustrate how differential mortality can give rise to changes in *reported* behaviour at the population level when there has not actually been any change in the *actual* behaviour of individuals. Emphasise national representative surveys rather than small surveys.

In answer to (2) it is extremely difficult to attribute behaviour change to programmatic effects. For example, we are still discussing what really gave rise to the declines in HIV prevalence in Thailand/Uganda. We recommend the impact of the exposure to funerals, death of relatives *etc*… on sexual behaviour be investigated through analysis of DHS and other data.

What indicators should be added to data collection instruments on knowledge, skills and behaviour?

a) Include questions on marital history in the DHS and simplified marital history in ANC. b) Ensure questions in the DHS that allow indirect estimates of adult mortality continue to be asked and analysed together with sexual behaviour and marital data.

Further research that can help address the evaluation of trends in knowledge, skills and behaviour

Examine the importance of different types/measures of sexual behaviour for HIV incidence at different stages of the epidemic through analysis of empirical data and models of sexual behaviour. e.g. is sexual behaviour (condom use *etc*..) within 'monogamous' unions more important in determining HIV incidence later on in a generalised epidemic.

We raise the issue of the importance of creating "safe archives" of data so that we do not repeat the problem of having data lost through staff changes, hard-drive crashes, computer thefts *etc*.

3. Modelling the sexual transmission of HIV

Objective
To apply the age-structured incidence model to all nine countries using data presented here and show results for influence of behavior change and natural epidemic dynamics on conclusions about incidence trends. Carry out separate fits to urban (or capital city) and rural data. Explore feasibility of participants from national programmes having access to a version of the model for their own use.

Timeline
A formal data request was to be issued by December 1st providing a standardized form for data entry, which should be returned to Tim Hallett by December 22nd. If, for whatever reason, this was not possible data would still be accepted until mid-January. By mid-February Tim Hallett will have applied data from each country to the age-structured model and have discussed the results with country representatives. In collaboration with representatives from all countries participating in the exercise, Tim Hallett was to prepare an initial draft paper by the end of February.

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1. **Asamoah-Odei, E. et al.** HIV prevalence and trends in sub-Saharan Africa: no decline and large subregional differences. *Lancet. 364*: 35-40 (2004).
2. **Parekh, B.S. et al.** Quantitative detection of increasing HIV type 1 antibodies after seroconversion: A simple assay for detecting recent HIV infection and estimating incidence. *AIDS Res Human Retrovir. 18* (4): 295-307 (2002).
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Appendix A – Meeting Agenda and Participant List

Monday 15th November

9:00	Welcome to Zimbabwe	Dr E Xaba *Permanent Secretary* *Ministry of Health, Zimbabwe*
9:10	Introductory remarks	Shannon Hader *CDC Zimbabwe*
9:15	Welcome and meeting aims	Peter Ghys *UNAIDS Geneva*
	Overview	Chair: Neff Walker
9:30	HIV prevalence trends in sub-Saharan Africa	Emil Asamoah-Odei and Txema Calleja
10:00	Trends in reported knowledge and sexual behaviour in countries with generalised epidemics from national surveys	Roeland Monash
10:30	*Coffee/Tea*	
10:45	Models of sexual behaviour and HIV transmission in countries with generalised epidemics	Geoff Garnett
11:00	The relationship between reported sexual behaviour and HIV infection	Tim Hallett
11:45	Use of marital history data in assessing sexual risk behaviour in the context of generalised HIV epidemics	Basia Zaba
12:15	Comparison of UNAIDS/WHO and empirical estimates of mortality in Africa: What are the implications for estimating HIV incidence?	Rob Dorrington
12:45	Discussion	
13:00	*Lunch*	
	Country reviews (1)	Chair: Karen Stanecki
14:00	Uganda	Wilford Kirungi, Joshua Muzunguzi and Wolfgang Hladik
14:30	Ethiopia	Shabbir Ismail, Abbas Aseged Woldu, Tsehaynesh Messele and Wolfgang Hladik
15:00	Zambia	Mwaka Monze
15:30	*Tea*	
16 :00	Côte D'Ivoire	Kunomboa Ekra, Kouassi Lucien and Kassim Sidibe
16 :30	Kenya	Boaz Cheluget, Larry Marum, John Stover

17:00	Discussion	
17:30	Close	

Tuesday 16th November

	Country reviews (2)	Chair: John Stover
9:00	Zimbabwe	Owen Mugurungi, Simon Gregson and A.D. McNaghten
9:30	Declining HIV prevalence and incidence in women attending maternity clinics in Harare, Zimbabwe: a pattern emerging in east and southern Africa?	John Hargrove
10:00	Manicaland cohort study, Zimbabwe	Simon Gregson
10:30	Discussion	
11:00	*Coffee/Tea*	
11:15	Malawi	George Bello, John Chipeta and John Aberle-Grasse
11:45	Rwanda	Eugénie Kayirangwa and Jeffrey Hanson
12:15	Haiti	Louis-Marie Boulos, Michel Cayemittes, Eric Gaillard and Kassim Sidibe
12:45	Discussion	
13:00	*Lunch*	
13:30	**Issue working groups** **The interpretation of trends in HIV prevalence and behaviours in countries with generalised epidemics**	
15:30	*Tea/Coffee*	
16:00	Working Groups contd.	
16:30	**Plenary** **Feedback from Working Groups**	Chair: Peter Ghys
17:30	Close	

Wednesday 17th November

9:00	**Country working groups** **Planning implementation of country models and drafting of papers with country analyses**	
	Coffee/Tea/lunch as before	
16:30	**Plenary** **Feedback from Working Groups**	Chair: Geoff Garnett
17:30	Close	

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Appendix B – Example template for country analyses

Evidence for changes in sexual behaviour and HIV incidence in country X?

Executive Summary

Summarise findings of review and analysis to answer key questions:

Is there evidence for a declining prevalence of HIV, either nationally or in a region?

If yes, is there also evidence for a declining incidence of HIV, either nationally or in a region?

If yes, is the decline in incidence likely to be the result of behaviour change or simply AIDS mortality?

1. Introduction

2. Data and analysis

2.1 Prevalence of HIV/AIDS

Antenatal clinics with consistent reporting over time

Describe trends in HIV prevalence from antenatal clinic (ANC) sentinel sites with consistent reporting over time for 15-49 year old attendees.

Prevalence trends based on the 2004 national estimate

Describe trends in prevalence based on the most recent national estimate (e.g. use EPP if estimated using this software)

2.2 Incidence of new HIV infections

Inferred incidence from trends in prevalence among young ANC attendees

Describe trends in HIV prevalence for young ANC attendees (15-24 year olds, 15-19 year olds, and 20-24 year olds) – declines are likely to indicate declines in incidence since these people are only recently exposed to infection. Also describe trends in prevalence among ANC attendees by parity – HIV prevalence among pregnant

women expecting their first or second child may be a reasonable marker of HIV incidence (*4*)

Inferred incidence from EPP and Spectrum

Use EPP and Spectrum to estimate incidence from prevalence data.

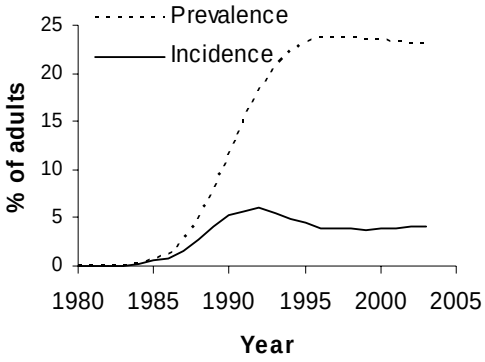

Figure example HIV prevalence and incidence for the 2003 Zimbabwe national HIV estimate (*5*). Note incidence decline in early 1990s can be explained by AIDS mortality and hence lower HIV prevalence among sexual contacts.

Inferred incidence from age profile of prevalence among young people in population based surveys

The age distribution of prevalence among young people in population surveys can reflect trends in incidence (*6, 7*). Assuming that all individuals are equally likely to become infected once they become sexually active then a convex distribution of prevalence suggests increasing incidence over time, and a concave distribution decreasing incidence (see Figure below).

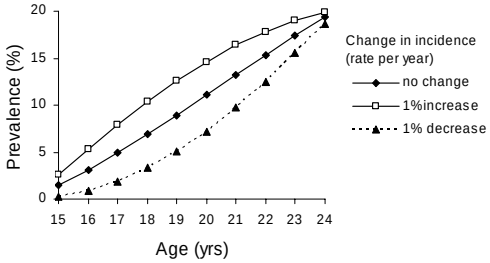

Figure example Model HIV prevalence by age for a cohort of young people with median age at first sex of 19 years where HIV incidence over time has shown a linear increase, a linear decrease or no change.

Evidence from other sources (military recruits, cohort studies, etc..)

Any additional evidence here

2.3 Sexual behaviour and knowledge

A decline in incidence can occur even without any changes in sexual behaviour due to death of higher risk individuals infected with HIV, and declining prevalence and hence a lower probability that a sexual contact is HIV positive. Is there any behavioural surveillance data that suggests a reduction in risky behaviour?

Some example, indicators that can be used to assess levels of knowledge and of sexual behaviour in the population are given below. The denominator population for these questions should ideally be young men and women (15-24 years old) and adult men and women (15-49 years old) (except where indicated).

Note, however, the analysis is likely to be restricted by the amount of data available from comparable surveys that have been carried out at different times. We therefore recommend that data is presented for any relevant indicators that are available from more than one time point.

Key indicators

1. Percentage of respondents who have been sexually active in the last 12 months and have had sex with a non-marital, non-cohabiting partner in the same period.
2. The percent of respondents who say they used a condom the last time they had sex with a non-marital, non-cohabiting partner, of those who have had sex with such a partner in the last 12 months.
3. Percentage of young people (15-25) who have had sex before the age of 15.
4. The proportion of young women who have had sex in the preceding 12 months with a partner who is 10 or more years older than themselves.
5. The percent of men respondents reporting sex with a sex worker in the last 12 months.
6. The percent of men respondents reporting condom use the last time they had sex with a sex worker, of those who report having had sex with a sex worker in the last 12 months.
7. Percentage of respondents (adults or young people) who both correctly identify ways of preventing the sexual transmission of HIV and reject major misconceptions about HIV.
8. etc…

Data sources

National population-based surveys such as Demographic and Health Surveys (DHS) supported by USAID or Multiple Indicator Cluster Surveys (MICS) supported by UNICEF can provide this data if implemented in more than one year. Need to ensure comparability of questions in each year.

Cohort studies

Others….

2.4 Exposure to prevention programmes

Exposure to prevention programmes

Key indicators
Examples:

1. Percentage of schools with teachers who have been trained in life-skills-based HIV/AIDS education and who taught it during the last academic year
2. Percentage of large enterprises/companies that have HIV/AIDS workplace policies and programmes
3. The proportion of people who had an HIV test in the preceding 12 months and know the results.

2.5 Mortality

Trends in adult mortality suggested by vital registration data, census data, cohort studies or household surveys (e.g. DHS).

2.6 Sexually transmitted infections other than HIV

Sexually transmitted infections (STIs) other than HIV can act as markers for unsafe sexual behaviour and therefore may be suitable 'biomarkers' for HIV incidence (*8*). Trends in STIs treated at public clinics and other sources of data may therefore provide a useful supplement to the analysis of HIV prevalence and sexual behaviour data.

3. Integrated analysis

Is there evidence for a declining incidence of HIV at the national or sub-national level? If so, is it likely to be explained by mortality or changes in sexual behaviour?

4. Discussion

…

5. Appendix references

1. **Asamoah-Odei, E. et al.** HIV prevalence and trends in sub-Saharan Africa: no decline and large subregional differences. *Lancet. 364*: 35-40 (2004).
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