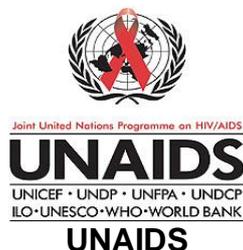# Estimation of the size of high risk groups and HIV prevalence in high risk groups in concentrated epidemics

Report of a meeting of the UNAIDS Reference Group on Estimates, Modelling and Projections held in Amsterdam, the Netherlands, Dec 9-10th 2008

TECHNICAL REPORT AND RECOMMENDATIONS

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 the complex topic of estimation methods for HIV prevalence in high risk groups and the size of high risk groups in concentrated and low level epidemics in order to inform new guidelines for surveillance and estimation.

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 29 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.

Methods for estimating the size of high risk groups in concentrated and low level epidemics

Presentations reviewed the available methods and examples of their results to share experience in estimating the size of high risk populations.

1. Sex worker populations and capture-recapture method

Capture-recapture (CRC) method has been used in a range of settings to quantify the size of hard to reach populations. Typically, this method is initiated with detailed mapping to identify "hotspots" of the high risk population, then two samples are taken with the overlap determining the overall size.

In Côte d'Ivoire, where multiple methods have been used to quantify the size of sex worker populations, capture-recapture was utilised in three cities in 2008 in an effort to update the mapping of sex worker sites, provide a better estimate of the size of the female sex worker population, promote the services available to sex workers and evaluate the level of coverage of these services. The results were compared with previous enumeration methods of estimation and the use of CRC resulted in the identification of two to four times as many sex worker "hotspots" in each site and resulted in a greater population size estimation compared to previous estimates (with the exception of census data). Capture-recapture was identified as a feasible method for estimating the size of this hard to reach population in Côte d'Ivoire. Ethical issues regarding mapping were raised and it was iterated the mapping should only include the place of work and omit any information identifying place of residence.

2. Multiplier method

The multiplier method is mathematically simple and straight forward and relatively easy to implement with proper preparation. The basic principle is that the number of persons belonging to the hard to reach population who appear at selected locations or services over a specified time frame is equal to the total size of the estimated population multiplied by the proportion of the population who attended the services. The method assumes there are two overlapping but independent data sources, specific to the group being counted, and that the population has a non-zero probability of inclusion in both sources. This method is arithmetically equivalent to the CRC formula but different in its implementation.

Multipliers can be applied on the basis of 1) service statistics e.g. recorded by NGOs serving the population to be counted (many challenges selecting a valid multiplier due to different NGOs using different documentation methods); 2) tagging based on certain criteria or a population definition; 3) a unique object identifier which is distributed in advance of the survey. The unique object identifier method is advantageous in that it is controlled by the survey team and may reduce potential bias; however, it was noted that confidence intervals will be larger when only a small number of people receive the object.

Multiplier methods in conjunction with probability sample surveys are potentially powerful and easy-to-use tools for size estimation. Behavioural surveys conducted in India surveyed high risk groups captured by time location sampling or respondent driven sampling which allowed the multiplier method to be used. The Avahan project found that use of the multiplier method yielded lower size estimates than the mapped programme data. It is uncertain why this occurred, it may be due to inflated mapping estimates or due to interdependence between the data sources. When utilising this

method, it is imperative to spend time getting a good multiplier; in the absence of a multiplier based on service statistics, the unique object identifier method can be used.

3. Estimating the size of IDU populations

The Reference Group to the UN on HIV and injecting drug use (IDU) recently conducted reviews on the use of methamphetamine around the world and the association of methamphetamine injection and HIV, a review on the injection of pharmaceutical opioids and a systematic review on the global epidemiology of injecting drug use and HIV.

Globally, 148 countries report injecting drug use, 61 countries have some form of prevalence estimates of IDU and 40 countries use indirect estimates of IDU. Multiple methods are used in conjunction with many different surveys to estimate the size of IDU populations. Multiplier methods are most commonly utilised, but CRC is also employed while modelling methods, such as back projection, are less frequently applied.

Administrative datasets are commonly used for IDU estimation and include: hospital data, drug dependence treatment data, opioid substitution treatment data, overdose data, arrest data, and drug user registration data. These data sources often have an opioid focus and may be unable to capture, or imprecisely capture, the IDU population. Miscoding or a lack of coding is a common problem with these datasets. In addition, questions arise regarding the definition of an injecting drug user and estimates may vary in capture to include current IDU, past IDU or lifetime IDU.

Examples from Australia (Hallett et al, 2000; Degenhardt et al, 2004; McKetin et al 2004; Law et al, 2006; Kimber et al, 2008) illustrate that the use of multiple methods have produced a range of population size estimates. Concern was expressed that IDU populations are dynamic and one should be aware of the limitations of the data used. Multiple, indirect methods are preferable and sensitivity analyses are critical.

4. Direct and indirect methods for client estimates

There is evidence that DHS data underestimates the proportion of males who are clients of female sex workers (FSWs). The indirect method of estimation is to extrapolate based on census data estimating the number of FSWs together with the number of clients FSWs report and the number of client acts per year FSWs report to identify the number of male clients.

A direct method of estimation was employed in West Africa, using a polling booth method where questions were read aloud and voting cards were placed into a box depicting yes/no answers while respondents were isolated from each other in private booths. The cards were compiled to produce aggregate data and provided the proportion who had visited a sex worker. This method does not require literacy, is completely anonymous and results in less uncertainty than the indirect method.

The implementation of large-scale polling booth surveys may be a method to improve estimates on the size of FSW client populations. The data can be extrapolated to the national level with adjustments made for rural and urban differences. To improve estimation with indirect methods, it would be advantageous to modify behavioural surveys to provide better understanding of the level of FSW activity over a one-year time period.

5. Comparison of different methods used in India for size estimation of high risk groups

Since 2003, the Avahan project has conducted intervention programmes among at-risk populations in areas with high HIV prevalence in 83 districts across six states in India. In order to monitor and evaluate the interventions, Integrated Behavioural and Biological Assessment (IBBA) is conducted. When this project began, NGOs performed initial size estimates of the high risk populations and these estimates are updated every six months to one year with a mapping exercise fed into by peer educators.

The methods used by the Avahan project for estimating the size of high risk groups in India include: programme estimates from census data, capture-recapture with a unique object identifier, multiplier method, and a new approach, the reverse tracking method. The reverse tracking method (mathematically similar to the Hansen-Hurwitz method) requires comprehensive mapping of hotspots followed by sampling frame development containing both time location clusters and conventional clusters. Cluster size was determined by key informants thus this probability based sample is not suitable for hidden populations (e.g. IDU).

The use of multiple methods identified many potential problems. For the multiplier method there was difficulty choosing a multiplier due to NGOs operating services in overlapping areas, migration and double counting of populations and avoidance of programme services for fear of being identified. CRC highlighted the importance of timely recapture. The strengths of the estimates from the Avahan project are that they are from community established interventions and trust built among the community has helped to identify hidden sub-populations. The estimates can readily and easily be updated and mobility patterns can be monitored.

6. Direct measurement of high risk populations in a national survey

The National Survey of Sexual Attitudes and Lifestyles (NATSAL) is a cross-sectional, national probability sample undertaken in Britain; it is a household survey and thus has several limitations.

The limitations that may impact size estimates of high risk populations include selection biases, variance in population definitions, desirability biases and insufficient power. Populations that are not queried include prisoners, homeless people, people in hostels, hospitals and nursing homes and non-responders. It is possible that high risk groups are more likely to be non-responders. Population definitions vary, for example gay men versus MSM, (identification as gay versus reporting homosexual sex) and the choice and wording of questions may result in different capture. Desirability bias and differences in social acceptability of behaviours over time may result in different levels of disclosure over time.

The strength of this national probability sample is that it provides an opportunity for triangulation with convenience samples, respondent driven sampling and general population estimates. Repeated cross-sectional surveys with consistent methodology will also allow for estimation of calendar and cohort effects. It was discussed that changes in the wording of questions may account for a proportion of the changes observed and it was noted that consistent methodology is necessary to identify trends.

7. Network scale-up method in large area surveys

The network scale-up method has been used to estimate size of small and large hidden populations. The basic principle is that, "people's social networks are, on

average, representative of the population." The estimate requires three pieces of information: the number of HRG known (collected in the survey), the network size of respondent (estimated from the survey) and the number of people in the entire population (known). The social network size of the respondent can be identified through back estimation or summation (McCarty et al, 2001). This simple estimate can be improved by averaging over many respondents (Killworth et al, 1998). The method requires a random sample of the general population but does not require contact with the hidden population. It can be added to a nationally representative survey to produce sizes for many hidden populations at the same time and may be useful for estimation of IDU, MSM and CSW populations.

A disadvantage of the network scale-up method is that barrier effects (non-random mixing or uneven distribution of hidden populations) will increase the variance and lead to bias if the sampling frame is incomplete. In addition, respondents may be unable or unwilling to answer questions accurately regarding IDUs, MSM and CSWs. Currently, there is no sound procedure for applying confidence intervals to the estimates.

This method has been used predominantly in the United States and needs to be applied to other countries in a research setting. More theoretical research is needed on the statistical procedures focusing on the variance and magnitude of biases. Research on the accuracy of responses is also needed in addition to further development of procedures that will improve measurement of network size.

Estimating HIV prevalence in high risk groups in concentrated and low level epidemics

1. The use of respondent driven sampling as a surveillance tool

Respondent driven sampling (RDS) is a variant of chain-referral sampling consisting of two components, recruitment and analysis. Recruitment is initiated with non-randomly selected members of target populations (seeds) who in turn recruit others in their network. After a number of rounds of recruitment those sampled should be representative and prevalence can be measured. RDS has successfully been used in numerous countries among many different populations including Thailand for recruitment of clients of sex workers and Albania for recruitment of street working children.

Respondent driven sampling has advantages in that little formative research is required, there is no mapping, target members recruit for you and less visible and invisible populations are reached. The implementation and analysis tools of RDS have already been developed, there are representative estimates and confidence bounds and RDS can provide multipliers for population size estimation.

The challenges of RDS are that it only works on populations that are socially networked and willing to recruit their peers and it may be difficult to verify group membership. Logistical training is required and there are dangers that the method is poorly implemented, partly as a result of the complex theoretical parameters, the difficult-to-use software and the analysis tools which need further development. In addition, it is particularly difficult to deal with selective non-response bias. Homophily, where there is a bias to recruit similar individuals into the sample, needs to be addressed as there may be sub-populations that are not connected, for example, street sex workers may not know sex workers in bars or clubs and HIV may be particularly focused in one of these populations.

2. Time location sampling

Time location sampling (TLS) or time location cluster sampling (TLCS) is a probability sampling method that is similar to conventional cluster sampling. This method is preferable for non-networked populations and is potentially useful for interventions if locations where they are required are identified. The use of TLS results in a clear understanding of who is "captured", the geographic area is clearly defined, the criteria and methods for selection are under the control of the survey team and refusals can be tracked. This method may capture a more relevant population than other methods if subjects are sampled where and when risk behaviour is concentrated and can additionally provide multipliers for population size estimation.

Compared to RDS, the TLS tools for analysis are more user-friendly and provide more analysis options (batch processing, documented programming, ease of moving between data cleaning/recoding and analysis, flexibility for analysis of continuous variables, sub-group analysis is less constrained). In addition, there is easier coverage of broad geographic areas and easier analysis for subgroups; however, TLS is more resource intensive with the development of the sampling frame being particularly time consuming. Time location sampling will miss the less visible or hidden populations and it can be biased as it requires a "counter" and "selector" who can correctly identify eligible respondents.

3. Comparison of national survey prevalence to sentinel surveillance prevalence in concentrated epidemics

Many countries use ANC prevalence data as a substitute for prevalence among the low risk population, either for women only, or for both men and women. The question arises whether an adjustment will be required for ANC data, equivalent to the adjustment for generalised epidemics to correct for bias that is largely due to the geographical non-representativeness of ANC sites. National surveys are not recommended in low-level and concentrated epidemics; however, some countries and states with concentrated epidemics have conducted national prevalence surveys (6 states in India, the Dominican Republic, Cambodia, US, Peru, and one province in Vietnam). ANC prevalence data can be compared to these national prevalence surveys. This work is ongoing and raises questions regarding patterns across different countries, differences in women only, versus women and men combined, and differences in rural areas versus urban areas and differences by age. Further work is necessary to identify if ANC sentinel surveillance is different from routine testing for PMTCT; if a general adjustment factor should be used with ANC data in concentrated epidemics, when to use an adjustment, and of what magnitude the adjustment should be. It is recommended that where national surveys are available, they should be used for comparison with sentinel surveillance.

Recommendations

It is clear that estimating the numbers and associated prevalence for high risk populations is a fundamentally difficult exercise. There is currently no one correct approach and the potential pitfalls of the methods are unclear. In such circumstances, good documentation of methods and appropriate caution in interpreting results are extremely important.

Specific recommendations for estimating the size of high risk groups and HIV prevalence in high risk groups:

➢ Triangulate estimation methods. Use more than one method for estimating the size of high risk groups and compare the results obtained from different methods.

➢ All types of available data should be used for size estimation of high risk groups but should be interpreted with caution

➢ The population and its characteristics need to be explicitly defined.

➢ The reliability and representativeness of survey data needs to be addressed.

➢ Further research is needed for the potentially promising network scale-up method including the generalisability of results, the degree of extrapolation and the possibility for use as a national estimate.

➢ Different estimation methods should be used for different situations (e.g. RDS is not an appropriate method to use for clients of sex workers).

➢ Detailed, explicit documentation and definition of the sample frame methodology is important. It is essential that the documentation process is understood and adhered to.

➢ The biases of sampling methods need to be acknowledged and presenting bias should be viewed as a strength as opposed to a weakness.

➢ Detailed documentation and explanation of extrapolation, adjustment and estimation methods used for national estimates of HIV prevalence should be provided.

➢ Funding for evaluation is essential. Donors need to support the processes, the research and the technical support necessary to make this happen. There cannot be reliance solely upon national programs.

➢ There needs to be a route for publication of these findings, a journal for HIV surveillance.

Modelling of national HIV epidemics in concentrated settings

1. *Applying the Modes of Transmission model to countries in West Africa*

Ongoing work is being conducted applying the Modes of Transmission, (MoT) model to West African countries. It was found that a high proportion (25-50%) of new infections occur in low risk populations due to past experience of risk behaviour or due to having a high risk partner, while 15-35% of new infections occur among the partners of medium and high risk people and 10-30% of new infections are due to sex work. IDU transmission was highlighted as a major factor in Nigeria but there is a lack of data on IDU transmission in other West African countries. Similarly, MSM transmission is not well understood and better information is needed regarding the population size, the number of partners and acts per partner and condom use. It may also be useful to use scenario analysis to examine MSM and IDU transmission.

A critique of the MoT application to West African countries illustrated specific data issues, transmission dynamics issues and presentation issues. Specifically, the results are highly dependent upon components of population estimates for high risk groups in a context where size estimates are often based on small, unrepresentative studies (particularly for MSM and IDU). For some countries, estimations of FSW client populations were derived using DHS data despite suggestions these may be a gross underestimate. There remains a need for better understanding of the proportion of men who are clients of sex workers, how often clients visit sex workers and the number of contacts that are with the same sex worker.

In countries with largely concentrated epidemics, low risk cases are mostly due to the past experience of risky behaviour of partners or having a currently high risk partner thus modelling incidence over one year only will underestimate the contribution of high risk people and their partners to the total number of prevalent cases.

While absolute numbers and specific incidence rates are available from the MoT model, proportions are usually presented and this is problematic when comparing countries and distribution between different categories. An increase in the proportion in one group does not mean increased transmission in this group, and vice-versa. Current graphical representation does not take into account dependency between each category (i.e. if contribution of one category increases, at least one other will decrease). It was argued that with better data, the MoT model could be useful for assessing short-term impact of preventive activities, but could be misleading for medium and long-term impact.

It was recommended that absolute numbers and incidence rates should be considered and utilized. The reliability of DHS data needs to be assessed in addition to the representativeness of special population studies.

2. *EPP 2007 for national estimates in countries with concentrated epidemics*

The application of EPP to three countries with concentrated epidemics – Vietnam, Cambodia and Myanmar – highlighted many important issues to consider when using EPP for national estimates in countries with concentrated epidemics. The methodology of application will vary by type of epidemic. In Vietnam, the

methodology was to decompose into geographic clusters with at-risk populations, an intensive process that elucidated substantial geographic diversity. In Cambodia, the approach was to treat the epidemic like a general population one, and perform ANC fits coupled with male adjustments, while in Myanmar national fits were applied using at-risk populations (EPP fit then values recalibrated).

Issues arose with population size estimates, geographic diversity, data availability and quality. Specifically, there is a dearth in population size estimates for high risk groups, many of which are hidden or poorly characterised. Size estimates are not triangulated or validated with multiple sources and there is pressure to use "official" estimates which is problematic, especially in IDU dominated epidemics where results can be thrown off substantially.

The issue of sample representativeness needs to be addressed. Limited numbers of sites are used to provide supposed national coverage and data are heavily urban-centric. Convenience sampling is most commonly employed for high risk populations with samples taken from rehabilitation facilities, urban clinics and hospitals. The definitions of surveillance populations may be unclear and there may be shifts in at-risk populations and definitions of at-risk populations over time. The biases in surveillance are not assessed or understood. There remains a need for more surveillance "calibration studies" comparing to more systematic samples (e.g., IBBA and surveillance) and performed by independent organisations. Questions remain regarding ANC representativeness; recalibrations of ANC data can substantially affect results. Data is not reviewed or cleaned regularly and there are limited years of data availability, which allows considerable variability in fitting EPP. Uncertainty is particularly large if the epidemic has not reached a plateau.

It is recommended that the application of EPP goes hand-in-hand with careful review of surveillance. Problems and outliers need to be identified and removed and the data should be cleaned before fitting. Feedback mechanisms should be built so surveillance improves over time and surveillance data should be calibrated. Finally, the results should be validated against other sources.

3. Modelling concentrated epidemics with Asian Epidemic model

The Asian Epidemic model (AEM) is a deterministic process model patterned after Asian epidemics. It takes behavioural inputs, translates them into predicted HIV infection numbers and compares these against observed trends. The key inputs include the size of high risk populations, behaviour over time and the transmission parameters. Validation is by fitting to observed HIV prevalence; standardised outputs are provided. AEM provides essential information for prevention targeting in Asia, allows analysis of intervention impacts in specific groups and can be applied to cost-benefit or cost-effectiveness analysis. It has been successfully applied to many countries including China, Thailand, Bangladesh and Vietnam and has been applied in preliminary form to all Asian countries.

Key advantages of AEM over EPP include the linking of epidemiology and behaviour, but if behavioural patterns are wrong the shape of the epidemic is wrong; and the linking of populations. Recent work is being undertaken to make AEM easier for local application, automatic fitting (using Bayesian melding), uncertainty estimation, an affected children module and a new MSM module, expanded to include relationships, casual and commercial partners and segregated into high and low risk MSM.

4. Performance of estimation tools used for comparison with case reports of HIV infection

Different methodological approaches have been applied in research studies to estimate HIV prevalence in both the UK and the Netherlands. A recent application in the UK used the direct method. This method was found to be difficult to implement due to lack of available data for some high risk groups, potential biases, and data sources providing information only on mixtures of different risk groups. Assumptions were made to compensate for the lack of data and biases, and while sensitivity analyses were done, there was no real scope for proper quantification of uncertainty (no confidence intervals). In addition, there was no notion of relationship between sources of information with each parameter informed by a single item of data thus it was not possible to validate the results. There was no notion of model fit which resulted in the inability to discern if the results were credible.

An alternative approach, the Bayesian multi-parameter evidence synthesis (MPES) method was then applied. This is a probabilistic model in which a composition of mixed groups is explicitly modelled with explicit modelling of biases. The advantages of MPES are that the results come from a long process of model and data criticism. MPES has the ability to combine data on the basic parameters with data on the functions which results in more than one data item informing the estimation of a given parameter, providing more precise parameter estimation. MPES allows investigation of consistency between pieces of information and model fitting and allows correct propagation of uncertainty and provision of credible intervals for any quantity of interest.

The main disadvantage of MPES is that it is not user-friendly. It requires an in-depth understanding of data limitations, an understanding of the underlying estimation philosophy (Bayesian) and expert knowledge of the software it is implemented in (WinBugs). MPES is not an automatic process and each estimate can be approached in a different way according to the nature of the available information. Communication of the rationale and results of this complex model may be difficult.

5. Uncertainty around national prevalence estimates in concentrated epidemics

The assessment of uncertainty about national prevalence in concentrated epidemics is in a developing state. The Workbook equation in combination with Bayesian framework for uncertainty, or "Bayesian Workbook," is a method currently being used which combines uncertainty estimates from regions and risk groups. The Bayesian framework for uncertainty includes a posterior distribution for size of risk group by region and a posterior distribution for prevalence by risk group by region. Estimates for the size of risk groups and the HIV prevalence in risk groups may be based on different data so their posterior distributions may be independent. While the posterior distribution for prevalence might not be too difficult to obtain, the posterior distribution for the size of high risk groups and hidden populations can be a particular challenge. It is difficult to assess uncertainty in estimates due to confounding between population size and the probability of being counted, in other words, it is difficult to distinguish between low population size with high probability of being counted and high population size with low probability of being counted.

Methods exist for estimating uncertainty in CRC and multiplier methods, snowball sampling and network scale-up. Estimating uncertainty in population size from RDS needs further research. Capture-recapture is the gold standard when the assumptions hold, which they rarely do. The assumptions of CRC are that the two samples are independent, all capture probabilities are equal, all captures are correctly identified, and it is a closed population (no migration, births or deaths between samples). The most serious violation is heterogeneity of capture

probabilities. It was highlighted that information about the distribution of capture probabilities is useful and should be collected.

The Bayesian Workbook framework has the ability to combine different data types (CRC, RDS, network scale-up) and handle missing data. It allows for integration with EPP and it allows the use of prior information from other countries, regions, and time periods.

Recommendations

Specific recommendations for modelling national HIV epidemics in concentrated settings:

- ➢ ANC data should be used and adjusted as it is likely an overestimate of the general population prevalence for women. Examine ANC surveillance coverage (geographic, age distribution, attendance) and consider potential bias.

- ➢ Use cross country comparisons to inform definitions (MSM, urban versus rural, type of SW).

- ➢ Use scatter plots to strengthen assumptions (urban versus rural prevalence, ANC adjustments).

- ➢ Triangulate prevalence estimate and number diagnosed with proportion infected. In countries with strong reporting systems, case data can be included in triangulation for model validation (CD4 at diagnosis, AIDS case deaths).

- ➢ Examine the relationship between prevalence and the definition of high risk groups. A high prevalence should not be applied to a broad definition.

- ➢ Explicitly document all methods and note changes in protocol over time.

- ➢ Examine data for outliers and epidemiologic plausibility before fitting.

- ➢ The comments section of EPP needs to be utilised to document the source of prevalence data.

- ➢ Use the current Workbook method for uncertainty in national estimates.

- ➢ Further research is needed to explore uncertainty and should be tested, initially, with countries where there is access to the primary data. The methods need to first be tried and then applied to more politically sensitive locations.

Appendix I: Meeting Agenda

TO BE INSERTED IN PDF VERSION

Appendix II: List of Participants

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