Editorial: methodological developments in the Joint United Nations Programme on HIV/AIDS estimates

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Introduction

The Joint United Nations Programme on HIV/AIDS (UNAIDS) publishes estimates of the HIV epidemic every year [1]. For 2016, estimates are available for 160 countries representing 98% of the global population. These estimates are produced by countries with guidance from UNAIDS. The methods used in this process continue to evolve over time under the stewardship of the UNAIDS Reference Group on Estimates, Modelling and Projections [2].

In 2014, the WHO convened the Guidelines for Accurate and Transparent Health Estimates Reporting (GATHER) Working Group with the aim to define and promote good practice in reporting global health estimates [3]. The GATHER Statement is the outcome produced by this group. It defines a list of reporting requirements to allow for the accurate interpretation, and facilitate the appropriate use, of global health estimates [4]. UNAIDS fully endorses and supports the GATHER Statement.

The current special supplement, which details the methods used to produce the 2016 UNAIDS estimates, further supports the routine publication of data sources and methods used as part of an open and transparent process. It provides updates of the evolving understanding of the data on which the estimates are based, the methods used to derive the estimates, justification of changes in these methods, and the sources of new data available to inform these modifications. It follows a series of such collections [5–10] which have documented and described the evolving methods used to produce the UNAIDS Global AIDS estimates since 2004.

Key updates and modifications in Spectrum

The AIDS Impact Module and the Estimation and Projection Package (EPP) in Spectrum [11] are the core tools used by countries and endorsed by UNAIDS to produce HIV estimates. These tools are modified and updated as new data become available, in response to further method development, and to support the evolving needs of program planning, monitoring, and evaluation. Changes in the methods used can result in changes in both current and historical estimates.

A key change in the 2016 estimates is the reduction in the estimated number of children living with HIV (CLHIV) compared with previous estimates. Mahy *et al.* [12] describe the new evidence on the probabilities of mother-to-child HIV transmission and the age at which children initiate antiretroviral therapy, both of which are crucial assumptions. This leads to a 27% reduction in CLHIV compared with the 2015 estimates. The revised estimates are compared with the available empirical data which illustrate general consistency with nationally representative population-based surveys, although, given the paucity of empirical data on HIV incidence and prevalence, the potential for underestimation of HIV prevalence, especially among children at older ages, remains.

Among adults, new data available from the International Epidemiologic Databases to Evaluate AIDS Network are used to estimate revised model parameters in Spectrum for adult mortality on antiretroviral treatment (ART). Anderegg *et al.* [13] update a previous analysis from 2012 [14] and develop methods to adjust the observed all-cause mortality on ART to account for the unknown outcomes of patients that are ‘lost-to-follow-up’. Patient-level data from 43 countries across seven regions

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are used in this analysis. Mortality rates for each region are corrected on the basis of the ascertainment of vital status of those lost-to-follow-up from tracing studies in Kenya and linkage of data systems in South Africa. The revised estimates express higher on-ART mortality rates than those previously calculated. This is largely explained by this analysis benefiting from the data of many more sites than was possible previously. However, there remains a need for empirical data on the outcomes of patients' lost-to-follow-up, in countries outside of South Africa and Kenya, to further improve the accuracy of these parameters.

For countries with concentrated or low-level HIV epidemics, Mahiane *et al.* [15] describe the 'Fit to Program Data' tool in Spectrum which allows estimation of HIV incidence from case-report data and vital registration of AIDS mortality. This tool was developed to provide an alternative option to fitting to surveillance and survey data in EPP, data which are often unavailable in low-level epidemic settings, require nationally representative trends over time, and robust size estimates for key populations. This new fitting tool allows countries with strong case-reporting systems and relatively complete registration of AIDS deaths to take advantage of the strength of these data to develop estimates. In 2016, 62 countries used this tool to produce estimates, compared with 16 countries in 2015. Fitting to program data in these countries provided good alternative fits compared with EPP when information about the timing of diagnosis, the proportion of the population undiagnosed, and the potential for misclassification of AIDS-related deaths over time is known.

Other modifications in EPP and Spectrum described by Stover *et al.* [16] include the implementation of updated demographic data at the national and subnational level, adaptations to the program data input to better reflect WHO 2015 guidelines on ART, improved estimates of uncertainty at the regional level, additional options for estimating incidence in Spectrum, and technical changes related to the sharing of estimates between different modules within the framework.

Better understanding of the data used in the estimates

HIV prevalence measured from periodic sentinel surveillance of pregnant women attending antenatal clinics (ANC) has historically been the basis in EPP for estimating trends in HIV prevalence over time in generalized epidemic settings [17]. However, these data present a number of challenges, which new methods seek to better accommodate.

First, these data from pregnant women are subject to a bias caused by the reduced fertility associated with HIV. Corrections for this are already made in the estimation process, but accumulating data availability allows a more detailed analysis. Marston *et al.* [18] use data from population cohorts in Uganda, Tanzania, and Zimbabwe to estimate the relationship between duration of HIV infection and fertility before the availability of ART. This is done to understand how increases in population level subfertility by duration of infection affect the relationship between prevalence among pregnant women and the population over the course of the epidemic.

Second, these trends can exhibit greater variation than expected from random sampling error alone, due to changeable sampling practices, testing procedures or local epidemic shifts. If this is not factored-in to the model fitting, too much weight could be attached to those data compared with high quality data sources, such as national population-based surveys. Eaton and Bao [19] propose three approaches to account for the uncertainty of nonsampling error in HIV prevalence measured in ANC sentinel surveillance and tested these with data from nine countries in southern and eastern Africa. The authors find that incorporating an additional variance parameter in EPP to allow for nonsampling error, and estimating this variance term via Bayesian inference, results in improved fitting to household survey prevalence and appropriately increased uncertainty intervals in the early epidemic period. This approach is recommended for implementation in EPP and will also have further applicability for the inclusion of other types of data in EPP fitting, notably routine testing data from prevention of mother-to-child transmission programs.

Third, as the ANC surveillance sites were historically chosen more for their convenience than a belief that they faithfully represent the wider communities of which they are a part, it remains a question about how to interpret those data in a spatial context. To examine this, Wilson *et al.* [20] investigate whether HIV prevalence measures among women attending ANC clinics are representative of prevalence in the local area, or whether estimates may be biased by women who travel away from their home areas to attend nonlocal clinics. Data from periodic surveillance rounds conducted in 19 ANC clinics in Zimbabwe between 2000 and 2012 are used to compare HIV prevalence and nonlocal patterns of attendance. The authors find that while HIV prevalence in towns was slightly underestimated due to women from lower prevalence rural areas traveling to towns to attend ANC in 2000, there was no distortion in HIV prevalence in more recent surveillance rounds. Thus, prevalence measures among women attending ANC in Zimbabwe provide reliable estimates of HIV prevalence in pregnant women in the local area. Further studies are needed to establish the wider generalizability of these findings.

Finally, countries with generalized HIV epidemics are currently transitioning away from periodic sentinel surveillance in ANC to the use of routinely collected data from all ANC sites. This transition has important implications for generating HIV estimates and the greater spatial density of these data will be central in developing more spatially specific estimates. There are also challenges, as countries will no longer have the continuity of data from the same ANC sentinel surveillance trend data over time, but will instead include data from all sites, with testing requiring patient consent and conducted using rapid tests, and so potentially subject to a range of different biases. Sheng *et al.* [21] propose new methods that allow for the inclusion of both sentinel and routine surveillance data in EPP and address these biases, and generate recommendations and further considerations to further test and refine these methods as routine program data become available.

Validation of surveillance data and model estimates

The estimates produced for each country represent the compilation of a large amount of data but inevitably also rely to some extent on assumptions and judgments. It is, therefore, important to take every opportunity to compare the outputs of the estimation process to other data and to assess how faithfully estimates align with reality. Two approaches have recently been used.

To assess the performance of the models in estimating incidence and prevalence trends, Silhol *et al.* [22] produced a subnational model projection in Spectrum using surveillance data from women attending ANC, census data, and population survey data from an HIV cohort study in Manicaland, Zimbabwe. The estimates obtained from the Spectrum projection were compared with the empirical estimates. Overall, model estimates of the incidence and prevalence were in good agreement with the data. However, the Spectrum estimates of HIV incidence among women declined faster than empirical estimates, and there were inconsistencies in the Spectrum estimated age-patterns of adult all-cause mortality. Among children, the latest Spectrum estimates of child HIV prevalence closely matched survey prevalence, but discrepancies were observed in the estimates of maternal and paternal orphanhood.

To assess the performance of the models in estimating mortality trends, Masquelier *et al.* [23] compare the 2016 Spectrum estimates of adult mortality and orphanhood in 43 countries in sub-Saharan Africa to household survey and census data. Among adults, the authors find discrepancies in the levels, sex ratios and age patterns

of adult mortality. Although some of these differences may be explained by suspected systematic biases in the empirical measurements, some of the signals could point to factors affecting mortality that are not fully represented in the models. In particular, it appears that in high prevalence settings the bulge of AIDS deaths around ages 34–39 years for women in Spectrum is not found in empirical estimates, which show the spread of AIDS deaths is less concentrated and extends to younger women as well. For high-HIV prevalence countries, this analysis also indicates a higher prevalence of paternal orphans in the survey and census data than in the model estimates, which is consistent with findings by Silhol *et al.* [22], and suggests underestimation of HIV-associated male mortality in Spectrum. In low and intermediate HIV prevalence countries, both paternal and (especially) maternal orphanhood are lower in empirical estimates than in model-based ones. The ‘adoption effect’ – respondents reporting parental survival based on a current foster parent rather than the biological parent – may contribute to these discrepancies, particularly for maternal orphanhood.

Taken together, these highlight areas for further investigation and method development – particularly pointing toward the need to develop age-structured modeling of mortality data and prevalence and program data simultaneously – and indicates that, for now, caution should be taken in interpreting some estimates, notably age-specific estimates of child prevalence, age-specific estimates of mortality, and orphanhood estimates. Further work is currently underway to address these issues.

Development of new methods to inform future estimates

There is an increasing demand for estimates at the subnational level to inform program planning, decision-making, and resource allocation and to monitor and evaluate progress toward stated goals. A goal for future rounds is for estimates to be developed at much finer spatial scales and work to develop appropriate methods is progressing rapidly [24,25]. However, several developments that allow leveraging of available data to better represent subnational epidemics are already planned for use in the 2017 estimates round. In particular, Niu *et al.* [26] present a statistical model that incorporates a hierarchical structure in EPP to improve the precision of estimates at the subnational level. This method ‘borrows’ information from relatively data-rich areas to inform data-poor areas. The authors demonstrate the improvement of HIV estimates at the subnational level in both generalized and concentrated epidemic settings.

Conclusion

The 2016 UNAIDS estimates are informed by the best available data and evidence. The accuracy of these estimates is critical for HIV program planning, effective scale-up of services, and optimal use of resources. As such, the methods used to generate these estimates will continue to evolve in the future in support of continual refinement and enhanced precision. The generation of additional empirical data will be essential to further improve the ability to develop and validate model-based estimates.

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Conflicts of interest

There are no conflicts of interest.

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