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Lessons from the 2012 national HIV household survey to improve mathematical modelling for HIV policy

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Since the start of the HIV epidemic in sub-Saharan Africa, mathematical models fitted to surveillance data have been heavily relied on for estimating and projecting the future course of HIV epidemics (1). The establishment of HIV surveillance at antenatal clinics in the late 1980s created routinely available data for systematically monitoring HIV epidemics across Africa, but mathematical models are needed to relate these data to the outcomes that matter most for responding to HIV epidemics: HIV in the general population, new HIV infections, and HIV deaths.

Over time, HIV surveillance data have improved with developments such as HIV testing in nationally representative household surveys (2). Mathematical modelling methods capable of incorporating these new data have developed alongside, including new statistical methods for robustly fitting the models to data and quantifying uncertainty in estimates (3,4).

The most recent *South African National HIV Prevalence, Incidence and Behaviour Survey* conducted in 2012 incorporated new tools for generating greater information about the current state of the HIV epidemic from the national household survey. In addition to data included in previous surveys about HIV prevalence, sexual behaviour, and knowledge and attitudes towards HIV, the 2012 survey additionally tested blood samples for the presence of antiretroviral drugs, HIV viral load, and evidence of recent HIV infection (5). Overall, the survey estimated that HIV prevalence among adults aged 15–49 years was 18.8% (95% CI 17.5–20.3%), an increase from 16.9% in 2008, and HIV incidence was 1.72% (1.38%–2.06%) in the 15-49 years age group.

Rehle and colleagues compared how direct HIV incidence estimates from the multi-assay recent infection algorithm compared with more conventional approaches to estimating incidence with mathematical models fitted to HIV prevalence data and assumptions about HIV survival and the effects of antiretroviral treatment (ART) (6). The three models, all updated to incorporate prevalence data from the 2012 survey, included in the comparison were: (i) Thembisa, an HIV epidemic model developed specifically for South Africa (7), (ii) the EPP/Spectrum model used by UNAIDS for HIV epidemic estimates across the world (8), and (iii) a synthetic cohort method for estimating HIV incidence from two prevalence surveys (9). Estimates of HIV incidence in 2012 amongst those 15-49 years were remarkably consistent across the three models and the direct HIV incidence estimates from the multi-assay recent infection algorithm : 1.47% (1.23%–1.72%) from Thembisa, 1.52% (1.43%–1.62%) by EPP/Spectrum, 1.9% (0.8%–3.1%) from the synthetic cohort method and 1.72% (1.38%–2.06%) from the HIV incidence testing algorithm. , and. The consistency across estimation methods increases confidence in the sobering conclusion about the continuing spread of HIV in South Africa of over 1,000 new infections daily in 2012 (6).

Validating model projections

Mathematical models are also widely used for investigating the potential impact of HIV prevention strategies, recently with particular interest in 'treatment as prevention' (10). More than a dozen different mathematical models have been calibrated to the HIV epidemic in South Africa, and models have been in broad agreement that achieving high levels of ART coverage would be expected to substantially reduce HIV incidence in South Africa (11) and that earlier ART eligibility would be cost-effective (12). For the first time, the 2012 household survey data provided an opportunity to externally *validate* the model projections by comparing existing model predictions for HIV prevalence, incidence, and mortality to the new survey data. Crucially, the model projections were all created before the 2012 household survey data were analysed and published.

Overall, we found that the models accurately anticipated many of the important epidemiological changes that occurred in South Africa between the national household surveys in 2008 and 2012 (13). These included a substantial shift in the age pattern of HIV towards older ages as HIV incidence and prevalence declined among young adults while HIV positive adults survive to older ages owing to ART, and dramatic reductions in HIV deaths coinciding with the rapid scale-up of ART. However, models did not predict an increase in HIV prevalence between 2008 and 2012 as great as the 1.9% observed. Instead, models tended to predict that HIV prevalence in 2012 would be similar to that in 2008, because the number surviving longer with ART would be approximately offset by reductions in new infections. Changes in prevalence among young adults aged 15–24 years were similar between the models and survey data, but models systematically underestimated prevalence among adults aged 25–49 years, suggesting that HIV incidence among middle-aged adults may have been higher than expected. It is not possible to identify exactly why the models did not predict the prevalence increase, but potential contributing explanations could include: that models were not adequately calibrated to earlier epidemiological data; that there were unforeseen increases in sexual risk behaviour;, that models did not fully capture reductions in mortality; or that models were overly optimistic about the extent to which ART would reduce HIV incidence.

One further observation from this validation exercise was that models which were directly calibrated to earlier household survey data more accurately predicted the epidemic trends than did models which were primarily calibrated to trends in HIV prevalence among pregnant women in antenatal clinics. This made sense considering the steady increasing prevalence observed in three household surveys, while prevalence in pregnant women has been unchanged for nearly a decade. Deeper investigation of this, however, illustrated that within each age group prevalence trends among pregnant women were the same as in the general population—decreasing prevalence among the young women, but increasing HIV prevalence among older women (14). The apparent discrepancy in trends was explained by the unique age distribution of pregnant women, highlighting how HIV prevalence among pregnant women declines more rapidly than that among the general population, in mature HIV epidemics (15). The most recent global HIV epidemic estimates published by UNAIDS in July 2015 incorporated an adjustment in the model calibration to antenatal clinic sentinel surveillance data to account for the relationship between prevalence among pregnant women and the general population (16). In this way, findings from the 2012 household survey in South Africa have contributed to better understanding of the HIV epidemic not only in South Africa, but across sub-Saharan Africa.

Informing policy changes

The ultimate value of new survey data and mathematical models is measured through the extent to which they inform and shape policy around HIV treatment and prevention. After being calibrated to the 2012 household survey and other epidemiologic data in South Africa, the Thembisa model has recently been used for a comprehensive evaluation of HIV prevention priorities in the next National Strategic Plan on HIV, STIs, and TB in South Africa. One of the key changes made to the Thembisa model to achieve consistency with the 2012 household survey data was modifying the assumed levels of condom use based on the observed decline in condom use between 2008 and 2012. This decline may reflect a reduction in emphasis on HIV communication programs in recent years. The model-based evaluation of HIV prevention priorities in South Africa suggests that scaling up these HIV communication programs and promoting condom distribution are likely to be the most cost-effective HIV interventions over the next two decades. Modelling exercises such as these thus depend heavily on up-to-date surveillance data in identifying gaps in current programs. Prevention and treatment priorities will probably continue to shift as new surveillance data are published in future, and projections of the future should always be viewed with caution. However, mathematical modelling remains essential to the process of efficient resource allocation, and uncertainty about the future should not prevent efforts to predict the impact of future policy changes.

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