The consequences of age-specific fertility rates and HIV subfertility on national HIV epidemic estimates from antenatal clinic prevalence

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Abstract

National HIV epidemic estimates are generated by fitting a mathematical model to HIV prevalence among pregnant women attending antenatal care. We created an age-stratified version of the UNAIDS EPP model that calculates prevalence among pregnant women accounting for age-specific fertility rates and the effect of HIV on fertility. We estimated the effect of HIV on fertility by duration of HIV infection using data from three population-based cohort studies in the ALPHA network. The model was fitted to HIV surveillance data from nine countries in eastern and southern Africa. Estimates of prevalence, incidence and AIDS deaths in the recent were similar. But adjusting for age-specific fertility and HIV subfertility reduced peak HIV incidence during the 1990s by between 3 and 16% and reduced estimated adult AIDS deaths between 1985 and 2000 by 12%. Model fit and out-of-sample prediction for household-based prevalence surveys were modestly improved. Previous HIV epidemic estimates based on ANC survey data may overstate levels of historical HIV incidence and mortality.

Introduction

In countries with generalised HIV epidemic in sub-Saharan Africa, national estimates of trends in HIV prevalence, incidence, and mortality are created by fitting a mathematical model to data about HIV prevalence among pregnant attending antenatal care (ANC) and prevalence from nationally-representative household surveys such as Demographic and Health Surveys (DHS) [1]. Household survey prevalence estimates are used to calibrate the overall prevalence level, but because these surveys were not available before the mid-2000s and occur only around every 5 years, sentinel surveillance of ANC prevalence are the primary data for informing historical epidemic trends. This is achieved by assuming that the prevalence trend among pregnant women is the same as the general population, allowing for a constant bias between ANC prevalence and population survey prevalence [1–3].

In contrast with this assumption, in recent years HIV prevalence among pregnant women has declined more rapidly than general population HIV prevalence as the burden of HIV has shifted towards older ages [4,5]. Differences in the age-distribution of pregnant women versus the general population according to the age pattern of fertility and the effects of HIV on fertility are potential explanations for these discrepant trends. Analyses based on cross-sectional data have estimated that the relationship between HIV infection and fertility depends strongly on age. Among young women (age 15–19 years) ANC prevalence is higher than general population prevalence because both pregnancy and HIV risk occur among the subset of women who are sexually active, but among older age groups the fertility rate ratio among HIV-positive women becomes increasingly lower relative to HIV-negative women [4,6,7]. However, rather than a direct effect of age, the lower prevalence among older pregnant women may primarily be associated with reduced fertility during later stages of HIV infection. This distinction is potentially important because of its interaction with the stages of the HIV epidemic—during the early exponential growth period of the epidemic, many more women are recently infected, and so HIV-related subfertility will be less than later in the epidemic, even among older women.

We created an age/sex-structured version of the UNAIDS EPP model to evaluate the consequences of accounting for differences in the age distribution of pregnant women and HIV subfertility associated with duration of infection. Model parameters about the effects of HIV on fertility by duration of HIV infection were estimated using longitudinal data from population-based cohort studies in eastern Africa. We fitted the model to HIV surveillance data from nine countries in eastern and southern Africa with two or more household prevalence surveys and compared estimates of adult HIV prevalence, incidence, and mortality with those generated by the current assumption that the ANC prevalence trend is representative of the general population prevalence.

Methods

Mathematical model

Most countries with generalised HIV epidemics use the EPP r-spline model to generate estimates for HIV incidence and prevalence in most countries with generalized HIV-epidemics [1]. The model uses a smooth B-spline function for the force of infection to generate an epidemic curve [8]. Model inputs include the rate of HIV disease progression, the effects of antiretroviral treatment (ART) on mortality, and national programme data about ART eligibility and numbers on ART to relate HIV incidence to prevalence. The model is fit to ANC and household survey prevalence data in a Bayesian framework. The likelihood for the ANC prevalence includes clinic-level random-effects to account for different epidemic levels at different sentinel sites:

$$E[\mathrm{I}^{-1}(Y_{it})] = \mathrm{I}^{-1}\left(\rho_{15-49}(t)\right) + \alpha_{ANC} + b_i$$

where Y_{it} is the observed prevalence in clinic i at time t, I^{-1} is the probit transformation, $\rho_{15-49}(t)$ is the predicted HIV prevalence among all adults age 15–49 years, α_{ANC} is the bias between ANC prevalence and general population prevalence, and $b_i \sim N(0, \sigma^2)$ is the clinic random effect [1,9].

The EPP model treats the age 15–49 year population as a homogenous group. We extended the model to include two sexes and single-year age groups. The model is solved as a discrete difference equation with a 0.1 year time step, and aging is approximated by 10% of those in each age moving to the next age group each time step.

Demographic inputs including age/sex-specific background (non-HIV) mortality rates and age-specific fertility rates for each country were derived from the United Nations World Population Prospects 2012 [10], via interpolated single-age/year inputs prepared for the Spectrum model [11]. We assumed that demographic rates are the same for different regions within each country in the absence of other data about subnational demographic rates. Age-specific epidemiologic inputs were taken from default parameter values specified for the Spectrum model [11]. These included age/sex-specific HIV incidence rate ratios, HIV progression and mortality rates by age, and mortality on ART.

To account for differences in prevalence trends between pregnant women we calculated HIV prevalence among pregnant women as a function of the age-specific fertility rate $\phi_a(t)$, age-specific HIV prevalence, and the fertility rate ratio (FRR) $\omega_{a,m}$ for women age a in stage of infection $m = \{1, \ldots, 7, ART\}$. The calculation is as follows, the number of births to women in age group a:

$$B_a(t) = \phi_a(t) \cdot N_{F,a}(t)$$

The HIV prevalence among pregnant women in age group a is

$$\rho_{preg,a}(t) = \frac{\sum_{m=1}^{7} \omega_{a,m} I_{F,a,m}(t) + \omega_{a,ART} A_{F,a\cdot\cdot}(t)}{S_{F,a}(t) + \sum_{m=1}^{7} \omega_{a,m} I_{F,a,m}(t) + \omega_{a,ART} A_{F,a\cdot\cdot}(t)}$$

where $S_{F,a}$ is the number of HIV-negative (*susceptible*) women, $I_{F,a,m}$ is the number HIV-positive untreated women in stage m, and $A_{F,a..}$ is the number of women on ART. Prevalence among all pregnant women is

$$\rho_{preg}(t) = \frac{\sum_{a=15}^{45} \rho_a(t) \cdot B_a(t)}{\sum_{a=15}^{45} B_a(t)}$$

In the likelihood instead of relating observed ANC prevalence to prevalence among all adults ($\rho_{15-49}(t)$), we use the model prevalence among pregnant women:

$$E[\mathrm{I}^{-1}(Y_{it})] = \mathrm{I}^{-1}\left(\rho_{preg}(t)\right) + \alpha_{ANC} + b_i$$

The likelihood for household survey prevalence is the same as the EPP model [1].

Data and statistical analysis

We use data from three general population HIV cohort studies in eastern Africa to estimate the effects of HIV on fertility by age and duration of HIV infection—the $\omega_{a,m}$ parameters described above. Each cohort conducts demographic surveillance including recording of all births and conducts routine HIV testing in the general population, enabling identification of fertility events relative to when a woman seroconverted. Table 1 describes the cohorts included in the analysis.

We used Poisson regression to estimate the effects of HIV on fertility by age and duration of HIV infection, relative to HIV negative women. Age was stratified by 5 year age group, and duration categorized as 0 years (the year following seroconversion), 1-2 years, 3-4 years, 5-6 years, 7-8 years, and 9+ years. The effect of duration is presumed to capture the biological effects of HIV associated with advancing disease progression. The effects of age capture other factors related to the exposure to pregnancy associated with HIV, such as selection for sexually active women at the youngest ages, and perhaps increased widowhood or divorce among HIV positive older women. The model adjusted for age-specific fertility rates in each site and trend in population fertility by calendar time.

Data were only included prior to the availability of ART in 2005 in order to estimate the natural effects of HIV on fertility in the absence of treatment. For women observed to have seroconverted, the date of seroconversion was randomly imputed between dates of last negative and first positive HIV test. For women who were already HIV positive when first observed, seroconversion date was imputed based the site-specific distribution of incidence by age and the subsequent survival. Results are based on pooled results from 100 imputed datasets.

Finally, we estimated FRRs associated with each stage of infection (CD4 >500, 350–500, etc.) by varying the parameters $\omega_{a,m}$ such that the progression of subfertility by duration simulated by the EPP disease progression model matched trend estimated by the regression model. For women on ART, we assumed a fertility rate ratio of 0.8 relative to HIV negative women based on estimates from urban Malawi [12].

Analysis

We fit the model to HIV surveillance data from nine countries in eastern and southern Africa with two or more household-based HIV prevalence surveys: Kenya, Uganda, Tanzania, Malawi, Zambia, Zimbabwe, Botswana, South Africa, and Lesotho. For most countries, the model was fit separately to data from urban rural regions, except for Malawi (northern/central/southern) and South Africa (each of nine provinces), for a total of 26 regions as defined for the 2014 UNAIDS estimates [13].

For each country we fit the model (1) assuming that ANC prevalence is related to population prevalence (which we refer to as the 'EPP' assumption) and (2) assuming that ANC prevalence is related to the prevalence among pregnant women. We calculated HIV prevalence, HIV incidence rate, and the AIDS death rate for adults aged 15–49 years for each scenario, and the total number of AIDS deaths estimated to occur among adults aged 15+ years.

As model validation, we compared how well the model based on prevalence among pregnant women fit the prevalence trend from national surveys. The motivation for adjusting for prevalence among pregnant women was to account for discrepant prevalence trends between pregnant women and the general population [4], so we hypothesized that after adjusting for prevalence among pregnant women the model would give better predictions of general population prevalence. For each region we fit each model withholding the most recent national survey. We then calculated the absolute error and log-posterior predictive density (LPPD) for the prevalence observed in the withheld survey [14].

Results

Estimates of HIV subfertility by duration of infection

Table 2 summarizes the results of the regression analysis of the effects of HIV on fertility by duration of HIV infection and age group, adjusted for age-specific fertility rates in each site and a temporal trend in population fertility. The fertility rate ratio steadily declines with longer duration of infection, such that women seven to eight years post seroconversion have 39% (95% CI 23–51%) lower fertility than women in the first year after seroconversion. In the youngest age group 15–19 years, fertility among HIV+ women is much higher than HIV- women, as expected due to the selection for sexually active women. For ages 20–39 years, there was not a statistically significant effect of age on the HIV+ to HIV- FRR, after accounting for duration of infection. At age 40-44, HIV+ women had lower fertility than HIV- women, potentially due to factors affecting exposure to pregnancy such as increased widowhood.

The EPP model uses a Markov model for HIV progression through seven disease stages: CD4 >500, CD4 350–500, CD4 250–350, CD4 200–250, CD4 100–300, CD4 50–100, and CD4 <50 [11]. We estimated FRRs associated with each stage of infection such that the reduction in fertility over time matched predicted by the Markov model matched the age-adjusted subfertility by duration of infection. These parameter estimates are in Table 3. The trend in subfertility by duration of infection

predicted by these parameters closely match the empirical estimates from the population cohorts (Figure 1, left).

Effects on HIV prevalence, incidence, and mortality estimates

Figures 2, 3, and 4 illustrate the consequences for national estimates of adult HIV prevalence, incidence, and mortality, respectively, of incorporating age-specific fertility and HIV subfertility into the prevalence calculation in the ANC data likelihood. Green lines illustrate general population epidemic trends assuming that the general population prevalence trend follows the ANC prevalence trend, and red lines illustrated estimated trends with the revised assumption adjusting for prevalence among pregnant women. General population prevalence levels during the late 2000s are very similar from both approaches. This is because in both instances the epidemic level is calibrated to match the same household survey prevalence data.

The most dramatic difference is lower estimates for the epidemic during the 1990s. Estimates for the peak HIV incidence rate are between 3% and 16% lower, the year of peak incidence occurs slightly later, and incidence decline occurs somewhat more gradually (Figure 3).

Consequences for estimates of AIDS deaths

Across the nine countries, the model predicted 5.3 million adult AIDS deaths between 1985 and 1999 when assuming that ANC prevalence trends are representative of general population prevalence. This reduced to 4.7 million when adjusting for prevalence among pregnant women, a 12% reduction. Table 4 summarizes the percentage reduction in number of AIDS deaths by 5-year time period in each country. Reductions in estimated AIDS deaths are larger in earlier periods—19% reduction in AIDS deaths from 1985 to 1989, a 14% during 1990 to 1994, 10% during 1995 to 1999, 5% from 2000 to 2005, and essentially no change after that. The changes were largest in countries where HIV incidence is estimated to have peaked and declined in the early 1990s, such as Kenya, Tanzania, Malawi, Zambia, and Zimbabwe.

Out-of-sample prediction

To test model fit, we compared the current and proposed approach accounting for fertility by fitting each model to all of the ANC and national survey data, except for the most recent national survey in each region. We calculated the posterior distribution for the predicted prevalence in the year of the withheld survey, and calculated the log-posterior predictive density (LPPD) of the prevalence observed in the withheld survey. Higher LPPD values indicate a better prediction.

Table 5 presents the results of this comparison. The first columns indicate the year and observed prevalence of the withheld survey. The next two columns report the posterior mean and standard error for the predicted HIV prevalence in the same year as the withheld survey for each model fitting assumption. The next two columns report the absolute difference between the posterior mean predicted prevalence and the observed prevalence. Adjusting for prevalence among pregnant women reduces the prediction error by an average of 0.2 percentage points, a 10% relative

improvement. The final columns report the LPPD for each prediction, a measure which accounts for both the accuracy and precision of the prediction. In 16 out of 26 regions, the pregnancy-adjusted model resulted in better out-of-sample predictions, and on average the LPPD increased by 0.16.

Discussion

The relationship between HIV prevalence among pregnant women captured in ANC sentinel surveillance and HIV in the general population is crucial for generating general population HIV estimates from ANC surveillance data. We suggest unaccounted-for mechanisms for why this relationship changes over the course of the epidemic, and provide empirical estimates for these from general population HIV cohorts. First is differences in the age-composition of pregnant women compared to the general population, which becomes important as the burden of HIV shifts towards older ages. Second is accounting for the effects of HIV on fertility by stage of infection when calculating prevalence among pregnant women. During the early exponential growth phase of the epidemic, most women were recently infected, resulting in less HIV subfertility. Once the epidemic has matured, HIV positive women are in later stages of infection with reduced fertility—producing lower prevalence among pregnant women compared to all women. This relationship is expected to continue to change as ART coverage increases, which will be an important factor for using ANC surveillance or PMTCT prevalence to monitor epidemic trends going forward.

Compared to the assumption that prevalence trends among pregnant women are representative of the prevalence trend in the general population, accounting for these mechanisms resulted in lower estimates for the numbers of new HIV infections during the 1990s and, consequently, lower estimates for the number of AIDS deaths that occurred. We also found that accounting for the changing relationship between pregnancy and HIV resulted in better model fits to household survey prevalence data.

Overall, adjusting for prevalence differentials among pregnant women reduced the number of estimated AIDS deaths from 1985 to 2000 by 12%, with the largest reductions occurring in countries where HIV incidence was estimated to have peaked and decline in the early 1990s such as Kenya, Tanzania, Malawi, Zambia, and Zimbabwe. This downward revision of AIDS mortality goes some way to reconcile discrepancies reported elsewhere between mortality trends estimated by UNAIDS and direct empirical estimates of adult mortality in the 1990s from sibling survival data [15]. It should be noted that because, in this analysis, non-HIV mortality rates were a fixed model input, the consequence will be to simply reduce model estimates of overall all-cause adult mortality. A comprehensive estimate for all-cause mortality requires also iteratively changing the non-HIV mortality rates such that the combined HIV and non-HIV mortality are consistent with available mortality data.

Estimates presented here should not be considered as alternative to recent estimates published by UNAIDS. While the models here are fitted to the same data, the model has not incorporated important details such as urbanization or international migration. Rather the purpose here is to examine how accounting for previously neglected systematic differences in pregnant women, who have been the

focus for longitundal HIV surveillance, affects our understanding of HIV epidemic trends and adult mortality in sub-Saharan Africa over the last 30 years.

In the 2015 revision of global HIV estimates UNAIDS adopted an alternate approach to account for differential prevalence trends between pregnant women and the general population that involved adjusting ANC prevalence based on the ratio of pregnant women to general population estimates from the previous estimates [16]. The results were qualitatively similar to those presented here in terms of reductions in historical global incidence, prevalence, and mortality relative to previous estimates. This pragmatic approach did not require substantial modifications to the underlying EPP model structure. But it also exhibits limitations, including reliance on previous estimates from the same data and thus somewhat circular, and assumes subfertility is related to wholly age rather than stage of infection. In light of this, we propose the representation of demographic structure in the estimation model presented here as a feasible and preferable solution.

Moreover, the age-structured model implementation developed here provides a foundation for further extensions. This analysis retains assumptions embedded in the current Spectrum model, including that the age-specific HIV incidence rate ratios are fixed over time, and most countries adopt a set of reference rate ratios derived from cohort data [11]. With an age-structured model, age-specific prevalence data from national surveys and where available ANC surveys can be included the likelihood to estimate country-specific incidence patterns. Scope for estimating changes in age-specific incidence patterns over time may be limited though due to lack of age-stratified historical prevalence data.

Fertility among women on ART is a major source of uncertainty in this analysis and data are very sparse about this at present. We assumed that women on ART for less than one year have no increase in fertility and that after one year on ART women have slightly lower fertility than HIV-negative women (FRR = 0.8), which may be the case if women on ART have different contraceptive use, fertility intentions, or relationship status. Empirically studying fertility among women on ART is challenging because many women are diagnosed and start ART during and because of pregnancy. Thus looking at the recent fertility histories among women on and off ART will not provide an accurate estimate of conception on ART. Understanding fertility among on ART is an urgent priority if ANC populations are to continue to be used for surveillance of population epidemic trends and when collecting ANC and PMTCT surveillance data it should be recorded whether women were on ART prior to the current pregnancy.

Conclusions

Longitudinal data from population-based HIV cohorts indicate that sub-fertility associated with HIV increases with duration of infection. Not accounting for age-specific patterns of fertility and HIV sub-fertility has likely resulted in overestimating the growth, peak, and decline of HIV epidemics in sub-Saharan Africa during the 1990s—and hence overestimating adult mortality during the 2000s. Adjusting for prevalence among pregnant women improves model fit and out-of-sample prediction to household survey prevalence.

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Tables

Table 1: ALPHA Network sites included in analysis

Site	Years	Total PYs	HIV+ PYs	Births
Masaka, Uganda	1989–2005	57146	4668	9024
Kisesa, Tanzania	1994–2005	91401	4388	16510
Rakai, Uganda	1999–2005	150437	15576	18820

Table 2: Effects of HIV on fertility by age and duration of infection

	Adjusted FRR	95% CI
HIV status		
Negative	1 (Reference)	
Positive	0.78	(0.71, 0.86)
Duration of infection		
0 (Year after seroconversion)	1 (Reference)	
1-2 years	0.87	(0.72, 1.05)
3-4 years	0.64	(0.52, 0.77)
5-6 years	0.66	(0.54, 0.81)
7-8 years	0.61	(0.49, 0.77)
9+ years	0.58	(0.47, 0.71)
Effects of HIV by age		
15-19 years, HIV+	1.63	(1.30, 2.03)
20-24 years, HIV+	1 (Reference)	
25-29 years, HIV+	1.07	(0.92, 1.24)
30-34 years, HIV+	1.04	(0.87, 1.23)
35-39 years, HIV+	0.90	(0.71, 1.15)
40-44 years, HIV+	0.60	(0.37, 0.98)
45-49 years, HIV+	1.55	(0.47, 5.10)
Study site		
Kisesa	1 (Reference)	
Masaka	0.78	(0.71, 0.86)
Rakai	0.64	(0.60, 0.68)
Age group (Kisesa)		
15-19 years	0.50	(0.45, 0.55)
20-24 years	1 (Reference)	
25-29 years	0.96	(0.88, 1.05)
30-34 years	0.79	(0.72, 0.87)
35-39 years	0.60	(0.54, 0.67)
40-44 years	0.29	(0.25, 0.34)
45-49 years	0.06	(0.04, 0.08)
Age group x site		
15-19 years, Masaka	0.79	(0.68, 0.92)
20-24 years, Masaka	1 (Reference)	
25-29 years, Masaka	0.94	(0.82, 1.09)
30-34 years, Masaka	0.96	(0.82, 1.13)
35-39 years, Masaka	1.00	(0.83, 1.20)
40-44 years, Masaka	0.89	(0.67, 1.17)
45-49 years, Masaka	0.35	(0.14, 0.93)
15-19 years, Rakai	1.26	(1.12, 1.40)
20-24 years, Rakai	1 (Reference)	
25-29 years, Rakai	0.95	(0.87, 1.05)
30-34 years, Rakai	0.91	(0.82, 1.02)
35-39 years, Rakai	0.73	(0.64, 0.83)
40-44 years, Rakai	0.64	(0.52, 0.78)
45-49 years, Rakai	0.40	(0.22, 0.71)
Calendar year		
1998	4.7	(0.65, 34.21)
1999	1.29	(1.21, 1.37)
2000	1.05	(1.01, 1.10)
2001	1 (Reference)	
2002	1.06	(1.02, 1.11)
2003	0.91	(0.87, 0.95)
2004	0.85	(0.80, 0.89)
2005	0.61	(0.49, 0.75)

Results from Poisson regression of fertility rate as a function of HIV status by age, and duration of infection, controlling for interaction between study site and age, and calendar year. Pooled results based 100 datasets for imputed date of seroconversion.

Table 3: Estimated fertility rate ratios (FRRs) associated with stage of infection and age group.

Stage	FRR	Age group	FRR
CD4 >500	1.0	15–19 years	1.63
CD4 350–500	0.6	20–24 years	1.10
CD4 200–350	0.15	25–29 years	1.07
CD4 200–250	0.05	30–34 years	1.04
		35–39 years	0.90
On ART >1 year	0.8	40–44 years	0.70
		45–49 years	0.60

Table 4: Percentage reduction in adult (age 15+) AIDS deaths when accounting for age-specific fertility and HIV-subfertility.

	1985–89	**1990–94**	**1995–99**	**2000–04**	**2005–09**
Kenya	21%	18%	15%	8%	-1%
Uganda	8%	6%	-3%	-11%	-9%
Tanzania	27%	19%	13%	7%	4%
Malawi	16%	14%	10%	5%	0%
Zambia	16%	13%	8%	3%	-1%
Zimbabwe	35%	20%	15%	9%	2%
Botswana	-3%	8%	9%	7%	5%
South Africa	-6%	0%	4%	6%	3%
Lesotho	5%	11%	10%	6%	2%
Total	**19%**	**14%**	**10%**	**5%**	**1%**

Percentage reduction calculated as 1-[Prev Adj. AIDS deaths]/[EPP AIDS deaths].

Table 5: Log-posterior predictive density for out-of-sample prediction of withheld household survey prevalence data

	Withheld survey		Projected prevalence		Absolute error[a]		LPPD[b]		Change LPPD
	Year	Prev (SE)	EPP[c]	Preg adj[d]	EPP	Pr. adj.	EPP	Preg adj.	
Botswana - Urban	2012	21.5 (1.0)	20.8 (1.0)	21.5 (0.9)	0.7	0.0	1.98	2.18	0.20
Botswana - Rural	2012	22.4 (1.0)	26.2 (1.3)	26.6 (1.3)	3.8	4.2	-0.59	-0.99	-0.41
Kenya - Urban	2012	6.5 (1.1)	8.1 (0.8)	7.7 (0.7)	1.6	1.2	0.78	1.01	0.22
Kenya - Rural	2012	5.1 (0.8)	7.6 (0.7)	7.0 (0.5)	2.5	1.9	-1.08	-0.11	0.97
Lesotho - Urban	2009	27.2 (1.8)	31.0 (3.2)	31.3 (3.1)	3.8	4.1	0.84	0.72	-0.12
Lesotho - Rural	2009	21.1 (0.7)	21.6 (1.3)	22.2 (1.2)	0.5	1.1	2.01	1.86	-0.15
Malawi - Northern	2010	8.2 (0.7)	6.8 (1.1)	7.1 (1.1)	1.4	1.1	0.89	1.14	0.25
Malawi - Central	2010	9.0 (0.7)	6.7 (1.0)	7.3 (1.0)	2.3	1.7	-0.23	0.61	0.84
Malawi - Southern	2010	17.6 (0.7)	12.6 (1.1)	13.2 (1.1)	5.0	4.4	-3.60	-3.45	0.15
Tanzania - Urban	2012	7.2 (0.5)	7.6 (0.8)	7.9 (0.8)	0.4	0.7	1.70	1.59	-0.12
Tanzania - Rural	2012	4.5 (0.3)	4.5 (0.4)	4.4 (0.4)	0.0	0.1	2.06	2.09	0.02
Uganda - Urban	2011	8.7 (0.7)	10.9 (1.3)	9.8 (1.2)	2.2	1.1	0.39	1.28	0.89
Uganda - Rural	2011	7.0 (0.3)	6.6 (0.5)	6.2 (0.4)	0.4	0.8	1.85	1.12	-0.73
South Africa - MP	2012	21.8 (2.4)	27.1 (2.1)	27.3 (2.1)	5.3	5.5	0.05	-0.07	-0.11
South Africa - GP	2012	17.8 (1.8)	15.0 (1.3)	15.8 (1.3)	2.8	2.0	0.66	1.08	0.42
South Africa - KZN	2012	27.9 (1.4)	23.8 (1.4)	24.6 (1.4)	4.1	3.3	-0.23	0.49	0.73
South Africa - WC	2012	7.8 (1.4)	5.3 (0.9)	5.9 (1.0)	2.5	1.9	-0.10	0.44	0.54
South Africa - EC	2012	19.9 (1.5)	16.0 (1.5)	16.8 (1.4)	3.9	3.1	-0.08	0.45	0.54
South Africa - LP	2012	13.9 (2.2)	13.9 (1.7)	14.3 (1.7)	0.0	0.4	1.16	1.15	-0.01
South Africa - FS	2012	20.4 (2.8)	20.5 (2.4)	21.1 (2.3)	0.1	0.7	1.13	1.12	-0.01
South Africa - NW	2012	20.3 (1.5)	18.3 (2.1)	18.9 (2.1)	2.0	1.4	1.11	1.27	0.16
South Africa - NC	2012	11.9 (3.3)	9.2 (1.6)	9.7 (1.6)	2.7	2.2	0.40	0.52	0.12
Zambia - Urban	2007	19.7 (1.1)	21.2 (2.0)	21.7 (1.8)	1.5	2.0	1.39	1.26	-0.12
Zambia - Rural	2007	10.3 (0.6)	9.6 (1.0)	9.8 (1.0)	0.7	0.5	1.56	1.67	0.11
Zimbabwe - Urban	2010	16.7 (0.8)	14.9 (0.9)	14.5 (0.8)	1.8	2.2	0.85	0.29	-0.56
Zimbabwe - Rural	2010	14.6 (0.5)	13.8 (0.8)	14.3 (0.8)	0.8	0.3	1.91	2.19	0.28
Average					**2.04**	**1.84**			**0.16**

[a] Absolute error—absolute difference between posterior mean predicted prevalence and observed survey prevalence.

[b] Log-posterior predictive density—measure of accuracy of model prediction to withheld data. Higher values indicate a better prediction, also accounting for the precision of the prediction and uncertainty about the data.

[c] Model fit assuming ANC prevalence data are related to prevalence trend among all adults (current EPP assumption).

[d] Model fit assuming ANC prevalence data are related to simulated prevalence among pregnant women.

Figures

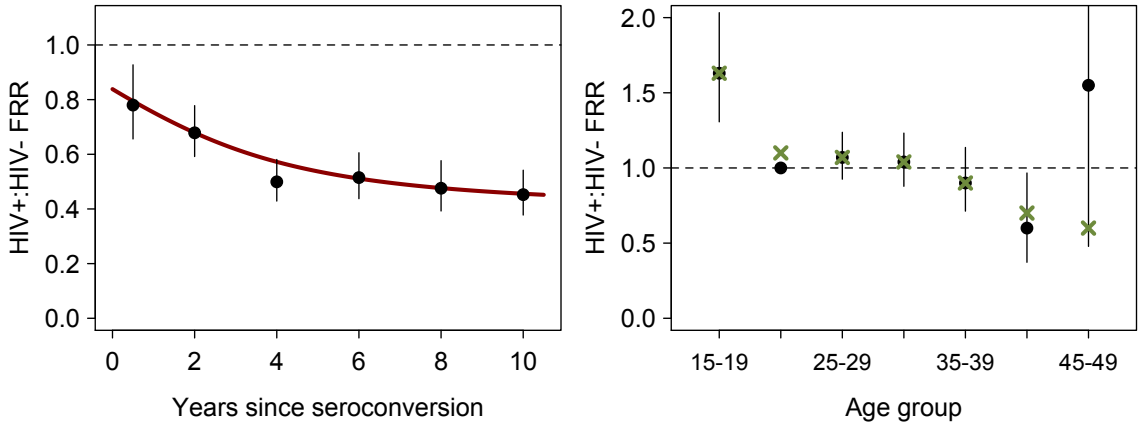

Figure 1: (Left) Trend in fertility rate ratio (FRR) by duration of infection, relative to HIV- women. Black points and vertical 95% CIs represent estimates from population cohort data reported in Table 2. Red line illustrates FRR trend by duration predicted by CD4 category FRRs in Table 3. (Right) Model parameter values for HIV+:HIV- FRR by age (green crosses; Table 3) compared with estimates from general population cohorts (points and 95% CIs, Table 2).

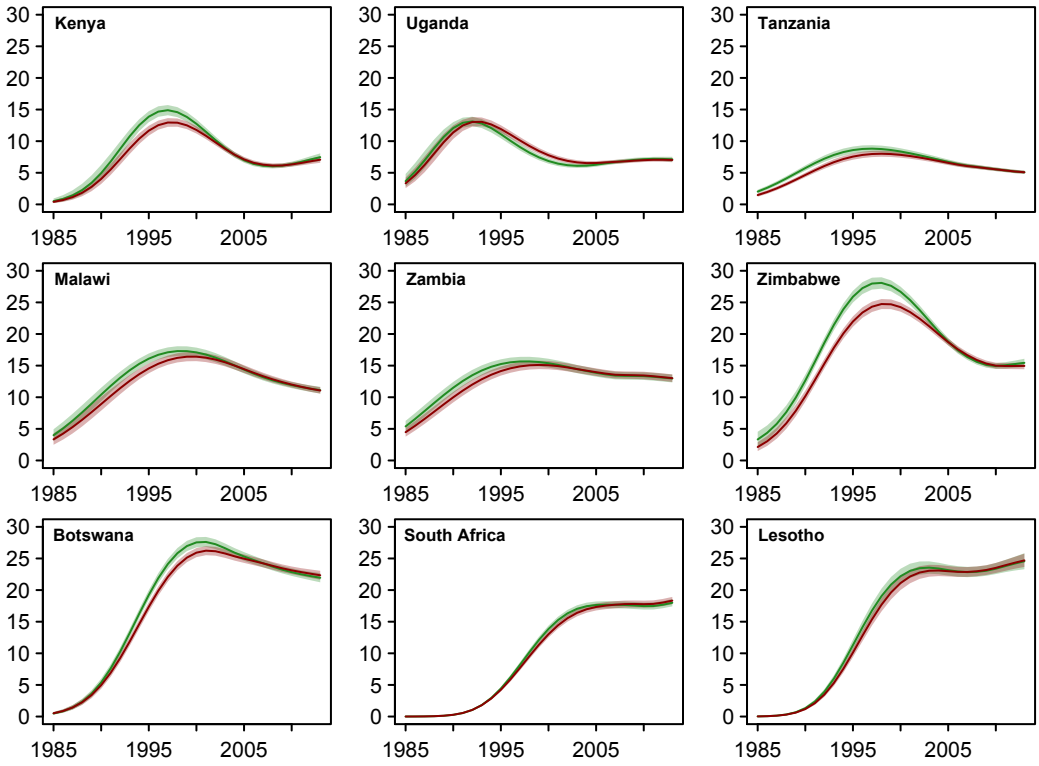

Figure 2: HIV prevalence (%) among all adults aged 15–49 years. Green lines represent prevalence estimate assuming ANC prevalence data are representative of general population HIV trends and red lines indicate prevalence estimates adjusting prevalence among pregnant women. Shaded areas indicate 80% credible intervals

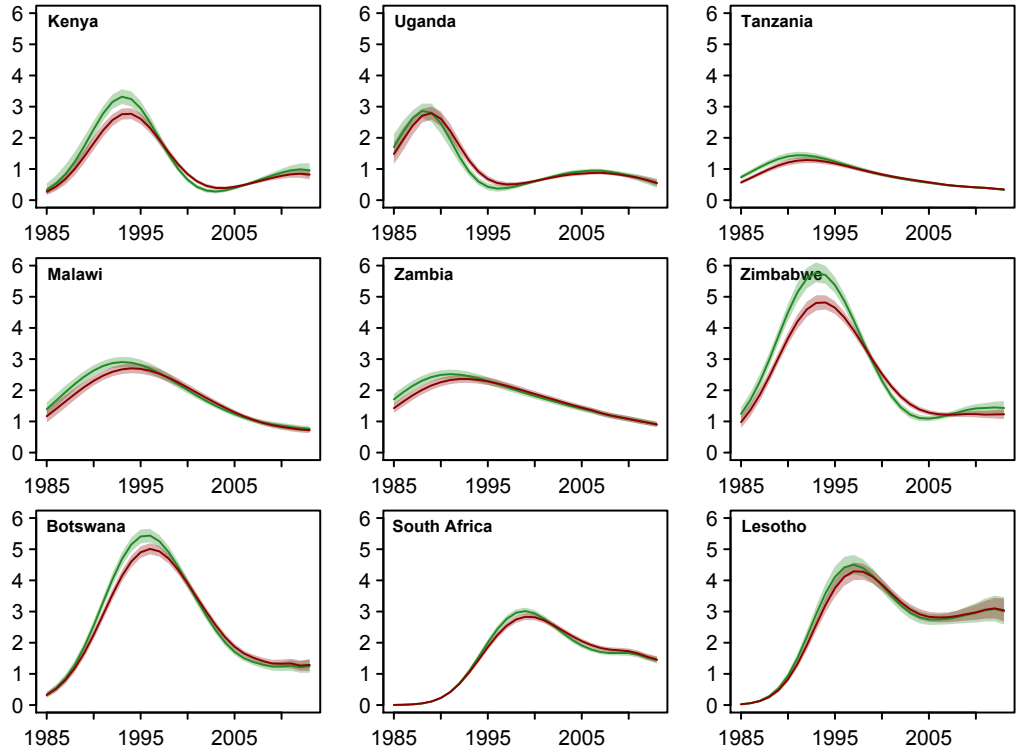

Figure 3: HIV incidence rate (per 100 person-years) among adults aged 15–49 years. Green lines represent estimate assuming ANC prevalence are representative of general population trends and red lines indicate incidence estimates inferred when adjusting prevalence among pregnant women. Shaded areas indicate 80% credible intervals.

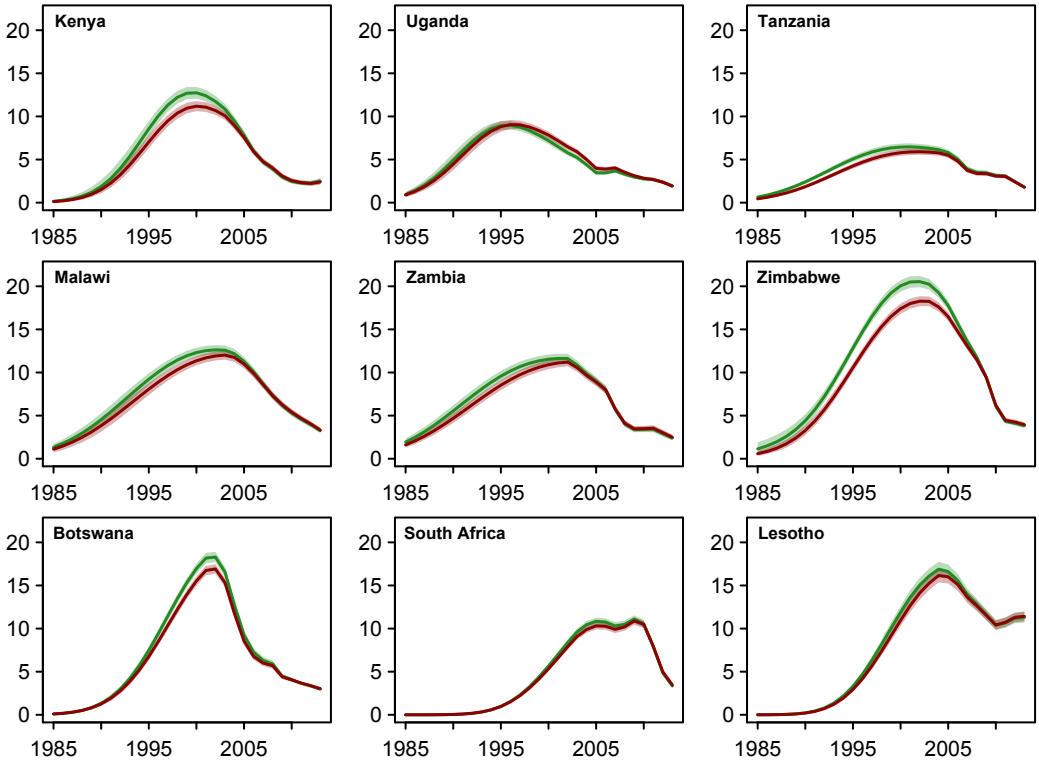

Figure 4: AIDS deaths per 1000 adults (age 15–49 years). Green lines represent estimate assuming ANC prevalence are representative of general population trends and red lines indicate mortality estimates accounting for prevalence among pregnant women. Shaded areas indicate 80% credible intervals.