

Recent HIV prevalence trends among pregnant women and all women in sub-Saharan Africa: implications for HIV estimates

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Objectives: National population-wide HIV prevalence and incidence trends in sub-Saharan Africa (SSA) are indirectly estimated using HIV prevalence measured among pregnant women attending antenatal clinics (ANC), among other data. We evaluated whether recent HIV prevalence trends among pregnant women are representative of general population trends.

Design: Serial population-based household surveys in 13 SSA countries.

Methods: We calculated HIV prevalence trends among all women aged 15–49 years and currently pregnant women between surveys conducted from 2003 to 2008 (period 1) and 2009 to 2012 (period 2). Log-binomial regression was used to test for a difference in prevalence trend between the two groups. Prevalence among pregnant women was age-standardized to represent the age distribution of all women.

Results: Pooling data for all countries, HIV prevalence declined among pregnant women from 6.5 [95% confidence interval (CI) 5.3–7.9%] to 5.3% (95% CI 4.2–6.6%) between periods 1 and 2, whereas it remained unchanged among all women at 8.4% (95% CI 8.0–8.9%) in period 1 and 8.3% (95% CI 7.9–8.8%) in period 2. Prevalence declined by 18% (95% CI –9–38%) more in pregnant women than nonpregnant women. Estimates were similar in Western, Eastern, and Southern regions of SSA; none were statistically significant ($P > 0.05$). HIV prevalence decreased significantly among women aged 15–24 years while increasing significantly among women 35–49 years, who represented 29% of women but only 15% of pregnant women. Age-standardization of prevalence in pregnant women did not reconcile the discrepant trends because at older ages prevalence was lower among pregnant women than nonpregnant women.

Conclusion: As HIV prevalence in SSA has shifted toward older, less-fertile women, HIV prevalence among pregnant women has declined more rapidly than prevalence in women overall. Interpretation of ANC prevalence data to inform national HIV estimates should account for both age-specific fertility patterns and HIV-related sub-fertility.

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Introduction

The establishment of sentinel surveillance of HIV prevalence among pregnant women attending antenatal clinics (ANC) in the early 1990s in countries with generalized HIV epidemics in sub-Saharan Africa [1] enabled HIV to become one of the better-quantified disease burdens in global health [2]. These prevalence surveys are repeated in the same clinics every 1–2 years and HIV prevalence estimates derived from women attending sentinel ANC have been used as a proxy measure to estimate the levels and trends in HIV prevalence among all adults aged 15–49 years using mathematical models [3–6]. In addition, data from these surveys are used to indirectly derive estimates of HIV incidence using mathematical models that incorporate other information about survival after HIV infection and antiretroviral use [7,8].

Since 2001, national household surveys including HIV testing, such as the Demographic and Health Surveys (DHS) and AIDS Indicator Surveys (AIS), have provided statistically representative estimates of population-wide adult HIV prevalence, including men and nonpregnant women. Based on the assumption that household prevalence surveys provide an unbiased estimate of HIV prevalence in the general population, these data have been used to calibrate the level of HIV prevalence estimates derived from ANC sentinel surveillance [9]. But, because such household HIV prevalence surveys are less frequent and, until recently, few countries had conducted more than one, ANC surveillance has continued to be relied upon as the primary information source for estimating the HIV epidemic trend in the general population.

The veracity of estimates derived from ANC prevalence data thus relies on the assumption that HIV prevalence trends among women attending ANC are representative of HIV trends among all adults aged 15–49 years. Two recent epidemiologic phenomena particularly motivate investigation of this assumption: recent declines in HIV incidence being especially great among younger adults [10,11] and the scale-up of antiretroviral treatment, which has resulted in treated persons living with HIV to older ages than they might have previously. Both changes could have shifted the age-distribution of prevalent HIV infections to older age groups, who are less fertile and thus less represented in ANC surveillance [12].

We pool data from serial cross-sectional household surveys in sub-Saharan Africa to compare recent trends in HIV prevalence between all women and women currently pregnant at the time of the survey.

Methods

Data

We used nationally representative household-based HIV prevalence survey data from countries in sub-Saharan Africa with at least two surveys in which women's HIV serostatus could be linked to her self-reported pregnancy status at the time of the survey. All surveys were conducted using a stratified two-stage cluster design. In most countries, these consist of DHS and AIS [13]. For South Africa, we used data from the HSRC National HIV Prevalence, Incidence, and Behaviour Surveys [14,15]. For Swaziland, we compared data from the 2007 DHS to estimates from the 2011 Swaziland HIV Incidence Measurement Survey [16]. In Swaziland, data were for women aged 18–49 years, the sampling frame for the latter survey. In all other countries, we restricted analysis to women aged 15–49 years, the age-range for which ANC prevalence trend is assumed to be representative in the Joint United Nations Programme on HIV/AIDS (UNAIDS) global HIV estimates [8].

To analyze HIV trends over time, we divided surveys into two periods with each country having one survey in each period. All surveys during the first period were conducted between 2003 and 2008 and all surveys during the second period between 2009 and 2012. In countries with more than two available surveys (Kenya, South Africa, Tanzania), we used the two most recent surveys. Table 1 summarizes the countries, year conducted, and sample sizes for each of the surveys included in the analysis.

We combined data from multiple countries into SSA regions according to standard UNAIDS classifications (Western, Eastern, Southern), and all countries together. For pooled multicountry analyses, survey sampling weights were de-normalized using the population size for women aged 15–49 years in 2012 from the UN World Population Prospects 2012 [17]. Thus, regional and continental pooled statistics and trends are representative of the aggregated population of the countries included in the analysis.

Statistical analysis

We calculated the percentage of women currently pregnant at the time of the survey. We calculated HIV prevalence among all women and currently pregnant women in each time period. Ninety five percentage (95%) confidence intervals for proportions were calculated using the logit method. Prevalence trends among all women aged 15–49 years and men aged 15–49 years were also compared.

We tested for a difference in recent HIV prevalence trends between pregnant and not currently pregnant women by estimating a log-binomial regression model with an

Table 1. Countries and surveys included and percentage of women currently pregnant at the time of survey.

Country	Region	Female 15–49 pop size 2012 (millions)	Period 1				Period 2			
			Survey year	N females HIV tested 15–49 (unadjusted)	N currently pregnant 15–49 (unweighted)	% curr. pregnant (SE)	Survey year	N females HIV tested 15–49 (unadjusted)	N currently pregnant 15–49 (unweighted)	% curr. pregnant (SE)
Burkina Faso	Western	3.8	2003	4189	426	10.1 (0.6)	2010	8346	818	10.2 (0.4)
Cameroun	Western	5.1	2004	5154	534	10.5 (0.5)	2011	7253	716	10.1 (0.5)
Côte d'Ivoire	Western	4.7	2005	22681	1954	7.9 (0.6)	2010–2011	4655	484	10.6 (0.6)
Senegal	Western	3.3	2005	4466	394	7.9 (0.5)	2010–2011	5590	470	7.7 (0.5)
Ethiopia	Eastern	21.5	2005	5942	474	8.4 (0.5)	2011	15505	1221	7.4 (0.3)
Kenya	Eastern	10.5	2008–09	3811	270	6.6 (0.6)	2012	5870	365	6.3 (0.4)
Rwanda	Eastern	2.8	2005	5663	432	7.6 (0.4)	2010	6952	478	7.0 (0.3)
Tanzania	Eastern	10.9	2007–2008	8711	770	9.2 (0.4)	2011–2012	10299	982	9.3 (0.5)
Lesotho	Southern	0.5	2004	3020	198	6.7 (0.6)	2009	3849	182	4.6 (0.4)
Malawi	Southern	3.5	2004	2864	379	13.5 (0.8)	2010	7396	698	9.1 (0.5)
South Africa	Southern	14.1	2008	4823	156	4.7 (0.5)	2012	8253	240	4.5 (0.5)
Swaziland ^a	Southern	0.3	2006–2007	3840	217	5.6 (0.4)	2011	11042	764	7.0 (0.3)
Zimbabwe	Southern	3.4	2005–2006	7494	494	6.8 (0.4)	2010–2011	7852	625	8.3 (0.4)
Western		17.0		36490	3308	9.2 (0.3)		25844	2488	9.8 (0.3)
Eastern		45.6		24127	1946	8.1 (0.3)		38626	3046	7.6 (0.2)
Southern		21.9		22041	1444	6.8 (0.4)		38392	2509	6.1 (0.3)
All		84.4		82658	6698	8.0 (0.2)		102862	8043	7.7 (0.2)

SE, standard error.
^aSwaziland for 18 to 49-year-old women.

interaction between survey period and pregnancy status at the time of the survey. Country-level fixed-effects were included in regressions to adjust for different fertility levels across countries:

$$\log(P(HIV+)) = \beta_{0i} \cdot [\text{country}]_i + \beta_1 \cdot [\text{pregnant}] + \beta_2 \cdot [\text{period} = 2] + \beta_3 \cdot [\text{pregnant}] \cdot [\text{period} = 2]$$

The regression was also estimated separately for women in age groups 15–24 years, 25–34 years, and 35–49 years to evaluate prevalence differences between pregnant and nonpregnant women in each age group. We standardized the age distributions of the two prevalence measures by re-weighting the 5-year age-specific prevalence among pregnant women according to the age distribution of all women in the general population.

Analyses were conducted in R version 3.1.0 [18] using the ‘survey’ package [19] to account for the stratified two-stage cluster sampling design of the surveys. R code for reproducing analyses is available at <https://github.com/jeffeaton/currpreg-hiv-trends>.

Results

Age distribution of fertility and changes in age-specific prevalence

Figure 1a compares the age distribution of all women in the population and the age distribution of currently pregnant women. Figure 1b illustrates changes in age-specific HIV prevalence among women aged 15–49 years between surveys conducted in period 1 (2003–2008) and period 2 (2008–2012). Younger adult women were disproportionately represented among currently pregnant women. Across all countries, women aged 15–34 years accounted for 85% of pregnant women compared with only 71% of the overall female population. Results were similar in each region: 86 versus 73% in Western Africa, 85 versus 72% in Eastern Africa, and 85 versus 69% in Southern Africa. There was not a statistically significant change in the age distribution of currently pregnant women between periods 1 and 2.

Between periods 1 and 2, HIV prevalence shifted to older ages (Fig. 1b). Among women aged 15–24 years, HIV prevalence decreased significantly from 5.1 (95% CI 4.6–5.5%) to 3.6% (95% CI 3.2–3.9%) and among those aged 35–49 years increased significantly from 9.4 (95% CI 8.7–10.2%) to 11.7% (95% CI 10.9–12.7%). This pattern was the same in all three regions (Fig. 1b). Taken together, HIV prevalence has declined among the age groups of women who are overrepresented among samples of pregnant women, whereas it increased among age groups underrepresented among samples of pregnant women.

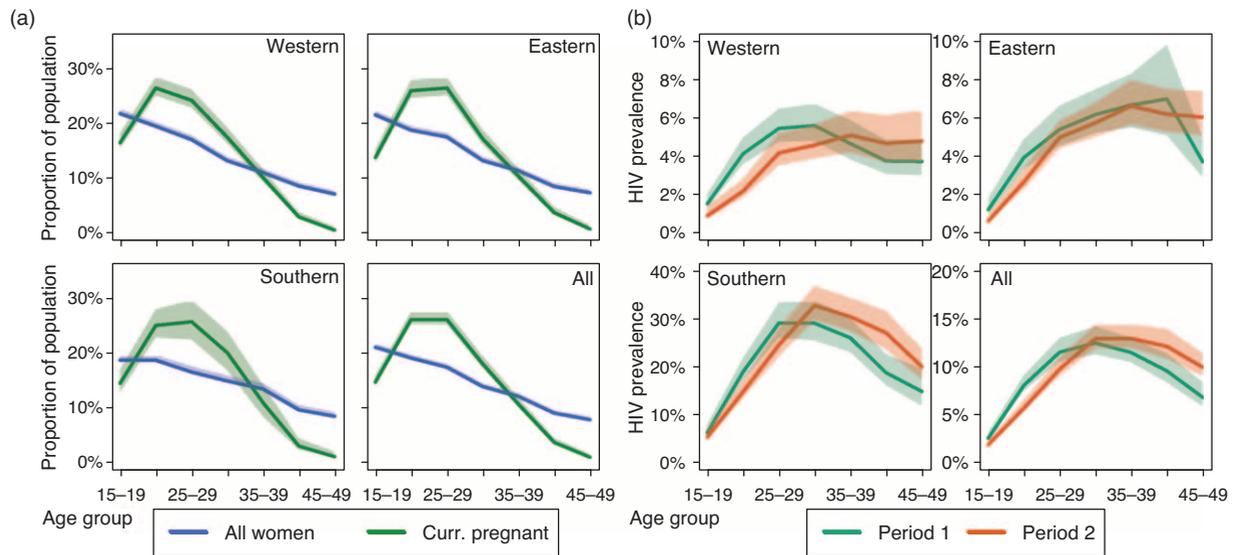


Fig. 1. (a) Age distribution of all women aged 15–49 years and currently pregnant women (both periods combined). (b) Age-specific HIV prevalence among all women aged 15–49 years in period 1 (surveys conducted 2003–2008) and period 2 (surveys 2008–2012). Shaded regions indicate 95% confidence intervals. Note vertical axes are not the same in (b).

Prevalence trends between pregnant women and all women

Figure 2a illustrates the HIV prevalence trend in each country among all women aged 15–49 years and currently pregnant women. Point estimates in 11 of 13 countries indicated that between the two most recent surveys HIV prevalence declined more or increased less among currently pregnant women than all women (Fig. 2b). Note that the standard errors for the change in HIV prevalence among pregnant women are large (Fig. 2a; Table S1, <http://links.lww.com/QAD/A559>), and the difference in prevalence trend is not statistically significant in any country. Relative changes in prevalence among adult men aged 15–49 years were similar on average to relative prevalence changes in adult women (Figure S1, <http://links.lww.com/QAD/A559>).

Pooling all countries, HIV prevalence among currently pregnant women declined from 6.5 (95% CI 5.3–7.9%) to 5.3% (95% CI 4.2–6.6%), a 19% decline, whereas it remained relatively unchanged at 8.4% (95% CI 8.0–8.9%) in period 1 to 8.3% (95% CI 7.9–8.8%) in period 2 among all women aged 15–49 years. In Western Africa, prevalence among pregnant women declined from 4.3 (95% CI 3.4–5.4%) to 2.9% (95% CI 2.2–3.9%) among pregnant women and 4.0 (95% CI 3.7–4.4%) to 3.4% (95% CI 3.1–3.7%) among all women, in Eastern Africa from 3.6 (95% CI 2.6–4.9%) to 2.9 (95% CI 2.2–3.9%) for pregnant women and 4.5 (95% CI 4.1–4.9%) to 4.1% (95% CI 3.8–4.5%) for all women, and in Southern Africa from 17.3% (95% CI 12.8–22.9%) to 16.1% (95% CI 11.6–22.0%) for pregnant women and increased from 20.1% (95% CI 18.8–21.4%) to 20.9% (95% CI 19.6–22.3%) for all women (Table S1, <http://links.lww.com/QAD/A559>).

Adjusting for country, HIV prevalence was lower among currently pregnant women than nonpregnant women during period 1 [relative risk (RR) 0.89, 95% CI 0.73–1.08; Table 2]. Based on the estimated interaction between current pregnancy and survey period, prevalence among pregnant women declined 18% more than prevalence among nonpregnant women between periods 1 and 2 (RR 0.82, 0.62–1.09; Table 2). The same pattern was found in all regions, with the prevalence trend among pregnant women being lower than that for all women by 22, 21, and 13% in Western, Eastern and Southern regions, respectively, although none were statistically significant (Western: RR 0.78, 0.54–1.14; Eastern: 0.79, 0.51–1.22; Southern 0.87; 0.57–1.33).

Age-standardized prevalence and age-specific prevalence trends among pregnant women

Based on the discrepancy in the age-distribution of pregnant women compared with all women (Fig. 1a), a natural approach to adjusting for the bias in prevalence among pregnant women would be to re-weight age-specific ANC prevalence with the population age distribution. Figure 2c illustrates the effect of age-standardizing prevalence among pregnant women on the estimated prevalence trend. Pooling all countries, the relative change in age-standardized prevalence was somewhat more similar to the change in general population prevalence, but not substantially so; age standardized prevalence declined by 17.4% compared with a 18.8% decline in crude prevalence among pregnant women. Standard error estimates for age-standardized prevalence among pregnant women were large, similar to the standard errors for crude prevalence among pregnant women (Table S1, <http://links.lww.com/QAD/A559>), preventing formal comparison of trends in age-standardized prevalence.

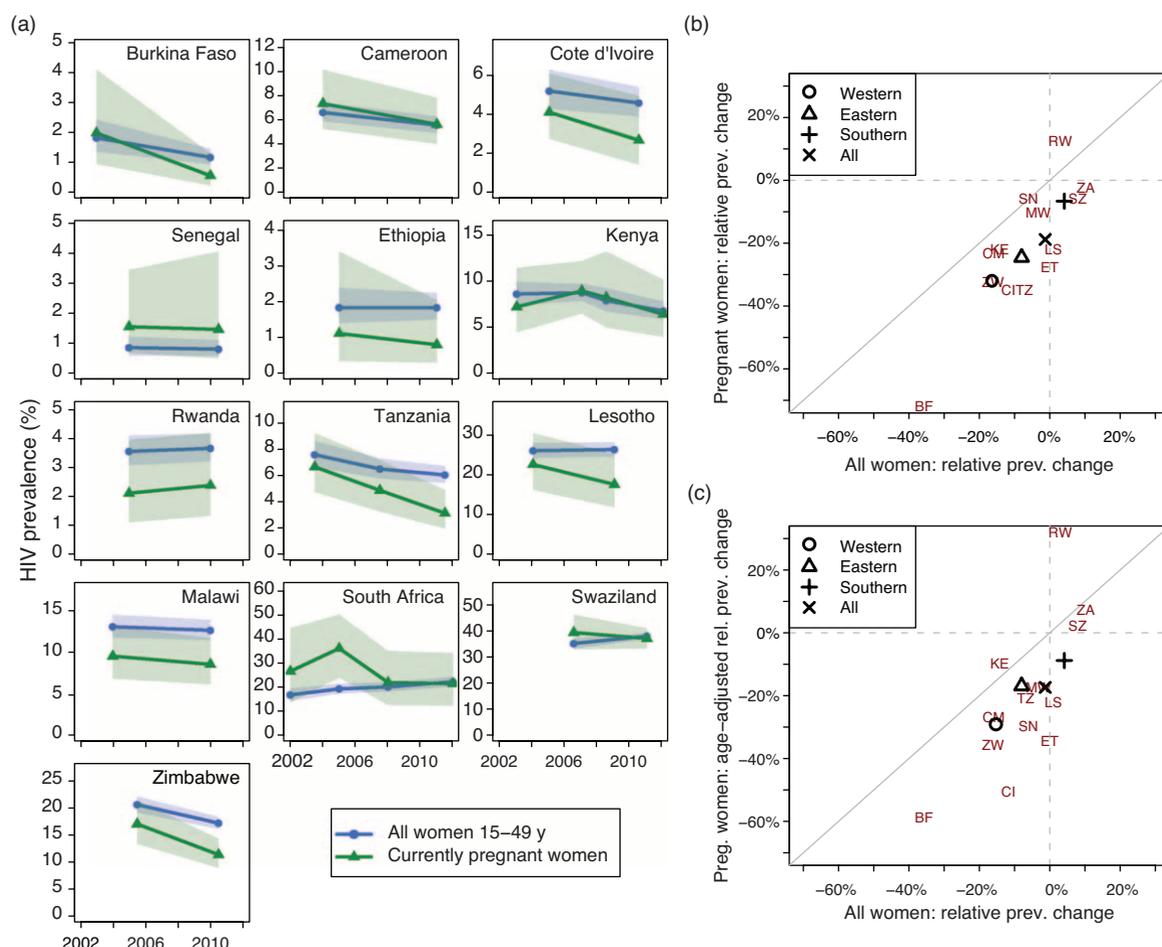


Fig. 2. (a) HIV prevalence trend in all women aged 15–49 years and currently pregnant women in all countries included in the analysis. Note: earlier surveys for Kenya, Tanzania, and South Africa are also plotted, which are not included in pooled analysis. Swaziland illustrates women aged 18–49 years. (b) The relative change [$100 \times (\text{period 2 prevalence})/(\text{period 1 prevalence}) - 1$] in prevalence from period 1 to period 2 among all women (horizontal axis) and currently pregnant women. BF, Burkina Faso; CM, Cameroon; CI, Côte d’Ivoire; SN, Senegal; ET, Ethiopia; KE, Kenya; RW, Rwanda; TZ, Tanzania; LS, Lesotho; MW, Malawi; SZ, Swaziland; ZA, South Africa; ZW, Zimbabwe. (c) Comparison of relative change in prevalence among all women and in age-standardized prevalence among pregnant women.

Furthermore, age-standardization increased the extent to which HIV prevalence among pregnant women underestimated HIV prevalence for all women. For example, pooling all countries, in period 1, age-standardization reduced HIV prevalence among currently pregnant women from 6.5 to 5.5%, compared with a prevalence of 8.4% among all women aged 15–49 years (Table S1, <http://links.lww.com/QAD/A559>).

The increased discrepancy in age-standardized prevalence was explained by examining the age-specific prevalence trends between pregnant women and all women (Fig. 3). Among young women aged 15–24 years, levels and HIV prevalence among pregnant women were representative of all women. However, among women aged 25–34 years and 35–49 years, prevalence was lower among pregnant women than all women. Adjusting for country-level

Table 2. Log-binomial regression estimating the relationship between HIV prevalence and current pregnancy and survey period.

	Western	Eastern	Southern	All
Currently pregnant vs. not	1.04 (0.82, 1.33)	0.80 (0.59, 1.09)	0.89 (0.66, 1.20)	0.89 (0.73, 1.08)
Period 2 vs. period 1	0.86 (0.75, 0.98)	0.93 (0.82, 1.05)	1.04 (0.95, 1.13)	0.99 (0.93, 1.06)
Currently pregnant · period 2 ^a	0.78 (0.54, 1.14)	0.79 (0.51, 1.22)	0.87 (0.57, 1.33)	0.82 (0.62, 1.09)

Estimates indicate relative risk ratios (RR) and 95% confidence intervals, adjusted for country.

^aInteraction between current pregnancy and survey period estimates excess prevalence decline in HIV prevalence among currently pregnant women vs. not currently pregnant women.

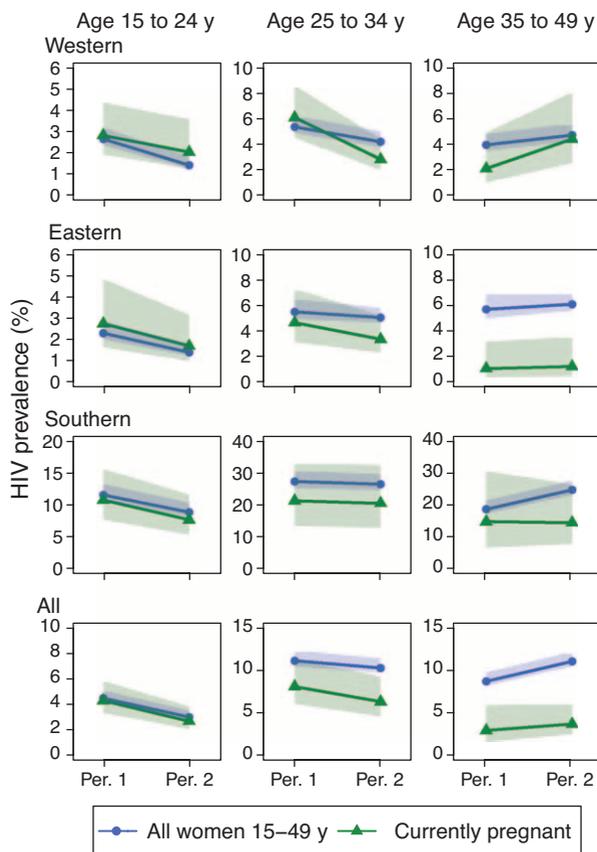


Fig. 3. Trends in age-specific prevalence among pregnant women and all women by age group and region.

differences in fertility, for women 25–34 years, HIV prevalence was 24% (95% CI –4–45%) lower among pregnant women than nonpregnant women in period 2. For women aged 35–49 years, prevalence was 54% (36–79%) lower among pregnant women (data not shown).

Discussion

Observed reductions in HIV prevalence in ANC surveillance systems may exaggerate the extent of HIV prevalence declines that are occurring in the wider female population. This is because HIV epidemics in sub-Saharan Africa are aging into older age groups of women, who experience lower fertility and thus are likely to be less represented among ANC clinic attendees. This is consistent across all three sub-Saharan regions of Western, Eastern and Southern Africa, and this pattern will be expected to continue and be exacerbated as ART programmes mature and HIV positive patients survive to older ages.

Point estimates in all three regions suggested that prevalence declined more rapidly among currently pregnant women than all women between surveys

conducted from 2003 to 2008 and 2008 to 2012 in the same countries. The downward bias in prevalence among pregnant women compared with not currently pregnant women was around 18% across all countries, but the difference was not statistically significant and CIs for prevalence among pregnant women were large. Using population sizes at the time of each survey to de-normalize sampling weights in pooled analyses rather than standardizing to 2012 population sizes had a negligible effect on the results. Other data sources offer the potential to improve the precision of these estimates, such as population-based HIV cohort studies embedded within demographic surveillance sites [20] and by comparing national household survey prevalence trends with the actual age-specific ANC HIV prevalence surveillance data, which have larger samples of pregnant women. Mathematical modelling will further elucidate how biases may vary over time, with ART programme scale-up, and across epidemics with different recent and future HIV incidence trends [21].

Modelling will also quantify the potential magnitude of biases in HIV incidence estimates resulting from downward biases in prevalence among pregnant women. National epidemic estimates for HIV incidence are generated by fitting a model to HIV prevalence trends in ANC data and using information about natural HIV survival and ART uptake to determine what previous incidence would be required to match the observed prevalence. Thus, overestimating declines in HIV prevalence based on trends in ANC data could also overstate the extent to which HIV incidence has declined. Because recent prevalence patterns represent the accumulation of HIV incidence and mortality from several years previous, the relationship between the magnitude of bias in prevalence trends and incidence trends over the same period may vary across epidemics and biases in prevalence trends in recent years may affect estimates of HIV incidence in earlier periods.

HIV prevalence trends among women aged 15–24 years who were currently pregnant were very similar to trends for all women aged 15–24 years. This is consistent with previous research finding that prevalence trends among young women attending ANC were representative of prevalence trends in all young women [11,22], which justified the recommendation of using ANC prevalence among women aged 15–24 years as proxy indicator for recent incidence trends [23]. This may be inappropriate going forward because an increasing proportion of prevalence in young adults will be accounted for by long-term survivors of mother-to-child HIV transmission [24,25], particularly as paediatric ART programmes mature.

Among older adult women, however, prevalence in pregnant women was significantly lower than in the general population. The implication of this is that simply

re-weighting age-specific prevalence among pregnant women to represent the age distribution of the general population may not resolve the downward bias in HIV prevalence trends among pregnant women. One reason for the lower prevalence is thought to be the lower fertility among HIV-positive pregnant women at older ages [26–28]. To the extent that this subfertility is due to the effects of HIV infection, antiretroviral treatment may ameliorate HIV-related subfertility [29]. Thus, with high levels of ART coverage, prevalence among older pregnant women may again become more similar to general population prevalence.

In light of the different age patterns of prevalence among pregnant women and the general population and potential future changes owing to ART, we recommend that HIV prevalence surveillance among antenatal clinic attendees should be stratified by age and whether HIV-positive women were on ART prior to the pregnancy or initiated ART during their pregnancy. The latter will enable appropriate adjustment for the effects of ART on fertility when interpreting future ANC prevalence trends. Ascertainment of ART status could be done anonymously using biomarker testing for antiretrovirals on blood samples from the first ANC visit [15,30], or biomarker testing could be used to confirm self-reported ART status. These recommendations for reporting ANC prevalence also apply to sentinel surveillance in pregnant women based on HIV testing for prevention of mother-to-child transmission (PMTCT), which must additionally ensure that women who opt out of PMTCT testing because of prior knowledge of HIV status are reflected in PMTCT surveillance reporting and that information on ART status be collected for such women [31].

This analysis did not consider factors beyond pregnancy that could influence the representativeness of HIV prevalence trends among ANC attendees. These could include changing patterns in ANC attendance over time or systematic differences in ANC attendance according to factors that are also correlated with risk of HIV infection, such as education, socioeconomic status, parity, or contraceptive use [6,32,33]. Although we found that HIV prevalence among pregnant women was lower than among all women, at the national level, HIV prevalence derived from ANC surveillance has tended to overestimate general population prevalence [34]. Reasons for this apparent discrepancy include: general population prevalence includes men who tend to have a lower prevalence than women [6], sites initially chosen for ANC surveillance may have been in higher prevalence areas [35], and potential systematic differences among women who attend public antenatal clinics as opposed to those who attend private facilities or do not attend any health facility for their prenatal care.

Sentinel surveillance of HIV prevalence among pregnant women attending antenatal care has been invaluable for

quantifying HIV epidemics in sub-Saharan Africa and will continue to be useful for informing HIV estimates. However, naïve interpretation of prevalence trends among pregnant women as representative of all women aged 15–49 years may lead to downward biases in model-derived estimates of HIV prevalence and incidence in the general population. To correct for this bias, HIV incidence and prevalence estimates in the general population should account for both the age-pattern of fertility and the effects of HIV and ART on fertility when interpreting trends in ANC prevalence.

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Conflicts of interest

There are no conflicts of interest

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