

Bias in HIV prevalence estimates from refusals to be tested in seroprevalence surveys

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Abstract

Nationally-representative HIV seroprevalence surveys are increasingly being relied upon for HIV prevalence estimates. We explore the potential for bias in these estimates because of non-response due to the refusal to be tested. The few studies on this topic have failed to identify any substantial bias, but they typically ignore bias due to refusals that are informed by prior knowledge about one's HIV status. In a sample of respondents from Malawi that had been tested before, we find that HIV positives are five times more likely to refuse a subsequent test than HIV negatives. We use this parameter in simulations that further rely on empirical data from the Demographic and Health Surveys and demonstrate that this factor alone may lead to significant bias in HIV prevalence estimates; particularly in urban areas where HIV prevalence, refusal rates, and coverage of VCT are often higher.

Background

Most published estimates of HIV prevalence in sub-Saharan Africa are based on inputs from sentinel surveillance data in antenatal clinics (ANC). Because of the importance of reasonably accurate HIV prevalence figures for policy formulation and resource allocation, the validity of these estimates have been subject to extensive scrutiny and often found to overestimate true prevalence [1-13]. Bias in ANC-based HIV prevalence estimates is attributed to the representativeness of women attending antenatal clinics and/or the under-representation of remote rural areas in surveillance systems. The identification of bias has led to the development of correction schemes to improve extrapolations from ANC surveillance data [2, 14-16], but questions continue to surround the uniform applicability of adjustment procedures in a variety of settings [12].

Expanding resources and progress in medical technology has brought HIV testing increasingly within reach of nationally representative household surveys and that has generated new prospects of resolving the type and magnitude of bias in ANC sentinel surveillance estimates, or, to provide a new gold standard for HIV prevalence estimates altogether [10, 17-20]. The inclusion of HIV serostatus testing in several Demographic and Health Surveys (DHS) is pushing the agenda in that respect. Data from such community-based surveys are indeed a valuable addition to ANC estimates, but they are also

subject to bias due to limitations of the sampling frame (e.g., the exclusion of high risk groups in army barracks, prisons or migrant worker hostels) and non-response because of population mobility and refusal. The association of population mobility with HIV infection has been documented extensively [12, 21-28]. In comparison, relatively little is known about the relationship between refusal and HIV infection in community-based studies [10, 18, 20]. A number of small-scale studies in STD and antenatal clinics most often conclude that refusals are positively associated with HIV status [29-37]. A few studies remain inconclusive about the nature of the relationship or suggest the opposite pattern [38-40].

In aggregate, population-based seroprevalence surveys are believed to underestimate true HIV prevalence, but the studies that have addressed this issue failed to identify significant bias due to non-response [13, 20, 41-43]. These studies do not, however, account for the possibility that individuals refuse testing based on prior knowledge of their HIV status. We hypothesize that HIV positive individuals who are aware of their HIV status are much less likely to consent to testing in a seroprevalence survey than those who previously tested negative and those who have not had a previous HIV test. Furthermore, we claim that this form of selective refusal may bias HIV seroprevalence estimates based on nationally representative serosurveys; particularly in settings where HIV prevalence, refusal rates, and VCT coverage are relatively high.

First we describe levels of prior testing and refusal rates in a number of Demographic and Health Surveys (DHS) in sub-Saharan Africa and explore their relationship with HIV prevalence. Secondly, we investigate the relationship between prior knowledge of HIV status and consent for testing using longitudinal survey data from Malawi with multiple rounds of HIV testing. We then develop a model of bias in HIV seroprevalence surveys that is based on HIV prevalence, the level of prior testing in a population, the refusal rate and the relationship between prior knowledge and consent for testing. Using that model, we simulate bias in estimates of HIV prevalence and the sex ratio of infections using empirical values of refusal and prior testing rates that we derive from the DHS surveys.

Levels of prior testing and refusal rates in sub-Saharan Africa

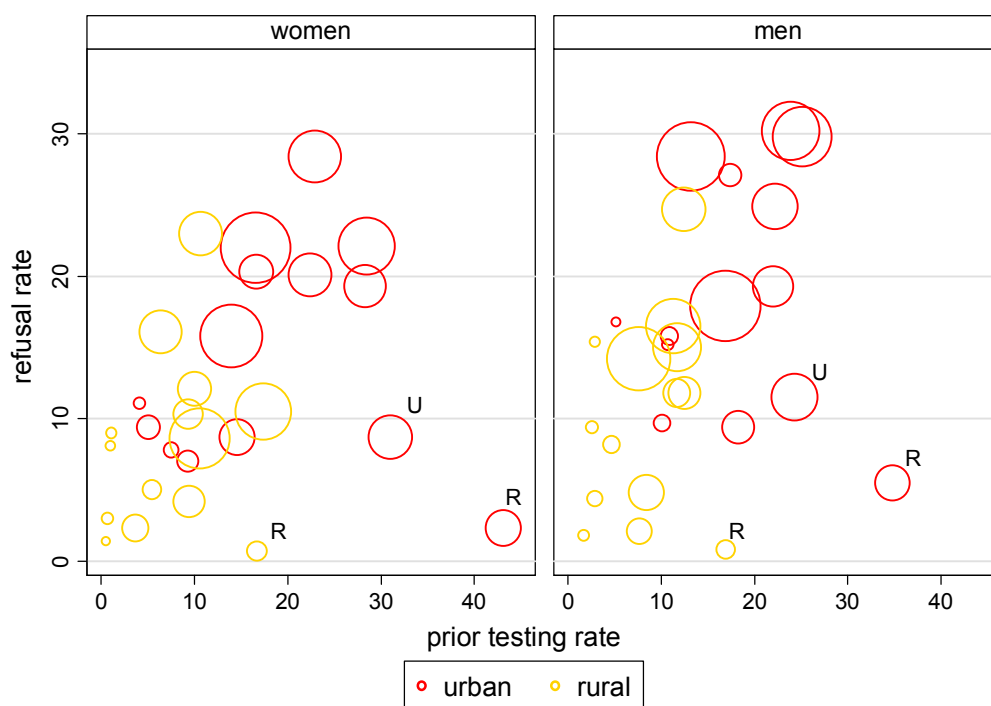
The prior testing rate, HIV prevalence and the refusal rate by urban/rural residence and gender for fourteen African countries where the DHS included an HIV testing component is illustrated in Figure 1. Refusal rates range from under 1% in rural Rwanda and exceed 25% in the urban (mainly male) population of Malawi, Ethiopia, Lesotho and Zimbabwe. Refusal rates vary quite importantly by urban/rural residence: the median refusal rates in urban and rural areas are 16.3% and 8.8% respectively. The median refusal rate for men is 14.6% and 9.2% for women. The prevalence rates reported by the DHS range from under 1% in Senegal, to 20% and above in Lesotho and a few population subgroups in Zambia and Zimbabwe. Rates of prior testing vary from under 1% for females in rural Guinea and Niger to 43% for females in urban Rwanda. The median rate of prior testing in urban areas is 17.2% compared to 8.1% in rural areas. The median rate of prior testing is 11.7%, and is a little higher for men than for women. The differences in terms of place of residence are much larger: 8.1% and 17.2 percent for rural and urban areas respectively.

Figure 1 is also very suggestive of a three-way aggregate-level relationship between HIV prevalence, prior testing and refusal. The only deviation from that pattern is Rwanda. It stands out as the country with high prior testing rates and relatively low refusal rates (the observation points for Rwanda in Figure 1 are labeled with an 'R'). Excluding Rwanda, the ecological correlation between either of these variables is greater than 0.5. Provided that the relationship between prior testing and refusal is not spurious¹, that could mean that refusal to be tested in HIV prevalence studies is informed by prior knowledge about one's HIV status. The fact that refusal rates increase with HIV prevalence as well,

¹ We verified the ecological correlation in five DHS surveys. The odds of a refusal are between 1.38 and 2.29 times higher among respondents that have been tested before compared to those who have never been tested for HIV.

further suggests that it is HIV positive individuals in particular who are more likely to refuse. That assertion, however, cannot be verified using DHS data because the HIV status of those who do not consent to testing is unknown (one just knows whether the respondent has been tested before or not).

Figure 1: Prior testing and refusal rates in 14 sub-Saharan African countries by HIV prevalence (size of the circles), disaggregated by rural/urban residence and sex (in %)



Notes: countries included in the graph are Cameroon (2004), Ethiopia (2005), Ghana (2003), Guinea (2005), Kenya (2003), Lesotho (2004), Malawi (2004), Niger (2006), Rwanda (2005), Tanzania (2003-04), Senegal (2005), Uganda (2004-05), Zambia (2002) and Zimbabwe (2005-06). The circles labeled with an R or U denote subpopulations in Rwanda and Uganda respectively. Compared to the other populations, they are characterized by relatively low refusal rates for the level of prior testing. The prior testing rate is defined as the proportion of respondents who have ever been tested for HIV and received the results of the last test. In Zambia and Tanzania, it is the percentage that has been tested before (irrespective of post-test counseling). The refusal rate is defined as the percentage of respondents that refused the HIV test conditional on having completed the survey interview. Source: Demographic and Health Surveys and AIDS Indicator Survey (Uganda)

Prior knowledge of HIV positive status and consent for testing

In order to obtain an empirical estimate of the relationship between prior knowledge of HIV status and consent for testing, we rely on data from the Malawi Diffusion and Ideational Change Project (MDICP). These are longitudinal survey data in three rural district of Malawi whereby respondents were approached for testing in wave three (MDICP3, 2004) and wave four (MDICP4, 2006). The original MDICP sample that was taken in 1998 included around 1,500 ever-married women and their spouses. In MDICP3, the sample was augmented with a group of adolescents (both sexes). In MDICP3, a total of 2,864 individuals were tested using OraSure® saliva swabs. These were processed in the UNC Lilongwe

lab with ELISA and Western Blot diagnostics². Post-test counseling was offered in VCT tents in or close by the villages of the respondents one to three months after testing. The second round of HIV testing and counseling took place in 2006, this time using a finger-prick rapid tests (Determine® and UniGold). The respondents could choose the testing location (either in the home or in a VCT tent in the village) and post-test counseling was done 20 to 30 minutes after the test. Respondents were given the option to be tested and counseled about their HIV status or just to provide a drop of blood for research purposes but without post-test counseling or disclosure of the test results.

Of the 2,878 respondents that were tested in MDICP3, 1,954 or 71.8% came back for post-test counseling (1,828 HIV negatives 117 HIV positives and 9 with undetermined result). Of these, 1,444 HIV negatives and 56 HIV positives were contacted again for testing in MDICP4. In this group of respondents, the relative risk of a refusal was 4.94 times higher among HIV positives than in among HIV negatives (95%-CI: 2.55 – 9.57, see Annex I).

Simulations of bias in HIV prevalence rates in national seroprevalence rates

The finding that refusals are informed by prior knowledge of HIV positive status does not automatically mean that refusals are a source of substantial bias in national or local estimates of HIV prevalence. Both levels of refusal and especially levels of prior testing have been relatively low in many sub-Saharan African countries and the magnitude of bias may therefore be negligible. In order to evaluate the magnitude of this bias, we carry out simulations designed to model the sampling process of individuals for a stratified population-based serological survey such as a DHS.

The model creates a large fictitious population stratified by urban/rural residence and assigns each individual an HIV status and whether or not the individual knows his or her HIV status from a previous HIV test. These individual characteristics are assigned such that the population level aggregates match the estimate obtained in the DHS. That is, if the DHS in Ghana estimates that urban females have HIV prevalence of 2.5 percent, then urban females in the simulated population will have prevalence of 2.5 percent. Similarly if 4.7 percent of rural males in the DHS have had a previous HIV test and received the result, then in the simulated population 4.7 of all rural males will know their HIV status.

The model currently assumes that HIV status and having had an HIV test prior to the survey are independently assigned. This assumption is almost certainly not true; several studies have suggested that individuals who are HIV positive are more likely to know their status [45]. Under this assumption, the model will thus provide conservative estimates of bias in HIV prevalence. In future versions of the model we may seek to quantify and include the relationship between HIV status and knowledge about one's status.

From this large simulated population a stratified random sample is drawn of the same size as in the corresponding DHS. In the case of Ghana, for example, a sample of 11,294 individuals was drawn to match the 2003 DHS. The sample is stratified such that males and females are sampled in equal proportions and individuals are sample proportionally from urban and rural areas following the distribution reported for the year 2000 in the World Urbanization Prospects [46].

Of the sampled population, a random set individuals are identified as 'absent' at the time of testing such that the proportion of missing individuals matches that recorded in each group in the DHS survey. In the model, being absent is assumed to be independent of HIV status. This is also likely to be untrue (Cfr. *Infra*), but again, this leads to conservative estimates of bias in HIV prevalence.

² A description of the MDICP project, the data and survey instruments can be found at <http://www.malawi.pop.upenn.edu>. The testing protocol for MDICP3 is described in [44]

Finally, for sampled individuals who are ‘present at the time of interview’ the model probabilistically assigns whether or not each individual refuses to be tested depending on the individuals’ HIV status as well as their knowledge about their HIV status. For each individual a random number between zero and one is generated. Those who are unaware of their HIV status ‘refuse the test’ if the random number is smaller than the proportion in the HIV status naïve population in the corresponding DHS that refused. If the number is greater, then the individual in the simulated sample participates in the HIV test. For example, in the Ghana 2003 DHS 14.35 percent of all urban HIV status naïve men refused. If an urban male in the simulated sample generated a random number of 0.063452 then he would refuse, if the generated random number is 0.44241, then he would accept the test. In aggregate, 14.35 percent of the HIV status naïve urban males sampled will refuse the test, although the exact refusal rate will vary slightly for each model draw.

The process is similar for individuals who know their HIV status. Each individual is assigned a random number. However the likelihood of accepting the test will now depend on the individuals HIV status. Based on the MDICP data, an individual who knows he is HIV positive is 4.94 times as likely to refuse as an individual who knows he is HIV negative. The likelihoods of refusal for each of these two groups is calculated so that in aggregate approximately the proportion of individuals who refuse is the same as the proportion of individuals who knew their status in the DHS survey refused. For example, if the HIV prevalence is 15 percent and the refusal rate among those that have been tested before is 10 percent, then a simple calculation reveals that about 31 percent of the individuals who know they are positive must refuse and 6.3 percent of those who know they are negative must refuse.

Finally, the HIV prevalence is calculated amongst the individuals who accepted to participate in the sero-survey. The bias can be assessed by comparing the sample prevalence to the actual fixed HIV prevalence in the population from which the sample is drawn. The comparison may be made across the entire population or within each stratified subgroup.

The model is considered in three different scenarios, where individuals who know they are positive are 2.55, 4.94 and 9.57 times as likely to refuse as individuals who know they are negative (corresponding to the relative risk point estimate and the 95% confidence interval limits). For each country the model is run 500 times for each scenario, producing a distribution of HIV prevalence estimates.

Results

Simulation results are presented for the Malawi 2004 DHS. Table 1 shows the relevant parameters recorded in the DHS. A total of 7868 individuals were eligible for HIV testing in the DHS. Of these 9.7 percent were not available at the time of testing. Of those present for the household survey, 13.4 percent reported that they had previously received the result of an HIV test. Of those who had been tested previously, 22.1 percent refused to be tested, and of those who had not been tested previously 24 percent refused to be tested for HIV³. The national adult HIV prevalence estimated by the DHS is 11.6 percent. For the purposes of parameterizing the simulation model, each of these figures is stratified by gender and urban/rural residence. These can be seen in Table 1.

³ Note that in the Malawi 2004 DHS, individuals who had been tested previously were overall *less* likely to refuse than individuals who had not been tested previously. In fact, out of the 10 countries with DHS surveys including HIV testing reported above, Malawi is the only country for which this is true. However, this does not affect the hypothesis that *amongst individuals who know their status*, HIV positive individuals are more likely to refuse than those who have tested negative.

Table 1: Parameters reported in Malawi 2004 DHS

	Males		Females		Total	
	Urban	Rural	Urban	Rural		
% Tested Previously	25.1	12.4	22.9	10.7	13.4	Sample Size = 7868
% Refusal - Tested Previously	25.4	19.7	27.1	21.7	22.1	% Urban = 15.1
% Refusal - Not Tested Previously	28.6	23.5	28.9	23.0	24.0	
% Absent	19.8	13.1	7.0	5.1	9.7	
DHS Sample HIV Prevalence	16.3	8.8	18.0	12.5	11.6	

Table 2 shows the results of the sample simulations based on the Malawi 2004 DHS parameters in Table 1. The first column shows the actual HIV prevalence in the simulated population, for the entire population and each sub-group. Columns two through four give the mean estimate of HIV prevalence in the sample drawn over 500 simulations for the ‘low’, ‘medium’, and ‘high’ assumptions about the likelihood of refusing for individuals who know their HIV status. The ‘low’ scenario corresponds to the assumption that individuals who know they are HIV positive are 2.55 times more likely to refuse than individuals who have tested negative, the ‘medium’ to 4.94 times, and the ‘high’ to 9.57 times. Columns five through seven represent the ratio of the actual population prevalence to the estimate of the prevalence produced by the sample.

In the sample population, the true population prevalence is 11.63 percent, but under the ‘medium’ assumption the sample prevalence is 10.48 percent. The stratified sample underestimates the actual population by about 11 percent. Under the low assumption, the bias is a relatively modest five percent, and under the high assumption the sample prevalence is about 16 percent too low.

However, the amount of bias is considerably greater for selected subpopulations that are more likely to have been tested previously and have high HIV prevalence and refusal rates. For example, while urban males make up only 7.55 percent of the entire population, the sample underestimates prevalence in this group by 23 percent under the medium assumption. Thus, while the bias may be modest in the national estimates of HIV prevalence, it is likely much more severe for subgroups of the population. This finding has potentially severe consequences for appropriately allocating resources for local ARV and VCT programs and generally providing healthcare services to populations that might have a greater burden of disease than that projected by national serological surveys. Furthermore, this suggests that the amount of bias in nationally representative serological surveys may increase in the future as VCT and ARV programs rollout and testing becomes more common.

Table 2: Preliminary Simulation Results for Malawi 2003 DHS

	Population Prevalence	Sample HIV Prevalence			Population Prev/Sample Prev		
		Low	Medium	High	Low	Medium	High
Malawi	11.63	11.03	10.48	10.02	1.05	1.11	1.16
Urban Males	16.30	14.57	13.25	12.08	1.12	1.23	1.35
Rural Males	8.80	8.48	8.04	7.67	1.04	1.09	1.15
Urban Females	18.00	16.29	15.03	13.76	1.10	1.20	1.31
Rural Females	12.50	12.07	11.61	11.19	1.04	1.08	1.12

Discussion

In this paper, we challenge the optimistic inclination in the literature that bias in HIV prevalence estimates due to the refusal for testing is minimal; if not negligible. Most previous studies that have

assessed bias in HIV serostatus, acknowledge that refusals correlate with sociodemographic and behavioral characteristics, but ignore that it is informed by prior knowledge about one's HIV status. The latter turns out to be important, and might lead to substantial bias in HIV prevalence estimates. This is particularly the case for sub-populations where prior testing and refusal rates are high. This is often the case for urban populations of countries with high prevalence rates, and our results suggest that HIV prevalence estimates in these settings might be underestimated by as much as 30 percent in the extreme scenario. Ironically, this finding implies that urban areas weigh less than they should in population-based survey estimates of HIV prevalence, while they were usually overrepresented in ANC based estimates of seroprevalence.

Even though the extrapolation from these static observations to trends over time need to be made with the necessary caution, our finding that bias is largest in populations where prior testing rates are highest implies that the potential for bias in seroprevalence estimates will increase in conjunction with efforts for increasing VCT coverage.

Our model is merely suggestive, however, and should not be considered a procedure for adjusting the HIV prevalence estimates from nationally representative surveys. One of the weaknesses of this study is that we had access to only one sample for estimating the likelihood of refusal conditional on prior knowledge of one's HIV status. This parameter is not likely to be fixed, and may vary under a variety of conditions such as gender, urban/rural residence, access to antiretroviral therapy, and possibly also with the level of refusal itself. In populations where the refusal rate is higher, refusal may be less selective, and as a consequence to a lesser degree informed by prior knowledge. Despite the uncertainty around this parameter, modest bias is observed even under the most conservative estimate of this parameter.

Our estimates of bias are also conservative because of a number of other reasons. First, we assume that HIV positives and negatives are as likely to have ever been tested before. Secondly, because we require survey information for estimating one of the parameters in our model, we only account for refusals conditional on a completed survey interview. This is problematic because HIV positives who know their status are not only more likely to refuse testing, but also to refuse an interview, particularly if it contains discomfiting questions about current and prior sexual behavior. Third, our model does not account for the potential relationship between perceived risk of infection, true HIV status and refusal in the subgroup that has never been tested before. Fourth, our model does not account for sources of bias related to the sampling frame and non-response for other reasons than refusal (e.g. population mobility).

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Annex 1: relative risk of refusal in MDICP4 (t₂) by prior test result (conditional on post-test counseling in MDICP3 (t₁))

	t1 HIV+	t1 HIV-	Total
t2 refusal	9	47	56
t2 consent	47	1397	1444
Total	56	1444	1500
Risk	.1607143	.0325485	.0373333
	Point estimate		[95% Conf. Interval]
Risk difference	.1281658		.03154 .2247917
Risk ratio	4.93769		2.548762 9.565734
Attr. frac. ex.	.7974761		.6076527 .8954602
Attr. frac. pop	.1281658		
1-sided Fisher's exact P = 0.0001			
2-sided Fisher's exact P = 0.0001			

Alternative estimate using poisson regression:

```
. poisson refusalt2 hivt1 if hivt1<8 & postvctt1==1, irr
```

```
Iteration 0: log likelihood = -236.25674
Iteration 1: log likelihood = -233.44745
Iteration 2: log likelihood = -233.42932
Iteration 3: log likelihood = -233.42931
```

```
Poisson regression              Number of obs   =       1500
                                LR chi2(1)         =        13.38
                                Prob > chi2         =       0.0003
                                Pseudo R2           =       0.0279
Log likelihood = -233.42931
```

refusalt2	IRR	Std. Err.	z	P> z	[95% Conf. Interval]
hivt1	4.937699	1.796586	4.39	0.000	2.419993 10.07477

Gives the same point estimate but slightly larger confidence intervals

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