Short Communication

Lack of a Decline in HIV Incidence in a Rural Community with High HIV Prevalence in South Africa, 2003–2007

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Abstract

To understand the dynamics of the HIV epidemic and to plan HIV treatment and prevention programs, it is critical to know how HIV incidence in a population evolves over time. We used data from a large population-based longitudinal HIV surveillance in a rural community in South Africa to test whether HIV incidence in this population has changed in the period from 2003 through 2007. We observed 563 seroconversions in 8095 individuals over 16,256 person-years at risk, yielding an overall HIV incidence of 3.4 per 100 person-years (95% confidence interval 3.1–3.7). We included time-dependent period dummy variables (in half-yearly increments) in age-stratified Cox regressions in order to test for trends in HIV incidence. We first did regression analyses separately for women and men. In both regressions, the coefficients of all period dummy variables were individually insignificant (all $p \geq 0.338$) and jointly insignificant ($p = 0.764$ and $p = 0.111$, respectively). We then did regression analysis using the pooled data on women and men, controlling for sex and interactions between sex and age. Again, the coefficients of the eight period dummy variables were individually insignificant (all $p \geq 0.387$) and jointly insignificant ($p = 0.701$). We show for the first time that high levels of HIV incidence have been maintained without any sign of decline over the past 5 years in both women and men in a rural South African community with high HIV prevalence. It is unlikely that the HIV epidemic in rural South Africa can be reversed without new or intensified efforts to prevent HIV infection.

ESTIMATES OF THE DEVELOPMENT OVER TIME of HIV incidence in the general population are crucial for understanding the dynamics of the HIV epidemic, assessing the population impact of HIV prevention strategies, and predicting antiretroviral treatment need. Several countries in sub-Saharan Africa have in recent years experienced declines in HIV prevalence among pregnant women attending antenatal clinics, including Botswana,¹ Ethiopia,² Kenya,³ Malawi,⁴ Zambia,⁵ and Zimbabwe.⁶ In South Africa, the country with the largest absolute number of HIV-positive people worldwide, HIV prevalence among women attending antenatal clinics has been reported to be leveling off after nearly two decades of steady increase.^{7,8} Trends in antenatal HIV prevalence are sometimes taken to suggest similar trends in HIV incidence in the general population.^{1,7} However, such inference may be incorrect. Findings based on surveys of women in antenatal care may not generalize to the population as a

whole.^{8,9} Moreover, changes in HIV prevalence are a function of both the rate of new infections and mortality in HIV-positive people, so that trends in HIV prevalence do not imply specific trends in incidence. For instance, Wawer and colleagues find that “HIV-related mortality contributed most to the [HIV] prevalence decline” observed in Uganda from 1990 to 1992, while HIV incidence did not change significantly over the period.¹⁰

Population trends in HIV incidence can be directly measured through repeated HIV testing of the same individuals in longitudinal HIV surveillance. However, longitudinal surveillances are rare, because they are difficult to establish and costly to maintain.¹¹ Only a few past studies in Africa have thus analyzed population trends in HIV incidence using longitudinal data.^{10,12–15} We use data from a large population-based longitudinal HIV surveillance conducted by the Africa Centre for Health and Population Studies, University of

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KwaZulu-Natal, in a rural community in the Umkhanyakude district of KwaZulu-Natal, South Africa, to test whether HIV incidence in this population has changed in the period from 2003 through 2007. Previous studies in this community found high levels of crude HIV prevalence in adults (21.4% in 2003/4)¹⁶ and crude HIV incidence (3.2 per 100 person-years from 2003 through 2005).¹⁷ Over the past years, the community in which the surveillance took place has been exposed to HIV prevention campaigns organized both at the national level (such as the *loveLife* campaign)¹⁸ and the local level (such as the *Star for Life* program),¹⁹ and has had access to voluntary counseling and testing (VCT) in the public and private sector.^{20,21} A public-sector antiretroviral treatment program was established in the study area in October 2004; by July 2008, more than 5200 patients were receiving antiretroviral medication through the program.

The data for this study were collected between July 2003 (the start of the HIV surveillance) and December 2007, covering the first four rounds of the surveillance. The study area, data collection, and laboratory methods of the surveillance have been described elsewhere.²² All participants in the surveillance provided written informed consent for the analysis of their information, including HIV status. Residents in the surveillance area had to meet age eligibility criteria (women between 15 and 49 and men between 15 and 54 years of age) in order to participate in the HIV surveillance. Of 36,813 eligible residents ever contacted in the first four rounds of the surveillance 21,709 consented at least once to provide a blood sample for HIV testing (i.e., the participation proportion over the first four surveillance rounds was 59%). We enrolled all individuals into the HIV incidence cohort for this study who met the following additional eligibility criteria. First, they had to have tested HIV-seronegative when they first participated in the HIV surveillance. Second, they had to be eligible for participation in at least one round of the HIV surveillance following the round in which they had initially participated (up to and including the fourth round of the surveillance).

Of the 12,494 individuals who tested HIV-seronegative in one round of the surveillance and were eligible for HIV testing in at least one later round, 8095 individuals participated at least one more time in the HIV surveillance and could thus be included in the HIV incidence analysis (i.e., the overall follow-

up proportion of the population eligible for participation in this study was 65%). Table 1 shows the sex-age distribution of the eligible population, the sample included in the HIV incidence analysis, and the follow-up proportion. Across 5-year age categories, the follow-up proportion varied between 64% and 74% in women and between 56% and 66% in men, although most of the sex-age specific proportions were not significantly different from each other (Table 1). At enrollment, the average age in the eligible population of 12,494 was 25.5 years [standard deviation (SD) 10.8] compared to 25.7 years (SD 11.0) in the 8095 individuals included in the sample for incidence analysis; 54.8% (SD 0.50) of the individuals in the eligible population and 58.5% (SD 0.50) of the individuals included in the sample for incidence analysis were women.

We determined the date of seroconversion by random draws from a uniform distribution of days between the date of an individual's first positive HIV test and the date of the last negative HIV test available in the surveillance. Such random assignment of the time point of HIV seroconversion has the advantage over the commonly used midpoint imputation^{12,14} that it avoids heaping of seroconversions in the middle of the study period. To test the robustness of our findings to the method of imputing seroconversion dates, we repeated all analyses described below using the midpoint of the seroconversion intervals (i.e., the expected value of random draws from a uniform distribution on the seroconversion interval) as the date of seroconversion. None of our results differed significantly by method of imputing seroconversion dates. Below, we thus show only the results based on the random assignment of dates.

The 8095 individuals included in the HIV incidence analysis contributed 16,256 person-years at risk and 563 seroconversions to the analysis (Table 2), yielding an overall HIV incidence of 3.4 per 100 person-years [95% confidence interval (CI) 3.1–3.7]. Figure 1 shows the point estimates and 95% CIs of crude HIV incidence by half-year calendar period from June 2003 through December 2007. The 95% CIs of HIV incidence in each calendar period overlap with the 95% CIs of the incidence estimates in all other periods. To test whether HIV incidence varied significantly by time period, we included calendar period at risk as a time-dependent covariate in half-yearly increments (from the period July 2003–December 2003

TABLE 1. SEX-AGE DISTRIBUTION OF ELIGIBLE POPULATION, SAMPLE INCLUDED IN THE HIV INCIDENCE ANALYSIS, AND FOLLOW-UP PROPORTION

	Eligible		Included in analysis		Follow-up proportion			
	Women	Men	Women	Men	Women		Men	
	(n)	(n)	(n)	(n)	mean (%)	95% CI ^a	mean (%)	95% CI
15–19	2963	3076	2066	1853	70	68–71	60	58–62
20–24	1080	1017	695	568	64	61–67	56	53–59
25–29	481	356	310	205	64	60–69	58	52–63
30–34	442	238	305	145	69	64–73	61	54–67
35–39	578	218	408	143	71	67–74	66	59–72
40–44	697	249	502	143	72	69–75	57	51–64
45–49	607	279	447	172	74	70–77	62	56–67
50–54		213		133			62	56–69
Total	6848	5646	4733	3362	69	68–70	60	58–61

^aCI, confidence interval.

TABLE 2. COX REGRESSION ANALYSIS OF HIV ACQUISITION^{a,b}

Regression	(1) Women	(2) Men	(3) Women and men
2004/I	1.07 (0.36)	0.76 (0.53)	0.99 (0.30)
2004/II	0.842 (0.37)	0.694 (0.72)	0.963 (0.32)
2005/I	0.757 (0.30)	0.865 (0.86)	0.776 (0.30)
2005/II	0.87 (0.32)	1.33 (0.60)	0.99 (0.28)
2006/I	0.681 (0.30)	0.656 (0.39)	0.964 (0.24)
2006/II	0.94 (0.38)	0.90 (0.46)	0.92 (0.30)
2007/I	0.853 (0.40)	0.875 (0.62)	0.780 (0.34)
2007/II	0.85 (0.37)	0.56 (1.58)	0.76 (0.41)
Female sex	—	—	5.89 (1.17)
Sex*Age 20–24	—	—	<0.0001 0.34 (0.09)
Sex*Age 25–29	—	—	<0.0001 0.16 (0.05)
Sex*Age 30–34	—	—	<0.0001 0.16 (0.07)
Sex*Age 35–39	—	—	<0.0001 0.14 (0.06)
Sex*Age 40–44	—	—	<0.0001 0.14 (0.07)
Sex*Age 45–49	—	—	<0.0001 0.10 (0.05)
N	4733	3362	8095
Seroconversions	427	136	563
Person-years at risk	9776	6480	16,256
Log likelihood	–2710	–743	–3750
LR χ^2	4.94	13.03	139.53
p value	0.764	0.111	<0.00001

^aThe numbers in the cells are the adjusted hazard ratio (aHR), standard error of the aHR, and p value. LR = likelihood ratio, I = first half of a year, II = second half of a year, *indicates interaction.

^bThe Cox baseline hazard is stratified by 5-year age category. The reference category in regressions (1) and (2) is 2003/II. The reference categories in regression (3) are 2003/II, male sex, and Sex*Age 15–19.

to the period July 2007–December 2007) in Cox regression analysis of HIV acquisition. When we included age (at the time of the first negative HIV test) in a number of different functional forms on the right-hand side of the Cox regressions

FIG. 1. Crude HIV incidence by half-year period.

equations (linear age term, third-order polynomial of the centered age variable, and 5-year age categories), the Cox proportional hazards assumption was consistently violated, as diagnosed by the Grambsch–Therneau test.²³ We thus stratified the Cox baseline hazard by age category (in 5-year increments, starting at age 15).

We know from previous studies in this population that the age pattern of HIV incidence differs by sex.^{17,24} We first did regression analyses separately for women and men [Table 2, regressions (1) and (2)]. In both regressions, the coefficients of the eight time-dependent period dummy variables were individually insignificant (all $p \geq 0.338$) and jointly insignificant [likelihood ratio test of joint significance, χ^2 4.94 ($p = 0.764$) in regression (1) and χ^2 13.03 ($p = 0.111$) in regression (2)]. To maximize the statistical power to detect significant differences in the hazard of HIV acquisition by time period, we then did regression analysis using the pooled data on women and men. In this regression, we controlled for sex and interactions between sex and the 5-year age strata. No interaction term between sex and the oldest age stratum (50–54 years of age) was included in the regression because women older than 49 years of age were not eligible to participate in the surveillance. The results of the regression using the pooled data confirmed the results of the separate regressions for women and men. The coefficients of the eight period dummy variables were individually insignificant (all $p \geq 0.387$) and jointly insignificant [likelihood ratio test of joint significance, χ^2 5.52 ($p = 0.701$)] [Table 2, regression (3)]. In none of the three final regressions was the proportional hazards assumption violated [for any of the individual independent variables (all $p \geq 0.104$) or globally (all $p \geq 0.517$)]. All analyses were undertaken using STATA 10.1.

A previous longitudinal population-based study in another rural community in South Africa (in Limpopo province) between 2001 and 2004 found HIV incidence levels similar to those in this community (4.9 and 2.2 per 100 person-years in women and men, respectively).²⁵ Our study demonstrates for the first time that such high levels of HIV incidence in women and men have been maintained in a rural South African community without any sign of decline over the past 5 years. This finding supports the conclusion in the 2008 UNAIDS Report that “there is no evidence yet of major changes in HIV-related behaviour” in South Africa.²⁶

While our study cannot answer the counterfactual question about how high the HIV incidence level in this community

would have been without past and present HIV prevention efforts, it is clear from our findings that the prevention strategies used are not sufficient to reduce the spread of the epidemic, primarily because they do not reach sufficient numbers of people, they do not reach the right target groups, or they are ineffective. It is unlikely that the HIV epidemic in rural South Africa can be reversed without new approaches (such as male circumcision programs²⁷ and behavioral interventions targeting HIV-positive people)^{27,28} or intensified effort to prevent HIV infection using established methods (such as school-based sexual health interventions).^{29,30}

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No competing financial interests exist.

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