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Effect of hormonal contraceptive use on HIV progression in female HIV seroconverters in Rakai, Uganda

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Abstract

Objective—To assess the association between hormonal contraceptive use and HIV progression.

Design—A retrospective analysis of 625 female HIV seroconverters from a Ugandan cohort study.

Methods—Multivariate Cox regression analyses incorporating time-varying hormonal contraceptive exposure were used to estimate the adjusted hazard ratios of death, and a composite outcome of AIDS or death, associated with hormonal contraceptive use. Sensitivity analyses included lagging hormonal contraceptive exposure, varying comparison groups, and separately assessing effects of oral and injectable contraceptives.

Results—A total of 27.5% of women reported ever using hormonal contraception. Of 625 women, 104 (16.6%) died and 291 (46.6%) progressed to AIDS or death during observation. Time-varying hormonal contraceptive use was not associated with an increased hazard of death as compared with nonuse of hormonal contraception (adjusted hazard ratio 0.76, 95% confidence interval 0.41–1.39, $P = 0.37$), and was associated with a significantly reduced hazard of progression to AIDS or death (adjusted hazard ratio 0.70, 95% confidence interval 0.50–0.97, $P = 0.03$). None of the sensitivity analyses suggested an adverse effect of hormonal contraception on HIV progression.

Conclusion—Hormonal contraceptive use was not associated with faster progression to death, and was associated with a reduced hazard of progression to the composite outcome of AIDS or death.

Keywords

family planning; HIV progression; hormonal contraception; survival analysis; Uganda

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Introduction

Over 120 million women worldwide use hormonal contraception, and methods such as injectable contraceptives are rapidly growing in popularity [1–3]. For HIV-positive women who wish to prevent pregnancy, use of an effective contraceptive method carries benefits including increased reproductive autonomy, reduced risks of maternal morbidity and mortality, reduced demand for abortion, reduced risk of perinatal HIV transmission, and avoidance of antiretroviral prophylaxis for prevention of mother-to-child HIV transmission, which can result in generation of resistant viral strains [4,5].

Potential risks of hormonal contraceptive use must be weighed against potential risks of pregnancy. Although studies in developed countries do not suggest cause for concern, in less developed countries, mixed evidence exists on the effects of pregnancy and breastfeeding on HIV progression [6–12].

Conversely, benefits of hormonal contraceptive use must be balanced against concerns about effects on HIV disease progression. One randomized controlled trial suggested that hormonal contraceptive use increased the hazard of progression to AIDS or death [13,14]. However, HIV disease progression associated with hormonal contraceptive use was not an *a priori* hypothesis, and high and differential rates of attrition and contraceptive discontinuation may have biased the results. An observational study conducted among Kenyan commercial sex workers also suggested a potential detrimental effect [15–18]. The biological mechanism by which hormonal contraception may influence HIV disease progression is unknown, but several theoretical mechanisms exist [17–22]. Borderline protective effects of hormonal contraception against mortality were found among Rwandan women [23], but most observational studies to date have found no association between hormonal contraception and HIV disease progression [24]. However, most observational studies have enrolled women with prevalent HIV infection, used small sample sizes, or had limited follow-up.

The purpose of our study was to assess the association between hormonal contraceptive use and progression to AIDS or death among women with incident HIV infection in a population-based cohort study in Rakai, Uganda.

Methods

The Rakai community cohort study

Since 1994, the Rakai Health Sciences Program has followed an open cohort of all consenting adults aged 15–49 years from 50 communities in the Rakai district of southwestern Uganda. Participants of the Rakai Community Cohort Study (RCCS) are consented and privately interviewed by same-sex interviewers every 12–15 months, using a standardized questionnaire [25,26]. Venous blood is collected at each survey for HIV-1 testing. Over 90% of eligible individuals have participated in any given survey round. Institutional Review Board (IRB) approvals for the RCCS were obtained from the Uganda Virus Research Institute's Science and Ethics Committee, the Uganda National Council for Science and Technology, and from the Western IRB in the United States.

Population and variable definitions

This analysis included all sexually experienced female participants who seroconverted to HIV between 1995 and 2006 while under observation in the RCCS. Outcome information was collected through 2008. As antiretroviral therapy (ART) became available in Rakai in mid-2004, the vast majority of person-time analyzed (98%) was treatment-naïve.

The date of HIV infection was estimated as the midpoint between the last HIV-negative and first HIV-positive antibody test dates. Seroconversion was defined as a positive result for two ELISA assays (Vironostika HIV-1, Organon Teknika, Charlotte, North Carolina, USA and Cambridge Biotech, Worcester, Massachusetts, USA) confirmed by western blot (Calypte Biomedical Corporation, Rockville, Maryland, USA). If the presero-conversion blood sample was PCR positive (AMPLI-COR HIV-1 MONITOR version 1.5, Roche Molecular Systems, Branchburg, New Jersey, USA) and ELISA negative, indicating acute infection, then visit date was considered the date of HIV seroconversion. Women with an indeterminate test (i.e., ELISA-positive and a negative or indeterminate western blot) between a previous negative and subsequent positive HIV antibody test were considered to have seroconverted at the date of the indeterminate western blot.

Hormonal contraceptive use was defined as use of either oral or injectable contraceptives, and as of 1999, the definition also included contraceptive implants, as Norplant became available during that year.

Date of death was ascertained from information collected during an annual census and surveys. We were unable to definitively distinguish between HIV-related and HIV-unrelated deaths, but previous analyses in Rakai have found that over 90% of all deaths among HIV-positive persons are HIV-related [27,28].

Prior to 2004, CD4 cell counts were collected only on a subset of individuals. For individuals with available CD4 cell counts, AIDS onset was defined as a CD4 cell count of 250 cells/ μ l or less (the criteria for ART initiation in Rakai). Date of AIDS onset was estimated as the midpoint between last CD4 cell count above 250 cells/ μ l and first CD4 cell count below 250 cells/ μ l. If a person's first CD4 cell count was below 250 cells/ μ l, then that date was used as date of AIDS onset. The majority (70%) of AIDS diagnoses were based on CD4 cell counts. For women without available CD4 cell counts, AIDS onset was defined as date at which self-reported symptoms met the criteria for WHO clinical stage 3 or 4 disease in adults in resource-limited settings [29]. For individuals with both CD4 cell count information and clinical symptoms information, the earlier of the two dates was used.

Statistical analysis

We calculated descriptive statistics to assess differences between hormonal contraceptive users and nonusers. To explore for the possibility of self-selection of healthier women into hormonal contraceptive use, we used *t*-tests to compare mean 'baseline' CD4 cell counts (the average of all CD4 cell counts obtained during the year-long survey period subsequent to seroconversion) in women who never versus ever used hormonal contraception during follow-up.

We estimated event rates per 100 person-years for periods of hormonal contraceptive use and nonuse, and for sociodemographic and behavioral covariates. Univariate associations of hormonal contraceptive use and time to event were evaluated using Kaplan–Meier analyses and univariate Cox regression models. The log-rank test was used to test for equality of survival functions. We fitted two continuous multivariate Cox models to estimate adjusted hazard ratios (adjHRs) and 95% confidence intervals (95% CIs), with time-varying hormonal contraceptive exposure and other covariates, using nonuse of hormonal contraception as the referent category. Model 1 controlled for all variables associated with both hormonal contraceptive use and time to event in univariate analyses at a *P* value of 0.15 or less (socioeconomic status, number of sex partners, educational status, breastfeeding, and time period for the time to death analysis; socioeconomic status and number of sex partners for time to AIDS or death analysis). Model 2 controlled for variables in Model 1, and other variables selected for theoretical concerns and comparability with previous studies. The proportional hazards assumption was tested using

Schoenfeld and scaled Schoenfeld residuals [30]. All analyses were done using STATA.SE, version 10.1 (StataCorp LP, College Station, Texas, USA).

Sensitivity analyses

Time-varying confounding may occur if a change in health status results in a change in exposure [31]. For example, if women who become sicker due to HIV discontinue hormonal contraceptive use, they may be more likely to experience progression following hormonal contraceptive discontinuation, which could underestimate any potential adverse effect of hormonal contraception. To address this concern, we replicated our statistical models using only information provided at baseline, and separately using a lagged exposure variable (reported use of hormonal contraception at previous interview). In addition, we assessed whether women who discontinued hormonal contraception were more likely to have symptoms of opportunistic infections or lower CD4 cell counts than women who continued using hormonal contraception.

Our initial analysis compared hormonal contraceptive users to all other women, regardless of nonhormonal contraceptive use, so we also compared hormonal contraceptive users separately against women using nonhormonal contraceptive methods and against non-contracepting women.

Finally, we analyzed oral contraceptive pills and injectables separately, to assess for differential effects due to different doses and hormones in these products.

Results

Of 625 seroincident women, 172 (27.5%) reported using hormonal contraception at any point during follow-up. Of 1294 time intervals contributed, 273 (21%) represented intervals of reported hormonal contraceptive use, of which 22% involved oral contraceptive pills (61 intervals), 72% involved injectables (197 intervals), and 5% involved Norplant (15 intervals). Women who reported use of hormonal contraception at any point contributed an average of 3.92 years for the time to death analysis, and 3.72 years for the composite outcome of AIDS or death. Women who never reported use of hormonal contraception contributed an average of 3.04 years ($P \leq 0.00$) for the time to death analysis, and 2.98 years ($P \leq 0.00$) for the composite outcome of AIDS or death. Follow-up times ranged from 0.25 to 12.39 years. Of 625 women, 104 (16.6%) died during observation and 291 (46.6%) progressed to AIDS or death. Among women ever reporting hormonal contraceptive use, 12.8% (22/172) died and 45.9% (79/172) progressed to AIDS or death. Among women who never reported hormonal contraceptive use, 18.1% (82/453) died and 46.8% (212/453) progressed to AIDS or death.

At baseline, 18% of women reported hormonal contraceptive use (Table 1). These women were more likely to have higher education and to report having at least one sex partner during the last year, and they were less likely to be in either the youngest (15–24 years) or oldest (35+ years) age categories, to be currently pregnant, to be nulliparous, and to report use of condoms. In 128 women with postseroconversion baseline CD4 cell counts available, average baseline CD4 cell counts were 633 (SD 290) cells/ μ l in 92 women who never used hormonal contraception compared with 713 (SD 249) cells/ μ l in 36 women who ever reported hormonal contraceptive use ($\Delta=80.1$ cells/ μ l, $P=0.15$). In the Rakai program in which ART is initiated when the CD4 cell count is below 250) cells/ μ l, none of the hormonal contraceptive users were ART eligible (0/36) at baseline compared with 4.4% of never users (4/92, $P=0.2$).

Table 2 shows the event rates per 100 person-years by participant characteristics, and univariate hazards of progression. In univariate analysis, time-varying hormonal contraceptive use was associated with a lower hazard of death, which was of borderline statistical significance (hazard

ratio 0.58, 95% CI 0.33–1.05, $P = 0.07$), and with a significantly lower hazard of progression to AIDS or death (hazard ratio 0.70, 95% CI 0.51–0.96, $P = 0.03$). The hazard of progression was significantly increased among women reporting multiple recent sex partners, whereas increased education and a later date of seroconversion were associated with a lower hazard of death. Median time to death was 7.06 years [interquartile range (IQR) 4.86–9.55 years], and median time to AIDS or death was 4.5 years (IQR 2.4–6.3 years). As shown in the Kaplan–Meier survival curves for time-varying hormonal contraceptive use (Figs 1 and 2), hormonal contraception was associated with improved survival with borderline significance (log-rank $P = 0.07$), and with a significantly reduced hazard of progression to AIDS or death (log-rank $P = 0.03$).

Table 3 presents the multivariate Cox hazards regression analyses. The hazard of progression to death was not significantly different between hormonal contraceptive users and nonusers (Model 1 adjHR 0.76, 95% CI 0.41–1.39, $P = 0.37$; Model 2 adjHR 0.77, 95% CI 0.41–1.44, $P = 0.41$), but hormonal contraceptive use was significantly associated with a reduced hazard of progression to AIDS or death (Model 1 adjHR 0.70, 95% CI 0.50–0.97, $P = 0.03$; Model 2 adjHR 0.71, 95% CI 0.51–1.01, $P = 0.05$).

We found no evidence that hormonal contraceptive use was detrimental in sensitivity analyses assessing the possibility of time-dependent confounding. In a model using only time-fixed, baseline covariates, the adjHR was 0.64 (95% CI 0.32–1.25, $P = 0.19$) for time to death, and 0.81 (95% CI 0.58–1.13, $P = 0.21$) for time to AIDS or death. The lagged exposure model generated an adjHR of 0.89 (95% CI 0.47–1.67, $P = 0.71$) for time to death, and 0.76 (95% CI 0.50–1.14, $P = 0.19$) for time to AIDS or death. We also assessed whether hormonal contraceptive discontinuation was due to declining health, and women who continued or discontinued hormonal contraception had similar average CD4 cell counts (t -test = 0.81) and symptoms suggestive of opportunistic infections ($P = 0.51$).

The adjHR comparing hormonal contraceptive users against women using nonhormonal contraceptive methods was 0.73 (95% CI 0.33–1.61, $P = 0.43$) for time to death, and 0.73 (95% CI 0.47–1.13, $P = 0.16$) for time to AIDS or death. The adjHR comparing hormonal contraceptive users against women who did not use any contraceptive method was 0.70 (95% CI 0.37–1.33, $P = 0.28$) for time to death and 0.68 (95% CI 0.49–0.96, $P = 0.03$) for time to AIDS or death.

For injectable contraception the adjHR was 0.93 (95% CI 0.46–1.86, $P = 0.84$) for time to death and 0.72 (95% CI 0.50–1.05, $P = 0.08$) for time to AIDS or death. For oral contraceptive pills, the adjHR was 0.73 (95% CI 0.23–2.37, $P = 0.61$) for time to death, and 0.65 (95% CI 0.33–1.28, $P = 0.21$) for time to AIDS or death.

Discussion

Hormonal contraceptive use among treatment-naïve HIV-positive women was not associated with increased risks of progression to death in our study. Additionally, as suggested in a previous study [23], hormonal contraceptive use may have been associated with reduced hazards of HIV disease progression, but given the potential for self-selection in observational data, this finding should be interpreted cautiously. Most importantly, and in contrast to two previous studies [13–18], our data suggest no detrimental impact of hormonal contraception on HIV disease progression.

Our study has several strengths. Considering the largest sample of incident seroconverters ever analyzed on this issue increased our power to detect an effect, and our study was population-based, meaning that results may be more generalizable than studies assessing high-risk groups. Originating the survival analyses from an estimated date of HIV infection reduced the potential

for survivor bias and improved the precision of survival time measurement. Using time-varying exposure and covariate information reduced misclassification. Although shorter intervals between interviews could have further reduced potential misclassification, this study benefited from follow-up times ranging through 12 years; shorter studies (which may have shorter intervals between interviews) may not provide sufficient information to observe long-term progression events [24]. We attempted to minimize the potential for time-dependent confounding by including several sensitivity analyses, and we reduced concerns about selection bias by assessing for potential self-selection of hormonal contraceptive use by healthier women.

Our study also had several limitations. The length of time between study rounds may have decreased precision for estimating dates of seroconversion, but is unlikely to be differential between hormonal contraceptive users and nonusers. Using symptoms to determine AIDS onset is imperfect, but was used for only 30% of AIDS diagnoses. We were unable to definitively diagnose AIDS-related deaths, but the vast majority of deaths in HIV-positive individuals are AIDS-related in this population [27,28]. As in all observational studies, there is a possibility of self-selection. There were differences in baseline characteristics of hormonal contraceptive users and nonusers (Table 1), and adjustment increased hazard ratios in the time to death analysis (Tables 2 and 3), suggesting possible confounding, but we did not find evidence of differences in disease stage at enrollment. Although baseline CD4 cell count could not be included in multivariate analysis, this limitation is less concerning than in studies of women with prevalent HIV infection. Finally, formulations of oral contraceptives may have changed over time, and the possibility of recall error exists with all self-reported information.

Conflicting information about the effect of hormonal contraception on HIV disease progression has hindered contraceptive counseling for HIV-positive women. Our findings should assuage these concerns. Given the results of our study and the preponderance of existing evidence, HIV-positive, treatment-naïve women should be counseled that hormonal contraception is not believed to accelerate HIV progression. Beyond assisting HIV-positive women in controlling their reproductive health, effective family planning is important for reducing mother-to-child HIV transmission and for prevention of AIDS orphanhood. Given the high level of unmet need for contraception among HIV-positive women, efforts to further integrate family planning and HIV services are urgently needed.

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Fig. 1.
Survival by time-varying hormonal contraceptive (HC) use in Rakai, Uganda.

AIDS/death by HC use (time-varying), Rakai, Uganda

Intervals at risk (progressions)

No HC	513	(166)	93	(77)	3	(3)	0
HC	112	(31)	29	(12)	2	(2)	0

----- No HC ——— HC

Fig. 2.
AIDS or death by time-varying hormonal contraceptive (HC) use in Rakai, Uganda.

Table 1

Relationship of hormonal contraceptive use with demographic, socioeconomic, fertility, and sexual characteristics among female HIV seroconverters in Rakai, Uganda, at baseline ($n = 625$).

	No hormonal contraceptive use at baseline (N = 513)		Hormonal contraceptive use at baseline (N = 112)		
	n	%	n	%	P
Demographic and socioeconomic					
Age (years)					0.006
15–24	196	38.2	39	34.8	
25–34	196	38.2	59	52.7	
35+	121	23.6	14	12.5	
Socioeconomic status*					0.191
Poor	38	7.4	4	3.6	
Average	296	57.7	59	52.7	
Above average	158	30.8	42	37.5	
Missing	21	4.1	7	6.3	
Education*					0.018
None	117	22.8	18	16.1	
Primary	291	56.7	56	50.0	
Secondary	88	17.2	22	29.5	
Technical/university	17	3.3	5	4.5	
Marital status					0.102
Never married	118	23.0	22	19.6	
Previously married	115	22.4	17	15.2	
Currently married	280	54.6	73	65.2	
Nonmarital relationship	143	27.9	39	34.8	0.143
Fertility and sexual behaviors					
Number of total births*					0.002
None	47	9.2	1	0.9	
1	71	13.8	15	13.4	
2–4	207	40.4	60	53.6	
5+	188	36.7	36	32.1	

	No hormonal contraceptive use at baseline (N = 513)		Hormonal contraceptive use at baseline (N = 112)		P
	n	%	n	%	
Currently pregnant*	73	14.2	0	0.0	<0.001
Breast feeding*	50	9.8	5	4.5	0.096
Condom use*					<0.001
No	407	79.3	111	99.1	
Yes	53	10.3	1	0.9	
Not asked because pregnant	53	10.3	0	0.0	
Sex partners in last year*					0.001
None	55	10.7	1	0.9	
One	404	78.8	100	89.3	
Two or more	54	10.5	11	9.8	

* P value calculated with Fischer's exact test due to small (n <10) cell size.

Table 2
Event rates and univariate Cox regression models for time-to-event among 625 female HIV seroconverters in Rakai, Uganda.

Time to death analysis							Time to AIDS or death analysis					
Variable	Deaths	Person-years at risk	Death rate per 100 person-years	Hazard ratio	95% CI	P	AIDS or death	Person-years at risk	Failure rate per 100 person-years	Hazard ratio	95% CI	P
Hormonal contraceptive use												
No	91	1264.0	7.20	1.00		0.07	246	1282.0	19.19	1.00		0.03
Yes	13	293.0	4.44	0.58	0.33–1.05		45	311.0	14.47	0.70	0.51–0.96	
Demographic and socioeconomic												
Current age (years)												
15–24	20	395.3	5.06	1.00		0.38	61	412.6	14.78	1.00		0.67
25–34	49	711.8	6.88	0.73	0.43–1.24		148	750.3	19.73	0.95	0.70–1.29	
35+	35	449.9	7.78	0.68	0.38–1.20		82	430.0	19.07	0.86	0.61–1.22	
Socioeconomic status												
Poor	5	70.4	7.10	1.00		0.15	16	69.9	22.89	1.00		0.09
Average	73	931.8	7.51	0.62	0.25–1.54		185	945.3	19.57	0.63	0.37–1.05	
Above average	26	516.7	5.03	0.42	0.16–1.11		88	540.7	16.28	0.54	0.32–0.93	
Education												
None	17	246.0	6.91	1.00		0.04	53	265.8	19.94	1.00		0.30
Primary	70	933.4	7.50	0.73	0.43–1.24		172	949.6	18.11	0.81	0.59–1.10	
Secondary or higher	17	377.6	4.50	0.42	0.21–0.84		66	377.6	17.48	0.76	0.53–1.10	
Marital status												
Never married	21	299.3	7.02	1.00		0.41	50	314.8	15.89	1.00		0.23
Previously married	42	496.7	8.46	0.79	0.47–1.35		111	481.9	23.03	1.24	0.88–1.73	
Currently married	41	760.9	5.39	0.70	0.41–1.19		130	796.2	16.33	1.01	0.72–1.40	
Nonmarital relationship												
No	69	1107.2	6.23	1.00		0.24	201	1134.4	17.72	1.00		0.32
Yes	35	449.7	7.78	1.28	0.85–1.93		90	458.6	19.62	1.14	0.88–1.46	
Time of interview												
1996–1998	18	230.27	7.82	1.00		0.00	39	254.20	15.34	1.00		0.24
1999–2002	55	534.39	10.29	0.97	0.56–1.66		109	577.50	18.87	1.24	0.85–1.82	

Variable	Time to death analysis					Time to AIDS or death analysis						
	Deaths	Person-years at risk	Death rate per 100 person-years	Hazard ratio	95% CI	P	AIDS or death	Person-years at risk	Failure rate per 100 person-years	Hazard ratio	95% CI	P
2002–2006	31	792.31	3.91	0.19	0.10–0.35		143	761.25	18.78	1.01	0.70–1.45	
Fertility and sexual behaviors												
Number of total births												
None	5	87.7	5.70	1.00		0.61	18	91.2	19.74	1.00		0.35
1	9	154.4	5.83	1.08	0.36–3.23		26	154.0	16.88	0.95	0.52–1.73	
2–4	43	649.0	6.63	0.80	0.32–2.04		123	703.0	17.50	0.71	0.43–1.16	
5+	47	665.9	7.06	0.70	0.28–1.77		124	644.7	19.23	0.74	0.45–1.22	
Currently pregnant												
No	96	1399.8	6.86	1.00		0.61	264	1434.9	18.40	1.00		0.39
Yes	7	150.7	4.64	0.96	0.45–2.10		25	152.5	16.39	1.07	0.71–1.62	
Uncertain	1	6.5	15.38	2.64	0.36–19.20		2	5.5	36.36	2.52	0.62–10.2	
Breast feeding												
No	98	1477.1	6.63	1.00		0.10	281	1509.9	18.61	1.00		0.58
Yes	6	79.8	7.52	1.99	0.87–4.57		10	83.0	12.05	0.83	0.44–1.57	
Condom use												
No	90	1288.3	6.99	1.00		0.71	242	1321.9	18.31	1.00		0.77
Yes	9	156.8	5.74	0.75	0.38–1.50		29	159.9	18.14	0.97	0.66–1.43	
Not asked	5	111.8	4.47	0.89	0.36–2.21		20	111.1	18.00	1.18	0.74–1.86	
Sex partners in last year												
None	18	241.2	7.46	1.00		0.01	47	228.7	20.55	1.00		0.01
One	76	1206.0	6.30	1.31	0.78–2.21		219	1257.9	17.41	1.05	0.76–1.44	
Two or more	10	109.8	9.11	3.40	1.54–7.54		25	106.3	23.52	2.04	1.24–3.37	

Hazard ratios may not approximate the ratio of event rates, in part, because the Cox model depends on the rank order of time to deaths, and because the hazard ratio estimates use time-varying hormonal contraceptive exposures, whereas the event rates depend on the length of time to event during use and nonuse of hormonal contraceptives, and ascribe person time to periods of exposure or nonexposure without accounting for ordering of events. CI, confidence interval.

Table 3

Multivariate Cox hazards regression models with time-varying exposure for HIV progression among female HIV seroconverters in Rakai, Uganda.

Variable	Time to death (<i>n</i> = 1294 records among 625 women)					Time to AIDS or death (<i>n</i> = 1168 records among 625 women)				
	Model 1			Model 2		Model 1			Model 2	
	Hazard ratio	95% CI	<i>P</i>	Hazard ratio	95% CI	<i>P</i>	Hazard ratio	95% CI	<i>P</i>	95% CI
Hormonal contraceptive use (time-varying)	0.76	0.41–1.39	0.37	0.77	0.41–1.44	0.41	0.70	0.50–0.97	0.03	0.51–1.01
Socioeconomic status			0.41			0.45			0.14	
Poor	1.00	–	–	1.00	–	–	1.00	–	–	–
Average	0.68	0.27–1.70	0.41	0.71	0.28–1.80	0.47	0.64	0.38–1.07	0.09	0.40–1.14
Above average	0.54	0.20–1.44	0.22	0.56	0.21–1.52	0.26	0.56	0.33–0.95	0.03	0.34–1.01
Sex partners in last year			0.05			0.04			<0.00	0.03
None	1.00	–	–	1.00	–	–	1.00	–	–	–
One	1.44	0.84–2.48	0.19	1.60	0.87–2.96	0.13	1.13	0.82–1.56	0.46	0.83–1.70
Two or more	2.75	1.23–6.16	0.01	2.90	1.29–6.52	0.01	2.17	1.31–3.58	<0.00	1.19–3.32
Education			0.08			0.04				0.65
None	1.00	–	–	1.00	–	–	–	–	–	–
Primary	0.60	0.35–1.05	0.07	0.54	0.30–0.99	0.05	–	–	–	0.36
Secondary or higher	0.44	0.21–0.91	0.03	0.37	0.17–0.81	0.01	–	–	–	0.52
Current breastfeeding	1.25	0.49–3.17	0.64	1.29	0.48–3.41	0.61	–	–	–	0.73
Time of interview			0.00			<0.00				0.30
1996–1998	1.00	–	–	1.00	–	–	–	–	–	–
1999–2002	1.04	0.57–1.87	0.91	0.93	0.48–1.80	0.83	–	–	–	0.71
2002–2006	0.20	0.11–0.40	0.00	0.17	0.08–0.36	<0.00	–	–	–	0.56
Number of total births			0.81			0.81				0.55
None	–	–	–	1.00	–	–	–	–	–	–
1	–	–	–	1.46	0.45–4.79	0.53	–	–	–	0.96
2–4	–	–	–	1.18	0.39–3.53	0.77	–	–	–	0.28
5+	–	–	–	0.98	0.31–3.09	0.97	–	–	–	0.39
Current age (years)			0.58			0.58				0.42
15–24	–	–	–	1.00	–	–	–	–	–	–
25–34	–	–	–	1.34	0.69–2.63	0.39	–	–	–	0.67
35+	–	–	–	1.10	0.51–2.40	0.81	–	–	–	0.55

Variable	Time to death (<i>n</i> = 1294 records among 625 women)					Time to AIDS or death (<i>n</i> = 1168 records among 625 women)				
	Model 1		Model 2			Model 1		Model 2		
	Hazard ratio	95% CI	<i>P</i>	Hazard ratio	95% CI	<i>P</i>	Hazard ratio	95% CI	<i>P</i>	<i>P</i>
Currently pregnant						0.64				0.41
No	–	–	–	1.00	–	–	–	–	1.00	–
Yes	–	–	–	0.74	0.32–1.69	0.48	–	–	0.96	0.62–1.48
Uncertain	–	–	–	1.82	0.24–13.91	0.56	–	–	2.58	0.63–10.64
Marital status						0.71				0.36
Never married	–	–	–	1.00	–	–	–	–	1.00	–
Previously married	–	–	–	1.25	0.62–2.54	0.53	–	–	1.29	0.87–1.91
Currently married	–	–	–	1.01	0.52–1.95	0.97	–	–	1.08	0.75–1.57

CI, confidence interval.