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Hormonal Contraceptive Use and Discontinuation among HIV-infected Women in Uganda and Zimbabwe

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Abstract

Introduction—Hormonal contraception (HC) use by HIV-infected women has been identified by the WHO as important strategy for reducing vertical HIV transmission. Little is known about factors associated with HC discontinuation among HIV-infected women.

Methods—We analyzed data from a prospective study of HC use among 231 HIV-infected oral contraceptive (OC) or injectable depot medroxyprogesterone acetate (DMPA) users in Uganda and Zimbabwe. We used Kaplan-Meier survival curves to estimate the median duration of OC and DMPA use and use of any highly effective contraceptive method. Cox proportional hazards models were used to investigate factors associated with HC discontinuation.

Results—Median duration was 36 months (95% CI 14, 61) for OC use and 19 months (95% CI 14, 24) for DMPA use. Median duration of any highly effective method was 36 months (95% CI 26, N/A) for OC users and 22 months (95% CI 14, 38) for DMPA users. In multivariable analyses, living in Zimbabwe (HR 0.39; 95% CI 0.18, 0.83), no partner (HR 7.18; 95% CI 3.05, 16.88) and cervical infection (HR 1.99; 95% CI 0.90, 4.41) were associated with OC discontinuation. No partner (HR 2.00; 95% CI 1.12, 3.58), nausea (HR 1.84; 95% CI 1.02, 3.34) and excessive night sweats (HR 1.80; 95% CI 0.95, 3.40) were associated with DMPA discontinuation.

Discussion—Long-term use of HC methods is acceptable to HIV-infected women. Women discontinue for a variety of reasons, primarily unrelated to HIV. Alternative methods and ongoing contraceptive counseling is essential to reduce unplanned pregnancies and vertical HIV transmission.

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Keywords

vertical transmission; unplanned pregnancy; hormonal contraception; contraceptive discontinuation

Introduction

Over 16.8 million women are HIV-infected worldwide[1]. HIV-infected women face complex reproductive and sexual health choices involving managing their fertility and contraceptive choices[2–4]. The use of highly effective contraceptive methods, including hormonal contraception (HC), by HIV-infected women has been recognized by the WHO as an important strategy to prevent unintended pregnancies, reduce vertical transmission and increase a woman's reproductive control[5–7]. However, little is known about long-term patterns of use or factors associated with HC discontinuation among HIV-infected women.

Expanding access to highly active antiretroviral therapy (HAART) likely influences the fertility intentions and contraceptive needs of HIV-infected women[8–12]. Changes in the WHO's recommended CD4 threshold for HAART initiation has translated into over 8 million people on treatment worldwide[7,13]. Additionally, improved HAART regimens and better access to treatment have led to declines in pediatric HIV infections[14]. Currently, several countries in sub-Saharan Africa are considering changing national policies to place all pregnant HIV-infected women on lifelong HAART, regardless of CD4 count[15,16]. In this changing context, HIV-infected women need effective options for managing their fertility and achieving their reproductive goals[17].

While HC is highly effective for preventing pregnancy, many healthcare providers emphasize condom use for HIV-infected women and put less emphasis on use of highly effective contraception. Healthcare providers may also be reluctant to put HIV-infected women on HC because of concerns about possible interactions between HC and antiretroviral drugs, which could theoretically reduce contraceptive or antiretroviral efficacy[18]. Concerns have also been raised about whether HC may increase HIV acquisition in women or transmission to men and/or accelerate disease progression[19–21]. However, several recent prospective studies and systematic reviews suggest that HC use is not associated with time to AIDS, death or HAART initiation, but further investigation is needed about whether DMPA increases the risk of HIV transmission[22–27]. In 2012, the WHO affirmed its recommendation that women living with HIV can continue to use all existing HC methods without restriction[28].

The goal of this study was to examine factors associated with HC use among HIV-infected women by evaluating use of oral contraceptive pills (OC) and depot medroxygprogesterone acetate (DMPA) over an eight year period in a prospective cohort study of HIV-infected women in Uganda and Zimbabwe. The specific objectives of this analysis are (1) to describe the median duration of HC use among HIV-infected OC and DMPA users through a) first method-specific discontinuation and b) discontinuation of a highly effective method and (2) to examine factors associated with discontinuation of HC among HIV-infected OC and DMPA users.

Methods

We analyzed data from a prospective study of HC use among women who became HIV-infected while participating in the *Hormonal Contraception and Risk of HIV Acquisition (HC-HIV) Study* and a subsequent study of contraceptive use among HIV-infected women

(*Hormonal Contraception and HIV-1 Genital Shedding and Disease Progression (GS) Study*) conducted from 2001 to 2009. Study procedures have been described previously[29]. Briefly, we recruited 86 Ugandan and 145 Zimbabwean (n=231) HIV-infected women ages 18 to 45 years who used either DMPA (150 mg administered quarterly), OCs (low-dose pills containing 30 mcg ethinyl estradiol and 150 mcg of levonorgestrel), or no hormonal method. Women were ineligible if they had an abortion or miscarriage in the 10 days prior to screening or if they had undergone hysterectomy. The institutional review boards of collaborating institutions in the United States, Uganda and Zimbabwe approved the study. All women provided written informed consent prior to study participation.

We conducted follow-up visits at 4, 8, and 12 weeks after enrollment and at 12-week intervals thereafter. At each study visit, women were interviewed about their contraceptive use, sexual behavior and reproductive health. We provided contraceptive, HIV risk reduction, and condom use counseling and free contraceptives and condoms. Each study visit also included physical examinations, pregnancy and reproductive tract infections (RTIs) testing as previously described[30]. We treated participants on-site for vaginal infections and recalled women diagnosed with asymptomatic chlamydia, gonorrhea, or syphilis for treatment. Beginning in 2003, we offered HAART and trimethoprim–sulfamethoxazole to women who developed severe symptoms of HIV infection (WHO clinical stage 4 or severe stage 3) or who within a six-month period had two CD4 counts ≤ 200 cells/mm^3, in accordance with national ARV guidelines at the time.

For the analyses of contraceptive discontinuation and risk factors, we analyzed HIV-infected participants with at least one follow-up visit with valid contraceptive use data who (1) used either OCs or DMPA at the start of the GS study or (2) were not using HC at study enrollment but began using it during follow-up. For women using OCs or DMPA at enrollment, the contraceptive start date was the date of their first study visit. For women who began using OCs or DMPA during follow-up, the contraceptive start date was the first visit at which they reported OC or DMPA use. At each study visit, women were asked about contraceptive use since their last visit and reported start and stop dates for any method used. Time to discontinuation was calculated as the number of months from contraceptive start date to date of method discontinuation. For OC users, discontinuation was defined as any gap in the start and stop dates for OC use. For DMPA users, discontinuation was defined as not returning for an injection within 121 days of a woman's last injection.

Our primary endpoint was the number of months from the contraceptive start date to either (1) method-specific contraceptive discontinuation or (2) the last study contact, whichever occurred earlier. A secondary endpoint was defined as the number of months from the contraceptive start date to (1) stopping use of a highly effective method (defined as OC, DMPA, IUD, implants or sterilization) or (2) the last study contact, whichever occurred earlier. For women who became pregnant during follow-up, if the estimated pregnancy date occurred prior to the date of method of discontinuation they were not counted as discontinuing their method and were right censored at the estimated pregnancy date. Women contributed person-time on a method prior to becoming pregnant, but were censored at their estimated pregnancy date because they would no longer eligible to discontinue contraception. Because HAART was not available throughout the entire study period, women who initiated HAART or who underwent hysterectomy were right-censored at the visit of the event.

We calculated the median number of months from contraceptive start date to method-specific discontinuation for all women who used HC during the study period. We compared the probability of discontinuation in OC and DMPA users over time using Kaplan–Meier survival analysis and log-rank tests. We conducted two sensitivity analyses. For the first, the

contraceptive start date was calculated retrospectively going back before enrollment based on contraceptive calendar information obtained at the first study visit. The retrospective start date was not used as the primary contraceptive start date because covariate information between seroconversion and study entry was not available for all women. Because we were interested in understanding HC use after HIV-infection, person-time for women who continuously used OCs or DMPA before HIV infection were truncated at their estimated date of HIV infection. In the second, the analysis population was restricted to women on HC at their first study visit.

We evaluated factors related to OC or DMPA method-specific discontinuation (primary endpoint) using Cox proportional hazards models. Factors significant in bivariate analyses (at alpha ≤ 0.10) were included in full multivariable models and variables were eliminated using backwards selection with an alpha 0.10 cut-off. We decided to include *a priori* the following variables in all multivariable models: country, age and CD4 count. To estimate the effect of time-varying variables (e.g. sexual behaviors, condom use) on method discontinuation, a participant's time was divided into segments corresponding to the periods between study visits[30]. All analyses were conducted using SAS statistical software, version 9.3 (SAS Institute, Cary, NC).

Results

Of 231 enrolled women, 62 (27%) used OCs and 128 (55%) used DMPA at their first study visit. An additional 18 (8%) began OCs and 23 (10%) began DMPA during follow up. DMPA use was more popular than OCs, with 151 (65%) women either using DMPA at baseline or initiating use during follow up (Table 1). Women contributed a total of 1886 visit segments and were followed for a mean of 25 months and a median of 16 months. Over the follow-up period, 151 women discontinued their original method; 41 (18%) OC users and 110 (48%) DMPA users. Twenty (9%) women were censored due to pregnancy and 18 (8%) due to HAART initiation. The cumulative pregnancy rate was higher in Uganda (14.4 per100 person years) than Zimbabwe (7.7 per100 person years). The combined cumulative pregnancy rate was 10.1 per 100 person years[31].

Women in the study were approximately equally distributed among the age groups 19–24, 25–29 and 30+. The majority of women had at least two children (78%) and reported 0–14 sexual acts in a typical month (72%). Among women with partners, self-reported condom use was high but inconsistent; only 60 (26%) women reported always using a condom. Only 16 (7%) reported no condom use due to no partner (Table 1).

HIV-related side effects such as excessive night sweats and loss of appetite or weight were uncommon. Nausea was slightly higher among DMPA than OC users (7% vs 3%). Slightly more OC than DMPA users had a current cervical infection (CT or GC) at baseline (13% vs 9%). CD4 counts in the study population were relatively high at baseline; 125 (54%) had CD4 counts ≥500 cells/mm^3 (Table 1).

Over the eight year study period, OC users continued on their method about twice as long as DMPA users. The median time to discontinuation for OC users was 35 months (95% CI 14, 61) and 19 months (95% CI 14, 24) for DMPA users (Figure 1). However, among women in Uganda the median times to discontinuation for each method were nearly identical; 21 months (95% CI 6, 36) for OC users and 21 months (95% CI 14, 31) for DMPA users. Conversely, in Zimbabwe median DMPA use was 17 months (95% CI 12, 24) while OC discontinuation never reached the median (50^{th}) percentile (Figure 2). Similar trends were seen in sensitivity analyses when the duration of contraceptive use included time before enrollment (36 months for OCs; 21 months for DMPA) and likewise, when the analysis

population was restricted to women on HC at study enrollment (36 months for OCs; 16 months for DMPA). Within the first year of use, discontinuation did not vary by method (36% of OC users and 37% of DMPA users).

At the time of discontinuation, women were asked the main reason for not continuing use of their current method. Of five possible answers, other non-medical reasons (such as no longer having a sexual partner) was the most common (32%), followed by bleeding problems (9%), other side-effects (8%), desires/desired pregnancy (3%) and unintended pregnancy (2%). Bleeding problems were more commonly cited as a reason for discontinuation among DMPA users (11% vs 2% among OC users), whereas 'other' side-effects was more commonly cited among OC users (12% vs 6% for DMPA users). Results were similar for reasons for discontinuation of any highly effective method; with a slightly higher proportion reporting desires/desired pregnancy (3%) and unintended pregnancy (3%).

The median time to discontinuation of any highly effective method was also 36 months (95% CI 26, NA) for OC users and 22 months (95% CI 14, 38) for DMPA users. Compared to the median time to method-specific discontinuation, median use of any highly effective method was shorter for DMPA users in Uganda (16 months; 95% CI 11, 38) and longer for DMPA users in Zimbabwe (32 months; 95% CI 12, 49). We found a significant country by method interaction for the hazard of discontinuation (p-value 0.01), and therefore constructed separate multivariable models for OC and DMPA users.

Among women who discontinued their original method but stayed on a highly effective method, all 12 originally on OCs switched to DMPA at their first visit after discontinuing OCs. Among 26 DMPA users who switched to another highly effective method, 25 (96%) switched to OCs and one woman had tubal ligation. At the visit a woman discontinued her original method, 28 (68%) of OC users and 87 (79%) of DMPA users reported having a primary partner.

In bivariable analyses among OC users, younger age (19–24), never using a condom, no sexual partner, participant behavioral risk (defined as multiple partners, new partner, commercial sex work or had sex with another man in the last 3 months) and having a current cervical infection were associated with an increased hazard of OC discontinuation. Increased coital frequency (15–29 acts) and living in Zimbabwe were protective against OC discontinuation. In multivariable analyses, living in Zimbabwe remained significantly protective against OC discontinuation (HR 0.39; 95% CI 0.18, 0.83), while not having a partner (HR 7.18; 95% CI 3.05, 16.88) remained associated with an increased hazard of discontinuation and current cervical infection (HR 1.99; 95% CI 0.90, 4.41) was marginally associated with increased OC discontinuation (Table 2).

Among DMPA users in bivariable analyses, no sexual partner, nausea, excessive night sweats and loss of appetite or weight were significantly associated with an increased hazard of discontinuation. Having a primary partner spend any nights away from home in the last month and baseline CD4 count 201–499 cells/mm3 were protective against discontinuation. In multivariable analyses, no sexual partner (HR 2.00; 95% CI 1.12, 3.58) and nausea (HR 1.84; 95% CI 1.02, 3.34) were significantly associated with an increased hazard of discontinuation and excessive night sweats (HR 1.80; 95% CI 0.95, 3.40) was marginally associated with increased DMPA discontinuation (Table 3).

Discussion

In this prospective, multi-site cohort study of hormonal contraceptive use among HIV-infected women, overall median time to discontinuation within the eight year study period was relatively long; over 35 months for OC users and 19 months for DMPA users. In

sensitivity analyses, median time to discontinuation did not change dramatically when time on HC between seroconversion and study enrollment was included or when the study population was restricted to women on HC at study enrollment. Many women were enrolled in the study soon after HIV seroconversion, therefore time on HC after seroconversion and before study entry was generally short. In a similar analysis of HC discontinuation among HIV-uninfected women, median duration of use from study entry was the same for DMPA users (19 months) but shorter for OC users (16 months), however participants were only followed for 15–24 months[32]. The median time to discontinuation of any highly effective method was similar; nearly 36 months for OC users and 22 months for DMPA users. Despite the extensive duration of HC use, 65% of women discontinued their original method at some point during follow-up.

While overall OC use was nearly twice as long as DMPA use, the length of time on a method varied by country. Living in Zimbabwe, compared to Uganda, was associated with over a 60% reduction in the hazard of discontinuing OCs. In contrast, among DMPA users, country was not an important factor for time to discontinuation. Historical country-specific programming may explain these observations. In Zimbabwe, family planning programs have traditionally emphasized OC use over DMPA and 41% of currently married Zimbabwean women use OCs[33]. In Uganda women tend to prefer injectables, however fewer women overall use modern contraception and only 14% use injectables[34].

Little research on HC use by HIV-infected women has focused on contraceptive use over an extended time period or included time-varying factors related to contraceptive use[35–37]. By incorporating time-varying factors into our study, including side-effects related to HIV infection and HC use, as well as sexual behavior characteristics, we were able to assess how these factors influence HC discontinuation over time.

Throughout the follow-up period, few HIV-related side effects were associated with increased HC discontinuation. Symptoms suggesting opportunistic infections have previously been inversely associated with HC use[38], however, in our study this was not the case. Consistent with previous work, higher CD4 counts were protective against DMPA discontinuation, although these results were not statistically significant[39]. The reverse was true for OC users; however, due to sparse data the estimates for the association between CD4 count and discontinuation among OC users are imprecise. Women in our analysis were censored at HAART initiation (HAART was not available throughout the study); therefore we cannot assess the impact of HAART use on HC discontinuation. However, our results suggest that pre-HAART initiation, HIV-related symptoms do not contribute significantly to HC discontinuation.

Few non-HIV related side-effects or health conditions were significant predictors of HC discontinuation in our study. Previous work has shown that side effects are often a primary reason for HC discontinuation[37,40]. In a similar analysis among HIV-uninfected women, side-effects including breast tenderness, nausea and bleeding problems (DMPA users) were significantly associated with HC discontinuation[32]. However, in our analysis only nausea was associated with DMPA discontinuation. Having a cervical infection was the only other health condition associated with OC discontinuation. The most commonly reported reason for discontinuation of original method was ‘other non-medical reasons’ (59% among OC users and 22% among DMPA users), suggesting that the decision to switch contraceptive methods may have more to do with preferences unrelated to side-effects.

Consistent with previous studies, not having a partner was strongly associated with discontinuation for both DMPA and OC users[41–43]. However, at the time of original method discontinuation, 86% of OC users and 79% of DMPA users reported having a primary

partner. Such a large proportion of HIV-infected women with sexual partners highlights the importance of HC as an option for managing their reproductive choices.

Among HIV-uninfected women, younger age has been associated with HC discontinuation[32,44]. In our study, younger age (19–24 years) at method start was associated with discontinuation for OC users, although the results were not statistically significant. Age was not associated with DMPA discontinuation. Upon learning they are HIV-infected, many women choose to switch from combined oral contraceptive pills to an injectable contraceptive[8,32,45]. Our results suggest that injectables may be preferable in particular for younger HIV-infected women interested in long-term HC use[46].

Discontinuation of a woman's original method due to pregnancy, intended or unintended, was notably low in our analysis. Other studies have reported parity as being associated with HC use[35,38]. However, neither having two or more children at baseline or breastfeeding during follow-up (for DMPA users) were associated with HC discontinuation. This is likely explained by parity being relatively high among study participants, since most women already had at least two children. Further, while HIV-infected women may continue to desire children, they may choose to have fewer children overall, compared to HIV-uninfected women[10–12].

Our study has several important strengths. We were able to collect extensive information on both clinical and behavioral factors that influence contraceptive use, and had the ability to analyze how these factors changed over an extended period of time. In addition, we evaluated how morbidity associated with HIV infection and disease progression influenced contraceptive use over time. A limitation of our study was the inability to account for multiple contraceptive method switches and only evaluate the median time to first method switch. In addition, because HAART was not available for the entire study women were censored at HAART initiation and therefore we could not evaluate contraceptive use after treatment initiation. Fertility preferences were not included in the multivariable analysis, however at the time of discontinuation only 5% of women reported discontinuing due to intended or unintended pregnancy, suggesting that fertility intention was not a primary reason for HC discontinuation.

Providing safe and effective contraceptive choices for HIV-infected women is critical to prevent unintended pregnancies and reduce vertical HIV transmission. As access to HAART expands and the risk of vertical transmission decreases, HIV-infected women will increasingly need effective contraception to attain their reproductive goals. Our results suggest that HC methods are acceptable and feasible for HIV-infected women to use over longer periods of time, but that women often chose to discontinue a method for a variety of reasons. Providing HIV-infected women with an expanded range of contraceptive choices, including longer-acting reversible methods (e.g., IUDs, implants), is urgently needed. Access to a range of contraceptive options and ongoing contraceptive counseling are essential components of improving HIV-infected women's reproductive control and decreasing HIV transmission.

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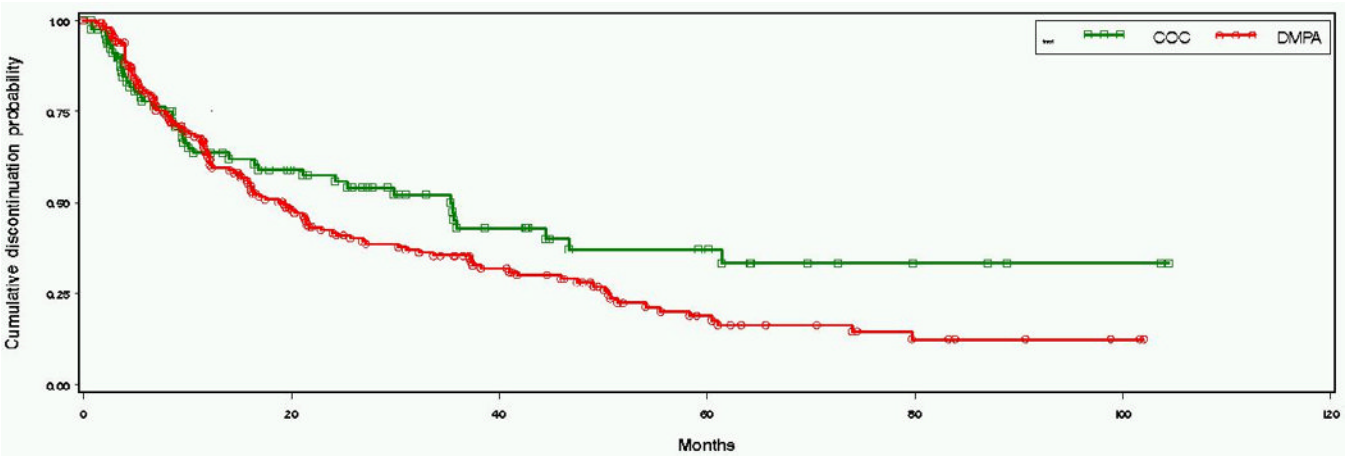

Figure 1. Kaplan-Meier estimation of discontinuation probabilities by contraceptive groups
Log rank test for the distributions of time to discontinuation (p-value): 0.069.

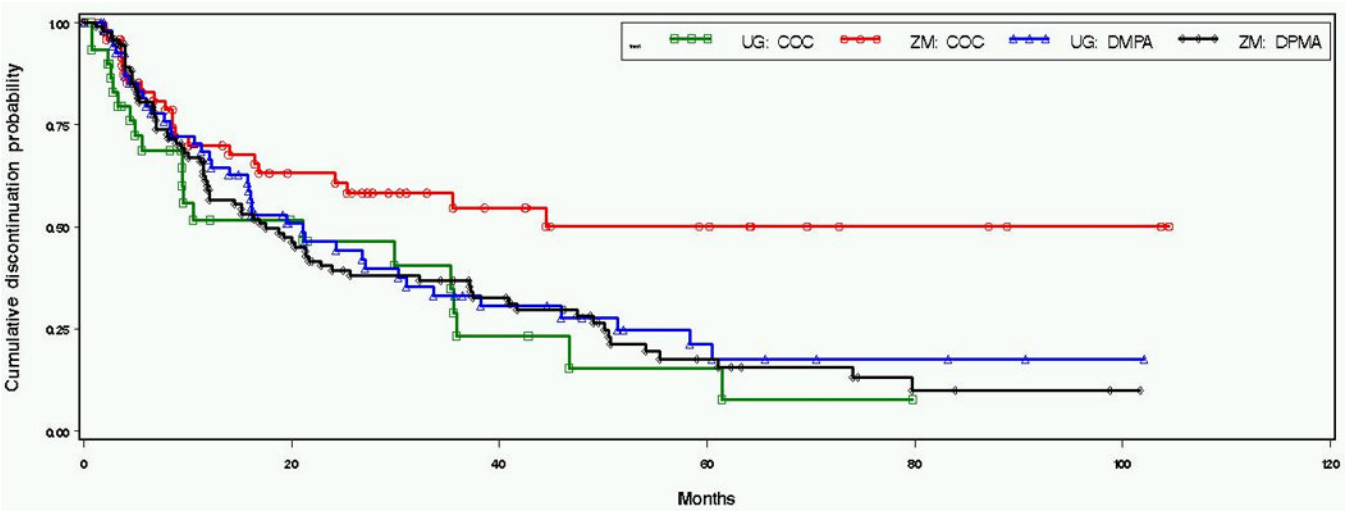

Figure 2. Kaplan-Meier estimation of discontinuation probabilities by contraceptive groups and country

Log rank test for the distributions of time to discontinuation (p-value): 0.021.

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Table 1

Baseline characteristics for OC and DMPA HIV-infected users in Uganda and Zimbabwe

Information on education was collected at the HC-HIV study baseline visit. Participant behavioral risk is defined as: multiple partners, new partner, commercial sex work or had sex with another man in the last 3 months. Missing data includes, primary partner spend any nights away from home in the last 30 day (n=4); current cervical infection (n=7) CD4 count (n=3). Column percentages calculated including missing values.

Characteristic	OC N (%) N =80 (35.0)	DMPA N (%) N =151 (65.0)	Total N(%) N =231
Sociodemographic characteristics			
Uganda	30 (37.5)	56 (37.1)	86 (37.2)
Zimbabwe	50 (62.5)	95 (62.9)	145 (62.8)
Age at method start (years)			
19–24	27 (33.8)	48 (31.8)	75 (32.5)
25–29	29 (36.3)	56 (37.1)	85 (36.8)
30+	24 (30.0)	47 (31.1)	71 (30.7)
Education ≤9 years	40 (50.0)	70 (46.4)	110 (47.6)
Reproductive and sexual health characteristics			
Lifetime live births ≥2	54 (67.5)	125 (82.8)	179 (77.5)
Currently breastfeeding	5 (6.3)	15 (9.9)	20 (8.7)
Coital Frequency (typical month in last 3 months)			
0–14 acts	55 (68.8)	111 (73.5)	166 (71.9)
15–29 acts	21 (26.3)	33 (21.9)	54 (23.4)
30+ acts	4 (5.0)	7 (4.6)	11 (4.8)
Condom use (typical month in last 3 months)			
Always	22 (27.5)	38 (25.2)	60 (26.0)
Sometimes	22 (27.5)	44 (29.1)	66 (28.6)
Never	31 (38.8)	58 (38.4)	89 (38.5)
No sexual partner	5 (6.3)	11 (7.3)	16 (6.9)
Behavioral Characteristics			
Participant behavioral risk in last 3 months	2 (2.5)	10 (6.6)	12 (5.2)

Characteristic	OC N (%) N =80 (35.0)	DMPA N (%) N =151 (65.0)	Total N(%) N =231
Primary partner spend any nights away from home in the last 30 day	39 (48.8)	75 (49.7)	114 (49.4)
Reported symptoms and conditions			
Nausea	2 (2.5)	10 (6.6)	12 (5.2)
Current cervical infection (CT, GC)	10 (12.5)	13 (8.6)	23 (10.0)
HIV-related symptoms and clinical characteristics			
Excessive night sweats	7 (8.8)	9 (6.0)	16 (6.9)
Loss of appetite or weight	3 (3.8)	10 (6.6)	13 (5.6)
CD4 count			
≤200 cells/mm3	4 (1.3)	4 (2.7)	8 (3.5)
201–499 cells/mm3	32 (40.0)	63 (41.7)	95 (41.1)
≥500 cells/mm3	43 (53.8)	82 (54.3)	125 (54.1)

Table 2

Factors associated with discontinuation of OCs among HIV-infected women in Uganda and Zimbabwe

Additional factors investigated which were not significant in bivariable models include: living with a partner, education, parity, currently breastfeeding, primary partner's HIV status, primary partner spent nights away, alcohol use, severe headaches, nausea, breast tenderness, bleeding between periods, abnormal vaginal discharge, current vaginal infection (TV, BV, Candida, unexplained fever, excessive night sweats, loss of appetite or weight and fatigue that interferes with daily living.

Characteristic	Bivariable HR (95% CI)	p-value	Multivariable HR (95% CI)	p-value
Time-invariant covariates				
Uganda	1.00		1.00	
Zimbabwe	0.48 (0.26, 0.84)	0.01	0.39 (0.18, 0.83)	0.01
Age at method start (years)				
30+	1.00		1.00	
25–29	0.96 (0.44, 2.10)	0.92	0.98 (0.45, 2.10)	0.95
19–24	2.00 (0.96, 4.14)	0.06	1.72 (0.74, 4.01)	0.21
Time-varying covariates				
Coital Frequency (typical month in last 3 months)				
0–14 acts	1.00		N/A	
15–29 acts	0.48 (0.20, 1.16)	0.10	N/A	
30+ acts	0.67 (0.15, 2.97)	0.60	N/A	
Condom use (typical month in last 3 months)				
Always	1.00		1.00	
Sometimes	1.32 (0.36, 4.83)	0.67	1.03 (0.28, 3.79)	0.97
Never	2.43 (1.01, 5.85)	0.05	1.26 (0.51, 3.12)	0.62
No sexual partner	7.02 (2.94, 16.78)	<0.01	7.18 (3.05, 16.88)	<0.01
Participant behavioral risk in last 3 months	5.81 (1.18, 28.53)	0.03	N/A	
Current cervical infection (GC or CT)	2.01 (0.87, 4.66)	0.10	1.99 (0.90, 4.41)	0.09
CD4 count				
≤200 cells/mm^3	1.00		1.00	
201–499 cells/mm^3	0.68 (0.21, 2.21)	0.52	1.22 (0.30, 4.95)	0.78
≥500 cells/mm^3	1.45 (0.49, 4.29)	0.50	1.54 (0.45, 5.33)	0.49

Table 3

Factors associated with discontinuation of DMPA among HIV-infected women in Uganda and Zimbabwe

Additional factors investigated which were not significant in bivariable models include: living with a partner, education, parity, participant's behavioral risk, primary partner's HIV status, alcohol use, coital frequency, severe headaches, breast tenderness, bleeding between periods, abnormal vaginal discharge, current vaginal infection (TV, BV, Candida), current cervical infection (CT or GC), unexplained fever and fatigue that interferes with daily living.

Characteristic	Bivariable HR (95% CI)	p-value	Multivariable HR (95% CI)	p-value
Time-invariant covariates				
Uganda	1.00		1.00	
Zimbabwe	1.10 (0.75, 1.63)	0.63	0.85 (0.54, 1.34)	0.49
Age at method start (years)				
30+	1.00		1.00	
25–29	1.08 (0.66, 1.75)	0.77	1.17 (0.71, 1.92)	0.53
19–24	1.05 (0.63, 1.75)	0.85	1.03 (0.60, 1.75)	0.93
Time-varying covariates				
Condom use (typical month in last 3 months)				
Always	1.00		1.00	
Sometimes	0.89 (0.49, 1.63)	0.71	0.86 (0.45, 1.65)	0.65
Never	0.76 (0.46, 1.24)	0.26	0.68 (0.38, 1.21)	0.18
No sexual partner	2.24 (1.22, 4.11)	<0.01	2.00 (1.12, 3.58)	0.02
Primary partner spend any nights away from home in the last 30	0.72 (0.48, 1.07)	0.10	N/A	
Nausea	1.94 (1.05, 3.59)	0.04	1.84 (1.02, 3.34)	0.04
Excessive night sweats	2.08 (1.11, 3.90)	0.02	1.80 (0.95, 3.40)	0.07
Loss of appetite or weight	1.89 (0.96, 3.71)	0.06	N/A	
CD4 count				
≤200 cells/mm3	1.00		1.00	
201–499 cells/mm3	0.52 (0.24, 1.11)	0.09	0.58 (0.27, 1.24)	0.16
≥500 cells/mm3	0.57 (0.26, 1.21)	0.14	0.72 (0.33, 1.54)	0.39