

Original Research Article

Is long-acting reversible contraceptive method use associated with HIV testing frequency in KwaZulu-Natal, South Africa and Lusaka, Zambia? Findings from the CUBE study

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ABSTRACT

Objectives: To assess differences in HIV testing at 6-months intervals over 24 months among intramuscular depot medroxyprogesterone acetate (DMPA-IM) injectable, levonorgestrel implant, or copper intrauterine devices (IUD) users in KwaZulu-Natal, South Africa, and Lusaka, Zambia. Testing at recommended intervals has not been previously assessed in long-acting reversible contraceptive (LARC) users (implant and IUD users) compared to those using effective but shorter-acting methods (such as DMPA-IM) in sub-Saharan Africa.

Study design: As part of the longitudinal contraceptive use beyond ECHO (CUBE) study, we measured HIV testing over 24 months. Participants were considered continuous users of DMPA-IM, levonorgestrel implant, or copper IUD if they used the same method across all months of their study participation, or not continuous users of their baseline CUBE method if they switched or discontinued their method. We used multivariable logistic regression models with generalized estimating equations and robust standard errors, stratified by country, to assess differences in HIV testing.

Results: Among the 498 participants, HIV testing rates were higher in Zambia for all methods compared to South Africa. In bivariate analyses, continuous implant or IUD users (the LARC users) were significantly less likely to report having received HIV testing at the 6-months and 24-months surveys, compared to continuous DMPA-IM users. In adjusted longitudinal models, continuous IUD users (adjusted odds ratio: 0.42, 95% CI: 0.24, 0.74), continuous implant users (adjusted odds ratio: 0.23, 95% CI: 0.12, 0.42) in South Africa had significantly lower odds of HIV testing compared to continuous DMPA-IM users. There were no significant differences in Zambia in the adjusted models.

Conclusion: LARC use may reduce opportunities for HIV testing and users should be counseled on regular HIV testing and the option of HIV self-testing.

Implications: Due to infrequent clinical contacts which may lead to lower rates of HIV testing at recommended intervals, LARC users should be provided opportunities to test for HIV at home or when seeking other health services.

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1. Introduction

The availability of long-acting reversible contraceptives (LARC), including contraceptive implants and intrauterine devices (IUDs), can increase method choice, reducing the unmet need for contra-

ception [1–4]. Global data has indicated a steady increase in LARC use in sub-Saharan African (SSA) countries over the last 10 years, although use remains fairly low overall [5].

Countries in SSA bear an unequal burden of HIV, accounting for 55% of all people living with HIV (PLHIV) in 2020 [6]. South Africa has one of the highest HIV prevalence rates in SSA among those aged 15 to 49 years (20.6%), with a higher prevalence in women (26.3%) compared to men (14.8%) [7]. Zambia has a lower HIV prevalence: 11.1% of the population aged 15 to 49 years living

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with HIV [8]. However, similar gender disparities exist in Zambia, with three times the rate of young women aged 15 to 24 living with HIV (11.9%) compared to young men (3.7%) [8].

Across SSA, knowledge of one's own HIV status has increased from 5.7% in 2000 to 84% in 2020 [9]. National surveys show significant increases in HIV testing rates in South Africa over the last 20 years [7,10–12]. In a 2017 national HIV survey, 79.3% of female respondents had been tested at least once in their lives [7]. Statistics from Zambia also show that HIV testing increased between 2007 and 2018, from 45% to 92% among pregnant women, and 10% to 58% among nonpregnant women [13].

LARC use relieves the burden on women to make frequent clinic visits for method resupply, however, the impact of fewer contraceptive clinical contacts on HIV testing at recommended intervals has not been assessed in SSA, especially in countries with high HIV prevalence. Cross-sectional survey data from 2011 to 2015 United States National Survey of Family Growth assessed sexually transmitted infection (STI) and HIV service receipt or uptake among a range of contraceptive users and nonusers aged 15 to 24 years [14]. There were no differences in any STI testing service receipt between LARC users and moderately effective (oral contraceptive pills, injectable contraception, patch, and ring), or less effective method users (condoms, diaphragm, and withdrawal); however, continuing LARC users were significantly less likely to be tested for HIV than those using moderately effective methods [14].

The South African Department of Health guidelines recommends HIV testing be offered to all clients every 6 to 12-months [15], particularly for high-risk groups such as adolescent girls and young women. In Zambia, healthcare workers are mandated to offer HIV testing services to all individuals presenting to health facilities at every clinical visit or point of contact [16]. Therefore, it is important to understand if the recent gains in regular HIV testing frequency could be impacted by the increasing availability of LARCs in moderate to high HIV prevalence settings. The goal of this analysis was to better understand HIV testing dynamics among users of LARC compared to non-LARC users over time. To investigate this association, we compared HIV testing at any 6-months interval over 24 months among a sample of women using three different contraceptive methods (DMPA-IM, levonorgestrel (LNG) implant, and copper IUD) at study baseline in South Africa and Zambia.

2. Methods

2.1. Study population and sample

The data for this analysis come from the contraceptive use beyond ECHO (CUBE) study, a 24-months longitudinal study examining contraceptive continuation and discontinuation patterns following their exit from the evidence for contraceptive options and HIV Outcomes (ECHO) Trial [17]. Women were recruited from three sites: two in the KwaZulu-Natal Province in South Africa and one in Lusaka, Zambia. Women were recruited through phone calls to ECHO participants who had already had their exit visit.

CUBE study design and eligibility have been described previously [18], but specifically, women had to be using one of the ECHO study methods (DMPA-IM, LNG implant (Jadelle), or the copper IUD) at ECHO exit to participate in CUBE. Of the 688 women contacted to participate, 674 were eligible, consented, and completed the first survey. Participants completed four surveys (one every 6-months) over 24 months between 2018 and 2021, in which they reported contraceptive method use and HIV testing over the previous six months. The study was approved by FHI 360's Protection of Human Subjects Committee, the University of the Witwatersrand Human Research Ethics Committee (HREC), the University

of North Carolina at Chapel Hill Institutional Review Board, and the University of Zambia Biomedical Research Ethics Committee.

2.2. Measures

The primary outcome of this analysis was HIV testing at 6-months intervals over 24 months. In the first CUBE survey, respondents were asked if they had undergone HIV testing since ECHO exit. Then, in the subsequent three CUBE surveys, they were asked if they had undergone HIV testing since the previous survey. The main independent variable was contraceptive method use. To reduce confounding in the outcome due to varying contraceptive use over the survey periods, respondents were categorized as continuous DMPA-IM users, continuous LNG implant users, continuous copper IUD users, and not continuous users of the baseline CUBE method. The few DMPA-IM users who switched to using a 2-months injectable, but had no interruptions in injectable use, were included in continuous DMPA-IM users for ease of categorization. Continuous users were defined as respondents who reported continued method use every month over their enrollment in the study, with no discontinuation or switching. Those who were not continuous users of their baseline CUBE method were those who switched from the method they were using at CUBE enrollment at any point or discontinued all contraceptive use and were using no contraceptive method. We included sociodemographic and relationship variables hypothesized a priori to confound the relationship between the contraceptive method used and HIV testing. These included baseline age, highest education level completed, parity, travel time to the ECHO clinic (as a proxy for distance traveled to obtain health care services), employment status, partner status, and whether the respondent had sex in the last 3 months.

2.3. Analysis

Research staff entered responses into password-protected data collection forms in an online REDCap database [19]. We linked each woman's CUBE record to her ECHO study data to describe the overall characteristics of the sample and obtain HIV status, which was ascertained in ECHO. For all analyses, we excluded those participants who were HIV-positive at the end of ECHO ($n = 21$). For the main analysis, we also excluded 155 respondents who reported taking PrEP currently or at any time since their previous CUBE survey, since PrEP users undergo HIV testing to initiate PrEP use and then every 3-months, potentially confounding HIV testing responses. The final analytic sample was 498 respondents, 261 in South Africa and 237 in Zambia.

We described the baseline characteristics of the respondents, overall and by country, and used chi-square tests and paired t -tests to test for differences in proportions and means, respectively. To test for differences in HIV testing over 2-years, we used generalized estimating equations with logit link and robust standard errors for repeated measures analysis and to account for within-respondent correlation over time. We examined bivariate associations and then added the potential confounders. In all models, we stratified the analyses by country (South Africa vs Zambia) due to the differences in HIV prevalence and country-specific HIV-testing recommendations. In order to test the robustness of the results, we also conducted sensitivity analyses, assessing any bivariate differences in sociodemographic characteristics between DMPA-IM, implant, and IUD users at baseline and sociodemographic characteristics, contraceptive patterns, and HIV testing between excluded PrEP users and the analysis sample in South Africa. All analyses were conducted in Stata version 15.1.

Table 1
Characteristics of analysis sample at study baseline, South Africa and Zambia CUBE study sites, 2018 to 2021 (n,%)

	South Africa (n = 261)	Zambia (n = 237)	Total (n = 498)
Age at CUBE enrollment (mean, SD) ^a	25.7 (3.8)	27.4 (4.7)	26.5 (4.3)
19–24	133 (51.0)	80 (33.8)	213 (42.8)
25–30	100 (38.3)	97 (40.9)	197 (39.6)
31–38	28 (10.7)	60 (25.3)	88 (17.7)
Level of education ^b			
No schooling	0 (0.0)	14 (5.9)	14 (2.8)
Primary school	0 (0.0)	91 (38.4)	91 (18.3)
Secondary school, not complete	81 (31.0)	93 (39.2)	174 (34.9)
Secondary school, complete	117 (44.8)	32 (13.5)	149 (29.9)
Attended post-secondary school	63 (24.1)	7 (3.0)	70 (14.1)
Parity (mean, SD) ^b	1.2 (0.9)	2.6 (1.3)	1.8 (1.3)
Distance from home to ECHO clinic ^b			
Less than 30 min	120 (46.0)	20 (8.4)	140 (28.1)
30–60 min	132 (50.6)	154 (65.0)	286 (57.4)
>1 h	9 (3.4)	63 (26.6)	72 (14.5)
Employment status ^c			
Homemaker/Unemployed/Other	116 (44.4)	172 (72.6)	288 (57.8)
Student	74 (28.4)	4 (1.7)	78 (15.7)
Part or full-time employment	71 (27.2)	61 (25.7)	132 (26.5)
Partner status ^c			
Living together (married/unmarried)	15 (5.7)	203 (85.7)	218 (43.8)
Not living together (married/unmarried)	232 (88.9)	32 (13.5)	264 (53.0)
No current partner*	14 (5.4)	2 (0.8)	16 (3.2)
Sex in last 3-mon ^{c**}	240 (92.0)	229 (96.6)	469 (94.2)
Wants another child in future ^c			
Yes	203 (77.8)	197 (83.1)	400 (80.3)
No	36 (13.8)	12 (5.1)	48 (9.6)
Undecided/No response	22 (8.4)	28 (11.8)	50 (10.0)
Any previous contraceptive use (before ECHO) ^b	251 (96.2)	211 (89.0)	462 (92.8)
Contraceptive method at ECHO exit/CUBE enrollment			
3-mo injectable (DMPA)	106 (40.6)	95 (40.1)	201 (40.4)
Copper IUD	75 (28.7)	56 (23.6)	131 (26.3)
LNG implant (Jadelle)	80 (30.7)	86 (36.3)	166 (33.3)
Contraceptive method continuation			
Continuous use of DMPA	59 (22.6)	45 (19.0)	104 (20.9)
Continuous use of IUD	61 (23.4)	37 (15.6)	98 (19.7)
Continuous use of implant	57 (21.8)	58 (24.5)	115 (23.1)
Not continuous use of baseline method	84 (32.2)	97 (40.9)	181 (36.3)

^aCalculated based on age at ECHO enrollment and date of CUBE enrollment;^bCollected at ECHO enrollment;^cCollected at CUBE 6-month survey; *Includes widowed/separated/divorced; **1 “no response” in South Africa;^dCollected during ECHO participation.

3. Results

Overall, participants in South Africa were younger than participants in Zambia, had achieved more education, had lower mean parity, had to travel a shorter distance to reach the ECHO clinic, were more likely to be students and were less likely to be homemakers or unemployed (Table 1). They were also more likely to report not currently living with their partner than respondents in Zambia, less likely to want a child in the future, and more likely to have used contraception before enrolling in ECHO. In South Africa, there were no significant demographic differences by method use at baseline, and in Zambia, those using IUDs at baseline had a significantly higher number of children (2.9 vs 2.3 among DMPA users and 2.6 among implant users) and were also significantly more likely to report not wanting to have another child in the future (12.5%), compared with 2.1% of DMPA users and 3.5% of implant users. The only sociodemographic difference between excluded South African PrEP users and the South African analysis sample was that PrEP users were significantly less likely to report wanting a child in the future (69.7%) compared to the those in analysis sample (77.8%).

In bivariate analyses, there were significant differences in HIV testing rates by method across the survey waves. In the 6-months survey, continuous IUD or implant users were significantly less likely to report having undergone HIV testing (IUD: 68.3%; implant:

71.5%) than continuous DMPA-IM users (86.2%). While this pattern was attenuated in the 12- and 18-months surveys, it reappeared in the 24-months survey (IUD: 73.1% and implant: 77.3% vs DMPA-IM: 93.2%). Reported rates of HIV testing were generally lower in South Africa than in Zambia across all survey waves and methods (Fig. 1), with testing rates at each 6-months interval in South Africa ranging from 57.8% to 91.1%, depending on the contraceptive method and survey. Continuous DMPA-IM users were more likely to report HIV testing than those using other methods in both countries and across all survey intervals. When the testing frame was expanded to the previous 12 months, there were no significant bivariate differences in testing by the method in South Africa at the 12-months survey (DMPA: 95.5%, IUD: 85.3%, implant: 81.3%) or the 18-months survey (DMPA: 96.4%, IUD: 94.8%, implant: 83.9%). However, there were significant differences in testing by method over the previous 12 months at the 24-months survey (DMPA: 95.8%, IUD: 94.7%, implant: 77.4%).

In sensitivity analyses, there were no differences in the categories of method use between South African PrEP users and the South African analysis sample, but PrEP users were significantly more likely to report HIV testing at 6 months (78.7%) and 12 months (85.3%) than the analysis sample (66.3% and 75.8%, respectively). While there were no differences in HIV testing rates for DMPA-IM users between South African PrEP users and the analysis sample at any point, PrEP users using LARC had a significantly

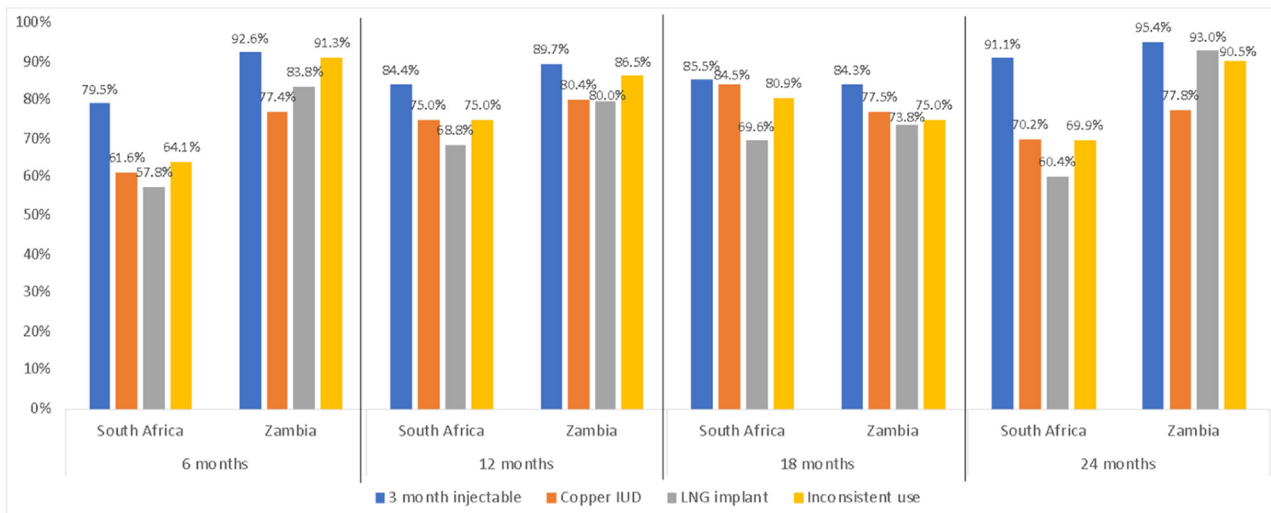


Fig. 1. HIV testing rates, by method, survey, and country.

higher rate of HIV testing at 6 months (but not any other time point) (81%) compared to South African LARC users not using PrEP (59.7%).

Among the women who completed all 4 surveys, the proportion of those who tested at least twice over the 24-month study period was slightly higher in Zambia (95.2%, $n = 231$) compared to South Africa (88.6%, $n = 202$). This significantly varied by the method in South Africa (DMPA: 97.9%, IUD: 87.7%, implant: 79.3%), but not in Zambia. In Zambia, zero women reported never testing across the four surveys, while in South Africa 4.8% ($n = 11$) reported never testing.

In the unadjusted longitudinal analysis, South African respondents who were continuous IUD or implant users or not continuous users of their baseline CUBE method had significantly lower odds of reporting HIV testing at any 6-months interval compared to continuous DMPA-IM users (Table 2). After adjusting for sociodemographic and other characteristics, this pattern persisted for IUD and implant users. Continuous IUD users had almost two-thirds lower odds of HIV testing than DMPA-IM users (adjusted odds ratio : 0.42, 95% confidence interval (CI): 0.24, 0.74), while continuous implant users had around one-fifth of the odds of HIV testing (adjusted odds ratio: 0.23, 95% CI: 0.12, 0.42). While the Zambia results trended in a similar direction, they did not achieve statistical significance.

4. Discussion

In this sample, we find evidence that continuous LARC users, especially in the high HIV prevalence setting of South Africa, had lower HIV testing than DMPA-IM users over four 6-months intervals over 24 months. This finding may be a direct result of a reduced need for clinic attendance for repeat method administration among LARC users. The 2019 Ideal Clinic initiative in South Africa promotes HIV testing using an integrated service approach [20], and this may have resulted in more participants being offered an HIV test when they returned for contraceptive resupply, such as for continuous DMPA-IM users. While one of the key benefits of LARC is extended length of use without the need for re-supply [21], additional HIV and other STI prevention counseling for women who desire and initiate LARC methods in high HIV prevalence settings tailored to each woman's unique situation may be needed.

The relationship between LARC versus DMPA-IM use and HIV testing in Zambia was not significantly different at any of the 6-months intervals, although there was a trend towards higher test-

ing rates among DMPA users, with the highest testing seen in this group across all four time points. As per Zambian policy [16], HIV testing must be offered at every clinical contact, and therefore, the frequency of DMPA re-injection visits may result in higher testing rates than among the LARC users.

The testing rates at each 6-months interval in South Africa are in line with 2017 to 2018 national survey data on HIV testing among young South African women [7,22]. Although testing rates in this study were lower in South Africa, most women were testing per the country's six to twelve monthly testing recommendations [15]. The higher Zambia HIV testing rates of 73.8% to 95.4% across the survey intervals were also in line with those reported in its national surveys [8]. One strategy to increase HIV testing rates among LARC users could be to make HIV self-testing kits available for women to use between clinic visits. South Africa has a comprehensive HIV self-testing policy [23], while the Zambia Consolidated Guidelines for Treatment and Prevention of HIV Infection 2020 [16] only promotes HIV self-testing as a strategy in key populations. This recommendation could be expanded to include LARC users.

The interrelationship between HIV and unintended pregnancy particularly underpins their need for integration [24–27]. However, the increasing uptake of LARC, which provides highly effective pregnancy prevention but not protection against STIs and HIV, also strongly supports the argument for integrated family planning and HIV prevention services. Clients who view HIV testing as part of routine care (for example, in provider-initiated prenatal screening), maybe more comfortable requesting HIV tests in future visits [28–29].

More counseling on HIV testing is not a novel recommendation, but a possible outcome of growing LARC use in high HIV-prevalence settings may be a reduction in regular HIV testing. For people using shorter-acting methods, returning to a facility is routine, and those visits can be more easily coupled with HIV testing without as much stigma. Therefore, we would not propose a decoupling of contraceptive care from HIV screening, but rather underscore the need for integration of HIV testing into all areas of health care, especially for LARC users returning to facilities for other non-contraceptive health services. Providers should highlight the importance of regular HIV testing to LARC users at the time of IUD and implant insertion, especially in areas of high HIV prevalence, and be aware that LARC clients may not have undergone HIV testing recently.

Table 2

Associations between continuous contraceptive use and HIV testing at any 6-month interval over 24 months, South Africa and Zambia CUBE study sites, 2018 to 2021

	South Africa (n = 261)		Zambia (n = 237)	
	Unadjusted OR	Adjusted OR	Unadjusted OR	Adjusted OR
Contraceptive use (ref: Continuous DMPA use)				
Continuous IUD use	0.44 (0.25, 0.78)	0.42 (0.24, 0.74)	0.52 (0.24, 1.12)	0.56 (0.25, 1.25)
Continuous implant use	0.27 (0.15, 0.48)	0.23 (0.12, 0.42)	0.58 (0.28, 1.20)	0.64 (0.31, 1.34)
Not continuous users of baseline method	0.51 (0.28, 0.94)	0.58 (0.31, 1.09)	0.66 (0.33, 1.36)	0.76 (0.36, 1.61)
Age (ref: 19–24)				
25–30	0.79 (0.54, 1.17)	–	0.72 (0.41, 1.27)	–
31–38	0.81 (0.42, 1.56)	–	0.80 (0.42, 1.52)	–
Highest education (ref: Secondary school, not completed)				
No schooling	–	–	0.53 (0.20, 1.43)	–
Primary	–	–	0.60 (0.35, 1.03)	–
Secondary school, complete	1.05 (0.67, 1.63)	–	0.70 (0.32, 1.51)	–
Attended postsecondary school	0.95 (0.57, 1.59)	–	0.40 (0.07, 2.23)	–
Live births (ref: 1)				
0	0.90 (0.57, 1.42)	–	–	–
2+	0.92 (0.60, 1.42)	–	0.71 (0.39, 1.30)	–
Travel time to ECHO clinic (ref: Less than 30 min)				
30–60 min	0.86 (0.59, 1.27)	–	0.57 (0.21, 1.56)	–
>60 min	0.68 (0.32, 1.46)	–	0.79 (0.27, 2.32)	–
Employment status (ref: Housewife/Unemployed/Other)				
Student	1.09 (0.73, 1.63)	–	4.72 (0.18, 126.87)	–
Part or full-time employment	0.85 (0.59, 1.23)	–	0.79 (0.48, 1.32)	–
Partner status (ref: Living together)				
Not living together	1.45 (0.79, 2.68)	–	0.94 (0.48, 1.81)	–
No current partner	0.90 (0.37, 2.24)	–	–	–
Sex in last 3-mo (ref: No)	1.55 (0.91, 2.64)	–	1.05 (0.41, 2.69)	–
Wants another child in future (ref: No)				
Yes	1.19 (0.74, 1.89)	–	0.97 (0.22, 4.36)	–
Undecided/No response	1.82 (0.82, 4.04)	–	1.08 (0.22, 5.36)	–
Time (6-mo intervals)	1.03 (1.00, 1.05)	–	1.00 (0.97, 1.02)	–

Unadjusted and adjusted odds ratios and 95% confidence intervals from multivariable logistic regression analyses that adjusted for age, education, live births, travel time to clinic, employment status, partner status, sex in last 3 months, intention for future children, and time. Unadjusted odds ratios are based on 261 women who contributed 830 observations in South Africa and 237 women who contributed 785 observations in Zambia. Adjusted odds ratios are based on 260 women who contributed 829 observations in South Africa and 237 women who contributed 775 observations in Zambia.

This was a secondary analysis conducted upon completion of data collection and so specific questions related to why participants may or may not have tested for HIV were not asked. Another important limitation of this analysis is that some of the 18- and 24-months surveys were carried out during the COVID-19 pandemic, which may have affected HIV testing access. However, we do not have a reason to believe that LARC and DMPA users would have been differentially affected. This also is a unique sample who had participated in the ECHO study and received targeted HIV prevention counseling every 3-months during their participation in the study; however, testing rates appear to be in line with national estimates. Other limitations are some differences in sociodemographic characteristics at baseline which may result in over or understating differences in testing between the groups. In addition, there was a higher loss-to-follow-up rate in South Africa than in Zambia by the 24-months survey, particularly among those who were continuous DMPA-IM and those who were not continuous users of their baseline CUBE method. Yet, because testing rates were higher among DMPA-IM users, we would not expect the differential loss to follow-up to have a demonstrable impact on differences in testing between DMPA-IM and LARC users. There may have been potential measurement bias because of self-reported testing and recall issues. Finally, while significant differences in HIV testing were not detected in Zambia, it may be that due to the high testing rates reported overall, we lacked sufficient sample size to detect variability in testing over the 24-months study period.

In conclusion, LARC use reduces the frequency of contraceptive method clinic visits. Contraceptive methods with more frequent return schedules may trigger increased opportunities to discuss HIV

risk and testing. This is important because routine HIV testing has been found to moderately reduce HIV incidence in a high-risk population [30] and can decrease late HIV diagnosis [31]. LARC users should be reminded about the need for and offered routine HIV testing as per country guidelines and the option of HIV self-testing. Providers should consider the discussion of HIV testing for at-risk patients even when women present for noncontraceptive services.

Conflicts of interest

The authors declare no conflicts of interest.

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