Published in final edited form as:

AIDS. 2009 November ; 23(Suppl 1): S89–S95. doi:10.1097/01.aids.0000363781.50580.03.

Successful increase in contraceptive uptake among Kenyan HIV-1 serodiscordant couples enrolled in an HIV-1 prevention trial

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Abstract

Objective—To evaluate a multi-pronged approach to promote dual contraceptive use by women within heterosexual HIV-1 serodiscordant partnerships.

Methods—For 213 HIV-1 serodiscordant couples in Thika, Kenya participating in an HIV-1 prevention clinical trial, contraceptive promotion was initiated through a multi-pronged intervention that included staff training, couples family planning sessions, and free provision of hormonal contraception on-site. Contraceptive use and pregnancy incidence were compared between two time periods (before versus after June 2007, when the intervention was initiated) and between Thika and other Kenyan trial sites (Eldoret, Kisumu, and Nairobi). Generalized estimating equations and Andersen-Gill proportional hazards modeling were used.

Results—Non-barrier contraceptive use increased after implementation of the intervention: from 31.5% to 64.7% of visits among HIV-1 seropositive women (odds ratio [OR] 4.0, 95% confidence interval [CI] 3.0–5.3) and from 28.6% to 46.7% of visits among HIV-1 seronegative women (OR 2.2, 95% CI 1.4–3.5). In comparison, at the other Kenyan sites, where the intervention was not implemented, contraceptive use changed minimally, from 15.6% to 22.3% of visits for HIV-1 seropositive women and from 13.6% to 12.7% among HIV-1 seronegative women. Self-reported condom use remained high during follow-up. Pregnancy incidence at the Thika was significantly lower after compared with before June 2007 (hazard ratio [HR] 0.2, 95% CI 0.1–0.6), and was approximately half that at other Kenyan sites during the intervention period (HR 0.5, 95% CI 0.3–0.8).

Conclusions—A multi-pronged family planning intervention can lead to high non-barrier contraceptive uptake and reduced pregnancy incidence among women in HIV-1 serodiscordant partnerships.

Keywords

Africa; contraception; pregnancy; HIV-1 serodiscordant couples

Introduction

Sub-Saharan Africa has the highest prevalence and incidence of HIV-1 infection in the world [1,2], and the region also has high fertility rates, with approximately 14 million pregnancies annually considered unintended [3]. As an example, in Kenya, HIV-1 seroprevalence is 7.1%, 60% of HIV-1 infected adults are women, the total fertility rate is 4.7 births per woman, and it has been estimated that there is a 25% unmet need for family planning among married women [4–6]. Studies in Kenya have reported low contraceptive uptake among HIV-1 seropositive women [7, 8]. For women with or at-risk for HIV-1 infection, dual-contraceptive use (i.e., use of an effective non-condom contraceptive method in conjunction with condoms) is the optimal strategy to prevent both pregnancy and HIV-1 transmission. Moreover, for HIV-1 seropositive women, prevention of unwanted pregnancies through contraceptive use is an important adjunctive, and cost-effective, method to reduce mother-to-child transmission of HIV-1 [6, 9–11]. Unfortunately, family planning and HIV-1 care programs are often not integrated, and few examples of successful programs to increase contraceptive uptake within the context of HIV-1 prevention have been described [8–12]. In addition, few reports have described the importance and opportunity to involve male partners in family planning decision-making.

Recent population surveys and mathematical modeling studies have found that stable HIV-1 serodiscordant couples – i.e., in which one partner is HIV-1 infected and the other is HIV-1 uninfected – may be responsible for a majority of new HIV-1 transmissions in Africa [1]. Thus, HIV-1 serodiscordant couples should be considered a high priority population for both HIV-1 prevention efforts and family planning interventions. Here, we describe a successful multi-pronged intervention to increase contraceptive use among HIV-1 serodiscordant couples enrolled in an HIV-1 prevention trial in Thika, Kenya.

Methods

Population and procedures

The Partners in Prevention HSV/HIV Transmission Study was a phase III, randomized, placebo-controlled, clinical trial of daily acyclovir herpes simplex virus type 2 (HSV-2) suppressive therapy provided to HIV-1 seropositive members within heterosexual HIV-1 serodiscordant couples [13]. The primary aim of the trial was to assess the effect of acyclovir on HIV-1 transmission to the seronegative partners. The trial enrolled participants at 14 African sites in East and southern Africa between December 2004 and May 2007, with individual study sites initiating enrollments in a staged fashion between December 2004 and June 2006. The last study follow-up visits were completed by October 2008. The present study reports on contraceptive use and pregnancy incidence from the Thika, Kenya site, where the supplementary family planning intervention was implemented, and compares findings against composite results from the other three Kenyan study sites (located in

Eldoret, Kisumu, and Nairobi). All Kenyan sites recruited from urban, peri-urban, and rural areas in a radius up to 150 kilometers from the study site.

For the Partners in Prevention HSV/HIV Transmission Study, couples were eligible if they reported 3 episodes of vaginal intercourse during the three months prior to enrollment. HIV-1 seropositive partners were 18 years of age, seropositive for HSV-2, had a CD4 count ≥ 250 cells/mm³ and no history of AIDS-defining conditions, and were not on antiretroviral therapy (ART). HIV-1 infected women who were pregnant at the time of study screening were excluded from enrollment. HIV-1 seronegative partners were 18 years of age.

Study visits occurred monthly for HIV-1 seropositive participants and quarterly for HIV-1 seronegative participants, for a maximum of 24 months (until trial closure). Visits included individual and couple risk reduction counseling, with provision of free male and female condoms. HIV-1 infected women who became pregnant were discontinued from study medication during the pregnancy but remained in the study. HIV-1 infected participants who met national guidelines for initiation of ART during follow-up were referred to local HIV-1 care clinics.

All participants provided written informed consent for study participation. The protocol was approved by institutional review boards at the University of Washington, Kenyatta National Hospital, Kenya Medical Research Institute, and Moi University.

Family planning interventions at the Thika study site

At all study sites, contraceptive methods were offered on site or by referral on voluntary basis as a part of routine clinical care. During its first year of operation (June 2006–May 2007), the Thika site offered injectable depot medroxyprogesterone acetate and oral contraceptive pills free-of-charge at the research clinic, while other methods were offered by referral. In June 2007, site staff instituted a combination of interventions (Table 1) to increase dual contraceptive uptake (i.e., condoms plus another effective contraceptive method) in part to minimize the time off study drug among HIV-1 seropositive female participants, a protocol requirement, and to prevent unplanned pregnancies among both HIV-1 seropositive and seronegative participants. The Kisumu and Eldoret sites did not provide non-condom methods at the research clinic and referred women to nearby medical facilities, whereas the Nairobi site offered injectable depot medroxyprogesterone acetate and oral contraceptive pills free-of-charge at the research clinic.

Statistical analysis

Data were analyzed using SAS version 9.2 (SAS Institute, Cary, NC). Analyses were conducted using data collected at quarterly study visits. The primary study measure was self-reported use of contraception other than condoms, defined as current use of an intrauterine device, surgical method, or injectable, implantable, or oral hormonal methods. Contraceptive use and pregnancy incidence were compared between time periods (before and after June 2007, when the multi-pronged intervention was initiated). Comparisons within the Thika site study population, within the other Kenyan sites, and between Thika and the other Kenyan sites were performed. Use of non-condom contraception over time was analyzed using generalized estimating equations (GEE). Pregnancy incidence was analyzed

via Andersen-Gill proportional hazards modeling, to account for pregnancy as a potential recurrent event. Adjustment for potential confounding by age and number of children did not result in meaningful changes; thus, only unadjusted rates are presented.

Results

Participant characteristics

Between June 2006 and April 2007, the Thika site enrolled 213 HIV-1 serodiscordant couples, including 159 (74.7%) in which the female partner was the HIV-1 seropositive partner. The median age of HIV-1 seropositive and seronegative women was 30.2 (interquartile range [IQR] 26.3–34.0) and 30.9 years (IQR 26.0–37.7), respectively, and 89.3% and 90.8% had at least 1 living child (Table 2). Most women were married to their study partner (91.2% and 94.6%, respectively). Unprotected sex during the month prior to enrollment was reported by 25.2% of HIV-1 seropositive women and 25.9% of HIV-1 seronegative women. The median duration of follow-up was 18 months (IQR 15–24) for HIV-1 seropositive women and 18 months (IQR 18–24) for HIV-1 seronegative women, and HIV-1 seropositive and seronegative women each completed a median of 6 visits (IQR 5–7 and IQR 6–7, respectively). In Thika, 66.9% of visits by HIV-1 seropositive and 68.7% of visits by HIV-1 seronegative women occurred after June 2007.

A total of 1216 couples were enrolled by the other 3 Kenyan sites (Eldoret, Kisumu, and Nairobi) from December 2004 to May 2007. Of these, 832 (68.4%) were couples in which the HIV-1 seropositive was female. Enrollment characteristics, including age, marital status, and frequency of unprotected sex, were similar for female participants from the 3 Kenyan sites compared with participants at the Thika site (data not shown), except that HIV-1 seropositive participants were slightly younger at the other Kenyan sites (median 28.2 years, IQR 24.0–33.0) compared to the Thika site (Mann-Whitney $p=0.002$). Participants from the other Kenyan sites had longer median follow-up (24 months for both HIV-1 seropositive and seronegative women) than participants at the Thika site, reflecting that the Thika site was the last site to initiate the study.

Contraceptive uptake

Between June 2006 and May 2007, HIV-1 seropositive women in Thika used non-condom contraception at 31.5% of visits (117/372), while after June 2007 (i.e., between June 2007 and September 2008), use rose to 64.7% of all visits (486/751) (odds ratio [OR] 4.0, 95% confidence interval [CI] 3.0–5.3) (Figure 1). Among HIV-1 seronegative women in Thika, there was also a significant increase in use of non-condom methods of contraception, from 28.6% of visits (34/119) prior to June 2007 to 46.7% of visits (122/261) after June 2007 (OR 2.2, 95% CI 1.4–3.5). The most common contraceptive method used was injectable methods (reported at 31.7% of visits by HIV-1 seropositive women and 23.2% of visits by HIV-1 seronegative women) followed by oral methods (7.2% and 9.2%, respectively), tubal ligation or other surgical procedure (6.8% and 5.0%), implants (5.8% and 1.3%), and IUDs (2.2% and 2.4%).

In the other Kenyan sites, non-condom contraceptive use did not change substantially in the time periods before and after June 2007. In these sites, among HIV-1 seropositive women, contraceptive use increased from 15.6% (523/3344) to 22.3% (604/2712) of visits (OR 1.5, 95% CI 1.3–1.9), while among HIV-1 seronegative women, used decreased slightly, from 13.6% (187/1373) to 12.7% (176/1389) of visits (OR 0.9, 95% CI 0.7–1.3). Thus, after June 2007, non-condom contraceptive use was substantially higher among HIV-1 seropositive women from Thika (64.7%) compared with the other Kenyan sites (22.3%) (OR 6.4, 95% CI 4.6–8.9). Similarly, after June 2007, non-condom contraceptive use among HIV-1 seronegative women was higher at Thika (46.7%) than at the other at other Kenyan sites (12.7%) (OR 6.0, 95% CI 3.4–10.7).

Reported condom use was high throughout the entire study follow-up period for both HIV-1 seropositive and seronegative women from all sites (87.8% and 91.4% of sex acts, respectively).

Pregnancy Incidence

Among HIV-1 seropositive women in Thika, pregnancy incidence declined after June 2007, from 13.5 to 8.7 per 100 woman-years (7 events in 52 woman-years to 16 events in 183 woman-years, respectively). Among HIV-1 seronegative women in Thika, pregnancy incidence also declined, from 21.1 to 11.0 per 100 woman-years (3 events in 14 woman-years to 7 events in 64 woman-years, respectively). However, at the other Kenyan sites, pregnancy incidence increased during this same time period: from 16.8 to 21.9 per 100 woman-years among HIV-1 seropositive women (101 events in 602 woman-years to 140 events in 640 woman-years, respectively) and from 14.6 to 19.7 per 100 woman-years (34 events in 233 woman-years to 64 events in 326 woman-years, respectively) among HIV-1 seronegative women. Within the Thika study population (i.e., including both HIV-1 seropositive and seronegative women in the analysis), pregnancy incidence was significantly lower after June 2007 compared with before June 2007 (hazard ratio [HR] 0.2, 95% CI 0.1–0.6). In addition, after June 2007, pregnancy incidence was significantly lower at Thika compared with the other Kenyan sites (HR 0.5, 95% CI 0.3–0.8), while there was no statistically significant difference in pregnancy incidence for Thika versus the other sites for the time period before June 2007 (HR 1.0, 95% CI 0.5–1.9).

Discussion

Within the setting of a biomedical HIV-1 prevention trial among Kenyan HIV-1 serodiscordant couples, we implemented a multi-pronged strategy focused on increasing contraceptive uptake. Our efforts substantially increased dual contraceptive use – i.e., use of condoms plus another effective method – among both HIV-1 seropositive and HIV-1 seronegative women in HIV-1 serodiscordant partnerships. Pregnancy incidence declined during this same time period. Given the low utilization of both barrier and non-barrier contraceptive services in many African populations, particularly within stable sexual partnerships, successful initiatives promoting family planning and dual contraceptive use may inform programmatic efforts to prevent unplanned pregnancies and decrease HIV-1 risk.

While our family planning intervention was not randomized, we were able to evaluate the uptake of dual contraceptive methods and pregnancy incidence by a time-series comparison from the Thika site, using data from the year prior to the intervention. In addition, we compared Thika data to that from the other three Kenyan sites that participated in this same clinical trial and which provided 'standard' contraceptive services and referrals to community family planning programs. In both comparisons, we found that dual contraception uptake was substantially higher among both the HIV-1 seropositive and HIV-1 seronegative women in the Thika cohort during the intervention period. Major components of the Thika family planning intervention were provision and enhanced promotion of free contraceptive services at the research clinic and staff training in family planning methods and counseling. Our experience is that both of these components were instrumental in achieving high rates of contraceptive use by study participants. Prior studies have shown that accessibility is an important factor to increase contraceptive use [9], and our results illustrated a potential opportunity to provide contraception in a research clinic which women are attending for other purposes. In addition, many health care workers lack knowledge of effective family planning options, particularly for women with HIV-1 [10,11], and we found that staff training in contraceptive methods and counseling for HIV-1 serodiscordant couples was an essential part of our intervention.

A potentially valuable role for male involvement in family planning provision has been suggested by previous studies [7,14]. We followed both members of HIV-1 serodiscordant couples as part of our clinical trial procedures, and thus were able to integrate male partner participation in contraceptive counseling into routine quarterly study visits. Condom use was high among these HIV-1 serodiscordant couples, for whom counseling of the HIV-1 positive partners was done monthly and counseling of both partners was done quarterly; approximately 90% of sex acts were reported to be protected by condoms.

In addition to a significant increase in contraceptive use for both HIV-1 seropositive and seronegative women during the intervention period at the Thika site, pregnancy incidence was also lower in Thika during the intervention period, both compared to the pre-intervention period and compared to the other Kenyan sites during the intervention period. We did not assess fertility intentions in this cohort and future studies among HIV-1 serodiscordant couples should assess fertility planning and contraceptive decision-making. Interventions to increase contraceptive uptake may benefit from follow-up visits to focus on factors that lead to early discontinuation of dual contraception, including myths, side effects, and changing fertility desires.

In our population, HIV-1 seropositive women had a higher contraceptive uptake compared with HIV-1 seronegative women. There are several possible explanations for this finding. First, HIV-1 seropositive women were seen monthly, while HIV-1 seronegative women were seen quarterly, and thus HIV-1 seropositive women had greater opportunity to discuss family planning intentions, receive counseling about contraceptive options, and identify acceptable contraceptive methods. Second, HIV-1 seropositive women may have had a greater desire to avoid unwanted pregnancies, in order to prevent possible HIV-1 transmission to a child. Finally, our clinical trial protocol required discontinuation of study drug for HIV-1

seropositive women who became pregnant, which may have been an incentive for study staff to focus family planning messages more strongly towards HIV-1 seropositive women.

Many HIV-1 prevention clinical trials are currently being conducted among women at-risk for HIV-1 and women in HIV-1 serodiscordant couples in sub-Saharan Africa [15]. Biomedical prevention trials, such as those testing oral antiretroviral medications and candidate vaginal microbicides, frequently require that women who become pregnant during follow-up be removed from the investigational product or discontinued from the study [16]. High numbers of pregnancies can result in a substantial proportion of study follow-up being unexposed to study product, thereby reducing the statistical power for the trial to demonstrate efficacy. Our results are particularly relevant to clinical trial populations, where periodic study visits can permit opportunities for ongoing counseling regarding family planning options.

Strengths of this study include the relatively large sample size, longitudinal follow-up, and inclusion of both HIV-1 seropositive and HIV-1 seronegative women. We were able to compare Thika to the other Kenyan sites, where the same clinical trial procedures were performed during the same time period. A limitation was that our intervention package was comprised of a combination of services and thus it is not possible to evaluate the impact of each separately. Our intervention was conducted within a clinical trial setting, which limits the generalizability of our findings to other family planning and HIV-1 prevention and care programs with fewer resources and less frequent follow-up.

In summary, we found a substantial increase in dual contraceptive uptake, and a concomitant decrease in incident pregnancy, among women in HIV-1 serodiscordant partnerships after an intervention to integrate family planning promotion into a clinical trial setting. Our results suggest that a multi-pronged intervention including training of counselors and clinical staff, counseling sessions that include the male partner, and provision of free contraceptive services on-site, can lead to a significant increase in uptake of contraceptive methods without decreasing condom use. This approach may be able to be adapted from the research clinic setting to HIV-1 service delivery settings.

Acknowledgments

We thank the principal investigators and study coordinators at the Kenyan sites of the Partners in Prevention HSV/HIV Transmission Study for use of site data for this analysis (Drs. Elizabeth Bukusi, Craig Cohen, Carey Farquhar, Kenneth Fife, Grace John-Stewart, James Kiarie, Harrison Tamoo, Edwin Were, and Cosmas Apaka and Josephine Oduyo) for use of their site data. We are grateful to Paul Musingila for assistance with data management.

Funding Source: The Partners in Prevention HSV/HIV Transmission Study was funded by the Bill and Melinda Gates Foundation (grant ID #26469, to the University of Washington).

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Figure 1. Non-condom contraceptive use prevalence by calendar month in Thika and other Kenyan sites, for a) HIV-1 seropositive and b) HIV-1 seronegative women.

Table 1

Multi-pronged approach to increase contraceptive uptake among HIV-1 serodiscordant couples participating in an HIV-1 prevention trial: Thika, Kenya

1	Training of clinical and counseling staff on contraceptive methods, including practical demonstrations and discussions of common myths and barriers to contraceptive use.
2	Provision of free contraceptive methods (oral contraceptive pills, injectables, implants, and intrauterine devices) to study participants at the research clinic.
3	Use of contraceptive appointment cards with clear dates for renewal of the time dependent methods (e.g., injectable depot medroxyprogesterone acetate) to avoid lapses in hormonal contraception.
4	Designation of one staff member to ensure that staff received ongoing training in contraceptive counseling and that sufficient contraceptive supplies were always available on site.
5	Introduction of checklists in chart notes to remind staff to discuss and provide contraceptive methods during study visits.
6	Weekly meetings with clinicians, counselors, and pharmacy staff to share their experiences discussing contraception with study participants.
7	Discussion of challenges to contraceptive uptake with study couples individually and in psychosocial support groups. The insights from these sessions were reported back to the study team to strengthen contraceptive messages for other couples.
8	Involvement of male partners during contraceptive counseling sessions during routine study visits.
9	Review of unintended pregnancies among HIV-1 seropositive women to identify reasons why these pregnancies were not avoided.

Table 2

Baseline characteristics of women enrolled at the Thika study site.

	HIV-1 seropositive (N=159)	HIV-1 seronegative (N=54)
	n (%)	n (%)
Age, years		
18–24	27 (18.2)	11 (20.4)
25–34	89 (60.1)	27 (50.0)
35–44	25 (16.9)	13 (24.1)
45 and older	7 (4.7)	5 (5.6)
Number of children		
0	17 (10.7)	5 (9.3)
1	34 (21.4)	9 (16.7)
2 or more	108 (67.9)	42 (74.1)
Married to study partner	145 (91.2)	53 (94.4)
Unprotected sex with study partner, prior month	40 (25.2)	14 (25.9)