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## HIV Testing and Counseling Leads to Immediate Consistent Condom Use among South African Stable HIV-discordant Couples

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### Abstract

**Introduction**—Effective behavioral HIV prevention is needed for stable HIV-discordant couples at risk for HIV, especially those without access to biomedical prevention. This analysis addressed whether HIV testing and counseling (HTC) with ongoing counseling and condom distribution lead to reduced unprotected sex in HIV-discordant couples.

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**Methods**—Partners in Prevention HSV/HIV Transmission Study was a randomized trial conducted from 2004–2008 assessing whether acyclovir reduced HIV transmission from HSV-2/HIV-1 co-infected persons to HIV-uninfected sex partners. This analysis relied on self-reported behavioral data from 508 HIV-infected South African participants. The exposure was timing of first HTC: 0–7, 8–14, 15–30, or >30 days before baseline. In each exposure group, predicted probabilities of unprotected sex in the last month were calculated at baseline, month one, and month twelve using generalized estimating equations with a logit link and exchangeable correlation matrix.

**Results**—At baseline, participants who knew their HIV status for less time experienced higher predicted probabilities of unprotected sex in the last month: 0–7 days, 0.71; 8–14 days, 0.52; 15–30 days, 0.49; >30 days, 0.26. At month one, once all participants had been aware of being in HIV-discordant relationships for 1 month, predicted probabilities declined: 0–7 days, 0.08; 8–14 days, 0.08; 15–30 days, 0.15; >30 days, 0.14. Lower predicted probabilities were sustained through month twelve: 0–7 days, 0.08; 8–14 days, 0.11; 15–30 days, 0.05; >30 days, 0.19.

**Conclusions**—Unprotected sex declined after HIV-positive diagnosis, and declined further after awareness of HIV-discordance. Identifying HIV-discordant couples for behavioral prevention is important for reducing HIV transmission risk.

### Keywords

HIV; condom; unprotected sex; HIV counseling and testing; discordant couple; South Africa

### Introduction

Within stable HIV-discordant couples, HIV-uninfected partners are at ongoing risk for HIV acquisition<sup>1</sup>. In sub-Saharan Africa, stable HIV-discordant couples account for as few as 14% to as many as 94% of new infections<sup>2–3</sup>. Even if the fraction of new infections is on the lower end of the range, the absolute number of persons acquiring HIV from stable HIV-infected partners is substantial, given an estimated 1.8 million annual infections in sub-Saharan Africa<sup>4</sup>.

Within HIV-discordant couples, antiretroviral therapy taken by HIV-infected partners or pre-exposure prophylaxis taken by HIV-uninfected partners can reduce HIV incidence<sup>5–7</sup>. However, many HIV-infected partners are not eligible for antiretroviral therapy, and pre-exposure prophylaxis is not yet available in most settings.

Behavioral interventions, such as individual and couples HIV testing and counseling (HTC) remain viable approaches to prevention within HIV-discordant couples. Couples HTC is associated with increased condom uptake<sup>8–12</sup>. However, timing of condom uptake is not well understood, nor is whether those who continue engaging in unprotected sex engage in fewer unprotected acts. Although recent World Health Organization guidance recommends couples HTC, it indicates that the quality of evidence is weak, which suggests additional research is needed<sup>13</sup>.

The objective of this analysis is to assess whether HIV-infected persons in stable HIV-discordant couples increase condom uptake after individual or couples HTC and whether this behavior is maintained in the presence of monthly counseling for HIV-infected partners, three-monthly HTC for HIV-uninfected partners, and condom access for both partners. We also assess the impact of HTC on number of sexual acts among persons who continue to engage in unprotected sex. To assess these questions we use behavioral data from South African HIV-discordant couples enrolled in Partners in Prevention HSV/HIV Transmission Study<sup>14</sup>.

## Methods

### Participants

Partners in Prevention HSV/HIV Transmission Study was a randomized placebo controlled trial to assess the impact of acyclovir taken twice daily by HIV-1/HSV-2 coinfecting persons on HIV-1 disease progression<sup>15</sup> and HIV-1 transmission to HIV-1 uninfected sex partners<sup>14</sup>. Couples were followed for up to 24 months from 2004–2008 or until death, drop-out, or site closure. This analysis uses data from 508 HIV-infected participants enrolled in the South African sites: Gugulethu, Orange Farm, and Soweto. Three HIV-infected participants enrolled with two HIV-uninfected partners, but for this analysis, only sexual behavior of the first HIV-uninfected partner is analyzed.

Couples were screened to identify which were HIV-discordant and eligible. HIV-infected participants were eligible if they had CD4  $\geq$  250, no AIDS-defining illness, and were HSV-2 seropositive. Couples who were not in stable relationships (i.e. those who did not expect to remain together  $\geq$  24 months and those with no sexual activity for  $\geq$  3 months) were excluded. Detailed descriptions of recruitment, eligibility, and baseline characteristics are available<sup>14–17</sup>.

### Ethical Approval

The trial was approved by the Human Subjects Review Committee at University of Washington, and ethical review committees at participating sites. This analysis was approved by the Public Health-Nursing Institutional Review Board at University of North Carolina, Chapel Hill.

### Behavioral Interventions

Many HIV-infected participants, especially in Soweto, had learned that they were HIV-positive months before baseline. Some of these participants had initially learned their HIV status through individual HTC and others had learned their HIV status through couples HTC. By baseline all HIV-discordant couples, even those who had been tested previously, had participated in couples HTC, typically in the month before baseline. Couples HTC emphasized the risk for HIV transmission within the couple, as well as risk reduction through abstinence or consistent condom use. Additionally, HIV-infected participants were counseled about HIV risk reduction and provided with free condoms monthly. They were not re-tested for HIV. HIV-uninfected participants received HTC quarterly, typically with the HIV-infected partner, and also had access to free condoms.

### Data collection

Trained research staff collected demographic and sexual behavior information at baseline and monthly follow-up using interviewer-administered questionnaires.

### Factors of Interest and Outcome Assessment

The primary factor of interest was timing of HTC for the HIV-infected participant. At baseline, HIV-infected participants reported the date of their first HIV-positive test. This date was subtracted from the baseline date to determine the number of days since HTC. Some HIV-infected participants had been tested  $>30$  days before baseline (previously tested). Others learned their HIV status  $<30$  days before baseline (newly tested). For some analyses, the newly tested group was further divided into three categories: HTC 7, 8–14, and 15–30 days before baseline. We explored cut-points within the previously tested category, but did not observe meaningful differences if this category was divided at HTC  $>60$  days ( $p=0.7$ ) or  $>365$  days ( $p=0.3$ ).

The primary outcome was unprotected sex self-reported by the HIV-infected participant. At baseline and each month thereafter, HIV-infected participants were first asked the total number of vaginal and anal sex acts they had with their study partner in the last month and, of those acts, the number of times a condom was used. From these responses, numbers of sex acts and unprotected sex acts in the last month were calculated.

At baseline, for previously tested persons (>30 days), all unprotected sex acts must have occurred *after* HTC. For newly tested participants, unprotected sex could have occurred *before* becoming aware of their HIV status or soon after. Persons tested < 7 days before baseline were unaware of their HIV status for most of the month preceding baseline and serve as a proxy for persons unaware of their HIV-positive status. At all subsequent visits, all HIV-infected participants were aware of being HIV-infected and in HIV-discordant relationships for the full month preceding the visit (Figure 1).

We compared the sexual behavior of newly and previously tested persons at baseline and months one, six and twelve. We hypothesized that at baseline the persons tested < 7 days before baseline would have the highest prevalence of unprotected sex and the highest number of unprotected acts, but by month one all groups would be comparable.

### Baseline Analyses

At baseline, the primary comparison of interest was whether HIV-infected participants aware of their HIV status for a fraction of the previous month (< 7 days) reported more sexual risk than HIV-infected participants aware of their HIV status for the entire previous month. This comparison assesses whether learning one's own HIV-positive status through individual or couples HTC is protective. To assess this question a Zero-Inflated Negative Binomial (ZINB) model was implemented. A ZINB model was appropriate because data were over-dispersed and there were a large number of zero counts. By solving two simultaneous equations, ZINB models generate two sets of parameters<sup>18</sup>. The first set, generated using logistic regression, estimates the odds of being in a group that can only get a zero count (i.e. zero unprotected sex acts in the last month). The second set, generated using negative binomial regression, estimates the relative number of unprotected sex acts between the exposed and unexposed, conditional on not being in the first group. To mitigate influence of extreme observations, values >15 sex acts (N=20, median number of acts=25) were truncated.

### Longitudinal Analyses

In longitudinal analysis, the primary comparison of interest was whether there had been a decline in unprotected sex after baseline among those tested <7 days before baseline. At month one, this comparison assessed whether couples HTC was associated with a rapid decline in unprotected sex. At months six and twelve, this comparison assessed whether HTC and ongoing counseling and condom distribution was associated with a sustained decline in unprotected sex. We used generalized estimating equations to assess the effect of HTC timing on sexual behavior at baseline, and months one, six, and twelve among couples remaining HIV-discordant. Logistic models were used in the entire population and negative binomial (NB) models were restricted to persons reporting ≥ 1 unprotected sex act in a given period. In both logistic and NB models, to account for within subject correlation, robust variance estimators with exchangeable correlation matrices were used<sup>19</sup>. We calculated odds ratios (OR), relative numbers of unprotected acts, predicted probabilities of unprotected sex, predicted numbers of unprotected sex acts, and 95% confidence intervals (CI).

Both baseline and longitudinal models were restricted to persons sexually active with their study partners. Analyses were conducted in SAS v.9.2. (SAS Institute, Cary, North Carolina).

## Covariates

A directed acyclic graph was used to identify possible confounders of the association between time since HTC and unprotected sex<sup>20</sup>. Individual-level variables were gender, age, education, having a living child, having ≥1 sex partner in the previous month (including ≥1 study partner), and study site. Couple-level variables were marital and cohabitation status, relationship length, relationship violence in the past 3 months, and male-female age difference.

To determine which variables to include in the final adjusted analyses, we first implemented models with all covariates presented in Table 1 and interaction terms for age, gender, and site. Interaction terms were retained if they reached statistical significance at alpha=0.1. Covariates were removed one-by-one, and retained if removal resulted in >10% change in estimate<sup>21–22</sup>. Fully adjusted models were implemented as sensitivity analyses.

## Results

### Descriptive Statistics

Soweto was the most common enrollment site (47%), followed by Gugulethu (39%), and Orange Farm (14%) (Table 1a). Most HIV-infected participants (77%) were female. The mean age of HIV-infected participants was 33 years and 29% had completed secondary school. Most HIV-infected participants (82%) had at least one child and few (4%) reported >1 sex partner in the last month. Two thirds of couples were married or cohabitating; 79% had been together for >1 year (Table 1b). On average, males were 4.1 years older than females, regardless of which partner was HIV-infected. Few HIV-infected participants (4%) reported recent relationship violence.

At baseline, 13% of HIV-infected participants were tested 7 days before baseline, 26% 8–14 days before baseline, 11% 15–30 days before baseline, and 50% >30 days before baseline (Table 1a). The median time since HTC was 29 days (IQR: 11 days, 9.2 months) overall and 9.2 months (IQR: 3.8 months, 25.6 months) among the previously tested.

At baseline, almost all HIV-infected participants reported ≥1 sex act in the last month with their study partner (new: 94.1%, previous: 96.1%, p=0.3) (Table 2). Among those newly tested, 53% reported ≥1 unprotected sex act in the last month compared to 25% of those previously tested (OR: 3.3, CI: 2.3, 4.8). Of those reporting any unprotected sex, the mean numbers of unprotected acts were eight (newly tested) and six (previously tested).

One month after baseline, most HIV-infected participants reported sexual activity with study partners (new: 87.9%, previous: 89.1%, p=0.7). Nine percent of those newly tested and 13% of those previously tested reported any unprotected sex in the last month (OR: 0.7, CI: 0.4, 1.3). Of those reporting any unprotected sex, the mean numbers of unprotected acts were eight (newly tested) and seven (previously tested).

Twelve months after baseline, most HIV-infected participants continued to report sexual activity with study partners (new: 73.6%, previous: 78.2%, p=0.3). Six percent of those newly tested and 14% of those previously tested reported any unprotected sex in the last month (OR: 0.4, 95% CI: 0.2, 0.8). The mean number of unprotected sex acts was 6 in both groups.

## Baseline Analyses

In multivariable analysis with adjustment for study site and marital status, the odds of being in a group engaging in unprotected sex were higher among those tested  $\leq 7$  days before baseline compared to those tested  $>30$  days before baseline [aOR: 9.3 (CI: 3.6, 24.2)]. Similarly, the number of unprotected sex acts was higher among those tested  $\leq 7$  days before baseline compared to those tested  $>30$  days before baseline [adjusted relative number: 1.7 (CI: 1.2, 2.6)]. The final adjusted model differed minimally from the unadjusted model (Table 3) or the fully adjusted model (2%, logistic parameter estimate; 8%, NB parameter estimate). Both the adjusted odds and adjusted relative number of unprotected sex acts were higher among those tested 7–14 and 15–30 days before baseline compared to those tested  $>30$  days before baseline (Table 3).

## Longitudinal Analyses

At baseline, the odds of unprotected sex in the last month were substantially higher among those tested  $\leq 7$  days before baseline than those tested  $>30$  days before baseline [OR 7.01 (CI: 3.80, 12.94)], but these groups were more comparable by month one [OR 0.53 (CI: 0.18, 1.58)] and remained so at months six [OR 0.45 (CI: 0.15, 1.34)] and twelve [OR 0.40, CI (0.10, 1.53)].

The odds of unprotected sex were lower at month one compared to baseline within each group:  $\leq 7$  days OR=0.03, 8–14 days OR=0.09, 15–30 days OR=0.19,  $>30$  days OR=0.45. In all groups, the odds of unprotected sex remained lower at month six compared to baseline:  $\leq 7$  days OR=0.04, 8–14 days OR=0.17, 15–30 days OR=0.16,  $>30$  days OR=0.69. Similarly, in all groups the odds of unprotected sex remained lower at month twelve compared to baseline:  $<7$  days OR=0.04, 8–14 days OR=0.10, 15–30 days OR=0.06,  $>30$  days OR 0.66 (Figure 2a.) All ORs were significant at an alpha level of 0.05. Model-building resulted in no adjustment. Full adjustment resulted in a 7% change in the primary comparison of interest (month one versus baseline among persons tested  $\leq 7$  days before baseline).

In longitudinal NB analysis, all newly tested participants ( $<30$  days) were analyzed together due to sparse data. The number of unprotected sex acts was higher among the newly tested than the previously tested at baseline [1.4 (CI: 1.1, 1.8)] but the groups were the same by month one [relative number: 1.0 (CI: 0.6, 1.8)] and remained so at month six [relative number 0.9 (CI: 0.5, 1.7)] and twelve [relative number: 1.1 (CI: 0.6, 2.0)]. Among the newly tested, the number of unprotected sex acts in the last month was similar at months one [0.8 (CI: 0.5, 1.3)], six [0.7 (CI: 0.4, 1.1)], and twelve [1.0 (CI: 0.6, 1.7)] compared to baseline, but results were imprecise. Among previously tested persons, the number of unprotected sex acts was the same at months one [1.1 (CI: 0.9, 1.5)], six [1.0 (CI: 0.7, 1.5)], and twelve [1.2 (CI: 0.9, 1.7)] compared to baseline, though also imprecise (Figure 2b). Model-building resulted in no adjustment variables, so results are not presented. Full adjustment resulted in a 6% change in the primary comparison of interest (month one versus baseline among newly tested persons).

## Discussion

These findings strongly suggest that HTC, and particularly couples HTC, lead to the adoption of consistent condom use in these stable HIV-discordant couples. At baseline, HIV-infected participants who had just learned their HIV status were much more likely to report unprotected sex (71%) than HIV-infected participants who had known their HIV status for the full month (26%). One month later, after both groups had received couples HTC, the proportion reporting unprotected sex declined from 71% to 8%. In the presence of

monthly counseling for the HIV-infected participant, three-monthly HTC for the HIV-uninfected participant, and condom access for both, these low levels of unprotected sex persisted for one year (8%).

The protective nature of couples HTC for HIV-discordant couples is consistent with findings from earlier work in Africa. Couples HTC is associated with high condom uptake among HIV-infected persons<sup>23–24</sup>, particularly persons in HIV-discordant relationships<sup>8–12</sup>. Our analysis is one of the first to show that condom uptake occurs within the first week after couples HTC<sup>9</sup>.

Our findings further suggest that a couple's mutual awareness of HIV-discordance is more protective than a person's individual awareness of HIV-positive status. This finding is supported by the modest decline in unprotected sex observed from baseline to month one among HIV-infected persons who had received HTC previously. Although these persons had sought HTC before, some may have sought individual HTC and not disclosed to sex partners, learned their partner's HIV status, or received counseling with partners until just before baseline when they received couples HTC with study partners. The finding that mutual awareness is more protective than individual awareness is complemented by findings from the full trial: HIV-uninfected participants reported less frequent unprotected sex with study partners, whose HIV status was known, than with outside partners, whose HIV status was often unknown<sup>25</sup>.

After baseline, all HIV-infected persons received individual counseling monthly, partners received individual or couples HTC quarterly, and condoms were provided. These factors may have contributed to consistent condom use, though we cannot determine how influential these factors were compared to the initial impact of couples HTC.

In spite of behavioral prevention, some HIV-infected persons continued engaging in unprotected sex with study partners, without reducing the number of unprotected acts. Reasons for ongoing risk behavior may include fertility desires, condom dislike, or disinhibition, but cannot be assessed formally in these data. Assessing reasons for nonuse, as well as acceptability of other prevention strategies, is important in this subpopulation.

Understanding the impact of HTC on HIV prevention is critical given its rapid scale-up. However, HTC is difficult to assess in randomized settings because withholding HTC is unethical and observational studies are typically subject to confounding. This trial provided an opportunity to address the impact of couples HTC on HIV prevention in an ethical, rigorous way. Our results are unlikely to be heavily biased by unmeasured confounding because the main difference between exposure groups was the timing of HTC with respect to study enrollment. This typically differed by only a few months and *a priori* seems unlikely to be strongly influenced by social or biomedical factors. The similar distribution of observed covariates between exposure groups (Table 1) and the need for minimal adjustment support this contention.

In our study, we knew the precise timing of when someone learned their HIV status, but could only determine when sexual behavior occurred within a one-month interval. The discrepancy in the timing of these measures leaves ambiguity regarding the temporal order of HTC and sexual behavior for newly tested persons. For example, someone tested 10 days prior to baseline spent the first 20 days of the month unaware of their HIV status and the final 10 days aware. If they reported unprotected sex during this thirty-day period, it could have occurred before, after, or both before and after HTC. Two features of our study design lend evidence to the strong possibility that unprotected sex occurred predominantly *before* HTC. First, once newly tested persons had been aware of their HIV status for at least one month they reported lower levels of unprotected sex. Second, at baseline, the relationship

between the amount of time someone was unaware of their HIV status and the odds of unprotected sex was monotonic. The more time someone spent unaware of their HIV status, the more likely they were to report any unprotected sex at baseline. If this trend were to continue a group unaware for the entire month would be expected to experience an even higher probability of unprotected sex than those who were most recently tested.

This analysis relied on self-report which is subject to social desirability. If persons were more likely to over-report condom use after HTC than before, effect measures would be exaggerated. Biomarkers suggest that these differences are unlikely to be explained entirely by this concern. In the full trial population, consistent condom use was strongly associated with reductions in HIV acquisition<sup>26</sup>. Additionally, there was strong correlation (84%) between the HIV-infected and HIV-uninfected partners with respect to the number of self-reported unprotected sex acts at baseline.

Caution is needed when generalizing results beyond these stable HIV-discordant couples. Persons enrolling in HIV prevention trials may be more motivated to adopt HIV prevention behaviors than the general population. Additionally, persons who are willing to enroll with partners may differ from persons who are unwilling. Most couples were in long-term marital or cohabiting relationships and levels of intimate partner violence were low<sup>27</sup>. Couples HTC may not be as protective in segments of the population in less stable, more violent partnerships<sup>28</sup>. Understanding effectiveness of couples HTC in these less stable partnerships is an area for future investigation.

Our findings raise questions about the current HTC paradigm, which is not typically couple-oriented. When stable couples learn that they are in HIV-discordant relationships they adopt consistent condom use quickly, but such marked behavior change is not typically reported after individual HTC<sup>29–30</sup>. Couples HTC assures simultaneous disclosure, has a substantial impact on sexual behavior<sup>30</sup>, and may have an impact on adherence to biomedical prevention<sup>7, 31</sup>. However, most current HTC efforts are aimed at individuals, not couples, leading to missed HIV prevention opportunities. Strategies, such as home-based testing<sup>32</sup>, supportive HIV-disclosure counseling<sup>33</sup>, and partner notification,<sup>34–35</sup> can be used to inform persons of HIV-discordance. Such couple-oriented strategies have recently been recommend in the World Health Organization's *Guidance on Couples HIV Testing and Counseling*.<sup>13</sup>

In summary, our results add to a growing body of evidence demonstrating that couples HTC is effective at rapidly increasing condom-uptake, facilitating ongoing condom use, and likely lowering rates of HIV transmission<sup>10–11, 26</sup>. Although initial findings were published nearly two decades ago, most countries have been slow to implement couple-based strategies. With expanding HTC capacity in Africa<sup>36</sup>, decision-makers now need to consider how to reach couples. Such expansion will help a high risk group make informed sexual health decisions and likely prevent a substantial number of HIV infections.

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NER conceptualized the study, in collaboration with AEP, WCM, DW, FB, SM, SD and GdB. SD, GdB, and DC were site PIs on the parent study. SD, GdB, DC, and MK oversaw laboratory and clinical aspects of the parent study, as well as data collection. Data analysis and interpretation were performed by NER, under the guidance of WCM and AEP. NER prepared the initial draft manuscript and revisions were made by AEP, WCM, SD, GdB, DW, FB, SM, DC, and MK.



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#### Conflict of Interest and Source of Funding

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Since the completion of data collection, Guy de Bruyn accepted a position at Sanofi Pasteur. SP had no role in this manuscript.

## References

1. Serwadda D, Gray RH, Wawer MJ, et al. The social dynamics of HIV transmission as reflected through discordant couples in rural Uganda. *AIDS*. 1995 Jul; 9(7):745–750. [PubMed: 7546420]
2. Dunkle KL, Stephenson R, Karita E, et al. New heterosexually transmitted HIV infections in married or cohabiting couples in urban Zambia and Rwanda: an analysis of survey and clinical data. *Lancet*. 2008 Jun 28; 371(9631):2183–2191. [PubMed: 18586173]
3. Gray R, Ssempiija V, Shelton J, et al. The contribution of HIV-discordant relationships to new HIV infections in Rakai, Uganda. *AIDS*. 2011 Mar 27; 25(6):863–865. [PubMed: 21326076]
4. UNAIDS. Global Report: UNAIDS Report on the Global AIDS Epidemic 2010. 2010.
5. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012 Aug 2; 367(5):399–410. [PubMed: 22784037]
6. Abdool Karim Q, Abdool Karim SS, Frohlich JA, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*. 2010 Sep 3; 329(5996):1168–1174. [PubMed: 20643915]
7. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011 Aug 11; 365(6):493–505. [PubMed: 21767103]
8. The Voluntary HIV-1 Counseling and Testing Efficacy Study Group. Efficacy of voluntary HIV-1 counselling and testing in individuals and couples in Kenya, Tanzania, and Trinidad: a randomised trial. *Lancet*. 2000 Jul 8; 356(9224):103–112. [PubMed: 10963246]
9. Kamenga M, Ryder RW, Jingu M, et al. Evidence of marked sexual behavior change associated with low HIV-1 seroconversion in 149 married couples with discordant HIV-1 serostatus: experience at an HIV counselling center in Zaire. *AIDS*. 1991 Jan; 5(1):61–67. [PubMed: 2059362]
10. Allen S, Tice J, Van de Perre P, et al. Effect of serotesting with counselling on condom use and seroconversion among HIV discordant couples in Africa. *BMJ*. 1992 Jun 20; 304(6842):1605–1609. [PubMed: 1628088]
11. Allen S, Serufilira A, Bogaerts J, et al. Confidential HIV testing and condom promotion in Africa. Impact on HIV and gonorrhoea rates. *JAMA*. 1992 Dec 16; 268(23):3338–3343. [PubMed: 1453526]
12. Allen S, Meizen-Derr J, Kautzman M, et al. Sexual behavior of HIV discordant couples after HIV counselling and testing. *AIDS*. 2003 Mar 28; 17(5):733–740. [PubMed: 12646797]
13. World Health Organization. Guidance on couples HIV testing and counselling, including antiretroviral therapy for treatment and prevention in serodiscordant couples. 2012.
14. Celum C, Wald A, Lingappa JR, et al. Acyclovir and transmission of HIV-1 from persons infected with HIV-1 and HSV-2. *N Engl J Med*. 2010 Feb 4; 362(5):427–439. [PubMed: 20089951]
15. Lingappa JR, Baeten JM, Wald A, et al. Daily aciclovir for HIV-1 disease progression in people dually infected with HIV-1 and herpes simplex virus type 2: a randomised placebo-controlled trial. *Lancet*. 2010 Mar 6; 375(9717):824–833. [PubMed: 20153888]

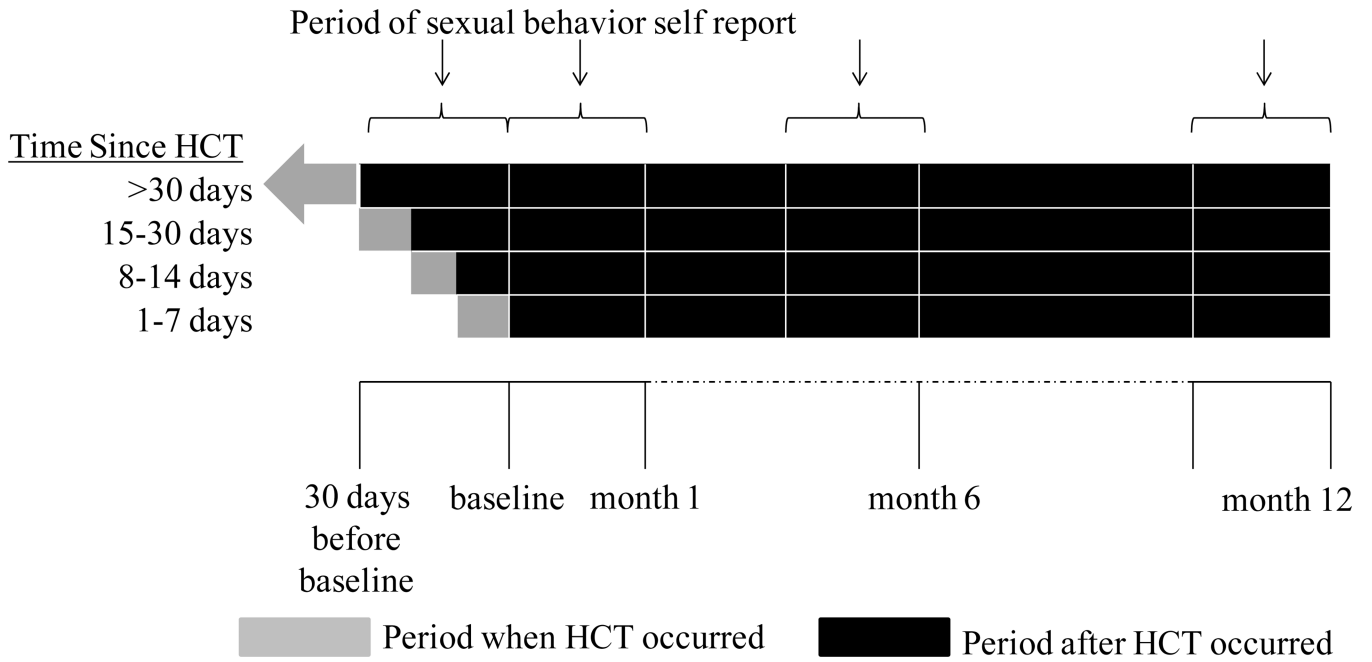
16. Lingappa JR, Lambdin B, Bukusi EA, et al. Regional differences in prevalence of HIV-1 discordance in Africa and enrollment of HIV-1 discordant couples into an HIV-1 prevention trial. *PLoS One*. 2008; 3(1):e1411. [PubMed: 18183292]
17. Lingappa JR, Kahle E, Mugo N, et al. Characteristics of HIV-1 discordant couples enrolled in a trial of HSV-2 suppression to reduce HIV-1 transmission: the partners study. *PLoS One*. 2009; 4(4):e5272. [PubMed: 19404392]
18. Long, JS.; Freese, J. *Regression Models for Categorical Dependent Variables Using Stata*. College Station, TX: StataCorp LP; 2006.
19. Liang KY, Zeger SL. Longitudinal data analysis using generalized linear models. *Biometrika*. 1986; 73:13–22.
20. Greenland S, Pearl J, Robins JM. Causal diagrams for epidemiologic research. *Epidemiology*. 1999 Jan; 10(1):37–48. [PubMed: 9888278]
21. Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. *Am J Epidemiol*. 1989 Jan; 129(1):125–137. [PubMed: 2910056]
22. Rothman, KJ.; Greenland, S.; Lash, TL. *Modern epidemiology*. 3rd ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2008.
23. Turner AN, Miller WC, Padian NS, et al. Unprotected sex following HIV testing among women in Uganda and Zimbabwe: short- and long-term comparisons with pre-test behaviour. *Int J Epidemiol*. 2009 Aug; 38(4):997–1007. [PubMed: 19349481]
24. Weinhardt L, Care M, Johnson B, Bickman N. Effects of HIV Counseling and Testing and Sexual Risk Behavior: A Meta-Analytic Review of Published Research, 1985–1997. *American Journal of Public Health*. 1999
25. Ndase P, Celum C, Thomas K, et al. Outside sexual partnerships and risk of HIV acquisition for HIV uninfected partners in African HIV serodiscordant partnerships. *J Acquir Immune Defic Syndr*. 2012 Jan 1; 59(1):65–71. [PubMed: 21963939]
26. Hughes JP, Baeten JM, Lingappa JR, et al. Determinants of Per-Coital-Act HIV-1 Infectivity Among African HIV-1-Serodiscordant Couples. *J Infect Dis*. 2012 Feb; 205(3):358–365. [PubMed: 22241800]
27. Were E, Curran K, Delany-Moretlwe S, et al. A prospective study of frequency and correlates of intimate partner violence among African heterosexual HIV serodiscordant couples. *AIDS*. 2011 Oct 23; 25(16):2009–2018. [PubMed: 21811146]
28. Jewkes RK, Dunkle K, Nduna M, Shai N. Intimate partner violence, relationship power inequity, and incidence of HIV infection in young women in South Africa: a cohort study. *Lancet*. 2010 Jul 3; 376(9734):41–48. [PubMed: 20557928]
29. Becker S, Mlay R, Schwandt HM, Lyamuya E. Comparing couples' and individual voluntary counseling and testing for HIV at antenatal clinics in Tanzania: a randomized trial. *AIDS Behav*. 2010 Jun; 14(3):558–566. [PubMed: 19763813]
30. Kennedy CE, Medley AM, Sweat MD, O'Reilly KR. Behavioural interventions for HIV positive prevention in developing countries: a systematic review and meta-analysis. *Bull World Health Organ*. 2010 Aug 1; 88(8):615–623. [PubMed: 20680127]
31. Ware NC, Wyatt MA, Haberer JE, et al. What's Love Got to Do With It? Explaining Adherence to Oral Antiretroviral Pre-exposure Prophylaxis (PrEP) for HIV Serodiscordant Couples. *J Acquir Immune Defic Syndr*. 2012 Jan 19.
32. Tumwesigye E, Wana G, Kasasa S, Muganzi E, Nuwaha F. High uptake of home-based, district-wide, HIV counseling and testing in Uganda. *AIDS Patient Care STDS*. 2010 Nov; 24(11):735–741. [PubMed: 21067357]
33. Kairania RM, Gray RH, Kiwanuka N, et al. Disclosure of HIV results among discordant couples in Rakai, Uganda: a facilitated couple counselling approach. *AIDS Care*. 2010 Sep; 22(9):1041–1051. [PubMed: 20824557]
34. Brown L. HIV Partner Notification is Effective and Feasible in Sub-Saharan Africa: Opportunities for HIV Treatment and Prevention. *J Acquir Immune Defic Syndr*. 2011; 56(5):437. [PubMed: 22046601]
35. Mohlala BK, Boily MC, Gregson S. The forgotten half of the equation: randomised controlled trial of a male invitation to attend couple VCT in Khayelitsha, South Africa. *AIDS*. 2011 May 21.

36. WHO, UNAIDS, UNICEF. HIV Testing and Counseling. Towards Universal Access: Scaling up Priority HIV/AIDS Interventions in the Health Sector, Progress Report 2010.

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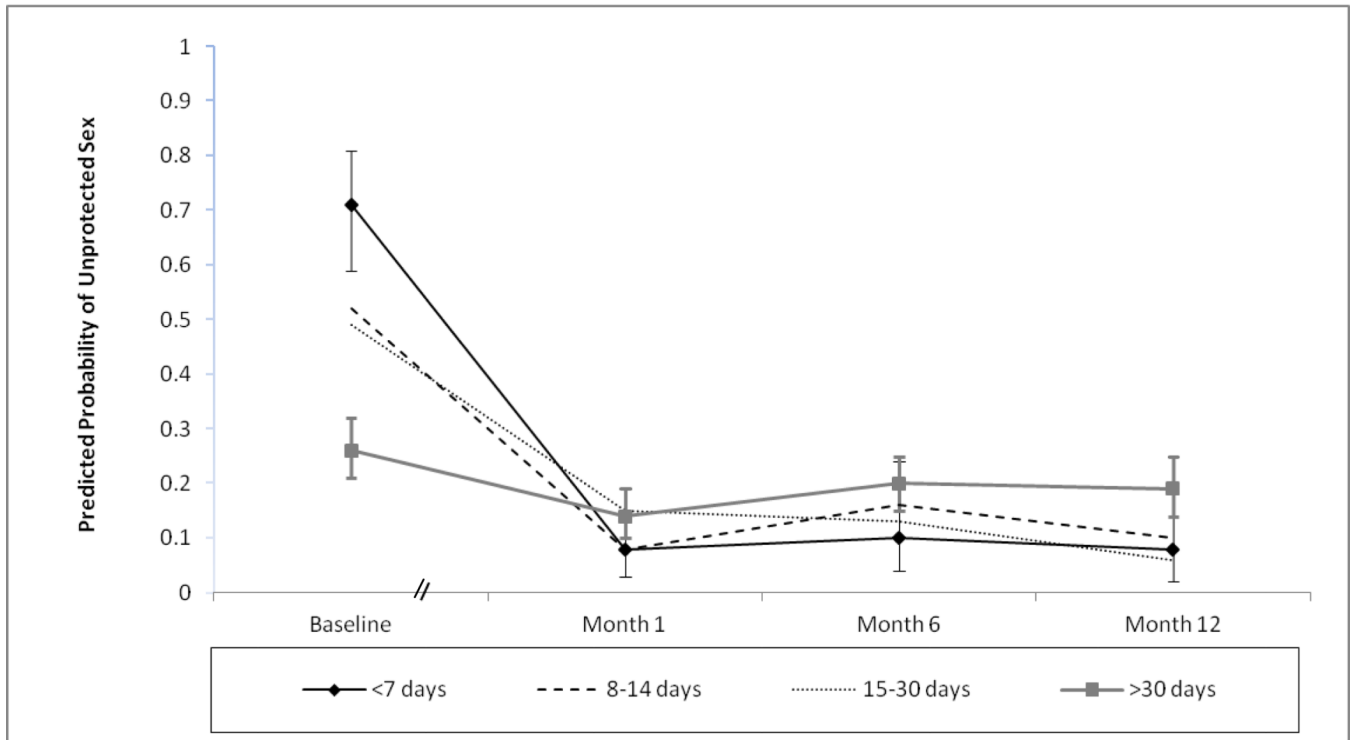
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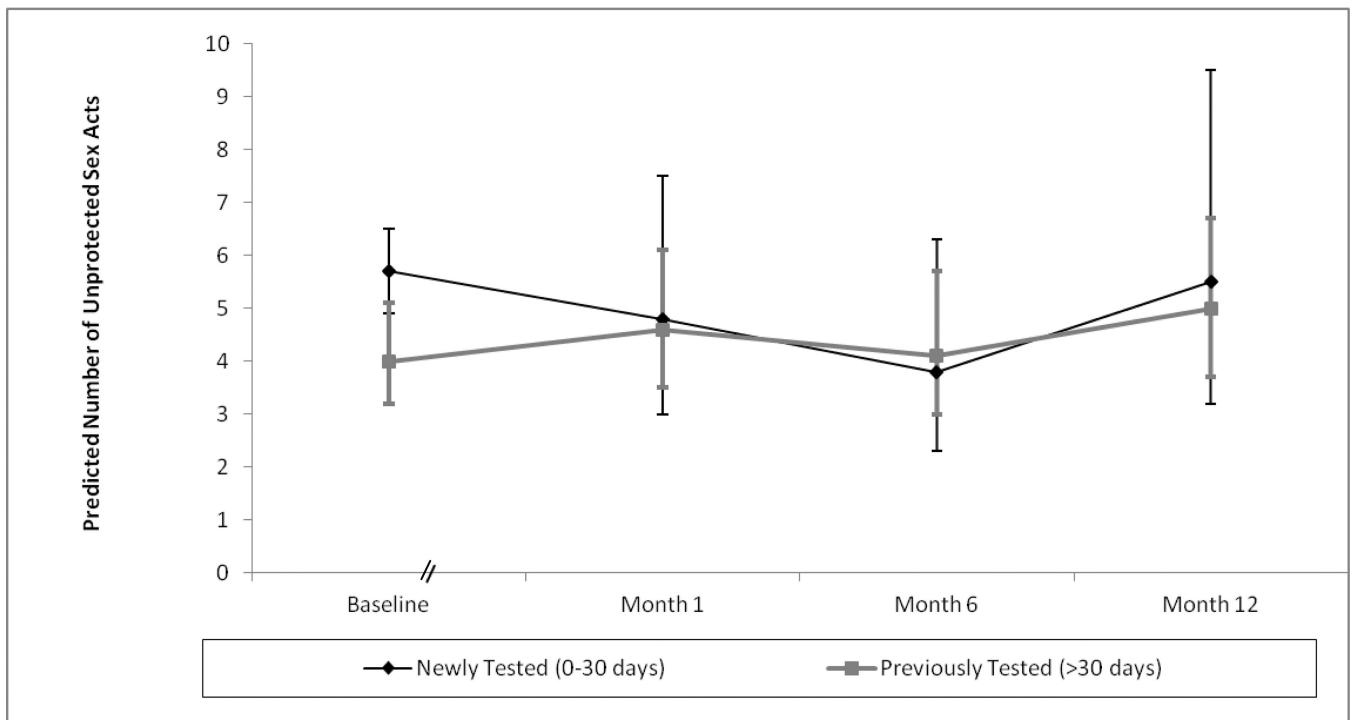
**Figure 1. Schematic of Baseline and Longitudinal Analyses**

Figure 1 displays the four exposure groups and time periods when outcomes are assessed. At baseline, those in the newly tested groups ( 7 days, 8–14 days, 15–30 days) are aware of their HIV status for only part of the month before baseline (indicated in gray), whereas those in the previously tested group (>30 days) are aware of their HIV status for the entire month before baseline (indicated in black). The more recently someone was tested, the longer they spent unaware of their HIV status. By months one, six and twelve, persons in all groups had known their HIV status for >30 days. After baseline, HIV-infected partners had access to counseling and condoms each month. HIV-discordant couples had access to couples HIV counseling and testing at 3, 6, 9 and 12 months.

**a. Unadjusted Predicted Probability of Any Unprotected Sex Acts (95% CIs) by Time Since HTC**



**b. Unadjusted Predicted Number of Unprotected Sex Acts (95% CIs) by Time Since HTC**



**Figure 2.**

Figure 2a depicts the predicted probability of unprotected sex among sexually active persons in all four groups over a one-year period. At baseline, the more recently someone had learned their HIV status, the higher the probability of unprotected sex. By month one, the predicted probability of unprotected sex declined in all four groups and remained lower over time. Figure 2b depicts the predicted number of unprotected sex acts among persons who engaged in unprotected sex at four time points over a one-year period. All newly aware groups are collapsed together due to sparse data. At baseline persons who were newly tested reported more unprotected sex acts in the last month than persons who were previously tested. One month after baseline, the predicted number of unprotected sex acts declined in the newly tested group and remained constant (though imprecise) in both groups over time.

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Table 1

<b>a. Baseline characteristics of HIV-infected participants by time since HTC</b>			
Characteristics	Newly Tested		
	7 days N=65 (13%)	8–14 days N=134 (26%)	15–30 days N=55 (11%)
			Previously Tested >30 days N=254 (50%)
Gender			
Male	14 (21.5)	31 (23.1)	16 (29.1)
Female	51 (78.5)	103 (76.9)	39 (70.9)
Age*			
<25	12 (18.8)	18 (13.6)	4 (7.3)
25–34	27 (42.2)	53 (40.2)	35 (63.6)
35	25 (39.1)	61 (46.2)	16 (29.1)
Education			
<Secondary	44 (67.7)	111 (82.8)	37 (67.3)
Secondary	21 (32.3)	23 (17.2)	18 (32.7)
Has a living child			
Yes	55 (84.6)	100 (74.6)	44 (80.0)
No	10 (15.4)	34 (25.4)	11 (20.0)
>1 sex partner			
Yes	4 (6.2)	6 (4.5)	1 (1.8)
No	61 (93.8)	128 (95.5)	54 (98.2)
Study Site			
Gugulethu	24 (36.9)	79 (59.0)	30 (54.5)
Orange Farm	13 (20.0)	22 (16.4)	10 (18.2)
Soweto	28 (43.1)	33 (24.6)	15 (27.3)
			164 (64.6)

<b>b. Baseline characteristics of HIV-infected couples by time since HTC, as reported by HIV-infected participant</b>			
Characteristics	Newly Tested		
	7 days N=65 (13%)	8–14 days N=134 (26%)	15–30 days N=55 (11%)
			Previously Tested >30 days N=254 (50%)
Marital/Cohabitation Status			
Not married, not cohabitating	16 (24.6)	48 (35.8)	26 (47.3)
			81 (31.9)

**b. Baseline characteristics of HIV-infected couples by time since HTC, as reported by HIV-infected participant**

Characteristics	Newly Tested			Previously Tested	
	7 days N=65 (13%)	8-14 days N=134 (26%)	15-30 days N=55 (11%)	>30 days N=254 (50%)	
Not married, cohabitating	40 (61.5)	70 (52.2)	23 (41.8)	120 (47.2)	
Married	9 (13.9)	16 (11.9)	6 (10.9)	53 (20.9)	
Relationship length*					
<1 year	15 (23.1)	40 (30.1)	14 (25.5)	38 (15.1)	
1-3 years	14 (21.5)	46 (34.6)	17 (30.9)	90 (35.9)	
>3 years	36 (55.4)	47 (35.3)	24 (43.6)	123 (49.0)	
Age Difference**†					
<5 years	35 (55.6)	70 (53.0)	32 (59.3)	134 (53.2)	
5 years	28 (44.4)	62 (47.0)	22 (40.7)	118 (46.8)	
Partner Violence 3 Months					
Yes	3 (4.6)	5 (3.7)	1 (1.8)	11 (4.3)	
No	62 (95.4)	129 (96.3)	54 (98.2)	243 (95.7)	

\*Results may not add to column totals due to missing data.

†Male age minus female age regardless of which partner is HIV-infected



**Table 2**  
Sexual behavior in the previous month comparing newly to previously tested at baseline, month one, and month twelve

Timing of testing	Baseline (N=508)			1-Month (N=487)			12-Month (N=376)		
	New	Previous	n	New	Previous	n	New	Previous	n
<b>Entire Population</b>	<b>n=254 (50%)</b>	<b>n=254 (50%)</b>	<b>n=239 (49%)</b>	<b>n=248 (51%)</b>	<b>n=202 (54%)</b>	<b>n=174 (46%)</b>	<b>n=174 (46%)</b>	<b>n=202 (54%)</b>	<b>n=202 (54%)</b>
Total sex acts									
N (%) 1	239 (94.1)	244 (96.1)	210 (87.9)	221 (89.1)	128 (73.6)	158 (78.2)	128 (73.6)	158 (78.2)	158 (78.2)
N (%) = 0	15 (5.9)	10 (3.9)	29 (12.1)	27 (10.9)	46 (26.4)	44 (21.8)	46 (26.4)	44 (21.8)	44 (21.8)
Mean (SD) count	7.1 (10.3)	6.9 (9.3)	5.3 (6.5)	6.3 (7.7)	4.4 (5.3)	4.9 (5.6)	4.4 (5.3)	4.9 (5.6)	4.9 (5.6)
Median (IQR) count	4 (3.8)	4 (3.8)	3 (2.5)	4 (2.8)	3 (0.7)	3 (1.7)	3 (0.7)	3 (1.7)	3 (1.7)
Unprotected sex acts									
N (%) 1	134 (52.8)	64 (25.2)	22 (9.2)	31 (12.5)	11 (6.3)	29 (14.4)	11 (6.3)	29 (14.4)	29 (14.4)
N (%) = 0	120 (47.2)	190 (74.8)	217 (90.8)	217 (87.5)	163 (93.7)	173 (85.6)	163 (93.7)	173 (85.6)	173 (85.6)
Mean (SD) count	4.1 (9.7)	1.5 (5.1)	0.7 (3.8)	0.9 (4.4)	0.4 (2.1)	0.8 (3.2)	0.4 (2.1)	0.8 (3.2)	0.8 (3.2)
Median (IQR) count	1 (0.4)	0 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mean (SD) proportion unprotected acts	0.4 (0.4)	0.2 (0.4)	0.1 (0.2)	0.1 (0.2)	0.0 (0.2)	0.1 (0.3)	0.0 (0.2)	0.1 (0.3)	0.1 (0.3)
Median (IQR) proportion unprotected acts	0.3 (0.1)	0 (0.0, 0.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Persons with 1 unprotected act	n=134 (68%)	n=64 (32%)	n=22 (42%)	n=31 (58%)	n=11 (28%)	n=29 (73%)	n=11 (28%)	n=29 (73%)	n=29 (73%)
Total sex acts									
Mean (SD) count	9.4 (12.2)	7.5 (9.6)	13.1 (12.9)	10.2 (10.4)	9.0 (5.1)	7.8 (6.0)	9.0 (5.1)	7.8 (6.0)	7.8 (6.0)
Median (IQR) count	5 (3, 12)	4.5 (2.5, 9)	7 (4, 20)	8 (4, 12)	8 (4, 12)	7 (4, 9)	8 (4, 12)	7 (4, 9)	7 (4, 9)
Unprotected sex acts									
Mean (SD)	7.8 (12.2)	5.8 (9.0)	7.7 (10.5)	7.1 (10.8)	6.1 (6.4)	5.7 (6.6)	6.1 (6.4)	5.7 (6.6)	5.7 (6.6)
Median (IQR)	4 (2, 9)	3 (1, 6)	2.5 (1, 8)	4 (2, 8)	2 (1, 12)	3 (2, 6)	2 (1, 12)	3 (2, 6)	3 (2, 6)
Mean (SD) proportion unprotected acts	0.8 (0.3)	0.8 (0.3)	0.6 (0.3)	0.7 (0.3)	0.6 (0.4)	0.7 (0.3)	0.6 (0.4)	0.7 (0.3)	0.7 (0.3)
Median (IQR) proportion unprotected acts	1.0 (0.6, 1)	1.0 (0.5, 1.0)	0.4 (0.3, 1)	0.8 (0.3, 1)	0.3 (0.3, 1)	0.7 (0.4, 1)	0.3 (0.3, 1)	0.7 (0.4, 1)	0.7 (0.4, 1)

SD=standard deviation, IQR=inter-quartile range

**Table 3**

Unadjusted and Adjusted Baseline ZINB Models by Time Since HTC

	Unadjusted Models		Adjusted Models*	
	OR of any unprotected sex (95% CI)	Relative # of unprotected acts (95% CI)	OR of any unprotected sex (95% CI)	Relative # of unprotected acts (95% CI)
Time Since HTC				
>30 days	1.	1.	1.	1.
15–30 days	2.6 (1.2, 5.4)	1.5 (0.9, 2.4)	3.2 (1.5, 7.0)	1.7 (1.1, 2.8)
8–14 days	3.5 (1.9, 6.4)	1.1 (0.8, 1.6)	4.2 (2.2, 8.0)	1.2 (0.8, 1.7)
7 days	9.0 (3.4, 23.9)	1.7 (1.2, 2.6)	9.3 (3.5, 24.2)	1.7 (1.2, 2.6)

ZINB=zero-inflated negative binomial; HTC=HIV testing and counseling; OR=odds ratio;

CI=confidence interval

\* Adjusted for marital status and study site