

New approaches to HIV prevention in African HIV serodiscordant couples:
antiretrovirals and mobile technology

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Abstract

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This dissertation informs the future implementation of HIV prevention for HIV serodiscordant couples in Africa. The research objectives include: 1) reviewing effective HIV prevention interventions, 2) evaluating the use of daily short message service (SMS, i.e. text message) surveys to measure sex and pre-exposure prophylaxis (PrEP) adherence, and 3) examining the acceptability of initiation of antiretroviral therapy (ART) at higher CD4 counts, a powerful HIV prevention tool.

After the necessary first step of HIV testing and counseling, HIV serodiscordant couples may be offered appropriate HIV prevention interventions, including condoms, male circumcision, treatment of sexually transmitted infections, and two recent biomedical strategies: initiation of ART by the HIV-infected partner and PrEP by the HIV-uninfected partner. Importantly, the widespread implementation and effectiveness of HIV prevention interventions requires understanding and encouraging behaviors for acceptance, adherence, and correct use. We conducted a prospective study of HIV-related behaviors and qualitative research to answer key implementation questions regarding the feasibility of PrEP and acceptability of early ART among HIV serodiscordant couples.

Within a clinical trial of PrEP, we evaluated the use of daily SMS surveys to examine patterns in sexual behavior and PrEP use. Daily SMS data collection was acceptable, obtained high response rates, and provided an assessment of temporal patterns of HIV risk behaviors and PrEP use over a 60-day period. Participants were more likely to adhere to daily PrEP doses when they were sexually-active, PrEP use was not associated with unprotected sex, and anticipating sex was difficult. In addition, HIV risk behaviors were reported on more days through daily SMS surveys compared to monthly interviewer-administered questionnaires, highlighting the potential of SMS to collect more accurate self-reported data. SMS may offer a new method for measuring and promoting behaviors related to HIV risk and adherence as well as enhancing communication between patients and providers.

Qualitative research with HIV serodiscordant couples familiar with HIV prevention methodologies highlighted common perceived advantages and concerns related to early initiation of ART, and an important conceptualization of ART as the “final stage” before dying. This negative meaning of ART initiation poses a challenge to acceptance of early ART and indicates that new messages regarding ART initiation are needed. These new messages should emphasize the benefits of HIV prevention and maintaining good health; acknowledge concerns such as side effects and life-long adherence; and ultimately, portray a positive image of individuals on ART.

Social and behavioral factors, in particular sustained adherence as well as individual and community acceptance, will be fundamental to successful implementation of early ART and PrEP and should remain a focus of HIV prevention and treatment initiatives.

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Introduction

More than 30 years into the HIV epidemic and years away from an effective vaccine, cure, or complete treatment coverage, there is an urgent need to improve and implement current strategies for HIV prevention. Heterosexual transmission is the key driver of the epidemic in sub-Saharan Africa, where 69% of all people infected with HIV worldwide live and an estimated 1.8 million people are newly infected each year [1]. With limited resources and over-burdened health systems, it is critical to focus HIV prevention efforts to have the greatest impact, specifically, highly-efficacious interventions for populations at greatest risk of transmitting or acquiring HIV. HIV serodiscordant couples, where one partner is HIV infected and the other is not, are an important priority population for HIV prevention in Africa due to ongoing risk and the opportunity to intervene to prevent HIV transmission. Recent success in a number of HIV prevention clinical trials has brought forward a new set of HIV prevention strategies for couples and raised questions about how to incorporate into ongoing prevention efforts for optimal impact.

Antiretroviral-based HIV prevention for HIV serodiscordant couples

Antiretroviral-based HIV prevention strategies are an exciting new arena for HIV prevention; these include (1) ART for HIV infected persons to decrease their infectiousness and (2) pre-exposure prophylaxis (PrEP) for high-risk HIV uninfected persons to prevent HIV acquisition. According to recent results from a multinational randomized clinical trial (HPTN 052), an HIV-infected individual's initiation of and high adherence to ART reduced the risk of HIV transmission to HIV-uninfected partners by 96% [2]. In addition, recent clinical trials have demonstrated the efficacy of PrEP in reducing the risk of HIV acquisition (Table 1). The Partners PrEP Study, a randomized controlled trial of daily oral PrEP among HIV serodiscordant couples

in East Africa, demonstrated high efficacy of tenofovir and emtricitabine/tenofovir in preventing HIV transmission in HIV serodiscordant couples, 67% and 75% respectively [3]. Among participants adherent to PrEP, protection from HIV was estimated to be approximately 90% [3].

This dissertation answers key implementation questions regarding the feasibility of PrEP and acceptability of early initiation of ART treatment among HIV serodiscordant couples. HIV serodiscordant couples represent an identifiable population at high-risk of new HIV infection and are considered a priority group for early initiation of ART and/or PrEP. In 2012, the World Health Organization (WHO) revised their guidelines on ART to recommend ART initiation by HIV-infected individuals in an HIV serodiscordant relationship regardless of their CD4 count and issued guidance on PrEP use for couples, particularly those in which the HIV-infected partner delays or is unable to adhere to ART [4]. The U.S. Food and Drug Administration (FDA) approved one combination antiretroviral, Truvada® (emtricitabine/tenofovir), for use by HIV-uninfected adults for HIV prevention in 2012 and ongoing demonstration projects are evaluating “real-world” effectiveness of PrEP in priority populations such as HIV serodiscordant couples.

This dissertation sought to answer questions about how to most effectively deliver HIV prevention strategies to HIV serodiscordant couples in Africa. We review effective HIV prevention interventions for HIV serodiscordant couples, evaluate the use of daily short message service (SMS, i.e. text message) surveys to describe sexual behavior and adherence to antiretroviral-based HIV prevention, and examine the acceptability of novel antiretroviral-based HIV prevention strategies to this priority population. The first chapter provides a review of HIV prevention strategies and considerations for HIV serodiscordant couples in sub-Saharan Africa. Chapters 2 and 3 present an evaluation of daily SMS surveys as a new method to measure self-reported behaviors related to HIV prevention. In Chapter 2, we describe results from this study of the use of SMS for collecting daily sex and medication adherence data in

Kenya. Next, these self-reported sex and adherence behaviors collected over daily SMS are compared to self-reported measures from monthly interviewer-administered surveys in Chapter 3. Finally, Chapter 4 highlights key findings from a qualitative study exploring Kenyan HIV serodiscordant couples' attitudes toward initiation of antiretroviral therapy (ART) for HIV prevention.

Review of HIV prevention strategies for HIV serodiscordant couples: Chapter 1

What is the epidemiology of HIV in HIV serodiscordant couples in sub-Saharan Africa? Which HIV prevention strategies should be included in a combination prevention approach?

A substantial fraction of new HIV infections in Africa occur within stable relationships, that is cohabitating or married couples—a population that has been previously considered 'low-risk' [5]. Approximately half of married or cohabitating couples in which one person is HIV-infected are estimated to be serodiscordant [6-9]. Models and studies of HIV incidence suggest that an important fraction of new HIV infections occur among HIV serodiscordant couples in Africa, making them a critical population for HIV prevention (Table 2, Figure 1). In Chapter 1, we review epidemiological evidence of behavioral and biological factors related to HIV transmission within HIV serodiscordant couples. We assess the effectiveness of various HIV prevention interventions, including recent clinical trials of antiretroviral medications taken by either partner, plus, factors to consider for successful implementation.

Daily SMS surveys to measure sex and PrEP use: Chapters 2 & 3

What is the feasibility of SMS to collect sensitive health information? What are the patterns in sexual risk behavior and PrEP adherence? Is anticipated sexual activity associated with actual

sexual behavior? What is the agreement between self-reported sex and adherence behaviors reported over daily SMS surveys and monthly interviewer-administered questionnaires?

We conducted a novel pilot study to test the use of mobile phones and text messaging to conduct a “real time” assessment of HIV risk and PrEP adherence in a prospective cohort of HIV serodiscordant couples on a regimen of daily, oral PrEP. The collection of daily data allowed us to explore patterns in sex, condom use, and daily PrEP use. This study examined whether pill use varied with sexual behavior and if participants could anticipate when they would have sex, thus effectively employ pre-coital PrEP dosing.

Mobile phone data collection.

In Africa, researchers and health practitioners have begun to use mobile technology to collect data on health behaviors and deliver health interventions. Few published studies in Africa have explored the use of mobile phone SMS to collect health data directly from patients [10, 11]. The survey of sensitive health behaviors over SMS on personal phones has the potential to reduce measurement bias. The collection of private and sensitive data by mobile devices may improve accuracy by shortening the period of recall and having more frequent sampling times (i.e. daily or weekly vs. monthly) [10]. Data collection through mobile technology may also minimize social desirability bias, the tendency of respondents to report more favorable behaviors, with the sense of privacy and anonymity provided [12].

In addition, the concurrent collection of self-reported sex and adherence behaviors by daily SMS and monthly interviewer-administered questionnaire provided an opportunity to compare these two survey methods. Previous studies suggest that more frequent (i.e. daily) collection of sexual behavior data may improve the quality and accuracy. The reliability of data on sex frequency diminishes with longer periods of recall of more frequent sexual behaviors (e.g. vaginal sex)

[12]. The use of diaries as a data collection tool for sexual behavior were preferable to study participants than recall questionnaires and provided greater report of HIV risk behavior, suggesting more reliable data [13, 14].

Qualitative study of HIV serodiscordant couples' attitudes towards early ART: Chapter 4

How do Kenyan HIV serodiscordant couples view the use of ART for HIV prevention? What factors influence their decision to initiate ART?

ART for HIV-infected partners may be preferable and more effective for some couples. It is unknown whether the proven HIV prevention benefit will outweigh previously identified barriers to ART initiation – feeling healthy, fear of side effects, concern for drug resistance, unable to disclose, stigma, abstaining from alcohol, as well as the economic and opportunity cost of seeking care [15-19]. In one survey of Kenyan HIV serodiscordant couples enrolled in the Partners PrEP Study, close to one third of HIV-infected adults reported reluctance to initiating ART at CD4 >350 cells/ μ L (Kenya's current medical criteria) [20]. Few previous studies, and no published qualitative research to date, have examined attitudes and beliefs about early initiation of ART, at CD4 counts >350 cells/ μ L.

In Chapter 4, we present results from a qualitative study on HIV serodiscordant couples' willingness to initiate ART early. We conducted focus groups and in-depth interviews to explore how environmental, social, and individual factors play a role in decision-making regarding initiation of ART. This qualitative research explains resistance to early initiation of ART and provides new insight into the meaning of ART for this Kenyan population.

Summary

HIV researchers, policy makers, advocates, and medical providers are currently considering how to most effectively implement “combinations” of appropriate and effective HIV prevention strategies, including ART and PrEP. This dissertation presents studies using multiple methods, including mobile technology for prospective daily data collection and qualitative research, to explore African HIV serodiscordant couples’ behaviors related to, and interest in, these new HIV prevention strategies.

Table 1. Randomized controlled trials of the efficacy of oral PrEP for HIV prevention

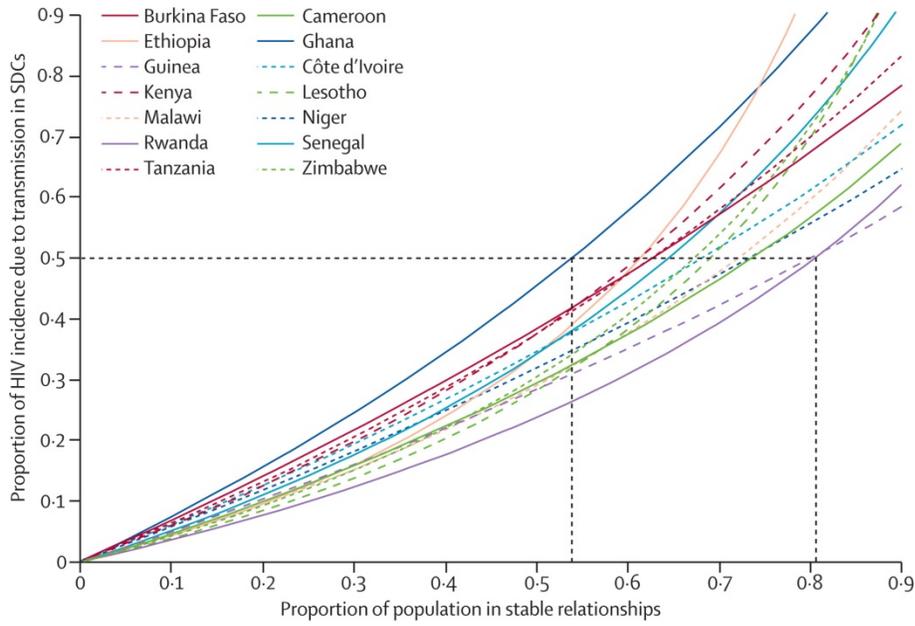
Trial	Population & Setting	Intervention	Efficacy results	Efficacy with high adherence
Partners PrEP Study [3]	4,758 HIV serodiscordant heterosexual couples in Kenya & Uganda	Daily oral TDF; daily oral TDF/FTC	67% reduction in HIV among TDF arm 75% reduction in HIV among TDF/FTC arm	>97% dispensed doses taken across entire study 86% (TDF) and 90% (TDF/FTC) reduction among participants with detectable study-drug
TDF2 [21]	1,219 heterosexual men and women in Botswana	Daily oral TDF/FTC	63% reduction in HIV among TDF/FTC arm	78% reduction in analysis excluding HIV infections occurring >30 days after last drug dose
Bangkok Tenofvir Study [22]	2,413 injection drug users in Thailand	Daily oral TDF	49% reduction in HIV among TDF arm	drug administration directly observed 87% of study time 70% reduction among participants with detectable study-drug
iPrEX [23]	2,499 men who have sex with men in Brazil, Ecuador, Peru, South Africa, Thailand, & U.S.	Daily oral TDF/FTC	44% reduction in HIV among TDF/FTC arm	73% reduction in HIV among high adherers ($\geq 90\%$ pill use) 92% reduction among participants with detectable study-drug
FEM-PrEP [24]	2,120 women in Kenya, South Africa, & Tanzania	Daily oral TDF/FTC	No efficacy	<40% HIV-uninfected women had detectable study-drug in subgroup analysis
VOICE [25]	3,019 women in South Africa, Uganda, & Zimbabwe	Daily oral TDF; daily oral TDF/FTC	No efficacy	30% samples from TDF arm & 29% from TDF/FTC arm had detectable study-drug in random sample of active arms

Abbreviations: PrEP: pre-exposure prophylaxis, TDF: tenofovir; FTC: emtricitabine

Table 2. Comparison of estimated proportion of within-couple HIV transmissions by study and location

Reference	Location	Estimated drivers of epidemic
UNAIDS, 2008 [26]	Kenya	44.1% of incidence due to heterosexual sex within <u>regular partnership</u> & 20.3% to casual heterosexual sex
UNAIDS, 2008 [26]	Lesotho	23% due to sex with a single marital or cohabitating partner & 65% of incidence due to casual sex
UNAIDS, 2008 [26]	Uganda	43% new HIV infections in adults occurred in <u>discordant monogamous relationships</u> , 46% among persons reporting multiple partners and their partners, 10% due to sex work & 1% MSM and IDU
UNAIDS, 2008 [26]	Mozambique	48% incidence due to <u>steady partnerships</u> , 23% casual partnerships, 19% SW, 5% MSM, 3% IDU, & 2% medical injections
Dunkle et al, 2008 [8]	Kigali, Rwanda	92.5-92.7% of new HIV infections occur in <u>marriage/cohabitation</u>
Dunkle et al, 2008 [8]	Lusaka, Zambia	55.1-77.0% of new HIV infections occur in <u>marriage/cohabitation</u>
Gray et al, 2011	Rakai, Uganda	18.3% incident HIV during pre-ART & 13.7% during post-ART period occurred within <u>identifiable HIV serodiscordant couples</u> ; 29.3% incident HIV during pre-ART & 17.6% during post-ART period occurred among married individuals with a partner of unknown HIV status

Figure 1. Proportion of country-level HIV incidence due to transmission by stable discordant couples versus the proportion of the population in stable relationships lasting a year or more [42]



Abbreviations: SDC: stable discordant couples

Chapter 1: HIV-1 Prevention for HIV-1 Serodiscordant Couples

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HIV-1 Prevention for HIV-1 Serodiscordant Couples

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Abstract

A substantial proportion of HIV-1-infected individuals in sub-Saharan Africa are in stable relationships with HIV-1-uninfected partners, and HIV-1 serodiscordant couples thus represent an important target population for HIV-1 prevention. Couple-based HIV-1 testing and counseling facilitates identification of HIV-1 serodiscordant couples, counseling about risk reduction, and referrals to HIV-1 treatment, reproductive health services, and support services. Maximizing HIV-1 prevention for HIV-1 serodiscordant couples requires a combination of strategies, including counseling about condoms, sexual risk, fertility, contraception, and the clinical and prevention benefits of antiretroviral therapy (ART) for the HIV-1-infected partner; provision of clinical care and ART for the HIV-1-infected partner; antenatal care and services to prevent mother to child transmission for HIV-1- infected pregnant women; male circumcision for HIV-1-uninfected men; and, pending guidelines and demonstration projects, oral pre-exposure prophylaxis (PrEP) for HIV-1-uninfected partners.

Introduction

Sub-Saharan Africa has the highest prevalence of HIV-1 globally and has high incidence with approximately 1.8 million new HIV-1 infections in 2009 [27]. All HIV-1 transmissions occur from an infected to an uninfected partner, but sub-Saharan Africa is unique in that a high proportion of HIV-1 transmissions may occur in stable, long-term partnerships, in which one member is HIV-1-infected (i.e., an HIV-1 serodiscordant couple). We focus this review on HIV-1 prevention in HIV-1 serodiscordant couples, with an emphasis on sub-Saharan Africa. We address testing, couples counseling, and prevention interventions, including recent evidence of the strong prevention benefits of antiretroviral therapy (ART) for the HIV-1-uninfected partner [2] and pre-exposure prophylaxis (PrEP) for the HIV-1-uninfected partner [28]. We also review prevention strategies based on modifiable biological risk factors (e.g., lack of male circumcision) and behavioral risk factors (e.g., lack of condom use, multiple partners) associated with HIV-1 transmission in couples (Table 3).

Epidemiology of HIV-1 serodiscordance among heterosexual African couples

HIV-1 serodiscordance is common in sub-Saharan Africa. National population surveys and epidemiologic studies indicate that the majority of African HIV-1-infected individuals are married or in a stable, long-term relationship [29-31], and approximately half of couples in which at least one partner is HIV-1-infected are HIV-1 serodiscordant [6, 30, 32], resulting in 2-8% of all stable couples being HIV-1 serodiscordant in some settings [30, 31, 33]. Mathematical models suggest that a substantial proportion of new HIV-1 infections occur among HIV-1 serodiscordant couples in Africa, demonstrating that HIV-1 serodiscordant couples are an important population for HIV-1 prevention [26, 34, 35]. Women are equally likely as men to be the HIV-1-infected member in a serodiscordant couple [36].

Many HIV-1 serodiscordant couples are unaware of their serodiscordant status, primarily because one or both partners have not been tested or have tested separately and not disclosed their HIV-1 status to their partner. More than three-quarters of stable couples with at least one HIV-1-infected partner sampled in nationally representative HIV-1 serosurveys in Kenya [31], Malawi [29], and Uganda [6] were unaware of their partner's HIV-1 status. Moreover, couples often report low levels of condom use; across five African countries, fewer than 11% of cohabiting couples reported condom use at last sex [29, 30]. Finally, the term 'stable HIV-1 serodiscordant partnerships' does not capture the reality of dynamic partnerships, as indicated by viral linkage of transmission pairs from recent studies of HIV-1 serodiscordant couples, which documented that 25-29% of HIV-1 transmissions occur from an outside partner [2, 37]. Some of these HIV-1 transmissions occurred after dissolution of the HIV-1 serodiscordant partnership and formation of a new partnership, often with someone of unknown HIV-1 serostatus, with whom they were less likely to use condoms [38].

Couples HIV Testing and Counseling (CHTC)

HIV-1 testing is the essential first step in the identification of HIV-1 serodiscordant couples, and disclosure is facilitated if couples test for HIV-1 together with a counselor trained in pre- and post-test counseling techniques for couples, called Couples HIV Testing and Counseling (CHTC) [39, 40]. The Centers for Disease Control and Prevention (CDC) curriculum for CHTC training has been used in many parts of sub-Saharan Africa, and has recently been adapted for brief counseling in clinical settings [41]. Couples counseling involves risk assessment with sensitivity in order to foster facilitated disclosure, avoid blame, and provide counseling messages about HIV-1 serodiscordance and referral for HIV-1 care and prevention (Figure 2) [42-45]. Importantly, knowledge of serostatus within serodiscordant couples is likely a highly

effective HIV-1 prevention strategy. African and U.S. HIV-1 serodiscordant couples who have received CHTC report increased condom use, contraceptive use, and uptake of prevention of mother-to-child transmission (PMTCT) services [43-49]. HIV-1 transmission rates were as high as 20-25% per year among HIV-1 serodiscordant couples unaware of their HIV-1 status and before ART scale-up in Africa [43, 50]. In contrast, annual HIV-1 incidence rates of 6% were observed in couples who had participated in CHTC in an observational study [43] and 2% a randomized trial of a biomedical HIV-1 intervention among HIV-1 serodiscordant couples [37]. Facilitated disclosure of serostatus within a stable partnership also fosters family support, which has been associated with improved engagement in HIV-1 care for HIV-1-infected partners and high adherence to ART [51, 52].

The counselors who communicated with thousands of African HIV-1 serodiscordant couples in the multi-site Partners in Prevention HSV/HIV Transmission Study and Partners PrEP Study indicate that denial, disbelief, and misconceptions about discordance are frequently encountered and require additional counseling. Common reactions expressed by couples upon learning their HIV-1 serodiscordant status include disbelief in the accuracy of the test results, desire for re-testing in hope of a different outcome, anger, blaming their partner for infidelity, sadness, fear, and concerns about their children's HIV-1 status. Studies in Kenya and Uganda found that misconceptions about HIV-1 serodiscordance were common among health care providers (e.g., that HIV-1 serodiscordance reflect that the HIV-1-uninfected partner is in the 'window period' of seroconversion and is always already infected) as well as among the newly-identified HIV-1 serodiscordant couples (e.g., believing that the HIV-1-uninfected partner is immune or has undetectable and latent virus) [53, 54].

HIV-1 serodiscordant couples have a range of needs that emerge after the initial couples counseling and testing session and are critical to ongoing HIV-1 prevention and treatment. Couples learning of their HIV-1 serodiscordance cannot be expected to retain all messages

from the first counseling session, and may need additional support to understand that HIV-1 serodiscordance is common and does not reflect inaccurate test results or immunity for the uninfected partner. Common challenges reported by HIV-1 serodiscordant couples include feeling isolated, fear of disclosing their serodiscordance, personal desires and family pressures to have more children, relationship discord over perceived infidelity and blame, union dissolution, and in some cases physical violence and threats over refusal to have sex [54-57]. Some studies have found higher rates of divorce, separation, and intimate partner violence among HIV-1 serodiscordant couples than among HIV-1 seroconcordant couples, although most reports have found intimate partner violence to be relatively rare [54, 58-60]. Counselors can identify couples at risk of violence based on a history of abuse, help ensure safety and care for those who experience violence, and make appropriate referrals, including peer support groups for HIV-1 serodiscordant couples [61].

HIV-1 re-testing is suggested for HIV-1 serodiscordant couples, as with other populations at high risk of exposure to HIV-1, in order to promote early detection of HIV-1 infection and timely referral to care and treatment [62]. The World Health Organization (WHO) recommends that individuals with a known HIV-1-infected partner re-test in four weeks to assess for recent HIV-1 transmission and annually thereafter if they continue to be sexually active [62]. The frequency of HIV-1 testing for the HIV-1-uninfected partner couple should typically be annual, and informed by the couples' risk of transmission, fertility intentions, and symptoms suggestive of acute HIV-1. Messages about referrals for care, support in disclosure, initial relationship concerns, and methods to reduce risk of HIV-1 transmission should be reinforced at follow-up counseling and testing visits. Clinical follow-up for the HIV-1-infected partner should be emphasized and include a) CD4 cell count testing and evaluation of their eligibility for ART according to national policies to ensure timely initiation and ongoing adherence, b) correct and consistent condom use, c) discussion of family planning, safe conception, and pregnancy, and d) PMTCT for HIV-1-

infected pregnant women (Figure 2) [63]. In addition, prevention strategies should be recommended for the HIV-1 uninfected partner, including condoms, male circumcision, and PrEP, as it becomes available (Figure 2).

Antiretroviral-based strategies to reduce HIV-1 transmission in serodiscordant couples

Antiretroviral therapy for HIV-1-infected partners

ART dramatically improves the health and survival of HIV-1- infected individuals [64, 65] and also significantly reduces their infectiousness and likelihood of transmitting HIV-1 to partners (Table 4) [2, 37, 66-68]. A recent multi-national randomized clinical trial (HPTN 052) with HIV-1 serodiscordant couples demonstrated that early initiation of ART between CD4 counts of 350-550 cells/mm³ reduced the risk of HIV-1 transmission by 96%, compared to delayed ART initiation at CD4 of 250 cells/mm³ [2]. Importantly, HPTN 052 used intensive measures throughout the study to maximize the prevention benefits of ART: quarterly viral load monitoring and enhanced adherence counseling for those who had detectable HIV-1 RNA on ART. Thus, HPTN 052 demonstrates that ART markedly reduces HIV-1 transmission, if adherence is sufficient to achieve and sustain virologic suppression. Encouraging data from observational studies of HIV-1 serodiscordant couples, in which ART was provided following national guidelines and with less intensive adherence counseling and typically without virologic monitoring, found 80-92% reduction in HIV-1 transmission from HIV-1-infected patients who initiated ART [66-69].

The WHO will be releasing guidelines on CHTC which will include recommending earlier ART for serodiscordant couples to reduce transmission to HIV-1-uninfected partners. Expanded use of ART for HIV-1 prevention will require careful analysis of resources and implementation strategies, including ethical, programmatic, and cost factors of earlier ART for HIV-1-infected

partners who are in a serodiscordant partnership. A mathematical model predicted that treating HIV-1 serodiscordant couples in countries like Malawi and Lesotho, with high HIV-1 prevalence (7.1% and 19.5%) and where a large percentage of couples are serodiscordant (9.7% and 13.6%), could result in a substantial reduction in population-level HIV-1 incidence [70]. Primary prevention strategies will also be needed for HIV-1 serodiscordant couples, as ART will not protect those who become infected from outside or new partners, which accounted for 25-29% of HIV-1 transmissions in HPTN 052 and the Partners in Prevention HSV/HIV Transmission Study [37, 71], but will be preventive for new partners of the HIV-1 infected partner on ART for prevention.

The success of ART for HIV-1 prevention depends on key implementation factors, including earlier identification of HIV-1-infected persons so that they can promptly initiate ART when they meet national guidelines and retention in care both pre- and post-ART, sustained adherence to ART, minimizing drug resistance, and reducing rates of treatment failure. These challenges will require expanded HIV-1 testing initiatives, strong linkages to care, and effective follow-up of HIV-1 infected persons who do not yet meet national ART guidelines. An additional consideration will be the acceptability and willingness of HIV-1-infected partners to initiate ART when they are asymptomatic. Importantly, some studies have found a substantial minority of HIV-1-infected persons who are aware of being in an HIV-1 serodiscordant partnership, are reluctant to initiate ART, as demonstrated by 37% of HIV-1-infected partners eligible for ART in a cohort of Kenyan HIV-1 serodiscordant couples who did not initiate ART within 1 year of referral for free treatment [15]. Higher CD4 count (>100 cells/mm³) and lower socioeconomic status, measured in home ownership and rent cost, were strong predictors of non-initiation of ART [15]. In addition to economic obstacles and structural challenges such as drug stock-outs, fear of ART side effects, stigma and disclosure, concerns over sustainability of care, food insecurity, and preference for alternative medicines pose barriers to ART initiation and ongoing

adherence [72]. However, if these barriers can be overcome through counseling, other support, and strengthening of health care systems, HIV-1 infected partners who initiate ART could benefit from adherence support and involvement of their partner [51, 52].

Pre-exposure prophylaxis

Topical and oral tenofovir (TDF)-based PrEP have shown substantial efficacy in some but not all trials (Table 4). Relevant to the focus of this review, in the Partners PrEP Study, daily oral TDF and FTC/TDF were shown to have 62% and 73% efficacy, respectively, among HIV-1-uninfected partners in East African HIV-1 serodiscordant couples [28]. Very high adherence to study drug was observed in the Partners PrEP Study [73], with qualitative interviews indicating that adherence to pill-taking was fostered by support from their partner [74]. Peri-coital use of vaginal 1% tenofovir gel showed a 39% reduction in HIV-1 acquisition and 51% reduction in HSV-2 acquisition among South African women in the CAPRISA 004 study [75]. Daily oral emtricitabine/tenofovir (FTC/TDF) was shown to have an efficacy of 44% among men who have sex with men in the multinational iPrEx study [23] and 62% in young heterosexuals in Botswana [76]. In contrast, FEM-PrEP, a trial of daily oral FTC/TDF in high-risk women was recently stopped early due to lack of efficacy [77] and the daily oral tenofovir and daily vaginal 1% tenofovir arms of the VOICE trial were stopped due to inability to demonstrate efficacy in HIV-1 prevention [78]. Further data, available in 2012, will be important to understand whether lack of efficacy in the FEM-PrEP and VOICE trials was due to insufficient adherence or other biological and behavioral factors.

A rapid review ('rapid advice') of the PrEP efficacy data, including guidelines about PrEP for HIV-1 serodiscordant couples, will be issued by the CDC and WHO in 2012. It is important to consider both the prevention promise and the implementation challenges of PrEP among HIV-1

serodiscordant couples, for whom the efficacy data are substantial, and interest and adherence could be high. Demonstration projects for PrEP in serodiscordant couples will need to implement CHTC with messages about ART-based prevention and evaluate targeting of PrEP to highest-risk couples, cost-effective delivery strategies, adherence support tools, and provision of a comprehensive risk reduction package [79-83]. The use of PrEP in HIV-1 serodiscordant couples should be considered as part of a combination HIV-1 prevention strategy; PrEP could be most appropriate as an effective biomedical prevention strategy under the control of the HIV-1 uninfected partner if their HIV-1 infected partner is not on ART, not adherent with ART, or if they have multiple partners or partners of unknown HIV-1 status. Mathematical modeling suggests that a cost-effective 'staged' use of antiretrovirals for HIV-1 prevention could involve PrEP by the HIV-1 uninfected partner in a serodiscordant relationship before the HIV-1 infected partner initiates ART, with PrEP discontinuation a few months after ART is started (to allow time to achieve viral suppression) [84]. Based on the high levels of efficacy of PrEP observed in the Partners PrEP Study and assuming PrEP costs less than 40% that of ART, PrEP could be as cost-effective, and potentially cost-saving, if very high-risk couples are targeted, as a prevention strategy for couples compared to ART initiated before CD4 of 350 cells/ μ L for the HIV-1 infected partner [84].

Family planning safe pregnancy, and prevention of mother to child transmission (PMTCT)

Many HIV-1 serodiscordant couples have high fertility; both HIV-1 infected and uninfected partners often report desires for having children with their partner [85-88]. Over half of serodiscordant couples recruited from HIV-1 care centers in Uganda wished to have children in the future [89]. Regardless of fertility intentions, rates of highly effective contraception are often low and there are high rates of pregnancy among women of reproductive age in sub-Saharan

Africa [90, 91]. Annual pregnancy rates among HIV-1 serodiscordant couples were 16.0% in the Partners in Prevention HSV/HIV Transmission Study and 9.7% in an observational cohort in Kenya [91, 92]. Pregnancy is a time of increased risk of sexual HIV-1 transmission and acquisition; pregnant women had a two-fold increased risk of male-to-female and female-to-male HIV-1 transmission in the Partners in Prevention HSV/HIV Transmission Study [88].

Counselors and clinicians need to assess fertility intentions of HIV-1 serodiscordant couples and discuss contraceptive choices for couples not desiring children and safe conception strategies for couples who plan to have children. Less than two-thirds of women in HIV-1 serodiscordant couples surveyed in Rwanda and Zambia had ever used any contraceptive method, despite high awareness of contraception, with many citing concerns with side effects [93]. HIV-1 serodiscordant couples' childbearing desires are not always expressed to their health care providers [86]. Health care workers' knowledge may be incomplete and perpetuate misconceptions, and women may feel pressured by providers to terminate pregnancy or not report pregnancy intentions if they are HIV-1-infected [90, 94, 95]. An intervention that provided family planning counseling and free contraception to HIV-1 serodiscordant couples in Thika, Kenya led to significant declines in pregnancy and sustained high reports of condom use [96]. Thus, it is important to ascertain fertility desires of HIV-1 serodiscordant couples, counsel about available data on HIV-1 transmission risks during pregnancy, and encourage dual condom and contraceptive use for those not wanting to conceive [88, 97]. HIV-1 serodiscordant couples who do not want to conceive should be provided a choice of contraceptive options, including long-acting methods such as IUDs and implants.

HIV-1 serodiscordant couples who wish to conceive must consider options to reduce the risk of HIV-1 transmission to the HIV-1 uninfected partner. When intrauterine or intravaginal insemination is unavailable or too expensive, low technology options to reduce the risk of transmission during conception should be discussed, including delaying unprotected sex until

viral load is suppressed using ART for the infected partner, screening and pre-treatment for sexually transmitted infections that might facilitate HIV-1 transmission, limited and timed unprotected sexual encounters, and male circumcision if the man is HIV-1 uninfected [98]. Safe conception may be feasible when the HIV-1 infected partner is virally suppressed on ART [99, 100]; a Swiss study of 46 HIV-1 serodiscordant couples noted no seroconversions when the HIV-1-infected male partners were on fully suppressive ART, practiced timed intercourse, and used PrEP pericoitally [101].

Further evaluation of antiretroviral-based prevention is warranted, including ART for the HIV-1 infected partner or periconception PrEP in the HIV-1 uninfected partner if their partner is not on ART or virally-suppressed, in combination with timed unprotected intercourse during the most fertile days of the menstrual cycle [101, 102]. Advantages of periconception PrEP include autonomy of administration, which is important for HIV-1 uninfected partners, and shorter period of use which would have lower costs and may be associated with higher adherence than continuous PrEP [102].

Behavior change

Behavior change strategies available to HIV-1 serodiscordant couples to prevent HIV-1 transmission include sexual abstinence, correct and consistent condom use, and reduction of outside sexual partnerships. Couples-focused HIV-1 prevention behavioral interventions have reduced reported unprotected sex and dramatically increased reported condom use [43, 45-47]. In some studies, couples where the man was HIV-1 uninfected had higher sustainability of condom use than couples with an HIV-1 uninfected woman [43, 45]. In the Partners in Prevention HSV/HIV Transmission Study, in which HIV-1 serodiscordant couples received monthly risk reduction counseling and free condoms, self-reported unprotected sex decreased

from 29% at baseline to 7% over up to 24 months of follow-up ($p < 0.001$) [37]. Correct and consistent use of condoms is a highly effective tool for HIV-1 prevention; analyses from the Partners in Prevention HSV/HIV Transmission Study found that male condoms were associated with 79% lower risk of HIV-1 transmission on a per-contact basis [103]. However, introducing condoms into a long-term sexual relationship can be challenging. Couples often stop using condoms when they commit to a partner and if they are trying to conceive [104]. Additional challenges include perceptions that condoms interfere with sexual pleasure, spontaneity, and are a cause of sexual dysfunction [55, 104, 105]. Finally, alcohol use has been linked to unprotected sex in serodiscordant couples [106-108]. Couples should be counseled about the high efficacy of condoms for HIV-1, STIs and pregnancy, how condoms can enhance sexual pleasure by reducing anxiety about risk of HIV-1 transmission and pregnancy, and can become a symbol of love and commitment to the partner's well-being [109].

Sexual abstinence is an effective strategy to eliminate risk of HIV-1 transmission, but it may not be a desirable or feasible, life-long strategy for many couples [54, 104]. Cultural and social norms of sex and childbearing within marriage and long-term relationships, as well as personal desires to conceive, present a major impediment to sexual abstinence for couples. Sexual partners outside of the marriage or primary relationship present additional risks for HIV-1 infection. HIV-1 uninfected partners may perceive new outside partners to be a safer option for unprotected sex than their infected partners. The Partners in Prevention HSV/HIV Transmission Study and HPTN 052 study found through viral linkage that 25-29% of HIV-1 infections were from outside partnerships [2, 37]. In the Partners in Prevention HSV/HIV Transmission Study, a significant increase in reported new partnerships was observed, however, most of these were not concurrent or overlapping partnerships and most were reported after partners reported no longer having sex with their known HIV-1 infected partner [38]. Condom use was reported to be much lower with their new partners than with their known HIV-1 infected partners. Some prior

studies have noted lower reported condom use during extramarital sex [45, 110]. Risk reduction counseling for HIV-1 uninfected partners in serodiscordant relationships should emphasize the risk of infection from any unprotected sex and encourage HIV-1 testing, disclosure, and protection with all sex partners.

Male circumcision

Three randomized controlled trials provide strong evidence that male circumcision reduces the risk of female-to-male HIV-1 transmission by 50-60% [111-113]. Circumcision is not generally recommended for HIV-1-infected men, given conflicting evidence between observational data and a clinical trial in terms of reduced male-to-female HIV-1 transmission [42, 114, 115]. However, male circumcision should be strongly promoted for HIV-1 serodiscordant couples in which the male partner is HIV-1 uninfected and uncircumcised. HIV-1 discordant couples may also represent early adopters of infant male circumcision: over 90% of HIV-1 serodiscordant couples in Uganda were interested in circumcision for their male children for HIV-1 risk reduction [116].

Screening and treatment of sexually transmitted infections

The treatment of sexually transmitted infections in HIV-1 infected persons lowers genital viral load in most studies. Studies of stable HIV-1 serodiscordant couples suggest that the prevalence of curable STIs is low [117] and thus not a major driver of HIV-1 transmission within couples. However, treatment of STIs, when detected through laboratory screening or by symptomatic assessment, particularly in HIV-1 infected partners, should be done. Herpes simplex virus type 2 (HSV-2) infection is highly prevalent in HIV-1 serodiscordant couples, but

acyclovir (400 mg bid) did not reduce HIV-1 transmission in three efficacy trials of HSV-2 suppression for HIV-1 prevention [37, 118, 119]. A recent cross-over study indicates that higher doses of HSV-2 suppression achieved $>1 \log_{10}$ reduction in plasma HIV-1 levels [120]; further consideration of higher doses of herpes suppression as a pre-ART intervention to reduce HIV-1 disease progression and infectiousness may be warranted.

Conclusion

HIV-1 prevention within HIV-1 serodiscordant couples encompasses a combination of strategies tailored to their needs and fertility intentions, including CHTC, disclosure of HIV-1 test results, condom promotion, ART for the HIV-1 infected partner, contraceptive use or safe conception strategies depending on their fertility intentions, male circumcision for HIV-1 uninfected male partners, treatment of sexually transmitted infections, and potentially, pending guidelines and demonstration projects, the use of PrEP by the HIV-1 uninfected partner. Couples HIV-1 testing and counseling is a fundamental core of HIV-1 prevention that needs to be scaled up, particularly in high prevalence settings in sub-Saharan Africa. Scale-up of counselor and clinician training in CHTC is needed to build skills in risk assessment, facilitated disclosure, discussion of HIV-1 serodiscordance and risk reduction strategies, and addressing the common challenges faced by HIV-1 serodiscordant couples. HIV-1 testing programs must ensure that knowledge of HIV-1 serostatus is coupled with strong linkages with ART and PMTCT programs and referrals for HIV-1 uninfected persons to effective prevention interventions. Partner testing should be consistently promoted and strongly encouraged in HIV-1 care settings. Forthcoming WHO guidelines will provide recommendations based on the recent HPTN 052 and Partners PrEP Study findings of significant efficacy of antiretrovirals to reduce HIV-1 risk within HIV-1 serodiscordant couples [40]. Implementation of ART for HIV-1-infected

partners and PrEP for HIV-1 uninfected partners in HIV-1 serodiscordant couples must be informed by public health impact modeling, cost-effectiveness analyses, and demonstration projects. Antiretroviral-based strategies will be an important part of combination HIV-1 prevention among HIV-1 serodiscordant couples, delivered in the context of scale-up of couples HIV-1 testing and counseling to maximize the prevention impact of these effective biomedical tools.

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Table 3. Epidemiology of HIV-1 discordance among heterosexual African couples

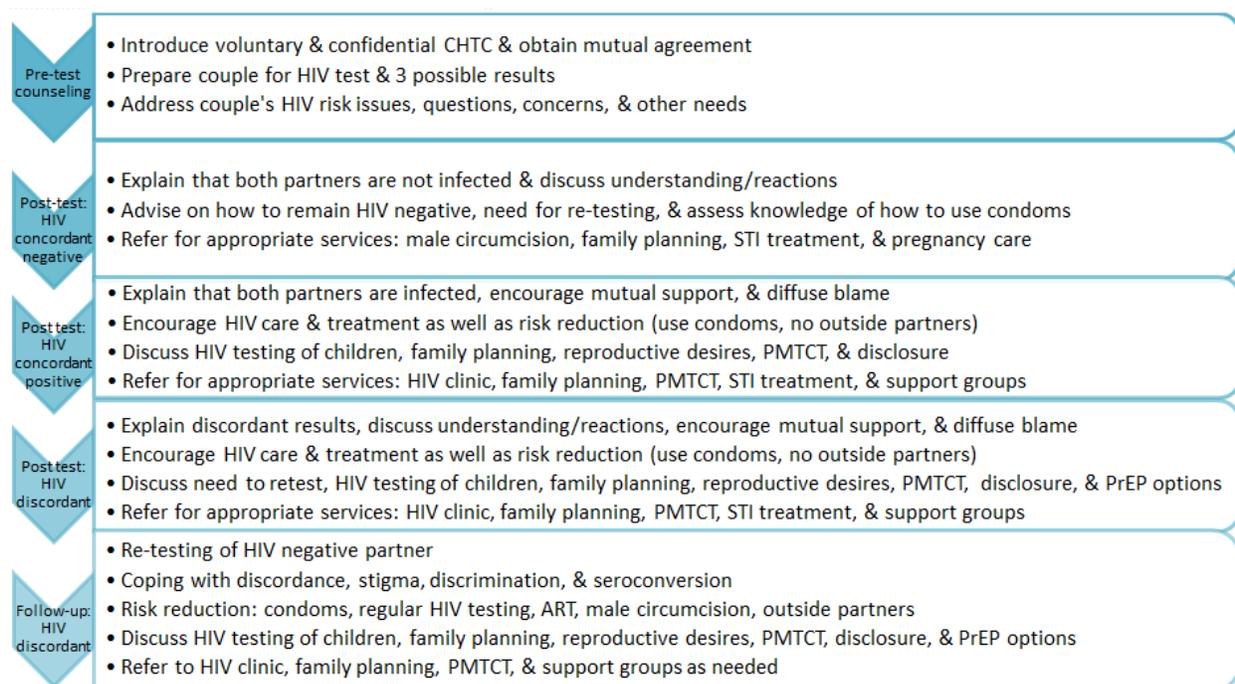
HIV-1 serodiscordance is common	
	<ul style="list-style-type: none"> ▪ Half to two-thirds of HIV-1-infected adults in a cohabiting relationship in Africa have an HIV-1-uninfected partner [6, 31-33] ▪ Population-based studies indicate that the HIV-1-uninfected partner in heterosexual serodiscordant couples is equally as likely to be male as female [36]
HIV-1 transmission rates are high	
	<p>HIV-1 incidence in studies with HIV-1 serodiscordant couples ranges from 2.0 to 11.8/100 person-years (p-y):</p> <ul style="list-style-type: none"> ▪ 2/100 p-y with regular counseling and provision of free condoms [2, 37] ▪ 4/100 p-y for men and 9/100py women in couples VCT cohort study[43] ▪ 8.7/100 p-y for men and 9.2/100py for women in a population-based cohort with low condom use [121] ▪ 11.8/100 p-y in a retrospective cohort prior to ART scale-up [122, 123]
There are modifiable risk factors for HIV-1 transmission	
Plasma viral load	<ul style="list-style-type: none"> ▪ High viral load is significantly associated with increased risk of transmission, with 2.3-2.5 increased risk per each log₁₀ increase in plasma viral [50, 122, 124]
ART use by HIV-1 infected partner	<ul style="list-style-type: none"> ▪ Early initiation of ART at CD4 350-550 cells/mL reduces risk of transmission to HIV-1-uninfected partners by 96% in context of viral load monitoring, adherence support and risk reduction counseling [37] ▪ Observational studies indicate 80-92% reduced HIV-1 transmission in context of ART use by HIV-1-infected partners without virologic monitoring [66-69] ▪ In one observational study, equal transmission rate from HIV-1-infected partners on & off ART in context of limited monitoring and adherence counseling [125]
Contraception	<ul style="list-style-type: none"> ▪ Effective methods can prevent unintended pregnancies ▪ Hormonal contraception associated with two-fold increased risk of HIV-1 acquisition and transmission among HIV-1 serodiscordant couples [97]; thus, dual condom use and contraceptive options need to be promoted
Pregnancy	<ul style="list-style-type: none"> ▪ Pregnancy in the HIV-1-infected or uninfected female associated with two-fold increased risk of male to female and female to male HIV-1 transmission [88]
Condom use	<ul style="list-style-type: none"> ▪ Low condom use among couples, especially among those unaware of their serostatus [6, 29, 43, 46, 121] ▪ Condom use is highly protective with 79% lower rate of transmission among HIV-1 serodiscordant couples on a per-act basis [103] ▪ Lower infection rates among couples reporting consistent condom use [43, 45, 125] ▪ Alcohol use associated with lower condom use [106]
Outside partners	<ul style="list-style-type: none"> ▪ Risk from outside partners of unknown HIV-1 serostatus with whom condom use is lower [38] ▪ Partners in Prevention HSV/HIV Transmission study: viral linkage indicates 29% of HIV-1 infections in serodiscordant couples were acquired from outside partners [37]. Most outside partnerships reported when the HIV-1-uninfected partner did not report sex with their known HIV-1- infected partner (i.e. were not concurrent) and condom use was lower with outside partners [38]. ▪ HPTN 052: viral linkage indicates 25% of HIV-1 transmissions from outside partners [2]
Male circumcision	<ul style="list-style-type: none"> ▪ Lack of male circumcision is associated with increased risk of HIV-1 acquisition in men and women [122, 123] ▪ Circumcision of HIV-1-uninfected men significantly reduced risk of HIV-1 acquisition [111-113] ▪ Observational data indicate circumcised HIV-1-infected men at lower risk of HIV-1 transmission to their female partners, most of whom were likely to have been circumcised prior to becoming HIV-1-infected [114], but circumcision of HIV-1-infected men did not reduce risk of transmission to female partners in randomized clinical trial [115]

Table 4. Antiretroviral-based HIV-1 prevention strategies for HIV serodiscordant couples

Trial	Population & Setting	Intervention	Status/Outcome
Partners PrEP Study [28]	4758 HIV-1 serodiscordant heterosexual couples in Kenya & Uganda	Daily oral TDF; daily oral FTC/TDF	62% (95% CI: 34-78%) reduction in HIV-1 in TDF arm 73% (95% CI: 49-85%) reduction in HIV-1 in FTC/TDF arm
HPTN 052 [2]	1763 HIV-1 serodiscordant couples with HIV-1-infected partners' CD4 count 350-550 in Botswana, Kenya, Malawi, South Africa, Zimbabwe, Brazil, India, Thailand, & U.S.	Immediate ART for HIV-1-infected partners with CD4 350-550 cells/mm ³ vs. ART at CD4 of 250 cells/mm ³ (delayed arm)	96% (95% CI: 73-99%) reduction in HIV-1 among early ART arm

Abbreviations: ART: antiretroviral therapy, PrEP: pre-exposure prophylaxis, TDF: tenofovir; FTC: emtricitabine

Figure 2. Couples HIV-1 testing and counseling topics [39]



Abbreviations: CHTC: couples HIV testing and counseling, STI: sexually transmitted infections, PMTCT: prevention of mother-to-child transmission, PrEP: pre-exposure prophylaxis, ART: antiretroviral therapy

Chapter 2: Daily short message service surveys to measure sexual behavior and pre-exposure prophylaxis use among Kenyan men and women

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**Daily short message service surveys to measure sexual behavior and pre-exposure
prophylaxis use among Kenyan men and women**

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Abstract

Pre-exposure prophylaxis (PrEP) is a novel HIV prevention strategy which requires high adherence. We tested the use of daily short message service (i.e., SMS/text message) surveys to measure sexual behavior and PrEP adherence in Kenya. Ninety-six HIV-uninfected adult individuals, taking daily oral PrEP in a clinical trial, received daily SMS surveys for 60 days. Most participants (96.9%) reported taking PrEP on $\geq 80\%$ days, but 69.8% missed at least one dose. Unprotected sex was reported on 4.9% of days; however, 47.9% of participants reported unprotected sex at least once. Unprotected sex was not correlated with PrEP use (OR=0.95). Participants reporting more sex were less likely to report PrEP non-adherence and those reporting no sex were most likely to report missing a PrEP dose (adjusted OR=1.87). PrEP adherence was high, missed doses were correlated with sexual abstinence, and unprotected sex was not associated with decreased PrEP adherence.

Background

Antiretroviral pre-exposure prophylaxis (PrEP) is a novel HIV prevention strategy that is being investigated for optimal use. Recent clinical trials have demonstrated the efficacy of PrEP for HIV prevention, and implementation projects are underway to determine uptake of and adherence to PrEP outside of clinical trial settings [3, 21, 75]. Adherence to PrEP is key for effective HIV prevention, and understanding patterns of adherence related to sexual behavior may be especially important [24, 126, 127]. In addition, different options for effective PrEP delivery, including intermittent or coital-dependent dosing, are being investigated, but little is known about the potential for PrEP users to anticipate sexual activity, which would be necessary for non-daily PrEP use.

Mobile technologies offer promising possibilities in Africa and other low-income country settings for promoting and measuring health behaviors, with mobile phone text messaging, otherwise known as short message service (SMS), representing an emerging low-technology and low-cost option. Mobile phone ownership is common and rapidly growing in Africa – for example, of 43 million persons in Kenya, an estimated 29.2 million are mobile phone subscribers and 89% of the population has access to mobile phones [128]. Two randomized controlled trials conducted in Kenya have demonstrated increased antiretroviral therapy (ART) adherence through SMS interventions [129, 130]. SMS has also been used to conduct data collection, including medication adherence data [10, 11, 131] and for clinic visit reminders [132]. Health data collected through mobile devices can be received immediately and more frequently, allowing for medical providers to monitor behavior and outcomes remotely in “real time” [133].

We assessed the use of daily SMS surveys to measure sexual behavior and PrEP use in real time among HIV-uninfected members of HIV serodiscordant couples.

Methods

Participants

HIV-uninfected participants were recruited from the Thika, Kenya site of the Partners PrEP Study. Thika is a peri-urban and farming community 45 kilometers north of Nairobi. The Partners PrEP Study is a randomized, controlled trial of daily oral tenofovir and emtricitabine-tenofovir PrEP among 4,758 HIV serodiscordant couples in 9 sites in Kenya and Uganda; study procedures and eligibility criteria have been previously described [117]. In July 2011, the study demonstrated daily oral PrEP to be highly efficacious in preventing HIV [3]; participants were informed of the study results and the placebo arm was offered active PrEP. Data for this pilot evaluation study were collected between December 2011 and April 2012, when all HIV-uninfected participants were taking active PrEP (either tenofovir or emtricitabine-tenofovir).

Eligible participants were HIV-uninfected, taking PrEP, literate, owned a mobile phone that they did not share, knew how to send and receive SMS, had regular access to an electrical outlet to charge their phone, and had to respond to ≥ 5 of 7 daily surveys during the first week run-in of the SMS study.

Study design and procedures

The target sample size for this pilot evaluation was 100 participants. Study staff briefly described this study and offered enrollment to participants during clinical trial visits. At enrollment, after eligibility was confirmed and participants were trained on SMS study questions and procedures, participants selected a time for survey delivery (8:00, 12:00, or 20:00), language (English, Kiswahili, or Kikuyu), and an alpha or numeric password <8 digits. Participants then completed a practice survey on their phone. Surveys were automated to send daily for 60 days. The survey began with a password question (“what is your secret password?”) to ensure the intended user was completing the survey. An SMS encouraging participants to retry entering their password was sent up to two times upon receipt of incorrect passwords or non-response (after a 15 minute delay). After successful password completion, participants received sequential questions on sexual activity (question 1: “did you have sex yesterday?”), condom use (if “yes” to 1, question 2: “did you or your partner use a condom when you had

sex?”), expectation of sex (question 3: “do you think you will have sex tomorrow?”), and PrEP use (question 4: “did you remember to take your study pill yesterday?”). Accepted response options included 1 for “yes,” 2 for “no,” and 3 for “I choose not to respond.” The survey question was resent if the participant responded with anything other than “1”, “2”, or “3.” Participants received an SMS thanking them for their participation after successfully completing each survey. SMS responses received after survey completion prompted an SMS with a brief message and the number to a study mobile phone managed by staff. Participants were compensated with delivery of phone credit to their mobile phone twice a week: 5 Kenyan Shillings (KSH) (approximately 0.05 USD) for each SMS response and 50 KSH (approximately 0.50 USD) for each completed survey. On days selected by convenience, study staff conducted quality assurance interviews by phone after participant completion of the SMS survey to ask the exact same questions to later evaluate concordance; participants were randomly chosen to complete the interview and were contacted after the next SMS survey completed if they were unable to complete the interview on the first attempt.

SMS survey system

An SMS system for automated delivery and recording of SMS surveys and responses was developed (Dimagi, Inc., Cambridge, USA). The software was written using the RapidSMS open source framework. The SMS web database was hosted in an Amazon Elastic Compute Cloud (EC2) and messages were sent through the MACH SMS gateway. Study investigators could access the SMS web database to view survey responses, track survey completion by participant, day, and time, as well as send messages to participants and edit participant information (i.e., phone numbers, passwords) as needed.

Statistical analysis

Participant characteristics and survey responses were analyzed using descriptive statistics. Chi-square tests of homogeneity (frequency) and Wilcoxon-Mann-Whitney test

(medians) were used to compare characteristics of enrolled participants to those from the Thika site who did not participate in the study.

To assess correlates of unprotected sex and missed PrEP doses, univariate and multivariate generalized estimating equation (GEE) logistic models with robust standard errors were used to calculate odds ratios and 95% confidence intervals, taking into account within-individual correlation over time in the longitudinal dataset. Logistic regression analyses were restricted to surveys with “yes” or “no” responses; responses of “choose not to respond” were treated as missing data and no attempt was made to impute missing responses. An independent correlation structure was used for greatest flexibility, although GEE is not sensitive to the specification of correlation structure [134]. Covariates that were significant at $p < 0.10$ in univariate analyses were included in the respective multivariate models.

To compare reports of anticipated sex and actual sex, percent agreement and Kappa correlation coefficients, which correct for the proportion of agreement due to chance, were calculated. Lag variables were used to link reports of anticipated sex with reports of actual sex when participants had data for 3 consecutive days. Accurate sexual prediction was defined as agreement (“yes” or “no”) between expectation of sex (“tomorrow”) and sexual activity (“yesterday”) provided on SMS surveys 2 days apart.

Data were analyzed using STATA version 11.0 (College Station, Texas, USA).

Ethics

The University of Washington Human Subjects Review Committee and the Kenyatta National Hospital Ethics Review Committee approved the study protocol. The Partners PrEP Study is registered with ClinicalTrials.gov (NCT00557245). All participants provided written informed consent.

Results

Participant enrollment and characteristics

A total of 206 HIV-uninfected participants were approached for the study: 79 were ineligible, 17 declined, and 110 eligible participants were enrolled, of whom fourteen failed to meet the criterion of high response (≥ 5 of 7 daily surveys completed) during the first week run-in, resulting in 96 participants followed with daily SMS surveys for 60 days (Figure 3). The most common reasons for ineligibility were not knowing how to send SMS (42/79, 53.2%) and not owning a phone (28/79, 35.4%). One participant became pregnant and discontinued PrEP (a requirement of the parent clinical trial protocol), and thus stopped participation after 28 days in this SMS study.

The majority of the 96 participants were male (75.0%), married (96.9%), and earning some type of income (93.8%) (Table 5). The median age of participants was 33.3 (interquartile range [IQR]: 30.9-37.3) years and the median years in school was 11.0 (IQR: 8.0-12.0). When participants enrolled in the SMS study, they had been in the Partners PrEP Study clinical trial for a median of 2.1 years (IQR: 1.7-2.4). Based on monthly interviewer-administered questionnaires, only 8 (8.3%) reported unprotected sex with their HIV-infected study partner in the month prior to starting the SMS surveys and 7 (7.3%) reported sex with someone other than their study partner. The median number of sex acts in the prior month was 4.0 (IQR: 2.0-8.0). SMS survey participants ($n = 96$) tended to be younger (33.3 vs. 37.4 years, $P = 0.003$), had significantly more education (11 vs. 7 years, $P < 0.001$), and were more likely to have electricity (47.9% vs. 11.4%, $P < 0.001$) compared to other HIV-uninfected participants who were in the Partners PrEP Study clinical trial but were not eligible for the SMS study ($n=79$). Eligible participants who declined to participate or had poor response the first week ($n=31$) did not significantly differ from SMS survey participants ($n=96$) for any factors in Table 5.

Survey response rates

There were 5,760 daily surveys planned for delivery to the 96 participants over 60 days (Figure 3). Of these planned surveys, 5,412 were distributed, with the remainder failing to distribute due to technical errors (and, in the case of the participant who became pregnant,

study exit). A total of 5,085/5,412 (94.0%) distributed surveys were answered. The median number of unanswered surveys during the 60 day study period was 2 (IQR: 1-4); 20.8% (20/96) of participants completed every survey, 7.3% (7/96) had >10 unanswered surveys, and one participant had >20 unanswered surveys (1/96, 1.0%). Unanswered surveys were more likely to occur during later weeks of the study (test for trend, $P=0.02$).

Sexual behavior

Among 5,085 answered surveys, sex was reported on 1,686 days (33.2%) and unprotected sex was reported on 251 days (4.9%) (Table 6). Nearly half of participants (46/96, 47.9%) reported sex unprotected by a condom at least once during the 60 day study period. The proportion of participants reporting sex without a condom in the first 30 days of the SMS survey was significantly greater than the proportion who reported unprotected sex in the previous month (with any partner) at the monthly clinic visit prior to enrollment in the SMS study (36.5% vs. 13.5%, $P=0.004$).

In multivariate analyses, unprotected sex was significantly correlated with not living with study partner, having 8 or more years of education, and reporting any weekly alcohol consumption (Table 7). Unprotected sex was not significantly associated with whether or not participants reported taking their PrEP medication that same day.

Prediction of Sex

The question about the expectation of sex was answered “choose not to respond” for 16.9% of days—a substantially higher proportion than any other survey question (Table 6). Among 3,716 surveys with a “yes” or “no” response to anticipated sex and subsequent report of sexual activity, there was 71.7% agreement (2,666/3,716 response matches) and a Kappa indicating fair agreement (Kappa=0.38, $Z=22.93$, $P<0.001$) between expected sexual activity and subsequently-reported sexual activity. Participants’ reported sexual expectations had a positive predictive value of 57.4% (95% confidence interval [CI] 54.7-60.1%; 760/1,325) and a negative predictive value of 79.7% (95% CI 78.1-81.3%; 1,906/2,391).

PrEP adherence

Among 5,085 answered surveys, participants reported missing a daily PrEP dose on 215 surveys (4.2%) (Table 6). However, of the 96 participants, 67 (69.8%) reported missing a PrEP dose at least once during the survey period. The median number of days that participants reported not taking PrEP during the 60-day study period was 2 (IQR: 0-4). Most participants reported taking PrEP on at least 80% (93/96, 96.9%) or 90% (80/96, 83.3%) of days. Most reports of non-adherence to PrEP (178/215, 82.8%) were isolated, with only 17.2% (37/215) of missed PrEP doses occurring on ≥ 2 consecutive days. Participants reporting no sex (odds ratio [OR] = 3.29, 95% CI 1.42-7.60, $P=0.005$), 1-10 sex acts (OR=2.93, 95% CI 1.76-4.87, $P<0.001$), or 11-20 sex acts (OR=1.96, 95% CI 1.09-3.56, $P=0.03$) were significantly more likely to miss a PrEP dose than participants reporting 20 or more sex acts during the study period (test for trend, $P<0.001$).

In multivariate analysis, sexual activity and living with study partner were predictors of PrEP adherence. Specifically, participants who did not report sex that day were significantly more likely to have missed that day's PrEP dose than those who had reported sex (adjusted odds ratio [AOR] = 1.87, 95% CI 1.35-2.60, $P<0.001$) (Table 8). Participants who were not living with their study partner were also significantly more likely to report non-adherence (AOR=2.09, 95% CI 1.15-3.78, $P=0.02$). Having a study partner on ART and having unprotected sex were not correlated with missing a PrEP dose.

Quality Assurance interviews

Study staff completed 101 quality assurance interviews by phone among 68 participants. The interviewer-administered question "did you have sex yesterday?" had 90.0% agreement (90/101 response matches) with the SMS response and a Kappa indicating substantial agreement (Kappa=0.78, $Z=7.97$, $P<0.001$). Responses to the condom use question had 100% agreement (29/29) and excellent agreement according to Kappa (Kappa=1.00, $Z=5.39$, $P<0.001$). The PrEP adherence question had 97.0% agreement (96/101) and an uninterpretable

Kappa (Kappa=-0.01, Z=-0.14, P=0.6) due to the highly skewed distribution of responses (e.g., 96 “yes” responses and 2 “no” responses).

Discussion

In this study, we demonstrated that SMS surveys elicited high response rates (>90%) and captured daily sexual behavior and PrEP adherence in an African heterosexual population. Our results suggest that SMS data collection of sensitive health information, such as sexual behavior and pill taking, is feasible and acceptable. Participants reported high adherence to daily oral PrEP – with higher sexual activity a strong predictor of greater daily PrEP adherence. Over a third of participants reported unprotected sex during the first 30 days of the study (and nearly half over the 60-day study period), which was over twice as many than at the monthly clinic visit prior to the study start. Notably, sex without a condom was not associated with reduced PrEP use. Finally, participants had difficulty predicting when they would have sex. Thus, SMS data collection provided frequent and timely accounts of health behaviors and appeared to provide high-quality self-reported data.

Previous studies employing two-way SMS communication in Africa have had varying response levels [10, 129, 131]. In a randomized controlled trial of weekly SMS questions to Kenyan ART patients over one year, approximately 76% of questions were answered in time [129]. That trial also reported high acceptance of SMS communication [129]. However, a study using daily SMS to collect sexual behavior data among HIV-uninfected men who have sex with men and female sex workers in Kenya had a median daily response rate of 33% [131]. In that study, participants were given mobile phones, SIM cards, and airtime, though many of them already owned phones and were familiar with SMS [131]. The high response rate found in the present study could reflect a selection only of adherent responders, a shorter survey period, use of own phone rather than study phone, a more stable telecom network, and/or a more technologically-savvy or motivated population.

Notably, participants more frequently reported unprotected sex in daily SMS surveys compared to monthly clinic reports. The sense of privacy and anonymity provided by mobile technology may have minimized social desirability bias, the tendency of respondents to report more favorable behaviors [12]. This has been noted for other technology-based sexual self-reported data collection, though not always consistently [135, 136]. Also, the reliability of data on sex frequency diminishes with longer periods of recall or more frequent sexual behaviors [12]. Daily SMS data collection thus may be both acceptable and collect more accurate data regarding sexual behavior in this population than periodic and face-to-face surveys.

Sex was strongly correlated with adherence to PrEP: there was higher PrEP use with daily sexual activity. In addition, participants who were not sexually active or having sex less frequently in the study were significantly more likely to report missing doses of PrEP than those who reported more frequent sex. Thus, PrEP adherence appeared to be greatest among participants most at risk of HIV infection. Importantly, there was high agreement between SMS responses to sexual behavior and PrEP adherence questions in the quality assurance interviews.

Results from this SMS survey and quality assurance interviews indicated that it was difficult for participants to accurately predict sexual activity, even within the context of daily behavioral surveys. The sexual expectations question resulted in the highest proportion of “choose not to respond” answers (16.9%). In addition, for those who answered the question in the affirmative, there was relatively low agreement between participants’ expectation of sex and reports of sexual activity and a positive predictive value below 60%. This population of HIV serodiscordant couples, with moderate frequency of sex, were better at accurately predicting when they would not have sex (negative predictive value = 79.7%) than when they would have sex (positive predictive value = 57.4%). These data suggest that daily PrEP dosing may be better at achieving optimal adherence than intermittent or peri-coital PrEP dosing regimens that depend on the ability to anticipate sex.

There were limitations and implementation challenges to this pilot study. The greatest limitation is the small, selected population – participants were enrolled in a clinical trial, literate, owned a mobile phone, and had a high response rate during the first week. Daily surveys may have served as reminders for condom use and adherence. Conduct of the study among clinical trial participants, who received monthly counseling on HIV risk reduction and PrEP adherence and who were highly motivated, may limit the generalizability of study findings to a broader research-naïve population. However, it should be noted that despite frequent counseling and high awareness of HIV prevention methods, nearly half of participants reported unprotected sex during the two months of the study. Resources did not allow for a comparison of self-reported PrEP adherence to biological measures of adherence and thus the accuracy of self-reported behaviors is unknown and a possible limitation. The frequent reporting of less socially desirable behaviors, such as missed PrEP doses (69.8% ever during the study period) and unprotected sex (47.9% ever during the study period), is notable. Also, the use of an existing cohort of clinical trial provided additional insight into PrEP use and sexual risk behavior among participants taking a known active drug. Missing data in bivariate analysis may have not been missing at random and may have introduced bias. However, the total proportion of missing and “choose not respond” replies was low (2.1% for condom use, 4.3% for PrEP use) and should not substantially affect the results. Finally, in future studies, systematic approaches to conducting quality assurance interviews may be valuable.

The study also faced a few implementation challenges: 1-2 hours twice a week of staff time for manual reimbursement for SMS responses, a few mobile phones reported lost by participants, and a temporary, mid-study block on survey delivery by one of the major mobile phone providers in Kenya. To our knowledge, the lost phones did not lead to any breach of sensitive information or other harmful consequences. Automated reimbursement for SMS responses and a locally hosted messaging system (versus a Kenyan phone card hosted in Europe, as was used in this study) could eliminate these challenges and increase response

rates. Inclusion of individuals who are illiterate or do not own mobile phones should be considered when planning mobile health interventions.

Conclusion

This study of PrEP use and sexual behavior among HIV-uninfected Kenyan men and women highlights the strengths and growing potential of daily SMS data collection. Reported PrEP adherence rates were high and sexual risk behavior was greater than anticipated from monthly interviewer-administered questionnaires. High response rates and participant retention provides evidence that SMS can be used to collect health data in this setting. Two-way SMS communication between research clinics or health facilities and patients may eliminate the need for certain types of visits, promptly identify potential health problems, and ultimately save time and money.

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Figure 3. Flow chart of participant enrollment, survey distribution and response rates

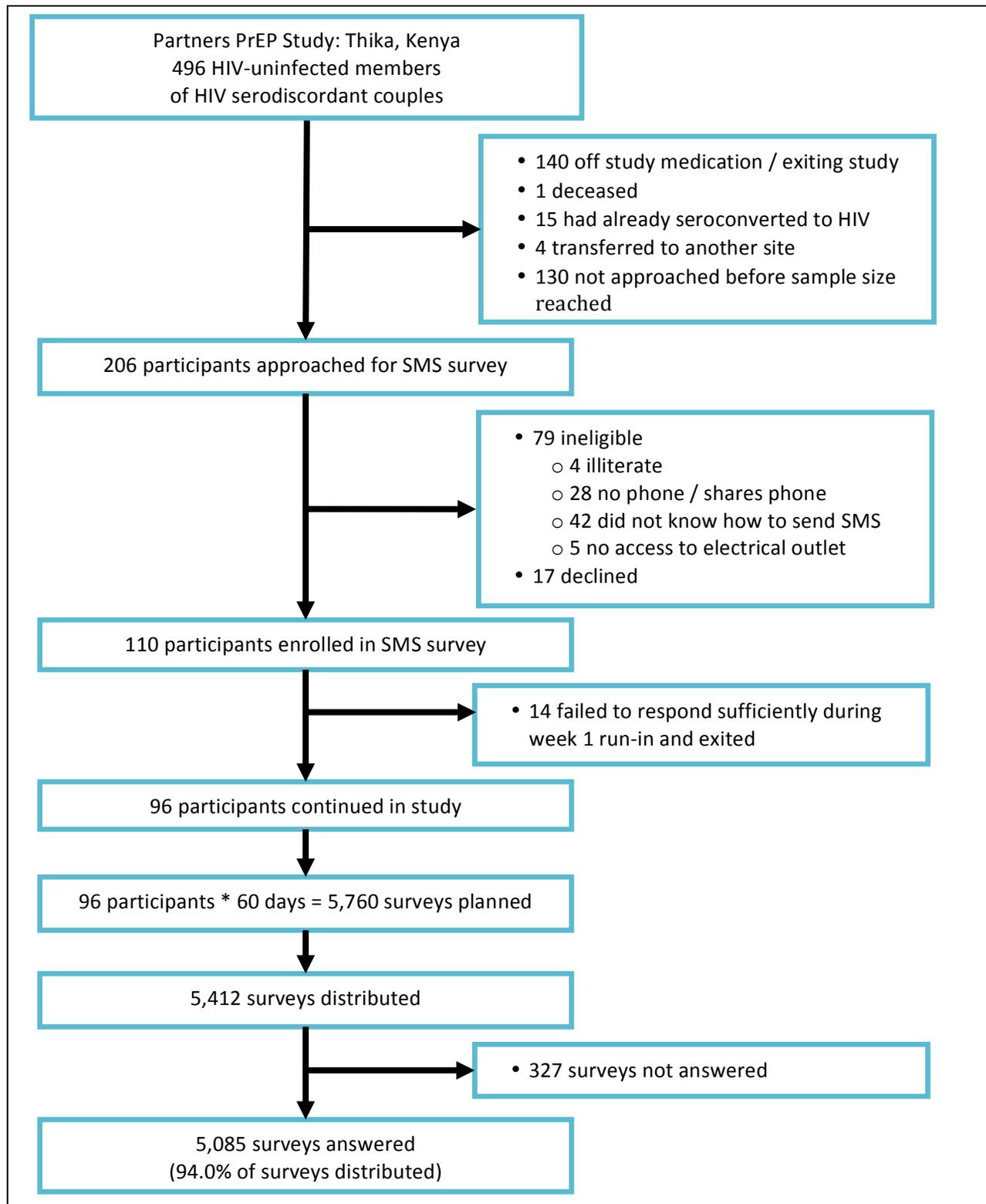


Figure 3 legend.

Flow chart of participant enrollment, survey distribution and response rates. The target sample size for this study was 100. Study staff approached Partners PrEP clinical trial participants for enrollment during their monthly clinic visits. Some participants had already completed maximum follow-up for the Partners PrEP Study clinical trial at the time this pilot evaluation was conducted. A total of 110 participants were enrolled in the study, of which 96 participants responded to ≥ 5 of 7 daily surveys during the first week run-in. Of 5,760 surveys planned for 96 participants over 60 days, 5,412 surveys were distributed, 32 surveys were cancelled after one participant exited due to pregnancy, and 316 surveys were not delivered due to a mid-study block by a local mobile phone provider.

Table 5. Socio-demographic and behavioral characteristics of participants (N = 96)

	N (%) or Median (IQR)
Male	72 (75.0%)
Age, years	33.3 (30.9 – 37.3)
Married	93 (96.9%)
Living with study partner	91 (94.8%)
Number of children with study partner	1 (0-2)
Number of years in school	11 (8-12)
Earning any income	90 (93.8%)
Electricity available in the home	46 (48.9%)
Time spent in Partners PrEP Study, years	2.1 (1.7-2.4)
HIV-infected study partner on antiretroviral therapy*	29 (30.2%)
Number of sex acts, prior month*	4 (2-8)
Any unprotected sex with study partner, prior month*	8 (8.3%)
Any sex with other partners, prior month*	7 (7.3%)
Any unprotected sex with any sexual partner, prior month*	13 (13.5%)

* Reported through interviewer-administered questionnaire at clinic visit prior to enrollment in text message survey.

Table 6. Text message survey questions, responses, and response rates among answered surveys (N = 5,085)

Survey Questions & Responses	N (%)
Did you have sex yesterday?	
Yes	1,686/5,085 (33.2%)
No	3,300/5,085 (64.9%)
Choose not to respond	92/5,085 (1.8%)
<i>Missing (question not answered)</i>	<i>7/5,085 (0.1%)</i>
Did you or your partner use a condom when you had sex?*	
Yes	1,399/1,686 (83.0%)
No	251/1,686 (14.9%)
Choose not to respond	8/1,686 (0.5%)
<i>Missing (question not answered)</i>	<i>28/1,686 (1.7%)</i>
Do you think you will have sex tomorrow?	
Yes	1,463/5,085 (28.8%)
No	2,678/5,085 (52.7%)
Choose not to respond	860/5,085 (16.9%)
<i>Missing (question not answered)</i>	<i>84/5,085 (1.7%)</i>
Did you remember to take your study pill yesterday?	
Yes	4,651/5,085 (91.5%)
No	215/5,085 (4.2%)
Choose not to respond	71/5,085 (1.4%)
<i>Missing (question not answered)</i>	<i>148/5,085 (2.9%)</i>

* Survey question dependent on “yes” response to previous question.

Table 7. Crude and adjusted odds ratios for reports of unprotected sex, for survey days when sex was reported

Correlates	Survey days N (%)*	Unprotected sex N (%)*	OR (95 % CI)	P	AOR (95% CI)**	P
Gender						
Male	1,254 (76.0)	205 (16.4)	1.49 (0.55, 4.01)	0.4		
Female	396 (24.0)	46 (11.6)	REF			
Age (years)						
<30	402 (24.4)	47 (11.7)	REF			
30-35	591 (35.8)	56 (9.5)	0.79 (0.23, 2.69)	0.7		
35+	657 (39.8)	148 (22.5)	2.20 (0.73, 6.61)	0.2		
Lives with partner						
Yes	1,580 (95.8)	216 (13.7)	REF		REF	
No	70 (4.2)	35 (50.0)	6.31 (1.24, 32.23)	0.03	3.88 (1.10, 13.67)	0.04
Children together						
Yes	966 (58.6)	167 (17.3)	REF			
No	684 (41.5)	84 (12.3)	0.67 (0.26, 1.75)	0.4		
Education						
5-8 years	725 (43.9)	53 (7.3)	REF		REF	
>8 years	925 (56.1)	198 (21.4)	3.45 (1.26, 9.46)	0.02	3.05 (1.16, 8.00)	0.02
Any monthly income						
Yes	1,540 (93.3)	232 (15.1)	0.85 (0.16, 4.60)	0.9		
No	110 (6.7)	19 (17.3)	REF			
Electricity at home						
Yes	803 (48.7)	129 (16.1)	REF			
No	847 (51.3)	122 (14.4)	0.88 (0.35, 2.19)	0.8		
Alcohol use (weekly)						
None	1,234 (74.8)	143 (11.6)	REF		REF	
Any	416 (25.2)	108 (26.0)	2.68 (1.01, 7.10)	0.05	2.63 (1.00, 6.90)	0.05
HIV-infected study partner on ART						
Yes	496 (30.1)	70 (14.1)	0.88 (0.30, 2.64)	0.8		
No	1,154 (69.9)	181 (15.7)	REF			
PrEP use (same day)						
Yes	1,540 (97.2)	227 (14.7)	REF			
No	45 (2.8)	10 (22.2)	1.65 (0.83, 3.28)	0.2		

OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; P: p value; ART: antiretroviral therapy; PrEP: pre-exposure prophylaxis.

* There were 1,650 surveys with “yes” or “no” responses for condom use; 8 “choose not to respond” responses and 28 unanswered questions were treated as missing data.

** Multivariate model includes lives with study partner, education, and alcohol use.

Table 8. Crude and adjusted odds ratios for reports of missing doses of PrEP

Correlates	Survey days N (%)*	Missed PrEP N (%)*	OR (95 % CI)	P	AOR (95% CI)**	P
Gender						
Male	3,685 (75.7)	145 (3.9)	REF		REF	
Female	1,181 (24.3)	70 (5.9)	1.54 (0.99, 2.40)	0.06	1.39 (0.90, 2.14)	0.1
Age (years)						
<30	1,025 (21.1)	51 (5.0)	REF			
30-35	1,842 (37.9)	79 (4.3)	0.86 (0.46, 1.60)	0.6		
35+	1,999 (41.1)	85 (4.3)	0.85 (0.49, 1.45)	0.5		
Lives with partner						
Yes	4,635 (95.3)	196 (4.2)	REF		REF	
No	231 (4.8)	19 (8.2)	2.03 (1.03, 4.02)	0.04	2.09 (1.15, 3.78)	0.02
Children together						
Yes	3,154 (64.8)	153 (4.9)	REF			
No	1,712 (35.2)	62 (3.6)	0.74 (0.40, 1.35)	0.3		
Education						
5-8 years	1,969 (40.5)	82 (4.2)	REF			
>8 years	2,897 (59.5)	133 (4.6)	1.11 (0.71, 1.73)	0.7		
Any monthly income						
Yes	4,572 (94.0)	194 (4.2)	REF		REF	
No	294 (6.0)	21 (7.1)	1.74 (0.93, 3.25)	0.09	1.52 (0.78, 2.95)	0.2
Electricity at home						
Yes	2,362 (48.5)	98 (4.2)	REF			
No	2,504 (51.5)	117 (4.7)	1.13 (0.71, 1.80)	0.6		
Alcohol use (weekly)						
None	3,711 (76.3)	170 (4.6)	REF			
Any	1,155 (23.7)	45 (3.9)	0.84 (0.50, 1.43)	0.5		
HIV-infected study partner on ART						
Yes	1,543 (31.7)	80 (5.2)	1.29 (0.82, 2.03)	0.3		
No	3,323 (68.3)	135 (4.1)	REF			
Sex (same day)						
Yes	1,598 (32.8)	46 (2.9)	REF		REF	
No	3,182 (65.4)	168 (5.3)	1.88 (1.34, 2.64)	<0.001	1.87 (1.35, 2.60)	<0.001
Unprotected sex						
Yes	237 (4.9)	10 (4.2)	0.95 (0.53, 1.72)	0.9		
No	4,629 (95.1)	205 (4.4)	REF			

OR: odds ratio; CI: confidence interval; AOR: adjusted odds ratio; P: p value; ART: antiretroviral therapy.

* There were 4,866 survey responses with “yes” or “no” responses for PrEP use; 71 “choose not to respond” responses and 148 unanswered questions were treated as missing data.

** Multivariate model includes gender, lives with study partner, income, and sex.

Chapter 3: Daily short message service surveys detect greater HIV risk behavior than monthly clinic questionnaires in Kenya

**Daily short message service surveys detect greater HIV risk behavior than
monthly clinic questionnaires in Kenya**

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Abstract

Background: Accurate measurement of HIV risk behaviors is challenging. Technology-based approaches offer novel opportunities to record behaviors in real-time, potentially reducing biases related to recall and social desirability that are inherent in other methods of self-report. We compared self-reported sexual and pill-taking behaviors collected over daily short message service (SMS, i.e., text message) to concurrent monthly questionnaires among HIV-uninfected Kenyan adults participating in a clinical trial of pre-exposure prophylaxis (PrEP).

Methods: Eighty-five participants contributed 145 observation-months. SMS data were collected daily through an automated survey; clinic-based questionnaires were completed monthly. We assessed agreement between reporting of sexual activity, sex unprotected by condoms, and missed PrEP doses.

Results: The proportion of observation-months with reports of any sex (93.8% vs. 85.5%), any unprotected sex (35.2% vs. 15.9%), or any missed PrEP doses (54.5% vs. 13.1%) were significantly greater by daily SMS data collection than monthly questionnaires, respectively (all $p < 0.0001$).

Conclusion: Daily SMS surveys delivered to personal mobile phones elicited significantly greater reports of sex, unprotected sex, and missed PrEP doses compared to monthly questionnaires, likely providing more accurate self-reported HIV risk behavior through enhanced privacy and reduced recall period. SMS diaries offer a promising method to assess sensitive or repetitive health behaviors (such as medication-taking) in real-time.

Key words: HIV prevention, pre-exposure prophylaxis, sexual behavior, adherence, survey methodology, reporting biases

Background

The measurement of sexual behavior in populations at risk of HIV has been critical to HIV epidemiology, targeting of HIV prevention responses, and monitoring potential risk compensation from HIV prevention interventions. However, measures of sexual behavior and repetitive prevention health behaviors often rely on self-report. Self-reported health behaviors are prone to error from inaccurate recall of repeated or less salient behaviors and social desirability, reporting, and telescoping biases, particularly for stigmatizing behaviors. A number of approaches to improving collection of sensitive behavioral data have been developed, including ecological momentary assessment technologies such as physiological sensors, daily or weekly diaries to shorten recall periods, and phone- or computer-assisted self-administered interviews (CASI) to remove the effect of the interviewer [137, 138]. Approaches that offer both short recall and privacy could have greater accuracy than approaches that rely on behaviors to be summarized over a longer period and/or reported in face-to-face interviews [139].

The use of electronic data capture to measure daily health behaviors have been described in a variety of settings: interactive voice response (IVR) and uni- and bi-directional short message service (SMS, i.e. text message) to measure antiretroviral therapy adherence [10], ecological momentary assessment of substance use over automated mobile phone calls [140], call-in reporting of smoking behavior [141], and hand held computers to record hemophilia home-therapy [133]. Electronic data capture of sexual and other HIV risk behaviors has been conducted through SMS and online surveys [11, 142, 143]. Coital diary data collected electronically can include automated prompts to complete surveys and time-stamps for when data are entered [136, 144, 145]. Precision in timing of sexual behavior may be valuable for identifying periods of HIV risk and correlating behaviors with use of HIV prevention interventions. There is a continued

need for methodological research to develop and evaluate reliable, cost-effective assessments of HIV risk behaviors [137, 139, 146].

We previously reported the results of a pilot evaluation of daily SMS surveys to measure sexual behavior and pill taking in a study of pre-exposure prophylaxis (PrEP) for HIV prevention among HIV uninfected members of HIV serodiscordant couples [147]. We found high response rates to daily SMS surveys, a positive correlation between sexual activity and PrEP use, no association between unprotected sex and PrEP use, and poor ability to predict sexual activity in the next day [147]. In the present analysis, we compare data collected by daily SMS from that study to concurrently-collected data measured by monthly counselor-administered questionnaires. We hypothesized that daily SMS data collection would reduce recall and social desirability biases, yielding greater reports of unprotected sex and missed PrEP doses than monthly, clinic-based questionnaires.

Methods

Participants

We conducted a study of daily SMS to collect sexual behavior and PrEP adherence data nested within the Partners PrEP Study, a randomized clinical trial of daily oral PrEP among African HIV serodiscordant couples. The ancillary SMS study was implemented at one peri-urban site in Kenya between December 2011 and April 2012, after the clinical trial demonstrated efficacy of PrEP for preventing HIV and participants had been offered active PrEP and continued follow-up [3]. The 96 participants included in the SMS study were HIV-uninfected, taking PrEP, literate, owned a mobile phone that they did not share, knew how send and receive SMS, had regular access to an electric outlet, and responded to ≥ 5 of 7 daily surveys during the first week run-in of the SMS study.

Study design and procedures

As part of the Partners PrEP Study clinical trial, monthly clinic visits were scheduled every 28 days (Figure 4). At these visits, nurse counselors administered standardized questionnaires to assess sexual activity (in the past month, how many times did you have sexual intercourse with your study partner? or someone other than your study partner?), condom use (how many times was a condom used?), and PrEP adherence (how many days did you take the study tablet?). The “past month” was defined as the period since the last regularly scheduled clinic visit.

During the SMS study, participants received computer-automated SMS surveys on their mobile phones at the same time every day for 60 consecutive days (Figure 4). After successfully answering a personal password question, questions about sexual activity (“did you have sex yesterday?”), condom use (if sex was reported then: “did you or your partner use a condom when you had sex?”), and PrEP adherence (“did you remember to take your study pill yesterday?”) were delivered sequentially. Participants were trained and reminded in each SMS survey question to respond 1 for “yes,” 2 for “no,” and 3 for “I choose not to respond.” In the SMS study, participants responded to 94.0% of daily surveys delivered to their mobile phones; non-response was most often related to disruption in survey delivery [147].

SMS study participants who completed monthly clinic visits during their participation in the 60-day SMS study were eligible for the present analysis which compared self-reported sex and adherence behaviors from daily SMS surveys to monthly clinic questionnaires. Monthly clinic visits were included in this comparison if 1) they occurred 21-35 days since the previous monthly clinic visit and 2) ≥ 21 SMS surveys were completed during the time period covered by the monthly clinic survey.

Statistical analyses

Participant characteristics and self-reported behavior were analyzed using descriptive statistics. To calculate the total behavior reported over one observation-month through daily SMS surveys, we summed the daily responses occurring between monthly clinic visits. Since the SMS question on sexual behavior asked only whether sex had occurred but not the number of acts, we assumed one vaginal or anal sexual act for each day that sex was reported. For daily SMS surveys that were not delivered or completed, we imputed the participant's mean daily value for each SMS survey outcome (sex, condom use, missed PrEP dose).

To assess agreement between daily SMS and monthly clinic-based self-reported behavior during the same observation-month, percent agreement and McNemar's χ^2 test statistic were calculated for binary outcomes (any sex, any unprotected sex, any missed PrEP doses). Concordance correlation coefficients (scaled indexes that measure the variation of a pair of values from the 45° line of perfect concordance [148]) were calculated for continuous outcomes (number of sex acts, number of unprotected sex acts, number of missed PrEP doses). Generalized Linear Latent Mixed Models (GLLAMM) were used to measure incidence rate ratios for continuous outcomes (using Poisson distribution and logistic link function), specifying unique participant observation-months as a random effect and survey method as a fixed effect [149]. Data were analyzed using STATA version 11.0 (College Station, Texas, USA).

Results

Study participants and survey inclusion

Of 179 observation-months occurring during the SMS study, 145 were included in this analysis; 34 months were excluded: 8 were shorter or longer than the defined time range (21-35 days); 26 had <21 SMS surveys completed between clinic visits (Figure 5).

The 145 observation-months were contributed by 85 participants: 64 contributed two observation-months and 17 contributed one observation-month. The median time period between clinic visits was 28 days (interquartile range [IQR]=28-28, range=23-34).

The majority of participants were male, married, and earning some income (Table 9). Over half lacked running water in their homes. They had a median age of 33 years and had been enrolled in the Partners PrEP Study for a median of 2.2 years. At SMS study enrollment, 30.6% of participants' HIV-infected partners had initiated antiretroviral therapy and 8.2% reported sex with someone other than their study partner in the previous month.

Participants completed a median of 27 daily SMS surveys (IQR=24-28, range=21-33) in each observation month. Survey responses were imputed for 275 missing daily SMS surveys (6.7% of 4,089 days covered during the 145 observation-months).

Sexual activity

The proportion of observation-months with any sex reported was higher when assessed by daily SMS data collection than by the monthly questionnaire (93.8% vs. 85.5%, $p=0.004$; Figure 6 and Table 10). There was 89.0% agreement between reporting any sex on the SMS survey and monthly questionnaire. For 14 observation-months (9.7% of 145), sex was reported by SMS survey but no sex was declared in the monthly questionnaires. Sex was reported on monthly clinic questionnaires but not on SMS surveys for just two observation-months (1.4% of 145).

The frequency of sex was greater by SMS than by monthly clinic-based questionnaire: participants reported a median of 9 sex acts per month over daily SMS surveys and a median of 5 sex acts through monthly interviewer-administered questionnaire (Table 10). A concordance correlation coefficient of 0.5 indicated poor

absolute agreement between the number of sex acts reported over the two survey methods. Figure 7a shows the majority of observations above the (dotted) line of perfect concordance, illustrating more reports of sex acts in daily SMS surveys compared to monthly questionnaires. Among the 145 observation-months, 25 (17.2%) had the same number of sex acts on both survey methods, 93 (64.1%) had greater reporting of sex in daily SMS surveys, while 27 (18.6%) had a greater report of sex on the monthly questionnaire. Overall, participants reported a median of 2 more sex acts per month on the daily SMS survey than the monthly questionnaire (IQR=0-5, range=-9-24); this resulted in a 1.5 fold increase (95% confidence interval [CI]: 1.3-1.7, $p < 0.001$) in the frequency of days with sex reported in the past month for SMS surveys compared to monthly questionnaires.

Condom use

There was only 71.0% agreement between participants' reports of any sex without a condom reported on daily SMS surveys and monthly questionnaires, and poor absolute agreement between total number of unprotected sex acts reported through daily SMS surveys and monthly questionnaires (Concordance Correlation Coefficient [CCC]=0.6). In daily SMS data, 35.2% of observation-months included reports of unprotected sex – twice as many as by monthly questionnaires ($p < 0.0001$, Table 10). On nearly a quarter of observation-months (35/145, 24.1%), SMS surveys included reports of sex without a condom when no unprotected sex was recorded on the monthly questionnaire.

The median number of unprotected sex acts in a month reported in both daily SMS surveys and monthly questionnaires was zero. Among 145 observation-months in the comparison analysis, 88 (60.7%) indicated the same number of unprotected sex acts reported in the past month on both survey methods. Participants reported a greater

number of unprotected sex acts through the daily SMS surveys for 41 observation-months (28.3%) and through monthly questionnaire for 16 observation-months (11.0%). Comparing SMS to monthly questionnaires, there was a slight but non-statistically significant increase in days with unprotected sex reported in the past month (Incidence Rate Ratio [IRR]=1.2, 95% CI:0.8-1.8, p=0.4).

Figure 7b shows a substantial number of observations with >1 unprotected sex acts reported through daily SMS and 0 unprotected sex reported on monthly questionnaires. One observation appeared to be an outlier (0 unprotected sex on daily SMS, 20 unprotected sex acts on monthly questionnaire), but its exclusion did not substantially change the line of reduced major axis or concordance correlation coefficient.

PrEP adherence

Daily SMS surveys included a significantly greater proportion of observation-months with reports of any missed PrEP dose compared to monthly questionnaires (54.5% vs. 13.1%, p<0.0001). However, the total number of missed PrEP doses was generally small by both survey methods. Participants reported a median of 1 missed PrEP dose per month over daily SMS surveys and 0 missed PrEP doses at the clinic visit. Among 145 observation-months, 59 (40.7%) had the same number of missed PrEP doses reported in the past month on both survey methods, 76 (52.4%) reported more missed PrEP doses through the daily SMS surveys, and 10 (6.9%) reported more missed PrEP doses on the monthly questionnaire. Any missed PrEP was recorded on daily SMS surveys but not monthly questionnaires for 68 (46.9%) observation-months.

The mean number of missed PrEP doses reported was 0.2 for monthly questionnaires and 1.2 for daily SMS surveys. Figure 7c illustrates greater reporting of missed PrEP doses over daily SMS compared to monthly questionnaires. The incidence

rate of days with missed PrEP reported in the past month was 5 times greater for SMS surveys compared to monthly questionnaires (IRR=5.1, 95% CI:=3.0-8.5, $p<0.001$).

Discussion

This study compared two modalities for measuring self-reported sexual activity and PrEP pill-taking behaviors among Kenyan HIV-uninfected adults in HIV serodiscordant relationships: daily self-administered SMS and monthly staff-administered paper surveys. We found greater reporting of sex, unprotected sex, and missed PrEP doses through daily SMS surveys compared to monthly interviewer-administered questionnaires. According to both survey methods, most observation-months included sexual activity, over half of the observation-months had no unprotected sex reported, and the majority contained reports of perfect PrEP adherence or only a small number of missed PrEP doses in the previous month. However, close to a quarter of observation-months had reports of at least one unprotected sex act in the SMS survey data and no unprotected sex in monthly interviews. SMS surveys are a viable data collection option for this population and may reveal more frequent HIV risk behavior than alternative survey methods.

Higher cumulative monthly reports of sex, missed PrEP doses, and unprotected sex on SMS surveys compared to monthly clinic surveys most likely reflects under-reporting on the monthly interviewer-administered questionnaires. Social desirability bias, recall bias, and/or question format may explain the tendency of participants to under-report these sensitive behaviors in a face-to-face interview at monthly clinic visits. Previous studies have assessed agreement between more frequent diaries and retrospective questionnaires and found similar results. Sex workers in Cameroon reported a mean of 1.5 more sex partners per week over coital diaries than on retrospective monthly surveys [150]. A randomized trial of weekly, prospective sexual

behavior diaries (recorded online, via SMS, or paper) among young adults in Australia demonstrated high correlation between sex acts and condom use reported through the three diaries and 3 month end point retrospective survey, yet slightly lower reporting of any sex and new partners over the 3 month retrospective questionnaire [142]. Similarly, a comparison of web-based diaries (every 2 weeks, once a week, or twice a week) to a retrospective 3 month web-based survey among a cohort of young men who have sex with men (MSM) in the U.S. found overall high concordance of reporting, worse agreement with more frequent behaviors (i.e., anal sex), and slightly higher reports of sexual behavior (i.e. number new partners, anal sex, unprotected anal sex) over diaries [143]. Overall, SMS and web-based diaries with real-time data collection tend to capture greater reporting of sensitive health behaviors and, thus may be more accurate than retrospective interviews. They may be most useful technologies to measure counts, timing, sequence, and within-person variation [143]; check regularly collected survey data; assess patterns in misreporting of data; and closely examine the context of HIV risk behavior [151].

SMS surveys may be more effective than paper diaries at capturing HIV risk behaviors in real-time, more accurate in their recording of more sensitive behaviors (unprotected sex, non-adherence) and actual counts of more frequent behaviors (sex acts), and better suited for scientific questions concerning a temporal relationship between multiple, co-occurring behaviors. Health data collected through mobile devices can allow real-time remote monitoring of behavior[133] and intervention to prevent medical problems between clinic visits [10]. SMS has the advantages of high mobility, convenience, time stamps, and increasing ubiquity as an inexpensive, instantaneous mode of communication, and possibly reduced marginal cost [152, 153]. Similar to diaries, daily SMS surveys may be ideal for short periods of frequent data collection when the order and exact occurrence of behaviors is important, allowing for complex

analyses to examine patterns and whether one type of behavior predicts another behavior. Through daily SMS surveys, we discovered a significant correlation between days that sex was reported and daily PrEP adherence, yet no correlation between unprotected sex and PrEP adherence [147]. The advantages of SMS data collection for accuracy are clear, but must be balanced by the initial technology set-up cost, requirement for literacy, as well as participant burden and potential burnout over longer periods of time (beyond the 2 months in this study).

This study had limitations. Our population was relatively small and, as participants in a clinical trial, may not be generalizable. The survey question format varied somewhat between the two instruments, with the daily SMS surveys assessing whether sex occurred on the previous day, whereas monthly interviews recorded the total number of sex acts. We conservatively assumed only one sex act per day that sex was reported through the daily SMS survey, thus our measure of the frequency of sex and unprotected sex may be underestimated through this method. Both methods relied on self-reported data and we did not have a biological measure for comparison or validation of sexual activity, such as Y chromosome PCR or prostate specific antigen testing from vaginal samples.

Conclusion

Daily SMS surveys of sexual activity and PrEP adherence elicited high response rates and significantly greater reports of sex, unprotected sex, and missed PrEP doses compared to monthly interviewer-administered questionnaires. Daily SMS surveys delivered to personal mobile phones may provide more accurate self-reported HIV risk behavior through enhanced privacy and reduced recall period. As with any new technology, good exposure measurement and survey design remains important [154]. Mobile phone SMS diaries offer a promising method to assess sensitive health

behaviors over short periods of time, particularly in settings where text messaging is ubiquitous and more frequent and timely reporting of behavior is desirable.

Acknowledgements

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Figure 4. Description of daily SMS survey and monthly clinic questionnaire

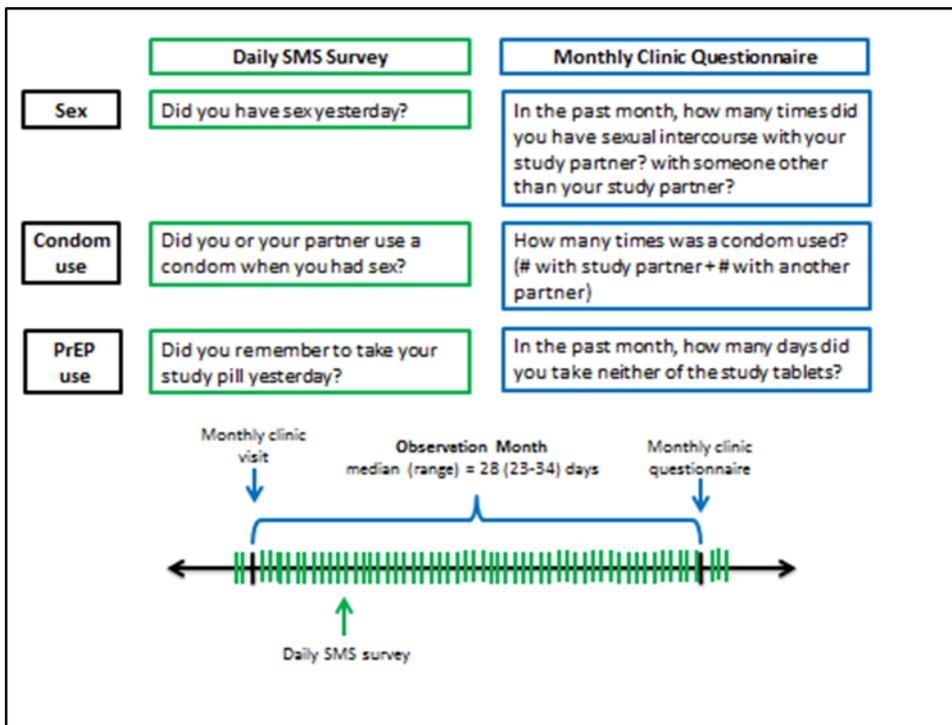


Figure 5. SMS study participants included in comparison analysis

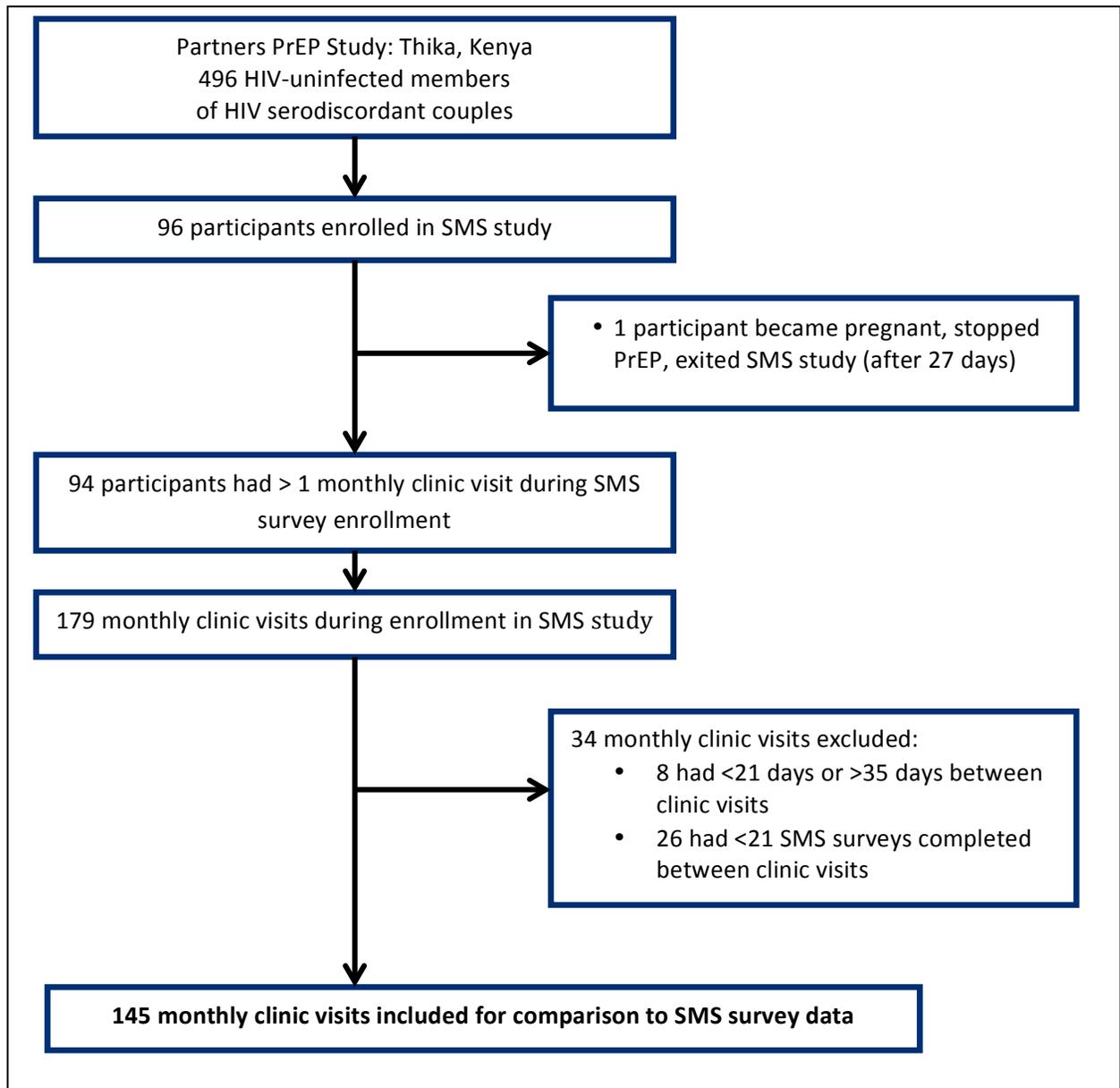


Figure 5 legend.

Flow chart of participant enrollment and inclusion in analysis to compare daily text message surveys to monthly interviewer-administered questionnaires.

96 HIV-uninfected participants enrolled in a 60-day SMS study. Of 179 monthly clinic visits occurring during the SMS study, 34 were excluded. Overall, 85 eligible participants contributed 145 person-months to the present analysis.

Figure 6. Observation-months with any sex, any unprotected sex, and any missed PrEP, by survey method (N = 145)

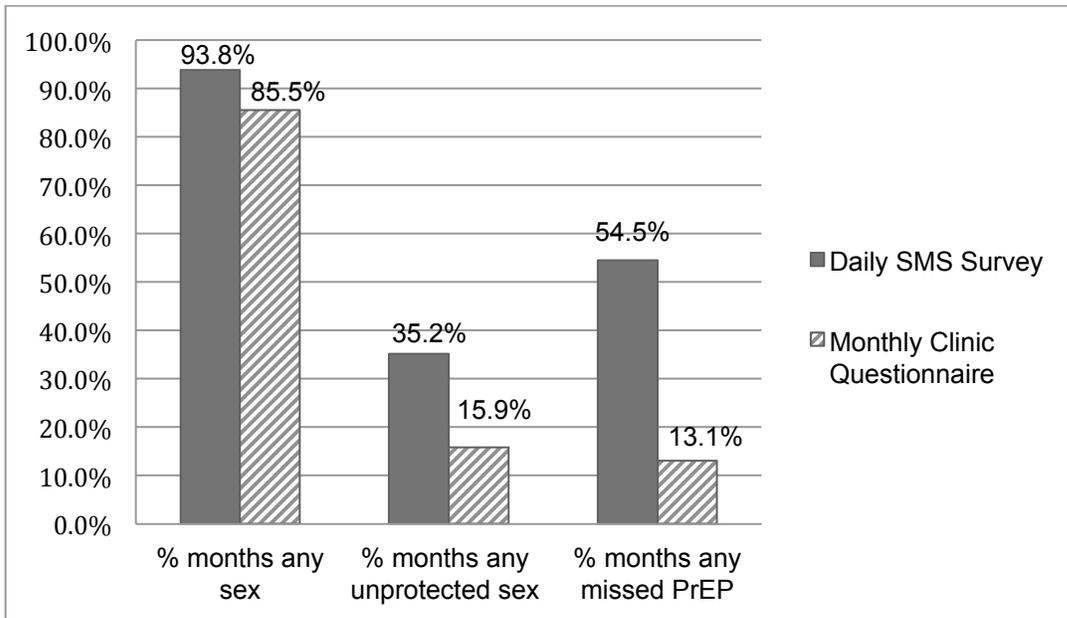


Figure 6 legend.

Proportion of observation-months with any sex, any unprotected sex, and any missed PrEP by survey method. The frequencies of reporting any sex, any unprotected sex, and any missed PrEP in the past month, were significantly greater over daily SMS surveys than on the monthly clinic questionnaire, according to McNemar's Chi² test at $p < 0.01$.

Figure 7. Plots comparing sex, unprotected sex, and missed PrEP doses by survey method

Figure 7a.

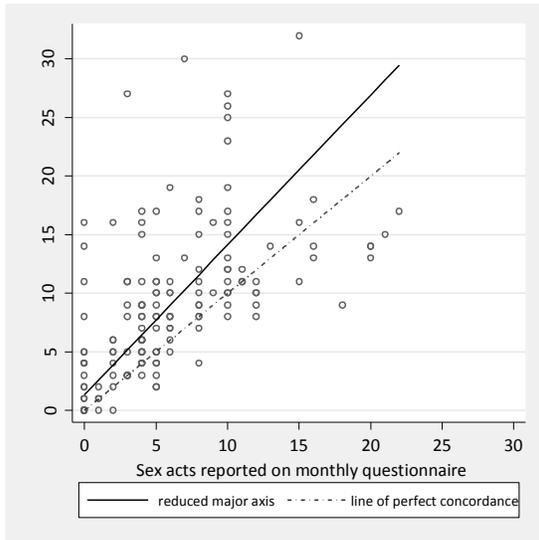


Figure 7b.

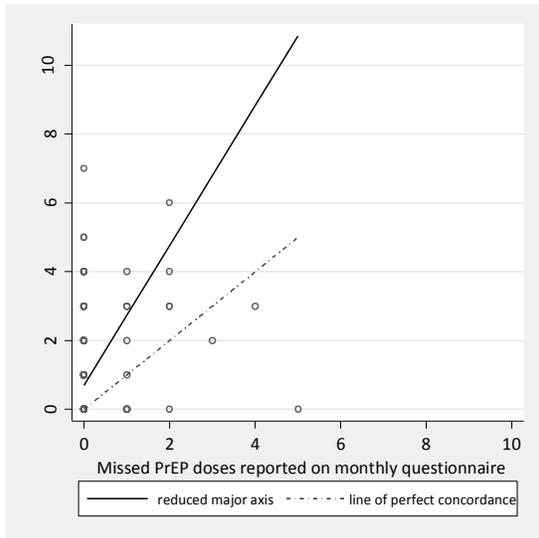


Figure 7c.

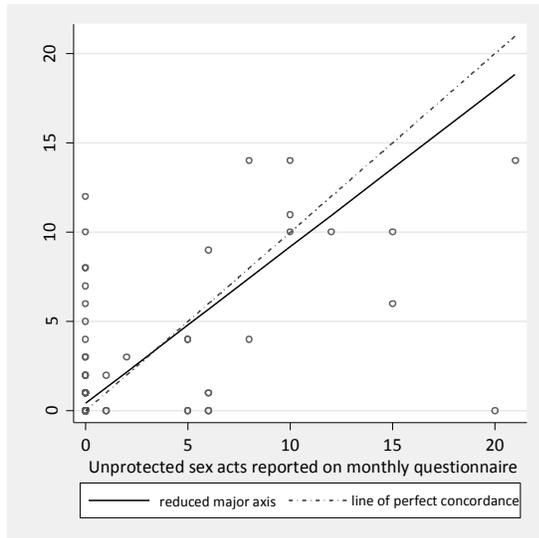


Figure 7 legend.

Plots comparing sex, unprotected sex, and missed PrEP doses by survey method.

Each plot includes total monthly counts for each behavior reported through monthly questionnaire on the x-axis and daily SMS survey on the y-axis. Circles represent observation-months. The dotted line of perfect concordance is the 45° line whereby each observation-month has equal values reported by monthly questionnaire and daily SMS survey. The solid line shows the reduced major axis or standard deviation line, which passes through the intersection of the means, with slope the ratio of the standard deviations, taking the sign of Pearson's correlation coefficient. The concordance correlation coefficient (CCC) measures the agreement of the two different survey methods by determining how far the observed data deviate from the line of perfect concordance.

In figure 7a, the majority of observations lie above the line of perfect concordance, illustrating an overall trend for participants to report more sex acts via daily SMS surveys than on monthly questionnaires (CCC=0.5). In figure 7b, while the data scatter around the line of perfect concordance, a substantial number of observations have >1 unprotected sex acts reported through daily SMS but no unprotected sex reported on monthly surveys (CCC=0.6). In figure 7c, most observations fall above the line of perfect concordance, representing more missed PrEP doses reported in daily SMS compared to monthly questionnaires (CCC=0.1).

Table 9. Socio-demographic and behavioral characteristics of participants (N = 85)

	N (%) or Median (IQR)
Male	65 (76.5%)
Age, years	33 (31-37)
Married	82 (96.5%)
More than one wife*	7 (8.2%)
Living with study partner	81 (95.3%)
Number of children with study partner	1 (0-2)
Number of years in school	11 (8-12)
Earning any income	80 (94.1%)
Running water in the home	39 (44.9%)
Time spent in Partners PrEP Study, years	2.2 (1.7-2.4)
Weekly alcohol use reported at Partners PrEP Study enrollment	21 (24.7%)
HIV-infected study partner on antiretroviral therapy**	26 (30.6%)
Reported sex with someone other than study partner, past month**	7 (8.2%)

IQR: interquartile range, PrEP: pre-exposure prophylaxis.

* Among 65 men.

** Reported through interviewer-administered questionnaire at clinic visit prior to enrollment in text message survey.

Table 10. Comparison of reported sexual behavior and PrEP use between daily SMS surveys and monthly interviewer-administered questionnaires (N = 113)

	Daily SMS survey N(%) or Median (Range)	Monthly questionnaire N(%) or Median (Range)	Under-reporting on monthly questionnaire N(%) or Median (Range)	Percent agreement or concordance correlation coefficient	Incidence Rate Ratio (95% CI), P**
SEX					
Any sex reported, past month	136 (93.8%)	124 (85.5%)	14 (9.7%)	89.0%	
Number of sex acts, past month	9 (0-32)	5 (0-22)	93 (64.1%)	0.5	1.5 (1.3-1.7), p<0.001
UNPROTECTED SEX					
Any unprotected sex reported, past month	51 (35.2%)	23 (15.9%)	35 (24.1%)	71.0%	
Number of unprotected sex acts, past month	0 (0-14)	0 (0-21)	41 (28.3%)	0.6	1.2 (0.8-1.8), p=0.4
MISSED PREP DOSE					
Any missed PrEP doses reported, past month	79 (54.5%)	19 (13.1%)	68 (46.9%)	47.6%	
Number of missed PrEP doses, past month	1 (0-7)	0 (0-5)	76 (54.2%)	0.1	5.1 (3.0-8.5), p<0.001

PrEP: pre-exposure prophylaxis, SMS: short message service (i.e., text message), CI: confidence interval.

* Generalized Linear Latent Mixed Models were used to estimate incident rate ratios for continuous outcomes, specifying unique observation-months as a random effect and survey method as a fixed effect.

Chapter 4: “If I am given antiretrovirals I will think I am nearing the grave”: Kenyan HIV serodiscordant couples’ attitudes regarding early initiation of antiretroviral therapy

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 Kenyan HIV serodiscordant couples’ attitudes regarding early initiation of antiretroviral therapy. *AIDS*. 2013. [Epub ahead of print].

“If I am given antiretrovirals I will think I am nearing the grave”: Kenyan HIV serodiscordant couples’ attitudes regarding early initiation of antiretroviral therapy

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Abstract

Objectives: Early initiation of antiretroviral therapy (ART) – i.e., at higher CD4 counts (>350 cells/ μ L) – is a potent HIV prevention strategy. The World Health Organization recommends ART initiation by all HIV-infected individuals in HIV serodiscordant relationships to prevent HIV transmission, yet the acceptability of early ART among couples has not been well studied.

Design: Qualitative study exploring HIV serodiscordant couples' attitudes towards early initiation of ART.

Methods: We conducted 8 focus group discussions and 20 in-depth interviews with members of heterosexual HIV serodiscordant couples in Kenya. Investigators iteratively applied inductive and deductive codes, developed matrices to identify patterns in codes, and reached consensus on key attitudes (motivations and barriers) related to early ART and one central, emerging theme.

Results: Most participants expressed interest in early initiation of ART, with maintaining health and preventing HIV transmission as key benefits. However, many identified personal concerns and potential barriers to wider community acceptance, including side effects, adherence to life-long treatment, and stigma. The meaning of ART emerged as a fundamental consideration, with initiating therapy perceived as emblematic of the final stage of AIDS, when one was “nearing the grave.” One particular challenge was what early ART might signify for someone who looks and feels healthy.

Conclusions: HIV serodiscordant couples recognized the potential benefits of early ART, but ART was frequently viewed as signifying AIDS and approaching mortality. Potential implementation of early ART presents challenges and an opportunity to re-orientate individuals towards a new image of ART as health-preserving for patients and partners.

Background

Initiation of antiretroviral therapy (ART) by HIV-infected persons – i.e., at higher CD4 counts (>350 cells/ μ L) – is a potent HIV prevention strategy [2, 155]. The World Health Organization (WHO) recommends ART initiation irrespective of CD4 count for HIV-infected members of HIV serodiscordant couples [4]. Studies from a variety of settings have reported that some HIV-infected individuals are not willing to initiate ART [16, 156-158], but few studies have directly explored early ART initiation. Among 181 HIV-infected Kenyan individuals with CD4 counts >350 cells/ μ L and known HIV-uninfected partners, approximately 40% reported reluctance to consider early ART, citing side effects, stigma, pill burden, and ART resistance [20]. In the control arm of HPTN 052, nearly 20% of HIV-infected participants declined ART when offered after the trial demonstrated HIV protection – many stating that they were not ready to begin ART or believed their CD4 was too high [159]. Recent studies have suggested that higher CD4 counts are associated with delayed ART initiation or refusal [15, 17, 160].

Socially-constructed perceptions of HIV are important to understand refusal, uptake, and adherence to HIV treatment and prevention. In high-income settings, the social definition of HIV has been shifted from a universally fatal disease to a chronic, manageable illness since the advent of highly effective ART [161, 162]. The reconceptualization of HIV as a treatable disease has a profound social and psychological impact: restored hope, a return to normalcy, and potentially reduced stigma [162, 163], but also the burden of managing an ongoing, unpredictable illness and adhering to treatment [161, 162, 164]. It is hypothesized that the transition of HIV to a chronic illness will reduce stigma, an important barrier to engagement in HIV services, as HIV-infected individuals on ART can remain healthy and maintain a 'normal' identity and life, concealing their HIV status and avoiding potential negative reactions from

others. Less has been described about reconceptualization of HIV as a chronic, treatable illness in Africa, where ART availability is more recent and ART is generally initiated at low CD4 counts. Particularly unknown is the conceptualization of earlier initiation of ART. This qualitative study explored HIV serodiscordant couples' attitudes towards the early initiation of ART.

Methods

Between February and April 2012, 8 focus group discussions (FGD) and 20 in-depth interviews (IDI) were conducted with members of HIV serodiscordant couples in Thika, Kenya. Couples were participants in the Partners PrEP Study, a randomized trial of pre-exposure prophylaxis (PrEP) for HIV prevention [117]. Thika is a peri-urban and farming community approximately 25 miles from Nairobi. Participants were engaged in HIV prevention and care through the study clinic, including couples counseling, condom distribution, and HIV primary care. HIV-infected participants received WHO staging every 3 months, CD4 counts every 6 months, co-trimoxazole (Septrin) prophylaxis, multivitamins, and referral to ART care centers when eligible by Kenyan guidelines (i.e., ART initiation at CD4 counts <350 cells/ μ L or at \geq 350 cells/ μ L with WHO stage III or IV).

HIV serodiscordant couples in which the HIV-infected partner had not initiated ART were eligible for this qualitative study. A Kenyan female ethnographer not otherwise involved in study clinic activities (SV) invited eligible individuals to participate in the study. Two FGDs of 5-8 participants each were conducted according to gender and HIV status: HIV-uninfected women, HIV-infected women, HIV-uninfected men, and HIV-infected men, for a total of eight focus groups. In addition, ten couples were interviewed individually, 5 in which the woman was HIV-infected and 5 in which the man was HIV-infected. FGDs and IDIs were semi-structured, based on a standardized guide, and conducted in Kiswahili or English. After first exploring general attitudes towards ART, the

facilitator described the HPTN 052 study results, including the magnitude of prevention benefit and concurrent clinical benefit, and asked about attitudes towards starting ART early. Three HIV-infected women were discovered to have recently initiated ART after commencing the focus group; their data were included.

SV translated and transcribed all audio recordings into English. KC, KN, and SV read all transcripts and agreed on a codebook. Investigators followed an iterative process of reading transcripts, applying inductive and deductive codes, and comparing and revising codes in ATLAS.ti (version 7.0, Berlin, Germany). Consensus was reached on key attitudes (motivations and barriers) related to early ART and one central, emerging theme. Matrices were used to identify patterns in attitudes across FGDs and IDIs as well as by gender and HIV status. Results were validated through the use of multiple independent coders, triangulation of emerging codes, themes, and patterns across interviews and focus groups, and the search for negative cases [165, 166].

The University of Washington Human Subjects Review Committee and the Kenyatta National Hospital Ethics Review Committee approved the study protocol. All participants provided written informed consent.

Results

A purposeful sample of 68 volunteers (32 men, 36 women) participated (Table 11). All participants were aware of ART and some recalled drastic improvements when ART was introduced into their communities: “the death rates reduced and people were uplifted” (HIV+ man, FGD). The research was initiated with an intention of describing motivations for and barriers related to early ART. In addition, one important theme emerged in review of the data: the meaning of ART initiation.

Motivations for early ART initiation

Most participants expressed interest in the concept of early initiation of ART and described maintaining health and HIV prevention as important motivators. Some HIV-infected individuals were eager to start immediately; almost all HIV-uninfected men and women were in favor of their partners starting ART early. Many participants reasoned that initiating ART while healthy would allow one to keep the body strong, preserve immunity, and control the virus.

You should start ARVs [antiretrovirals] immediately so that your CD4 can be maintained there. Because this issue of waiting until the CD4 goes down, the body loses its strength. –HIV+ man, FGD

I usually see those who start when they have 150 [CD4], they come when they are very weak. So now I feel when your CD4 is high the body will have strength. –HIV+ woman, IDI

Some believed that starting ART when the body was weak might exacerbate one's illness, even leading to death. Several participants noted that, once infected with HIV, the virus was "still in the body" and early ART could "prevent the virus [from] multiplying."

In addition, many participants stated that early initiation of ART would help avoid negative HIV-related health consequences: opportunistic infections and stigma from appearing ill and thus being "known."

I have never been sick, if I start now there is no way that people will ever come to know the way I am...it is good to start early. –HIV+ woman, FGD

When you go somewhere, when you pass they laugh ... and you know it is about you. When someone has HIV [he] is usually recognized if he is not using those drugs... when someone is using the drugs they can't know very fast. –HIV-man, IDI

Finally, the ultimate benefit of good health was the ability to "live and work normally," including taking care of children. Although all were told of the prevention benefits of ART during previous routine counseling in the trial and at the time of the interview, only a small number emphasized that early ART would be beneficial for preventing HIV transmission to partners.

Barriers to early ART initiation

Most participants also identified personal concerns and potential barriers to wider community acceptance of early ART, including side effects, life-long adherence, and stigma. ART side effects posed a significant concern in two ways—physical discomfort and inadvertent disclosure of HIV status to others.

Let's say I have started using [ART] and I have never had rashes or pimples, then I have that effect, now that way one can know how our status is. –HIV+ woman, FGD

Sometimes your body doesn't adjust to the ARVs... it is better you don't take the ARVs... There is [a] side effect like itching, maybe your body had not become weak to use those drugs...the main fear is of that person's skin changing, you see your skin changes until you are not able to recognize yourself...–HIV+ woman, IDI

In interviews and all FGDs, except among HIV-uninfected men, life-long adherence to ART was raised as a concern, particularly for HIV-infected individuals initiating at higher CD4 counts.

Starting ARVs early when your CD4 is still high is something that is very hard, because when you start that way the ARVs you know that you have already signed a contract forever, there is no day you are going to stop. –HIV+ man, FGD

I could say monotony, because [he] will take them for a very, very long time that is life time, so when he starts early when the CD4 is high, I think it will be too early...and maybe he gets bored along the way which is not good in terms of his health. –HIV- woman, IDI

Likewise, some participants remarked on the potential difficulty of ART adherence if one had initiated when healthy, without ever experiencing HIV-related problems. For these reasons, some HIV-infected men in FGDs and women in IDIs declared they preferred taking co-trimoxazole to stay healthy.

HIV-related perceived stigma emerged as a central challenge to initiating ART early. Participants discussed how fear and shame—of being seen carrying ART, taking drugs, or accessing HIV services—were major barriers to ART initiation.

People talk a lot of things until you even feel ashamed. It can prevent you from taking the drugs... They say she was doing this, she was moving out with other people's husbands. –HIV+ woman, IDI

Many participants believed public disclosure of HIV would lead to gossip, judgment, isolation, and discrimination – threatening their social and work identities, as well as those of their family. While a few viewed stigma as a barrier to early ART, many described strategies to avoid stigma: keeping their ART use secret and traveling to clinics farther from their home where they would not be recognized.

The meaning of ART initiation and “nearing the grave”

A recurring theme that was discussed in FGDs and IDIs, across HIV status and gender, was a reluctance to start ART early due to its meaning as the final stage before dying. Participants highlighted a widespread community belief that the initiation of ART signals the last stage of disease – “the last lap” or when “your life has come to an end.”

Respondent #4: Now if you start and you haven't reached 350, you will feel like you have reached another stage.

Respondent #3: You know the mentality that is there when you take the ARVs, it means you are at the lowest stage and that is why people fear ARVs.

Respondent #6: Like me, if I am given the ARVs I will think I am nearing the grave.

–HIV+ women, FGD

ART initiation was strongly associated with images of graves or very ill individuals on their deathbed, a reminder of HIV as a highly stigmatized terminal illness. An HIV-infected man described how this visual imagery originated from HIV treatment campaigns and the profound, positive health benefits from ART as well as the

internalized connotation of ART initiation as indicative of the “last stage” when someone is extremely sick:

The way in which our minds have been fed since we started these drugs [Septrin], we were told ARVs is the last stage and we see billboards drawn showing someone who was wasted and when they start taking the ARVs their bodies become good. –HIV+ man, FGD

In contrast, co-trimoxazole was considered a medication for an earlier, less serious stage of HIV. One HIV-infected woman described how people did not think of themselves as HIV-infected until they started ART:

You know when you take Septrin and multivitamin, you don't count yourself among the people who have HIV but those ones [ART], aaih, you feel like you are inside it. –HIV+ woman, FGD

A shift in HIV care from daily co-trimoxazole prophylaxis to ART represented a profound change in identity – how one perceived their own illness and reactions from others.

When you take this Septrin you consider yourself to be in another stage, you have not reached the final stage of the ARVs and we know when you start ARVs, it is a lifetime engagement... Now if these stages are brought forward and then I start taking them here, you see this person will know now I am in the last stage. So even the benefits... which is very good, but then we will have the negative effect, the psychological effect. That I am now heading to the grave. –HIV+ man, FGD

Furthermore, HIV-infected participants expressed concerns in how their partners would react when they heard that they were now at the stage of ART, a powerful reminder that they were “sick.”

He could react in a different way from what I know, he is a good person, maybe when he sees me take Septrin he sees it is normal because other people are taking them, but if I start things like those [ART] maybe he will feel it is true this person is sick. –HIV+ woman, IDI

This participant acknowledged her partner's acceptance of co-trimoxazole since it was “normal” medication used by people without HIV, yet she was worried that her partner would react differently to her, and, in a sense, her HIV status if she started ART. In

FGDs, HIV-infected women raised concerns about their partners' reactions to early ART and the emotional burden their ART initiation would bring.

He feels like you are almost going [to die]. –HIV+ woman, FGD

Sometimes he goes with you to the clinic, he has heard ...when your CD4 goes below 350 you will start ARVs. When you start he will feel, 'Right now, let me plan myself because I can see she is going [to die]'...he knows ARVs are taken when people are too sick.

–HIV+ woman, FGD

Finally, some participants felt that the negative connotation of ART as the “final stage” could be amended with revised counseling messages:

We could change people's thinking, they should be told it is not that they are in the last stage, but we are trying to protect your body...it needs counseling and counseling should start early. –HIV+ man, FGD

Discussion

This qualitative study improves understanding of attitudes towards initiation of ART at higher CD4 counts and highlights important incentives, concerns, and potential barriers to acceptance. Among Kenyan HIV serodiscordant couples who were well-informed about HIV prevention, many expressed interest in early initiation of ART, with a focus on health benefits but considerable attention to possible side effects, inadvertent HIV disclosure, and stigma. A novel, important barrier to early ART was the significance of ART initiation as the last stage of disease, for use when one is close to dying. There is an opportunity to modify messages regarding ART initiation in order to appropriately emphasize the personal benefits of earlier initiation, acknowledge concerns, and ultimately change community perceptions about the meaning of ART.

HIV-infected participants commonly articulated willingness to initiate ART at a CD4 > 350 cells/μL for the sake of maintaining good health, avoiding opportunistic infections, and protecting children and HIV-uninfected partners, although many expressed reservations and a small number conveyed resistance to early ART. There

were not substantial gender differences in attitudes towards ART, compared to previous literature that suggests men are more likely to delay ART initiation [17], which may reflect the motivated population of clinical trial participants. The near universal support of HIV-uninfected partners suggests a potentially important role of partner involvement in couples' decisions to initiate treatment.

Consistent with previous literature, ART side effects, stigma, and adherence emerged as primary concerns for early ART [16, 20, 72, 167]. A fear of unintended disclosure, from visible side effects or being seen accessing HIV services, underscored how perceived stigma in the community motivates HIV-infected individuals to hide their HIV status, ultimately influencing HIV care behaviors [168-173]. Notably, concerns about visible side effects were voiced both related to not initiating ART (signs of disease progression) and to initiating ART (as a side effect). Early ART was more acceptable when it enabled HIV-infected individuals to conceal their HIV status and minimize stigma and discrimination. Importantly, participants were concerned that life-long adherence to ART would be more challenging when initiated early.

The meaning of ART initiation as the last stage before the end of life emerged as a barrier unique to early ART. All HIV-infected participants were engaged in pre-ART care and they and their partners viewed taking co-trimoxazole, a prophylactic medicine with non-HIV indications, as helpful and positive. Thus, while daily pill use was acceptable, ART initiation itself was a "psychological" challenge because it symbolized proximity to the end of health, normalcy, and life. Initiation of ART marked a transition from living a normal life to being sick and potentially stigmatized. This perception of ART as the final stage may be an unintended consequence of HIV guidance to promote "positive living" to encourage HIV-infected individuals to adopt healthy behaviors to prevent disease progression and thus delay ART initiation. Among HIV-infected adults in Uganda, internalized stigma declined after ART initiation but did not disappear [174].

HIV-infected individuals have been stigmatized in the absence of visible symptoms [161] and efforts to lead a 'normal' life are dependent on reliable access to ART, social support, and financial stability [164].

HIV/AIDS has long been described by metaphors of death. Before ART, HIV was defined as a fatal acute illness and diagnosis was seen as a "death sentence" [161]. ART has saved lives and offers a return to health, hope, and normalcy [168, 175], described by some as "coming back from the dead"[164]. ART could potentially counteract HIV-related stigma through lengthening life expectancy and drastically improving the appearance of HIV-infected individuals—by making HIV a "manageable chronic condition rather than a terminal illness" [162, 168]. Alternatively, the image of visibly ill, near-death individuals starting ART and the nature of ART as life-long treatment as opposed to a cure may impede this transition. In a qualitative study in rural Tanzania, ART was known as "life prolonging drugs" and recognized for a return to health, yet AIDS was still referred to as "six by six," the dimensions of a grave, because there was no cure [176]. Similarly, study participants viewed ART as a way to remain physically healthy and conceal one's HIV status, yet also a reminder that they or their partners were in fact infected with a life-threatening illness. They appreciated the hope and normalcy that ART provides, but they have not completely overcome the perception of HIV as a death sentence.

There are limitations to this study. Questions about early ART were hypothetical since Kenyan guidelines did not include ART for asymptomatic persons with higher CD4 counts. Participants enrolled in a clinical trial of PrEP that included ongoing HIV risk reduction counseling may have been more likely to support early ART for prevention and limit generalizability. This is balanced by the strength of using a sample of HIV serodiscordant couples who were well-informed about HIV prevention, mutually disclosed, and engaged in pre-ART care.

Conclusion

In this qualitative study among Kenyan HIV serodiscordant couples, most had positive attitudes and interest in early ART. However, many participants' description of ART as the final stage before death, regardless of the reason for initiation, revealed a profound view of HIV and ART in this Kenyan community. The implementation of early ART for HIV prevention presents an opportunity to re-orientate conversations to the benefits of early ART, emphasizing the role of ART in maintaining health and HIV prevention, capitalizing on positive attitudes of partners regarding earlier ART, and portraying a new image of individuals on ART.

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Author contributions

KC wrote the manuscript. JMB was the principal investigator of this study and oversaw manuscript preparation. SV conducted all interviews and focus group discussions. KC, KN, SV, and BSD analyzed the data. All authors reviewed and provided comments on the study protocol, results, and final manuscript.

Conflicts of interest

None declared.

Table 11. Participant characteristics

	HIV-infected women (n=18)	HIV-uninfected men (n=17)	HIV-infected men (n=15)	HIV-uninfected women (n=18)
	n (%) or median (range)			
Age	29.5 (20-38)	36 (22-63)	42 (31-60)	40 (24-50)
Married	18 (100%)	17 (100%)	15 (100%)	18 (100%)
Children	2 (1-5)	2 (1-7)	3 (0-5)	3 (1-5)
CD4 count*	637.5 (394-1102)	--	477 (261-1164)	--

* CD4 count from most recent measurement taken at study clinic visit prior to invitation to participate in the qualitative study.

Discussion

This dissertation describes the epidemiology of African HIV serodiscordant couples and effective HIV prevention strategies, evaluates an innovative mobile technology method for collecting self-reported HIV risk behavior in this key population, and explores couples' behavior, use, and attitudes related to new strategies for ART for HIV prevention. HIV serodiscordant couples are an important priority population for HIV prevention in Africa. We drew from the experiences of HIV serodiscordant couples enrolled in a clinical trial of PrEP to inform about practical considerations for future implementation of early ART and PrEP for HIV prevention.

The studies presented in this dissertation were nested within an ongoing randomized controlled trial of PrEP among 4,758 HIV serodiscordant couples in Kenya and Uganda [3]. This population was ideal for examining sexual risk behavior within stable couples over time and investigating critical questions about the future use of antiretroviral-based HIV prevention. Specifically, these studies improve scientific knowledge and clinical practices related to:

- HIV serodiscordant couples: frequency of sex and condom use; whether sex is planned or spontaneous; whether there are identifiable periods of high-risk of HIV infection;
- Services for HIV serodiscordant couples: potential of delivering of PrEP during high-risk periods; feasibility and considerations for implementing antiretroviral-based HIV prevention, including the initiation of early ART;
- mHealth: feasibility and acceptability of daily and monthly mobile phone data collection on sensitive topics such as sexual activity, condom use, and HIV risk perception.

Our findings can provide valuable insight for future policy decisions and implementation of early ART and PrEP among this priority population.

The first chapter reviewed the evidence of HIV prevention in HIV serodiscordant couples and highlighted key, effective interventions to be applied in a combination prevention approach. HIV transmission rates are high within HIV serodiscordant couples and observational studies provide evidence that rates are highest in couples unaware of their serodiscordant status, reporting low condom use, having uncircumcised male partners, and/or with high viral loads in the HIV-infected partner [37, 43, 121-124]. Thus, HIV testing and counseling remains an important and necessary first step to HIV prevention, especially for identifying and promoting HIV disclosure and risk reduction within couples. Our review underscored modifiable risk factors for HIV transmission: plasma viral load, ART use by HIV-infected partner, contraception, pregnancy, condom use, outside partnerships, and male circumcision. After learning their HIV serostatus, HIV serodiscordant couples may be provided appropriate HIV prevention interventions, including condoms, male circumcision, treatment of sexually transmitted infections, initiation of ART by the HIV-infected partner, and PrEP by the HIV-uninfected partner.

As described in Chapter 2, daily SMS surveys were acceptable to this population and had high completion rates. Daily SMS provided a “real-time” assessment of HIV risk behaviors and study medication use over a 60-day period when all HIV-uninfected participants were taking active study drug. Analysis of daily self-reported behaviors provided evidence that overall PrEP adherence was high, participants were more likely to adhere to daily PrEP doses when they were sexually-active, PrEP use was not associated with unprotected sex, and anticipating sex was difficult. A complementary analysis presented in Chapter 3 found that daily SMS surveys elicited greater reporting

of HIV risk behaviors compared to monthly interviewer-administered questionnaires, highlighting the potential of SMS to collect more accurate self-reported data.

In Chapter 4, the qualitative analysis of rich discussions and interviews with HIV serodiscordant couples familiar with these HIV prevention methodologies highlighted common perceived advantages and concerns related to early initiation of ART. Notably, this study identified a powerful theme about the meaning of ART as the “final stage” before dying. Although many HIV-infected participants reported a willingness to start ART immediately and their partners were supportive, they believed this negative connotation of ART initiation could pose a considerable challenge to implementation of early ART in the wider community. Couples expressed a desire for counselors to inform communities of the benefits of starting ART earlier: HIV prevention and maintaining good health.

Mobile technology for health

MHealth is an emerging field that harnesses low-cost mobile technology to improve public health in resource-limited settings. Our evaluation of automated, recurring SMS surveys delivered through mobile phones in Kenya contributes to mobile health (mHealth), a growing field that evaluates the use of mobile technology to improve public health. The study presented in Chapter 2 demonstrated several important advantages of SMS surveys over traditional data collection methods: anonymity/privacy, reduced recall period, capture of behaviors that participants may not have been comfortable reporting to study counselors, and the ability to capture HIV risk behaviors in real-time to enable response.

Mobile phones have been used to send SMS to remind and motivate patients to take medications and attend clinic appointments. A few studies have successfully implemented mobile phone interventions to improve HIV-infected patients' adherence to antiretroviral therapy (ART) and retention in care [129, 130, 177, 178]. Medical providers and community health workers have used mobile phones and personal digital assistants (PDA) for data collection, disease reporting, and two-way communication about patient visits [152, 179-183]. Research staff have contacted study participants on their mobile phones for daily interviews [184] or to collect data when clinic visits were missed [185]. The majority of people in rural areas of Eastern African have access to a mobile phone and willingness to receive SMS appeared high, though potential challenges such as the shared use of phones and ability to respond have been documented [10, 177, 186-188].

There are several key logistical advantages to the use of SMS to mobile phones to collect data in resource-limited settings (Table 12). SMS has the benefits of high mobility, instantaneous communication speed, low cost, convenience (messages stored until recipient is ready to read), limited time to communicate to multiple recipients, and popularity as an inexpensive mode of communication [152, 153]. Most people in rural areas of Eastern African own a mobile phone and are willing to receive SMS [10, 177, 186-188]. The automated delivery of SMS quickly and efficiently reaches many participants in a wide geographic area with fewer human resources [130, 189]. After initial set up, staff have more time to focus on people who are not responding. Health data collected through mobile devices can be received immediately and more frequently, allowing for medical providers to monitor behavior and outcomes remotely in real time [133]. The instant collection of adherence data through SMS quickly flags medical problems such as treatment interruptions so that medical providers can promptly intervene, without waiting until the next clinic visit [190].

In the context of expansion of HIV prevention and ART treatment programs and overburdened health systems, there is an urgent need for inexpensive health interventions to promote compliance to HIV prevention, high adherence to ART and PrEP, and retain patients in care. Studies utilizing SMS to communicate with ART patients demonstrated significant improvements in ART adherence and biological outcomes [129, 130].

According to the Weltel study, SMS ART adherence reminders were successful by cultivating a sense of connection and caring between the health care provider and patients [129]. An ongoing randomized trial in Kenya is evaluating whether weekly SMS questions designed to “check in” with patients will improve retention in HIV care and time to ART initiation over the first year after HIV diagnosis [191].

The SMS study described in Chapter 2 informed the development of a large-scale SMS survey within the Partners Demonstration Project, a newly initiated evaluation of the implementation of ART and PrEP in HIV serodiscordant couples in Kenya and Uganda as follow-up to the Partners PrEP Study. This SMS survey will test the use of toll-free, daily assessment of PrEP adherence and sexual behaviors over a longer time frame and at different time intervals: one week before and one week after quarterly clinic visits.

Future research should continue to evaluate innovative ways for mobile phones and automated SMS to enhance communication between health care providers and patients in resource-limited settings and monitor and retain patients in PrEP interventions, pre-ART care, and ART programs.

HIV prevention for HIV serodiscordant couples

Social and behavioral considerations for implementation of biomedical HIV prevention interventions. Social and behavioral factors are critical to the effective implementation of

biomedical HIV prevention interventions such as PrEP and early initiation of ART [81, 192-194]. While antiretroviral-based HIV prevention strategies are biomedical in nature, their wide-spread implementation and ultimate effectiveness requires understanding and encouraging behaviors for acceptance, adherence, and correct use. Three key behaviors are required for ART and PrEP to be successful: the adoption (and for PrEP, by individuals at high risk of infection), high adherence to drug regimens, and sustained HIV risk reduction practices [194]. Divergent results from PrEP clinical trials reiterate that PrEP efficacy is dependent on acceptance and adherence (Table 1, Introduction). Individuals must also first accept HIV testing and learn their serostatus. Important social considerations include stigma, disclosure of HIV status, gender, socioeconomic status, education level, and relationships with health care providers. In situations where women have less power and control in sexual decisions such as condom use, PrEP promises an urgently needed, female-controlled, discrete HIV prevention strategy [192, 193].

Researchers have also raised concerns of potential behavioral disinhibition or sexual risk compensation with the adoption of partially-effective HIV prevention strategies, including PrEP and initiation of ART [193-195]. This potentially comprises increased engagement in risk behaviors, such as less condom use or more sex partners, under the belief that one is protected against this health risk [196]. A survey about PrEP intentions with high-risk men in the U.S. demonstrated high interest in PrEP if it were at least 80% effective and evidence that some would hypothetically decrease their condom use while on PrEP [197]. A prospective study in Uganda found no evidence of behavioral disinhibition, but instead a decrease in risky sex among ART patients in home-based program who received prevention counseling and free condoms [198].

Considerations for the implementation of PrEP. In light of these concerns, findings from the evaluation of daily PrEP use and sexual risk behaviors over 60 days among Kenyan HIV-uninfected adults in HIV discordant relationships were reassuring. We found that, for the most part, PrEP users made rational decisions about their use of PrEP and condoms. Overall, daily PrEP adherence was high. Most used PrEP consistently, while those that more regularly missed doses were not having sex. Poor prediction of sex highlighted the potential challenge of adherence to coitally-dependent PrEP regimens, favoring implementation of daily regimens of PrEP. PrEP use was not correlated with greater reports of unprotected sex, suggesting there was not risk compensation. Additional social science research might explain why adherence has been low in other priority populations and confirm the absence of risk compensation.

Considerations for the implementation of early ART. Strong evidence of HIV prevention through early ART initiation has shifted the ongoing debate on when HIV-infected individuals should initiate ART, including enthusiasm for a “test and treat” approach as well as a call for more research into when to initiate ART in Africa [199]. The success of ART for HIV prevention will depend on timely initiation, life-long adherence, and retention in care. New guidance and policies on ART initiation will require careful efforts to change the mindset and attitudes regarding ART. There is a need to bridge the disconnect between high-level policy setting on treatment standards and the populations the guidance is intended to serve. We need to develop clear, effective messages about ART in consideration of how communities currently understand treatment. Future research should also assess the acceptability of early ART in other key, priority populations, including HIV serodiscordant couples who have not been in an HIV prevention clinical trial.

At present, we have an opportunity to modify messages regarding ART initiation and in turn, bring new meaning to ART. In a focus group, one HIV-infected emphasized the need to “change people’s thinking” through counseling to explain that the initiation of ART is not the “last stage,” but a viable way for one to protect one’s body. New messages should emphasize the benefits of HIV prevention and maintaining good health; acknowledge concerns such as side effects, life-long adherence, drug resistance, diet; and ultimately, present a new, positive image of individuals on ART. It is an opportune time to once again change the face of the AIDS epidemic.

Conclusion

Current HIV prevention research focuses on how best to deliver a package of HIV prevention interventions to different priority populations. Recent HIV prevention trials have found positive results and presented exciting, new biomedical prevention strategies to be included: early ART and PrEP. New international guidance promotes the implementation of these new HIV prevention strategies among HIV serodiscordant couples, while ongoing demonstration projects evaluate their “real world” effectiveness. Social and behavioral factors, in particular sustained adherence as well as individual and community acceptance, will be fundamental to successful implementation and should remain a focus of HIV prevention and treatment initiatives.

Table 12. Advantages and limitations of mobile phone data collection

Advantages	Limitations
<p>Real time data collection</p> <ul style="list-style-type: none"> • Reduces recall period and memory error [139] • Timely information to permit prompt intervention 	<p>Real time data collection</p> <ul style="list-style-type: none"> • Poor response rate [10] • Disruptive • Reactive [139] • Limited availability and response to phone calls [189]
<p>Reach users in remote areas through mobile networks</p> <ul style="list-style-type: none"> • Quick, easy way to contact patients [185] • Does not require clinic visit or related time and cost of transport 	<ul style="list-style-type: none"> • Dependent on mobile provider server and SMS gateways; potential outages [11] • Limited by type of information can collect over phone: short text or audio
<p>Automated delivery of SMS</p> <ul style="list-style-type: none"> • Ease of use: shorter interaction & accurate data [153] • One server to reach thousands of patients over large geographic area [130] • Fewer human resources required [189] 	<ul style="list-style-type: none"> • Potential habituation with repeat SMS [130] • Participant effort & commitment required – possible fatigue [139] • Cost of SMS response falls on participant
<p>Use of low-cost ubiquitous technology [10]</p> <ul style="list-style-type: none"> • SMS can be used with any type of phone; familiar to mobile phone owners as cheap mode to communicate [153] • Reduces human resources needed beyond initial set-up, data management, quality control / monitoring 	<p>SMS requires literacy and familiarity with mobile phones [153]</p> <ul style="list-style-type: none"> • Expensive to distribute mobile phones; risk of losing phone • Higher tech programming, knowledge, and oversight needed for larger-scale endeavors
<p>More privacy and anonymity than face-to-face data collection and visits to clinic [139]</p> <ul style="list-style-type: none"> • Less social desirability bias than face-to-face interviews [12] • SMS considered more private than phone call [177] 	<ul style="list-style-type: none"> • Risk of loss of privacy if others overhear phone conversation, see SMS on phone, SMS intercepted, or phone lost or stolen [186, 189] • Phone sharing is a common • No interviewer to clarify questions or responses [12] • Phone number to link data

Abbreviations: SMS: short message service (i.e. text message)

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- Liaison between U.S. and Tanzania collaborators on a National Institute of Mental Health funded randomized controlled trial assessing a community-based HIV voluntary counseling and testing intervention
- Supervised 5 ethnographers, 1 data manager, 2 data clerks, and 2 translators; recruited and trained new staff in research methods, ethics, and project activities
- Oversaw the logistics of quantitative and qualitative data collection procedures
- Assisted in the development of journal manuscripts, study instruments, and research protocols

Johns Hopkins Bloomberg School of Public Health

Baltimore, Maryland

Graduate Research Assistant

March 2007-May 2007

Supervisor: Dr. Michael Sweat

- Conducted survey of HIV prevention interventions for HIV positive people for a World Health Organization project

SHARAN, Society for Urban Poverty

Delhi, India

Graduate Research Assistant

June-December 2006

Supervisor: Dr. Michael Sweat

- Conducted qualitative research to examine the post-detoxification needs of injection drug users enrolled in a National Institute of Drug Abuse funded HIV prevention study
- Trained and led a team of 3 interviewers
- Coded and analyzed data from in-depth interviews for final report and MHS thesis

Education Development Center, Inc.

Newton, Massachusetts

Research Assistant

February 2004-July 2005

Supervisor: Ms. Cheryl Vince Whitman

- Assisted in proposal and grant writing
- Summarized research on emerging health fields for Global Programs and for the National Center for Mental Health Promotion and Youth Violence Prevention
- Wrote, developed, and revised materials, guides, and presentations

World Health Organization

Geneva, Switzerland

Intern

October-December 2003

Supervisors: Dr. Herbert Peterson & Mr. Jack Jones

- Aided in implementation of international conference on family planning guidelines
- Assisted in summarization of results and recommendations from conference for publication, titled "WHO Medical Eligibility Criteria for Contraceptive Use"
- Planned and executed pilot test of new document, titled "Information Series on School Health: Creating an Environment for Emotional and Social Well-being"

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Awards:

- Young Investigator Award for the 20th Conference on Retroviruses and Opportunistic Infections in Atlanta, GA (*March 2013*)
- The University of Washington STD/AIDS Research Training Fellowship (*September 2012-present, NIH T32-A1007140*)
- The University of Washington International AIDS Research Training Fellowship (*September 2011-April 2012, NIH D43 TW000007*)