Tenofovir-based oral preexposure prophylaxis prevents HIV infection among women

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Purpose of review
Despite tremendous promise as a female-controlled HIV prevention strategy, implementation of preexposure prophylaxis (PrEP) among women has been limited, in part because of disparate efficacy results from randomized trials in this population. This review synthesizes existing evidence regarding PrEP efficacy for preventing HIV infection in women and considerations for delivering PrEP to women.

Recent findings
In three efficacy trials, conducted among men and women, tenofovir-based oral PrEP reduced HIV acquisition in subgroups of women by 49–79% in intent-to-treat analyses, and by >85% when accounting for PrEP adherence. Two trials did not demonstrate an HIV prevention benefit from PrEP in women, but substantial evidence indicates those results were compromised by very low adherence to the study medication. Qualitative research has identified risk perception, stigma, and aspects of clinical trial participation as influencing adherence to study medication. Pharmacokinetic studies provide supporting evidence that PrEP offers HIV protection in women who are adherent to the medication.

Summary
Tenofovir-based daily oral PrEP prevents HIV acquisition in women. Offering PrEP as an HIV prevention option for women at high risk of HIV acquisition is a public health imperative and opportunities to evaluate implementation strategies for PrEP for women are needed.

Keywords
adherence, effectiveness, efficacy, HIV prevention, preexposure prophylaxis, women

INTRODUCTION
HIV/AIDS is the leading cause of death among women of reproductive age, and a combination of biological, behavioral, and sociocultural factors result in women bearing a disproportionate burden of the global HIV epidemic [1,2]. HIV prevention strategies available to women at risk of sexual transmission include abstinence from sexual activity, female and male condoms, and antiretroviral therapy (ART) use or voluntary male medical circumcision by their partners; however, all of these strategies depend on male partner cooperation. Tenofovir disoproxil fumarate/emtricitabine (TDF)-based preexposure prophylaxis (PrEP) is a novel prevention strategy in which HIV uninfected individuals use an oral antiretroviral medication, such as chemoprophylaxis to reduce HIV acquisition [3]. PrEP holds tremendous promise as a female-controlled prevention approach, and international normative bodies recommend PrEP for persons at substantial HIV risk, including women [4,5,6–8]. However, the delivery of PrEP to women at high risk of HIV is underdeveloped because of complicated results from clinical trials that assessed PrEP efficacy among women. In addition, cost, policies, infrastructure, and limited availability of antiretroviral medications are logistical factors limiting the scale-up of PrEP in areas of high HIV burden. To maximize the impact of PrEP, it is important to understand the different PrEP efficacy results across trials, draw a definitive conclusion

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KEY POINTS

- Clinical trial data demonstrate that daily tenofovir-based oral PrEP prevents HIV acquisition among women, when taken with sufficient adherence.
- Pharmacokinetic studies provide evidence that daily dosing of tenofovir-based oral PrEP reaches concentrations in vaginal tissues that are consistent with levels needed for HIV prevention.
- Evidence from clinical trials and emerging data from open-label studies demonstrate that women who are at risk of HIV and motivated to use PrEP can adhere sufficiently to the daily regimen and be protected against HIV.
- Innovative strategies to motivate women at risk to use daily PrEP and scalable adherence support strategies need to be identified and integrated into delivery models.

about the HIV prevention benefit of PrEP for women, and identify elements from clinical trials and open-label studies that are important to address within programs delivering PrEP to women.

TEXT OF REVIEW

Randomized clinical trials of preexposure prophylaxis among women

Five double-blinded, placebo-controlled randomized clinical trials of daily oral TDF-based PrEP that included heterosexual women were conducted [9,10**,11**,12–14,15**] (Table 1). All trials were carried out in settings with high HIV burden and study subjects received a comprehensive package of HIV prevention services, including frequent HIV testing, risk reduction and adherence counselling, condoms, and treatment for sexually transmitted infections (STI). Participants received intensive adherence counseling to take study drug once per day, and multiple methods were used to measure adherence, including self-report, daily diaries, clinic-based counts of returned pills and bottles, and testing archived blood samples for tenofovir. Despite similarities in study design and analytic approach, the primary intent-to-treat efficacy results varied substantially across trial populations.

Three of the five studies found that daily oral PrEP reduced the risk of HIV acquisition overall and in subgroup analyses of women. In the Partners PrEP Study, which included 1785 Kenyan and Ugandan women with a mutually disclosed HIV-infected partner, PrEP efficacy among women was 66 and 71% for the two PrEP medications tested, and PrEP efficacy did not differ substantially between men and women [9]. In further analyses, the protective effect of PrEP was consistent in subgroups of women at high risk for HIV acquisition [10**]. PrEP efficacy among women in the TDF2 (Safety and Efficacy of Daily Oral Antiretroviral Use for the Prevention of HIV Infection in Heterosexually-Active Young Adults in Botswana) study was 49%, although the small sample size limited statistical precision [12]. Although women comprised only 20% of participants in the Bangkok Tenofovir Study (BTS), PrEP efficacy among this subgroup was 79% [13]. In contrast, two trials among African women, (FEM-PrEP (Preexposure Prophylaxis Trial for HIV Prevention among African Women), conducted among 2120 women from Kenya, Tanzania, and South Africa, and VOICE (Vaginal and Oral Interventions to Control the Epidemic) conducted among 3019 women from South Africa, Zimbabwe and Uganda), demonstrated no effect of daily oral PrEP on HIV acquisition [14,15**].

Data from all five trials consistently demonstrated that HIV acquisition occurred during periods of low or no adherence to PrEP. Having tenofovir detected in blood samples was associated with ≥85% protection from PrEP [11**] and the frequency of tenofovir detection in each overall trial population strongly paralleled the HIV protection observed in each study. In the three trials that demonstrated a protective effect from PrEP, tenofovir was detected in 67–83% of samples from a random subset of participants [9,12,13], compared with 24–30% in the two trials with null results [14,15**,16**], leading to the conclusion that PrEP protects women from HIV infection when it is used.

Biological factors influencing preexposure prophylaxis efficacy among women

Several biological factors have been hypothesized to influence the protective effect of PrEP in women. Foremost among these is the presence of adequate PrEP medication at the time of HIV exposure. Preventing HIV acquisition through sexual contact likely depends on sufficient adherence to achieve tenofovir levels in genital (or rectal) tissues that can prevent viral replication and dissemination. Men who have sex with men (MSM) and transgender women, for whom rectal exposure carries the greatest HIV risk, appear to benefit from near-complete HIV protection with blood levels reflecting as few as four doses of TDF-based PrEP per week [17*]. MSM who used an event-driven, coitally dependent PrEP regimen achieved high rectal concentrations of tenofovir and reduced HIV acquisition by 86% [18*]. The body of evidence to define the level of
### Table 1. Double-blinded placebo-controlled randomized trials that included HIV uninfected heterosexual women to assess the efficacy of daily oral tenofovir disoproxil fumarate-based preexposure prophylaxis for HIV prevention

<table>
<thead>
<tr>
<th>Name</th>
<th>Study population</th>
<th>Sample size</th>
<th>Oral PrEP agent</th>
<th>Plasma TDF in a random sample of participants, %</th>
<th>Overall efficacy</th>
<th>Female subgroup efficacy</th>
<th>Additional analyses among women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partners PrEP Study, Baeten et al., Murnane et al., Donnell et al. [9,10**,11**]</td>
<td>Heterosexual HIV-1 uninfected persons in HIV-1 serodiscordant relationships: Kenya, Uganda</td>
<td>4747</td>
<td>TDF-FTC</td>
<td>81</td>
<td>75% (55, 87%)</td>
<td>66% (28, 84%)</td>
<td>Tenofovir &gt;40 ng/ml: 94% (−17, 100%)</td>
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<td></td>
<td></td>
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<td></td>
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<td></td>
<td>Age &lt; 30 years: 72% (25, 90%) Partner viral load &gt;50,000 copies/ml: 72% (13, 91%)</td>
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<td>Tenofovir &gt;40 ng/ml: 85% (−90, 99%) Age &lt; 30 years: 77% (29, 92%)</td>
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<td></td>
<td>Partner viral load &gt;50,000 copies/ml: 84% (29, 96%)</td>
</tr>
<tr>
<td>TDF2, Thigpen et al. [12]</td>
<td>Heterosexual men and women: Botswana</td>
<td>1219 (557 women)</td>
<td>TDF-FTC</td>
<td>79</td>
<td>62% (22, 83%)</td>
<td>49% (−22, 81%)</td>
<td>With censoring after self-reported discontinuation of study medication: 75% (24, 94%)</td>
</tr>
<tr>
<td>BTS, Choopanya et al. [13]</td>
<td>Male and female injection drug users: Thailand</td>
<td>2413 (489 women)</td>
<td>TDF</td>
<td>67</td>
<td>49% (10, 72%)</td>
<td>79% (17, 97%)</td>
<td></td>
</tr>
<tr>
<td>FEM-PrEP, Van Damme et al. [14]</td>
<td>Heterosexual women: Kenya, Tanzania, and South Africa</td>
<td>2120 women</td>
<td>TDF-FTC</td>
<td>24</td>
<td>6% (−52, 41%)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>VOICE, Marrazzo et al. [15**]</td>
<td>Heterosexual women: South Africa, Uganda, Zimbabwe</td>
<td>3019 women</td>
<td>TDF-FTC</td>
<td>29</td>
<td>−4% (−49, 27%)</td>
<td>NA</td>
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</table>

BTS, Bangkok Tenofovir Study; FEM-PrEP, Preexposure Prophylaxis Trial for HIV Prevention among African Women; PrEP, preexposure prophylaxis; TDF, tenofovir disoproxil fumarate; TDF2, Safety and Efficacy of Daily Oral Antiretroviral Use for the Prevention of HIV Infection in Heterosexually-Active Young Adults in Botswana; TDF/FTC, tenofovir disoproxil fumarate/emtricitabine; VOICE, Vaginal and Oral Interventions to Control the Epidemic.
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Tenofivir and number of doses required to confer this level to women are limited, particularly studies linking pharmacokinetics to in-vivo pharmacodynamics. Available data suggest that more consistent dosing is required to achieve sufficient levels of tenofovir in vaginal tissue than rectal tissues [14,19*,20*,21]; however, as demonstrated in the efficacy clinical trials of PrEP, women who were generally adherent to a daily PrEP regimen were strongly protected against HIV.

Additional hypotheses have questioned whether the benefits of PrEP may be compromised in younger women who are more susceptible to HIV because of immature genital mucosa, in women with STIs, in women who encounter a high viral inoculum (i.e., because of high viral concentrations or acute HIV infection in partners), and because of interactions with hormonal contraceptives [14,22,23,24*]. Physiological features, including a higher proportion of exposed cervicovaginal epithelium tissues, and increased levels of pro-inflammatory cytokines in genital secretions and inflammatory immune cells in cervicovaginal fluid, may put younger women at higher risk of HIV acquisition [25]. On average, HIV-uninfected participants in the Partners PrEP Study, TDF2, and BTS were older than women in FEM-PrEP and VOICE [9,14,15**]; however, the protective effect of tenofovir-based PrEP was 72–77% in a subgroup analysis of women <30 years old in the Partners PrEP Study [10**]. The baseline prevalence of bacterial STIs was lower in the Partners PrEP Study, as compared with VOICE and FEM-PrEP [14,15**,26], and differences in recurrent and undiagnosed STIs or vaginal washing and drying may have heightened women’s susceptibility to HIV [27]. However, in the Partners PrEP Study, the protective effect of PrEP was 67–71% in a subgroup analysis of couples diagnosed with an STI in the past 3 months, and 83% of all HIV-uninfected women in the study reported daily vaginal washing [10**,26].

HIV incidence among women in the Partners PrEP Study placebo arm was 2.8 per 100 person years, substantially lower than incidence rates seen in FEM-PrEP (5.0 per 100 person years) and VOICE (4.2–4.6 per 100 person years) [9,14,15**]. One proposed explanation for this difference is that women in the Partners PrEP Study were primarily exposed to HIV by chronically infected men, who were potentially less infectious than acutely infected men [27]. Although infectivity is a strong predictor of HIV transmission, most infections in generalized HIV epidemics are transmitted from persons with chronic HIV [28,29]; and thus it is likely that most transmissions in FEM-PrEP and VOICE were as well. The overall protective effect of PrEP was 76–78%, among all HIV uninfected participants and 72–84%, among women whose partner had a viral load ≥50,000 copies/ml in the Partners PrEP Study, providing evidence that the prevention benefit of PrEP was not attenuated with exposure to high HIV viral load [10**]. Animal models have demonstrated that the protective effect of TDF-based PrEP does not diminish over time, regardless of the number of challenges, suggesting that there may not be a threshold effect of PrEP when taken with sufficient adherence [30*,31].

The high pregnancy incidence rate among women initiating oral contraceptives during FEM-PrEP initially suggested a potential interaction between oral contraceptives and PrEP [32,33*]. However, low adherence to oral contraceptives, especially among new users, is thought to be the driving factor behind this pregnancy incidence and women who adopted oral contraceptives at study enrollment were also less likely to adhere to study drug [16**,34**]. TDF-based PrEP does not interact with oral, injectable or implantable contraception to reduce either the effectiveness of contraceptives to prevent unintended pregnancy nor the HIV prevention benefit of PrEP [33*,35*]. Indeed, PrEP is one strategy that could mitigate concern regarding the potential increased risk for HIV acquisition among women using progestin-based injectable contraception [36].

Behavioral factors influencing preexposure prophylaxis effectiveness among women

Although challenging to accurately measure, motivation to prevent HIV acquisition is likely tied to self-perceived risk, which in turn influences adherence to HIV prevention strategies [37**]. Despite inclusion criteria based on objective measures of HIV risk and the high observed HIV incidence among placebo arm participants [38**], 50% of women enrolled in FEM-PrEP thought they had ‘no chance’ of acquiring HIV in the next 12 weeks and seroconverters described understimating their risk and rationalizing their risk behavior(s) [14,37*,39**]. Adherence was highest among older participants in BTS, VOICE, and the Partners PrEP Study [15**,40*,41]; younger participants in VOICE and FEM-PrEP were likely less experienced navigating personal risk and this may have influenced their HIV prevention decision-making [24*]. In qualitative interviews, VOICE participants acknowledged that their trial participation was motivated by increased HIV risk from male partners with additional sexual partners, however women often had to compromise study drug adherence and keep their trial participation covert to maintain these relationships [42**].

Across trials, personal assessment of high HIV risk, coupled with social and clinic-based support,
facilitated greater self-efficacy to adhere to daily oral PrEP. HIV-uninfected participants in the Partners PrEP Study had known exposure to HIV from their mutually disclosed HIV infected study partner and both partners received adherence counselling during the trial [39**]. PrEP provided a solution to the ‘discordance dilemma’ by simultaneously preventing HIV acquisition and maintaining the partnership, especially prior to ART initiation by the HIV infected partner [43]. Low or no adherence to PrEP in the Partners PrEP Study was associated with no or infrequent sex with a study partner, suggesting that participants modified their PrEP use based on fluctuations in their sexual activity and perceived HIV risk [11**,41]. Participants in the BTS were self-identified injection drug users attending drug treatment centers who had potential for parenteral and sexual exposure, and 93% of participants elected to attend daily study visits [40*]. Although participants did receive compensation for each study visit, these characteristics also suggest a high motivation for risk reduction.

Despite PrEP being a discrete female-controlled prevention method, community-level stigma related to HIV infection impacted women’s adherence to study drug [44**,45**]. Women in VOICE described the importance of taking their study drugs secretly to preserve their healthy, HIV uninfected image [45**]. Women perceived stigma associated with HIV and encountered suspicion from community members about why an HIV uninfected person would take antiretrovirals [45**]. It was taxing for women to manage social relationships while participating in the VOICE study; these challenges contributed to women concealing study participation and missing PrEP doses [45**,47**].

Features of clinical trials also influenced the behaviors of trial participants. Overall study retention in FEM-PrEP and VOICE was 82–91%, and quality clinical care, education, and modest financial reimbursement in settings with limited opportunity for income generation, motivated women to maintain their participation [9,12–14,15**,42**, 47**,48,49*]. However, retrospectively, participants in FEM-PrEP and VOICE expressed ambivalence about research and the importance of adhering to study medication, including reluctance to use investigational drugs with the potential for side-effects and unknown levels of HIV protection [15**,42**,49*]. Inaccurate self-reported adherence was common in the trials. Participants in FEM-PrEP cited perceived consequences, such as trial termination, negative reactions from study staff, and additional time needed to explain their nonadherence during study visits, as reasons for over-reporting adherence [42**,49*]. Some VOICE participants believed that tenofovir testing would rectify inaccurate self-reported adherence, and poor adherence by some women could be overcome by high adherence from others [42**].

**The HIV prevention benefit of preexposure prophylaxis requires adherence**

The conflicting results across trials regarding the benefit of PrEP for women have challenged the HIV prevention community. However, when analyzed collectively, there is a clear conclusion that daily oral TDF-based PrEP is protective for women, established through subgroup analyses, consistency across studies when adherence is evaluated, and bolstered by analogous data from men. Like any medication, adherence is required for PrEP to be efficacious. Pharmacokinetic studies suggest that consistent adherence is required to achieve sufficient concentrations of tenofovir in vaginal tissues and a substantial proportion of women across studies attained this level of high adherence. The lack of a protective effect observed in FEM-PrEP and VOICE can be attributed to overall low adherence to study medication and is not because of biological features unique to women [50,51]. Although adherence challenges observed across all trials have important implications for PrEP delivery to women, they should not detract from the overall conclusion that PrEP protects women from HIV acquisition when taken with sufficient adherence (Fig. 1).

**DELIVERING PREEXPOSURE PROPHYLAXIS TO WOMEN**

The next steps for PrEP delivery to women include implementation within routine healthcare, in the context of a now-proven protective benefit from PrEP and without the incentives of clinical trials. Clinical trial data suggest that PrEP is tolerant of some missed doses, and additional research is needed to understand how many doses can be missed and still provide HIV protection for women, as well as whether that differs in the presence of cofactors influencing HIV susceptibility.

**Integrating time-limited preexposure prophylaxis into existing reproductive health services**

Integrating HIV risk assessment and PrEP dispensation into established sexual and reproductive health
services that women access routinely, including HIV/STI testing and counselling, antenatal care, and contraceptive counselling, is a natural strategy to maximize the impact of PrEP [24]. Delivery strategies for time-limited PrEP use during periods when a woman’s HIV risk is greatest – including new partnerships with men of unknown HIV status, with HIV infected male partners prior to ART initiation, during pregnancy and pregnancy attempts when condom use is reduced – are feasible, safe, and cost-effective [52–54, 55–58, 59]. Providers can use risk scoring tools to identify women with the highest risk for HIV acquisition using routinely collected clinical and demographic data [60, 61].

Facilitating adherence in public health settings

Individuals’ adherence patterns changed relatively little during the clinical trials; in general, those who initiated PrEP maintained their adherence, especially if they adhered through the end of the first month [11, 15]. Greater public health impact may come from prioritizing PrEP for those who will achieve this sustained high adherence, directing adherence support to the subset with adherence challenges, and assisting women to assess their risk and match PrEP use with their most vulnerable periods [58]. PrEP delivery to women must be coupled with realistic expectations of and mechanisms to facilitate adequate adherence, including personal risk assessment and social support [24, 62–64]. Community sensitization regarding antiretroviral medications for prevention, not just treatment, of HIV may create a context that is more receptive to PrEP use. When it is safe for a woman to share her desire for HIV prevention, her invitation to a male partner to participate in decision-making about PrEP may facilitate her high adherence.

Initial data suggest that adherence to and HIV protection from PrEP is higher in open label-studies when the HIV prevention benefit is well understood by users. Among MSM enrolled in the PROUD (Pre-exposure option for reducing HIV in the UK) study, high self-reported adherence to daily oral TDF-based PrEP was substantiated by blood tenofovir levels and provided 86% protection from HIV [65]. Among HIV serodiscordant couples enrolled in the Partners Demonstration Project using PrEP as a ‘bridge’ until the HIV-infected partner sustains ART use, tenofovir was detected in 86% of samples tested and contributed to an estimated 96% reduction in HIV [66, 67].

Open-label studies also suggest that adherence to daily dosing may be preferred over intermittent or event-driven dosing, perhaps because it fits into daily routines and does not require anticipating sex [68, 69]. In ADAPT (Alternative Dosing to Augment Pre-Exposure Prophylaxis Pill Taking) (HPTN 067), an open-label study of oral PrEP dosing frequency among young South African women, adherence was assessed through Wisepill monitoring.

FIGURE 1. Schematic depicting the totality of evidence for tenofovir-based oral preexposure prophylaxis to prevent HIV among women.
Women randomized to a daily dosing schedule had higher adherence overall and 75% of sexual acts covered by PrEP, as compared with 52–56% of sex acts among women randomized to less than daily or intermittent dosing to align with sexual activity [68*]. Long-acting formulations of PrEP delivered as injectables or vaginal rings, including multipurpose technologies that provide dual protection against HIV and unintended pregnancy, are currently being evaluated and may provide alternative strategies to daily oral PrEP in the future [70,71,72,73*]. Analogous to contraception, for which multiple methods permit choices to accommodate individual women’s needs, multiple delivery mechanisms for PrEP may allow more women to achieve HIV protection [74].

CONCLUSION
Tenofovir-based oral PrEP is an effective HIV prevention strategy for heterosexual women. Significant public health impact from PrEP will require delivery strategies that integrate PrEP into existing health services and address the individual, community, and structural level factors that influence adherence. More than 30 years into the HIV epidemic, oral PrEP is the first intervention that women can control themselves and it offers highly efficacious prevention against HIV.

Acknowledgements
We are grateful for the dedication of the thousands of men and women who have participated in the PrEP clinical trials and open-label demonstration projects.

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None.

Conflicts of interest
There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING
Papers of particular interest, published within the annual period of review, have been highlighted as:
** of special interest
*** of outstanding interest

   These guidelines recommend daily oral PrEP as TDF/FTC for heterosexual women who are at substantial risk of HIV acquisition, including during the periconception and pregnancy periods.

   These guidelines state that PrEP is not contraindicated during pregnancy and is a recommended strategy for HIV uninfected women who are at high risk of HIV acquisition before and during pregnancy, including PrEP as a safer conception strategy for HIV-serodiscordant couples.


   The study presents robust estimates of daily oral PrEP efficacy among subgroups of HIV-uninfected women enrolled in the Partners PrEP Study that facilitate comparison to female study populations enrolled in other PrEP efficacy trials.

   The study presents estimates of TDF-based oral PrEP efficacy within subgroups of the Partners PrEP Study defined by plasma tenofovir levels. High adherence to TDF-based PrEP provided high protection (>99%) from HIV among both men and women, and patterns of adherence were consistent throughout follow-up.


   The article presents the primary intent-to-treatment analysis from the VOICE double-blind placebo controlled randomized controlled trial of tenofovir-based PrEP among young African women. Specifically, the study did not demonstrate that daily oral PrEP prevents HIV acquisition; however, adherence to daily study medication was very low (<30%).

   In this subcohort analysis from three FEM-PrEP trial sites, oral TDF-based PrEP concentrations, as measured by plasma tenofovir levels, were 28.6% at all visits. Only 12% of participants achieved good adherence throughout the study and adherence was lower among women initiating oral contraceptive pills at the time of trial enrollment.


   Men who have MSM enrolled in the open-label Ipergay study achieved high rectal concentrations of TDF-based PrEP and reduced HIV acquisition by 86% with an event-driven, cohort dependent dosing schedule.

   The article presents a comprehensive review of antiretroviral pharmacokinetics, including evidence that suggests higher and/or more consistent dosing of antiretroviral is needed to achieve HIV protection in the female genital tract as compared with rectal tissues.
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20. Cotrell MI, YK, Prince Ha, Sykes C, et al. Predicting effective Truvada® PrEP by dosing strategies with a novel PK-PD model incorporating tissue active metabolites and endogenous nucleotides. HIV research for prevention in South Africa. 2014. Results from a phase I study and population pharmacokinetic models indicate that higher and/or more consistent dosing of oral PrEP is needed to achieve sufficient levels of tenofovir in vaginal or cervical tissues, as compared with rectal tissues.


The review article describes a range of options for HIV prevention specific to young African women, and summarizes barriers and opportunities to implementing PrEP among this population. Importantly, this article comprehensively draws upon behavioral, health economic, and biomedical approaches to HIV prevention and includes discussion on the relationship between cognitive development and risk perception among young women.


The study demonstrated that female macaques developed T-cell responses while on topical or oral PrEP and exposed to multiple simian/human immunodeficiency virus (SHIV) vaginal challenges, suggesting that PrEP can confer protection in vaginal tissues over time, even when faced with repeat challenges.


The study describes the self-perceived HIV risk among a subcohort of women enrolled in the FEM-PrEP trial, and identifies that having some level of self-perceived HIV risk was associated with higher adherence to study medication during follow-up.


Adherence to daily oral TDF-based PrEP was higher among women and older injection drug users enrolled in the BTS, and higher adherence was associated with a higher degree of protection from HIV.


The qualitative substudy nested within the VOICE PrEP trial analyzes female participant experiences navigating individual, household, organizational, and community level factors to adhere to study medication. Although blood tenofovir-levels later revealed that <30% of women adhered to study medication, few women were willing to acknowledge their own extended low or nonuse.


Using data from both men and women, this qualitative substudy nested within the VOICE PrEP trial discusses the direct and indirect influences that male partners had on their female partner’s trial participation and adherence to study medication.


The qualitative substudy nested within the VOICE PrEP trial highlighted community level factors that influenced female participants adherence to study medication, including stigma associated with HIV infection, the importance of preserving a healthy, HIV uninfected image, and confusion over taking antiretrovirals as an HIV prevention strategy.


The qualitative substudy nested within the VOICE PrEP trial explores the tension between attending clinical trial participation and the socioeconomic context of women’s lives. Competing priorities such as work, school, and caregiving made it difficult for women to attend study visits and refill prescriptions of study medications.


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The mixed methods study identified multiple and concurrent sexual partners, transactional sex, low condom use, and unknown HIV status of male partners as risk factors that contributed to the high HIV incidence rate observed among female participants in the FEM-PrEP trial.
The PrEP revolution: from clinical trials to routine practice


The subgroup analysis found that HIV-uninfected women who became pregnant during the Partners PrEP Study had high adherence to study medication in the three months prior to pregnancy. There was no difference in adherence between women who became pregnant and those who did not, providing evidence that PrEP may be an acceptable HIV prevention strategy for women who are attempting pregnancy.


Results from this study show that pregnancy incidence, birth outcomes, or infant growth did not differ between women randomized to the active TDF-based PrEP arms versus placebo in the Partners PrEP Study.


The study estimates the cost effectiveness of and number of HIV infections averted by providing PrEP and ART to HIV serodiscordant couples in both an open-label demonstration project setting and a government program setting in Uganda.


The review includes a comprehensive overview of considerations for prevention-effective adherence to PrEP in the context of public health programs, including a comparison of tools to measure adherence and guidance on counseling messages.


65. McCormack S, Dunn D. Pragmatic open-label randomised trial of preexposure prophylaxis: the PROUD study. Conference on Retroviruses and Opportunistic Infections (CROI); Seattle, WA. 2015.22LB.

Self-reported adherence to daily oral TDF-based PrEP was high among men who have MSM enrolled in the open-label PROUD study and confirmed by blood tenofovir levels. Daily oral PrEP provided 86% protection from HIV.


Preliminary results from HIV serodiscordant couples enrolled in the open-label Partners demonstration project show a 96% reduction in HIV when the HIV-uninfected partner uses daily oral PrEP as a ‘bridge’ until the HIV infected partner sustains ART use.


Among HIV serodiscordant couples followed in the open-label Partners demonstration project, 95% of HIV uninfected partners initiated PrEP at enrollment, and 91 and 84% of participants whose HIV infected partner had not yet initiated ART, continued to use PrEP at 6 and 12 months, respectively. These data provide evidence that PrEP as a ‘bridge’ is an acceptable and feasible risk reduction strategy until the HIV-infected partner achieves and sustains viral suppression.


Overall adherence was higher and a higher proportion of sex acts were protected by oral TDF-based PrEP among women who were randomized to a daily dosing regimen in the open-label ADAPT study, as compared with women who were randomized to less frequent dosing regimens.


71. Clinicaltrials.Gov. Phase 3 safety and effectiveness trial of dapivirine vaginal ring for prevention of HIV-1 in women (ASPIRE) (#NCT01617096); 2015.


Given the very low adherence to daily oral study medication observed in two PrEP efficacy trials alternate delivery mechanisms are needed to offer women additional choices. The review summarizes recent and ongoing studies of PrEP delivered as a vaginal ring.


Given the very low adherence to daily oral study medication observed in two PrEP efficacy trials alternate delivery mechanisms are needed to offer women additional choices. The review summarizes recent and ongoing studies of PrEP delivered as a long acting injectables, including the potential challenges and opportunities for implementing injectables in public health settings.