

Feasibility of Postexposure Prophylaxis (PEP) against Human Immunodeficiency Virus Infection after Sexual or Injection Drug Use Exposure: The San Francisco PEP Study

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The feasibility of providing postexposure prophylaxis (PEP) after sexual or injection drug use exposures to human immunodeficiency virus (HIV) was evaluated. PEP was provided within 72 h to individuals with exposures from partners known to have or to be at risk for HIV infection. PEP consisted of 4 weeks of antiretroviral medications and individually tailored risk-reduction and medication-adherence counseling. Among 401 participants seeking PEP, sexual exposures were most common (94%; $n = 375$). Among sexual exposures, receptive (40%) and insertive (27%) anal intercourse were the most common sexual acts. The median time from exposure to treatment was 33 h. Ninety-seven percent of participants were treated exclusively with dual reverse-transcriptase inhibitors, and 78% completed the 4-week treatment. Six months after the exposure, no participant developed HIV antibodies, although a second PEP course for a subsequent exposure was provided to 12%. PEP, after nonoccupational HIV exposure, is feasible for persons at risk for HIV infection.

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The Committee on Human Research at the University of California, San Francisco, approved the study protocol. Each participant provided written informed consent.

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Initiating prompt antiretroviral treatment after perinatal and occupational exposures to human immunodeficiency virus (HIV) significantly reduces the risk of viral acquisition [1–7] and is now integrated into treatment guidelines [8–10]. The effectiveness of postexposure prophylaxis (PEP) in the occupational and perinatal settings raises the question of whether PEP should also be used for HIV exposures resulting from sexual activity or injection drug use (IDU) [11]. Providing PEP outside the occupational setting is relevant, because sexual activity is the most common route for new infections, and, although PEP is standard for occupational exposures, the risk for acquiring HIV infection across mucosal surfaces is similar to the risk for occupational exposures [12, 13].

Providing PEP after sexual or IDU exposures presents different challenges than for occupational or perinatal exposures [12–14]. Persons exposed to HIV from sexual or IDU activities may not accurately assess their risk for infection and may delay seeking treatment. In the occupational or perinatal setting, the source for the exposure is apparent, and a patient's HIV infection status is easily determined. By contrast, identifying a person's source partner and determining his or her HIV infection status after sexual or IDU exposure may be problematic. Concerns also exist that, if PEP were provided for sexual or IDU exposures, individuals would experience unacceptable side effects or would inadequately adhere to antiretroviral medications or would refuse follow-up for a repeat HIV antibody test. Another concern is whether regimens for PEP would suboptimally suppress HIV and rapidly induce resistance to these agents. Finally, it is uncertain whether the availability of PEP for sexual or IDU exposures might paradoxically increase the behaviors that might lead to viral acquisition. Thus, we initiated the San Francisco PEP study, to assess the feasibility of providing PEP after sexual or IDU exposure to HIV. We designed this study to determine the characteristics of individuals seeking PEP, including the circumstances of their exposure, their recent HIV risk behavior, and the feasibility of identifying their source partners for HIV testing. We also sought to determine the adherence to and side effects of a 4-week course of antiretroviral treatment and the feasibility of retaining participants for repeat HIV testing.

Methods

Study Design

Individuals were eligible to participate if they presented within 72 h after sexual or IDU exposures to source partners with known or suspected HIV infection. Individuals received 4 weeks of antiretroviral medications, as well as risk-reduction and medication-adherence counseling. These individuals subsequently were evaluated for medication adherence and toxicities at 1, 2, and 4 weeks after exposure. HIV antibody determinations were performed 4 weeks and 6 months after the exposure. Repeat requests for PEP for subsequent exposures were allowed.

Participants

Inclusion criteria included potential exposure to HIV within the previous 72 h, age \geq 13 years, and ability to give informed consent. Exposures included receptive or

insertive anal or vaginal intercourse without a condom or with a condom that failed to prevent genital fluid exposure (tore, fell off, etc.); receptive oral intercourse with ejaculation; sharing of IDU equipment; or other activities that resulted in exposures to blood or genital fluids on a mucous membrane or broken skin. These exposures had to be associated with a source partner known by the participant either to be HIV infected or to have an established or possible risk factor for HIV infection. Risk factors included men who have sexual intercourse with men (MSM), past or present IDU, a commercial sex worker, or an anonymous source. All patients seeking to participate in this study were enrolled. Participants were excluded if they were unable to commit to serial evaluations or if established HIV infection was suspected.

Community-based organizations, including the local HIV/AIDS hotline, disseminated information regarding the PEP study. Billboards, leaflets, and palm cards were distributed in locations frequently visited by persons with high risk for HIV exposure. Participants presented to either the sexually transmitted diseases clinic in San Francisco, a county-sponsored community health center, or the San Francisco General Hospital. Study clinicians staffed a 24-h hot line and assessed eligibility criteria and referred participants to the study facilities. The clinician prescribed an initial dose of medication if the participant was evaluated between 6 p.m. and 8 a.m. Participants were encouraged to contact and refer the source of their exposure to the study for HIV antibody testing and ascertainment of antiretroviral treatment history.

Interventions

Antiretroviral medications. If the participant's source's HIV infection status or antiretroviral therapy history was unknown, the fixed combination of zidovudine plus lamivudine (Combivir; Glaxo-Wellcome) administered twice daily was recommended as initial PEP treatment. If the source was receiving or the participant refused a zidovudine-containing regimen, didanosine (200 mg, twice daily) plus stavudine (40 mg, twice daily) were administered. Dual antiretroviral agents had the advantage over other more complex treatment regimens, because adherence was likely to be higher with 2 rather than 3 agents, and the toxicities with 2 agents would probably be lower than with 3 agents. In addition, we hypothesize that the low levels of virus burden associated with initial exposure would probably require fewer active agents than is necessary when treating patients with established infection. Also, there were no data to suggest that 3 agents would provide enhanced clinical value versus 2 agents. Nelfinavir (750 mg, 3 times daily) was added to the dual reverse-transcriptase inhibitor regimen if the source's plasma HIV RNA levels, on treatment, were above the limits of detection. If the source was receiving nelfinavir and had detectable plasma HIV RNA levels, an alternative to nelfinavir as the third agent was left to the investigator's discretion. Individuals were allowed to decline antiretroviral medications and to remain in the study.

Risk-reduction counseling. During the first 5 weeks, participants were provided with 5 risk-reduction counseling sessions (baseline and weeks 1, 2, 4, and 5). Trained counselors, who did not participate in other study assessments, conducted the 20–30-min sessions. The determination of the exposure that led to the participant seeking PEP was obtained before risk-reduction counseling was provided. The intervention was individually tailored on the basis of social cognitive theory, incorporating strategies from motivational interviewing, and included elements of coping

effectiveness training [15–17]. The objectives for the first session included reducing anxiety, exploring the circumstances of the HIV exposure, discussing personal and social barriers to safer practices, and developing an individualized risk-reduction plan. The objectives of the second and subsequent sessions included reviewing and, if needed, revising the risk-reduction plan, reinforcing positive behavior change, and identifying contextual factors that might increase the behaviors associated with HIV transmission.

Medication-adherence counseling. Participants were provided with medication-adherence counseling at baseline, week 1, and week 2. Individually tailored counseling consisted of a review of the treatment regimen, identification of activities in the participant's daily schedule that could serve as "cues" to completing their medication course, and problem-solving potential barriers to adherence. Each session reviewed and developed corrective strategies for any problems that emerged during the course of treatment. The counseling also emphasized that medication did not confer absolute protection against HIV transmission and underscored the importance of the risk-reduction plan. For quality assurance, a clinical supervisor (K.F.) reviewed weekly a sample of all sessions. Medication adherence was measured by self-reported use of medications in the 4 days preceding a study visit.

Measurements and Study Events

After consent was obtained, information on demographic and behavioral history (including information on the exposed participant's perception of the source partner's HIV infection status) was obtained through interviewer-administered questionnaires. Blood was obtained for the following tests: HIV antibody, complete blood cell count, aspartate transferase (AST), alanine transferase (ALT), creatinine, and amylase. A urine pregnancy test was obtained for all women. A 1-week supply of antiretroviral medications was provided, and risk-reduction and medication-adherence counseling were initiated. One week later, participants returned for the HIV antibody result. If the test confirmed unsuspected HIV infection, participants were referred for primary care, and the antiretroviral therapy was discontinued. If HIV antibodies were not detected, the patient was given another week of antiretroviral therapy. An assessment of medication-related toxicities and medication adherence was performed, and risk-reduction and medication-adherence counseling were provided. One week later (week 2), risk-reduction counseling, medication-adherence counseling, and an assessment of medication toxicities and adherence were performed again. If significant toxicities were detected, medications were adjusted. At week 2, an additional 14-day supply of antiretroviral medication was provided, to complete a 28-day course. After 4 weeks of treatment, HIV antibody, complete blood count, AST, ALT, creatinine, and amylase tests were performed. Medication adherence and toxicities were ascertained, and risk-reduction counseling was provided. Participants returned 1 week later to obtain their previous HIV antibody results and for a final assessment of residual toxicities and risk-reduction counseling. Twenty-six weeks after the initial exposure, participants returned for a third HIV antibody test and for further risk-reduction counseling (antibody results were provided at week 27).

Statistical Analysis

Associations between categorical variables at baseline were evaluated with the χ^2 test. Determination of the probability of participants undergoing a second course of PEP, after accounting for those lost to follow-up, was performed by Kaplan-Meier estimation [18]. All analyses were performed with either Stata (Stata) or SAS (SAS Institute) software. All *P* values are 2-tailed.

Results

We enrolled 401 participants, ~1 patient every other day to 1 patient per day from December 1997 through March 1999. Participants were predominantly men (91%; *n* = 363) and were white (69%; *n* = 276), and the median age was 32 years (range, 17–72 years; [table 1](#)). The majority of participants were college educated (59%) and employed (83%), although 6% reported homelessness. Three hundred thirteen participants (78%) reported previous testing for HIV. Most participants (94%; *n* = 375) were residents or lived within 50 miles of San Francisco, although 6% traveled >50 miles to enroll.

Table 1. Baseline characteristics of participants in postexposure prevention study.

Three hundred and seventy-five (93.5%) of the 401 participants sought PEP because of a sexual exposure. Eight (2%) participants reported sharing of IDU equipment. Sexual exposure and sharing IDU equipment were reported by 4 (1%) participants. Fourteen (3.5%) participants had either a nonoccupational needle stick accident (*n* = 9) or another traumatic exposure (3 assaults and 2 bites). Of the 379 participants exposed via sexual activity or via sexual activity and IDU, 327 (86%) were MSM, 20 (5%) were heterosexual men, and 32 (8%) were heterosexual women. Among the sexually exposed participants, receptive (40%) and insertive (27%) anal intercourse were involved in 67% of the exposures ([table 2](#)). Forty-five (12%) individuals reported >1 potential sexual exposure to HIV: 43 of these 45 exposures involved insertive (*n* = 35) and/or receptive (*n* = 40) anal intercourse. Thus, 79% of the sexual exposures involved anal intercourse.

Table 2. Sexual exposure prompting postexposure prophylaxis (*n* = 379).

Type of sexual exposure	Men	Women	Total
Anal intercourse	132	1	133 (40)
Receptive	102	N/A	102 (32)
Insertive	N/A	36	36 (10)
Sexual activity	17	N/A	17 (5)
Anal receptive intercourse	44	1	45 (13)
Other ^a	11	0	11 (3)
Other ^b	11	0	11 (3)

^aNOTE: Data are no. or no. (%) of sexual or sexual and injection drug use exposure. N/A, not applicable.
^b Includes caustic or blood on abrasion or other mucous membrane.

Table 2. Sexual exposure prompting postexposure prophylaxis (*n* = 379).

One hundred seventy-four (43%) participants reported that their source partner was HIV infected, and the remaining 227 (57%) were uncertain about their source's HIV-infection status. Of the 227 participants who were uncertain about their source's HIV

infection status, 174 (77%) reported that their source was an MSM. The remainder identified their source as an injection drug user ($n = 9$), a commercial sex worker ($n = 5$), a person who had intercourse with a commercial sex worker ($n = 1$), an individual with multiple risk factors ($n = 19$), or an anonymous partner for whom they had no risk factor information ($n = 19$). Among MSM presenting with a potential sexual exposure ($n = 327$), there was no difference in the distribution of sexual acts between those with a known HIV-infected source and those with a source whose HIV infection status was uncertain ($P = .7$).

For the majority of participants exposed during sexual activity, the sexual exposure that prompted enrollment represented a lapse in safe sex practices rather than habitual high-risk behavior. The median number of sex partners among MSM in the 3 months before enrollment was 5 sex partners (interquartile range [IQR], 2–10 sex partners). Despite the large number of sex partners, the median number of partners with whom the men practiced various unprotected sex acts was low (figure 1). Seventeen percent of the MSM reported unprotected receptive anal intercourse, and 15% reported unprotected insertive anal intercourse with ≥ 2 different men during the 3 months before study participation. The median number of partners among heterosexual men and among women during the 3 months before enrollment was 2 (IQR, 1–3) and 1 (IQR, 1–2), respectively. Condoms were not used in 246 (65%) of the 379 sexual exposures and either broke or were used incorrectly for the remaining 133 (35%) exposures. Participants who identified their source partner as definitely HIV infected were no more likely to have used a condom (and to have experienced a condom failure) than were participants who were uncertain about the source's HIV infection status (relative risk, 1.1; 95% confidence interval [CI], 0.80–1.4).

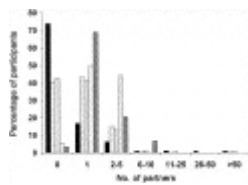


Figure 1. No. of unprotected sex partners for participants in the 3 months before postexposure prevention exposure. *Solid bar*, Men who have receptive oral sex with men; *bar with grid lines*, men who have receptive anal intercourse; *vertically striped bar*, men who have insertive anal intercourse; *dotted bar*, men who experience insertive vaginal sex; *checkered bar*, women who experience receptive vaginal sex with men.

The 401 participants recruited 64 source partners for HIV testing, and 50 (76%) source partners were HIV infected. Of the 174 participants who identified their source as HIV infected, 50 (29%) brought in their source partner; 49 agreed to be tested, and all had detectable HIV antibodies. By contrast, of the 227 participants who were uncertain of their source's HIV infection status, only 14 (7%) brought in their source partner for HIV testing, and HIV infection was detected in 1 (7%) of these source partners. The newly detected HIV infection was unsuspected by the source partner.

The median time from exposure to initial treatment was 33 h (IQR, 18–53 h). Four individuals declined to initiate medications. The source partner's treatment history was usually unknown, and thus the combination of zidovudine plus lamivudine was initially prescribed for 351 (86%) of the 397 individuals who elected to be treated (table 3). Didanosine and stavudine were prescribed for 31 exposures (8%). Nelfinavir was prescribed infrequently and according to the prespecified criteria for adding a third agent (3%).



Table 3. Antiretroviral treatment (ART) course among patients in postexposure prevention study.

A total of 309 (78%) participants completed 4 weeks of treatment ([table 4](#)). Significantly more patients treated with didanosine plus stavudine completed 4 weeks of therapy than did those receiving zidovudine plus lamivudine (94% vs. 76%; $P = .01$). Among participants who completed 4 weeks of therapy, the percentage of persons reporting complete adherence during the 4 days before the clinic visit ranged from 84% to 78% during the 4-week course of medication ([table 4](#)). The percentage of treatment completion and adherence that was observed occurred despite considerable subjective toxicity, including nausea (52%), fatigue (44%), headache (24%), diarrhea (15%), and anorexia (12%). Laboratory toxicity occurred among <2% of the participants and was reversible in all cases. Other than the 37 participants who were lost to follow up, the principal reasons for discontinuing treatment were medication toxicities ($n = 27$) and reevaluation of risk for HIV exposure, including a determination that the source of exposure was not HIV infected ($n = 10$). Three participants discontinued medications after they were diagnosed with HIV infection (unsuspected for each individual). After 6 months of follow up, 300 (75%) participants were available for repeat HIV antibody testing, and none of the patients (95% CI, 0%–1.0%) had developed detectable HIV antibodies. Six months after the initial exposure, 39 participants (12% by Kaplan-Meier estimation) had sought to repeat PEP for a second exposure.

Table 4. Adherence to medications among participants completing 4 weeks of therapy in the postexposure prevention study.

Medication regimen	Week 1	Week 2	Week 4
Zid + 3TC	21 (18%)	18 (17%)	17 (17%)
ddI + ddC	11 (10%)	10 (10%)	11 (11%)
Zid + 3TC + ddI	4 (3%)	4 (3%)	4 (4%)
ddI + ddC + ddI	1 (1%)	1 (1%)	1 (1%)
Total	27 (23%)	23 (22%)	23 (23%)

NOTE: Data are no. (%) of participants reporting 100% adherence to medication regimen during the previous 4 days. 3TC, lamivudine; ddI, didanosine; ddC, didanosine; ddI + ddC, didanosine/didanosine; Zid + 3TC, zidovudine/lamivudine.

Table 4. Adherence to medications among participants completing 4 weeks of therapy in the postexposure prevention study.

Discussion

The theoretical benefits and risks of PEP after sexual and IDU exposures to HIV have been extensively debated [[7](#), [9](#), [11](#), [12](#), [14](#), [19](#)], but no data on the actual practice of providing PEP have been gathered. Accordingly, the Centers for Disease Control and Prevention neither support nor oppose the provision of PEP after nonoccupational exposures [[11](#)]. Although our study does not resolve all the questions regarding PEP after sexual or IDU exposures, it has addressed several critical concerns regarding the feasibility of providing PEP in these settings.

We have demonstrated that persons with sexual exposures will seek PEP. For the majority of individuals presenting with a sexual exposure, the episode represented a lapse in safe sexual practices and was not part of a pattern of habitually high-risk behavior. Although our enrollment criteria were broadly inclusive for HIV transmission risks, the majority of those presenting with sexual exposures reported the highest risk acts, such as receptive anal and receptive vaginal intercourse. Only 4% of participants sought PEP solely for receptive oral intercourse.

Our program attracted few individuals reporting IDU exposures. This may reflect a lack of interest within this group, fear of disclosure of unlawful activities, inadequate

outreach by our program, or low levels of needle sharing because of San Francisco's needle exchange program. Localities where the prevalence of IDU is higher than in San Francisco, or where needle exchange programs are not available, may experience a higher demand for PEP among injection drug users than we observed.

In addition to demonstrating the feasibility of identifying persons with sexual exposures to HIV, our study also showed that exposed persons can be reliably and safely treated with a 4-week course. Despite a high incidence of subjective toxicity, 78% of our participants completed the treatment course, compared with 45%–62% of persons receiving PEP after an occupational exposure [20–22]. The higher completion rates that we observed probably resulted from several factors. First, we provided one-on-one medication-adherence counseling. Second, we dispensed only a limited supply of medications at each visit (1- and 2-week supplies). Our dispensing schedule necessitated several visits, and, at each visit, participants had considerable contact time with program staff. We believe that this contact and individualized attention increased our participants' motivation to complete the treatment course. Third, our most commonly prescribed medication regimen, the zidovudine plus lamivudine combination pill used twice daily, is probably associated with fewer side effects and greater ease-of-use than that associated with 3-drug regimens recently reported [20].

Finally, we have determined that is feasible to retain exposed individuals and to reevaluate them 6 months after exposure for HIV seroconversion and residual toxicity from the medication regimen. Because we observed a very low incidence of biochemical toxicity and no irreversible toxicity, we believe that PEP can be performed without routine laboratory monitoring for toxicity. Such monitoring should be reserved for persons with preexisting hematological, hepatic, or pancreatic disease. On the other hand, our finding of 3 unsuspected HIV infections in the 401 participants seeking PEP underscores the importance of testing patients seeking PEP for HIV infection at presentation. Although PEP should not be delayed until results are available, testing avoids the possibility of HIV-infected patients receiving a 28-day course of incompletely suppressive antiretroviral medications.

Although our study has addressed several of the fundamental issues regarding the feasibility of providing PEP after sexual or IDU exposures to HIV, other questions must be resolved before the overall utility of the intervention can be determined. The most important question is whether PEP is effective in preventing HIV transmission after nonoccupational exposures. Because we had no untreated comparison group, our study was not designed to evaluate efficacy. Although we did not observe any participants who developed detectable HIV antibodies at 6 months after exposure, this should not be considered evidence that PEP is efficacious. It is not unexpected to observe no seroconversions among 401 individuals, in light of the low per-contact risk for HIV transmission [13, 23] and the likelihood that many of the exposures in our study were not to individuals truly infected with HIV.

The efficacy of PEP after nonoccupational exposures is not known, but if PEP can prevent transmission, its efficacy is probably related to how quickly it can be administered [24, 25]. Despite our provision of 24-h physician coverage, the average time between exposure and treatment was 33 h. This is substantially longer than the average 1.75–4 h between exposure and treatment reported for occupational PEP [20, 21]. This may not bode well for the feasibility of sites that may have even fewer

resources than this project to rapidly administer PEP. The longer interval between exposure and treatment that we observed might include delays by the participants in recognizing the risk associated with the exposure and identifying treatment sites. Although it is likely that the success of PEP in preventing transmission after nonoccupational exposures also depends on other factors besides duration between exposure and treatment (such as size of the inoculum, viral pathogenicity, genetic predisposition for infection, and viral resistance to medications), it is essential that methods for optimizing the rapidity of medication delivery be developed. A first step in this process is educating a broader group of physicians on how to provide PEP in emergency and primary care settings.

The higher completion rates observed for participants using stavudine plus didanosine, compared with those taking zidovudine plus lamivudine, were unexpected because the stavudine plus didanosine regimen is more complex in terms of number of pills per day. The higher completion rate may be a product of our study protocol. Stavudine plus didanosine were administered when the source's past or present medications included zidovudine, in an attempt to provide treatment against a possibly resistant isolate. Therefore, when participants receiving didanosine plus stavudine developed tolerable adverse reactions, they were discouraged from changing to zidovudine plus lamivudine. By contrast, those receiving zidovudine plus lamivudine who experienced an adverse event were encouraged to switch to didanosine plus stavudine to complete their treatment course. It is also possible that the completion rate was higher for those using stavudine plus didanosine because they experienced less nausea and vomiting, although they did experience more diarrhea. Despite our observation of higher completion among those taking stavudine and didanosine, allocation of treatment was not random; therefore, we continue to recommend zidovudine plus lamivudine as the standard regimen. This recommendation stems from the relative ease of adherence to zidovudine plus lamivudine combined into a single pill administered twice daily. The nonnucleoside reverse-transcriptase inhibitors (NNRTIs) may have a role in this setting. However, we chose not to include this class of compounds, because available PEP data had used nucleoside therapy, and adding an NNRTI would probably lead to increased toxicity, reduced compliance, and higher costs.

In the occupational setting, the HIV serostatus of the source individual is often known, and, if it is not, it can usually be rapidly ascertained. By contrast, more than half of our participants did not know the HIV infection status of their source partner, on initial presentation, and, among these participants, only 7% subsequently contacted their source partner and facilitated his or her recruitment into the program for HIV testing. The relatively low referral rates of potential source partners is probably explained by the high rates of anonymous sexual activities, unclear legal ramifications of identifying a partner, and the lack of perceived clinical relevance to the participant if the source partner was not immediately identified and enrolled in the project. We justified treating persons who were uncertain about their source partner's serostatus on the high pretest probability that a source partner in San Francisco was HIV infected (31% of MSM in San Francisco are estimated to be infected) [14, 26, 27]. Clinicians in other localities should anticipate that most persons presenting for PEP will be uncertain of their source partner's serostatus and therefore will need to take into account the local prevalence of HIV among pertinent source risk groups [28]. Because optimizing the cost effectiveness of PEP in the nonoccupational setting requires that a

high percentage of treated individuals have been exposed to source partners who are truly infected with HIV, future work should focus on improved ascertainment of the source partner's serostatus. This could include novel techniques in partner notification or the use of home-based rapid testing of source partners that would eliminate the need for sources to come to testing sites.

This study did not include a cost-per-case determination. Others, however, have assessed the cost effectiveness of nonoccupational PEP. Cost-effectiveness models depend on a number of factors, including risk of infection, costs of establishing and maintaining the prevention infrastructure, efficacy of PEP, and reduction of future risky behaviors. A recent economic analysis determined that PEP could be cost effective when applied to persons exposed from an HIV-infected partner and to persons reporting unprotected anal intercourse with anonymous partners or possibly other partners with similar risk for HIV infection [29]. Other calculations suggest that indiscriminate use of PEP could be extremely expensive and perhaps beyond the budgetary scope of most programs [30, 31].

An ongoing concern is the possibility that some people will use PEP as their primary form of HIV prevention and will either fail to reduce or actually increase their high-risk exposures because they perceive that PEP will fully prevent virus transmission. If the availability of PEP were to facilitate behavioral disinhibition, the net effect would increase HIV incidence [32]. We do not have any data to suggest that offering PEP influenced risk-taking behavior in this community. Other studies provide conflicting information on whether risk behavior changes with knowledge or availability of PEP [33–35]. Our finding that 12% of participants (probably an underestimate of the true frequency of high-risk exposures) returned for a second course of PEP within 6 months of the initial exposure underscores this concern but should not necessarily be considered proof of long-term behavioral disinhibition. For example, an individual requiring repeated courses of PEP might learn to reduce his or her risk for HIV infection if the succeeding courses are accompanied by more intensive prevention counseling. The period immediately after an exposure to HIV is a unique opportunity for clinicians to provide education and counseling regarding the prevention of future exposures [36–38]. Because persons seeking PEP are highly motivated to avoid infection, they may be in a "window period" in which education and counseling will have significant influence. Providing PEP also promotes testing for other sexually transmitted diseases and for the provision of immunizations, such as those for hepatitis A and B. Therefore, the value of PEP may extend beyond any benefit of diminished probability of transmission associated with antiretroviral treatment of the presenting exposure.

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