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What is This?
Acceptability of Oral versus Rectal HIV Preexposure Prophylaxis among Men Who Have Sex with Men and Transgender Women in Peru

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Abstract

Objective: Oral preexposure prophylaxis (PrEP) with antiretrovirals (ARVs) is at the forefront of biomedical HIV prevention research, and ARVs are also being tested for rectal administration to target people practicing unprotected receptive anal intercourse (URI) and at risk of HIV infection. This study assessed the acceptability of daily oral PrEP and rectal PrEP during URI among men who have sex with men (MSM) and transgender women (TGW) in Peru. Methods: During the 2008 HIV sentinel surveillance survey conducted in 3 Peruvian cities (Lima, Iquitos, and Pucallpa), MSM and TGW reported being “versatile,” “most of the time receptive,” and “exclusively receptive” during anal sex behavior where surveyed on their acceptability of oral and rectal PrEP. Results: Among 532 individuals, high acceptance of either oral (96.2%) or rectal (91.7%) PrEP products was reported. If both products were efficacious/available, 28.6% would prefer a pill, 57.3% a rectal lubricant, and 14.1% either. A trend toward higher acceptance was observed as receptive anal sex behavior exclusivity rose (P = .013). Being receptive most of the time (adjusted odds ratio [aOR]: 9.1, P = .01) and exclusively receptive (aOR: 7.5, P = .01), compared to being versatile, were independently associated with oral PrEP acceptability. A similar association was found with the acceptability of rectal formulations (aOR: 2.3, P = .07; and aOR: 2.5, P = .02; respectively). Conclusions: Oral and rectal PrEP were highly acceptable among Peruvian MSM and TGW, particularly among those at the highest HIV infection risk. These data can guide the implementation of PrEP programs in Peru and similar settings and populations.

Keywords

HIV-1, preexposure prophylaxis, rectal microbicides, high-risk, homosexual men, transgender women, Peru

The use of antiretrovirals (ARVs) to prevent HIV acquisition before exposure (preexposure prophylaxis or PrEP) is at the forefront of current biomedical prevention research. Recently, proof-of-concept clinical trials of vaginally applied and daily oral tenofovir-based PrEP have proved to be efficacious in preventing HIV-1 infection in different populations at risk, with no major safety concerns or increase in sexual risk-taking behaviors.¹⁻⁴ However, other PrEP trials failed to show efficacy,⁵,⁶ presumably because of poor adherence or other biological factors presently unknown. Although the US Food and Drug Administration (FDA) has approved the use of Truvada for use as PrEP, the policy has not been universally adopted by all countries, and in Peru—where Truvada is not yet available for treating HIV—its use for prevention is still far off. Nonetheless, policymakers, with advocacy from populations at risk, are considering the implications of translating positive PrEP findings into programmatic priorities (to address the need to identify and implement innovative evidence-based HIV-prevention strategies). ARVs are in the early stages of being formulated and tested for rectal administration (as rectal

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microbicides—RMs), which would eventually be targeting people who have unprotected receptive anal intercourse (URAI) and are at risk of HIV infection, including men who have sex with men (MSM) and transgendered women (TGW).

Although data from recent PrEP subgroup analyses showed that efficacy was higher among more adherent study participants—pointing to further research on adherence and its effect on overall HIV prevention efficacy—it is still unknown which PrEP strategies (ie, oral or rectal—if efficacious) would work best to prevent HIV infection in populations at risk via URAI as well as to whom each strategy would be targeted and the specifics of usage (eg, daily or intermittent use, several hours prior to sexual intercourse, or before or during intercourse, etc). Nonetheless, it is clear that if these products are found to be efficacious and are eventually launched commercially then users will make choices about how and when to use them based on personal preferences.

In Peru, MSM and TGW would benefit from PrEP interventions based on their high HIV prevalence and incidence rates, which are comparable to those observed in some heterosexual populations of sub-Saharan Africa. In these populations, URAI is common and highly associated with prevalent and incident HIV infection. To better understand the feasibility of implementing potential PrEP interventions in MSM and TGW at high HIV risk in Peru, we assessed the acceptability of using efficacious ARV-based product formulations to prevent HIV administered either orally everyday or rectally in conjunction with URAI.

**Methods**

**Study Population and Study Design**

This sub-study was nested in a HIV sentinel surveillance survey of HIV and sexually transmitted infections (STI) among MSM and TGW at high risk that was conducted in 3 cities in Peru (the capital and coastal city of Lima, and Lquipos and Pucalla, the 2 largest cities of the Amazon River basin region) during 2008.

In this survey, males 18 years of age or older were enrolled if meeting the following criteria: reported anal sexual intercourse with one or more man during the preceding 6 months; residing in one of the study cities; of unknown HIV serostatus or not having their last HIV test at least twelve months before with a negative result and having any of the following sexual behaviors for acquiring HIV-1 infection in the previous 6 months: (1) no condom use during the last episode of anal intercourse; (2) anal intercourse with more than 5 sex partners; (3) the exchange of money, gifts, shelter, or drugs for anal sex; (4) an STI diagnosis; or (5) being the sex partner of an HIV-positive man.

Potential participants were referred to sentinel sites by peer outreach workers at socialization venues (eg, saunas, pornographic movie theaters, sex work areas, discoteques, bars, beauty parlors, sports events). At study sites, participants underwent a structured computer-assisted self-interview for demographics and sexual risk behavior assessment, including primary anal sexual role (5-point Likert scale: exclusively insertive, most of the time insertive, versatile, most of the time receptive, and exclusively receptive) and lubricant use during rectal anal intercourse; a medical history and targeted physical examination; and a peripheral venous blood draw for HIV-1 (Determine HIV-1/2 Rapid Antibody Test, Abbott Diagnostics, Abbott Park, Illinois; and Western blot, Biorad Laboratories, Hercules, California) and syphilis (rapid plasma reagin and microhemagglutination assay, both from Organon Teknika, Durham, North Carolina) testing. All participants received STI and HIV pretest and posttest risk reduction counseling and condoms, and syphilis treatment when indicated (in accordance with the 2006 US Centers for Disease Control and Prevention Guidelines). Participants with an HIV diagnosis were referred for standard care including access to antiretroviral therapy. Participants were provided with condoms and transportation cost reimbursement.

Only individuals reported being “versatile,” “most of the time receptive,” and “exclusively receptive” as their primary anal sexual role were included in this substudy.

To assess the acceptability of using oral or rectal PrEP formulations, we asked, “If it were available, would you use a pill every day to decrease your risk of becoming infected with HIV?” and “If it were available, would you use a lubricant during anal sex to decrease your risk of becoming infected with HIV?” Both questions had the following response choices: (1) yes, I definitely would use it; (2) yes, I probably would use it; (3) no, I probably would not use it; and (4) no, I definitely would not use it.

To assess acceptability of using any efficacious PrEP formulation (oral, rectal, or either), we asked, “If you could choose between taking a pill every day or using a lubricant applied only during anal sex to decrease your risk of becoming infected with HIV, which would you prefer?”; and provided the following response choices: (1) I definitely would use the pill; (2) I probably would use the pill; (3) I probably would use the lubricant; (4) I definitely would use the lubricant; and (5) I would use either the pill or the lubricant.

The study protocol, informed consent forms, and recruitment materials were approved by the Asociación Civil Impacta Salud y Educación and US Naval Medical Research Center Unit No. 6 Institutional Review Boards in compliance with all applicable Peruvian and US federal regulations governing the protection of human participants.

**Statistical Analysis**

Univariate analyses of selected variables were performed by chi-square and Fisher’s exact tests for categorical variables and Mann-Whitney U Test for 2 independent samples for continuous variables.

To predict the independent factors associated with acceptability for using specific formulations of HIV PrEP products (oral or rectal), we conducted adjusted binomial logistic regression analyses using backward stepwise selection procedures. Acceptability was assessed collapsing from 4 to 2 levels “yes, I would use it” (“yes, I definitely would use it” and “yes, I probably would use it”) and “no, I would not use it” (“no, I probably would not use it” and “no, I definitely would not use it”).
it”). Independent factors associated with the use of any efficacious PrEP product (oral, rectal, or either) were assessed by adjusted multinomial logistic regression analysis using backward stepwise selection procedures. Acceptability was collapsed in 3 categories “I would use the pill” (“I definitely would use the pill” and “I probably would use the pill”); “I would use the lubricant” (“I probably would use the lubricant” and “I definitely would use the lubricant”); and “I would use either the pill or the lubricant”. These analyses yielded adjusted odd ratios (aORs) and 95% confidence intervals (CI).

All reported P values represent 2-sided tests. Statistical analyses were computed using Statistical Package for the Social Sciences version 16.0 (SPSS Inc, Chicago, Illinois).

Results

Study Population and Participants Characteristics

We analyzed the data from 532 participants. Enrollment was fairly even across all the cities, with the least number (161) residing in Pucallpa, followed by 172 from Iquitos and 199 persons from Lima. A total of 111 reported being mainly versatile, 170 mostly receptive, and 251 exclusively receptive in their anal sex role.

The median age of our study population was 28 years (interquartile range [IQR]: 23–35) with a range of 18 to 68 years. Most had completed secondary education and described their sexual identity as homosexual. Among all participants, 40.2% had accepted money, food, gifts, or accommodations in exchange for sex in the previous 6 months. In the previous 3 months, 67.5% had used alcohol and 6.0% drugs before or during sex. Participants reported a median of 5 male partners (IQR: 2–10) and 36 (6.8%) also reported having at least 1 female partner in the previous 3 months. “Exclusively receptive” participants had lower education levels, self-identified as TGW, and reported less lubricant use. Up to 41.7% of the participants reported URAI during the last sexual intercourse, but this behavior varied by primary anal sexual role, among versatile it was 36.3%, among most of the time receptive it was 36.4%, and among exclusively receptive it was 47.6%. Lubricant use in the preceding 3 months was reported by 55.7% of the sample (Table 1).

Acceptability for Using Specific Formulations of Oral or Rectal Efficacious PrEP Formulations

High acceptance of either oral or rectal PrEP products was reported by the study participants. If both products were efficacious and available, there was a higher preference for using a rectal product compared to the use of an oral product. A trend toward higher PrEP acceptance was observed as receptive anal sex behavior was reported to be more exclusive (P = .013; Table 2).

After adjustment for age, city, and education, only being receptive most of the time (aOR: 9.1, 95%CI: 1.8–46.5, P = .01) and exclusively receptive (aOR: 7.5, 95%CI: 1.6–53.2, P = .01) during anal intercourse, compared to being versatile, were independently associated with acceptability for using oral PrEP products. A similar association was found with the acceptability of a rectal formulation (ie, lube; aOR: 2.3, 95%CI: 0.9–6.1, P = .07; and aOR: 2.5, 95%CI: 1.1–5.4, P = .02). No individual characteristic was found to be independently associated with the acceptability for using any efficacious PrEP product after an adjusted multinomial logistic regression analysis.

Discussion

Although several studies are emerging with regard to the acceptability of oral PrEP in different populations, to our knowledge, this is the first to assess the acceptability of oral versus rectal PrEP among MSM and TGW who mainly practice URAI. Importantly, data for this study were collected in 2008, before the results of the iPrEx study were disseminated in 2010, thereby providing a unique opportunity to assess the potential PrEP acceptability when the approach was still hypothetical. Our findings suggest that efficacious oral or rectally formulated HIV PrEP interventions would be highly acceptable among MSM and TGW practicing receptive anal sex and with concomitant high-risk sexual behavior. Additionally, acceptability of HIV PrEP increased as HIV risk (ie, receptive anal sex behavior) increased. Combined, these findings bode well for the potential uptake of future tailored PrEP interventions whether formulated as an oral tablet or as a rectal lubricant. In particular, the finding that the acceptability of oral PrEP was independently associated with being receptive exclusively or most of the time suggests some awareness among this population that an intervention such as PrEP may help to protect them from HIV infection.

The high acceptability of PrEP reported in this study is consistent with a growing body of research of PrEP acceptability globally. Specifically in Peru, 3 previous studies have assessed the acceptability of different PrEP interventions, including RMs alone,19 oral PrEP alone,20 and oral PrEP versus injectable PrEP.17 In this latter study, similar to ours, different PrEP administration routes were assessed, daily oral versus a monthly injection in the arm or bimonthly injections in the buttocks. Injections of either type were preferred to the oral formulation.17 A next research step would be to compare acceptability of oral versus topical (ie, rectal) versus injectable PrEP specifically within the context of sexual role. Although each study used different methodologies, the consensus is that among high-risk Peruvian MSM and TGW, PrEP of some type would be highly acceptable.

Unprotected receptive anal intercourse is the sexual behavior with the highest per act risk of HIV acquisition conferring approximately 10 to 20 times more risk than unprotected receptive vaginal intercourse, a behavior commonly practiced by MSM and TGW who are in need of new approaches to HIV prevention. Because rates of lubricant use are high in MSM and TGW practicing receptive anal sex, the development of an ARV-based RM gel may provide a safe and effective means of preventing HIV infection with an intervention that is likely to
### Table 1. Selected Demographic, Behavioral, and Clinical Characteristics of Study Participants According to Primary Anal Sex Rolea

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Versatile (N = 111)</th>
<th>Mostly Receptive (N = 170)</th>
<th>Exclusive Receptive (N = 251)</th>
<th>Total (N = 532)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Age, years</td>
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<td>&lt;25</td>
<td>45</td>
<td>40.5</td>
<td>58</td>
<td>34.1</td>
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<tr>
<td>≥25</td>
<td>66</td>
<td>59.5</td>
<td>112</td>
<td>65.9</td>
</tr>
<tr>
<td>Educationb</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>62</td>
<td>55.9</td>
<td>61</td>
<td>35.9</td>
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<tr>
<td>High school</td>
<td>48</td>
<td>43.2</td>
<td>96</td>
<td>56.5</td>
</tr>
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<td>More than high school</td>
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<td>0.9</td>
<td>13</td>
<td>7.6</td>
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<tr>
<td>Sexual orientationb</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Bi/heterosexual</td>
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<td>32.4</td>
<td>16</td>
<td>9.0</td>
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<tr>
<td>Homosexual</td>
<td>64</td>
<td>61.0</td>
<td>116</td>
<td>69.9</td>
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<tr>
<td>Transgender</td>
<td>7</td>
<td>6.7</td>
<td>35</td>
<td>21.1</td>
</tr>
<tr>
<td>Symptoms of STI in the past 6 monthsb</td>
<td>24</td>
<td>21.8</td>
<td>35</td>
<td>20.7</td>
</tr>
<tr>
<td>Gifts, favors, or place to sleep for sex</td>
<td>35</td>
<td>32.4</td>
<td>74</td>
<td>43.8</td>
</tr>
<tr>
<td>Alcohol consumption before or during sexc</td>
<td>77</td>
<td>72.0</td>
<td>112</td>
<td>59.6</td>
</tr>
<tr>
<td>Drug consumption before or during sexc</td>
<td>9</td>
<td>69.2</td>
<td>12</td>
<td>50.0</td>
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<tr>
<td>Number of male sexual partnersc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>7</td>
<td>6.3</td>
<td>21</td>
<td>12.5</td>
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<tr>
<td>1</td>
<td>13</td>
<td>11.7</td>
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<td>13.1</td>
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<td>2-5</td>
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<td>10+</td>
<td>25</td>
<td>22.5</td>
<td>43</td>
<td>25.6</td>
</tr>
<tr>
<td>Sex with womenc</td>
<td>21</td>
<td>19.1</td>
<td>10</td>
<td>6.0</td>
</tr>
<tr>
<td>Lubricant useb,c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>39</td>
<td>35.1</td>
<td>65</td>
<td>38.2</td>
</tr>
<tr>
<td>Sometimes</td>
<td>55</td>
<td>49.5</td>
<td>79</td>
<td>46.5</td>
</tr>
<tr>
<td>Always</td>
<td>17</td>
<td>15.3</td>
<td>26</td>
<td>15.3</td>
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<tr>
<td>Unprotected anal intercourseb,c</td>
<td>37</td>
<td>36.3</td>
<td>52</td>
<td>36.4</td>
</tr>
<tr>
<td>HIV infection</td>
<td>11</td>
<td>9.9</td>
<td>18</td>
<td>10.6</td>
</tr>
<tr>
<td>Syphilis infection</td>
<td>17</td>
<td>15.3</td>
<td>23</td>
<td>13.6</td>
</tr>
<tr>
<td>Early syphilis infection</td>
<td>5</td>
<td>4.5</td>
<td>9</td>
<td>5.3</td>
</tr>
</tbody>
</table>

a Total denominators varied slightly because of missing data.

b P ≤ .05, chi-square test for homogeneity.

c In the preceding 3 months.

### Table 2. Acceptability for Specific Formulations of Hypothetical Oral and Rectal Efficacious HIV PrEP Formulations

<table>
<thead>
<tr>
<th>PrEP Formulation</th>
<th>Versatile (N = 111)</th>
<th>Mostly Bottom (N = 170)</th>
<th>Exclusive Bottom (N = 251)</th>
<th>Total (N = 532)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Oral productb</td>
<td>104</td>
<td>93.7</td>
<td>160</td>
<td>94.1</td>
</tr>
<tr>
<td>Rectal productc</td>
<td>100</td>
<td>90.1</td>
<td>153</td>
<td>90.0</td>
</tr>
<tr>
<td>Any product</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral product</td>
<td>28</td>
<td>25.2</td>
<td>48</td>
<td>28.2</td>
</tr>
<tr>
<td>Rectal product</td>
<td>60</td>
<td>54.1</td>
<td>94</td>
<td>55.3</td>
</tr>
<tr>
<td>Any</td>
<td>23</td>
<td>20.7</td>
<td>28</td>
<td>16.5</td>
</tr>
</tbody>
</table>

Abbreviation: PrEP, preexposure prophylaxis.
b Preexposure prophylaxis.
c Provided as a pill.
d Provided as a rectal lubricant.
have high acceptability among the target population. Building on the results of before-and-after sex vaginally applied TDF 1% gel to prevent HIV infection, the RM field is now launching a phase II clinical trial to evaluate the safety and acceptability of Truvada tablet and rectally applied tenofovir reduced-glycerin 1% gel among MSM and TGW in several international settings including Peru. Although not powered for efficacy, the results of this study will nonetheless provide the data needed to, ideally, justify the progression to a large-scale efficacy trial.

The limitations of our study may be attributed to its design as a secondary analysis. This convenient sample was restricted to a relatively educated high-risk MSM population practicing receptive anal intercourse from 3 Peruvian cities. The outcome measures were based on single questions asking for potential acceptability of hypothetical efficacy products with answers having nominal categories which were further collapsed for statistical analysis, all of which could affect the interpretation of results. Potential frequency of use was not measured in our study but is an important factor to assess (ie, daily, intermittent, or coitally dependent). There was also a lack of power to assess the relationship between participant characteristics and expressed willingness to use PrEP products. Finally, the expressed attitudes about willingness to use hypothetical products may not be maintained when the actual product is available.

Oral PrEP is fast becoming a reality and is poised to receive FDA approval for its explicit marketing and use for HIV prevention in MSM, a move that could influence the decisions in other countries. Despite its limitations, this study provides important and novel information on the acceptability of oral and rectal PrEP among MSM and TGW practicing URAI in Peru that can guide the implementation of future programs in this and similar settings and populations.

**Authors’ Note**

The findings of this study were presented in part at the 18th International Society for Sexually Transmitted Disease Research Congress. London, England. June 28th-July 1st, 2009. Abstract no. OS 1.10.02. The study protocol and informed consents were approved by the Asociación Civil Impacta Salud y Educación and United States (US) Naval Medical Research Unit Six Institutional Review Boards in compliance with all applicable federal regulations governing the protection of human participants. Silvia M. Montano and Tadeusz Kochel are employees of the US Government. This work was prepared as part of their official duties. Title 17 U.S.C. 105 provides that Copyright protection under this title is not available for any work of the US Government. Title 17 U.S.C. 101 defines a US Government work as a work prepared by a military service member or employee of the US Government as part of that person’s official duties. The opinions and assertions contained in this manuscript are those of the authors and do not necessarily reflect the official policy or position of the US Department of the Navy, US Department of Defense, and the US Government or of any of the other organizations listed.

**Declaration of Conflicting Interests**

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