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Antiretroviral Medication Adherence and Amplified HIV Transmission Risk Among Sexually Active HIV-Infected Individuals in Three Diverse International Settings

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Abstract

Successful biomedical prevention/treatment-as-prevention (TasP) requires identifying individuals at greatest risk for transmitting HIV, including those with antiretroviral therapy (ART) nonadherence and/or ‘amplified HIV transmission risk,’ defined as condomless sex with HIV-uninfected/unknown-status partners when infectious (i.e., with detectable viremia or STI diagnosis according to Swiss criteria for infectiousness). This study recruited sexually-active, HIV-infected patients in Brazil, Thailand, and Zambia to examine correlates of ART nonadherence and ‘amplified HIV transmission risk’. Lower alcohol use (OR = .71, $p < .01$) and higher health-related quality of life (OR = 1.10, $p < .01$) were associated with greater odds of ART adherence over and above region. Of those with viral load data available (in Brazil and Thailand only), 40 % met Swiss criteria for infectiousness, and 29 % had ‘amplified HIV transmission risk.’ MSM had almost three-fold (OR = 2.89, $p < .001$) increased odds of ‘amplified HIV transmission risk’ (vs. heterosexual men) over and above region. TasP efforts should consider psychosocial and contextual needs, particularly among MSM with detectable viremia.

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Keywords

Adherence; Treatment as prevention; HIV transmission; Amplified risk; Alcohol use; MSM; Biomedical prevention

Introduction

Groundbreaking advances in biological HIV prevention have occurred recently, including studies definitively showing that viral suppression through early [1] or ongoing [2] HIV treatment with antiretroviral therapy (ART) can significantly eliminate HIV transmission in serodiscordant couples. Achievement of viral suppression with ART, however, requires optimizing and sustaining adherence to these regimens. Additionally, the rates of adequate uptake, adherence, and viral suppression may be higher in clinical trials and in identified stable serodisocordant partnerships than in many real-world HIV care settings. Thus, the extension of treatment as prevention (TasP) requires identifying factors associated with likely failure of TasP efforts across diverse HIV subgroups, including those who may be most likely to be ART nonadherent, and other biological factors that may amplify HIV transmission risk. The presence of untreated sexually transmitted infections (STIs) have been shown to increase HIV infectiousness through local inflammation and increases in genital tract HIV replication [3], which may undermine TasP efforts [4].

In 2008, the Swiss Federal Commission for HIV/AIDS developed a set of criteria for evaluating infectiousness, suggesting that individuals who have unsuppressed plasma viremia or a co-occurring STI are at greatest biological risk for sexually transmitting HIV [5]. Findings from the U.S. and Western Europe have identified that a substantial number of HIV-infected individuals engage in condomless sex, approximately 30 % across risk groups and settings, and that this includes sex with unknown or HIV-uninfected partners [6, 7]. Although many individuals in HIV care who engage in condomless sex will be virally suppressed and without STIs, and thus have reduced probability of transmitting HIV to others according to Swiss criteria, it is possible that a sizeable minority will have unsuppressed plasma viremia or presence of an STI, and therefore would continue to be at biological risk for transmitting HIV despite being offered ART as part of care.

Additionally, few studies have examined rates or variables associated with condomless anal and/or vaginal sex with HIV-uninfected or unknown status partners in the context of unsuppressed plasma viremia or a co-occurring STI (i.e., defined throughout as ‘amplified HIV transmission risk’). One exception is a study of U.S. MSM in HIV primary care that found heavy alcohol use, stimulant drug use, and having at least a college degree were each associated with approximately three times greater likelihood of amplified HIV transmission risk. Being more recently HIV infected was also associated with amplified HIV transmission risk, which could reflect younger age and/or less time to engage in care [8]. At the time of writing, we are unaware of a study that has examined factors associated with both ART adherence and amplified HIV transmission risk in international settings.

The current study recruited HIV-infected individuals with recent sexual HIV transmission risk from HIV care settings in three countries—two with high HIV prevalence in key

populations (in Brazil, Thailand) and one generalized setting (Zambia). Study aims included identifying psychosocial factors associated with (1) ART adherence and (2) 'amplified HIV transmission risk.' Psychosocial factors examined were drawn from existing literature and other HIV Prevention Trials Network (HPTN) and AIDS Clinical Trials Group (ACTG) trials [7, 9–12]. Amplified HIV transmission risk, described in more detail below, was defined as engaging in condomless anal or vaginal sex with HIV-uninfected or unknown-status partners and having biological risk for HIV transmissiblity (i.e. detectable viremia or positive STI test) [8].

Methods

Participants and Procedure

HPTN 063 was a multi-site, longitudinal, observational cohort study of high risk HIV-infected individuals (n = 749) in HIV care in Africa (Zambia), Asia (Thailand) and South America (Brazil). The current report uses data from the baseline assessment from this study. Adults (18 years and older) were recruited in Rio de Janeiro, Brazil, Chiang Mai, Thailand, and Lusaka, Zambia if they were HIV-infected (HIV testing performed outside of the study was acceptable as long as local guidelines were followed for testing) and met sexual risk criteria (participants needed to evidence some level of HIV transmission risk in the past 12 months by reporting either acquisition of an STI, vaginal or anal intercourse without a condom, difficulty negotiating condom use, or non-disclosure of HIV status to an HIV-uninfected partner or partner of unknown HIV serostatus). They also were required to be currently receiving HIV/AIDS care (defined as at least two visits in the nine months prior at a clinic or hospital). Participants were excluded if: (1) he/she was enrolled in any other study that included behavioral HIV risk reduction counseling or HIV prevention; (2) he/she reported having unprotected sex for the purpose of conceiving; (3) he/she was planning to relocate from the area in the following year; or (4) any condition that may make participation in the study unsafe or inappropriate as deemed by the primary investigator(s). Participants recruited included HIV-infected heterosexual men, heterosexual women, and men who have sex with men (MSM; Brazil and Thailand only), with roughly equal numbers of each demographic HIV risk group per site. Men who have sex with men, regardless of whether or not they also have sex with women, were considered as MSM. A total of 749 participants were recruited across the three sites, including 250 heterosexual men (100 in Thailand, 64 in Brazil, and 86 in Zambia), 299 heterosexual women (100 each in Thailand and Zambia, 99 in Brazil), and 200 MSM (100 per site in Thailand and Brazil).

Patients were recruited from several HIV clinics. Patients in Brazil were recruited from the Instituto de Pesquisa Clinica Evandro Chagas Clinical Research Site (IPEC CRS) in Rio de Janeiro, Brazil and the Matero Reference Clinic CRS and George Health Clinic CRS in Lusaka, Zambia. In Thailand, participants were recruited from several local HIV clinics and non-governmental organizations (NGOs). At all sites, patients were approached by study coordinators to discuss potential participation in this study. In Brazil and Zambia, this occurred while patients were waiting for their clinic appointments. In Thailand, recruitment occurred at voluntary counseling and testing (VCT) centers, including district/provincial hospitals in upper-northern Thailand, anonymous clinics, private laboratory/hospital/clinic

settings, and blood banks. Recruitment was targeted through mass media at these settings, through radio broadcasts, local newspapers, the Research Institute for Health Sciences/ Chiang Mai University website, newsletters, and magazines. All procedures were approved by the respective ethical review boards at each site. For Zambia, procedures were approved by University of Zambia, Zambia Ministry of Health, and the University of Alabama at Birmingham (UAB) institutional review board (IRB). In Thailand, procedures were approved by the Research Institute for Health Sciences at Chiang Mai University and Johns Hopkins Bloomberg School of Public Health. In Brazil, procedures were approved by the Evandro Chagas Clinical Research Institute and the National Committee for Ethics in Research.

At all sites, screening and enrollment occurred on the same day or separate days (within the following 30 days) depending on availability of participant and clinic staff. If a participant provided informed consent and met eligibility criteria for the study, they were enrolled. During the enrollment visit, the assessments included a general health assessment, a behavioral risk assessment, and STI testing. HIV viral load data was only available for participants in the Thailand and Brazil sites (at the time of the study, viral load tests were not part of routine care in Zambia).

Assessments

ART adherence was assessed using an interviewer-administered questionnaire [13] that assessed “in the last three months, on average, how would you rate your ability to take all your ART as your doctor prescribed?” Instructions were provided prior to the interview that normalized nonadherence. Participants were provided a response card with six ordinal response categories for rating adherence (very poor, poor, fair, good, very good, excellent). Prior research has documented the validity and reliability of using a single-item, self-report measure of adherence with an ordinal response rating [14]. Adherence was assessed among individuals who had been on ART in the past three months.

Depressive symptoms were measured using the Center for Epidemiologic Studies Depression Scale (CESD) [15], a 20-item measure of depressive symptoms validated in international settings. This was also interviewer administered. A score of less than seven is considered no depressive symptoms; 7–16 as mild to moderate depressive symptoms; and greater than 16 severe depressive symptoms.

Alcohol use was measured using the Alcohol Use Disorders Identification Test (AUDIT [16]), a 10-item interviewer administered screening and assessment of alcohol use severity. A score of eight or more reflects hazardous and harmful alcohol use, and possible alcohol dependence.

Other substance use was assessed via interview using a list of locally used substances at each site. Responses were dichotomized as yes/no for use of any drug in the past three months.

Quality of life was assessed using the interview administered ACTG SF-21 [17, 18], which has strong psychometric properties for assessing quality of life for people living with HIV.

There are eight subscales including: physical functioning, role functioning, pain, current health perceptions, emotional well-being, cognitive functioning, energy/fatigue, and social functioning. Scores were standardized, with a possible range of 1–100.

Social support was measured using nine items from the Multidimensional Scale of Perceived Social Support (MSPSS) [19], which assessed social support across family, friends, and partners. Higher scores reflect greater social support.

HIV disclosure was assessed using six items developed for this study assessing how the participant feels about disclosing their HIV status. Responses were on a four-point Likert scale ranging from disagree strongly to agree strongly. Sample questions were "I usually tell my sex partner(s) about my HIV positive status" and "I fear discrimination if I disclose my HIV positive status to others." We performed a principal component analysis using the six HIV disclosure items, which revealed two components (the first two components had an eigenvalue greater than 1, and the results of a scree plot also suggested that the first two components were meaningful [20]). Factor 1 was composed of the average of two disclosure items: "I usually tell my sex partner about my HIV positive status" and "If my partner does not disclose his/her HIV status to me I do not tell them mine." Factor 2 was composed of the average of four items related to fear of consequences of disclosure: "I fear discrimination if I disclose my HIV positive status to others," "I am afraid of violence if I disclose my HIV positive status to others," "I am afraid of losing my job if I disclose my HIV positive status to my boss or others," and "I fear being kicked out of my house if I disclose my HIV positive status to others." Higher scores indicate less disclosure of HIV status and greater fear related to consequences of disclosure, respectively.

HIV-RNA viral load measurement was extracted from the participants' medical records in Brazil and Thailand only (Zambia, at the time of study, did not conduct viral load tests as part of routine care). To be considered "current," the HIV viral load result had to be within six months of the study assessment date with no ART initiation in the interim.

Sexually transmitted infections (*STIs*) were tested (syphilis, gonorrhea, chlamydia) using urine, vaginal/rectal swabs, and blood specimens. Gonorrhea and chlamydia were assessed using urine and self- or clinician-collected rectal swabs for MSM, urine for men, and self- or clinician-collected vaginal swabs for women. Collected specimens were stored at each site. Test performance was also validated by quality assurance assessment with the guidance of the HPTN laboratory center at Johns Hopkins University (JHU) in Baltimore, MD. Rectal swabs, urine, and vaginal swabs for gonorrhea and Chlamydia were sent to the JHU laboratory center for storage and testing at the HPTN laboratory center at JHU. If an STI was identified, participants were called back into the clinic for re-testing and treatment. Syphilis serological testing was performed at the local laboratories in real-time using blood samples and a screening assay (either RPR or VDRL) and confirmed at the local site by a confirmatory assay (using MHA-TP or FTA-ABS), with quality assurance reviewed by the HPTN laboratory center at JHU. STI results included in all analyses for gonorrhea and chlamydia were based on the test results performed by the HPTN laboratory center at JHU.

Condomless sex was assessed via audio-computer assisted self-interview (ACASI) to maximize disclosure and accurate reporting. Specifically, participants were asked to report on the number of times they had vaginal, insertive or receptive anal sex with male or female partners who were HIV-uninfected or of unknown status in the past three months. Condomless sex was coded as "yes" if the participant reported having vaginal, insertive or receptive anal sex with an HIV-uninfected or unknown status partner in the past three months.

'*Amplified HIV transmission risk*' was coded as "yes" if a participant reported that he or she engaged in condomless sex (unprotected anal and/or vaginal sex with HIV-unin-fected or unknown status partner in the past three months) and had either a detectable viral load or an STI [8]. Amplified HIV transmission risk was examined among participants with HIV viral load, STI status, and sexual risk behavior data available. Amplified HIV transmission risk was coded as "no" if a participant had suppressed viral load in the absence of an STI OR no condomless sex in the past three months.

Statistical Analysis

Demographic and baseline characteristics were summarized by frequency distributions (for categorical variables) or median and interquartile range (for continuous variables). The percentage of individuals on ART, the percentage of those individuals who self-reported adherence at each level (very poor, poor, fair, good, very good, excellent), the percentage of individuals with detectable viremia, the percentage of individuals with a positive STI test, and the percentage of individuals with 'amplified HIV transmission risk' was calculated. Bivariate analyses were conducted to examine the associations of psychosocial (depression, alcohol/substance use, quality of life, social support, HIV disclosure) and sociodemographic (country, sexual group) factors with (1) ART adherence and (2) amplified HIV transmission risk in separate models. Multivariable logistic regression analyses (for amplified HIV transmission risk) and multivariable ordinal logistic regression analyses (for ART adherence) were conducted. Variables with $p < .1$ in the bivariate analyses were included in the multivariable models. Odds ratios (ORs) and 95 % confidence intervals (CIs) were calculated. For the ordinal logistic regression analysis of ART adherence, the OR indicates the odds of a higher category of adherence per one unit change in the covariate. Odds ratios for continuous covariates indicate a per 10 unit increase on the scale. Data analyses were implemented in SAS Version 9.2.

Results

Descriptive Data

Table 1 lists descriptive statistics for all independent variables for the total sample, by risk group, and by geographic region, and number of unprotected sex acts with serodiscordant or unknown status partners across the three risk groups (heterosexual men, MSM, heterosexual women). Of the total sample, 86 % were on ART. Of those, 18 % reported excellent adherence, 33 % very good, 35 % good, 11 % fair, 1 % poor, and 1 % very poor. Seventeen percent of the total sample had a positive STI test. MSM had the highest rates of STIs across sites, including 56 % of MSM with a positive STI test in Brazil (vs. 9 % for heterosexual

men and women) and 32 % in Thailand (vs. 5 % and 7 % for heterosexual men and women respectively). Of those who had viral load data available (i.e., in Brazil and Thailand; *n* = 475), 24 % had detectable viremia. Of those who had viral load and STI data available (*n* = 457), 40 % met Swiss criteria for biological infectiousness risk [5] (i.e., in that they had either detectable viremia or an STI). Among participants who met Swiss criteria for infectiousness (*n* = 182), 73 % engaged in condomless penetrative sex with an unknown or HIV-uninfected partner in the past three months, which means 29 % of the eligible sample with viral load and STI data available had 'amplified HIV transmission risk' (i.e., they had either a detectable viral load or an STI and had engaged in condomless sex with an unknown or HIV-uninfected partner in the past three months [8]). Regarding specific risk groups, 26.0 % of eligible heterosexual men (*n* = 131), 60.8 % of eligible MSM (*n* = 166), and 29.4 % of eligible heterosexual women (*n* = 160) met Swiss criteria for biological infectiousness. Of all individuals who met Swiss criteria for infectiousness (*n* = 182), 67.6 % of heterosexual men, 67.3 % of MSM, and 89.4 % of heterosexual women engaged in recent condomless sex with unknown or HIV-uninfected partners and thus had 'amplified HIV transmission risk'. See Table 1 for additional results.

ART Adherence

Table 2 lists the bivariate and multivariable analyses of sociodemographic and psychosocial factors associated with ART adherence on the six-point ordinal scale. In bivariate analyses, individuals with mild to moderate depressive symptoms had 42 % lower odds of ART adherence than individuals with no depressive symptoms (OR = 0.58; 95 % CI 0.41–0.81; $p < .01$), and individuals with severe depressive symptoms had 54 % lower odds of ART adherence than individuals with no depressive symptoms (OR = 0.46; 95 % CI 0.33–0.66; $p < .0001$). Each 10 point increase on the AUDIT was associated with a 37 % lower odds of ART adherence (OR = 0.63; 95 %CI 0.51–0.79; $p < .0001$), each 10 point increase on the ACTG SF-21 quality of life-health scale was associated with 16 % higher odds of ART adherence (OR = 1.16; 95 % CI 1.08–1.23; $p < .0001$), and each 10 point increase in social support was associated with 54 % higher odds of ART adherence (OR = 1.54; 95 % CI 1.18–1.99; $p < .01$). Being from Brazil or Zambia (vs. Thailand) was associated with 1.89- and 2.08-fold greater odds of ART adherence, respectively (Brazil vs. Thailand: OR = 1.89; 95 % CI 1.33–2.70; $p < .001$; Zambia vs. Thailand: OR = 2.08; 95 % CI 1.48–2.92; $p < .0001$).

In the multivariable model predicting ART adherence, each 10 point increase on the AUDIT was associated with a 29 % lower odds (OR = 0.71; 95 % CI 0.56–0.90; $p < .005$) of ART adherence, and each 10 point increase on the ACTG SF-21 quality of life-health scale was associated with 10 % higher odds (OR = 1.10; 95 % CI 1.02–1.19; $p < .01$) of ART adherence. Being from Brazil or Zambia, compared to Thailand, was associated with 2.35-(OR = 2.35; 95 % CI 1.62–3.41; $p < 0.0001$) and 1.70-(OR = 1.70; 95 % CI 1.20, 2.41; $p < .005$) fold greater odds of ART adherence, respectively. Although with borderline statistical significance, individuals with severe depressive symptoms had 34 % lower odds (OR = 0.66; 95 % CI 0.43–1.00; $p = .053$) of ART adherence than individual with no depressive symptoms. See Table 2 for additional details and results.

Amplified HIV Transmission Risk

Table 3 lists the bivariate and multivariable analyses predicting ‘amplified HIV transmission risk’ among individuals from Thailand and Brazil where HIV viral load and STI data were available (n = 457). In bivariate analyses, being from Brazil (vs. Thailand) was associated with 2.80-fold greater odds of amplified HIV transmission risk (OR = 2.80; 95 % CI 1.84–4.25; $p < .0001$), and identifying as MSM (vs. heterosexual man) was associated with a 3.26-fold greater odds of amplified HIV transmission risk (OR = 3.26; 95 % CI 1.89–5.63; $p < .0001$). Greater fear of consequences of HIV disclosure (Factor 2) was associated with 1.81-fold greater odds of amplified HIV transmission risk (OR = 1.81; 95 % CI 1.22–2.67; $p < .01$). Although at borderline statistical significance, no substance use in the past three months was associated with 40 % lower odds of amplified HIV transmission risk (vs. any use; OR = .60; 95 % CI 0.34–1.04; $p = .07$), and being a heterosexual woman (vs. heterosexual man) was associated with 1.67-fold greater odds of amplified HIV transmission risk (OR = 1.67; 95 % CI 0.94–2.96; $p = .078$).

In the multivariable model, MSM had 2.89-fold (OR = 2.89; 95 % CI 1.65–5.07; $p < .001$) greater odds of amplified HIV transmission risk compared to heterosexual men. Individuals from Brazil had 2.44-fold greater odds (OR = 2.44; 95 % CI 1.56–3.83; $p < .0001$) of amplified HIV transmission risk compared to individuals from Thailand. See Table 3 for additional details and results.

Discussion

Successful TasP efforts require identifying individuals at greatest risk for ART nonadherence, as well as individuals with other factors that increase biological risk for HIV transmission (i.e., detectable viral load or STI co-infections). The current study recruited a diverse sample (n = 749) of individuals with potential HIV transmission risk across HIV risk groups (MSM, heterosexual men, heterosexual women) from HIV care in three international settings (Brazil, Thailand, and Zambia). There were two study outcomes: ART nonadherence and amplified HIV transmission risk (condomless sex with HIV negative or unknown status partners in the context of higher likelihood of biological transmissiblity due to detectable viral load or STI co-infection). Regarding correlates of ART nonadherence, findings pointed to higher levels of alcohol use as an important modifiable factor associated with ART nonadherence. Regarding HIV transmissibility, findings pointed to focusing efforts specifically on MSM, as this risk group had the highest rates of STIs, and highest odds of engaging in condomless sex with HIV-uninfected or unknown-status partners in the context of detectable viremia and/or a recent STI.

Regarding ART use, 14 % of the sample was not on ART, and 82 % self-reported less than excellent ART adherence. Given typical inflation of self-reported ART adherence, this is likely an overestimate of actual rates of ART adherence. In the multivariable model, lower alcohol use severity and better health-related quality of life were associated with increased odds of ART adherence over and above significant site differences. Although it did not reach statistical significance ($p = .053$) in the multivariable model, having severe depressive symptoms was associated with decreased odds of ART adherence. Addressing alcohol use, as well as perceptions of health-related quality of life and depressive symptoms, may be

useful when considering TasP approaches with specific at-risk populations. Evidence-based interventions to improve ART adherence across a range of risk groups and international settings may consider including brief counseling to reduce alcohol use. Research is needed to better understand how to optimally integrate and implement evidence-based substance use interventions in HIV primary care in diverse resource-limited global settings.

With respect to infectiousness and amplified HIV transmission risk, approximately one-quarter of those analyzed had detectable viremia, and 17 % of the total sample had a positive STI result. A substantial portion (40 %) of individuals in this sample met Swiss infectiousness criteria (i.e., had detectable viral load or STI). Among those with biological risk, 73 % also engaged in behavioral transmission risk (i.e., condomless penetrative sex with an unknown or HIV-uninfected partner), thus meeting our definition of amplified HIV transmission risk. These data suggest that providing ART on its own may not be a successful TasP approach, which is in line with other literature suggesting that STI co-infections and frequent condomless sex may undermine TasP [4]. Findings point to the need, in some contexts, to enhance TasP by providing behavioral interventions to reduce STIs for those who may need it. According to the Swiss criteria, infectiousness is driven by viral suppression (i.e., ART adherence), as well as STI co-infection (i.e., condomless sex), and as such, for TasP to be successful, complementary behavioral interventions may be needed to address ART adherence and/or condomless sex depending on site, risk group, psychosocial characteristics, and fear of HIV disclosure.

Across risk groups, MSM had the highest rates of individuals with STI co-infection (56 % in Brazil and 32 % in Thailand) and highest rates of individuals meeting Swiss criteria for infectiousness (61 %). MSM who met Swiss criteria for infectiousness were approximately three times more likely to engage in behavioral risk compared to heterosexual men (the referent group for this analysis) who met Swiss infectiousness criteria. Although the rates of infectiousness and HIV transmission risk may be inflated given that anyone with no HIV transmission risk in the past 12 months was excluded in this study, findings highlight the need for tailored TasP efforts for MSM to also promote lower HIV transmission risk behavior.

Further, of note, 89 % of heterosexual women who met Swiss criteria for infectiousness engaged in recent condomless sex with unknown or HIV-uninfected partners; gender-related vulnerability may be an important factor associated with condom non-use and sexual HIV transmission among women in these sites. Future analyses focusing on the women enrolled in HPTN 063 may consider exploring specific factors associated with condomless sex with unknown or HIV-infected partners in this population.

Findings must be interpreted in the context of study limitations. First, the cross-sectional nature of the study does not allow for interpretations regarding causality of study findings. Second, there are inherent limitations of self-reported ART adherence. Here we used a measure with forced categories of responses, which provide a crude assessment of actual rates of adherence; though this question has shown particular validity compared to a “percent” question [13]. Additionally, self-report assessments may be influenced by social desirability and recall biases. More nuanced and accurate assessments of adherence would

require electronic monitoring of pill taking, which was not available in this study. A key limitation of measuring our 'amplified HIV transmission risk' criterion variable was that HIV viral load data was missing from 25 % of participants; at the time of the study, Zambia did not conduct viral load tests as part of regular care and HIV viral load testing was not available as part of study procedures. Thus, we were only able to calculate amplified HIV transmission risk in a subset of the sample were HIV viral load data was available, and the model of amplified HIV transmission risk is only with individuals in Thailand and Brazil. Additionally, MSM were not recruited at the Zambia site, largely due to concerns regarding stigma and likely nondisclosure of MSM status. This limitation suggests important future directions from this work to examine whether the current findings related to MSM and TasP replicate in an African setting, and if so, how TasP interventionists may appropriately and sensitively identify MSM in this setting for TasP efforts. Further, to fully assess the criteria for infectiousness outlined by the Swiss Consensus Statement, the duration of viral suppression would have to be known (i.e., six month duration), which was not available in our data.

Related to inclusion/exclusion criteria, these criteria were developed to prioritize inclusion of individuals at the greatest risk for HIV transmission who could realistically be identified in a clinic setting. Thus, any individuals with no HIV transmission risk in the past 12 months were excluded, which thereby may have inflated the proportion of the sample with HIV transmission risk. Additionally, exclusion of individuals who are trying to conceive may have excluded more heterosexual men and women than MSM, thereby potentially biasing the relative risk of MSM versus heterosexual individuals. Finally, regional differences should be interpreted with caution. Although there were meaningful differences by site, for instance in the higher rates of detectable viral load across risk groups in Brazil versus Thailand, and regional differences that emerged after controlling for risk group and other important variables in the multivariable models, there may be other factors that contribute to the site differences identified including cultural norms, country differences in ART availability, and potential cultural differences in self-reporting. If replicated and found to generalize to other sites within each region, these findings may have implications for how TasP is rolled out in these countries.

Conclusions

Despite the noted limitations, this study included a range of high-risk groups and geographical settings to answer questions regarding who may be most likely to benefit from interventions to promote TasP by identifying individuals at greatest risk for ART nonadherence and HIV transmission. Evidence-based interventions to promote ART adherence globally may be optimized if delivered alongside evidence-based treatment for alcohol use when clinically indicated. Additionally, our findings suggest that MSM may be a particularly important risk group to focus on to optimize the likelihood of TasP success. Providing more intensive behavioral interventions to individuals with greatest risk for ART nonadherence and who have the greatest likelihood of HIV transmission risk may amplify effectiveness of TasP in global settings.

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Table 1

Descriptive characteristic of study sample

	Thailand			Brazil			Zambia		Total
	Heterosexual men	MSM	Heterosexual women	Heterosexual men	MSM	Heterosexual women	Heterosexual men	Heterosexual women	
Total N enrolled	100	100	100	64	100	99	86	100	749
N taken ART in the last 3 months	98/100 (98 %)	96/100 (96 %)	96/100 (96 %)	53/64 (83 %)	59/100 (59 %)	70/99 (71 %)	83/86 (97 %)	88/100 (88 %)	643/749 (86 %)
ART adherence (last 3 months)[a]									
Missing	0/98 (0 %)	0/96 (0 %)	0/96 (0 %)	0/53 (0 %)	1/59 (2 %)	0/70 (0 %)	0/83 (0 %)	0/88 (0 %)	1/643 (< 1 %)
Very poor	1/98 (1 %)	0/96 (0 %)	1/96 (1 %)	1/53 (2 %)	0/59 (0 %)	3/70 (4 %)	1/83 (1 %)	0/88 (0 %)	7/643 (1 %)
Poor	1/98 (1 %)	0/96 (0 %)	2/96 (2 %)	1/53 (2 %)	1/59 (2 %)	1/70 (1 %)	1/83 (1 %)	0/88 (0 %)	7/643 (1 %)
Fair	19/98 (19 %)	10/96 (10 %)	13/96 (14 %)	4/53 (8 %)	9/59 (15 %)	9/70 (13 %)	5/83 (6 %)	2/88 (2 %)	71/643 (11 %)
Good	36/98 (37 %)	41/96 (43 %)	33/96 (34 %)	18/53 (34 %)	14/59 (24 %)	24/70 (34 %)	28/83 (34 %)	32/88 (36 %)	226/643 (35 %)
Very good	34/98 (35 %)	40/96 (42 %)	41/96 (43 %)	12/53 (23 %)	14/59 (24 %)	10/70 (14 %)	30/83 (36 %)	33/88 (38 %)	214/643 (33 %)
Excellent	7/98 (7 %)	5/96 (5 %)	6/96 (6 %)	17/53 (32 %)	20/59 (34 %)	23/70 (33 %)	18/83 (22 %)	21/88 (24 %)	117/643 (18 %)
Any STI (lab result)									
Missing	0/100 (0 %)	0/100 (0 %)	0/100 (0 %)	2/64 (3 %)	3/100 (3 %)	11/99 (11 %)	3/86 (3 %)	3/100 (3 %)	22/749 (3 %)
No	95/100 (95 %)	68/100 (68 %)	93/100 (93 %)	56/64 (88 %)	41/100 (41 %)	79/99 (80 %)	78/86 (91 %)	87/100 (87 %)	597/749 (80 %)
Yes	5/100 (5 %)	32/100 (32 %)	7/100 (7 %)	6/64 (9 %)	56/100 (56 %)	9/99 (9 %)	5/86 (6 %)	10/100 (10 %)	130/749 (17 %)
N with VL available	85/100 (85 %)	85/100 (85 %)	82/100 (82 %)	49/64 (77 %)	85/100 (85 %)	89/99 (90 %)	0/86 (0 %)	0/100 (0 %)	475/749 (63 %)
Detectable VL	13/85 (15 %)	11/85 (13 %)	8/82 (10 %)	12/49 (24 %)	40/85 (47 %)	31/89 (35 %)	0/0 (0 %)	0/0 (0 %)	115/475 (24 %)
N qualified for swiss infectious criteria	84/100 (84 %)	84/100 (84 %)	82/100 (82 %)	47/64 (73 %)	82/100 (82 %)	78/99 (79 %)	0/86 (0 %)	0/100 (0 %)	457/749 (61 %)
Met Swiss criteria for Infectiousness									
No	66/84 (79 %)	47/84 (56 %)	68/82 (83 %)	31/47 (66 %)	18/82 (22 %)	45/78 (58 %)	0/0 (0 %)	0/0 (0 %)	275/457 (60 %)
Yes	18/84 (21 %)	37/84 (44 %)	14/82 (17 %)	16/47 (34 %)	64/82 (78 %)	33/78 (42 %)	0/0 (0 %)	0/0 (0 %)	182/457 (40 %)
With unprotected sex	12/18 (67 %)	24/37 (65 %)	13/14 (93 %)	11/16 (69 %)	44/64 (69 %)	29/33 (88 %)	0/0 (0 %)	0/0 (0 %)	133/182 (73 %)
Unprotected sex with HIV-/unk partners									
Missing	1/100 (1 %)	3/100 (3 %)	0/100 (0 %)	0/64 (0 %)	0/100 (0 %)	0/99 (0 %)	9/86 (10 %)	4/100 (4 %)	17/749 (2 %)
No	33/100 (33 %)	35/100 (35 %)	8/100 (8 %)	28/64 (44 %)	23/100 (23 %)	21/99 (21 %)	12/86 (14 %)	5/100 (5 %)	165/749 (22 %)
Yes	66/100 (66 %)	62/100 (62 %)	92/100 (92 %)	36/64 (56 %)	77/100 (77 %)	78/99 (79 %)	65/86 (76 %)	91/100 (91 %)	567/749 (76 %)
Met criteria for amplified HIV transmission risk									

	Thailand			Brazil			Zambia		Total
	Heterosexual men	MSM	Heterosexual women	Heterosexual men	MSM	Heterosexual women	Heterosexual men	Heterosexual women	
No	72/84 (86 %)	60/84 (71 %)	69/82 (84 %)	36/47 (77 %)	38/82 (46 %)	49/78 (63 %)	0/0 (0 %)	0/0 (0 %)	324/457 (71 %)
Yes	12/84 (14 %)	24/84 (29 %)	13/82 (16 %)	11/47 (23 %)	44/82 (54 %)	29/78 (37 %)	0/0 (0 %)	0/0 (0 %)	133/457 (29 %)
Unprotected sex acts in past 3 months with HIV-unknown partners (among those who Qualified for Swiss Criteria)									
Median	2	2	3	4	4	4	–	–	3
25th, 75th %tile	0, 4	0, 10	2, 5	1, 18	1, 19	1, 28	–	–	0, 15
Min, max	0, 45	0, 64	0, 40	0, 30	0, 750	0, 2520	–	–	0, 2520
Social support score									
Median	35	34	35	33	34	33	36	36	35
25th, 75th %tile	32, 36	30, 36	30, 36	28, 36	29, 38	29, 38	33, 38	33, 37	30, 36
Min, max	24, 45	19, 45	23, 45	18, 45	14, 45	11, 45	13, 45	23, 45	11, 45
CESD score									
Median	10	11	11	13	16	16	6	9	11
25th, 75th %tile	6, 15	6, 18	6, 19	6, 25	8, 31	8, 32	2, 13	4, 16	6, 20
Min, max	2, 32	1, 37	0, 40	0, 51	1, 46	0, 53	0, 32	0, 40	0, 53
HIV disclosure (factor 1)									
Median	3	3	3	3	3	3	3	3	3
25th, 75th %tile	3, 3	3, 3	3, 3	3, 3	2, 3	3, 3	3, 3	3, 3	3, 3
Min, max	2, 4	1, 4	2, 4	1, 4	1, 4	2, 4	2, 4	1, 4	1, 4
Fear of consequences of disclosure (Factor 2)									
Median	2	3	2	3	3	3	2	2	3
25th, 75th %tile	2, 3	2, 3	2, 3	2, 3	3, 3	3, 3	2, 3	2, 3	2, 3
Min, max	1, 4	2, 4	1, 4	1, 4	2, 4	1, 4	1, 4	1, 3	1, 4
ACTG SF-21 subscales									
General health perception									
Median	75	71	67	58	58	58	75	75	67
25th, 75th %tile	58, 75	50, 75	50, 75	42, 83	33, 83	33, 83	58, 75	50, 75	50, 75
Min, max	8, 100	8, 100	0, 100	0, 100	0, 100	0, 100	25, 100	8, 100	0, 100
Physical functioning									
Median	100	100	100	88	100	88	100	100	100

	Thailand			Brazil			Zambia		Total
	Heterosexual men	MSM	Heterosexual women	Heterosexual men	MSM	Heterosexual women	Heterosexual men	Heterosexual women	
25th, 75th %tile	100, 100	88, 100	88, 100	63, 100	75, 100	63, 100	88, 100	88, 100	88, 100
Min, max	38, 100	50, 100	25, 100	13, 100	25, 100	0, 100	50, 100	0, 100	0, 100
Role functioning									
Median	100	100	100	100	100	100	100	100	100
25th, 75th %tile	100, 100	100, 100	100, 100	50, 100	50, 100	75, 100	100, 100	100, 100	100, 100
Min, max	50, 100	50, 100	0, 100	0, 100	0, 100	0, 100	25, 100	25, 100	0, 100
Social functioning									
Median	89	89	100	100	89	100	100	100	94
25th, 75th %tile	78, 100	78, 100	78, 100	72, 100	67, 100	67, 100	78, 100	67, 100	78, 100
Min, max	11, 100	33, 100	33, 100	0, 100	0, 100	11, 100	22, 100	33, 100	0, 100
Cognitive functioning									
Median	87	80	80	87	80	80	97	87	87
25th, 75th %tile	73, 100	67, 87	67, 87	70, 100	73, 100	67, 93	87, 100	73, 100	73, 100
Min, max	40, 100	27, 100	27, 100	0, 100	7, 100	0, 100	47, 100	33, 100	0, 100
Pain									
Median	89	89	78	72	67	56	100	89	78
25th, 75th %tile	67, 100	67, 100	67, 100	33, 100	44, 100	44, 78	67, 100	67, 100	56, 100
Min, max	44, 100	0, 100	22, 100	11, 100	0, 100	0, 100	22, 100	11, 100	0, 100
Mental health									
Median	67	67	60	60	53	53	67	60	60
25th, 75th %tile	60, 67	60, 67	53, 67	47, 67	40, 67	40, 67	53, 67	47, 67	47, 67
Min, max	33, 87	33, 80	20, 93	33, 100	7, 100	0, 87	27, 80	13, 73	0, 100
Energy/fatigue									
Median	80	80	80	70	70	70	90	80	80
25th, 75th %tile	70, 90	60, 90	60, 100	40, 95	40, 100	50, 90	60, 100	50, 100	60, 100
Min, max	40, 100	40, 100	0, 100	0, 100	0, 100	0, 100	20, 100	0, 100	0, 100

[a] ART adherence was assessed among individuals who reported being on ART in past three months

Table 2

Ordinal logistic regression model of ART adherence

Characteristics	Level	Bivariate model		Multivariable model[b]	
		OR (95 % CI)[a]	*p*	OR (95 % CI)[a]	*p*
Site	Brazil vs. Thailand	1.89 (1.33, 2.70)	.0004	2.35 (1.62, 3.41)	<0.0001
	Zambia vs. Thailand	2.08 (1.48, 2.92)	<0.0001	1.70 (1.20, 2.41)	.0030
Risk group	MSM vs. heterosexual men	1.02 (0.71, 1.48)	.8988		
	Heterosexual women vs. heterosexual men	1.12 (0.81, 1.55)	.4774		
Substance use	No vs. yes	1.58 (0.97, 2.58)	.0681	1.38 (0.82, 2.33)	.2210
CESD score	Mild to moderate depression vs. no depression	0.58 (0.41, 0.81)	.0013	0.74 (0.52, 1.05)	.0940
	Severe depression vs. no depression	0.46 (0.33, 0.66)	<0.0001	0.66 (0.43, 1.00)	.0525
ACTG SF-21 scales					
General health	General health (rescored in 10)	1.16 (1.08, 1.23)	<0.0001	1.10 (1.02, 1.19)	.0094
Physical functioning	Physical functioning	1.00 (0.99, 1.01)	.8761		
Role functioning	Role functioning	1.00 (1.00, 1.01)	.3864		
Social functioning	Social functioning	1.01 (1.00, 1.01)	.1457		
Cognitive functioning	Cognitive functioning	1.01 (1.00, 1.01)	.1665		
Pain	Pain	1.00 (0.99, 1.01)	.9652		
Mental health	Mental health	1.01 (0.99, 1.02)	.3199		
Energy/fatigue	Energy/fatigue	1.00 (1.00, 1.01)	.3337		
Social support	Social support (rescored in 10)	1.54 (1.18, 1.99)	.0013	1.30 (0.98, 1.71)	.0683
HIV disclosure	Factor 1 (disclosure)	0.93 (0.65, 1.33)	.6796		
	Factor 2 (fear of consequences of disclosure)	0.80 (0.61, 1.05)	.1099		
Alcohol score	AUDIT score (rescored in 10)	0.63 (0.51, 0.79)	<0.0001	0.71 (0.56, 0.90)	.0043

[a] The OR indicates the odds of a higher adherence associated with a one unit change in the covariate (rescaled for a 10 unit change on the log scale for general health, social score and AUDIT score)

[b] Covariates with $p < .1$ were included in the multivariable model

Table 3

Logistic regression model of ‘amplified HIV transmission risk’

Characteristics	Level	Bivariate model		Multivariable model[a]	
		OR (95 % CI)	*p*	OR (95 % CI)	*p*
Site	Brazil vs. Thailand	2.80 (1.84, 4.25)	<0.0001	2.44 (1.56, 3.83)	.0001
Risk group	Heterosexual women vs. heterosexual men	1.67 (0.94, 2.96)	.0782	1.50 (0.83, 2.74)	.1828
	MSM vs. heterosexual men	3.26 (1.89, 5.63)	<0.0001	2.89 (1.65, 5.07)	.0002
Substance use	No vs. yes	0.60 (0.34, 1.04)	.0702	0.86 (0.46, 1.60)	.6323
CESD	Mild to moderate depression vs. no depression	0.92 (0.55, 1.54)	.7586		
	Severe depression vs. no depression	1.42 (0.87, 2.32)	.1659		
ART adherence	Excellent vs. very poor	0.59 (0.09, 3.84)	.5841		
	Very good vs. very poor	0.35 (0.06, 2.23)	.2688		
	Good vs. very poor	0.50 (0.08, 3.14)	.4636		
	Fair vs. very poor	0.75 (0.11, 4.92)	.7644		
	Poor vs. very poor	1.50 (0.14, 16.54)	.7406		
ACTG SF-21 scales					
General health	General health	1.00 (0.99, 1.01)	.5030		
Physical functioning	Physical functioning	0.99 (0.98, 1.00)	.1320		
Role functioning	Role functioning	0.99 (0.99, 1.00)	.2321		
Social functioning	Social functioning	1.00 (0.99, 1.01)	.6076		
Cognitive functioning	Cognitive functioning	0.99 (0.98, 1.00)	.1504		
Pain	Pain	1.00 (0.99, 1.01)	.9297		
Mental health	Mental health	1.00 (0.98, 1.01)	.5761		
Energy/fatigue	Energy/fatigue	1.00 (0.99, 1.01)	.4415		
Social support	Social support	0.99 (0.95, 1.02)	.3948		
HIV disclosure	Factor 1 (disclosure)	0.77 (0.47, 1.25)	.2874		
	Factor 2 (fear of consequences of disclosure)	1.81 (1.22, 2.67)	.0029	1.39 (0.92, 2.08)	.1159
Alcohol score	AUDIT score	1.01 (0.98, 1.04)	.5319		

Amplified HIV transmission risk was defined as detectable viral load OR STI and engaged in condomless anal or vaginal sex with an HIV-uninfected or unknown status partner in past three months. Not being in this amplified HIV transmission risk category was defined as suppressed viral load and no STI or no condomless insertive or penetrative sex with an HIV-uninfected or unknown status partner in the past 3 months. This analysis only includes individuals where HIV RNA data were available (from Thailand and Brazil) and STI lab test results (n = 457)

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[a] Covariates with $p < .1$ were included in the multivariable model