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# Risky Sexual Behavior Among Individuals Receiving Buprenorphine/Naloxone Opiate Dependency Treatment: HIV Prevention Trials Network (HPTN) 058

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**Introduction:** Understanding the role of opiate dependency treatment in risky sexual behavior could help optimize interventions for people who inject drugs (PWID).

**Objectives:** We evaluated whether long-term medication-assisted treatment (LT-MAT) of opiate dependency with buprenorphine/naloxone influenced risky sexual behavior among HIV-uninfected PWID and identified predictors of risky sexual behavior.

**Methods:** We used data from HPTN 058, a randomized controlled trial of LT-MAT vs. short-term medication-assisted treatment among PWID in China and Thailand. We evaluated associations between randomized opiate dependency treatment group and self-reported risky sexual behaviors within the past month: condomless sex with primary partner, condomless sex with nonprimary partner, multiple partners, and more than 3 sexual acts. We used generalized estimating equations to conduct intention-to-treat, as-treated, and exploratory analyses of these associations.

**Results:** Of 1250 participants included in the analysis, 92% were male, with median age of 34 years (interquartile range 28–39). At baseline, referring to the past month, 36% of participants reported condomless sex with primary partner, 4% reported condomless sex with nonprimary partner, 6% reported multiple sex partners, and 30% reported more than 3 sexual acts. Risky sexual behaviors did not differ significantly between treatment groups at any point. Significant predictors ($P < 0.05$) of condomless sex with nonprimary partner were history of incarceration and noninjection drug use. Number of needle-sharing partners, noninjection drug use, and higher income were predictors for multiple sexual partners.

**Conclusions:** LT-MAT did not significantly modify risky sexual behavior among HIV-uninfected PWID. Interventions that reduce sexual risk should target PWID with history of incarceration, alcohol use, and needle sharing.

**Key Words:** risky sexual behavior, people who inject drugs, HIV prevention, opiate dependency treatment

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## INTRODUCTION

Injection drug use has been shown to increase the risk of HIV transmission and acquisition through both unsafe injection practices and risky sexual behavior.[1–4] According to the 2014 World Drug Report, 12.7 million people inject drugs globally, about 1.7 million of whom are living with HIV.[5] The population of people who inject drugs (PWID) in South East and East Asia is estimated to be nearly 4 million.[6] In China and Thailand, injection drug use is rampant due to illicit opium production.[2] In China, PWID accounted for approximately 39% of new HIV infections between 2005 and 2009,[7,8] whereas in Thailand, HIV prevalence among PWID in 2010 ranged between 11% and 24%.[9]

HIV and other infections have the potential to spread within the population of PWID and to the general population through sexual networks. In the region particularly in China, there has been a change in HIV transmission patterns among

PWID, from being predominantly due to unsafe injection practices to heterosexual transmission.[10–12] It is therefore important to determine whether long-term medication-assisted treatment (LT-MAT) with buprenorphine/naloxone (BUP/NX) of injection opiate dependency will lead to changes in risky sexual behavior in this region. Studies conducted in the United States suggest that LT-MAT with BUP/NX may lead to a reduction in risky sexual behavior in PWID.[13,14] BUP/NX has fewer clinical and regulatory barriers as well as comparable clinical effectiveness with methadone.[15–19]

Methadone maintenance treatment is widely used in PWID in the region through community-based treatment programs implemented by the Chinese and Thai governments, where opiate-dependent patients can be admitted.[20–25] Buprenorphine/naloxone treatment for opiate dependence was not yet licensed for treatment in Asia at the time of conducting the HIV Prevention Trials Network (HPTN) 058 study.[26] Policies on injection drug use management in the region are evolving, from being punitive through compulsory detoxification programs implemented through labor centers to these community-based rehabilitation.[21] These changes therefore increase the relevance of exploring other treatment options for injection drug use management such as buprenorphine/naloxone and further to determine the effect of LT-MAT on risky sexual behavior.

Risky sexual behavior has been defined in other studies to include multiple sexual partners, unprotected sexual acts, sexual frequency, having sex while under the influence of alcohol or drugs, and transactional sex.[4,27] Risky sexual behaviors among PWID are common, in particular, condomless sex, multiple partners, and transactional sex.[10,13,28–31] This makes this population vulnerable to both transmission and acquisition of sexually transmitted infections including HIV. Using data from the HPTN 058 study, it is important to determine predictors of risky sexual behavior to derive sexual risk prevention strategies.

HPTN 058 was a randomized controlled trial (RCT) of LT-MAT vs. short-term medication-assisted treatment (ST-MAT) among PWID in China and Thailand. The primary aim of the original study was to evaluate the effect of randomized treatment on the rates of new HIV infection and mortality. The study was stopped early at the recommendation of Data Safety Monitoring Board (DSMB) in October 2011 due to lower than expected overall HIV incidence.[32]

The purpose of this study is to evaluate if receipt of LT-MAT vs. ST-MAT influenced risky sexual behavior longitudinally among HIV-uninfected PWID and to identify other predictors of risky sexual behavior in this population. These analyses can provide new information about risky sexual behaviors among HIV-uninfected PWID globally, which may be helpful for designing behavioral intervention strategies to reduce risky sexual behavior among this population, which in turn impacts the general population.

# METHODS

## Study Population

HPTN 058 recruited HIV-uninfected PWID who were older than 18 years of age from 4 centers across China and Thailand.[32] The participants had to meet Diagnostic and Statistical Manual of Mental Disorders (DSM IV) criteria for opiate dependence, with positive urine test for opiates at time of enrollment, admit to injecting opiates at least 12 times in the previous 28 days, and either not be of reproductive potential or be willing to use contraception. Exclusion criteria included pregnancy, breastfeeding, enrollment for methadone treatment, and significant medical conditions. Between May 2007 and October 2011, 1251 participants were enrolled and randomized. Of the 1250 evaluable participants; 623 were randomized to LT-MAT and 627 randomized to ST-MAT. Participants randomized to LT-MAT received BUP/NX thrice weekly for 48 weeks coupled with 21 sessions of risk-reduction counseling, and followed by dose tapering.[32] Participants randomized to ST-MAT received BUP/NX detoxification for 15 days together with 21 sessions of risk-reduction counseling. Participants were followed for a minimum of 52 weeks to accommodate the time required for the LT-MAT plus dose tapering. We will refer to this 52-week period as the treatment phase.

## Measures

### Endpoints

The 5 primary endpoints for this analysis were binary indicators of risky sexual behaviors in the previous month: (1) any condomless sex with a primary partner, (2) any condomless sex with a nonprimary partner, c) multiple sexual partners ($>1$), and d) more than 3 sex acts in a month. Data regarding self-reported risky sexual behavior were collected through structured interview at baseline and again every 26 weeks.

### Predictors

The primary predictor for this analysis was type of opiate dependency treatment. Treatment was defined in 3 ways: (1) for the descriptive statistics and intention-to-treat (ITT) analyses, treatment was defined dichotomously as randomized arm (LT-MAT vs. ST-MAT), (2) for the first as-treated analysis, treatment was defined as percent adherence (proportion of doses taken vs. total expected doses) to BUP/NX in the past 28 days (participants in the ST-MAT arm were coded as having 0% adherence), and (3) for the second as-treated analysis, treatment was defined categorically with 3 levels based on cumulative percent adherence to BUP/NX during the treatment period (LT-MAT $\geq$75% cumulative adherence, LT-MAT $<$75% cumulative adherence, and ST-MAT). Participant BUP/NX dosing was assessed weekly during the treatment period, primarily through direct observation by study clinicians. Percent adherence refers to the proportion of completed dosing in the previous 28-day period.

To describe other risk factors and effect modifiers for risky sexual behavior by treatment arm, demographics and risky injection behavior covariates at baseline were included as other potential predictors of risky sexual behavior: age (10-year increment), sex, minority ethnicity (participants who did not identify as Han in China or Thai in Thailand), marital status (married/living with partner vs. not), years of

education, income (>$1000 annual income vs. not), employment (employed vs. unemployed), history of incarceration (any vs. none referring to past 6 months), alcohol use (any vs. none referring to the past 6 months), noninjection drug use (any vs. none referring to past 6 months), number of days injected (referring to past 6 months), average number of times per day injected (referring to the past month), mixing of different drugs (any vs. none referring to past 6 months), using front- or back-loaded syringes (any vs. none referring to past 6 months), passing (lending) drug injection needles after use (any vs. none, number of times, and number of people passed to referring to past 6 months), and sharing (receptive of) drug injection needles after others (any vs. none, number of times, and number of people shared with referring to past 6 months).

## Statistical methods

Study participant characteristics were summarized at baseline using frequencies and percentages for categorical variables and medians with interquartile ranges for continuous variables.

To describe risky sexual behaviors over time by treatment group, the proportion of participants with each risk behavior were plotted by treatment arm at each visit from baseline to week 104. Then, for each endpoint, odds ratios (ORs) associated with treatment were estimated at each time point. Each model included an interaction between treatment arm and visit, the main effects for treatment and visit, and adjustment for site. Differences between ORs at baseline and weeks 52 and 104 were evaluated using Wald tests.

To determine if LT-MAT (vs. ST-MAT) was associated with risky sexual behaviors, ITT and as-treated analyses were completed. For the ITT, ORs associated with treatment (as randomized) were estimated. Two models were used (both adjusted for site). Model 1 was used to test for an interaction between treatment arms and visit (an interaction indicating that the treatment effect was visit-dependent). If the interaction was nonsignificant (per Wald test), model 2 was used to estimate an overall OR.

Two as-treated analyses were conducted. First, to evaluate the effectiveness of treatment on risky sexual behavior during the treatment period, outcome data were limited to weeks 26 and 52, and ORs associated with 10 percentage points higher adherence in the past 28 days were estimated. Second, to evaluate the effectiveness of the treatment on risky sexual behavior after the treatment ended, outcome data were limited to weeks 52, 78, and 104, and ORs associated with cumulative adherence were estimated. Models were adjusted for site and visit.

Finally, to explore risk factors for risky sexual behaviors, ORs associated with each risk factor were estimated. Two models were fit for each endpoint. Model 1, a partially adjusted model, adjusted for site, treatment (as randomized), baseline vs. follow-up, and an interaction between treatment and baseline vs. follow-up (to allow for any treatment effects). Model 1 was run for each potential risk factor. Model 2 was a fully adjusted model. In addition to all Model 1 adjustment terms, Model 2 included any model 1 risk factors that had $P < 0.1$.

All ORs were estimated using generalized estimating equations using logistic regression to account for the binary endpoints and exchangeable correlation structures to account for the repeated measures. We used exchangeable covariance structure with the assumption that the correlation between visits for the participant is constant.

## Ethical Considerations

Institutional review boards/ethics committees at each of the 4 sites in China and Thailand approved the HPTN 058 trial. Written informed consent was obtained from all study participants. The HPTN ethical committees approved this data analysis.

# RESULTS

Recruited participants were active opiate drug injectors across 3 sites in China (n = 161 in Guangxi, Nanning; n = 411 in Heng County; and n = 477 in Xinjiang, Urumqi); and n = 202 in Chiang Mai, Thailand.

## Baseline Characteristics

Of the 1250 participants included in the analysis, 92% were male, with a median age of 34 years (interquartile range, 28–39). Baseline characteristics were similar in the randomized arms (Table 1).

At baseline, referring to the past month, 36% of participants reported condomless sex with their primary partner, 4% reported condomless sex with a nonprimary partner, 6% reported multiple sex partners, and 30% reported more than 3 sex acts.

## Adherence Over Time

Adherence to the induction phase of the study ranged from 88% (ST-MAT) to 91% (LT-MAT). Eighty percent (n = 502) participants completed the detoxification phase.

## Risky Sexual Behavior Over Time

Figure 1 shows the proportion of participants in each treatment arm with a given risky sexual behavior at each study time point. As you can see from the plots, rates of risky sexual behaviors were fairly consistent over the course of the study. Although there were slight differences between treatment groups at various time points, ORs associated with treatment were nonsignificant at every visit including baseline for all endpoints (Table 2).

## Effect of Treatment on Risky Sexual Behaviors

In the ITT analysis, the interaction between treatment and time was nonsignificant for all endpoints. This allowed us to estimate overall treatment effects for each risky sexual behavior. Supplemental Digital Content Table S1, http://links.lww.com/QAI/B140, presents the overall OR

**TABLE 1.** Baseline Characteristics by Treatment Arm

| | % (N) or Median (interquartile range) | | |
|---|---|---|---|
| | ST-MAT (N = 627) | LT-MAT (N = 623) | Total (N = 1250) |
| Demographics | | | |
| Age (yrs) | 34 (28–39) | 33 (27–39) | 34 (28–39) |
| Sex (male) | 92% (577) | 92% (574) | 92% (1151) |
| Ethnicity (minority status)* | 42% (260) | 42% (262) | 42% (522) |
| Married/living with partner | 51% (320) | 52% (327) | 52% (647) |
| Education (yrs) | 8 (6–9) | 8 (6–9) | 8 (6–9) |
| Employed | 55% (342) | 54% (334) | 54% (676) |
| History of incarceration†§ | 11% (68) | 12% (73) | 11% (142) |
| Alcohol use†§ | 50% (315) | 46% (288) | 48% (603) |
| Noninjection drug use†§ | 51% (319) | 53% (328) | 52% (647) |
| Injection drug use | | | |
| Days injected§ | 30 (30–30) | 30 (30–30) | 30 (30–30) |
| Passed needles after use§ | 22% (136) | 22% (140) | 22% (276) |
| Used needles after others§ | 19% (121) | 22% (136) | 21% (257) |
| Sex behaviors‡ | | | |
| Any sex | 49% (306) | 46% (289) | 48% (595) |
| Primary sex partner | 44% (273) | 41% (256) | 42% (529) |
| Any sex with primary | 43% (271) | 40% (252) | 42% (523) |
| Any condomless sex | 40% (249) | 36% (222) | 38% (471) |
| Nonprimary sex partner | | | |
| Any sex with nonprimary | 8% (53) | 8% (48) | 8% (101) |
| Any condomless sex | 6% (38) | 6% (36) | 6% (74) |
| No. of sex partners | | | |
| 0 | 51% (321) | 54% (335) | 52% (656) |
| 1 | 42% (265) | 41% (253) | 41% (518) |
| 2+ | 7% (41) | 6% (35) | 6% (76) |
| No. of sexual acts | | | |
| 0 | 51% (322) | 54% (336) | 53% (658) |
| 1–2 | 17% (105) | 17% (107) | 17% (212) |
| 3+ | 32% (200) | 29% (180) | 30% (380) |
| Transactional sex† | 3% (17) | 4% (22) | 3% (40) |

*Minority status refers to participants who did not identify as Han in China or Thai in Thailand.
†Missing data.
‡Past 1 month.
§Past 6 months.

for each endpoint, all of which were nonsignificant. Similarly, the as-treated analyses did not provide evidence of an association between medication-assisted treatment and risky sexual behaviors. Specifically, ORs associated with 10 percentage points higher 28-day adherence during the treatment period were all nonsignificant with point estimates extremely close to one (see Supplemental Digital Content Table S2, http://links.lww.com/QAI/B140). The ORs associated with cumulative adherences had more variation in terms of point estimates (see Supplemental Digital Content Table S3, http://links.lww.com/QAI/B140) however, they were also nonsignificant for all endpoints.

## Other Predictors of Risky Sexual Behaviors

We then looked at other potential predictors of each of the risky sexual behavior endpoints (Table 3).

Statistically significant ($P < 0.05$) predictors associated with higher odds of condomless sex with a primary partner in the fully adjusted model (adjusted for site, treatment, baseline vs. follow-up and interaction between treatment and baseline vs. follow-up) were being married/living with partner: adjusted odds ratio (AOR) = 4.34 [95% confidence interval (CI): 3.61 to 5.23], being employed: AOR = 1.22 (95% CI: 1.05 to 1.42), and alcohol use: AOR = 1.45 (95% CI: 1.24 to 1.70). Significant predictors associated with lower odds of condomless sex with a primary partner were incarceration: AOR = 0.75 (95% CI: 0.54 to 0.82) and mixing different drugs: AOR = 0.69 (95% CI: 0.47 to 0.85).

Significant predictors associated with higher odds of condomless sex with a nonprimary partner were incarceration: AOR = 1.62 (95% CI: 1.08 to 2.42) and noninjection drug use: AOR = 1.92 (95% CI: 1.40 to 2.64). Significant predictors associated with lower odds of condomless sex with a nonprimary partner were older age: AOR = 0.69 (95% CI: 0.54 to 0.87) and being married/living with partner: AOR = 0.65 (95% CI: 0.46 to 0.91).

Significant predictors associated with higher odds of having multiple sex partners were more years of education: AOR = 1.09 (95% CI: 1.01 to 1.16), annual income >$1000: AOR = 2.11 (95% CI: 1.32 to 3.39), noninjection drug use: AOR = 1.80 (95% CI: 1.33 to 2.43), and number of people with whom needles were shared after use: AOR = 1.25 (95% CI: 1.04 to 1.50). Significant predictors associated with lower odds of having multiple sex partners were older age: AOR = 0.71 (95% CI: 0.55 to 0.91) and being married/living with partner: AOR = 0.01 (95% CI: 0.46 to 0.90).

Finally, significant predictors associated with higher odds of more than 3 sexual acts were being married/living with partner: AOR = 2.71 (95% CI: 2.25 to 3.27), being employed: AOR = 1.25 (95% CI: 1.07 to 1.46), alcohol use: AOR = 1.32 (95% CI: 1.12 to 1.56), and number of people to whom drug injection needles were passed to after use: AOR = 1.21 (95% CI: 1.08 to 1.36). Significant predictors associated with lower odds of more than 3 sexual acts were older age: AOR = 0.72 (95% CI: 0.64 to 0.81), incarceration: AOR = 0.75 (95% CI: 0.58 to 0.97), number of days drugs were injected: AOR = 0.99 (95% CI: 0.98 to 1.00), and sharing of needles after use: AOR = 0.59 (95% CI: 0.44 to 0.81).

## DISCUSSION

This study was the first large RCT of opiate dependence treatment among PWID. In this analysis of risky sexual behavior of PWID enrolled into HPTN 058, we found that long-term BUP/NX treatment was not significantly associated with different risky

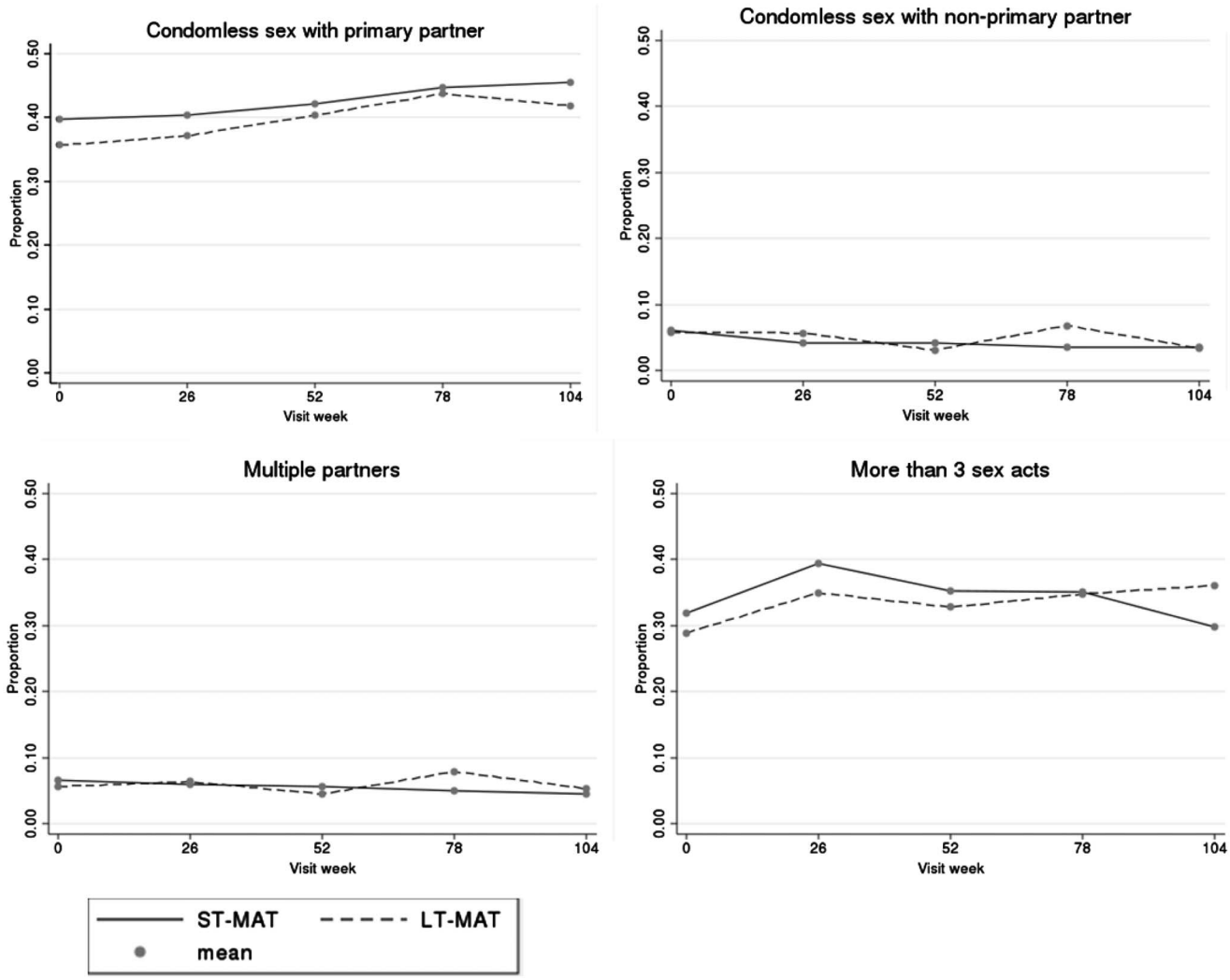


**FIGURE 1.** Changes in risky sexual behaviors by treatment arm.

sexual behavior than short-term treatment among PWID. This is consistent with previous smaller RCT and behavioral studies which have shown long-term BUP/NX to be significantly associated with a reduction in drug injection risk, but not leading to a reduction in risky sexual behavior.[33–36] Based on this finding, it is important that PWID on opiate dependence treatment be provided with sexual risk reduction counseling in addition to injection drug use risk-reduction interventions. Risky sexual behavior is an additional risk for HIV and hepatitis B and C transmission among PWID.

PWID have generally been known to have greater risky sexual behavior compared with general population.[2–4,28,30] In contrast to what has been previously reported in studies of injecting drug users, we found lower rates of risky sexual behavior at baseline and at all time points.[4,30,31,35] This could be because the trial offered additional sexual behavior risk-reduction counseling together with drug taking risk-reduction counseling at least monthly. This could also indicate effectiveness of sexual behavioral interventions in HIV prevention over time.

One factor significantly associated with lower risky sexual behaviors among this HIV-uninfected PWID population was older age. This could be due to less experimentation

**TABLE 2.** Odds of Risky Sexual Behaviors Associated With LT-MAT at Each Study Visit

| Risky Sexual Behavior | Baseline (N = 1250) | Week 26 (N = 897) | Week 52 (N = 697) | Week 78 (N = 561) | Week 104 (N = 410) |
|---|---|---|---|---|---|
| Condomless sex with primary partner | 0.84 (0.67–1.05) | 0.86 (0.66–1.11) | 0.92 (0.69–1.23) | 0.90 (0.65–1.24) | 0.73 (0.50–1.07) |
| Condomless sex with nonprimary partner | 0.95 (0.59–1.54) | 1.39 (0.75–2.58) | 0.68 (0.30–1.52) | 1.99 (0.90–4.39) | 0.87 (0.30–2.53) |
| Multiple partners in previous month | 0.85 (0.53–1.36) | 1.06 (0.61–1.84) | 0.76 (0.38–1.52) | 1.74 (0.85–3.54) | 1.16 (0.49–2.79) |
| More than 3 sex acts in a month | 0.87 (0.68–1.10) | 0.80 (0.61–1.04) | 0.88 (0.64–1.20) | 0.95 (0.68–1.34) | 1.21 (0.81–1.82) |

**TABLE 3.** Demographic and Behavioral Risk Factors for Risky Sexual Behavior Endpoints

| | Condomless Sex With Primary Partner | | Condomless Sex With Nonprimary Partner | | Multiple Partners | | More Than 3 Sex Acts | |
|---|---|---|---|---|---|---|---|---|
| | OR (95% CI) | AOR (95% CI) | OR (95% CI) | AOR (95% CI) | OR (95% CI) | AOR (95% CI) | OR (95% CI) | AOR (95% CI) |
| Demographics | | | | | | | | |
| Age (10 yrs difference) | 1.01 (0.90 to 1.14) | — | 0.59 (0.46 to 0.75)* | 0.69 (0.54 to 0.87)* | 0.63 (0.49 to 0.82)* | 0.71 (0.55 to 0.91)* | 0.81 (0.73 to 0.91)* | 0.72 (0.64 to 0.81)* |
| Sex (male) | 0.56 (0.41 to 0.77)* | 0.72 (0.51 to 1.02) | 1.10 (0.55 to 2.21) | — | 0.94 (0.50 to 1.75) | — | 0.76 (0.55 to 1.04) | 0.85 (0.60 to 1.20) |
| Ethnicity (minority status)† | 1.45 (1.15 to 1.84)* | 1.28 (1.00 to 1.64) | 1.62 (0.98 to 2.68) | 1.48 (0.87 to 2.51) | 1.43 (0.81 to 2.54) | — | 1.34 (1.05 to 1.70)* | 1.10 (0.86 to 1.43) |
| Married/living with partner | 4.65 (3.88 to 5.58)* | 4.34 (3.61 to 5.23)* | 0.58 (0.41 to 0.81)* | 0.65 (0.46 to 0.91)* | 0.59 (0.42 to 0.82)* | 0.64 (0.46 to 0.90)* | 2.50 (2.10 to 2.99)* | 2.71 (2.25 to 3.27)* |
| Education (yrs) | 0.99 (0.96 to 1.02) | — | 1.02 (0.95 to 1.11) | — | 1.11 (1.02 to 1.19)* | 1.09 (1.01 to 1.16)* | 1.03 (1.00 to 1.06) | 1.03 (0.99 to 1.06) |
| Employed | 1.32 (1.16 to 1.51)* | 1.22 (1.05 to 1.42)* | 0.88 (0.64 to 1.20) | — | 1.01 (0.75 to 1.35) | — | 1.34 (1.16 to 1.55)* | 1.25 (1.07 to 1.46)* |
| Income > $1000 | 1.26 (1.07 to 1.50)* | 1.19 (0.99 to 1.45) | 1.63 (1.00 to 2.66) | 1.64 (1.00 to 2.71) | 2.09 (1.34 to 3.27)* | 2.11 (1.32 to 3.39)* | 1.31 (1.09 to 1.59)* | 1.22 (0.99 to 1.50) |
| History of incarceration‡,‖ | 0.67 (0.54 to 0.82)* | 0.75 (0.59 to 0.95)* | 1.58 (1.06 to 2.36)* | 1.62 (1.08 to 2.42)* | 1.16 (0.76 to 1.78) | — | 0.69 (0.54 to 0.88)* | 0.75 (0.58 to 0.97)* |
| Alcohol use ‡,‖ | 1.38 (1.19 to 1.59)* | 1.45 (1.24 to 1.70)* | 1.32 (0.97 to 1.80) | 1.20 (0.88 to 1.64) | 1.16 (0.89 to 1.52) | — | 1.32 (1.13 to 1.55)* | 1.32 (1.12 to 1.56)* |
| Noninjection drug use‡,‖ | 0.92 (0.81 to 1.06) | — | 2.08 (1.52 to 2.84)* | 1.92 (1.40 to 2.64)* | 1.84 (1.37 to 2.47)* | 1.80 (1.33 to 2.43)* | 1.14 (0.99 to 1.30)* | 1.08 (0.93 to 1.25) |
| Injection drug use | | | | | | | | |
| Days injected‖ | 1.00 (0.99 to 1.00) | — | 0.99 (0.97 to 1.00) | — | 0.99 (0.98 to 1.01) | — | 0.99 (0.99 to 1.00)* | 0.99 (0.98 to 1.00)* |
| Times/day injected§ | 1.00 (0.97 to 1.03) | — | 0.89 (0.77 to 1.03) | — | 0.91 (0.80 to 1.03) | — | 0.98 (0.93 to 1.05) | — |
| Mixed different drugs‡,‖ | 0.63 (0.47 to 0.85)* | 0.69 (0.50 to 0.94)* | 1.03 (0.63 to 1.69) | — | 1.24 (0.78 to 1.97) | — | 0.73 (0.54 to 0.99) | 0.78 (0.57 to 1.07) |
| Any front- or back-loaded syringes‖ | 0.74 (0.51 to 1.08) | — | 1.79 (0.93 to 3.47) | 1.24 (0.61 to 2.52) | 1.65 (0.86 to 3.17) | — | 0.82 (0.54 to 1.24) | — |
| Passed needles after use‖ | 1.09 (0.89 to 1.33) | | 1.53 (0.98 to 2.41) | 1.01 (0.58 to 1.77) | 1.21 (0.77 to 1.92) | — | 1.01 (0.80 to 1.27) | — |
| No. of times passed | 1.00 (0.99 to 1.00) | | 1.01 (1.00 to 1.01) | 1.00 (0.99 to 1.02) | 1.00 (0.99 to 1.01) | — | 1.00 (0.99 to 1.00) | — |
| No. of people passed to | 1.03 (0.96 to 1.10) | | 1.08 (0.96 to 1.21) | — | 1.08 (0.97 to 1.21) | — | 1.08 (0.99 to 1.17) | 1.21 (1.08 to 1.36)* |
| Used needles after others used‖ | 0.81 (0.64 to 1.01) | | 1.37 (0.86 to 2.19) | — | 1.22 (0.77 to 1.95) | — | 0.76 (0.59 to 0.98)* | 0.59 (0.44 to 0.81)* |
| No. of times used after others | 1.00 (1.00 to 1.01) | | 1.01 (1.00 to 1.02)* | 1.00 (0.99 to 1.01) | 1.01 (1.00 to 1.01) | 0.99 (0.98 to 1.01) | 1.00 (0.99 to 1.01) | — |
| No. of people used after | 0.99 (0.90 to 1.09) | | 1.28 (1.07 to 1.52)* | 1.22 (0.98 to 1.51) | 1.26 (1.07 to 1.49)* | 1.25 (1.04 to 1.50)* | 1.04 (0.93 to 1.16) | — |

*Indicates $P$ value $< 0.05$ AOR: adjusted for site, treatment, baseline vs. follow-up and interaction between treatment and baseline vs. follow-up and all covariates that had $P < 0.1$ in the partially adjusted model.

†Minority status refers to participants who did not identify as Han in China or Thai in Thailand.

‡Missing.

and risk taking of older PWID compared with those of younger persons.[34,37]

Being married or living with a partner was significantly associated with higher frequency of condomless sex with the primary partner, higher frequency of sexual acts, as well as lower reports of condomless sex with a nonprimary partner and fewer sexual partners. Being married or living with a partner was therefore associated with a protective effect as there were significantly fewer reports of multiple sex partners and unprotected sex with a nonprimary partner. This is consistent with previous studies.[31,38,39] This could be because greater trust and caring have been shown to be characteristic of relationships with primary partners.[39,40] These findings also show that in sexual risk–reduction interventions, it is important to ascertain the nature of sexual relationships as there is a difference in behavior between primary and nonprimary partners among PWID, consistent with other studies.[40]

PWID in the HPTN 058 who also admitted to noninjection drug abuse were noted to be at significantly higher risk of unprotected sex with a nonprimary partner as well as higher risk of multiple partners. These findings are consistent with previously published literature,[30,38,41,42] and are of public health relevance for future education and intervention among HIV-uninfected PWID.

Income of >$1000/yr was significantly associated with higher risk of condomless sex with a nonprimary partner and with having multiple partners, consistent with previous reports in which higher socioeconomic status was a predictor of unsafe sex.[43,44] More research on higher income PWID might be necessary to further understand the social dynamics that might contribute to risky sexual behaviors among this population. This would be critical in tailoring prevention interventions among this group.

Alcohol use was significantly associated with unprotected sex acts with the primary partner as well as higher frequency of sex among HIV-uninfected PWID. This is consistent with existing literature.[40,45–49] Interventions to reduce alcohol consumption are important in HIV-uninfected PWID because they have a potential to reduce risky sexual behavior, which in turn reduces sexually transmitted infections including HIV. Furthermore, condom use messaging should be intensified in this population.

In this analysis, we were able to show the association of injection drug taking risk with the different risky sexual behaviors. The number of days that a participant injected opiate drugs was noted to be significantly associated with lower sexual acts and this could be because high levels of intoxication have a potential to reduce sexual activity.[50–52] The number of people with whom drug injection needles were used after others was significantly associated with higher risk of multiple sexual partners. It is important to target these specific populations in sexual risk–reduction interventions.

## Limitations

All data on risky sexual behaviors were collected retrospectively by self-report, potentially resulting in possible recall bias and social desirability bias. Studies have shown that sensitive information is more likely to be underreported.[53–56] In this study, this was minimized by having counselors not being involved in intervention acceptability assessments.

There was a possibility of selection bias; individuals who were more comfortable participating in this research project may not be representative of HIV-uninfected PWID in the general population. Finally, trial participants were mostly male (92%) and, therefore, results may not be generalizable to female PWID.

## CONCLUSIONS

In conclusion, LT-MAT did not significantly modify risky sexual behavior among HIV-uninfected PWID. Significant predictors of low frequency of unprotected sex with nonprimary partner and low odds of multiple partners among this population included older age and being married/living with a partner, whereas significant predictors of unprotected sex and multiple partners were incarceration, concomitant noninjection drug use, alcohol use, and needle sharing. Interventions that may lead to reduction in risky sexual behaviors should target these populations.

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