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# Participation in methadone programs improves antiretroviral uptake and HIV suppression among people who inject drugs in Kenya

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## Abstract

**Background:** HIV prevalence among people who inject drugs (PWID) in Kenya is estimated to be 18% compared to 4.5% in the general population. Studies from high-income countries have

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CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

**Loice Mbogo:** conceptualization, formal analysis, writing-original draft. **Betsy Sambai:** formal analysis. **Aliza Monroe-Wise**: writing – review & editing. **Natasha Ludwig-Barron:** writing -review & editing. **Brandon L. Guthrie:** formal analysis, data curation. **David Bukusi:** writing – review & editing. **Bhavna Chohan:** data curation, writing – review & editing. **Paul Macharia:** software programming. **Matt Dunbar:** software programming. **Emily Juma:** project administration. **William Sinkele:** project administration, writing – review & editing. **Esther Gitau:** project administration, resources. **Ashley Tseng:** writing – review & editing. **Rose Bosire:** writing – review & editing. **Sarah Masyuko:** writing – review & editing, **Helgar Musyoki:** writing – review & editing. **Tecla Temu:** writing – review & editing. **Joshua Herbeck**: funding acquisition, writing – review & editing. **Carey Farquhar:** funding acquisition, conceptualization, formal analysis, writing – review & editing.

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demonstrated that methadone use is associated with increased uptake of antiretroviral therapy (ART) and higher rates of viral suppression among PWID with HIV. However, it is unclear whether methadone use has the same effect among African PWID living with HIV.

**Methods:** We performed a cross-sectional study to evaluate associations between methadone program participation and ART uptake and viral suppression (HIV RNA viral load <1000 copies/ml) among PWID with HIV in Kenya. Participants were recruited from needle and syringe programs and methadone clinics, interviewed on site, and samples were obtained and assayed for HIV viral loads. Univariate and multiple logistic regression were used to determine associations.

**Results:** Among 679 participants, median age was 37 years, 48% were female, and 24% were in a methadone program. We observed higher proportions of ART use (96% vs. 87%, p=0.001) and HIV viral suppression (78% vs. 65%, p=0.012) among PWID on methadone compared to those not on methadone treatment. PWID who were not participating in a methadone program were 3-fold more likely to be off ART and approximately twice as likely to be viremic compared to those in methadone programs (adjusted odds ratio [aOR]=3.35, 95% confidence interval [CI]:1.35-8.35 and aOR=1.90, 95% CI:1.03-3.52, respectively).

**Conclusions:** In this study, Kenyan PWID living with HIV participating in a methadone treatment program were more likely to be on ART and to have achieved viral suppression. Scale-up of methadone programs may have a positive impact on HIV epidemic control for this key population.

### Keywords

Methadone; antiretroviral therapy; viral suppression; Kenya

## Introduction

Globally, it is estimated that 15.6 million people who inject drugs (PWID) are living with HIV (Degenhardt et al., 2017) and an estimated 600,000 of these individuals are in sub-Saharan Africa (SSA) (Mathers et al., 2008). In SSA only a handful of countries operate harm reduction services through needle syringe programs (NSP) and incarceration of drug users is common; however, due to civil society advocacy, academic research and international donor support, awareness of NSP (Gen, 2016) and integrated methadone and HIV programs are slowly being scaled up (Guise et al., 2019).

Within the region, the HIV epidemic continues to be a major public health concern and provision of optimal care to PWID living with HIV is a significant challenge (Degenhardt et al., 2010; Vickerman et al., 2014). In particular, gaps exist in engagement in HIV care services, uptake of antiretroviral therapy (ART), and viral suppression among PWID (Azar et al., 2015; Li et al., 2018; Zhang et al., 2011). Achieving optimal adherence to ART and sustaining viral suppression are essential to reduce morbidity and mortality associated with HIV (Mocroft et al., 1998; Rodger et al., 2013).

Despite the availability of subsidized HIV care integrated with other essential clinical services, PWID face many barriers to accessing services, including incarceration, displacement, homelessness, untreated psychiatric illness, transportation costs and stigma,

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which may complicate engagement in HIV care and affect ART adherence (Treisman, 2001; Wood et al., 2005). Studies in high-income countries have shown engagement in methadone treatment may reduce drug use and improve ART adherence (Palepu et al., 2006), and in the United States (US), viral suppression was associated with methadone use (Michael, 2000). Similar studies done in Vietnam examined buprenorphine plus naloxone and referral for methadone maintenance therapy and showed reduced heroin use, increased receipt of ART and HIV viral suppression with these interventions (Korthuis et al., 2021), while a study in Taiwan showed high retention among PWID on methadone (Chao et al., 2020). Integrated methadone and HIV care programs can provide promising infrastructure for promoting ART uptake and adherence by reducing transportation costs associated with traveling to multiple clinic sites, establishing trust with healthcare providers who are trained on the specific needs of PWID, and offering non-judgmental, safe-spaces for PWID (Berg et al., 2011; Tran BX, 2012).

In Kenya, key populations disproportionately contribute to the HIV epidemic and include female sex workers (FSW) and men who have sex with men (MSM) , all of which experience disproportionately high prevalence of HIV at 29.3% and 18.9% (Bhattacharjee et al., 2020; Musyoki et al., 2016; NASCOP, 2014). An estimated 18,000 PWID live in Kenya, primarily in Nairobi and coastal Kenya (NASCOP, 2019). Notably, HIV prevalence is approximately 18.3% among PWID (Kurth et al., 2015) compared to 4.5% in the general population in Kenya (National AIDS and STI Control Programme (NASCOP), Ministry of Health, 2018). NSP were introduced in 2013, providing harm reduction education and grassroots distribution of safe injection equipment through peer educators who are recovering PWID (NASCOP, 2013). In 2014, as a way to reduce opioid dependence and incident HIV infection in PWID communities, Kenya's government introduced integrated methadone programs, which provide methadone and HIV care (Rhodes et al., 2015). Integration of HIV care services has long been recognized as essential to enhance service access for key populations, particularly for PWID (NACC, 2015; NASCOP, 2018). However, few studies have examined the relationship between methadone use and HIV outcomes including ART uptake and viral suppression in resource-limited settings, particularly in sub-Saharan Africa.

There is a need to understand how methadone service settings that provide care to PWID living with HIV can affect HIV treatment uptake and adherence in sub-Saharan Africa and other resource-limited settings (Guise et al., 2019; Rhodes et al., 2015). In this study, we evaluated the association between methadone program participation, ART use and viral suppression among PWID living with HIV in Kenya, comparing those enrolled in methadone clinics to those enrolled in NSP. We hypothesized that methadone use would be associated with increased ART uptake and viral suppression among PWID who are living with HIV in Kenya.

## Methods

### Study setting and participants

We analyzed baseline data from participants enrolled in a prospective cohort study in Kenya. The study was established to evaluate the effectiveness of assisted partner services (APS)

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in identifying, testing, and linking to care the sexual and injecting partners of HIV-positive PWID. APS is the practice through which health care providers facilitate the notification, testing and linkage to care of partners who are exposed to HIV or other sexually transmitted infections by an individual known to be positive, without revealing the identity of the person who may have exposed them (Monroe-Wise et al., 2021).

## Study participants and procedures

The primary study recruited participants using convenience sampling through established needle and syringe programs and methadone clinics in the Nairobi and coastal region of Kenya. In Nairobi, participants were recruited from methadone sites at the Drug Rehabilitation Unit in Mathari Hospital and Ngara Health Center, and three NSP sites managed by a harm reduction organization, Support for Africa Addiction Prevention Treatment in Africa. At the coast region the participants were recruited from the methadone clinic at Malindi County Hospital and four NSP sites including the Reachout program in Mombasa, Muslim Education Welfare Association sites in Mtwapa and Kilifi, and the Omari Project in Malindi. In our analysis we included all participants enrolled in the parent study who had injected drugs at least once in the last year, were ≥18 years of age, and had a confirmed HIV diagnosis. We excluded newly HIV diagnosed participants from the analysis due to the short duration on ART.

The secondary analysis used data collected at baseline through a standardized questionnaire programmed through Open Data Kit software (Anderea Steiner, 2016), with iRespond (iris scan) software ensuring that each participant was assigned a unique identification number (Anne et al., 2021) to limit double-enrollments. Data collected included demographic information (e.g., age, sex, marital status, housing conditions, employment), current and previous drug use (e.g., types of drugs, drug administration practices, duration of injecting, alcohol use), sexual practices (e.g., types of partners, condom use) and HIV services (e.g., ART history and current use). All participants provided written informed consent and were compensated 400 Kenyan shillings ($4 USD) for their time and transportation. All study protocols and procedures were approved by the Ethics and Research Committee of Kenyatta National Hospital and the Institutional Review Board at University of Washington.

## Laboratory analysis

Blood samples collected at baseline were processed for HIV RNA viral loads conducted using a real time polymerase chain reaction (RT-PCR) (Abbott). Viral suppression was defined as an HIV-1 RNA viral load of <1000 copies/ml as per the Kenya guidelines (NASCOP, 2018)

## Statistical Analysis

Socio-demographic and behavioral characteristics were described using medians and interquartile ranges for continuous variables, and proportions for categorical variables. Differences in the distribution of these characteristics by methadone participation was assessed using chi-square tests for categorical variables and Mann Whitney U Test (Wilcoxon Rank Sum Test) for continuous variables. Univariate and multiple logistic regression models were used to determine whether enrollment in a methadone program

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was associated with ART use and HIV viral suppression controlling for region (Coast vs Nairobi), methamphetamine use, cocaine use and alcohol use. Analyses were conducted using Stata version 15.1 (College Station, TX).

## Results

Among 679 PWID, 391 (58%) were from Nairobi and 163 (24%) were on methadone. Median age was 37 (IQR 32-42) years, slightly over 50% were males, median duration of drug injection was 4 years (IQR 2-9), and 41 (6%) were homeless. Methadone use was more than two times higher among coast participants when compared to Nairobi residents (67% vs 33%, p<0.001) and males were more likely to be taking methadone compared to females (29% vs 19%, p=0.003). Individuals on methadone had injected longer than those not on methadone (5 years (IQR 3-10) vs 4 years (IQR 2-8), p<0.001). Most individuals reported polysubstance use with nearly 90% using heroin, 51% using marijuana and 32% using alcohol in the previous month. Heroin use was more likely to be reported by those not on methadone compared to those on methadone (79% vs 21%, p<0.001). Those who had lived longer with HIV were also more likely to be on methadone (p=0.045) (Table 1).

### Association between methadone program participation and ART uptake

We observed a greater proportion of ART use among PWID on methadone compared to those not on methadone (96% vs 87%, p=0.001). In the multivariable analysis, individuals who were not involved in a methadone program were 3.35 times more likely to report not taking ART (aOR=3.35, 95% CI: 1.35-8.35, p=0.009). Individuals were less likely to be off ART if they had had sex with an individual known to be HIV positive (aOR=0.41, 95% CI: 0.21-0.78, p=0.007), used condoms (aOR=0.42, 95% CI: 0.24-0.71, p=0.001), and were older (aOR=0.95, 95% CI: 0.92-0.99, p=0.011) (Table 2).

### Association between methadone program participation and viral suppression

Viral load results were available for a subset of 400 (59%) participants of whom 109 (27%) were on methadone. Our analysis showed a higher proportion of PWID on methadone (78%) were virally suppressed compared to those not on methadone (65%, p=0.011). In the multivariable analysis, individuals not involved in a methadone program were 1.90 times more likely to be viremic compared to those in a methadone program (aOR=1.90, 95% CI: 1.03-3.52, p=0.040). Those who had injected for more years were less likely to be viremic (aOR=0.95, 95% CI:0.91-0.99, p=0.049) and older age was associated with lower odds of viremia (aOR=0.97, 95% CI;0.94-0.99, p=0.046) (Table 3).

## Discussion

This finding suggest that methadone use was associated with both ART uptake and achieving HIV viral suppression among PWID in Kenya. These findings show differential uptake of methadone in Kenya and suggest that scaling up of methadone use could improve uptake of HIV care and retention and the achievement of viral suppression in this population.

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In SSA there is a dearth of evidence about the impact of interventions related to methadone use on HIV care outcomes, and only five countries in Africa now have harm reduction programs: Kenya, Mauritius, Senegal, South Africa and Tanzania (Guise et al., 2019). Tanzania established that integration of HIV and TB services in methadone programs is of benefit to both the patient and the healthcare provider (Bruce et al., 2014) and results in increased ART initiation (Hassan et al., 2019). In high income countries such as the US, studies have demonstrated a complex interplay between optimal ART adherence, current injection-related practices, and viral suppression (Shrestha Roman, 2019). In Canada, studies have found that engagement in a methadone maintenance program was associated with adherence to ART and achieved HIV-1 RNA suppression (Palepu et al., 2006). In Greece, expedited ART linkages for PWID identified by respondent-driven sampling surveys led to an apparent decline in HIV incidence (Sypsa et al., 2017) and other high income countries have shown improvement of ART uptake and viral suppression associated with methadone use. (Hogg et al., 2011; Miller et al., 2018).

Methadone programs have been scaled up in 8 out of the 47 counties within Kenya to curb addiction since 2014. Needle and syringe programs, which are key components of harm reduction initiatives, play an important role in endorsing individuals who are ready to be initiated in methadone treatment. They do this with the support and coordination of the Kenya National AIDS and STI Control Programme (NASCOP), the Ministry of Health and with international funding support (Guise et al., 2019; Salleh et al., 2021) . While rehabilitation programs are often associated with failing to prevent relapse, methadone engenders hope for a more profound recovery and reintegration into society. However, limitations such as lack of resources, stigma, and discrimination have been identified as barriers to accessing methadone treatment (Rhodes et al., 2015; Wolfe et al., 2010). Previous studies have also identified barriers to integrating HIV care into methadone programs at the policy, institutional, provider and client levels (Li et al., 2018). Individual who had injected drugs for a short period of time were more likely to be viremic. Consistent with previous literature, younger and ongoing drug use was associated with poorer ART uptake (Arnsten H et al., 2002). Programmatic data show that PWID on Kenya’s coast are more likely to be enrolled in an NSP program than those in Nairobi; furthermore, NSP participation has been linked to methadone use. As a result, the pipeline from NSP to methadone remains better utilized in Kenya’s coast than in Nairobi (Ndimbii et al., 2015; Rhodes et al., 2015).

Our study had several limitations. This was a cross sectional study, and therefore could not evaluate the sustainability of methadone uptake in this population. We limited enrollment in this study to people who had injected drugs within the previous year, introducing potential selection bias and limiting the generalizability to others who may not have recently injected drugs. Finally, ART use was self-reported, which may have introduced recall or desirability bias. Nevertheless, our study is among the first to show significant associations between methadone use and important HIV care outcomes among PWID in a low-resource setting.

Methadone treatment improves ART uptake in a variety of settings and populations (Sasha Uhlmann, 2011; Weber et al., 2009). Improving the engagement of people living with HIV who inject drugs in methadone programs will reduce morbidity and mortality caused by low viral suppression and nonadherence to ART (Altice et al., 2010; Mayer et al., 2013;

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Miller et al., 2018). In turn, this will decrease ongoing HIV transmission both within the PWID community and between PWID and the general population. In our study, out of 679 only 24% were taking methadone, an indication of the need to enhance the acceptability of, feasibility of and access to integrated methadone and HIV care (Guise et al., 2019; Saleem et al., 2016).

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### Conflicts of Interest

The authors declare that they have no conflicts of interest associated with this publication and there has been no significant financial support for this work that could have influenced its outcome. We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that this study was conducted with the ethical approval of the Institutional Review Board at the University of Washington and the Ethical Review Committee at Kenyatta National Hospital/University of Nairobi.

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**Table 1:**

Socio-demographic characteristics stratified by methadone program participation

| | Total N=679 | On Methadone n=163 | Not on Methadone n=516 | $a$ p-value |
|---|---|---|---|---|
| **Socio-demographics** | | | | |
| **Age years (Median, IQR)** | 37 (32-42) | 36 (31-41) | 37 (32-42) | 0.158 $b$ |
| **Sex** | | | | |
| **Male** | 355 (52%) | 102 (63%) | 253 (49%) | **0.003** |
| **Marital status** | | | | |
| **Single** | 244 (36%) | 52 (32%) | 192 (37%) | **0.033** |
| **Married** | 170 (25%) | 54 (33%) | 116 (22%) | |
| **Partnered** | 37 (5%) | 12 (7%) | 25 (5%) | |
| **Divorced/separated** | 159 (23%) | 30 (18%) | 129 (25%) | |
| **Widowed** | 69 (10%) | 15 (9%) | 54 (10%) | |
| **Living condition** | | | | |
| **Person/friends/relatives/hotel/rental** | 603 (89%) | 151 (93%) | 452 (88%) | 0.075 |
| **Improvised shelter/open** | 76 (11%) | 12 (7%) | 64 (12%) | |
| **Region** | | | | |
| **Coast** | 288 (42%) | 110 (67%) | 178 (35%) | **<0.001** |
| **Nairobi** | 391 (58%) | 53 (33%) | 338 (65%) | |
| **Number of sexual partners in the last 3 months** | | | | |
| **0** | 326 (48%) | 59 (36%) | 267 (52%) | **0.003** |
| **1** | 169 (25%) | 49 (30%) | 120 (23%) | |
| **2-5** | 103 (15%) | 35 (21%) | 68 (13%) | |
| **>5** | 81 (12%) | 20 (12%) | 61 (12%) | |
| **Years of HIV infection (Median (IQR))** | 5 (2-10) | 6 (2-10) | 5 (2-10) | **0.045** $b$ |
| **Years injecting (Median (IQR))** | 4 (2-9) | 5 (3-10) | 4 (2-8) | **<0.001** $b$ |
| **Type of drug used in the past month** | | | | |
| **Heroin** | 608 (89%) | 128 (78%) | 480 (93%) | <0.001 |
| **Methamphetamine/Speed** | 54 (8%) | 16 (10%) | 38 (7%) | 0.313 |
| **Cocaine** | 42 (6%) | 4 (2%) | 38 (7%) | 0.023 |
| **Marijuana** | 347 (51%) | 97 (59%) | 250 (48%) | 0.014 |
| **Alcohol use** | | | | |
| **Yes** | 216 (32%) | 38 (23%) | 178 (35%) | **0.008** |
| **Number of times injected drugs in the past month (Median (IQR))** | 60 (12-90) | 30 (0-90) | 60 (30-90) | **0.048** $b$ |
| **ART use** | | | | |
| **Yes** | 606 (89%) | 157 (96%) | 449 (87%) | **0.001** |

Abbreviations: IQR, Interquartile range

$a$ Pearson's chi square test used to test association between each row variable and methadone participation

$b$ Mann Whitney U Test (Wilcoxon rank sum test) for difference of medians between those on methadone and those not on methadone.

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**Table 2:**

Factors associated with not currently taking ART

| | Adjusted OR (95%CI)** | p-value |
|---|---|---|
| **Methadone participation** | | |
| **No** | 3.35 (1.35-8.35) | **0.009** |
| **Age years (Median,IQR)** | 0.95 (0.92-0.99) | **0.011** |
| **Sex** | | |
| **Female** | 0.67 (0.29-1.53) | 0.343 |
| **Marital status** | | |
| **Married** | 1.51 (0.73-3.14) | 0.409 |
| **Partnered** | 1.18 (0.30-4.62) | |
| **Divorced/separated** | 0.88 (0.41-1.85) | |
| **Widowed** | 1.96 (0.82-4.69) | |
| **Living condition** | | |
| **Improvised shelter/open** | 1.31 (0.59-2.92) | 0.504 |
| **Region** | | |
| **Coast** | 0.41 (0.21-0.79) | **0.008** |
| **Number of sexual partners in the last 3 months** | | |
| **1** | 1.39 (0.69-2.84) | 0.509 |
| **2-5** | 1.13 (0.46-2.82) | |
| **6+** | 2.14 (0.88-5.23) | |
| **Condom use** | | |
| **Yes** | 0.42 (0.24-0.71) | **0.001** |
| **Heterosexual** | | |
| **Yes** | 1.92 (0.39-9.34) | 0.418 |
| **Given money for sex** | | |
| **Yes** | 0.62 (0.29-1.30) | 0.204 |
| **Received money for sex** | | |
| **Yes** | 0.82 (0.39-1.71) | 0.601 |
| **Sex with known positive** | | |
| **Yes** | 0.41 (0.21-0.78) | **0.007** |
| **Years injecting (Median (IQR)** | 0.98 (0.93-1.03) | 0.467 |
| **Methamphetamine/Speed** | | |
| **Yes** | 0.40 (0.11-1.42) | 0.158 |
| **Cocaine** | | |
| **Yes** | 1.53 (0.58-4.02) | 0.392 |
| **Alcohol use** | | |
| **Yes** | 1.49 (0.81-2.71) | 0.197 |

** Adjusted odds ratios from the multivariable model that included all the variables in the table.

Reference group for methadone participation is (Yes), sex (male), marital status (single), living condition (person/friends/relatives/hotel/rental), region (Nairobi), Number of sexual partners in the last 3 months (0), condom use (No), heterosexual (No), given money for sex (No), received money for sex (No), sex with known positive (No), methamphetamine use (No), cocaine use (No) and alcohol use (No).

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**Table 3:**

Factors associated with HIV viremia

| | Adjusted OR (95%CI)** | p-value |
|---|---|---|
| **Methadone participation** | | |
| **No** | 1.90 (1.03-3.52) | **0.040** |
| **Age in years (Median, IQR)** | 0.97 (0.94-0.99) | **0.046** |
| **Sex** | | |
| **Female** | 0.83 (0.39-1.71) | 0.610 |
| **Marital status** | | |
| **Married** | 0.86 (0.45-1.65) | 0.292 |
| **Partnered** | 3.33 (0.97-11.40) | |
| **Divorced/separated** | 1.00 (0.54-1.87) | |
| **Widowed** | 1.26 (0.58-2.75) | |
| **Living condition** | | |
| **Improvised shelter/open** | 1.11 (0.53-2.32) | 0.775 |
| **Region** | | |
| **Coast** | 0.90 (0.48-1.70) | 0.749 |
| **Number of sexual partners in the last 3 months** | | |
| **1** | 1.54 (0.85-2.81) | 0.133 |
| **2-5** | 1.18 (0.56-2.52) | |
| **6+** | 2.43 (1.09-5.41) | |
| **Condom use** | | |
| **Yes** | 0.79 (0.49-1.28) | 0.352 |
| **Heterosexual** | | |
| **Yes** | 6.58 (1.25-34.42) | **0.026** |
| **Given money for sex** | | |
| **Yes** | 0.84 (0.46-1.57) | 0.595 |
| **Received money for sex** | | |
| **Yes** | 0.98 (0.52-1.83) | 0.945 |
| **Sex with known positive** | | |
| **Yes** | 0.64 (0.38-1.06) | 0.086 |
| **Years injecting** | 0.95 (0.91-0.99) | **0.049** |
| **Methamphetamine/Speed** | | |
| **Yes** | 0.94 (0.40-2.22) | 0.900 |
| **Cocaine** | | |
| **Yes** | 0.82 (0.32-2.10) | 0.679 |
| **Alcohol use** | | |
| **Yes** | 1.09 (0.65-1.86) | 0.733 |

** Adjusted odds ratios from the multivariable model that included all the variables in the table.

Reference group for methadone participation is (Yes), sex (male), marital status (single), living condition (person/friends/relatives/hotel/rental), region (Nairobi), Number of sexual partners in the last 3 months (0), condom use (No), heterosexual (No), given money for sex (No), received money for sex (No), sex with known positive (No), methamphetamine use (No), cocaine use (No) and alcohol use (No).