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ORIGINAL PAPER

Contingency Management for Integrated Harm Reduction Among Men Who Have Sex with Men Who Use Methamphetamine in Los Angeles: A Pilot Assessment

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Abstract

Methamphetamine (MA) use is associated with HIV transmission among men who have sex with men (MSM) and lapses in medication adherence. Contingency Management (CM) is effective in reducing MA use, but studies of CM to support adherence to HIV prevention or treatment are limited. We conducted a pilot trial of a CM intervention to reduce MA use and improve PrEP/ART adherence among MSM prescribed a tenofovir (TFV)-based regimen for HIV prevention or treatment. Participants were randomly assigned to receive escalating incentives for either MA abstinence or TFV adherence (based on point-of-care urine testing), and to a monitoring schedule of either 2 or 3 visits/week for 4 weeks. 19 MSM were randomized to either CM for MA use or CM for PrEP/ART adherence (median age: 38; IQR: 28–46) and 15 were living with HIV. Participants attended 95.7% (67/70) of scheduled visits in the 2x/week arm and 74.8% (74/99) in the 3x/week arm. TFV adherence was higher among participants in the TFV adherence arm with 93.5% (n = 72/77) of urine samples positive for TFV, compared to 76.6% (n = 49/64) in the MA abstinence arm (p = 0.007). Participants in the MA abstinence arm had more urine samples negative for MA metabolites (20.3%, n = 13/64) than those receiving CM for TFV adherence (6.5%, n = 5/77; p = 0.021). A CM model for MA abstinence and PrEP/ART adherence using twice-weekly visits and urine testing for MA and TFV for MSM who use MA is feasible and potentially effective as an integrated harm reduction strategy.

Keywords men who have sex with men · stimulant use · substance use · contingency management · adherence

Introduction

Men who have sex with men (MSM) are disproportionately impacted by the HIV epidemic and continue to experience HIV-related health disparities despite advances in antiretroviral therapy (ART) and pre-exposure prophylaxis (PrEP) [1, 2]. The link between methamphetamine (MA) use and HIV infection has been well established in the literature [3–5]. MA use has been associated with increased sexual risk behaviors (such as higher numbers of sexual partners and impaired condom negotiation), poor adherence to PrEP, and increased prevalence of STIs [3, 6, 7]. Among MSM living with HIV, MA use has been associated with impaired engagement along the HIV care cascade, including lower adherence to ART, and lack of virologic suppression [8, 9]. These factors contribute to HIV transmission within sexual networks as well as ongoing HIV-related health disparities that are experienced by MSM who use MA.

Between 2015 and 2019, the prevalence of MA use in the US has increased by 43% and overdose deaths have increased 180% [10]. In Los Angeles County, MA-related deaths have increased by over 700% in the past decade [11]. Despite rising rates of MA use, there are no pharmacologic

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treatment options for MA use disorder that are currently approved by the Food and Drug Administration and current evidence-based treatment options are centered around behavioral interventions [12, 13].

Contingency management (CM) is an evidence-based behavioral intervention for the treatment of MA use disorder that has proven efficacy in reducing frequency of MA use [14]. CM provides escalating financial rewards in exchange for consecutive biomarkers (e.g., urine drug screens) that confirm drug abstinence [13]. As MA use is typically associated with "Delay Discounting," or the prioritization of short-term rewards over long-term risks, the financial incentives provided for drug abstinence in CM may serve to supplant the association of MA use as a short-term reward [15–17].

Given the well-established links between MA use and HIV risk behaviors, several studies have evaluated the indirect impact of CM on HIV acquisition and transmission. Reductions in MA use have been associated with decreased frequency of condomless intercourse among MSM as well as reduced HIV viral loads in previous trials of CM [18, 19]. MA abstinence during CM has been associated with increased adherence to HIV post-exposure prophylaxis (PEP) following a high-risk sexual exposure among MSM who use MA [20, 21]. Additionally, CM interventions have been separately used to directly promote positive health behaviors and advancement along the HIV care continuum, such as attending medical visits, obtaining lab tests, completing vaccination series, improving medication adherence, and achieving virologic suppression among non-substance using populations [22–25]. Despite these indirect benefits of CM for MA use on preventing HIV acquisition and transmission, there are a paucity of interventions that have utilized CM as a combined approach to impact both MA use and PrEP/ART adherence.

While medication adherence is the cornerstone for treatment as prevention (TasP), limitations in the ability to accurately measure adherence to PrEP/ART represent an important barrier in utilizing CM as a strategy to promote HIV medication adherence among individuals who use MA. In clinical settings, medication adherence has traditionally been measured by self-report, which can be vulnerable to recall and social desirability biases [26]. Other methods to measure adherence have consisted of evaluating active prescriptions, pharmacy records, and pill counts – which can be cumbersome and have been found to have minimal improvements in accuracy compared to self-reported adherence [27, 28]. Remote medication adherence monitoring technologies, such as electronic pill boxes, video-based technologies, electronic medication management systems, and motion sensors, have been developed to provide more accurate assessments of medication taking, but these technologies rely on proxy measures of medication adherence [29]. To overcome these limitations, pharmacologic metrics of adherence, where drug levels are measured using liquid chromatography tandem mass spectrometry (LC-MS/MS) in a biomatrix have been developed [30]. However, the ability to utilize LC-MS/MS assays in real world scenarios, such as CM, is limited because LC-MS/MS is expensive, labor intensive, and can be subject to lengthy processing times to obtain results [30]. To address these obstacles associated with traditional therapeutic drug monitoring assays, a point-of-care, antibody-based assay for tenofovir (TFV) in urine has been developed that can be performed in less than 5 min and detects the presence of either tenofovir disoproxil fumarate (TDF) or tenofovir alafenamide (TAF) use within the previous 3 days [31]. The newly developed and validated point-of-care assay [32, 33] provides a unique opportunity to provide objective measurements of TFV adherence in real time that can be incorporated into novel, CM-based HIV treatment and prevention paradigms.

MA use and ineffective use of HIV treatment and prevention represent key facilitators for ongoing HIV transmission within the sexual networks of MSM who use MA. While CM is effective in reducing the frequency of MA use and accompanying sexual risk behaviors, it has yet to be paired with CM programs to directly support adherence to biomedical HIV prevention and treatment. To address this gap, we conducted a pilot trial examining the logistics and feasibility for a CM intervention designed to reduce MA use and improve PrEP/ART adherence among MSM in Los Angeles, using a novel point-of-care urine TFV assay to support CM. As a secondary outcome, we evaluated whether implementation of the CM intervention was associated with reported sexual behaviors, such as number of male partners within the past 7 days. The goal of this study is to determine how to design CM programs as an integrated strategy to address both substance use and HIV risk behavior and to control the spread of HIV in the networks of MSM who use MA.

Methods

Study Design, Participants, and Recruitment

We conducted a pilot RCT to evaluate the logistics and feasibility of CM as a strategy to promote MA abstinence and PrEP/ART adherence among MSM who use MA. Participants were recruited from a community-based university research clinic as well as community-based organizations that provide resources for lesbian, gay, bisexual, and transgender communities in Los Angeles, California. To avoid withholding an effective CM therapy intervention from individuals trying to limit their MA use, this pilot study limited enrollment to MSM not currently seeking substance use

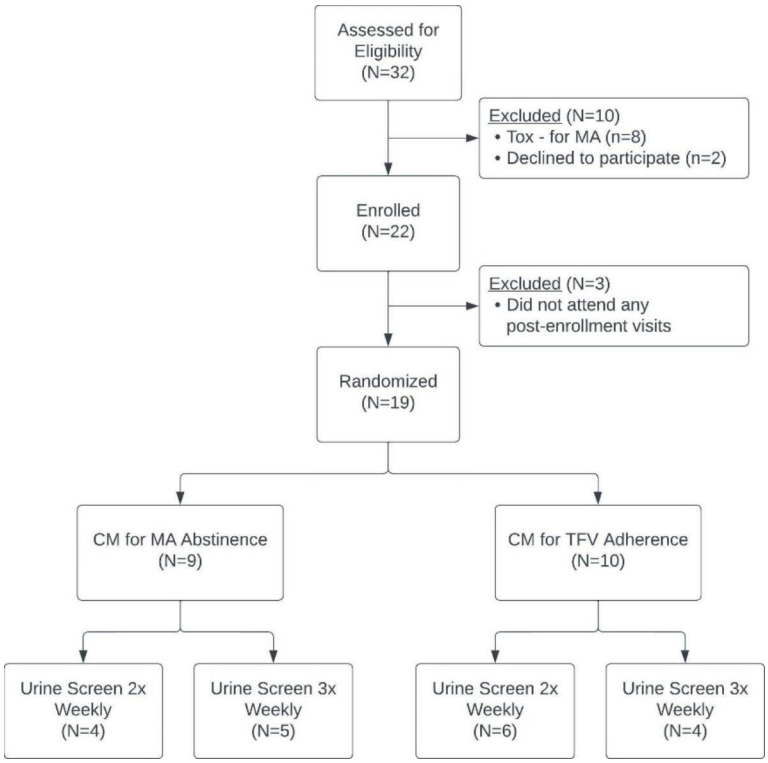

Fig. 1 Screening and randomization of participants

treatment. Inclusion criteria for study participation were as follows: (1) 18 years of age or older; (2) Biological male at birth; (3) Self-reported condomless anal intercourse with a male or transgender woman in the previous 6 months; (4) Report current MA use (at least once per week) with verified MA metabolites in urine at screening; (5) Currently taking TFV-based PrEP (if HIV-negative) or TFV-based ART regimen (if living with HIV), demonstrated by bottle of medication or active prescription; and (6) Willingness to complete study procedures. Exclusion criteria included: (1) Urine negative for MA metabolites at screening and (2) Unable or unwilling to take TFV-based regimens for HIV treatment or prevention.

Potential participants underwent telephone screening prior to being scheduled for an in-person enrollment visit. At the enrollment visit, participants provided written informed consent, were assessed for eligibility by a study clinician, and provided a urine sample that was tested for MA metabolites. After screening eligible, participants completed a computer-assisted self-interview (evaluating substance use, sexual behavior, PrEP/ART use), HIV/STI testing, and a urine sample to test for MA metabolites and TFV. At enrollment, participants were randomly assigned to (1) a CM program with incentives based on either MA abstinence or TFV adherence and (2) participating in CM visits either twice weekly or three times weekly (Fig. 1). We chose to randomly assign participants to either a twice weekly or three times weekly CM visit schedule to compare participant attendance rates and overall satisfaction, as both visit schedules are used in CM trials and have distinct benefits and tradeoffs [34]. Between March and July 2021, 32 participants were assessed for eligibility, and 13 participants were excluded due to (1) providing a urine sample negative for MA metabolites, (2) declining to participate in the study, and (3) not attending any post-enrollment visits. Following eligibility screening, 19 participants were randomized, with 9 participants assigned to CM for MA abstinence and 10 assigned to CM for TFV adherence. Randomization occurred using a computerized random number generator, stratified by HIV status. 10 participants were randomly assigned to twice weekly CM visits and 9 were assigned to three times weekly CM visits. CM visits occurred for a total of 4 weeks. Once a week, participants completed a computer-assisted self-interview that evaluated ART or PrEP adherence, sexual behavior, and substance use over the past 7 days. At the final visit, participants completed an exit survey that evaluated their satisfaction with the intervention and study procedures. Of the 19 participants randomized, 17 completed their final visit. Participants were compensated $50 for the enrollment visit, base payment of $10 for each CM visit (in addition to the CM visits described below), and $100 for completing the final visit. Participants received a $10 base payment for each CM visit to encourage visit attendance and to reduce the likelihood of missed visits due to anticipation that a urine sample would not be eligible for contingent rewards. The study was reviewed and approved

by the Office of Human Research Participant Protection (OHRPP) at the University of California, Los Angeles (IRB # 19-001996). This study was also registered with clinicaltrials.gov (NCT04563962).

Intervention

Participants completed CM visits either twice weekly or three times weekly for 4 weeks. At each CM visit, participants provided a urine sample that was tested at the point-of-care for the presence of MA metabolites and TFV. TFV was tested for via an antibody-based lateral flow assay, which can be performed in less than 5 min and indicates use of either TDF or TAF-based PrEP or ART in the prior 3-days [31]. Development and validation of this novel, point-of-care TFV assay has been previously described [31, 33]. Participants received financial incentives for each urine sample provided that was negative for MA metabolites (if randomized to MA abstinence) or positive for TFV (if randomized to TFV adherence). Financial incentives escalated in value during each week of the intervention, with $2/visit during Week 1, $6/visit during Week 2, $12/visit during Week 3, and $18/visit during Week 4. If a participant failed urine testing (e.g., tested positive for MA or negative for TFV, depending on randomization arm), their financial incentive schedule reset to the baseline value of $2/visit. The total possible incentives that could be earned during the 4-week CM intervention was $74 for participants randomized to twice weekly CM visits and $112 for those randomized to three times weekly CM visits. At each CM visit, study counselors conducted a brief check-in session using motivational interviewing techniques to encourage MA abstinence, TFV adherence, and condom use.

Outcomes

Our primary outcome was the number of urine samples that were positive for MA metabolites (for the MA abstinence arm) or TFV (for the TFV adherence arm). Our secondary outcomes included number of missed CM visits, number of male partners in last 7 days, and satisfaction with the intervention and study procedures at the end of the study. At enrollment, participants were asked demographic information, employment status, partnership status, number of male partners in the last month, PrEP/ART adherence, and MA use in past 3 months, and were tested for STIs. Participants were asked to categorize their current partnership status as one of the following "have primary or main partner, not living together", "living with primary or main partner", or "single/divorced/widowed". These options were combined into a dichotomous variable (partnered or not partnered). Participants self-reported the number of male sexual partners they had in the past month (potential range 1–20). HIV-uninfected participants were asked "On average, how often do you miss a dose of your PrEP medication?", and participants living with HIV were asked "How often do you miss a dose of your HIV medication(s)?" Potential response options for both questions included "Never", "Less than once a month", "Once a month", "Once a week", and "Several times a week". These variables were combined into one composite frequency of missed TFV doses variable with the following levels: never, once monthly or less, and once weekly or more. Participants were asked, "In the past three months, how often have you used MA (speed, crystal meth, ice, etc.)?" and potential response options included "Never", "Once or twice", "Monthly", "Weekly", and "Daily or almost daily". MA use in the past 3 months was trichotomized to: monthly or less, weekly, and daily or almost daily.

During weekly follow-up surveys, participants were asked to self-report the number of days they used MA in the past week. Participants also self-reported the number of male sexual partners in the past week. At the final visit, participants were asked a series of questions about the intervention and study procedures and were asked to rank their satisfaction for each study component from 1 to 5. Satisfaction questions included: "Overall, how satisfied were you with your experiences participating in this research study?" (1 [very unsatisfied] to 5 [very satisfied]); "How satisfied were you with the number and frequency of study visits?" (1 [too infrequent/not enough study visits] to 5 [too frequent/too many study visits]); "Do you think the behavioral counseling provided at each visit helped you to meet your treatment goals (either using PrEP/ART or abstaining from MA use)?" (1 [negatively affected my behavior] to 5 [positively affected my behavior]); "Do you think the CM incentives (the money provided for each visit where you met treatment goals) helped you to meet your goal (either using PrEP/ART or abstaining from MA use)?" (1 [negatively affected my behavior] to 5 [positively affected my behavior]).

HIV/STI Testing

At enrollment, urine samples, as well as rectal and pharyngeal swabs, were collected for gonorrhea/chlamydia (GC/CT) testing (Aptima Combo 2, Hologic, San Diego, CA). Blood was collected for HIV and syphilis testing. HIV testing was performed with a 5th generation HIV 1/2 antibody assay. Syphilis testing used rapid plasma reagin (RPR) with Treponema pallidum particle agglutination test (TPPA) confirmation. New syphilis infection (i.e., primary, secondary, or early latent) was defined using the Centers for Disease Control and Prevention determination following positive RPR results and local health department confirmation [35].

Table 1 Baseline characteristics and demographics of randomized participants (N = 19)

	MA (n = 9)	TFV (n = 10)
	n (%)	n (%)
Age (median [IQR])	37 (29–42)	41 (28–46)
HIV status		
HIV-negative	2 (22.2%)	2 (20.0%)
Living with HIV	7 (77.8%)	8 (80.0%)
Race/Ethnicity		
Latino	3 (33.3%)	4 (40.0%)
Black	5 (55.6%)	4 (40.0%)
White	0 (0.0%)	2 (20.0%)
Asian	1 (11.1%)	0 (0.0%)
Highest education completed		
Less than HS	4 (44.4%)	1 (10.0%)
HS	1 (11.1%)	1 (10.0%)
Some College/Technical school	4 (44.4%)	5 (50.0%)
College	0 (0.0%)	3 (30.0%)
Employment		
Full-time/Self-employed	1 (11.1%)	4 (40.0%)
Part-time	1 (11.1%)	4 (40.0%)
Not employed	7 (77.8%)	2 (20.0%)
Partnership status		
Partnered	4 (44.4%)	3 (30.0%)
Not partnered	5 (55.6%)	7 (70.0%)
GC/CT (genital, rectal)[a]		
Negative	7 (77.8%)	9 (90.0%)
Positive	2 (22.2%)	1 (10.0%)
Syphilis		
Negative	5 (55.6%)	2 (20.0%)
Prior infection	3 (33.3%)	5 (50.0%)
New infection	1 (11.1%)	3 (30.0%)
Male partners last month (median [IQR; range])	1 (1–2; 1–4)	3 (2–10; 1–20)
Frequency of missed TFV doses		
Never	3 (37.5%)	0 (0.0%)
Once monthly or less	3 (37.5%)	5 (50.0%)
Once weekly or more	2 (25.0%)	5 (50.0%)
MA use past 3 months		
Monthly or less	4 (44.4%)	0 (0.0%)
Weekly	4 (44.4%)	4 (40.0%)
Daily or almost daily	1 (11.1%)	6 (60.0%)
Urine test positive for TFV	6 (66.7%)	8 (80.0%)

MA = methamphetamine; TFV = tenofovir; IQR = interquartile range; HS = high school; GC/CT = gonorrhea/chlamydia

[a]Note – no pharyngeal GC/CT was detected at baseline

For the purposes of this analysis, we classified syphilis as either new syphilis infection (confirmed by local health department), prior syphilis infection (i.e., positive RPR and history of prior treatment), or negative syphilis testing. Participants with positive GC/CT and/or syphilis testing were provided appropriate antibiotic treatment and partner notification counseling.

Data Analysis

Descriptive statistics (frequency, percentage, median, interquartile range [IQR], and range) were utilized to characterize the population stratified by CM arm for MA abstinence or TFV adherence. Differences in number of missed visits, urine tests negative for MA metabolites, urine tests positive for TFV, self-reported MA use, sexual behavior, and exit survey satisfaction scores, were assessed using chi-square analysis (and Fisher's exact tests where appropriate) for categorical predictors and Kruskal-Wallis tests for non-parametric, continuous variables. Missing study visits were coded as missing in our analysis. All analyses were conducted using Stata 16 (StataCorp, College Town, TX).

Results

Demographics and Characteristics of Participants

Of the 19 participants randomized, median age was 38 years (IQR 28–46; range 27–50), and most (79.0%, n = 15/19) were living with HIV at baseline (Table 1). Almost half (47.4%) of participants were Black (n = 9/19), followed by 36.8% self-identifying as Latino (n = 7/19), 10.5% were White (n = 2/19), and one participant (5.3%) identified as Asian. The majority of participants (73.7%, n = 14/19) had at least a high school education, with 15.8% (n = 3) achieving a college degree and 47.4% (n = 9/19) attending some college/technical school. Most participants (63.2%, n = 12/19) were single/not in a partnership and 52.6% (n = 10/19) were employed. Three participants (15.8%) had genital and/or rectal GC/CT, but no participants had pharyngeal GC/CT at baseline. Four (21.1%) participants had a new syphilis infection, 8 had prior infection (42.1%), and 7 participants had negative syphilis testing at baseline. Median number of male partners in last month was 2 (IQR 1–4; range 0–20) among all participants at baseline. Most participants (60%, n = 6/10) randomized to the TFV adherence arm reported daily or almost daily MA use, with 40% reporting weekly (n = 4/10) use in the past 3 months. Among participants randomized to the MA abstinence arm, 44.4% reported weekly (n = 4/9), 44.4% reported monthly or less (n = 4/9), and 11.1% (n = 1/9) reported daily or almost daily MA use in the past 3 months. Participants randomized to the MA abstinence arm tended to self-report higher levels of adherence to TFV compared to those randomized to the TFV adherence arm, with 37.5% (n = 3/9) reporting never missing a TFV dose and 25.0% (n = 2/9) reporting missing TFV doses at least once weekly. In contrast, all participants in the TFV adherence arm reported missing some TFV doses, with half (n = 5/10) missing TFV doses at least weekly. However, 80%

Table 2 Follow-up visit adherence, substance use, tenofovir (TFV) adherence, and study satisfaction stratified by contingency management arm (N = 141 visits)

	MA (n = 64 visits)	TFV (n = 77 visits)	
	n (%)	n (%)	p-value
Number of missed visits[a]	19 (22.9%)	9 (10.5%)	**0.038**
Urine tests negative for MA	13 (20.3%)	5 (6.5%)	**0.021**
Urine tests positive for TFV	49 (76.6%)	72 (93.5%)	**0.007**
Self-reported past week MA use[b]			
0 days	2 (6.1%)	4 (10.5%)	**< 0.001**
1–2 days	22 (66.7%)	8 (21.1%)	
3–4 days	8 (24.2%)	11 (29.0%)	
5–7 days	1 (3.0%)	15 (39.5%)	
Male partners past 7 days (median [IQR; range])[b]	1 (0–1; 0–3)	2 (1–3; 0–6)	**< 0.001**
Exit survey satisfaction scores[c]	Median (IQR)	Median (IQR)	p-value
Overall	5 (4–5)	5 (4–5)	0.95
Visit frequency	3 (1–3)	3 (3–3)	0.22
Behavioral counseling	5 (5–5)	4 (3–5)	**0.024**
Effect of contingency management	4 (4–5)	4 (4–5)	0.96

MA = methamphetamine; TFV = tenofovir; IQR = interquartile range

[a]Calculated from total possible follow-up visits (n = 83 for MA arm and n = 86 for TFV arm)

[b]Calculated from weekly surveys (n = 71)

[c]Calculated from exit surveys (n = 17)

(n = 8/10) of participants in the TFV adherence arm tested positive for urine TFV at baseline, while 66.7% (n = 6/9) of those in the MA abstinence arm had urine TFV positivity.

Visit Attendance and Urine Test Results

Participants completed 83.4% (n = 141/169) of CM visits. Visit attendance was slightly higher among those in the TFV adherence arm with 89.5% (n = 77/86) follow-up visits completed, compared to a 77.1% (n = 64/83) visit completion rate among those in the MA abstinence arm (p = 0.038) (Table 2). Participants in the MA abstinence arm had more urine samples negative for MA metabolites (20.3%, n = 13/64) compared to those receiving incentives for TFV adherence (6.5%, n = 5/77; p = 0.021). Conversely, TFV adherence was higher among participants in the TFV adherence arm with 93.5% (n = 72/77) of urine samples being positive for TFV, compared to 76.6% (n = 49/64) TFV-positive urine samples among those in the MA abstinence arm (p = 0.007). Participants in the TFV adherence arm tended to self-report more frequent MA use and higher number of male sexual partners in the past week compared to those receiving CM incentives for MA abstinence. Satisfaction with the intervention and study procedures were high. Overall study satisfaction received the highest rating with a median of 5 ("very satisfied") and visit frequency scores had a median of 3 ("just the right number of study visits"). Participants in the MA abstinence arm tended to report higher levels of satisfaction with behavioral counseling compared to those in the TFV adherence arm. However, no differences in satisfaction scores regarding the overall study, visit frequency, or perceived effect of contingency management were observed between intervention arms.

Table 3 Follow-up visit adherence, substance use, tenofovir (TFV) adherence, and study satisfaction stratified by contingency management visit frequency (N = 141 visits)

	2 visits per week (n = 67 visits)	3 visits per week (n = 74 visits)	
	n (%)	n (%)	p-value
Number of missed visits[a]	3 (4.3%)	25 (25.3%)	**< 0.001**
Urine tests negative for MA	6 (9.0%)	12 (16.2%)	0.22
Urine tests positive for TFV	59 (88.1%)	62 (83.8%)	0.63
Self-reported past week MA use[b]			
0 days	5 (12.5%)	1 (3.2%)	0.24
1–2 days	13 (32.5%)	17 (54.8%)	
3–4 days	12 (30.0%)	7 (22.6%)	
5–7 days	10 (25.0%)	6 (19.4%)	
Exit survey satisfaction scores[c]	Median (IQR)	Median (IQR)	p-value
Overall	5 (5–5)	5 (3–5)	0.37
Visit frequency	3 (3–3)	3 (3–3)	0.67
Behavioral counseling	4 (4–5)	5 (4–5)	0.55
Effect of contingency management	4 (4–5)	4.5 (4–5)	0.56

MA = methamphetamine; TFV = tenofovir; IQR = interquartile range

[a]Calculated from total possible follow-up visits (n = 70 for 2 visits/weekly and n = 99 for 3 visits/weekly)

[b]Calculated from weekly surveys (n = 71)

[c]Calculated from exit surveys (n = 17)

When stratified by visit frequency, participants in the 2 visits/week arm had higher visit completion rates (95.7% visits completed, n = 67/70) compared to those in the 3 visits/week arm (74.8%, n = 74/99; p < 0.001) (Table 3). TFV adherence was similar between the two groups: TFV was detected in 83.8% (n = 62/74) of those participating in 3 visits/week and 88.1% (n = 59/67) of those participating in 2 visits/week. Participants who completed 3 visits/week had slightly more urine tests that were negative for MA metabolites (16.2%, n = 12/74) compared to those who participated in 2 visits/week (9.0%, n = 6/67), though this difference was not statistically significant. Rates of self-reported past week

MA use were similar across both groups. Satisfaction ratings with the intervention and study procedures were not different when stratified by visit frequency.

Discussion

This study is among the first to examine CM as a strategy to address substance use, PrEP/ART adherence, and HIV risk behavior among MSM who use MA. Our findings in this pilot project demonstrated a trend toward increased TFV adherence and MA abstinence following implementation of CM interventions using point-of-care urine assays to detect TFV and MA use, respectively. Furthermore, high visit completion rates and study satisfaction scores highlight the feasibility of CM as a potential tool to promote both PrEP/ART adherence and MA abstinence. These findings are particularly relevant given high rates of HIV transmission within the sexual networks of MSM who use MA and the lack of evidence-based interventions that address both substance use and HIV prevention. Collectively, this pilot project underscores the potential utility of utilizing CM to target both substance use and HIV transmission/outcomes and the need for future research to evaluate the effectiveness of an integrated CM strategy among people with or at risk of HIV with substance use.

Our findings demonstrate increased TFV-positive urine tests among participants randomized to receive contingent rewards based on TFV adherence. By using a novel, recently developed point-of-care test that can detect TFV in the urine, this study is the first to demonstrate that CM interventions utilizing contingent rewards based on detection of TFV in the urine may be a feasible approach to promoting PrEP/ART adherence. This point-of-care assay overcomes prior limitations in monitoring TFV adherence, such as delays in results from traditional LC-MS/MS testing [30, 31], that had previously served as a barrier to using CM (which relies on real-time metrics) for increasing PrEP/ART adherence. The availability of immediate feedback on TFV adherence allows for positive reinforcement and, in turn, operant conditioning through CM which supports habits and behaviors that promote PrEP/ART adherence [36, 37]. While CM has been demonstrated to reduce HIV risk behaviors and promote PrEP/ART adherence among MA users in prior studies, these findings are likely an indirect effect of reductions in MA use [18, 19]. Most HIV prevention studies have examined different HIV prevention strategies (e.g., HIV post-exposure prophylaxis, cognitive behavioral therapy, case management, motivational interviewing) that are delivered in parallel with a CM intervention that targets MA use [21, 38–40]. Our pilot study is the first to explicitly provide contingent rewards linked to biological evidence of PrEP/ART adherence, substantially contributing to the literature. Our findings suggest that linking contingent rewards to the results of a point-of-care urine TFV assay may be a promising strategy to promote TFV adherence among MSM who use MA, and future research exploring implementation of this strategy should be conducted.

Participants randomized to the CM arm that provided contingent rewards based on MA abstinence had higher frequency of urine tests that were negative for MA metabolites compared to those who participated in the TFV adherence arm. These results are consistent with previous trials demonstrating that CM promotes MA abstinence [14]. Even though participants in the MA abstinence arm did not receive incentives for TFV adherence, there was a trend toward increased TFV adherence among participants in the MA abstinence arm. As participants were informed of all their urine test results regardless of randomization, it is possible that being informed of TFV-positive urine tests may have served as a form of positive reinforcement that promoted TFV adherence among participants [41]. Furthermore, the receipt of motivational interviewing and frequent interactions with study staff could have promoted TFV adherence as well [42]. Additionally, such increases in TFV adherence may be related to MA abstinence itself, as prior studies have demonstrated that reductions in stimulant use are associated with reduced HIV risk behaviors and improved ART adherence [43, 44]. These findings highlight the impact that stimulant use has on HIV risk behaviors and the importance of developing combined interventions, such as this one, that address substance use in conjunction with HIV prevention and treatment.

In terms of visit frequency, attendance rates were higher for participants who were randomized to 2 visits per week compared to those who participated in 3 visits per week. As most point-of-care urine tests are able to detect MA use within the past 48–72 h and TFV use within the past 3 days, utilizing a 3 times weekly visit schedule maximizes the ability to accurately capture recent MA use and TFV adherence. However, a 3 times weekly CM schedule can be highly burdensome to the participant, particularly when navigating competing demands, such as employment or family needs. While twice weekly CM visits increase the potential for undetected MA use or missed TFV doses, this schedule is less cumbersome for participants, particularly for interventions of longer duration, and has been used in both National Institute on Drug Abuse (NIDA) Clinical Trials Network studies as well as a large-scale trial at the Department of Veteran's Affairs [34, 45, 46]. Other than visit attendance rates, we did not observe any differences in terms of study outcomes or satisfaction scores based on visit frequency.

Limitations

While our study evaluates a novel use of CM to promote MA abstinence and PrEP/ART adherence, it has limitations. As our primary goal was to evaluate the feasibility of this intervention, the small sample size of this pilot project limits the statistical power and our ability to determine the effectiveness of this intervention. Future implementation of this intervention in a larger, better powered trial to assess efficacy and effect size is needed. Since our primary objective was feasibility, study duration was limited to 4 weeks, instead of 8–12 weeks typically used in CM interventions [14], thus limiting our ability to determine whether our intervention resulted in a sustained response. As all participants provided urine test results for both MA and TFV regardless of intervention arm, it is possible that social desirability bias and positive feedback regarding urine test results may have indirectly promoted TFV adherence and MA abstinence even if participants were not randomized to receive contingent rewards for that behavior. It is also possible that participants may have failed to attend sessions when an MA-positive or TFV-negative urine was anticipated. However, we attempted to minimize this bias by providing a separate compensation schedule based on visit attendance, independent of urine test result. Additionally, frequency of MA use was lower in the MA abstinence arm at Baseline, which should be considered when interpreting our results. Since the point-of-care assay utilized in this study only detects TFV in the urine, this limits the generalizability of our intervention to other forms of non-TFV based PrEP/ART (such as long acting injectable cabotegravir). Finally, as our inclusion criteria was limited to MSM who use MA, our findings may not be generalizable to other types of substance use or populations who might be at risk for or living with HIV, which represent important directions for future research.

In conclusion, results from this project demonstrate that CM is feasible as an integrated strategy to address both substance use and HIV prevention and treatment among MSM who use MA. Findings from this study demonstrate that integrating point-of-care urine TFV assays into a CM strategy may be a feasible, scalable intervention designed to improve HIV outcomes and reduce HIV transmission among MSM who use MA and their sexual networks.

Declarations.

CM = contingency management; MA = methamphetamine; TFV = tenofovir.

Author Contributions SS, CB, MG, and JLC contributed to the study conception, design, and data collection. All authors contributed to the analysis. The first draft of the manuscript was written by CSB and all authors commented on multiple versions of the manuscript. All authors read and approved the final manuscript.

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Data Availability Available upon request from authors and approval from local institutional review board.

Declarations

Conflict of interest /Competing interests.
The authors declare that they have no conflict of interest.

Ethics Approval The study was reviewed and approved by the Office of Human Research Participant Protection (OHRPP) at the University of California, Los Angeles (IRB#19-001996).

Consent to Participate All participants provided written informed consent prior to enrollment.

Consent for publication Not applicable.

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