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Feasibility and acceptability of a phase II randomized pharmacologic intervention for methamphetamine dependence in high-risk men who have sex with men

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Abstract

Objective—To determine whether actively using, methamphetamine (meth)-dependent men who have sex with men (MSM) could be enrolled and retained in a pharmacologic intervention trial, and the degree to which participants would adhere to study procedures, including medication adherence.

Study design—Phase II randomized, double-blind trial of bupropion vs. placebo.

Methods—Thirty meth-dependent, sexually active MSM were randomized to receive daily bupropion XL 300 mg or placebo for 12 weeks. Participants received weekly substance use counseling, provided weekly urine specimens, and completed monthly audio-computer assisted self-interview (ACASI) behavioral risk assessments. Adherence was measured by medication event monitoring systems (MEMS) caps (the number of distinct MEMS cap openings divided by the number of expected doses) and self-report.

Results—Ninety percent completed the trial: 89% of monthly ACASIs were completed, 81% of study visits were attended, and 81% of urine samples were collected. Adherence by MEMS cap was 60% and by self-report was 81% and did not differ significantly by treatment assignment. The median number of positive urine samples was 5.5 out of a possible 11 (50%). Participants in both arms reported similar declines in the median number of sex partners ($P = 0.52$). No serious adverse events occurred and there were no significant differences in adverse events by treatment assignment ($P = 0.11$).

Conclusions—It is feasible to enroll and retain actively using, meth-dependent MSM in a pharmacologic intervention. Bupropion was well tolerated. Study participation and retention rates were high, however, study drug medication adherence was only moderate. Findings support a larger trial with improved adherence support to evaluate the efficacy of bupropion and other pharmacologic interventions for meth dependence in this population.

Keywords

bupropion; HIV prevention; men who have sex with men; methamphetamine

Introduction

Methamphetamine (meth) is a highly addictive drug with serious medical, societal, and economic consequences [1–12]. Nationally 0.5% of the civilian noninstitutionalized US population report using meth use in the prior 12 months [13]. Among men who have sex with men (MSM), meth use is up to 20 times more prevalent [14–16], compared to the general population, and is considered a major factor in driving the US MSM HIV epidemic: meth use is associated with high-risk sexual behavior [12,17–26], HIV seroconversion [27,28], sexually transmitted disease (STD) incidence [29,30], and drug-resistant HIV [31].

Pharmacologic therapies have proven successful in treating heroin, nicotine, and alcohol dependence. However, there are no pharmacologic therapies approved for meth dependence, limiting treatment options [32,33]. Behavioral interventions for meth users have reduced meth use and lowered drug-associated HIV risk behaviors [33–36], however, these interventions are time-intensive, and treatment trials report high rates of drop-out [37], loss to follow-up [38,39], and relapse [40]. Furthermore, few meth-using MSM access substance use treatment services [40,41]. A pharmacologic option for meth-dependent persons, either as a stand-alone treatment or as an adjunct to behavioral therapy, could provide an important and much-needed addition to current treatments for meth dependence.

Pharmacologic agents with the most promise to treat meth dependence include those that work on neurobiologic pathways dysregulated by meth use. Meth and other stimulants increase synaptic levels of dopamine by inhibiting the activity of dopamine reuptake transporters and by increasing release of vesicular dopamine stores [42]. The level of euphoria produced by meth is positively associated with dopamine levels and occupancy of the dopamine receptor [43–46]. Brain imaging research shows that amphetamines increase dopamine levels especially within the nucleus accumbens, the part of the brain that transacts reward and reinforcement in addictive disorders [47–52]. Whereas acute meth use disturbs dopamine levels, prolonged meth use results in chronically depressed CNS dopaminergic activity in the absence of meth [42,43,53–56].

Meth withdrawal symptoms vary in severity, but include anxiety, anhedonia, and depression [36,57–59] and are thought to be due to rapidly decreasing levels of dopamine in the nucleus accumbens following drug cessation [57,60,61]. Relapse is postulated to be driven by the desire to alleviate withdrawal symptoms by restoring CNS dopamine levels to the level found in the presence of drug [62–64].

Bupropion, a norepinephrine and dopamine reuptake inhibitor [65], is FDA-approved for the treatment of depression, smoking cessation, and seasonal affective disorder. Bupropion binds to the dopamine transporter and has been shown to increase dopamine transmission in both the nucleus accumbens and prefrontal cortex [66]. We hypothesized that bupropion would stabilize central dopamine tone in the absence of meth and alleviate meth withdrawal symptoms, thereby reducing relapse. Phase I, double-blind studies among meth users show that bupropion significantly attenuates subjective effects of meth: meth-dependent individuals who received escalating doses of meth after 6 days of bupropion treatment reported decreased feelings of being ‘high’ and had decreased cravings compared with those who received placebo [67].

Two randomized, placebo-controlled trials [68,69] evaluating bupropion for the treatment of meth dependence found that bupropion did not reduce meth use overall; however, there were reductions in meth-positive urines among lighter users. Limits to these trials include low retention rates (52% [68] and 34% [69]) and adherence measurement techniques that may overestimate adherence [70]. These trials enrolled mainly treatment-seeking heterosexuals

and did not measure adherence to study medication using electronic medication event monitoring systems (MEMS).

We are not aware of any pharmacologic trials for meth dependence that have focused exclusively on MSM populations at extremely high risk for transmitting or acquiring HIV in the context of their meth-related sexual behavior. Such populations would be an important target for any efficacious pharmacologic intervention, which would have the potential not only to reduce meth use but also HIV risk behavior. This is especially important as only a minority of meth-dependent MSM access substance use treatment services, even when behavioral treatment is available [40,41].

We sought to enroll actively using meth-dependent MSM who were not in meth treatment programs, in an effort to engage and retain a population not often represented in pharmacologic trials. Given the chaotic nature of meth-users' lives, it was important to determine whether this population can engage in a pharmacologic trial and adhere to study schedules and procedures. We also evaluated whether meth users could adhere to the study drug using self-report and MEMS.

Methods

Study participants

Thirty meth-dependent, sexually active MSM were randomized to receive bupropion ($n = 20$) or placebo ($n = 10$) for 12 weeks. Eligibility criteria included meth dependence by Structured Clinical Interview for DSM disorders (SCID), interest in reducing or stopping meth use, age 18–60 years, anal sex with men in past 3 months while using meth, meth-metabolite positive urine at screening, no acute medical or psychiatric illness, and baseline safety labs without clinically significant abnormalities. We excluded individuals with a history of seizure or high risk for seizure, evidence of current major depression by SCID or history of antidepressant use within the past 4 weeks, current use of pseudoephedrine-containing products (which may cause false-positive urines for meth use), and HIV-infected individuals with CD4 cell count below 200 cells/ μ l.

Study design

A randomized, double-blind, placebo-controlled, two-arm pilot study with 2 : 1 randomization to bupropion vs. placebo.

Study recruitment

Participants were actively recruited at the municipal STD and HIV clinics, by street outreach in gay neighborhoods, at bars and events such as circuit parties, at community-based organizations serving MSM, and at needle-exchange programs. Recruitment flyers were posted at locations of active recruitment, in local newspapers and gay print media, and on social networking websites. Participants were also given recruitment materials to pass on to others. Potential participants completed a brief telephone screen to assess initial eligibility and, if eligible, were scheduled for an in-person screening visit.

Informed consent

All participants gave informed consent using IRB-approved consent forms. A 10-item 'trial concept quiz,' containing true/false questions was used to verify participants' basic understanding of the trial. Participants were required to answer 100% of the questions correctly in two attempts before being enrolled.

Screening

After informed consent, all participants received the following during the two screening visits: a complete history and physical, complete blood count, metabolic panel liver function tests, and urine meth testing. Rapid qualitative urine meth testing was conducted onsite using immunochromatographic meth-metabolite detection tests provided by Medtox Diagnostics, Burlington, NC. Participants with unknown HIV status received HIV rapid testing and counseling; HIV-positive participants received CD4 and HIV viral load tests.

Randomization

Treatment assignment occurred through double-blinded block (blocks of four) randomization, ensuring that 10 participants received placebo and 20 bupropion. The study statistician provided the randomization code to the Drug Product Services Laboratory at University of California, San Francisco (UCSF).

Study procedures

All participants were seen weekly for urine specimen collection and substance-use counseling. Symptom-directed physical exams, safety labs, and behavioral assessments were performed at baseline and at the 4, 8, and 12-week visits. HIV risk-reduction counseling and testing was repeated for HIV-negative participants at the final visit. Participants were paid \$10 for weekly visits and \$35 for screening and at weeks 0, 4, 8, and 12.

Substance use risk reduction counseling

All participants received weekly 30-min substance use counseling. The counseling was modified from a standardized, manual-driven psychosocial treatment program using cognitive behavioral therapy [71] and motivational interviewing techniques [72,73], and incorporated the Stages of Change Model [74] that has been used in brief behavioral interventions to treat substance use [75–77]. Counseling was provided by trained study staff closely supervised by a clinical psychologist in weekly quality assurance sessions.

Medication procedures

Bupropion 150 mg XL and matching placebo were supplied by the Drug Product Services Laboratory at UCSF and dispensed in bottles with a MEMS cap. Participants were instructed to take one pill every morning for 1 week and then two pills every morning for the remainder of the study. After week 12, at the conclusion of the intervention part of the study, participants were instructed to taper by taking one pill daily for 14 days to avoid any untoward effects of bupropion discontinuation. All study staff and participants were blinded to treatment assignment. At study completion, participants were asked to guess treatment assignment.

Medication adherence counseling and evaluation

The study clinician provided medication adherence counseling including information about the importance of taking medication daily and how to handle missed doses. We used two common methods of assessing adherence in this study: adherence as measured by MEMS caps and self-reported adherence using the 4-day Structured Self-Report, the validated AIDS Clinical Trial Group measure [78,79], which inquires about the number of doses missed over each of the preceding 4 days to determine percent adherence. MEMS cap adherence was defined as the number of distinct days on which the MEMS cap bottle was opened during the study, divided by 84, the number of doses expected in 12 weeks.

Safety evaluation

All participants were asked weekly about potential adverse events; symptom-driven physical exams and safety laboratory monitoring were done at weeks 4, 8, and 12. Adverse events were classified using the 'Division of AIDS (DAIDS) Table for Grading Severity of Adult Adverse Experiences for HIV Prevention Trials Network.' [80]

Audio-computer assisted self-interview measures

The following measures were assessed using audio-computer assisted self-interview (ACASI) to minimize underreporting of risk activities [81–83] and to enhance standardization of data collection.

Drug use included the frequency of meth and other drug use, including route of administration, and the sharing of drug paraphernalia.

Substance use treatment included receipt of any substance use treatment services, self-help group participation, or drug-related hospitalizations.

Center for Epidemiologic Studies Depression Rating Scale (CES-D) was used to assess the degree of clinically significant depressive symptoms (scores >16) [84] in trial participants.

Severity of Dependence Scale was used to measure the severity of meth dependence. Each of the five scale items was scored on a 4-point scale (0–3). A higher summary score indicates a higher level of dependence.

Sexual risk behavior included the number of male anal sex partners; the number of unprotected anal sex episodes; and the number of HIV-positive, negative, and unknown serostatus anal sex partners and unprotected anal sex acts with these partners in the past 4 weeks.

Reasons for non-adherence were assessed by asking participants to choose from a list of common reasons for medication nonadherence including 'being high on meth,' 'being away from home,' 'busy with other things,' or 'simply forgot.'

Attitudes about trial participation assessed participants' level of satisfaction with the trial and whether they would participate in a similar trial in the future.

Statistical analysis

To assess feasibility of enrolling and retaining meth-dependent MSM, we computed the proportions of participants eligible and enrolled among those recruited and screened, the proportion of scheduled visits completed, scheduled urines collected, and the proportion of participants retained to the end of the study. We compared proportions across arms using Wilcoxon and Fisher's exact tests as appropriate to assess the comparability of participants by treatment assignment at baseline. Attendance at weekly visits and provision of urine samples were compared using binomial models with robust standard errors to accommodate potential overdispersion arising from within-person correlation.

To assess acceptability of bupropion and placebo, we examined adherence to study drug by the two measures described above. Percent adherence was compared by study arm using the Wilcoxon test. We compared time to the first study drug interruption of at least 1 week using the log-rank test.

To explore safety and tolerability, we computed the proportions of those experiencing adverse events and compared adverse event rates by treatment assignment using Fisher's exact test.

We used normal-logistic models fitted with random intercepts to assess between-group differences in meth-metabolite positive urine samples and self-reports of the number of serodiscordant anal sex partners. Analogous random effects negative binomial models, which are suitable for count outcomes with larger variance than under the Poisson model, were used to compare numbers of male partners as well as numbers of male partners with whom meth was used in the past 4 weeks. In these analyses, the baseline value was included, and the treatment effect was estimated by the interaction between treatment and follow-up. To be eligible for the study, participants had to provide a meth-metabolite-positive urine at a screening visit; however, not all urine results were positive at the randomization visit, at which the baseline values were ascertained. We omitted the week 1 urine result from the analysis of urine positivity because it takes approximately 1 week to achieve appropriate blood levels of bupropion. Sensitivity analyses were conducted that compared the inclusion and exclusion of the week one urine results.

Results

Screening, recruitment, and randomization

Figure 1 shows results for screening, recruitment, assignment and retention for the study period from October 2006 to August 2007. Three hundred and twenty-five people were assessed for initial eligibility by a telephone prescreen (Fig. 1). Of those eligible by telephone prescreen, 54 (17%) signed informed consent and were assessed further for eligibility. Of the 54, 17 were ineligible, seven declined further participation, and 30 were randomized. Thus 9% of the total of 325 prescreened were randomized (Fig. 2).

Baseline characteristics

We recruited a diverse sample (50% White, 20% Hispanic, and 10% Black), of whom 43% were HIV-positive (Table 1). Baseline demographic characteristics were similarly distributed in both arms with the exception of income ($P = 0.01$). Fifty-three percent reported using meth between 3 and 7 days/week and 53% of participants reported using meth with sex at least 50% of the time. The most common route of meth administration was smoking (87%), followed by injecting (50%) and snorting (47%). A minority (40%) of participants had previously sought substance use treatment or self-help programs for meth use. Mean severity of dependence scale score was high (5.9 ± 3.5) SCID score. Symptoms of depression were elevated (mean CESD score 20.1 ± 11.5) and 20 participants (67%) had CES-D scores at least 16 at baseline. At study completion, mean changes in CESD were $+2.9 \pm 10.1$ and -1.9 ± 13.3 in the placebo and bupropion arms, respectively. These differences were not statistically significant by Wilcoxon rank-sum test (P value = 0.21). Forty-seven percent reported having health insurance and 60% reported having a regular healthcare provider. The most commonly used other substances were marijuana (63% of participants), poppers (43% of participants), and club drugs including GHB, ketamine and ecstasy/MDMA (40% of participants) (data not shown).

Retention

Twenty-seven participants (90%) completed the trial with no significant differences by treatment assignment. Overall, 89% of monthly follow-up ACASI risk assessments were completed (bupropion 87%, placebo 93%; $P = 0.38$), 81% of weekly follow-up study visits were attended (bupropion 80%, placebo 81%; $P = 0.96$), and 81% of all scheduled weekly urine samples were collected (bupropion 80%, placebo 81%; $P = 0.96$).

Medication adherence

Adherence to study drug as measured by MEMS caps was 60% (59% bupropion, 62% placebo; $P=0.98$), whereas adherence by self-report was 81% (85% bupropion, 75% placebo; $P=0.21$). The correlation between adherence as measured by MEMS and by self-report was 54%. The most common reasons given for nonadherence included 'simply forgot' (18%), 'busy with other things' (18%), 'away from home' (16%), 'change in daily routine' (16%), 'slept through dose' (10%) and 'high on meth' (9%). Three participants in each group, including the three who did not complete the trial, had at least a week-long medication discontinuation prior to study completion ($P=0.37$). Time to the first week-long medication discontinuation did not differ by treatment assignment ($P=0.48$ by log-rank test).

Urine drug screen results

At randomization, 73% of participants had meth-metabolite-positive urines (bupropion 65%, placebo 90%; $P=0.21$). The proportion of meth-metabolite positive urines at follow-up visits decreased in both groups (Table 2). After accounting for the initial difference in meth-metabolite-positive urines, using a normal-logistic model, the reductions were similar in the two groups ($P=0.63$). Results were similar if week 1 meth-metabolite urine results were included and in an analysis imputing positive results for missing urine meth-metabolite results.

Sexual risk behavior

At baseline, the 20 participants in the bupropion group had a median of 3.5 male sexual partners in the past 4 weeks, whereas the 10 participants in the placebo group had a median of 13.5 partners ($P=0.11$ by Wilcoxon test; Table 3). After adjusting for the baseline difference, the declines were similar ($P=0.46$). The number of male partners with whom meth was used also declined during the trial. After adjusting for the baseline difference, the declines in male partners with whom meth was used were again similar ($P=0.71$). Comparable declines across both groups were also seen in unprotected insertive ($P=0.90$) and receptive ($P=0.62$) anal sex with serodiscordant partners. The declines in prevalence of unprotected serodiscordant anal sex were similar in both groups ($P=0.09$).

Safety and tolerability

There were no serious adverse events in the study. The most common adverse events were unrelated to study drug and were mild to moderate (grade 1 or 2) liver function test elevations, dermatologic conditions (grade 1 or 2), or electrolyte abnormalities (grade 1). There was one grade 3 ALT elevation. There were no significant differences in adverse events by treatment assignment ($P=0.11$). One participant in the bupropion arm was diagnosed with HIV and rectal gonorrhea. Another participant in the bupropion arm reported agitation which resolved after study drug dose reduction.

Attitudes about trial participation and assessment of blinding

At study completion, 96% of volunteers were highly satisfied or satisfied with study participation, whereas 11% (3/27) found study participation very or somewhat difficult. Ninety-three percent (25/27) of participants completing the study reported that they would be likely to participate in a similar study in the future. Participants at study completion were asked to guess their treatment assignment. In the placebo group, five of nine or 56% guessed they were on placebo. In the bupropion group, nine of 18 (50%) guessed correctly. Treatment guessing accuracy between two groups did not differ significantly by Fisher's exact test ($P=1.00$).

Discussion

In this randomized, double-blind, placebo-controlled trial, we demonstrated that it was feasible to enroll and retain actively using, high-risk, meth-dependent MSM in a pharmacologic intervention trial, outside of a drug treatment program, with excellent rates of participation in study visits, procedures, and follow-up evaluations. Given the high rates of meth use among MSM, the associations among meth use, sexual risk behavior and HIV, and the fact that most meth-dependent MSM have not accessed current treatment options, it was important to demonstrate that high-risk MSM are willing to participate in pharmacologic studies for meth treatment. We found a high level of enthusiasm for our study as indicated by high participation rates and interest in joining similar studies in the future. Retention rates were substantially higher than in the two previously reported studies of bupropion for meth dependence [68,69].

Stimulant use is associated with lower medication adherence, including to HIV medications among HIV-positive meth users [17,85–88]. Our adherence rates were comparable to adherence rates among drug users in other studies [86,88]; however, our rates were lower than reported in the previous bupropion studies [68,69]. We used the more rigorous MEMS measure, as is common in antiretroviral medication adherence trials [70,87]. Our findings that self-reported adherence (81%) was higher than MEMS-measured adherence (60%) is consistent with the evidence that self-report tends to overestimate antiretroviral adherence [70].

Consistent with behavioral studies of MSM [33,69], multiple measures of sexual risk behavior including the number of male partners, the number of male partners with whom meth was used, and unprotected serodiscordant anal intercourse, decreased during trial participation in both study arms. These findings indicate that meth-dependent MSM engaged in pharmacologic interventions with concomitant substance use counseling can reduce their sexual risk behaviors. Most adverse events were mild to moderate in nature, expected due to the known side effect profile of bupropion, and there were no differences by treatment assignment.

The study has limitations. We had a relatively low phone prescreen to randomization ratio (9%) which should be considered when interpreting conclusions regarding feasibility. Among those assessed in person for eligibility, the randomization ratio was much higher (56%). This was a phase II pilot study and was not powered to assess the efficacy of bupropion and thus our comparisons by treatment assignment should be interpreted with this limitation in mind. Also, compared with other drug treatment studies, often done in drug-treatment centers, our once-weekly study visit schedule may be considered ‘low intensity.’ More intensive study visit requirements would have likely reduced our relatively high participation rates.

Despite the above limitations, our study demonstrates that it is feasible to enroll actively using, meth-dependent MSM in a pharmacologic trial with excellent attendance, compliance with study activities, and retention. Results of participants’ assessment of whether they took bupropion or placebo show no compelling evidence of unblinding. Our modest adherence rates suggest that upcoming studies of pharmacologic interventions for meth dependence should be accompanied by adherence support measures that address the complex needs of this population. Sexual risk behavior declined during participation in this pharmacologic and substance use counseling intervention, suggesting potential of drug use reduction as a key part of HIV prevention interventions that target groups at highest risk. We must intensify our efforts to identify potential pharmacologic therapies for meth dependence, and to enroll

high-risk populations, both to reduce meth-related morbidity and to further prevent HIV acquisition and transmission.

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M.D. drafted the manuscript, assisted with the analysis, and primarily interpreted the data.

D.M.S. assisted in the conception and design of the study, acquisition, analysis and interpretation of data, and revising the manuscript for important intellectual content.

T.M. assisted in the conception and design of the study, acquisition of the data, and revising the manuscript for important intellectual content.

G.-M.S. assisted in the analysis and interpretation of data, and revising the manuscript for important intellectual content.

P.L.C. assisted in the analysis and interpretation of data, and revising the manuscript for important intellectual content.

E.V. assisted in the design of the study, analysis and interpretation of data, critical revision of the manuscript for important intellectual content, and the statistical analysis.

S.S. assisted in the conception and design of the study, interpretation of data, and critical revision of the manuscript for important intellectual content.

G.N.C. conceived and designed the current study, assisted with analysis, interpreted the data, and in the critical revision of the manuscript for important intellectual content. He also obtained funding and material support and provided supervision.

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Fig. 1. Participant flow diagram
F/U, follow-up.

Fig. 2.
Longitudinal trends of the percent positive urine meth screens by treatment assignment.

Table 1

	Bupropion		Placebo		P value
	n	Mean (%) (SD)	n	Mean (%) (SD)	
Demographics					
Age	38.1	(2)	33.3	(3)	0.24 ^a
Race					0.83 ^b
	African American	2 (10)	1 (10)		
	Latino/Hispanic	3 (15)	3 (30)		
	White	11 (55)	5 (50)		
	Other	4 (20)	1 (10)		
Education					0.73 ^b
	Less than high school	1 (5)	2 (20)		
	High school or GED	5 (25)	2 (20)		
	Some college	10 (50)	4 (40)		
	College and beyond	4 (20)	2 (20)		
Annual income					0.04 ^b
	Under \$10 000	12 (60)	2 (20)		
	\$10 000–29 999	3 (15)	7 (70)		
	\$30 000 and above	5 (25)	1 (10)		
Employed	6	(30)	4	(40)	0.69 ^b
Meth use					
Meth use (past 4 weeks)					0.26 ^b
	Less than 3 days a week	11 (55)	3 (30.0)		
	3–7 days a week	9 (45)	7 (70.0)		
Meth use with sex (past 4 weeks):					1.00 ^b
	50% of the time or less	9 (45)	5 (50.0)		
	Greater than 50% of the time	11 (55)	5 (50.0)		
Meth route of administration (past 4 weeks)					
	Smoked	17 (85)	9 (90)		1.00 ^b

	Bupropion		Placebo		P value
	n	Mean (%) (SD)	n	Mean (%) (SD)	
Injected	11	(55)	4	(40)	0.70 ^b
Snorted	11	(55)	3	(30)	0.26 ^b
Ingested orally	5	(25)	2	(20)	1.00 ^b
Inserted rectally	5	(25)	2	(20)	1.00 ^b
Severity of dependence scale (SDS) score	5.4	(1)	6.9	(1)	0.23 ^a
History of meth-related hospitalization	2	(10)	1	(10)	1.00 ^b
History of meth treatment/self-help program for meth	8	(40)	4	(40)	1.00 ^b
Clinical					
HIV status					0.26 ^b
Negative	13	(65)	4	(40)	
Positive	7	(35)	6	(60)	
Has health insurance	8	(40)	6	(60)	0.44 ^b
Has regular health provider	11	(55)	7	(70)	0.69 ^b
Ctr. for epidemiologic studies depression scale (CESD) score	22.4	(3)	18.2	(3)	0.44 ^a

^aUsing two-sample Wilcoxon rank-sum test.

^bUsing Fisher exact test.

Table 2

Percent urine positivity.

	Week			
	0	2-4	5-9	9-12
Bupropion	65	68	52	56
Placebo	90	81	79	74

Table 3

Sexual risk behaviors.

	Visit				
	Baseline	Week 4	Week 8	Week 12	
Mean (median) number of male partners	Bupropion 5.2 (3.5)	3.9 (4.0)	2.2 (2.0)	2.4 (1.0)	
	Placebo 10.5 (13.5)	7.1 (6.0)	4.8 (3.5)	3.6 (2.0)	
Mean (median) number of male partners with whom meth was used	Bupropion 4.1 (2.0)	3.1 (2.0)	1.6 (1.5)	1.8 (1.0)	
	Placebo 8.7 (12.0)	6.3 (4.0)	4.1 (3.0)	2.9 (1.0)	
Number (percent) reporting unprotected anal sex with SD ^a partner	Bupropion 4 (21%)	3 (18%)	2 (12%)	3 (17%)	
	Placebo 5 (50%)	0 (0%)	2 (20%)	1 (11%)	
Number (percent) reporting unprotected insertive anal sex with SD ^a partner	Bupropion 4 (21%)	2 (12%)	1 (6%)	3 (17%)	
	Placebo 3 (30%)	1 (11%)	1 (10%)	2 (22%)	
Number (percent) reporting unprotected receptive anal sex with SD ^a partner	Bupropion 5 (26%)	3 (18%)	1 (6%)	1 (6%)	
	Placebo 4 (40%)	1 (11%)	2 (20%)	0 (0%)	

^aSerodiscordant partner defined as HIV+ person with HIV-/unknown HIV status partner or HIV- person with HIV+/unknown HIV status partner.