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Drug Use and HIV Risk Outcomes in Opioid-Injecting Men in the Republic of Georgia: Behavioral Treatment + Naltrexone compared to Usual Care

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Abstract

Background—To test the initial feasibility of a novel 22-week comprehensive intervention pairing behavioral treatment with naltrexone that aimed at engaging, retaining, and treating opioid-injecting men in the Republic of Georgia.

Methods—Forty opioid-injecting males and their drug-free female partners participated in a two-group randomized clinical trial at the field site of the Union Alternative Georgia, in Tbilisi, Republic of Georgia. The comprehensive intervention that paired behavioral treatment with naltrexone for the male participants (n=20) included counseling sessions using Motivational Interviewing for both the male participant and the couple, monetary incentives for drug abstinence, and research-supported detoxification followed by naltrexone treatment. Male participants in the usual care condition (n=20) had the opportunity to attend once-a-week individualized education sessions and upon request receive referrals to detoxification programs and aftercare that could or could not have included naltrexone. Outcome measures included entry into inpatient detoxification and naltrexone treatment, urine drug screening, reduction in illicit substance use, use of benzodiazepines, injection of buprenorphine, and needle and syringe sharing.

Results—The comprehensive intervention condition showed significantly more weekly urine samples negative for illicit opioids during weeks 1 through 22 (7.0 *v.* 1.4; p<.001) and reported significant declines in use of benzodiazepines and injection of buprenorphine (both ps<.004).

Conclusions—The first behavioral treatment randomized clinical trial in the Republic of Georgia found that the use of tailored behavioral therapy paired with naltrexone is both feasible and efficacious for treating drug use and reducing HIV drug-risk behavior in Georgian men.

Keywords

opioid dependence; injection drug use; behavioral treatment; naltrexone; Republic of Georgia

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1.0 Introduction

Home-made opium and heroin were the main drugs of injection in Georgia in late 1990s-early 2000s (Gamkrelidze et al., 2004). In 2004 a sudden change in use of illicit opioids occurred, resulting in a significant increase of buprenorphine (Subutex®) injectors. In 2005, 39% (235 of 603) of all drug users in Georgia admitted for inpatient treatment were buprenorphine injectors (Javakhishvili et al., 2006). Importantly, buprenorphine at that time was not a registered medication in Georgia and was available only on the black market.

It is estimated that there were about 40,000 regular injecting drug users in Georgia in 2009 (Sirbiladze, 2010). Thus, problem drug use prevalence (in the case of Georgia defined as regular injecting use) is estimated as 1.5%, approximately 2.5 times higher than the average prevalence in Europe (European Monitoring Centre for Drugs and Drug Addiction, 2007). Injecting drug users comprised 60.4% of registered HIV cases in Georgia (Government of Georgia, 2010) and hepatitis C has been found in 50-60% of drug injectors (Shapatava et al., 2006; Tkeshelashvili-Kessler et al., 2005). Levels of HIV-risk-injecting behavior and unprotected sex are seemingly quite high throughout Georgia. Recent studies showed that sharing injecting equipment varied from 52% to 73% of injecting-drug users (Otiashvili et al., 2006; Tkeshelashvili-Kessler et al., 2005).

At the time of study implementation, few opioid-addicted individuals received any drug treatment in Georgia. If received, it was usually limited to a prohibitively expensive two-week inpatient detoxification with clonidine followed by outpatient individual and group therapy for 1-6 months (Georgian Research Institute of Addiction and NGO New Way, 2008). Most patients dropped out of treatment during the first month, and, as a result, relapse to substance use has been high (Javakhishvili and Sturua, 2009). Such treatment was provided to 600-1000 patients annually in 2006-2009 (Javakhishvili et al., under review).

At the time of data collection, methadone maintenance treatment (MMT) in Georgia was provided to only 230 patients, with the support of the Global Fund to Fight AIDS, Tuberculosis and Malaria (Georgian Research Institute of Addiction and NGO New Way, 2008). By the end of 2008 the Georgian government began funding MMT. Thus, several new MMT programs provided a total of 600 patient-slots.

The fear of police harassment and arrest further inhibited treatment access for drug dependence in Georgia. Since 2006 there has been a dramatic increase in police activity aimed at random street searches and (urine) testing of young people for drugs, which, in the event of a positive result, leads to harsh penalties (Otiashvili et al., 2008; Otiashvili et al., 2010). The result has been a situation in which drug users were driven deep underground and were reluctant to seek treatment services.

Given that the vast majority of opioid injectors were not receiving agonist medication and that naltrexone alone was unsuccessful in promoting continued illicit opioid abstinence, a multi-component behavioral therapy approach was developed for Georgian men (who comprise 99% of known drug-users), based on a successful intervention model developed in the US (Jones et al., 2011). Behavioral treatment components included individual Motivational Interviewing (MI) in order to foster treatment engagement (Miller and Moyers, 2002; Miller and Rollnick, 1991a; Rollnick et al., 1992), MI for the couple aimed at improving the couple's relationship and her support of the male participant's treatment episode, and concurrent rapid entry into detoxification followed by naltrexone maintenance. Drug-abstinence contingency management (CM), a method by which participants receive rewards with monetary value for providing drug-negative urine samples, was also used to initiate and sustain drug abstinence (Higgins et al., 1991; Petry et al., 2005). The decision to

engage female partners in the study was based on a commonly acknowledged feature of Orthodox Georgian society where traditional family bonds and interpersonal relations play an extremely important role (Nijaradze et al., 2005). Georgians tend to live in extended families, with three generations often co-existing together and sharing living space and expenses. Family members provide much of the economic, social, and psychological support to one another. In fact, the study targeted the 'typical' Georgian injecting drug user – male, regular opioid injector, married to a drug-free female, and never been in treatment (STI/HIV SHIP Project, 2007).

The present study's purpose was twofold. First, to determine the extent to which it was feasible to recruit and retain men and their drug-free female partners in a randomized controlled trial providing either a comprehensive intervention comprised of behavioral treatment, combined with contingency management, with the opportunity for detoxification followed by naltrexone treatment, or an active usual care control condition. Second, to examine the men's 1-, 3-, and 6-month post-treatment follow-up outcomes. It was hypothesized that non-treatment-seeking opioid-injecting men could be attracted into treatment and that the comprehensive intervention would result is less opioid use and reduced HIV drug-risk behaviors relative to the usual care condition.

2.0 Methods

2.1 Treatment Setting

The Union Alternative Georgia is an independent nonprofit research institution located in Tbilisi, Georgia. The study was conducted at its field site, conveniently located in the residential area of one of the city's central districts.

2.2 Participants

Participants were recruited by word-of-mouth, flyers, and advertisements given to hospital staff and harm reduction programs. Screening was a face-to-face interview at the research site. Of the 74 males contacting the research site between May, 2006 and January, 2009 (Figure 1), 55 were evaluated for eligibility. Eligibility criteria included: being a) male; b) at least 18 years old; c) having a current drug-free female sexual partner with whom they had regular contact; d) meeting current DSM-IV criteria for opiate dependence; e) no current suicidal ideation; f) not meeting current DSM-IV criteria for a thought disorder (e.g., schizophrenia); g) free of significant cognitive impairment that precluded them from completing study entry assessment; and h) screened negative for current physical abuse of their female partner.

The study was approved by the Institutional Review Boards of Johns Hopkins University and the Georgian HIV/AIDS Patients Support Foundation.

2.3 Treatment Conditions

2.3.1 Usual Care (UC)—Men assigned to this condition were asked to visit the research offices once per week for 22 weeks to provide an observed urine sample and participate in individualized manualized education sessions on topics of drugs of abuse, anger management, drug refusal skills, HIV/AIDS, hepatitis, and relaxation training. Upon request, information about community resources for common crises drug users face was available. Referrals to detoxification programs and aftercare were made, if requested.

2.3.2 Behavioral Treatment+Naltrexone (BT+N)—Male participants assigned to the BT+N condition were invited to participate in a 22-week program that was comprised of 4 major components. Participants were expected to come once a week to provide an observed

urine sample. If the urine sample was negative for opioids and buprenorphine, they received the cash equivalent of $9US for a maximum possible amount of $194US. All $US amounts reported herein are based on the exchange rate at the time of the outset of the study, and are rounded off to the nearest $US for convenience. In addition, they took part in a once-a-week MI counseling session. The first 6 sessions were designed to enhance motivation to stop or reduce drug use. Sessions 7-18 were couples counseling sessions using MI techniques to improve partner interactions and education about HIV/AIDS. The remaining sessions were individual sessions building on change behaviors and using MI techniques.

All participants in the BT+N condition had the opportunity to enter 14-day detoxification (in-patient pharmacological treatment with clonidine combined with abstinence-oriented psychological assistance, focusing mainly on the change of attitude towards drug use) shortly after study entry in order to aid their attempts at opioid abstinence. During detoxification, they were offered immediate access to a 22-week supply of oral naltrexone provided free-of-charge to them and monitored by the first author. Naltrexone was prescribed as a maintenance medication prior to completion of the detoxification program. Participants were opioid-free for 7-10 days and all participants who chose to intiate oral naltrexone passed a naloxone challenge test prior to such initiation. Naltrexone dosing regimens were individualized based upon patient response and need for supervision.

2.4 Follow-up Interviews

Male participants were contacted at 1, 3, and 6 months post-treatment to participate in follow-up interviews.

2.5 Female Partner Participation

Following male participant consent, his drug-free female partner was contacted, and asked to visit the study office and sign written informed consent. Female partners of male participants assigned to the BT+N condition were also asked to attend couples counseling sessions during weeks 7-18 of treatment.

2.6 Randomization

Eligibility of the potential participants was assessed by a study co-investigator, while all other assessments were performed by a research assistant. Following completion of the initial assessment battery, eligible male participants were randomly assigned by the research assistant to either the BT+N (n=20) or the UC (n=20) condition. Adaptive bias-coin randomization with urn design was used (Schouten, 1995). This allowed us to obtain a random allocation sequence with comparison groups of equal size (Lachin et al., 1988; Schulz and Grimes, 2002). All analyses reported in this paper are based on the data from these 40 male participants.

2.7 Procedures

All male and female participants in both conditions received the cash equivalent of $18US for completing the baseline (study entry) interview and $9US for completing 1, 3, and 6 month post-treatment follow-up interviews (for a maximum possible amount of $45 for participation in all four interviews). They also earned the cash equivalent of $9US for every attended study visit, for total possible earnings of $243US for completing all 4 interviews and attending all 22 study visits. Theefore, BT+N particpants could earn $437US (=$243US + $194US for negative urine samples; see *2.3.2*, above). Additional ancillary services such as refferal to an infection disease clinic, legal, and social assistance institutions were offered to all male participants in order to meet the needs of the population and overcome some study participation barriers. Specifically, they were given a community resources guide

developed by the Georgian research staff. Staff also helped the male participants call for services and initiate the steps to resolving crises such as legal or health care issues. Male participants were asked to provide a blood sample for HIV testing at study entry. Men received appropriate pre- and post-HIV testing counseling and were referred for treatment if needed.

2.8 Measures

2.8.1 Baltimore Risk Assessment Battery (BRAB)—HIV drug-risk was measured using a modified HIV Risk Assessment Battery (RAB), the Baltimore RAB (BRAB) (Chaudhury et al., 2010; Metzger et al., 1993). The BRAB includes 11 items that measure HIV drug-risk behavior. Drug-risk scores can range from 0-29, with higher scores indicating greater HIV drug-risk behavior. In addition, several supplementary drug risk items were included in the BRAB to measure drug risk in the Georgian population, notably whether the respondent had injected buprenorphine (Subutex®).

2.8.2 Urine Drug Screening—Urine specimens were collected weekly at the study site by male staff under direct observation following standard clinic procedures. Urine samples were tested for opioids by a research assistant at the research site using rapid test strips.

2.9 Outcome Measures

Treatment impact and drug-risk behaviors served as outcomes. Entered detoxification (yes *v.* no) and entered naltrexone treatment (yes *v.* no) were assessed at treatment completion, while number of weekly treatment sessions attended during the 22-week trial, and number of weekly positive and negative urine samples collected, were determined from study records. The remaining variables were measured at four time points: study entry, and 1-, 3-, and 6-month post-treatment follow-up. Drug risk was measured by the BRAB Drug-Risk Score, as well as with selected BRAB items measuring past 30-day drug use: drug injection, injection of buprenorphine, needle and syringe sharing, and use of benzodiazepines.

2.10 Statistical Analyses

The Type I error rate was set at .05. *t* tests (for age) and χ^2 likelihood ratio tests of independence (for all other variables) were used to compare the treatment conditions on relevant intake information. Because observations in the crosstabulation tables were sparse, exact test statistics were used to conduct significance tests.

For the binary outcomes of entered detoxification and entered naltrexone treatment, exact test statistics were again employed, due to the sparseness of the data. For the remaining outcomes, the simplest possible linear model was utilized. For number of (a) urine samples collected, (b) positive urines, and (c) negative urines, the explanatory variable in the statistical model was Treatment Condition (BT+N *v.* UC). For the continuous outcomes (BRAB Drug-Risk, and past 30-day: benzodiazepine use, buprenorphine use, and syringe sharing), a repeated-measures factor, assessment Time point (baseline *v.* 1-month *v.* 3-month *v.* 6-month follow-up), was added to the model, as was the Treatment Condition × Time interaction. Estimation and tests of significance were conducted with a generalized linear mixed model (GLiMM) approach, assuming a Poisson distribution for all variables except for BRAB Drug-Risk for which a normal distribution was assumed. Tests of simple main effects were conducted following detection of a significant interaction effect. Interpretation focused on the (exponentiated, except for BRAB Drug-Risk) model-derived least squares means.

Attempts to fit analogous GLiMM to the binary outcomes (past 30-day: injected drugs and shared needles) failed due to convergence problems caused by sparse data. Therefore, exact

tests were again utilized, testing difference between Treatment Conditions at each Time point (i.e., the simple main effect of Treatment Condition within Time).

3.0 Results

3.1 Participant Characteristics

Table 1 presents information regarding the attrition rate in the two Treatment Conditions at the four assessment Times. Overall, data from 43.3% of the follow-up assessments were not conducted due to failure of participants to show for their scheduled appointments. Table 1 also summarizes the background characteristics of the male participants. With one exception, all men injected drugs, with 33/40 injecting buprenorphine in the past 30 days – and all 40 having ingested buprenorphine during the same period. More than 50% shared needles or works (with this behavior more likely in the UC than the BT+N condition, as was sharing syringes). Finally, their mean past 30-day income at baseline assessment, determined from item E12 “Employment (net income)” from the ASI was $154.25US (*SD*=471.03, with n=30 with no past 30-day employment income).

3.2 Outcomes

Tables 2 and 3 summarize the results of the inferential analyses evaluating the differential impact of Treatment Condition. For the continuous outcomes, only the Treatment Condition × Time test statistic is reported in the table; any significant effect for the Treatment Condition or Time main effects for these outcomes are reported herein.

3.2.1 Treatment Impact Outcomes—The same 12 BT+N participants (60%) entered detoxification and naltrexone treatment, respectively, while no UC participant did so, both *p*s<.001. Moreover, positive urine drug screening results were more frequent, and negative urine drug screening results less frequent, in UC than in BT+N, both *p*s<.05 (see Table 2).

3.2.2 Drug Risk Behaviors—BT+N impacted several aspects of drug risk. The Treatment Condition × Time interaction was significant for both frequency of benzodiazepine use and frequency of buprenorphine injection, both *p*s<.001. Simple main effects tests of Time within each Treatment Condition revealed that Time was significant only within the BT+N Condition for both outcomes, both *p*s<.0001. The means decreased a minimum of seven-fold from baseline to 6-month follow-up in the BT+N condition, while remaining virtually unchanged in the UC condition (Table 3). Finally, although 95% in the BT+N condition and 100% in the UC condition were injecting drugs at baseline, only 17% in the BT+N condition versus 73% in the UC condition were injecting drugs at 6-month follow-up, *p*=.012. A similar pattern occurred with sharing needles (BT+N=0% *v.* UC=45%) at 6-month follow-up, *p*=.014. However, the Treatment Conditions differed at baseline in the number of participants sharing needles (25% *v.* 80%, respectively, *p*=.001).

Finally, there was a Time effect for BRAB Drug-Risk Scale score [*M*s(*SE*s) = 7.5(.6), 5.1(.7), 3.1(.8), and 2.6(.6), respectively] and sharing syringes [1.1(.2), 1.0(.2), .5(.2), and .5(.2), respectively], both *p*s<.001.

3.2.3 Participants' Earnings—Study participants earned on average $160US (*SD=83*) in the BT+N and $134US *(SD=89)* in UC group for attending study visits and participating in assessments. In addition, male participants in BT+N group earned on average $63 *(SD=59)* for providing drug-free urines.

4.0 Discussion

The study was the first randomized clinical trial in the field of substance abuse in Georgia, and its conduct was challenging. The whole notion of participation in a research study rather than in an expected “free, humanitarian kind of treatment program” needed a thorough explanation to each participant. The principle of random assignment to treatment conditions was another concept alien to our participants. An unexpected problem was the high attrition rate. Because Georgia is a former police state, drug-using individuals are understandably hesitant to provide suitable information to allow for subsequent contact. Future studies in Georgia require increased staff resources to track participants and perhaps increased monetary incentives for participation in follow-up assessment sessions.

In this randomized controlled trial, participants assigned to a comprehensive intervention that paired behavioral treatment with naltrexone were significantly more likely than usual care participants to enter detoxification and naltrexone treatment, and provide significantly more opioid-negative urine samples. Moreover, there were significant reductions in the use of benzodiazepines and buprenorphine injection in comprehensive treatment relative to usual care. Importantly, the two conditions did not differ significantly in the number of study sessions attended.

Moreover, as found in previous research, brief drug and HIV education and information provision without specific behavioral therapy and other research-supported treatment was ineffective either in facilitating the treatment entry (Booth et al., 1998) or in encouraging drug abstinence (Campbell et al., 2009). Although education sessions in the usual care condition did not make an impact on treatment initiation and illicit drug consumption, they did improve injection risk behavior, as would be expected (Gibson et al., 1999; Hershberger et al., 2003).

4.1 Challenges to Study Implementation

Several environmental factors deserve consideration when describing possible mechanisms behind treatment impact and study results interpretation. During study implementation, Georgian drug treatment consisted of prohibitively expensive detoxification programs. Although free, entry into MMT programs was highly competitive, with long waiting lists and the actual possibility of being admitted extended only to those individuals with HIV-positive status. Moreover, engagement of drug users in a long-term care employing research-supported behavioral therapy with additional incentives for that engagement, paired with tangible motivational incentives for drug abstinence, was viewed by Georgian drug injectors as an extremely novel approach to treatment.

Finally, the role of naltrexone in helping patients in the comprehensive intervention condition to achieve a drug-free state should be evaluated with caution. Although participants in the BT+N condition had free access to naltrexone, none of them requested the medication beyond an initial 10-tablet supply. Moreover, antagonist medication adherence was not the current study's primary focus, so it was not specifically targeted and controlled. Naltrexone likely supported early abstinence during the post-detoxification stage, but its overall contribution to reduced drug use in the BT+N condition should not be overestimated. Of some importance is the fact that naltrexone is available in Georgia without a prescription; however, is extremely expensive. Thus, although participants in UC condition in theory had a chance to initiate antagonist treatment, in reality it was necessary for them to remain opioid-free for a sufficient number of days to begin naltrexone treatment – and to be able to pay for the medication.

4.2 Study Limitations

The sample was small, thereby limiting our ability to draw firm conclusions. Moreover, the choice of an error rate of .05 increases cumulative error. However, a more conservative rate would have run the risk of failing to detect a small but potentially important difference between treatment conditions in an exploratory study.

Study results might have been adversely affected by a single counselor providing the MI. Although experienced, MI was new to her. Finally, the extent to which positive effects on drug use produced by the comprehensive intervention will be translated into long-term improvements are unknown.

Two other limitations merit discussion. The first issue is the sizeable attrition that occurred during the course of the conduct of the study. Such attrition does raise issues about the generalizability of the results. Although we have no data to support our contention, it is our belief that the major reason for dropping out of treatment was due to participants' fear of police street drug searches, as well as due to admission of some of study participants into the methadone maintenance treatment programs that had opened during the course of the study. The second issue is the fact that sample size was not chosen based on a power analysis prior to the conduct of the trial. However, the study was primarily a feasibility study with the primary intention of determining whether a large-scale randomized trial of behavioral treatment for opioid abuse in the Republic of Georgia was possible, and should be viewed from this perspective rather than from the viewpoint of randomized trial in a Western society in which the population of interest is well understood, and the ability to implement interventions under consideration are assumed to be quite practicable.

4.3 Strengths to the Study

Nevertheless, results show the feasibility of implementing a rigorously designed randomized clinical trial with Georgian opioid-injecting men and their partners. To our knowledge, no previous drug-free treatment has engaged patients with drug problems in Georgia and retained a large portion of them in such an extended treatment (22 weeks). Results also suggest that research-supported interventions that have been proven to be effective in other settings are well-accepted and produce positive results in the naïve-to-comprehensive long-term care Georgian substance-abusing men as well. This statement seems to be true for contingency management and to a lesser extent for MI.

Reducing treatment barriers facilitates entry into drug abuse treatment (Appel et al., 2004; Bobrova et al., 2006; Booth et al., 1998; Carroll et al., 2006; Laudet et al., 2009; Nyamathi et al., 2007). Thus, in the Georgian context of expensive detoxification treatment and extremely limited availability of methadone maintenance, offering free treatment was a powerful tool in facilitating treatment entry in our sample, with 60% of the male participants in the comprehensive behavioral intervention and 0% of the usual care participants entering inpatient detoxification. Efficacy of MI and contingency management separately has been demonstrated in previous studies (Dutra et al., 2008; Higgins et al., 1991; Miller and Moyers, 2002; Miller and Rollnick, 1991b; Rollnick et al., 1992; Weinstock et al., 2007). However, it is difficult to attribute positive outcomes of our study exclusively to any one comprehensive treatment component. This study was a feasibility study and not a dismantling study, so there was no intention to disentangle the possible explanations for treatment efficacy. Nonetheless, contingency management has been shown to improve both treatment retention and drug use outcomes (Peirce et al., 2006; Petry et al., 2005). In our study, and in some other studies, MI session attendance was not specifically targeted by contingency management (Peirce et al., 2006), while drug abstinence was. This factor may well explain why attendance did not differ significantly between the conditions. Despite the

fact that some studies with MI report improved retention in treatment, reductions in drug use are less commonly reported (Carroll et al., 2006). Thus, the significant reduction in drug use in the Intervention group was most likely the result of the combined effects of both MI and monetary incentives.

4.4 Conclusions

Findings do suggest the obvious direction of designing and implementing larger-scale confirmatory studies in this or other drug-using settings in Georgia. Another target group for these studies might be female drug users – the most understudied and underserved segment of the population with substance-use-related problems in this part of the world, and in Georgia in particular (International Harm Reduction Development Program, 2009). In Georgia, a country that is presently resource-limited, substantial consideration needs to be given to the costs of any intervention that might be adopted. Contingency management, although shown to be effective, often is problematic to implement in clinical settings due to its significant costs. Thus, future larger-scale trials of our BT+N intervention will need to examine not only its effectiveness, but also its cost effectiveness. Moreover, dismantling studies which systematically examine BT+N components clearly seem warranted in order to determine the effective ingredients for the model as appropriate to Georgian society.

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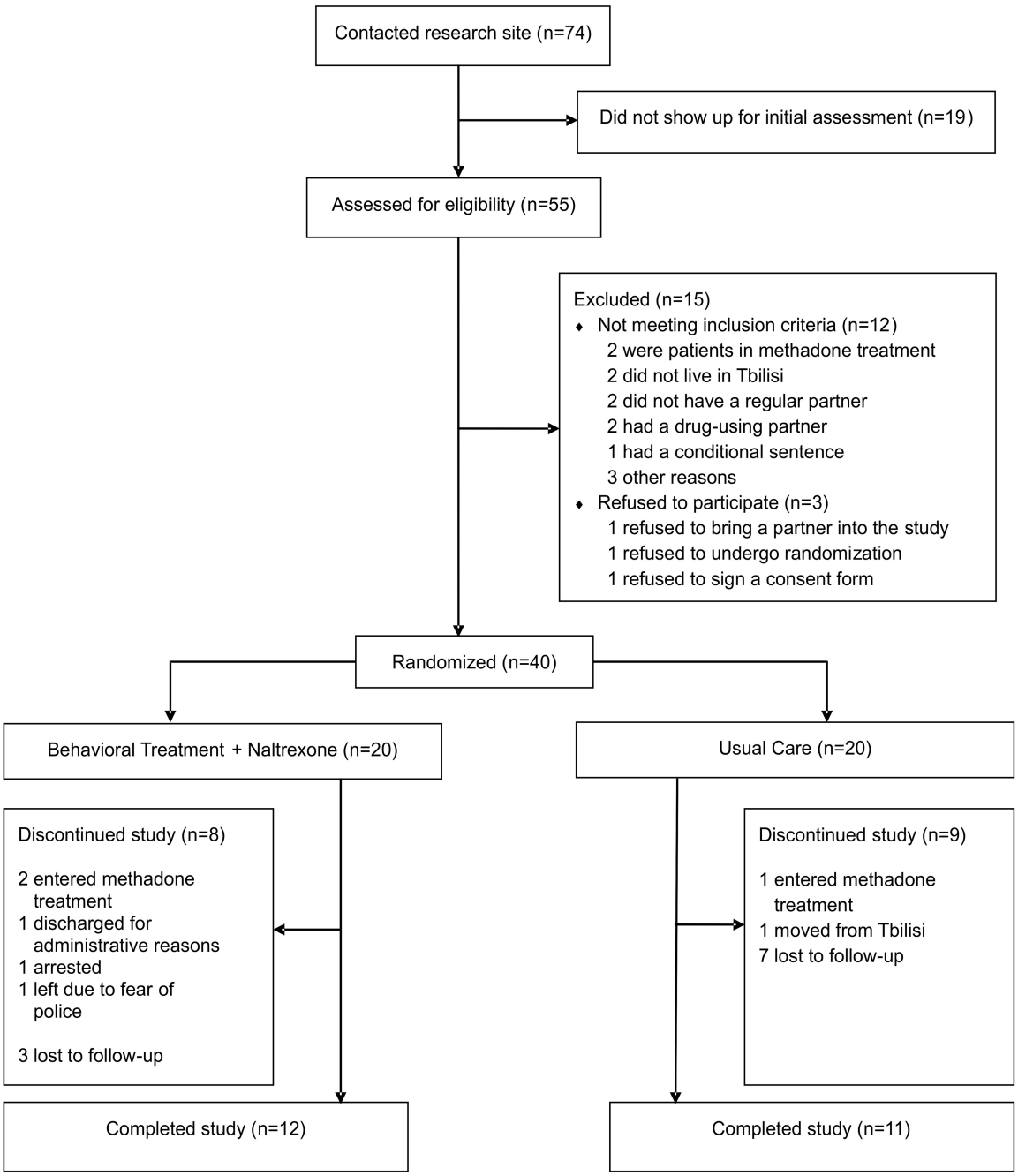

Figure 1. Study flow chart

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Table 1

Background Characteristics for the Total Sample and the Usual Care (UC) and Behavioral Treatment+Naltrexone (BT+N) Conditions (*N*=40)

	Total Sample (N=40)	UC (n=20)	BT+N (n=20)	Test Statistic (χ^2 or t)	p
	n (%)	**n (%)**	**n (%)**		
Baseline Assessments Conducted	40 (100%)	20 (100%)	20 (100%)	--	
1-month Follow-up Conducted	24 (60%)	9 (45%)	15 (75%)	3.8	.105
3-month Follow-up Conducted	23 (58%)	11 (55%)	12 (60%)	.10	1.0
6-month Follow-up Conducted	21 (53%)	9 (45%)	12 (60%)	.9	.527
	M (SD)	**M (SD)**	**M (SD)**		
Age	35.6 (6.7)	34.9 (5.5)	36.4 (7.9)	**t**(38)=-.7	.503
	n (%)	**n** (%)	**n** (%)		
HIV Status at Baseline				$\chi^2(3)=11.2$	.009
Positive	1 (3%)	0 (0%)	1(5%)		
Negative	22 (55%)	7(35%)	15(75%)		
Refuse	13 (33%)	11 (55%)	2 (10%)		
Drop-out	4 (10%)	2 (10%)	2 (10%)		
Hepatitis C Status at Baseline				$\chi^2(3)=4.8$	.240
Positive	24 (60%)	10 (50%)	14 (70%)		
Negative	5 (13%)	2 (10%)	3 (15%)		
Refuse	7 (18%)	6 (30%)	1 (5%)		
Drop-out	4 (10%)	2 (10%)	2 (10%)		
Past 30-day Ingested Buprenorphine					--
Not at all	40 (100%)	20 (100%)	20 (100%)		
Past 30-day Shared Needles or Works	21 (53%)	16 (80%)	5 (25%)	$\chi^2(1)=12.8$	.001
Syringe sharing				$\chi^2(3)=13.3$	.010
Not at all	15 (38%)	4 (20%)	11 (55%)		
A few times	11 (28%)	5 (25%)	6 (30%)		
A few times each week	7 (18%)	7 (35%)	0 (0%)		
Every day	7 (18%)	4 (20%)	3 (15%)		

Notes. Percentages are within the respective Treatment Condition. Past 30-day drug-risk questions were taken from the Baltimore Risk Assessment Battery (BRAB). All χ^2 tests of significance are likelihood ratio tests; all probability values are exact. - - indicates it was not possible to conduct inferential tests due to lack of variability in the outcome measure.

Table 2

Cell Frequencies (Percentages) and Least Squares Means (Standard Errors) and Tests of Significance for Treatment Impact Outcome Measures comparing the Usual Care (UC) and Behavioral Treatment+Naltrexone (BT+N) Conditions (N=40)

	UC (n=20)	BT+N (n=20)	Test Statistic	p
Treatment Impact				
	n (%)	**n (%)**	**Main Effect for Condition**	
Entered detoxification	0 (0%)	12 (60%)	$\chi^2(1)=21.9$	<.001
Entered naltrexone treatment	0 (0%)	12 (60%)	$\chi^2(1)=21.9$	<.001
	M (SE)	**M (SE)**		
Number of treatment sessions	9.8 (1.6)	12.1 (1.8)	$\chi^2(1)=.8$	.361
Number of urine samples collected	9.7 (1.6)	12.0 (1.8)	$\chi^2(1)=.8$	.360
Number of opioid-positive urine samples	8.4 (1.3)	5.1 (1.0)	$\chi^2(1)=4.9$	.043
Number of opioid-negative urine samples	1.4 (.6)	7.0 (1.3)	$\chi^2(1)=14.9$	<.001

Notes. Percentages reported for entering detoxification and entering naltrexone treatment are within the respective Condition. The 12 participants who entered detoxification were the same 12 participants who entered naltrexone treatment. All χ^2 tests of significance are likelihood ratio tests; the probability values for entering detoxification and entering naltrexone treatment are exact. Means, rather than percentages, are reported for number of positive and negative urine samples because participants varied in the number of urine samples provided, due to attrition.

Table 3

Cell Frequencies (Percentages) and Least Squares Means (Standard Errors) and Tests of Significance for Drug Risk Outcome Measures comparing the Usual Care (UC) and Behavioral Treatment+Naltrexone (BT+N) Conditions (N=40)

	UC (n=20)	BT+N (n=20)	Test Statistic	p
Drug Risk Behavior				
	n (%)	**n (%)**	**Simple Main Effect of Condition within Time**	
Past 30-day Injected Drugs				
Baseline	20/20 (100%)	19/20 (95%)	$\chi^2(1)=1.4$	1.0
1-month Follow-up (**n**=24)	8/9 (89%)	9/15 (60%)	$\chi^2(1)=2.5$	.191
3-month Follow-up (**n**=23)	7/11 (64%)	5/12 (42%)	$\chi^2(1)=1.1$	.414
6-month Follow-up (**n**=23)	8/11 (73%)	2/12 (17%)	χ^2 (1)=7.8	.012
Past 30-day Shared Needles				
Baseline	16/20 (80%)	5/20 (25%)	$\chi^2(1)=12.8$	.001
1-month Follow-up (**n**=24)	6/9 (67%)	2/15 (13%)	$\chi^2(1)=7.3$	.022
3-month Follow-up (**n**=23)	5/11 (45%)	1/12 (8%)	$\chi^2(1)=4.4$	.069
6-month Follow-up (**n**=23)	5/11 (45%)	0/12 (0%)	χ^2 (1)=8.9	.014
			Condition × Time Interaction Effect	
	M (SE)	**M (SE)**		
BRAB Drug Risk Scale Score			$\chi^2(3)=2.0$	.565
Baseline	8.1 (1.1)	5.5 (.8)		
1-month Follow-up	4.9 (1.1)	2.1 (.9)		
3-month Follow-up	4.7 (1.0)	1.3 (1.0)		
6-month Follow-up	5.5 (.8)	.4 (1.0)		
Past 30-day Used Benzodiazepines			$\chi^2(3)=8.61$	.035
Baseline	1.7 (.2)	1.7 (.2)		
1-month Follow-up	1.6 (.5)	.7 (.3)		
3-month Follow-up	1.1 (.4)	.6 (.2)		
6-month Follow-up	1.5 (.3)	.04 (.05)		
Past 30-day Injected Buprenorphine			$\chi^2(3)=23.9$	<.001
Baseline	1.3 (.2)	1.4 (.2)		
1-month Follow-up	1.9 (.4)	.5 (.1)		
3-month Follow-up	1.3 (.3)	.6 (.2)		
6-month Follow-up	1.3 (.3)	.2 (.1)		
Past 30-day Shared Syringes			$\chi^2(3)=5.2$	.158
Baseline	1.6 (.3)	.7 (.2)		
1-month Follow-up	1.6 (.4)	.4 (.2)		
3-month Follow-up	.8 (.3)	.3 (.2)		
6-month Follow-up	1.0 (.3)	.1 (.1)		

Notes. BRAB = Baltimore Risk Assessment Battery. Past 30-day drug-risk questions were taken from the BRAB. All χ^2 tests of significance are likelihood ratio tests; the probability values for the tests of simple main effects of Condition within Time are exact. See text for details regarding the need to conduct tests of simple main effects rather than interaction tests.