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Comparison of Behavioral Treatment Conditions in Buprenorphine Maintenance

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Abstract

Background and aims—The Controlled Substances Act requires physicians in the United States to provide or refer to behavioral treatment when treating opioid-dependent individuals with buprenorphine; however no research has examined the combination of buprenorphine with different types of behavioral treatments. This randomized controlled trial compared the effectiveness of 4 behavioral treatment conditions provided with buprenorphine and medical management (MM) for the treatment of opioid dependence.

Design—After a 2-week buprenorphine induction/stabilization phase, participants were randomized to 1 of 4 behavioral treatment conditions provided for 16 weeks: Cognitive Behavioral Therapy (CBT=53); Contingency Management (CM=49); both CBT and CM (CBT+CM=49); and no additional behavioral treatment (NT=51).

Setting—Study activities occurred at an outpatient clinical research center in Los Angeles, California, USA.

Participants—Included were 202 male and female opioid-dependent participants.

Measurements—Primary outcome was opioid use, measured as a proportion of opioid-negative urine results over the number of tests possible. Secondary outcomes include retention, withdrawal symptoms, craving, other drug use, and adverse events.

Findings—No group differences in opioid use were found for the behavioral treatment phase (Chi-square=1.25, p=0.75), for a second medication-only treatment phase, or at weeks 40 and 52 follow-ups. Analyses revealed no differences across groups for any secondary outcome.

Conclusion—There remains no clear evidence that cognitive behavioural therapy and contingency management reduce opiate use when added to buprenorphine and medical management in opiates users seeking treatment.

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Ethical Statement: The material in this paper has not been published in whole or part elsewhere; the paper is not currently being considered for publication elsewhere; all authors have been personally and actively involved in substantive work leading to the report and will hold themselves jointly and individually responsible for its content; all relevant ethical safeguards have been met in relation to patient or subject protection including clinical review by an appropriate ethical review committee and written informed patient consent. This research complies with the World Medical Association Declaration of Helsinki.

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Introduction

Worldwide, controlled clinical trials provide overwhelming support for the effectiveness of buprenorphine, a mu-opioid partial agonist approved in 2002 in the United States by the Food and Drug Administration (FDA) as a pharmacotherapy for opioid dependence (1-6). Buprenorphine has less potential for psychological and/or physical dependence than traditional full agonist opioids like methadone, has fewer side effects, and use in office-based settings allows patients to avoid the stigma sometimes attached to traditional opioid maintenance treatment programs. Buprenorphine treatment also allows patients to receive medication off-site by prescription, avoiding daily attendance at traditional opioid treatment programs.

The introduction of buprenorphine into the portfolio of treatment options was expected to substantially increase the number of patients seeking treatment for opioid dependence because of its ready availability at private office-based practices, less restrictive controls, and favorable safety profile (4,6-10). A possible barrier to prescribing buprenorphine may be the requirement that U.S. physicians treating opioid-dependent individuals with buprenorphine must provide ancillary treatment or referral to behavioral treatment, according to the Controlled Substances Act (11).

Because most private physicians may not have the training, time, space, or staff to provide on-site behavioral treatment, referrals are often made to local substance abuse treatment programs or 12-step programs. No research has assessed the true effectiveness of buprenorphine pharmacotherapy provided in conjunction with behavioral treatment as there has been no assessment of patients' acceptance and participation in behavioral programs. It remains unclear whether treatment outcome is improved by participation in behavioral treatments.

Controlled clinical trials have documented the efficacy of buprenorphine treatment (2,4,6,8,9) and of behavioral and cognitive therapies for optimizing pharmacotherapy outcomes (12-15). Currently popular and effective behavioral treatment methods for substance abusing populations include Cognitive Behavioral Therapy (CBT) and Contingency Management (CM).

Cognitive Behavioral Therapy (CBT) is associated with significant reductions in drug use (16-20), and in HIV-risk behaviors (21), and CBT benefits are sustained for significant durations after discontinuation of treatment (20,22). In a group or individual counseling session, CBT addresses intrapersonal and social/environmental influences that maintain substance use problems and provide coping skills training to prevent relapse. Sessions focus on behavior change principles including identifying relapse triggers, coping skills development, “breaking the cycle” of addictive behaviors, maintaining new lifestyle behaviors, and increasing self-efficacy.

Contingency Management (CM) interventions view behavior as controlled or shaped by its consequences (23-24), and drug use is maintained by positive reinforcement (25). As such, providing appropriate non-drug reinforcers should decrease substance use (26-30). CM procedures are successful in initiating periods of abstinence compared to standard treatment regimens (31) and have produced relatively long periods of abstinence (32-34). A variation of the CM procedure (35) provides opportunities to draw for prizes for meeting the target goal.

Although behavioral treatment methods have been found effective with opioid-dependent individuals, findings from research combining buprenorphine pharmacotherapy with different types of behavioral treatments are mixed. Bickel and colleagues (36) found that

community reinforcement therapy with reinforcers for opioid-negative toxicology tests was associated with longer retention (p=0.03) and higher rates of abstinence (p=0.03) compared to a standard treatment group in a 26-week outpatient opioid detoxification study. Conversely, no differences in any drug use outcome were found between a voucher-based reinforcement group (n=20) and yoked control group that received no performance reinforcers (n=21)(37) in polydrug cocaine- and opioid-dependent participants.

In a 24-week randomized trial comparing standard medical management (MM) with once- and thrice-weekly dose dispensing and enhanced MM with thrice-weekly dispensing, Fiellin (38) found no difference among groups in opioid-negative toxicology tests or retention. The onceweekly dispensing group reported greater treatment satisfaction than either of the two thrice-weekly treatment groups regardless of whether the treatment was standard or enhanced (p=0.04). Similar negative findings were found in a recent randomized trial of 141 opioid-dependent patients provided with buprenorphine in a primary care clinic (39). No differences in outcome were found between groups receiving the standard MM with and without a CBT component.

These studies either compared a behavioral component to a control group, or a standard behavioral component to a more extensive behavioral component. To our knowledge, no study has directly compared the effectiveness of multiple behavioral treatment conditions. The current study examined whether behavioral treatment added to buprenorphine pharmacotherapy increases successful outcome. Participants were provided with 16 weeks of buprenorphine with MM and random assignment to one of four behavioral conditions: 1) Cognitive Behavioral Therapy (CBT), 2) Contingency Management (CM), 3) Both CBT and CM (CBT+CM), and 4) No additional behavioral treatment (NT). Outcomes include opioid use, retention, withdrawal and craving symptoms other drug use, and adverse events (AEs).

Methods

Design

This was a 16-week randomized controlled trial to compare the effectiveness of four behavioral treatment conditions provided with pharmacotherapy and MM for treatment of opioid dependence. MM was designed to approximate care provided by physicians when prescribing buprenorphine in private practice. Following the behavioral treatment phase, participants entered a 16-week medication-only phase with follow-up assessments at weeks 40 and 52.

Participants

Individuals in the Los Angeles area were recruited through advertising, word of mouth, study flyers, and referrals from local addiction treatment programs, outreach programs, primary care providers, and mental health centers. Eligibility criteria included being 15+ years of age, meeting DSM-IV-TR criteria for opioid dependence, good general medical and psychiatric health, no sensitivity to buprenorphine or naloxone, no dependence on alcohol, benzodiazepines or any other drug that would require immediate medical attention, or a pattern of benzodiazepine use that could be unsafe in the context of the study. Females could not be pregnant or nursing, and must have agreed to use an acceptable birth control method.

Gift cards worth $410 were provided for completing all assessments: $25 for screening, $5 for each clinic visit; $25 each for Weeks 18 and 40, and $55 for the Week 52 assessment.

Procedures

Appointments were made with individuals who met preliminary screening criteria. After the informed consent process, assessments collected eligibility and baseline information.

Induction onto sublingual buprenorphine occurred over three days. Suboxone, a combination of buprenorphine and naloxone in a 4:1 ratio was used in two doses, 8:2mg and 2:0.5mg buprenorphine:naloxone. Participants were instructed not to use opioids for at least 10 hours prior to first dose. A 4mg dose (expressed as buprenorphine) was dispensed in clinic and participants were monitored for an hour. An additional 4mg dose could be provided at the physician's discretion. The total Day 1 dose was typically 8mg, but may have been up to 16mg. Day 2 doses were between 8-16mg, and Day 3 doses were between 12-24mg. Dose could be adjusted throughout the trial as clinically indicated.

At the end of the 2-week Induction Phase, participants were randomized to behavioral condition using a computerized urn procedure managed by the UCLA Data Management Center, which included stratification by gender, in blocks of 8. Participants were provided a detailed description of their assigned condition.

During the 16-week behavioral treatment phase, twice weekly clinic visits were scheduled to collect data and urine (UA), meetings with the study physician, and to receive study medication. CM was provided at each visit, and CBT was scheduled once weekly. A 16-week behavioral treatment period was selected to mirror the typical 3-4 month treatment duration used by many addiction treatment providers (40).

Participants assigned to CBT (CBT, CBT+CM) met with a master's level trained counselor for 45-minute individual sessions once weekly to address topics relevant to drug use and recovery. A CBT manual addressed 16 weekly session topics, exercises, and homework. Therapists were trained and supervised by a lead therapist experienced in CBT for drug dependent patients. Sessions were audio-taped and reviewed to ensure therapist fidelity.

Participants assigned to CM (CM, CBT+CM) met with a trained CM technician at each clinic visit to review opioid urine test results and receive incentives if earned. A “fishbowl” included 100 chips each corresponding to 1 of 4 dollar amounts. Participants drew chips for each opioidnegative UA, increasing the number of draws with consecutive clean UA. Missed visits or opioidpositive UAs received no draws and reset the draws. Some aspects of the CM schedule were changed mid-study in order to contain CM costs (e.g., The maximum number of chips drawn at one session was reduced from 32 to 10, and from 528 to 230 across all sessions. Total amount possibly earned across all sessions initially ranged from $528-$2,196, but was reduced to $230-$1460). Analyses comparing the two schedules found no difference in opioid use or retention by CM schedule (41). CM booster training sessions ensured fidelity to the procedures.

Limited counseling as typically provided in private office-based practice settings was provided at weekly MM sessions by study physicians. An MM checklist was used to confirm that physicians addressed each component of the visit such as reviewing the UA result, medication dosage, and adherence to the dosing schedule.

Assessments

Screening assessments included medical and psychiatric assessments to ensure eligibility. Weekly assessments included safety and drug use measures. UA samples were tested at each visit, and a dose log was maintained. At the completion of the behavioral treatment phase, assessments were completed similar to the battery used at baseline. Assessments used in the current analyses include the Addiction Severity Index (ASI)(42); Visual Analog Craving

Scale (VAS)(43-44); Clinical Opioid Withdrawal Scale (COWS)(45-46); Treatment Satisfaction, Substance Use Report; Dose Log, UA Drug Screen (opiates, oxycodone, propoxyphene, phencyclidine, barbiturates, benzodiazepines, cocaine, amphetamines, methamphetamines, marijuana, methadone, and ecstasy), and a dip test was used to confirm the presence of buprenorphine. All untoward events that occurred during the course of the study, whether or not deemed related to study drug or participation, were documented as adverse events (AEs) and categorized as to severity, relatedness, action taken, and resolution.

Analyses

Analyses include all randomized participants (47). Analyses of baseline characteristics were conducted using non-parametric univariate techniques to determine the adequacy of the randomization scheme. Analyses addressing opioid use during treatment compared opioid UA results by behavioral treatment condition. Analyses included univariate analyses of aggregate measures such as the Treatment Effectiveness Score (TES; 48) by condition for each treatment phase/follow-up. Chi-square tests were used to examine UA results across treatment conditions. Retention was analyzed using a Kaplan-Meier survival curve that tests the proportion of participants surviving by condition over the treatment phase. Listwise deletion was used for missing data. Distribution and composites of scores on drug craving and psychological tests were non-normal and analyzed by treatment condition using non-parametric Kruskal-Wallis test and Wilcoxon sign rank test for pre-post test comparisons. The statistical software used in the analysis includes SAS, version 9.3, and STATA 12.

Power analysis was conducted assuming a 70% follow up rate. Starting with a recruitment of 202 participants randomized into each condition allows us to determine a medium effect size difference between groups with a power of .80, and two-tailed alpha of .05. The study is therefore adequately powered at the behavioral treatment phase (n=202) and medication-only phase (n=143). The Weeks 40 and 52 follow-up samples (n≤100) are under-powered.

Results

Participants

A total of 366 individuals completed the consent process, 241 were inducted onto buprenorphine, and 202 were randomized to behavioral condition (figure 1). The first consent and randomization occurred in August, 2007, with the final follow-up assessment taking place in November, 2011.

Baseline characteristics are shown in Table 1. Percentages of participants who reported main opioid of abuse (heroin or prescription opioids) are included. Days of heroin or prescription opioid use in the last 30 days at baseline are shown for only the participants who reported that drug as their main drug of abuse.

Opioid Use

The TES calculated opioid use (opiate, oxycodone, propoxyphene, and/or methadone) as a percentage of the number of opioid-negative urine tests over the number of tests possible. UA assessments of buprenorphine were not reported as positive opioid UA results. The number of missing tests did not differ statistically across groups: CBT=9.4(sd=10.5); CM=8.5(sd=10.1); CBT+CM=8.2(sd=9.9); and NT=9.7(sd=9.9).

During the induction phase, 4 UA tests were possible, 32 during the behavioral treatment phase, 16 during the medication-only treatment phase, and 1 at each follow-up. The TES did not differ across groups at any treatment phase or follow-up (Table 2).

Analyses found no group differences in other measures of opioid use assessed for the behavioral treatment phase. The percentage of participants with 3+ consecutive opioid-negative UA test results included: CBT=66.04%, CM=73.47%, CBT+CM=75.51%, and NT=70.59% (p=0.74), and the percentage with 6+ consecutive opioid-free UA results included: CBT=54.72%, CM=61.22%, CBT+CM=69.39%, and NT=58.82% (p=0.48). The mean number of consecutive opioid-negative UA results also did not differ significantly by group: CBT=9.96(sd=11.1), CM=14.04(sd=12.3), CBT+CM=14.10(sd=12.7), and NT=10.86(sd=10.7) (p=0.16).

Analyses compared the TES of participants who attended at least 50% of behavioral treatment sessions. Results show no difference by group for either behavioral or medication phase.

Although no differences were found in opioid use across treatment groups, all groups reported a significant reduction in heroin use in the last 30 days at the end of the behavioral treatment phase compared to baseline For behavioral treatment phase completers (n=141), days of heroin use in the last 30 days were significantly reduced from baseline for all groups ($p<0.001$): CBT=3.30(sd=6.9), CM=4.71(sd=6.7), CBT+CM=4.11(SD=8.3), NT=5.36(sd=8.0). For those who dropped out of this phase but completed the subsequent interview (n=19), days of heroin use are: CBT=25.7(sd=9.6), CM=29.8(sd=1.2), CBT +CM=28.7(sd=3.2), NT=21.67(sd=13.3).

Other Drug Use

No difference in self-reported other drug use was found across groups by specific drug (amphetamines, cannabis, cocaine, sedatives) for any timepoint (Table 3). Similarly, no difference was found for other drug use as measured with the TES for the behavioral (p=0.14) or medication-only (p=0.91) treatment phases.

Retention

Study retention for the behavioral treatment phase was measured: 1) dichotomously by whether the participant completed the phase; 2) mean number of weeks retained (16 possible); and, 3) mean number of clinic visits attended (32 possible).

There were no differences in any retention measure across treatment groups. The percent of participants completing the behavioral treatment phase includes: CBT=71.7%, CM=69.4%, CBT+CM=73.5%, and NT=64.7% (p=0.79).

The mean number of weeks retained in this phase included: CBT=15.0(sd=5.1); CM=14.6(sd=5.3), CBT+CM=15.3(sd=5.0), and NT=14.6(sd=5.1)(p=0.89). The mean number of clinic visits included: CBT=22.4(sd=10.7), CM=22.3(sd=11.5), CBT+CM=23.6 (sd=10.1), and NT=21.5(sd=10.6)(p=0.81).

Withdrawal and Craving

No significant differences were found in withdrawal symptoms (COWS) or craving (VAS) across groups for the induction or treatment phases (Table 2).

ASI Domains

No significant difference was found across groups for any pre- or post-behavioral ASI composite score using non-parametric tests for non-normal distributions (not shown). No significant differences were found for pre-post scores within each group.

Adverse Events

A total of 253 AEs deemed possibly- or definitely-related to study drug were reported: CBT=29.2%, CM=24.5%, CBT+CM=24.1%, and NT=22.1%. Because the groups were similar, AE frequencies in Table 4 include the total sample: 31.6% occurred during the induction phase, before behavioral treatment was provided; and 68.4% occurred during the behavioral treatment phase. Assessing relation to study drug, 1.6% (4) were deemed definitely related to study drug, and 98.4% (249) were deemed possibly related. The severity of these AEs included 70.8% deemed mild; 29.2% moderate. No AEs were deemed serious or life-threatening. The majority of AEs did not require intervention (95.3%), whereas 3.6% were followed by a dose reduction, and 1.2% were followed by a dose increase. A total of 77.5% were resolved successfully, 2.4% were improving by study end; 10.3% had not changed; and 4.0 were worse or considered a chronic condition.

Medication and Treatment Compliance

Mean prescribed dose, and dose reported as taken by participants were compared across treatment groups. No difference in prescribed daily dose was found (p=0.53): CBT=15.36 (sd=5.1), CM=15.22(sd=4.9), CBT+CM=15.40(sd=4.8), and NT=14.13(sd=5.3). There was no difference across groups for self-reported mean daily dose taken (p=0.61); CBT=15.13(sd=5.3), CM=15.23(sd=5.3), CBT+CM=15.32(sd=4.9), and NT=14.09(sd=5.4).

No difference was found across groups in percentages of time dose was taken as prescribed (p=0.77); CBT=84.8%, CM=85.0%, CBT+CM=85.6%, and NT=87.7%. Additional analyses found no statistical differences in the percentages of each group who complied with the prescribed dosing schedule at least 80% (p=0.85) and 90% (p=0.62) of the time. A total of 69.8% of the CBT group complied 80% of the time, CM=69.4%, CBT+CM=71.4%, and NT=76.5%.

No differences were found in the percentages of each group that complied with behavioral treatment attendance: CBT=73.1%, CM =72.6%, CBT+CM=75.4% of assigned CBT and 73.8% of CM sessions. No difference in attendance at assigned weekly MM sessions was found: CBT=70.2%, CM= 73.1%, CBT+CM=73.9%, and NT= 68.9%.

Treatment Satisfaction

Small cell sizes in the treatment satisfaction items (Table 5) limit the use of chi-square analyses, so ANOVA was used to compare responses for each item. Most participants reported being “very satisfied” with treatment, and 85% of participants reported that Suboxone was “very effective.” Fewer participants (60%) reported that their behavioral treatment was “very effective.” Importantly, 21% of the NT group reported that their behavioral treatment was “not effective” as compared to 3% of the CBT group and 0% of the CM and CBT+CM groups (p=0.007). Most participants (87%) reported that they would participate again in this study.

Discussion

Although all groups in our study reduced their opioid use significantly from baseline to the end of the treatment phase, the addition of a behavioral treatment component (CBT, CM, CBT+CM) did not increase positive treatment performance as compared to a group (NT) that received only the standard MM provided to all participants. Opioid use, withdrawal symptoms, craving, pre-post status and functioning, other drug use, and AEs did not differ across the treatment groups. Additional analyses documented no differences in daily buprenorphine dose or treatment compliance across groups.

It may be surprising that behavioral treatment did not increase positive outcome over no behavioral treatment, especially as the provision of psychosocial treatment is a condition in the U.S. for use of buprenorphine as a medical treatment for opioid addiction. CBT and CM are perhaps the two psychosocial treatments with the best supporting research data for clinical utility, however, there have been a number of controlled studies, systematic reviews and meta-analysis (37-39), including a recently published Cochrane review (49), showing that adding behavioral treatment adds little to medical management of agonist maintenance treatment. The current findings do not suggest that behavioral interventions are of no use to patients, but that it is very difficult to demonstrate any added benefits to patients undergoing pharmacotherapy in these treatment settings.

Addressing treatment compliance in this study increases the usefulness of these results. Showing that the groups did not differ in treatment participation assures us that the outcomes reported here are valid –there is no systematic difference in treatment compliance that may be responsible for the outcome results.

Similarly, it is becoming increasingly apparent that participant beliefs, in addition to behaviors, are vital to assess. Using a treatment satisfaction measure in the current study records participant beliefs about what is most important in their treatment. Importantly, although 60% of the study participants reported that psychosocial treatment was effective, only 1% of the participants reported that their psychosocial treatment was the most effective study component as compared to 63% who reported medication as the most effective study component for treating their opioid dependence, and 36% who reported both are important. These results suggest that treatment programs should either focus on the provision of pharmacotherapy for increasing treatment satisfaction and positive outcome, or develop more effective psychosocial treatments satisfying to patients.

Importantly, the majority of our participants complied with treatment, attended study visits, reduced their opioid use, and reported satisfaction with treatment. Again, these results indicate that pharmacotherapy with buprenorphine is effective as shown in reductions in drug use and treatment retention. Whether behavioral treatment is beneficial or even necessary may be predicated on the needs of individual patients.

Limitations

We selected a treatment length similar to real-world settings, but better outcomes are associated with longer treatment periods. Different outcomes by group may have occurred had the treatment duration been longer. A related issue is that the MM in this study may not be representative of that offered in private practice or clinic settings. Few clinicians see patients twice-weekly for 18 weeks. Although this may be an issue when comparing our protocol with treatment plans in other settings, all participants received the same level of MM in this study.

Another limitation is generalizability of findings. Study eligibility criteria eliminated individuals with health issues so participants may be healthier, stable individuals with better resources. Comparisons between randomized participants (n=202) and a combined group of those who were not randomized (n=164) shows the non-randomized group reported more mean days of heroin use (15.3 (13.6) vs. 22.5 (11.5); 4.96, $p<0.0001$), and had a higher percentage of opioid-positive UA test results (90.7% vs. 80.2%; $p=0.009$).

Recommendations

Future research should study how private practice physicians provide behavioral treatment with buprenorphine to collect information about how buprenorphine treatment requirements

are being interpreted. A related investigation could examine how the MM plan is developed and implemented in treatment settings as compared to MM plans utilized in research.

These findings also suggest that buprenorphine-prescribing physicians need to take care in developing appropriate MM plans. We have found no study that has examined MM as a treatment component. Our MM included regularly scheduled appointments, which may contribute to improved outcomes, particularly when provided at the beginning of treatment.

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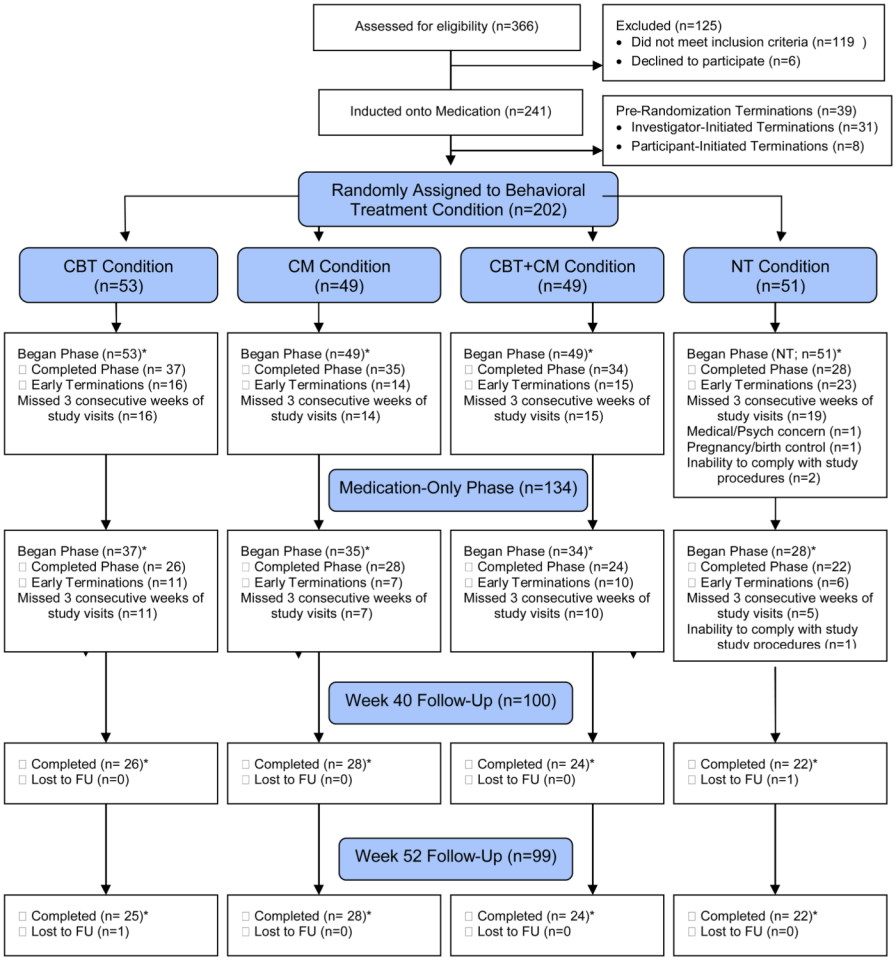

Figure 1.
Consort Flow Diagram.
*Analyses for each phase included participants who began the phase;follow-up analyses include those who completed follow-up.

Table 1

Demographic and Drug Use Characteristics of Randomized Participants at Screening/ Baseline by Treatment Condition

Characteristic	Treatment Condition			
	CBT (N = 53)	**CM (N = 49)**	**CBT+CM (n= 49)**	**NT (N = 51)**
Mean Age (sd)	35.2(12.4)	39.5(12.9)	38.8(12.2)	34.9(12.7)
Percentage Sex (n)				
Male	67.9 (36)	71.4 (35)	71.4 (35)	66.7 (34)
Female	32.1 (17)	28.6 (14)	28.6 (14)	33.3 (17)
Percentage Race/Ethnicity (n)				
White	54.7 (29)	51.0 (25)	53.1 (26)	51.0 (26)
Hispanic	17.0 (9)	22.5 (11)	16.3 (8)	25.5 (13)
Black	5.7 (3)	8.2 (4)	18.4 9)	7.8 (4)
Asian	9.4 (5)	2.0 (1)	2.0 (2)	7.8 (4)
Am Indian	1.9 (1)	6.1 (3)	2.0 (1)	2.0 (1)
Other/unknown	11.3 (6)	10.2 (5)	8.2 (4)	5.9 (3)
Mean Yrs. Education (sd)	13.3 (2.1)	13.1 (2.3)	13.5 (1.9)	13.4 (2.0)
Employment (past 30 days)				
Full-time	15.1 (8)	22.5 (11)	18.4 (9)	11.8 (6)
Part-time	30.2 (16)	26.5 (13)	26.5 (13)	25.5 (13)
Student	9.4 (5)	2.0 (1)	6.1 (3)	13.7 (7)
Unemployed	43.4 (23)	34.7 (17)	40.8 (20)	35.3 (18)
Retired/Disabled	1.9 (1)	12.2 (6)	8.2 (4)	9.8 (5)
Other	0	2.0 (1)	0	3.9 (2)
Opioid+ Drug Screen*	71.7%	87.8 %	87.8%	74.5%
Mean VAS (sd)	66.2 (31.3)	60.0 (31.5)	60.0 (31.5)	59.0 (28.3)
Mean COWS (sd)**	**3.6 (3.5)**	**1.7 (2.3)**	**2.3 (2.7)**	**2.1 (2.7)**
% Reporting Heroin as main drug of abuse				
	56.6%	57.1%	61.2%	62.0%
% Reporting Prescription Opioids as main drug of abuse				
	39.6%	38.8%	34.7%	30.0%
# Days of Drug Use in Past 30				
Alcohol	3.8 (6.9)	3.7 (5.7)	2.6 (4.2)	1.5 (1.9)
Heroin***	24.4 (8.9)	27.6(5.9)	24.6(9.2)	22.5(11.2)
Methadone	2.5 (7.3)	2.9 (7.7)	3.5 (8.2)	3.6 (8.8)
Other Opiates****	13.6 (12.8)	12.4 (14.1)	12.0 (13.7)	10.4 (12.5)

* results positive for opiate, oxycodone, propoxyphene, and/or methadone

** p=0.01

*** for those reporting heroin as main opioid of abuse

**** for those reporting prescription opioids as main opioid of abuse

Table 2

Mean Opioid Use (TES), Withdrawal (COWS) and Craving (VAS) Symptom Scores by Treatment Condition for the 2-Week Induction Phase and 16-Week Combined Pharmacotherapy and Behavioral Treatment Phase.

	CBT (n=53)	CM (n=49)	CBT+CM (n=49)	NT (n=51)	
Induction Phase (Weeks 1-2)					
TES	0.54 (0.35)	0.46 (0.39)	0.42 (0.36)	0.52 (0.33)	F=1.24, p=0.29
COWS	5.68 (1.93)	5.76 (2.87)	6.03 (2.10)	5.72 (2.43)	F=.22, p=0.88
VAS	57.26 (22.90)	51.94 (23.77)	56.67 (18.09)	49.14 (20.41)	F=1.28, p=0.28
Behavioral Treatment Phase (Weeks 3-18)					
TES	0.52 (0.38)	0.56 (0.39)	0.63 (0.37)	0.53 (0.36)	F=0.41, p=0.75
COWS	1.25 (1.06)	1.01 (1.16)	1.16 (1.15)	1.19 (1.17)	F=.48, p=0.69
VAS	26.59 (25.23)	19.72 (21.88)	19.86 (21.31)	19.25 (18.24)	F=.37, p=0.78
Medication-Only Treatment Phase (Weeks 19-34)					
TES	0.64 (0.49)	0.66 (0.47)	0.73 (0.44)	0.64 (0.47)	F=.34, p=0.79
Week 40 Follow-Up					
TES	0.62 (0.49)	0.65 (0.48)	0.73 (0.44)	0.62 (0.48)	F=.32, p=0.81
Week 52 Follow-Up					
TES	0.61 (0.49)	0.64 (0.48)	0.72 (0.44)	0.61 (0.48)	F=.29, p=0.83

Table 3

Self-Reported and TES Measures of Other Drug Use by Behavioral Treatment Group by Treatment Phase

Drug	Measure*	Treatment Phase	CBT	CM	CBT+CM	NT
Amphetamines	ASI	Screening	0.7 (3.0)	0.3 (0.8)	1.6 (4.8)	0.4 (1.0)
	TES	Behavioral Treatment Phase	0.95 (.16)	.91 (.19)	.92 (.20)	.91 (.21)
	ASI	End of Behavioral Treatment Phase	.09 (.62)	1.08 (3.27)	1.07 (6.96)	.69 (2.13)
	TES	Medication-Only Treatment Phase	.96 (.13)	.94 (.14)	.89 (.23)	.91 (.23)
Cannabis	ASI	Screening	5.6 (9.8)	5.5 (9.8)	2.1 (5.4)	6.8 (10.4)
	TES	Behavioral Treatment Phase	.72 (.36)	.78 (.33)	.83 (.31)	.62 (.43)
	ASI	End of Behavioral Treatment Phase	5.71 (9.34)	4.73 (9.41)	1.86 (4.32)	9.47 (12.69)
	TES	Medication-Only Treatment Phase	.72 (.40)	.81 (.33)	.88 (.29)	.65 (.43)
Cocaine	ASI	Screening	1.4 (4.8)	3.4 (8.1)	1.6 (3.0)	1.2 (3.1)
	TES	Behavioral Treatment Phase	.91 (.19)	.79 (.34)	.74 (.35)	.89 (.15)
	ASI	End of Behavioral Treatment Phase	.83 (3.2)	2.01 (4.93)	2.25 (5.78)	.53 (1.60)
	TES	Medication-Only Treatment Phase	.89 (.24)	83 (.33)	.81 (.34)	.86 (.24)
Sedatives	ASI	Screening	3.4 (7.5)	4.1 (8.6)	3.1 (5.7)	2.5 (5.3)
	TES	Behavioral Treatment Phase	.78 (.29)	.79 (.29)	.76 (.32)	.83 (.27)
	ASI	End of Behavioral Treatment Phase	5.4 (9.4)	3.42 (7.76)	4.44 (7.89)	4.24 (8.79)
	TES	Medication-Only Treatment Phase	.73 (.34)	.82 (.29)	.74 (.38)	.77 (.35)

*ASI = self-reported days of use in the last 30 days; TES = Treatment Effectiveness Score

Table 4

Frequencies of Adverse Events reported during induction and behavioral phases, deemed possibly or definitely related to study drug.

Constipation	51
Insomnia	40
Sweating/hot flashes	36
Headache	34
Fatigue/Lethargy	14
Nausea/Vomiting	9
aches/pains	8
decreased appetite	7
runny nose	5
anxiety	5
Diarrhea	4
Stomach Cramps	4
urinary retention	4
increased appetite/weight gain	3
numbness/tingling	3
restless/irritability	3
dry mouth	3
blurred vision	2
heartburn/acid reflux	2
decreased libido	2
dizziness	2
sleep movement	2
irregular periods	2
depression	1
heart palpitations	1
feeling cold	1
rash	1
nightmares	1
itchiness	1
incontinent	1
swelling	1
Total	253

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Table 5

Treatment Satisfaction Responses by Treatment Condition

	CBT	CM	CBT+CM	NT	Total
n=	**32**	**32**	**31**	**39**	**134**
How satisfied are you with the treatment you received? *					
Very satisfied	78% (25)	78% (25)	81% (25)	71% (27)	77% (102)
Satisfied	22% (7)	19% (6)	19% (6)	26% (10)	22% (29)
Dissatisfied	0	3% (1)	0	3% (1)	2% (2)
Very dissatisfied	0	0	0	0	0
How much do you think the treatment you received helped you?					
Helped very much	91% (29)	78% (25)	97% (30)	79% (31)	86% (115)
Helped somewhat	9% (3)	22% (7)	3% (1)	18% (7)	13% (18)
Did not make a difference	0	0	0	3% (1)	1% (1)
Was Suboxone effective in treating your opioid dependence?					
Very effective	94% (30)	78% (25)	90% (28)	79% (31)	85% (114)
Somewhat effective	3% (1)	16% (5)	10% (3)	15% (6)	11% (15)
Not effective	3% (1)	6% (2)	0	5% (2)	4% (5)
Was the psychosocial treatment you received effective in treating your opioid dependence?**					
Very effective	69% (22)	62% (20)	71% (22)	44% (17)	60% (81)
Somewhat effective	22% (7)	38% (12)	29% (9)	36% (14)	31% (42)
Not effective	9% (3)	0	0	21% (8)	8% (11)
Which treatment component do you think was most helpful?					
Suboxone	62% (20)	59% (19)	48% (15)	77% (30)	63% (84)
Psychosocial	0	3% (1)	3% (1)	0	1% (2)
Both equally helpful	38% (12)	38% (12)	48% (15)	23% (9)	36% (48)
Neither helpful	0	0	0	0	0
If you had to do it over again, would you still choose to participate in this treatment study?					
Definitely	91% (29)	84% (27)	96% (29)	79% (31)	87% (116)
Probably	6% (2)	9% (3)	3% (1)	15% (6)	9% (12)
Possibly	3% (1)	6% (2)	3% (1)	3% (1)	4% (5)
Probably not	0	0	0	3% (1)	1% (1)

	CBT	CM	CBT+CM	NT	Total
n=	**32**	**32**	**31**	**39**	**134**
Definitely not	0	0	0	0	0

* 1 person did not respond;

** p = 0.01