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Comparing adaptive stepped care and monetary-based voucher interventions for opioid dependence

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Abstract

This 6-month randomized clinical trial (with three month follow-up) used a 2×2 design to compare the independent and combined effectiveness of two interventions designed to improve outcomes in treatment-seeking opioid dependent patients ($n = 236$): Motivated Stepped Care (MSC) and Contingent Voucher Incentives (CVI). MSC is an adaptive treatment strategy that uses principles of negative reinforcement and avoidance to motivate both attendance to varying levels of counseling services and brief periods of abstinence (Brooner and Kidorf, 2002, Brooner et al., 2004). In contrast, CVI (Higgins et al., 1991) relies on positive reinforcement to motivate drug abstinence. The results showed that the combined approach (MSC+CVI) was associated with the highest proportion of drug-negative urine samples during both the randomized and three-month follow-up arms of the evaluation. The CVI-only and the MSC-only conditions evidenced similar proportions of drug-negative urine samples that were both significantly greater than the standard care (SC) comparison group. Voucher-based reinforcement was associated with better retention, while adaptive stepped-based care was associated with better adherence to scheduled counseling sessions. These results suggest that both CVI and MSC are more effective than routine care for reducing drug use in opioid dependent outpatients, and that the overall benefits of MSC are enhanced further by adding positive reinforcement.

Keywords

adaptive care; stepped care; behavioral reinforcement; opioid dependence; methadone

1.0 INTRODUCTION

The treatment of opioid dependence often requires varying types and amounts of clinical attention over long periods of time. Combination treatment approaches that include adequate doses of opioid agonist medications (e.g., methadone, buprenorphine) and verbal therapy have emerged as a core principle in many “best practice” models of care (McLellan et al., 1993, 2000; Strain, 2006), and this basic approach is associated with reduced drug use and some improvement in psychosocial functioning (e.g., Avants et al., 1999; Johnson et al., 2000; Strain,

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2006). While prior work has established the efficacy of methadone and produced empirically derived clinical guidelines on effective dose ranges (Strain and Stitzer, 2006), similar work is lacking in relation to most verbal therapies. Studies have shown that routine counseling and more specialized verbal therapies are often associated with improvement (see Kidorf et al., 2006, for a review), and that more counseling is sometimes better than less counseling (McLellan et al., 1993; Brooner et al., 2004; Kidorf et al., 2006). Less is known about when and how to adjust the amount of routine and enhanced counseling services to both initiate and sustain good psychosocial functioning over months and years of care (Brooner et al., 2004).

Stepped care interventions (e.g., Davison, 2000; Haaga, 2000; Sobell and Sobell, 2000) reflect an adaptive treatment planning strategy (Murphy et al., 2001; Murphy and McKay, 2004) that seems particularly well-suited for patients with persistent opioid and other drug dependence disorders. Adaptive treatment strategies employ ongoing (and ideally, objective) indicators of clinical response that are used to adjust both the amount and scope of clinical services over time to - prescribing more services for patients with partial and poor responses and less services for those doing well. An important goal of adaptive stepped care is to utilize the lowest and least intrusive amount of treatment services necessary to initiate and sustain an overall good clinical response. This objective can help reduce the demands of treatment participation by limiting more intensive counseling schedules to patients with well-documented partial and poor response to routine levels of counseling, an approach that may be particularly beneficial for people receiving long-term care. While adaptive stepped care strategies have been used to manage substance use and other persistent psychiatric problems (Newman, 2000; Sobell and Sobell, 2000; Wilson et al., 2000), the potential advantages of this approach can be neutralized by poor patient attendance to prescribed therapy services (Simpson et al., 1995; Magura et al., 1998; Strain et al., 1998; Morral et al., 1999; Sigmon and Stitzer, 2005).

Poor patient attendance to scheduled to prescribed counseling schedules is both commonplace in opioid-dependent patients and modifiable (Brooner et al., 2004; Kidorf et al., 2006). Behavioral reinforcement, for example, has been extensively used to reduce drug use and increasingly used to improve attendance to fixed (versus adaptive) schedules of routine drug abuse counseling (Stitzer et al., 1977; Higgins et al., 1991; Kidorf et al., 1994; Silverman et al., 1996; Kidorf et al., 1997; Epstein et al., 2003; Sigmon and Stitzer, 2005). A more recent study (Brooner et al., 2004) showed that behavioral reinforcement procedures are also effective in motivating attendance to changing amounts of verbal therapy delivered via an adaptive stepped care treatment paradigm. Opioid-dependent patients receiving methadone were randomly assigned to a Motivated Stepped Care (MSC) condition that included specific behavioral contingencies to reinforce counseling attendance or to a Standard Stepped Care (SSC) condition without the attendance contingencies. MSC patients were informed that any combination of missed counseling sessions or drug-positive urine samples would result in advancement to more intensive counseling schedules, and that continued missed counseling sessions and drug use during the most intensive step of care (Step 4; about 9 hrs of counseling per week) would lead to later (i.e. less undesirable) daily schedules of methadone dosing and the eventually to the onset of a 30-day methadone taper in preparation for discharge. These behavioral interventions were reversed following 1-week of attendance to scheduled counseling sessions and submission of a drug-negative urine specimen. Rates of counseling attendance, drug-negative urine specimens, and treatment retention were the primary outcome measures of the study. The results showed that subjects randomly assigned to the MSC versus SSC condition were significantly more likely to attend routine individual (94% vs. 70%, respectively) and intensified (76% vs. 28%, respectively) counseling sessions. The MSC condition was also associated with significantly less drug use, which was most strongly evident in subjects that were therapeutically transferred from the SSC to the MSC condition because of continuing partial and poor treatment response.

The MSC adaptive approach utilized in the Brooner et al. (2004) study is a good example of an stepped-care treatment intervention with one notable difference -- the treatment included a highly structured set of clinic-based contingencies to motivate patient attendance to scheduled counseling sessions (both routine and intensified) and at least brief periods of abstinence (i.e., 2 to 4 weeks). The efficacy of this approach is related to the behavioral principles of negative reinforcement and avoidance, and can be contrasted with interventions that rely primarily on "positive" reinforcement strategies. For example, contingent methadone dose increases and methadone take-home doses can be used as positive reinforcers, and studies have shown that they are often associated with reduced drug use, although effect sizes tend to be modest (Kidorf and Stitzer, 1999). Other types of positive reinforcement have produced notably larger effects. Contingent voucher incentives (CVI) have, for example, produced relatively large reductions in drug use by providing escalating levels of positive reinforcement through monetary-based incentives that are exchanged for goods and services. While the CVI intervention was developed originally for outpatient cocaine users (Higgins et al., 1991, 2003), it has been successfully extended to opioid-dependent patients receiving methadone (e.g., Silverman et al., 1996, 2004). Silverman et al. (1996), for example, showed that methadone maintenance patients receiving monetary vouchers for submitting cocaine abstinent urine samples (up to \$1155 over a 12-week period) produced more weeks of cocaine abstinence and demonstrated longer durations of sustained cocaine abstinence than those receiving vouchers on a non-contingent schedule. Many studies have since shown that contingent voucher-based incentives are effective across a variety of substance-dependent populations and treatment settings (Stitzer et al., 2006).

The MSC and CVI interventions both employ adaptive behavioral reinforcement to motivate improved treatment response, but rely on different mechanisms of escalating reinforcement (primarily negative vs. positive reinforcement, respectively), and employ very different counseling approaches (adaptive stepped care vs. fixed once per week counseling schedules). The similarities and differences of these interventions provide a rationale for studying the potential benefits of combining MSC and CVI. For example, while the MSC intervention provides substantial incentives for attending counseling services designed to reduce drug use and improve psychosocial functioning, the negative reinforcement aspects of this intervention (i.e., later clinic-based methadone dispensing times and onset of methadone dose tapers) may be insufficient to effect large reductions in drug use early in the course of treatment. An approach that combines MSC with CVI introduces positive reinforcement may facilitate a more rapid positive response to treatment. And increased attendance (Brooner et al. 2004) to the more frequent counseling sessions scheduled for patients with partial and poor responses may help sustain the potential benefits of voucher-based positive incentives even after the reinforcement is removed (Epstein et al., 2003). An evaluation of the effectiveness of each of these approaches separately is also warranted. CVI is potentially too costly to be of practical use in community treatment settings, particularly in patients with chronic substance use disorder who often require long-term treatment approaches. If an MSC approach utilizing clinic-based incentives can produce behavioral reinforcement of similar potency to voucher-based platforms (Brooner et al., 2004; Roll et al., 2005), community treatment settings would have an alternate strategy for using behavioral reinforcement to improve clinical outcomes.

The present study employs a 2×2 factorial design to evaluate the independent and additive effects of MSC and CVI in opioid-dependent patients seeking treatment with methadone in the Addiction Treatment Services program in Baltimore, Maryland. New admissions were randomly assigned to one of four treatment conditions: 1) MSC+CVI; 2) MSC-only; 3) CVI-only; or 4) Standard Care (SC). Subjects were followed for 6-months of randomized care and a 3-month follow-up period during which all subjects received standard care (SC). Treatment outcome was assessed using rates of attendance to scheduled counseling sessions, and rates of drug-negative urine specimens and treatment retention. We hypothesized that: 1) voucher-

based reinforcement as compared to non-voucher based reinforcement would be associated with lower rates of drug use, higher rates of retention, and earlier onset of drug-negative urine specimens; 2) MSC conditions vs. non-MSC conditions would be associated with lower rates of drug use and higher rates of attendance; and 3) that all three conditions (MSC+CVI, MSC only, CVI only) would have lower rates of drug use and higher rates of attendance and retention compared to the SC condition. The MSC+CVI versus the SC comparisons was also expected to produce larger improvements on drug use, attendance, and retention than the MSC only to SC and CVI only to SC group comparisons.

2.0 METHOD

2.1 Participants

A total of 333 subjects were recruited from a sample of 427 new admissions to the Addiction Treatment Services (ATS) program of the Johns Hopkins Bayview Medical Center in Baltimore, Maryland between February 1999 and November 2003. New admissions that were not enrolled (23%; 94/427) were ineligible to participate because of a psychiatric or medical problem that required immediate attention or refusal to enroll because of one or more protocol requirements (e.g., study assessment schedule and daily methadone dose parameter of 60 - 90mgs). The Johns Hopkins University Institutional Review Board reviewed and approved the evaluation; all subjects provided informed written consent to participate.

All study enrollees (n=333) met DSM-IV criteria for opioid dependence (physiologic subtype) and the Center for Substance Abuse Treatment's (CSAT; 2001) guidelines for long-term use of methadone. Ninety-seven (29%; 97/333) of these subjects were subsequently excluded from random assignment to treatment condition because they: 1) left the treatment program prior to random assignment (n = 37); 2) withdrew consent to participate (n = 12), or 3); were withdrawn from the study (n = 48) because of failure to complete the baseline assessment battery, requests for a daily methadone dose outside of study parameters (i.e., 60 mg – 90 mg), or marked clinical instability associated with the onset of exacerbation of a psychiatric or medical problem. This resulted in a final sample of 236 subjects randomized to treatment condition. Table 1 shows the demographic characteristics and baseline drug use of the final randomized sample. Comparison of the subjects withdrawn from the study prior to random assignment (n = 97) with those randomized to treatment condition (n = 236) on baseline demographic variables show that randomized group was marginally less likely to be male (53.8% vs. 64.9%; $\chi^2 = 3.50$; $p = .06$); no other significant differences were observed.

2.2 Routine Clinic Procedures

2.2.1 Methadone dosing—Subjects received daily oral doses of methadone. All subjects were inducted into treatment on a starting dose of 30 mg and stabilized at 75mg of methadone within the 4-week baseline period, although this dose could be adjusted up to 15 mg in either direction based on clinical observation and subject reports of dose adequacy and/or side-effects. Subjects who requested more than 90 mg or less than 60 mg of methadone were evaluated by medical staff and were removed from the study if a higher or lower dose was clinically indicated. As noted above, 8 subjects were withdrawn from the study prior to random assignment for this reason; an additional eight subjects were withdrawn following randomization and were considered study dropouts. The average methadone dose for randomized subjects was 77.9 mg; no differences were observed in mean methadone dose across the four treatment conditions.

2.2.2 Urine collection and testing—Subjects submitted urine samples under direct staff observation on a randomized scheduled one time per week. Two types of urine testing procedures were used. Three of the four monthly urine specimens were tested via an on-site

EMIT system that used immunoassay techniques to provide sensitive and specific assays for opiates, barbiturates, cocaine, alcohol, and some benzodiazepines. An additional specimen each month was tested at an off-site certified clinical laboratory that used both thin layer chromatography (TLC) and EMIT procedures for cocaine, alprazolam and clonazepam, and alcohol. Urine samples were included in the report only for subjects who remained active in the study (i.e., were in treatment and had not withdrawn consent or been removed from the evaluation).

2.2.3 Medication take-home doses—All subjects could earn methadone take-home doses after achieving 12-consecutive weeks of negative urine specimens and attendance to all scheduled counseling sessions. Employed subjects could also receive a second and a third weekly methadone take-home dose following additional 30-day periods of abstinence and attendance to scheduled counseling sessions. These incentives were available to all subjects independent of study assignment. Subjects could earn a range of 0 – 3 weekly take-homes of methadone during the study, although unemployed subjects could earn no more than one take-home per week.

2.2.4 Individual counseling—Individual drug abuse counseling was provided by the routine counseling staff with a bachelor's degree in the behavioral sciences. Individual counseling sessions were approximately 30 minutes long (+/- 10 minutes). Counselors completed a psychosocial assessment and master treatment plan for all subjects during the first 4-weeks of treatment (baseline period), and used cognitive-behavioral and motivational intervention approaches to help reduce drug and alcohol use and manage medical, occupational, and other psychosocial problems. Counselors were supervised weekly by masters-trained licensed professional counselors; all counselors worked with a similar number of subjects assigned to each of the four treatment conditions.

2.2.5 Intensified counseling sessions—Group-based counseling was primarily used to intensify the counseling schedule and overall care of subjects. Subjects were referred to one or more of the following groups based on assigned step of care: 1) Chemical Dependency Education (CDEG; 1x/wk), 2) Coping Skills (CSG; 2x/wk), 3) Community Support (CST; 1x/wk), 4) Relapse Control (RCG; 2x/wk), and/or 5) Cognitive-Behavioral Therapy (CBT; 2x/wk). Each group was manual-guided, with the exception of the Cognitive-Behavioral Therapy group. In general, subjects in Step 1 were assigned to attend CDEG, those advanced to Step 2 were referred to RCG, and those moved to Step 3 were assigned to attend CSG, CST, and CBT groups. Exceptions to this schedule were occasionally made to accommodate subjects with specific time constraints or other obstacles to attendance (e.g., previously scheduled appointments; work schedule). Groups were led by licensed professional counselors with a master's degree in the behavioral sciences, licensed clinical psychologists, or board-certified psychiatrists; all staff had a minimum of 3 years of experience in the treatment program. The only group that was not manually-guided (Cognitive-Behavioral Therapy) was led by a licensed clinical psychologist or psychiatrist.

2.3 Description of study conditions

All subjects were administered the Structured Interview for the DSM-IV (SCID-IV; First et al., 1995a & b) and other study assessments during the 4-week baseline. They were stratified on three variables commonly associated with treatment outcome: current cocaine dependence (e.g., Kidorf et al., 1998), antisocial personality disorder (APD; e.g., Woody et al., 1985; King et al., 2001), and current non-substance use Axis I or II psychiatric disorder other than APD (e.g., Rounsaville et al., 1986; Brooner et al., 1997), and then randomly assigned to one of four treatment conditions for 6-months.

2.3.1 Condition 1: Motivated Stepped Care (MSC-only) MSC is an adaptive stepped care service delivery model that adapts intensity of service delivery to objective indices of treatment performance. Subjects with a partial and poor treatment response (i.e., missed counseling sessions and/or drug-positive urine samples) are advanced to more intensive steps of weekly counseling. These subjects are returned to less intensive weekly counseling schedules after achieving a good clinical response (i.e., attendance to scheduled counseling and drug-negative urine samples).

As shown in Figure 1, subjects began at Step 1 and were scheduled to attend one individual drug abuse counseling session per week (30-minutes). Subjects who missed a scheduled counseling session or produced a drug-positive urine specimen (any tested substance) during any 2 consecutive weeks were advanced to Step 2 for 2 to 4 weeks. Subjects advanced to Step 2 were scheduled to attend one individual counseling session, and two group sessions per week. They returned to Step 1 after submitting drug-negative urine specimens and attending all scheduled counseling sessions for 2 consecutive weeks. Failure to meet the criterion for return to Step 1 within 4-weeks resulted in their movement to Step 3 for 8-weeks. Once in Step 3, subjects were scheduled to attend 2 individual counseling sessions and 5 hours of group sessions. They returned to Step 1 by submitting drug-negative urine specimens and attending all scheduled counseling for 4-consecutive weeks. Those who failed to meet this criterion within 8-weeks were started a 30-day methadone dose taper in preparation for discharge.

Additional behavioral contingencies to reinforce counseling attendance and reduced drug use were introduced in Step 3. Subjects who missed scheduled counseling sessions within the first 4 weeks of Step 3 were placed on a series of escalating methadone dosing time restrictions to enhance the inconvenience associated with receiving daily methadone. Participants could reverse the time restriction simply by attending all scheduled counseling sessions for one week. Missing counseling sessions or submitting drug-positive urine samples during the final 4-weeks of Step 3 resulted in a 30-day methadone dose taper that was stopped only after the participant produced one week of full counseling adherence and a drug-negative urine sample. Subjects who met this criterion restarted Step 3 for an additional 8-weeks and returned to their prior maintenance dose of methadone. Subjects who did not meet the criterion were tapered to a methadone dose of 0 and discharged from the program. All subjects discharged from the program were offered rapid readmission: those who attended over 50% of their counseling sessions during the taper were permitted readmission to Step 3 within 24-hours, while those who missed greater than 50% were offered readmission (Step 3) seven days following completion of their medication taper.

2.3.2 Condition 2: Contingent Voucher Incentives (CVI-only) Subjects assigned to the CVI-only condition were offered a system of voucher reinforcement similar to the one developed by Higgins and colleagues (e.g., Higgins et al., 1991) for cocaine-dependent, and later extended to opioid-dependent patients receiving methadone (e.g., Silverman et al., 1996). Subjects earned vouchers for each drug-negative urine submitted, which increased in value as the number of consecutive drug-free urine samples submitted increased. The initial voucher value was \$12.00, while the maximum voucher value was \$160.50. Thirty-dollar bonuses were provided for every string of 3-consecutive drug-free urine samples submitted. When the maximum voucher amount was achieved, subjects continued to earn vouchers worth \$160.50 as long as they submitted drug-free urine samples. Those who remained drug-free for the entire 24-weeks could earn a total of \$3,201.00. Subjects who relapsed to drug use had their voucher amount reset to the initial monetary value (\$12.00). All subjects could exchange vouchers for goods and services from the local community that were purchased by a research assistant. The research assistant also met weekly with counselors to report voucher earnings.

2.3.3 Condition 3: MSC+CVI Subjects assigned to this study condition were exposed concurrently to both the MSC and CVI models described above.

2.3.4 Condition 4: Standard Care (SC) SC subjects were scheduled for one individual counseling session per week throughout the study as a control condition that was designed to reflect standard treatment approaches in programs offering methadone. None of the behavioral contingencies on attendance and drug use that are described in the MSC approach were used in this condition.

2.4 Three-month follow-up

At the end of the 6-month randomized arm of the study, all subjects that remained in the study across the four treatment conditions were assigned to SC (1 individual counseling session per week without attendance contingencies or vouchers) for a 3-month follow-up evaluation to evaluate the stability of any effects observed in relation to the stepped care and/or the voucher-based incentives.

2.5 Data analyses

Chi square tests and analyses of variance (ANOVAs) were used to compare the four study conditions on baseline demographics and substance use, and scheduled and attended counseling sessions and proportion of sessions attended during the 6-month randomized arm of the study. Generalized Estimating Equations (GEE; Zeger et al., 1988; Liang, 1988) compared the study conditions on proportion of missing urinalysis data, using the SC condition as the reference group. Two sets of GEE analyses evaluated the occurrence of urine samples negative for opioids, cocaine, sedatives, (e.g., benzodiazepines), alcohol, or “any drug” use (opioids, cocaine, sedatives, alcohol). The first set used only available data and did not account for condition imbalances in missing data. GEEs were initially run treating “voucher-based” (CVI vs. non-CVI conditions) and “stepped-care” (MSC vs. non-MSC conditions) as main effects in separate regressions. Regressions were run again with both main effects plus an interaction term (MSC $\times$ CVI). Because the primary objective was to evaluate the effectiveness of each of the study conditions, GEE analyses were then run with a four-category condition variable using the SC condition as a reference group. Results are reported using odds ratios with 95% confidence intervals. To account for condition differences in missing urinalysis values, a second set of GEE analyses were conducted using the four-category condition variable and the SC condition as a reference group after imputing a drug-positive result for each missing data point.

Time to first drug-negative urine specimen was analyzed using the Cox proportional hazards regressions, with results reported as Hazards ratios with 95% confidence intervals. Treatment retention was also analyzed using the Cox proportional hazards regression, with results reported as Hazards ratios with 95% confidence intervals. An “event” was defined as leaving the study, either by leaving treatment against medical advice or electing a methadone dose beyond study parameters. Subjects completing the 9-month evaluation were censored to the end of the study period. The same modeling strategy was used for the Cox regressions as was used for the GEE analyses.

3.0 RESULTS

3.1 Baseline demographics and substance use

As shown in Table 1, the four study conditions did not differ in any demographic characteristics or percent of urine samples testing positive for opioids, cocaine, or sedatives during the first 4-weeks of treatment that constituted the baseline evaluation period.

3.2 Counseling attendance

As expected, a between-groups effect was found for both scheduled ($F(3, 232) = 37.2, p < .001$) and attended ($F(3, 232) = 26.4, p < .001$) individual and group counseling sessions during the 6-month randomized arm of the study. Participants in the adaptive stepped-care conditions (MSC+CVI and MSC-only) were scheduled to attend more counseling sessions (MSC+CVI: $M = 45.9, SD = 23.2$; MSC-only: $M = 47.3, SD = 23.2$) and in fact received more sessions (MSC+CVI: $M = 27.9, SD = 23.2$; MSC-only: $M = 26.7, SD = 22.1$) than those assigned to the other treatment conditions (scheduled: CVI: $M = 24.2, SD = 0.93$; SC: $M = 24.1, SD = 0.39$; $p < .05$; attended: CVI-only: $M = 8.5, SD = 5.7$; SC: $M = 7.9, SD = 5.8$; $p < .05$). A between-groups effect was also observed for proportion of scheduled sessions attended ($F(3, 232) = 13.2, p < .001$). Subjects assigned to either of the adaptive stepped-care conditions attended a higher proportion of their scheduled sessions (MSC+CVI: $M = 0.58, SD = 0.31$; MSC-only: $M = 0.52, SD = 0.28$) than subjects assigned to the other treatment conditions employing fixed (non-adaptive) amounts of once per week individual counseling (CVI-only: $M = 0.35, SD = 0.23$; SC: $M = 0.33, SD = 0.24$; $p < .05$).

During the 3-month follow-up arm of the evaluation, subjects in all treatment conditions were scheduled to attend the same amount of weekly counseling (once per week, totaling 12 sessions) without contingencies on attendance or voucher incentives. A between-groups effects was observed for both attendance ($F(3, 232) = 3.1, p < .05$) and proportion of sessions attended ($F(3, 232) = 3.1, p < .05$). Subjects assigned to the MSC+CVI condition received more counseling sessions ($M = 3.0, SD = 3.3$) than those in the MSC-only condition ($M = 1.7, SD = 2.4$; $p < .05$) and attended a higher proportion of their scheduled counseling sessions compared to the MSC only condition ($M = 0.25, SD = 0.27$ vs. $M = 0.14, SD = 0.20$; $p < .05$).

3.3 Drug use: Urinalysis results

GEE analyses showed that one of the treatment conditions (CVI-only) had a lower proportion of missing urinalysis data (9%) than the SC (22%) reference group (OR: 0.40, CI: 0.18-0.88). The remaining study conditions (MSC+CVI, MSC only) did not statistically differ from the SC condition in proportion of missing urinalysis data (MSC-only: 30%; MSC+CVI: 19%).

Urinalysis results are presented for opiate, cocaine, sedative, and “any drug” negative urine samples. Alcohol-positive urine samples were infrequent and did not differ by study condition and barbiturate use was not detected during the study. GEE analyses evaluating urinalysis results during the 6-months of randomized care showed a main effect for MSC for both sedative use (OR = 3.00; CI: 1.51 – 5.94) and “any drug” use (OR = 1.55; CI: 1.05 – 2.28); MSC participants (MSC+CVI and MSC conditions) were more likely to submit sedative-negative (97.7%) and “any drug”-negative (54.7%) urine samples compared to non-MSC participants (CVI-only and SC conditions; 92.2% and 40.2% negative urine samples, respectively). A main effect was also observed for CVI for cocaine use (OR = 1.50; CI: 1.02 – 2.21) and “any drug” use (OR = 1.92; CI: 1.30 – 2.84); CVI participants (MSC+CVI and CVI-only condition) submitted more cocaine-negative (73.3%) and “any drug”-negative (54.5%) urine samples than non-CVI participants (MSC-only and SC conditions; 63.5% and 38.4% negative urine samples, respectively).

Analyses of the MSC by CVI interaction shows that MSC+CVI subjects submitted a greater proportion of opiate, cocaine, sedative, and “any drug” negative urine samples than those in the SC condition (see Table 2). The MSC+CVI condition also generated the highest odds ratios (relative to the SC condition) across each of the study conditions and drug classes. Subjects in both the MSC-only and CVI-only conditions submitted a greater proportion of cocaine and “any drug” negative urine samples than those assigned to SC; MSC-only subjects also submitted a greater proportion of sedative negative urine samples than subjects in the SC

condition. The odds ratios of these two conditions (MSC-only and CVI-only) were similar although the MSC-only condition produced a much higher odds ratio than the CVI condition for sedative use. Analyses of the main effects for the 3-month follow-up show a MSC main effect for cocaine use (OR = 1.83; CI: 1.07-3.13); MSC participants submitted more cocaine-negative urine samples (75.3%) than non-MSC participants (62.0%). Analyses of the MSC $\times$ CVI interaction for the 3-month follow-up show that the MSC+CVI condition sustained significantly better treatment response compared to the SC condition for the cocaine, sedative, and “any drug” classes (see Table 2). In contrast, the MSC-only condition remained different for only cocaine-negative urine samples, while the CVI-only condition was similar to the SC condition across all drug classes.

Additional GEE analyses were conducted to evaluate urinalysis results across all study conditions for Months 1-6 and Months 7-9 after coding each missing urinalysis result as drug-positive. The results of these analyses show that both the MSC+CVI and CVI-only conditions exhibited higher proportions of drug-negative urine samples for cocaine and “any drug” in reference to the SC condition at both the Months 1-6 and Months 7-9 time points. The odds ratios ranged from 1.74 – 3.16 and were comparable across these study conditions. Both the MSC+CVI and CVI-only conditions also submitted a higher proportion of opiate-negative urine samples during Months 1-6 (but not Months 7-9) than the SC condition, while CVI-only participants submitted a greater proportion of sedative-negative urine samples during Months 1-6 (but not Months 7-9). In this set of analyses, the MSC-only condition, which had the largest amount of missing urine data, did not statistically differ from the SC condition.

3.4 Time to first negative urine specimen

Subjects in the MSC+CVI, MSC-only, and the CVI-only conditions were compared to the SC condition on time to first negative urine specimen. A significant main effect was observed for voucher-based incentives for the “any drug” use category, voucher incentives were associated with an earlier onset of first negative urine (OR: 1.50, CI: 1.11-2.03). As expected, significant interactions were observed between voucher incentives and stepped care. The combination of vouchers and stepped care (MSC+CVI) was associated with an earlier onset to first negative urine specimen for 3 of the 4 drug use categories evaluated in the study (opioid negative specimens: OR: 1.50, CI: 1.02 - 2.21; cocaine negative specimens: OR: 1.58, CI: 1.08 - 2.31; combined “any drug” negative specimens: OR: 1.92, CI: 1.24 – 2.98). In contrast, the vouchers only condition (CVI-only) was associated with an earlier onset of negative urine specimens compared to the SC condition for just one of the four drug use outcome measures (“any drug” negative: OR: 1.78, 1.15 – 2.75).

3.5 Treatment retention

Rates of retention for all study groups during the entire 9-month trial were as follows: CVI-only: 72.9%, MSC+CVI: 61.0%, SC: 57.6%, and MSC-only: 44.1%. The Cox proportional hazards regression shows a main effect for subjects assigned to voucher-based reinforcement conditions (MSC+CVI and CVI-only); subjects were more likely to complete the 6-month randomized arm (HR = 1.85; C.I.: 1.18 - 2.90; 73.7% completed randomized arm) and the 3-month follow-up arm of the study (HR = 1.74; C.I.: 1.16 – 2.61; 56.8%) compared to subjects assigned to non-voucher conditions (MSC-only and SC; 58.5% completed the randomized arm and 55.5% the follow-up; see Table 3). Analyses of the condition interactions show that none of the experimental conditions had significantly different retention at either 6-months or 9-months as compared to the SC reference condition.

4.0 DISCUSSION

The present study evaluated the individual and combined efficacy of two treatment approaches that employ primarily negative versus positive behavioral reinforcement strategies (MSC+CVI, MSC-only, CVI-only, respectively) with an adaptive or fixed amount weekly counseling schedule. While prior work has documented the efficacy of both behavioral reinforcement procedures in the treatment of chronic opioid dependence (e.g., Brooner et al., 2004; Silverman et al., 2004), this is the first known study to compare them separately and in combination with reference to a standard care comparison group. As expected, the combination of positive and negative reinforcement with an adaptive stepped-care counseling approach (MSC+CVI) produced the largest positive effects, during both the randomized and three-month follow-up arms of the evaluation. The CVI-only and MSC-only conditions produced similar reductions in drug use, outcomes that were generally better than the standard care (SC) comparison group. The study also showed that voucher-based reinforcement was associated with better retention and better drug use outcome when all missing urine data were coded as drug-positive. As expected, the adaptive stepped-based care conditions were also associated with better patient attendance to scheduled counseling sessions. The implications of these and related findings are discussed below.

4.1 Drug Use: Combining the MSC and CVI interventions

The MSC+CVI condition was associated with the highest rates of negative urine specimens across all categories of drug use. These findings provide additional support for the use of consistent and predictable behavioral reinforcement to improve rates of abstinence (Stitzer et al., 2006), and extends previous research by showing that the combination of escalating levels of negative and positive reinforcement may be more effective than either strategy alone. The fact that these reductions in drug use were largely maintained after removing both the negative (MSC) and positive (CVI) behavioral incentives seems particularly noteworthy. One concern often expressed about monetary voucher-based reinforcement is the potential loss of positive effects once the intervention is withdrawn (e.g., Rawson et al., 2002), which might be especially problematic for patients requiring long-term treatment (Brooner et al., 2004). In the present study, integration of voucher-based behavioral reinforcement with an adaptive stepped-care counseling approach may have helped preserve some of the acute benefits of monetary incentives, thereby rendering this intervention more practical for long-term treatment settings. This point is supported by the follow-up data showing that the MSC+CVI condition sustained comparatively more of their positive treatment response in the 3-month follow-up period compared to the MSC-only and CVI-only conditions. The benefit of combining positive and negative reinforcement with an adaptive care approach was also shown by the earlier onset of drug-free urine specimens in the MSC+CVI versus other treatment conditions.

4.2 Drug Use: Evaluation of the MSC-only and CVI-only conditions

The MSC and CVI conditions independently produced rates of both cocaine and “any drug” negative urinalysis results that were comparably good, and better than those attained by subjects assigned to the SC condition. While the use of monetary voucher-based incentives has a strong track record for reducing drug use in opioid- and cocaine-dependent patients (Stitzer et al., 2006), only one study has been reported on the efficacy of the MSC intervention and it was largely limited to a 90-day evaluation (Brooner et al., 2004). The present findings extend that work in two important ways. First, it extends the time course of the evaluation of MSC to six months. And perhaps most importantly, the present findings demonstrate the successful translation of some of the effectiveness of monetary reinforcement to clinic-based reinforcement procedures (Brooner and Kidorf, 2002; Kidorf et al., 2006), which may be a good (and potentially lower cost) alternative to the use of monetary-based vouchers to deliver effective doses of behavioral reinforcement.

4.3 Treatment retention

The positive association between voucher reinforcement and retention is consistent with prior work showing that monetary vouchers are often related to better retention compared to the use of non-contingent vouchers and treatments that do not employ voucher-based incentives (e.g., Silverman et al., 2004). The lower retention rate associated with stepped-based interventions also suggests that the problems of treatment drop-out associated with interventions that employ negative reinforcement procedures (e.g., Dolan et al., 1985) were not resolved by encouraging patients to attend more counseling (e.g., Simpson et al., 1997) or the specific procedures for rapid reversal of methadone dose tapers and readmission to the program. This issue clearly impacted some of the outcome comparisons in the study, particularly in the MSC-only condition. For example, the significantly lower rate of drug use observed in this MSC-only versus the SC condition was lost when all missing urine data from treatment drop-outs was replaced with drug-positive coding. While the basic analyses comparing these groups that did not adjust for difference in retention represents an “as treated” measure of response, the lower rate of retention in the MSC-only condition is problematic.

The overall findings of the study also suggest a solution to the retention problem. The fact that voucher-based reinforcement increased retention in the basic MSC condition suggest that the addition of positive reinforcement can extend the benefits of this treatment to more patients. Developing strategies to deliver comparable amounts of positive reinforcement without reliance on voucher-based incentives is perhaps the main challenge to this work. This effort would be facilitated by focusing more attention on the positive reinforcing value of the many aspects of routine care. Work in this area has already produced some promising findings and a basic methodology (e.g., Roll et al., 2005; Kidorf et al., 1995). For example, Roll et al. (2005) reported a surprisingly large number of routine treatment aspects that patients in “drug-free” settings rated as positive reinforcers, most of which are applicable to and expand the list of positive reinforcers already identified (e.g., take home doses, expanded medication dispensing times) in patients receiving methadone or other agonist medications (Brooner et al., 1998; Stitzer et al., 2006). More recent research using “low-cost” voucher reinforcement procedures may also make the use of monetary-based vouchers more feasible in community settings (Petry et al., 2005; Perice et al., 2006), although the long-term nature of treatment in many of these patients raise some question about the viability of sustaining even this approach over long periods of time. Strategies that mix low-cost voucher incentives with other positive reinforcement strategies derived from aspects of routine care may be the best approach to extend the benefits of stepped care to more patients.

4.4 Counseling attendance

The adaptive stepped-care conditions (MSC+CVI and MSC-only) were strongly associated with greater attendance to scheduled counseling sessions even though subjects assigned to these conditions were scheduled for a much larger number of sessions. This finding supports previous work showing that behavioral reinforcement can be used to improve counseling attendance and treatment engagement (e.g., Kidorf et al., 1994; Brooner et al., 2004), and that stepped-based models of care with behavioral reinforcement on attendance provide a platform to motivate patients to attend increasing rates of psychosocial care over long periods of time (Brooner and Kidorf, 2002; Kidorf et al., 2006). Counseling attendance and program involvement have been positively associated with better retention and lower rates of drug use in previous studies (e.g., McLellan et al., 1993; Simpson et al., 1997), although it was impossible to isolate the effect of these variables on outcomes in the present study (i.e., as distinguished from the effects of behavioral reinforcement).

4.5 Strengths and limitations

A primary strength of the study is the randomized factorial design that permitted a direct comparison of two approaches for delivering behavioral reinforcement (clinic-based vs. voucher-based) and drug abuse counseling (adaptive vs. fixed schedules) to improve adherence and reduce drug use in opioid-dependent patients receiving methadone, and an evaluation of the effectiveness of combining these two interventions. The study also used an objective measure of drug use (i.e., urine testing) obtained on a schedule of collection and assessment (i.e., 1x / wk) that conforms to rates of drug testing used in many community-based settings (Ball and Ross, 1991). A major weakness of the study is that results are based on a sample recruited from one community-based program that has considerable experience using the adaptive MSC treatment evaluated in the study. It is not clear how findings from this study and study setting will generalize to other populations and clinic settings. The final sample also excluded a number of subjects who left treatment or were removed from the evaluation prior to random assignment. While non-randomized subjects were comparable to randomized subjects on demographic and clinical characteristics other than gender (i.e., somewhat fewer males were randomized), these subgroups may have differed on variables that were not assessed. Finally, the study examined only 6-months of randomized care, which may not be long enough to fully evaluate outcomes in a chronic opioid-dependent population, and similarly too short a time to fully evaluate the effects of the additional verbal therapies received by subjects in the stepped care conditions (Carroll et al., 2000). Similarly, while the inclusion of a the 3-month follow-up evaluation is a strength of the study design, the time period may still have been too short to fully evaluate the stability of improvement after both the 6-month behavioral and stepped care interventions were withdrawn.

4.6 Summary

While each of the enhanced treatment approaches was superior to the standard care condition designed to reflect routine care of opioid-dependent patients receiving methadone, the combination of both positive and negative contingencies embedded within an adaptive stepped care counseling approach (MSC+CVI) produced the best outcomes. The implications of this finding on the further development of our MSC treatment approach is relatively clear -- increase patient exposure to positive contingencies to maximize reduction in drug use and increase retention in treatment. The difficulty is how to accomplish this without relying on the monetary-based voucher reinforcement employed in the present study. While this work will require considerable effort and thoughtfulness, progress in this area is being made (e.g., Roll et al., 2005). Behavioral reinforcement is simply too valuable an intervention to remain hindered by the lack of a more diverse range of platforms to effectively deliver it to patients. The present study also provides good evidence for the efficacy of negative reinforcement procedure to motivate patient attendance to scheduled therapy sessions and reduced drug use for those who remain in treatment, and the stepped care approach that used this behavioral paradigm was clearly more effective than the standard care condition that mimics routine care in many programs offering methadone. There is good evidence that verbal therapies can be helpful to patients suffering from drug dependence, and the MSC approach provides a replicable method for how to adapt the schedule and delivery of these services to patients over the course of treatment.

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Figure 1.

Subjects receiving MSC move to Step 2 for 2-4 weeks after missing any counseling sessions and/or submitting any drug-positive urine specimens during two consecutive weeks; they return to Step 1 after attending all scheduled counseling sessions and producing drug-negative urine specimens for 2-consecutive weeks. Subjects that do not produce at least two consecutive weeks of counseling attendance with drug-negative urine specimens are advanced to Step 3 (4-8 weeks) and must attend all scheduled counseling and provide drug-negative urine samples for 4-consecutive weeks to return to Step 1. Subjects that do not produce 4 consecutive weeks of counseling attendance with drug-negative urine specimens in Step 3 begin a 30-day methadone dose taper in preparation for discharge from the program which is discontinued by attending all counseling sessions for one week and providing a drug-negative urine specimen. Step 3 subjects tapered to a methadone dose of 0 are discharged and offered rapid readmission, starting at Step 3.

Table 1

Baseline demographic and drug use characteristics of sample¹

Variable	Combined Sample (n=236)	MSC-only(n=59) χ^2	CVI-only(n=59) χ^2	MSC+CVI(n=59)	SC(n=59) χ^2	F-test or χ^2	P-value
<u>Demographics Characteristic</u>							
Age (years)	38.46 (7.87)	38.14 (7.83)	38.17 (8.17)	39.03 (8.59)	38.51 (6.96)	0.164	NS
Education (years)	11.33 (2.02)	11.14 (1.94)	11.29 (2.00)	11.15 (2.23)	11.76 (1.89)	1.25	NS
Male (%)	54	56	53	49	58	1.01	NS
White (%)	35	32	36	32	39	0.82	NS
Employed (%)	27	27	19	27	36	4.29	NS
Married (%)	17	12	20	19	17	1.69	NS
<u>Baseline³ Urine Results</u>							
Opioid Positive (%)	47 (0.36)	54 (0.36)	40 (0.36)	48 (0.37)	47 (0.36)	1.54	NS
Cocaine Positive (%)	42 (0.38)	42 (0.37)	41 (0.39)	37 (0.37)	46 (0.38)	0.67	NS
Sedative Positive (%)	7 (0.18)	6 (0.14)	10 (0.23)	6 (0.16)	7 (0.18)	0.66	NS

¹ Means (standard deviation)

² MSC= Motivated Stepped Care; CVI= Contingent Voucher Incentives; SC= Standard Care

³ Baseline= Weeks 1-4 of treatment

Table 2

Comparison of drug negative urine samples across study conditions using GEE

Drug Class	SC(n=59) ¹	MSC-only (n=59) ¹	Odds Ratio(95% CI) ²	CVI-only (n=59) ¹	Odds Ratio(95% CI)	MSC+CVI (n=59)	Odds Ratio(95% CI)
Opioids							
Months 1-6	63.1%	73.3%	1.41 (0.88-2.25)	73.6%	1.52 (0.91-2.54)	77.8%	1.81 (1.14-2.89)
Months 7-9	74.4%	76.1%	1.09 (0.48-2.44)	74.0%	1.02 (0.52-2.03)	79.0%	1.29 (0.63-2.65)
Cocaine							
Months 1-6	56.4%	71.7%	1.76 (1.04-2.99)	70.9%	1.85 (1.08-3.17)	76.0%	2.10 (1.24-3.56)
Months 7-9	54.6%	74.8%	2.50 (1.14-5.49)	68.1%	1.92 (0.96-3.85)	75.7%	2.67 (1.28-5.55)
Sedatives							
Months 1-6	90.9%	97.3%	3.10 (1.24-7.78)	93.3%	1.36 (0.55-3.34)	98.0%	3.90 (1.49-10.22)
Months 7-9	87.5%	91.2%	1.51 (0.43-5.31)	89.5%	1.13 (0.41-3.14)	96.7%	4.12 (1.27-13.34)
Any Drug							
Months 1-6	29.3%	47.8%	1.91 (1.09-3.36)	49.6%	2.36 (1.31-4.24)	60.0%	3.04 (1.75-5.30)
Months 7-9	32.9%	47.8%	1.77 (0.82-3.84)	45.8%	1.69 (0.82-3.47)	53.1%	2.16 (1.04-4.48)

¹ SC= Standard Care; MSC= Motivated Stepped Care; CVI= Contingent Voucher Incentives

² Odds Ratios report the odds of submitting a drug negative urine sample using the SC condition as a reference group; CI=confidence interval; bolded values denotes statistical significance at p<.05.

Table 3
Retention across study conditions: Main effects of voucher-based¹ and stepped-care¹ approaches.

Condition	Six-Month Retention ²		Nine-Month Retention ²		Hazards Ratio (95% CI)
	CompletedStudy (#)	CompletedStudy (%)	CompletedStudy (#)	CompletedStudy (%)	
Voucher-based					
Yes (n=118)	87	73.7	79	56.8	1.74 (1.16-2.61)
No (n=118)	68	57.6	60	43.2	
Stepped-care					
Yes (n=118)	69	58.5	62	52.5	0.65 (0.43-0.97)
No (n=118)	86	72.9	77	65.3	

¹ Voucher-based: yes= MSC+CVI and CVI-only conditions, no= MSC-only and SC conditions; Stepped-care: yes= MSC+CVI and MSC-only conditions, no=CVI-only and SC conditions

² Retention is percent of patients completing study.

³ Hazards ratio= odds of completing study; CI=confidence interval; bolded values denotes statistical significance at p<.05.