Single- Versus Dual-Drug Target: Effects in a Brief Abstinence Incentive Procedure

Christopher J. Correia, Jesse Dallery, Elizabeth C. Katz, Kenneth Silverman, George Bigelow, and Maxine L. Stitzer
Johns Hopkins University School of Medicine

The number of drugs targeted may have an important influence on the ability of drug abusers to abstain during motivational incentive procedures. The authors investigated outcomes in methadone maintenance patients (n = 58), who had evidence of both opiate and cocaine use, when continuous abstinence from cocaine only (single target) or from both cocaine and heroin (dual target) was required to earn $200 in voucher incentives over a 4-day period. Study patients were equally likely to initiate and sustain abstinence from cocaine under the single- versus the dual-drug target. They were more likely to initiate opiate abstinence under the dual-target condition, demonstrating sensitivity to reinforcer effects. Results suggest that adding a second drug target does not impede short-term cocaine abstinence initiation.

The use of illicit drugs during methadone maintenance treatment is common. Despite the fact that methadone blocks or attenuates the effects of opiates, up to 60% of methadone patients continue to use heroin during their treatment (e.g., Stitzer & Chutuape, 1999). Studies have also reported high rates of cocaine use (Grella, Anglin, & Wugalter, 1997; Kidorf & Stitzer, 1993) and cocaine dependence (Brooner, King, Kidorf, Schmidt, & Bigelow, 1997) among methadone patients. Patients who continue using cocaine during methadone treatment are particularly difficult to treat (Condelli, Fairbank, Dennis, & Rachal, 1991) and are at greater risk for a host of negative outcomes, including HIV infection (Grella, Anglin, & Wugalter, 1995; Meandzija, O’Connor, Fitzgerald, Rounsaville, & Kosten, 1994), unemployment (Zanis, Metzger, & McLellan, 1994), and criminal activity (Hunt, Spunt, Lipton, Goldsmith, & Strug, 1986; Rothbard et al., 1999).

Voucher-based contingency management procedures have been used to effectively decrease drug use in a variety of clinical settings and contexts (for reviews, see Higgins & Silverman, 1999; Petry, 2000). In a typical program, patients earn vouchers in exchange for providing urine specimens that are free of the targeted drug or drugs. Thus, voucher programs give patients specific behavioral goals and provide them with tangible rewards when those goals are met. Earned vouchers can be used to purchase goods and services in the community, which are meant to facilitate drug-free treatment goals and increase the density of reinforcement derived from drug-free sources. The majority of studies demonstrating the efficacy of voucher-based contingency management procedures have targeted single drugs, including alcohol (Petry, Martin, Cooney, & Kranzler, 2000), marijuana (Budney, Higgins, Radonovich, & Novy, 2000), opiates (Silverman, Wong, et al., 1996), and cocaine (Higgins, Badger, & Budney, 2000; Higgins et al., 1993, 1994; Silverman, Chutuape, Bigelow, & Stitzer, 1999; Silverman et al., 1998; Silverman, Higgins, et al., 1996).

In contrast, relatively few studies have investigated the use of vouchers to promote abstinence from multiple drugs among methadone patients, and all but one (Petry & Martin, 2002) of these studies have reported only modest results. For example, Piotrowski et al. (1999) randomly assigned patients (n = 102) to methadone treatment alone or enhanced treatment with contingency management. Initially, contingency management patients received reinforcement for abstaining only from illicit opiates and cocaine; later (Months 2–4), voucher earnings were based on abstinence from alcohol, amphetamines, barbiturates, benzodiazepines, and marijuana, as well as opiates and cocaine. The mean duration of longest continuous abstinence was 2 times longer in contingency management (7.6 days) patients than in usual care control (3.3 days) patients, and this difference was also reflected in percentage of drug-free samples submitted during the study (28.5% vs. 16.3% drug-free samples). However, these results are clinically modest and nearly half of the participants offered the voucher program failed to produce a single drug-free urine specimen. Similarly, in a study by Downey, Helmus, and Schuster (2000) targeting polydrug abstinence among buprenorphine-maintained participants, there were no significant differences between ex-
perimental and usual care control groups on drug use outcomes, and more than half of the study participants failed to provide even a single drug-free urine that would have allowed them to come in contact with the reinforcer.

A study by Petry and Martin (2002) used a prize reinforcement system to target both opiate and cocaine abstinence in methadone patients. Patients in the contingency management condition earned chances to draw slips from a bowl and win prizes ranging from $1 to $100 in value. Patients earned a single draw for prizes when a urine free from either opiates or cocaine was submitted and additional draws for specimens negative for both drugs. The procedure ensured contact with the available reinforcers, and every patient earned at least one prize. Significant differences were obtained between contingency management and usual care groups for both percentage of opiate- and cocaine-free urines submitted and for longest duration of abstinence.

The studies reviewed above suggest that it is more difficult for opiate abusers enrolled in maintenance substitution treatment to respond to monetary-based contingency management interventions when abstinence from multiple versus single drugs is required to earn voucher reinforcers. Further, the studies suggest that one mechanism behind the poor outcomes is that a majority of patients are unable to initially meet the polydrug abstinence requirement in order to sample the reinforcer and potentially become engaged in the contingency management program. However, no study to date has directly compared the outcome of a contingency management program when single versus multiple drugs have been targeted while using a procedure that ensures more reliable reinforcer sampling.

Recently, a group of investigators (Robles et al., 2000) developed a procedure that they called the Brief Abstinence Test (BAT). This is a voucher-based contingency management procedure specifically designed to initiate abstinence in the largest possible proportion of patients by using a combination high reinforcer magnitude and low response requirement. The BAT uses quantitative urinalysis results to detect brief periods of abstinence by tracking changes in levels of drug metabolite; to date, this procedure has only been used to detect the cocaine metabolite, benzoylecgonine (Preston, Silverman, Schuster, & Cone, 1997). In the initial BAT study, patients could earn a $100 voucher for providing evidence of 2 days of cocaine abstinence, which was inferred if there was a 50% reduction in urinary benzoylecgonine concentrations over a 2-day period or if the urine specimen contained less than 300 ng/ml of benzoylecgonine. The procedure resulted in approximately 80% of the patients meeting the quantitative abstinence criteria. In contrast, only 36% and 32% met these abstinence criteria during the week before and the week after the incentive intervention, respectively, when no abstinence incentives were offered. A follow-up study (Katz et al., 2002) replicated the results of the initial study and extended the findings by demonstrating that the BAT procedure could be used to promote cocaine abstinence over a 2-week period.

The BAT procedure provides an efficient method to study the effect of variables, such as the number and type of drug targets, on abstinence initiation. By offering high magnitude reinforcers, this procedure maximizes the likelihood of abstinence initiation and therefore contact with the reinforcer. Further, the BAT potentially allows for a determination of drug-target effects under a variety of reinforcement conditions, one of which is tested here. Because the use of heroin and cocaine are closely associated in methadone patients (e.g., Hartel et al., 1995), it may be possible to target both simultaneously in a voucher incentive program without negatively affecting success rates. In this study, a within-subject design was used to compare abstinence initiation outcomes when a single-drug (cocaine) versus a dual-drug (cocaine and opiate) target was required to earn reinforcers. The study results are relevant to the design and clinical use of future voucher incentive interventions.

**Method**

**Sample Characteristics**

Study participants were 87 cocaine-using methadone maintenance patients enrolled between January 2000 and February 2001 at the Behavioral Pharmacology Research Unit’s methadone treatment research program. All patients were intravenous opiate users with at least 1 year of opiate dependence, as assessed by the Structured Clinical Interview for DSM–IV Axis I disorders (SCID; Spitzer, Gibbon, & Williams, 1986). Other inclusion criteria included being between the ages of 18 and 55, absence of serious medical and psychiatric disorders, and submission of an opiate- and cocaine-positive urine specimen during the intake and admission procedure. Because the study was designed to evaluate and compare two different drug targets, eligible participants were those who showed evidence of continued use of both heroin and cocaine during the study. Thus, 29 of the original 87 patients met the original inclusion criteria but were deemed inappropriate for an evaluation of the two experimental conditions and excluded from the analysis of outcomes. Of these 29, 18 failed to complete both experimental conditions, and 11 completely abstained from cocaine use, opiate use, or both during the study. The 58 remaining patients completed both interventions and displayed evidence of continued drug use during the study (defined as submitting at least one cocaine-positive urine test and one opiate-positive urine test over the course of the study), thus making them the most appropriate sample for evaluating the effects of the two experimental conditions in our within-subject design. Demographic, diagnostic, and baseline drug use information for all 87 patients initially screened—the 29 excluded and the 58 included patients—is presented in Table 1.

**Standard Treatment**

The study was conducted with new admissions to the methadone maintenance program. All patients received weekly individual counseling and group therapy. Methadone doses were stabilized during the first 3 weeks of treatment and were not disclosed to study patients or to staff in contact with them. All patients received an initial methadone dose of 30 mg and received 10-mg daily increases until they reached 60 mg. Patients were required to attend the clinic daily for the duration of the study to receive their methadone doses. Urine samples were collected three times per week on Monday, Wednesday, and Friday. Patients who completed the study were evaluated for admission into other ongoing studies or long-term methadone maintenance treatment. Those patients who were not retained were offered a 90-day methadone
detoxification. Patients were terminated from treatment and the study if they missed 3 consecutive dosing days.

**Experimental Design**

The study used a within-subject design in which each participant was exposed to two experimental conditions of 1-week duration with a 2-week washout period interposed. During each experimental week, single- and dual-drug target conditions were tested in counterbalanced order.

**Experimental Procedures**

Under the single-drug target condition, patients could earn voucher incentives for evidence of cocaine abstinence. Under the dual-drug target condition, patients were required to abstain from both cocaine and opiates to earn voucher incentives. Experimental conditions began on the Monday of treatment Weeks 4 and 7, when patients were told they would earn vouchers if their urine test results indicated that they abstained from the targeted drug or drugs, and the rules of the relevant incentive condition were explained. Voucher earnings were identical during both experimental conditions: Patient’s earned a $100 voucher if they met criteria for abstinence from the target drug or drugs between Monday and Wednesday; an additional $100 could be earned for evidence of continued abstinence until Friday. This 5-day test duration was selected because a previous study using a 2-week intervention (Katz et al., 2002) indicated that most relapse occurred by the second reinforcement opportunity. Voucher incentives had monetary value that could be exchanged for goods and services in the local community. All incentive purchases were made by staff, and no money was given directly to participants.

**Abstinence Criteria**

During Weeks 3 through 8 of the study, all urine specimens were subjected to on-site quantitative urinalysis testing. Cocaine and opiate metabolite concentrations were measured by an enzyme multiplied immunoassay technique. The assays were performed with Dade-Behring reagents (Dade-Behring Inc., Cupertino, CA) on a Syva 30R instrument (Syva Company, San Jose, CA) according to the manufacturer’s recommended procedures. The linear range of the assay was 0–3,000 ng/mL for cocaine and 0–4,000 ng/mL for opiates. Specimens that contained concentrations of cocaine, opiates, or both above the cutoff were diluted with distilled water until results fell within the linear assay range. Abstinence criteria for reinforcer delivery was based on quantitative urinalysis procedures developed by Preston and colleagues (Preston et al., 1997). Under the single-drug target condition (cocaine only), abstinence was inferred if there was a 50% reduction in urinary benzoylecgonine concentrations over a 2-day period (Monday to Wednesday or Wednesday to Friday) or if the urine specimen contained less than 300 ng/ml of benzoylecgonine. Under the dual-drug target condition (cocaine and opiates), abstinence was inferred if there was a 50% reduction in urinary concentration of both benzoylecgonine and morphine over a 2-day period or if the urine specimen contained less than 300 ng/ml of both benzoylecgonine and morphine.

**Data Analysis**

Three primary outcomes were measured during intervention Weeks 4 and 7: (a) number of vouchers earned, (b) percentage of participants abstinent from cocaine for 2 (Monday–Wednesday) and 4 (Monday–Friday) days, and (c) percentage of participants abstinent from opiates for 2 (Monday–Wednesday) and 4 (Mon-
Results

Percentage of Participants Abstinent: Preintervention

Baseline urine test results during 3 weeks prior to study intervention are shown in Table 1. Percentage of urines positive for cocaine, opiates, or both ranged from 78% to 84%. We also examined urine test results on the Monday of each experimental test week using qualitative (EMIT) testing. Percentage of urines testing negative on Monday of the single- and dual-target test weeks, respectively, was 15.5% and 17.5% for cocaine and 24.1% and 26.3% for opiates.

Voucher Earnings: Single- Versus Dual-Target Incentive Phase

Participants could earn zero, one, or two vouchers during each study condition. Mean vouchers earned was 1.22 and 1.09, respectively, under the single- and dual-target conditions. A chi-square test comparing the two conditions failed to reach statistical significance, $\chi^2(2, N = 58) = 3.65, p = .16$. The majority of participants (52%) earned vouchers under both conditions. A few (14%) failed to earn vouchers under either condition. Participants who earned under only one condition were equally likely to do so under the single (17%) or dual (17%) target.

Percentage of Participants Abstinent: Single- Versus Dual-Target Incentive Phase

Linear mixed models analysis revealed no statistically significant condition effects for either drug examined (cocaine, opiates). Significant time effects were found for both cocaine, $F(1, 171) = 13.4, p < .001$, and opiates, $F(1, 171) = 21.3, p < .001$. A significant Condition $\times$ Day interaction term was found only for opiates, $F(1, 171) = 6.8, p < .01$.

Figure 1 depicts rates of sustained cocaine abstinence over time as derived from quantitative urine testing outcomes. Percentage of participants initiating cocaine abstinence was virtually identical under the single- (69%) versus dual-drug (71%) target conditions. In both cases, rates of abstinence were substantially higher than rates of abstinence detected in qualitative testing on Monday. Relapse was observed from Wednesday to Friday in both study conditions, with the extent of relapse being similar under the two conditions. In planned comparison testing, there was not a significant difference across conditions in percentage of participants sustaining 4 days of cocaine abstinence (53% and 45% in single- versus dual-target conditions, respectively).

Figure 2 shows rates of sustained opiate abstinence over time. In contrast to cocaine, rates of opiate abstinence varied as a function of drug-target condition. The percentage of participants testing abstinent from opiates was significantly higher when opiates were included as a target drug and abstinence was required to earn incentives than when the incentives target was only cocaine (64% abstinent for the single target vs. 84% abstinent for the dual target; $Z = 2.56, p < .05$). In both cases, these rates of abstinence are higher than rates observed on Monday of the intervention weeks. The significant Condition $\times$ Day interaction term for opiates is seen in the steeper relapse function for opiates under the dual- versus under the single-drug target, such that there was no longer a significant difference between the groups when we examined the percentage of participants abstaining for 4 days (Monday–Friday) in post hoc testing (46.6% and 58.6% in single- versus dual-target conditions, respectively; $Z = 1.53, ns$).

Discussion

In this study we used a brief abstinence model to provide new evidence about the influence of single- (cocaine) versus dual-drug (opiate and cocaine) targets on the ability of opiate-dependent methadone maintenance patients to abstain from cocaine. Using a procedure in which high value reinforcers of $100 were offered for evidence of brief abstinence, the study revealed no significant differences in rates of cocaine abstinence initiation or rates of sustained...
(4-day) abstinence when one versus two drugs was targeted (see Figure 1). Consistent with the findings of Petry and Martin (2002), these results from a short-term abstinence procedure suggest that it may be possible to target both opiates and cocaine simultaneously in a voucher incentive program without negatively affecting success rates, particularly under conditions where reinforcer sampling is ensured.

The similar results seen for cocaine abstinence under the single- and dual-target conditions do not appear to be due to either the ineffectiveness of the intervention or the insensitivity of the study participants to the dual-drug target intervention. In other words, participants were sensitive to the demands of each condition. This is supported by the significant difference in rates of opiate abstinence observed when opiates were included as a target drug in the contingent reinforcement intervention (see Figure 2), a finding consistent with previous observations of voucher incentive effects in studies targeting opiate use (e.g., Silverman, Wong, et al., 1996). Thus, the dual-drug target increased rates of opiate abstinence initiation and did not have a negative effect on rates of cocaine abstinence initiation.

Results obtained in the present study for rates and patterns of cocaine abstinence during the BAT are consistent with observations from a previous study that used the procedures to motivate temporary cessation of cocaine use in methadone maintenance patients (Katz et al., 2002). Specifically, approximately 70% of participants initiated cocaine abstinence in both studies when $100 was offered as the reinforcer, and the extent of cocaine relapse was also similar, with about 50% of participants sustaining abstinence over 4 days when an additional $100 could be earned for doing so. This consistency of findings across studies using the same methods supports the reliability of the BAT. This is also a promising feature of the model that supports its use for examining variables that may influence the relapse process.

The findings of the present study have important implications for the use of voucher incentive programs in community clinical practice. With the notable exception of Petry and Martin (2002), most of the research conducted to date demonstrating the efficacy of contingency management procedures has focused on a single-drug target, with little consideration for any other drugs that the participants might be using (Higgins et al., 1993, 1994; Stitzer, Bigelow, Liebson, & Hawthorne, 1982). Fortunately, this approach has led to successful clinical outcomes that generalize beyond reductions in the targeted drug. In fact, reductions in secondary drug use (e.g., opiates) have frequently been observed when a primary drug such as cocaine is targeted (e.g., Jones, Haug, Silverman, Stitzer, & Svikis, 2001; Silverman et al., 1998), and this was also the case in the present study, as can be seen by comparing opiate abstinence under the single-target condition (see Figure 2) with baseline data. Nevertheless, clinicians may object to the use of single-drug targets because they feel the need to focus their clients’ attention on total abstinence from all drugs (Rounsaville, Petry, & Carroll, 2003). If multiple drugs could be targeted without loss of efficacy, this would make voucher incentive procedures more acceptable to clinicians. Thus, studies such as the present one are needed to provide information that can lead to further tailoring of voucher incentive procedures so that they can meet the needs of both treatment participants and clinicians without sacrificing efficacy.

The BAT was designed as a useful way to obtain time-efficient initial information about factors that influence relapse. However, the same feature (brevity) that makes the BAT useful as a model of abstinence initiation and relapse is also a limitation of the technique. It is worth noting, for example, that the slope of the cocaine relapse curve (see Figure 1) was slightly steeper in the dual- versus single-drug conditions. This, combined with the relapse to opiates observed in the dual-target condition (see Figure 2), suggests that over time, the slopes of these functions might have become increasingly disparate, with higher rates of relapse in the dual- than in the single-target condition. Thus, a limitation of the study is that different results might have been obtained if the interventions were carried out over a lengthier period of time. Given the clinical importance of the question, such a study would be warranted.

Two other limitations of the study are also worth noting. The study was conducted after only 3 weeks of stabilization in methadone maintenance treatment; different results might have been obtained if the study was conducted later in treatment. Finally, in the study we used a single high-monetary incentive value; we might have obtained different results had we used other monetary incentive values. In fact, it would be important to conduct additional studies using a
range of incentive values because the high-magnitude reinforcer used here may have produced a “ceiling” on behavior change and precluded observation of differences across experimental conditions.

In sum, this study replicates previous research by demonstrating that the BAT procedure can be used to initiate cocaine abstinence in a high percentage of methadone patients. It extends previous findings by using the BAT to investigate the effect of single- versus dual-drug target on a patient’s ability to initiate and sustain a limited period of abstinence. The study showed that under the conditions of high-magnitude reinforcement used, methadone maintenance patients who used both opiates and cocaine were equally likely to initiate and sustain brief abstinence from cocaine whether or not concurrent abstinence from opiate drugs was required to earn reinforcement. Thus, the study failed to support the view that it is more difficult for drug abusers to achieve short-term abstinence from multiple than from single drugs. However, because the BAT represents a special set of intervention circumstances (high-magnitude reinforcement delivered over a brief time period), more research is needed to further clarify the generality of these findings and to characterize the influence on rates and patterns of abstinence of both the number and type of drug targets selected for contingency management intervention.

References


