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Voucher-based reinforcement of opiate abstinence during methadone detoxification

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Abstract

Methadone detoxification is often used in the treatment of opiate dependence. This procedure, however, is frequently associated with continued opiate use, and high rates of attrition and relapse. In this study, a 90-day methadone detoxification was enhanced by adding voucher-based reinforcement of opiate abstinence before, during and after the dose tapering schedule. After 4 weeks of standard methadone maintenance (baseline), subjects were randomized to either the abstinence (n = 26), or attendance reinforcement (n = 22) condition. During the remaining 22 weeks of the study, the abstinence reinforcement group could receive vouchers with monetary value three times per week for providing opiate-negative urine specimens, while subjects in the attendance reinforcement group received vouchers of equal value for attending the clinic, regardless of urinalysis results. Methadone maintenance continued during weeks 5-10, dose tapering was implemented during weeks 11-23, and during weeks 24-26 the voucher schedule remained in effect but no medication was provided. Fifty percent of clients in both groups completed dose tapering, and 40% completed the vouchers-only phase. Subjects in the abstinence as compared with the attendance reinforcement group had lower rates of opiate use during the maintenance and detoxification phases, and longer periods of opiate abstinence during the detoxification phase. Cocaine use was also lower in the abstinence than the attendance reinforcement group during the maintenance and detoxification phases. In addition, abstinence as compared with attendance reinforcement subjects reported significantly fewer intravenous injections during the detoxification phase. Voucher-based reinforcement procedures could be useful for successfully transitioning patients into opiate antagonist therapy, or drug-free treatments. © 2002 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

Methadone detoxification is very frequently offered as a form of treatment for opiate dependence. For example, the Substance Abuse and Metal Health Services Administration (SAMHSA, 1999) reports that during 1997, of all opiate dependence admissions recorded in the Treatment Episode Data Set system (N = 232, 920), 50% received detoxification (short or long-term) as the primary form of treatment. In maintenance clinics, detoxification is regularly offered as a

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method to end substitution therapy with methadone or LAAM (*levo*-alpha-acetylmethadol). Time to detoxification varies widely from clinic to clinic, but a survey of methadone maintenance programs in the US has shown that clients are encouraged to detoxify after an average of 3 months of methadone maintenance (D'Aunno and Vaughn, 1992). Moreover, detoxification is often offered as a humane method to ameliorate withdrawal symptoms in cases of unrelated hospitalization or impending incarceration of narcotic dependent individuals. In short, detoxification from opiates is a standard feature of current narcotic addiction treatment practice in the US.

Although successful detoxification from opiates is achieved by some patients (Cushman and Dole, 1973;

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Jaffe, 1970; Stimmel and Rabin, 1974; Riordan et al., 1976), use of illegal opiates very often occurs before the detoxification schedule has been completed (Iguchi and Stitzer, 1991; Kleber, 1977; Sees et al., 2000). In addition, available figures indicate that 12-86% of the patients undergoing detoxification do not complete the program (Milby, 1988; Sees et al., 2000; Steer et al., 1978), and even fewer patients (0-10%) remain abstinent a year after undergoing detoxification (Canada, 1972; Maddux et al., 1980; Wilson et al., 1975). That is, evidence suggests that, despite being relatively inexpensive (at least in its outpatient form) and quite prevalent, gradual detoxification from opiates is of limited efficacy when provided as primary treatment for opioid addiction, and a predictor of poor outcome when given to most maintenance treatment clients.

Methadone detoxification could be potentially improved by reducing the number of patients who continue to use opiates during the procedure, and by increasing the number of patients who complete it. In general, attempts to enhance outcome from methadone detoxification have at most achieved modest levels of success. To date, one of the most promising strategies has been the addition of contingency management procedures during the detoxification. In the following paragraphs we describe some of those attempts.

In a study by McCaul et al. (1984), patients in an experimental group received \$10 and one take-home dose when they provided opiate-negative specimens during a 90-day (13-week) detoxification. These patients provided significantly more opiate-negative specimens than the control detoxification group during weeks 4-9; however, the difference was no longer significant after treatment week 10. Higgins and collaborators (1986) compared two procedures in which supplemental methadone was used to reinforce abstinence during a 90-day detoxification. Patients in one group received a choice of 5, 10, 15, or 20 mg of additional methadone per day when they provided an opiate-negative urine specimen. Patients in another group could receive similar amounts of additional methadone without being required to provide opiate-negative samples. The abstinence-contingent group consistently provided more opiate-negative specimens than the non-contingent and control groups, but as in the case of McCaul et al. (1984), the difference was no longer significant after treatment week 9. Overall, both studies show that contingency management procedures can aid in sustaining abstinence from opiates during detoxification. In addition, these studies reveal the long recognized importance of the methadone dose (Mintz et al., 1975) in sustaining opiate abstinence during the tapering procedure.

Recently, voucher-based reinforcement was successfully used to increase abstinence from illegal opiates in methadone maintenance patients (Silverman et al.,

1996). In that study, methadone patients received vouchers with monetary value for providing opiate-free urine specimens, using a schedule similar to that developed by Higgins et al. (1991, 1994). The study showed that the percentage of opiate-positive specimens decreased significantly from 78% during a 5-week prestudy baseline to 24% during the 12-week voucher intervention. When the voucher intervention was discontinued during an 8-week follow-up period, the peropiate-positive specimens centage increased significantly to 41%. However, illicit opiate use remained well below baseline levels during the final phase, suggesting lasting beneficial effects of opiate abstinence reinforcement in methadone patients. Voucher-based reinforcement was also recently used by Bickel et al. (1997) to sustain opiate abstinence and adherence to counseling requirements during a 90-day buprenorphine detoxification. Their results showed that patients receiving the behavioral treatment intervention remained in treatment significantly longer. In addition, significantly more patients in the behavioral treatment group achieved at least 8 weeks of continuous abstinence.

Since voucher-based reinforcement has effectively increased abstinence from opiates during methadone maintenance and has helped to sustain abstinence during a buprenorphine detoxification, we hypothesized that it might also be effective in establishing abstinence and then sustaining it through a methadone detoxification. The purpose of this study was to assess whether an escalating schedule of voucher-based reinforcement can sustain abstinence from illegal opiates before, during and after a 90-day methadone detoxification schedule.

2. Methods

2.1. Subjects

Fifty opiate dependent volunteers were recruited. One volunteer left the study before randomization and another received an alternative detoxification schedule; their data are not included in the analyses presented here. The screening interview was followed by a medical exam, urinalysis, blood work, and a battery of assessment instruments. The assessment instruments included the Structured Clinical Interview for DSM-IV (SCID. First et al., 1995), the Addiction Severity Index (ASI, McLellan et al., 1985), and the Beck Depression Inventory (BDI, Beck and Steer, 1987). Volunteers qualified to participate if they were between 18 and 65 years old, eligible for methadone maintenance according to US Food and Drug Administration guidelines, and reported intravenous opiate use during the past 30 days. Pregnant women, and applicants with current major

psychiatric disorders other than drug abuse or unstable serious medical illness were excluded. Volunteers signed a consent form approved by the local Institutional Review Board, and were tested to ensure they understood the study and procedures. Characteristics of the final study sample (n=48) are presented in Table 1. Information on diagnosis of Antisocial Personality Disorder (APD) is missing for one participant in the abstinence reinforcement group and two participants in the attendance reinforcement group. There were no significant differences (P>0.05) between the two groups on any of the characteristics listed on the table.

Table 1 Characteristics of the study sample^a

	Abstinence reinforcement group	Attendance reinforcement group
Demographic data:	N = 26	N = 22
Mean age (year)	41.0	40.4
% Male	69.2	59.0
% White	34.6	50.0
% Employed part-time	19.2	18.2
% Employed full-time	30.8	31.8
% Unemployed	50.0	50.0
Mean legal income (past 30 days)	732.9	754.3
Mean illegal income (past 30 days)	10.0	11.4
Mean ASI composite scores	:	
Medical	0.23	0.28
Employment	0.62	0.63
Alcohol	0.06	0.04
Drug	0.21	0.17
Legal	0.02	0.05
Family/social	0.07	0.03
Psychological	0.05	0.00
SCID diagnoses: % APD diagnosis % Current dependence	28 (N = 25)	15 (<i>N</i> = 20)
Opiates	100.0	100.0
Cocaine	53.9	59.0
Alcohol	11.5	9.0
Sedative/hypnotics	7.7	31.8
HIV-risk (Past 5 year):		
% HIV-positive diagnosis	7.1 (N = 18)	5.6 (N = 14)
% Reporting needle sharing	$55.6 \ (N=18)$	$78.6 \ (N = 14)$
% Reporting using condoms	66.7 $(N = 18)$	55.6 $(N = 14)$
Baseline drug use:		
% Opiate-positive tests	67.3	64.4
% Cocaine-positive tests	62.2	50.0
Mean total self-reported injections	0.5	0.4
Mean baseline methadone dose (mg/day)	76.4	70.3

^a Where data are missing, the sample size used for computations is reported in parentheses.

2.2. Standard treatment

All participants were stabilized on methadone during the first week and remained unaware of their methadone dose throughout the study. Maintenance doses ranged from 60 to 100 mg, with means of 76.4 and 70.3 mg for the abstinence reinforcement and attendance reinforcement groups, respectively (P = 0.25). Methadone maintenance treatment included daily methadone, one hour per week of individual counseling, and one hour per week of group therapy. Additionally, all participants were required to provide a urine sample three times per week, and were given a battery of computerized self-administered assessments each week.

2.3. Weekly self-report assessments

Assessments included the Beck Depression Inventory (Beck and Steer, 1987), the Past Week Non-IV Drug Use and Daily IV Use questionnaires, and the Lifestyle Changes, Weekly Dose Visual Analog Scale questionnaires (Silverman et al., 1999a). In addition, all participants completed the Drug Availability questionnaire, a six-item computerized assessment that explores current availability of cocaine and opiates in the participant's house and neighborhood, and the number of times that these drugs have been offered for sale or exchange in the last 7 days. The Daily IV questionnaire, a computerized self-administered instrument, required participants to recount separately the number of intravenous injections of heroin, other opiates, cocaine, speedball (i.e. heroin combined with cocaine), and other drugs for each of the preceding 7 days. Self-report of withdrawal symptoms was collected weekly using a computerized Visual Analog Scale (VAS) assessment (Jones et al., 1998).

2.4. Design and experimental procedures

The study lasted 26 weeks. During weeks 1–4 participants received the standard methadone maintenance treatment (methadone only). Random assignment to study conditions occurred at the end of week 4. During weeks 5–10 all participants continued receiving standard methadone maintenance treatment and they also received vouchers (methadone plus vouchers) according to their assigned treatment condition as described below. All participants received methadone dose tapering to 0 mg during the following 13 weeks (11–23) while they continued to receive vouchers according to their treatment condition (detoxification plus vouchers). Finally, during weeks 24–26 all medication was discontinued but voucher conditions remained in effect (vouchers only).

2.5. Detoxification schedule

Methadone dose was reduced gradually on a percentage basis to account for initial starting doses. The tapering schedule expressed as percentage of maintenance dose (detoxification weeks given in parentheses) was: 90% (1), 80% (2), 70% (3), 60% (4), 50% (5), 40% (6), 32% (7), 24% (8), 16% (9), 8% (10), and 0% (11–13). The volume of the liquid medication dispensed (methadone plus cherry syrup) remained constant at 40 cm³.

2.6. Urine collection and testing

Urine specimens were collected every Monday, Wednesday and Friday under observation by trained technicians, and immediately temperature-tested to determine their validity. If a urine specimen measured above 99°F or below 94°F, the participant's tympanic temperature was taken. If the ear temperature was 1.4° above the urine temperature, or if the urine temperature was greater than the ear temperature, the sample was discarded and the participant was required to leave a second specimen. All specimens were tested for opiates and cocaine using an on-site Enzyme Multiplied Immunoassay Technique system (EMIT; Behring-Syva Corp., Palo Alto, CA). Participants who did not deliver a urine specimen on a designated collection day were required to do so on the following day. However, those specimens were not included in data analyses.

2.7. Stratification and random assignment

At the end of week 4, participants were stratified and randomly assigned to either the abstinence reinforcement or the attendance reinforcement condition. Participants were stratified on six baseline characteristics: rate of opiate-positive urine specimens during baseline (100% vs. < 100%), rate of cocaine-positive urine specimens during baseline ($\geq 50\%$ vs. < 50%), diagnosis of Antisocial Personality Disorder (yes/no), employed full time during most of the past 3 years (yes/no), race (white, yes/no), and gender (M/F). Participants were assigned a binary score (0 or 1) on each of these six characteristics. The number of possible combinations of such binary scores (i.e. 011010) is 64. For each possible combination of stratification scores the first participant was randomly assigned to a study condition. The next participant with the same combination of characteristics was assigned to the other group. The third participant would again be randomly assigned, etc. This procedure assured that many participants were randomly assigned but that no single combination of characteristics would be significantly over-represented in a group. In order to follow the paired control procedure described in the following section, there was an exception to this stratification procedure; the first three participants reaching week 4 were assigned to the abstinence reinforcement group. As shown in Table 1, the resulting groups did not differ significantly in any of the categories used for stratification.

On the day of randomization, participants were informed of their group assignment and received a printed description of the voucher-based reinforcement contingencies for their treatment group. In addition, a member of the staff explained all relevant study procedures, gave each participant a quiz with feedback to assess their level of comprehension, and provided corrective feedback as needed. This quiz plus feedback procedure was repeated weekly with all participants during their first month in the study.

2.8. Paired control procedure

To ensure that participants in both groups received vouchers in equal amounts and temporal distribution, the voucher schedule of each participant randomized to the abstinence reinforcement group was linked to the schedule of a (control) participant in the attendance reinforcement group. Every time a participant in the abstinence reinforcement group received a voucher, the corresponding attendance reinforcement (control) participant was scheduled to receive a voucher for the same amount, for attending the clinic, submitting a urine sample, and completing scheduled assessments, regardless of that participant's urinalysis results. If a control participant missed a day when (s)he was scheduled to receive a voucher, the scheduled voucher was saved for the next urine collection day (MWF). Study subjects were not aware that their voucher schedule was linked to that of another participant.

2.9. Voucher reinforcement schedule

An escalating schedule of reinforcement similar to that developed by Higgins and collaborators (1991, 1994) was used. Participants in the abstinence reinforcement group could earn vouchers with monetary value on Monday, Wednesday and Friday by providing opiate-negative urine specimens. Upon providing the first opiate-free specimen, participants received a voucher worth \$2.50. Thereafter, the value of the vouchers increased by \$1.50 with every consecutive opiate-free specimen provided. Vouchers could be worth a maximum of \$40. Once earned, the voucher credits could not be lost. If an opiate-positive specimen was provided or if a participant did not provide a specimen on a given test day, the value of the voucher for the next opiate-free specimen provided was again worth \$2.50. In addition, participants earned bonus vouchers worth \$10 by providing three consecutive opiate negative samples. If a participant's voucher value was reset, then

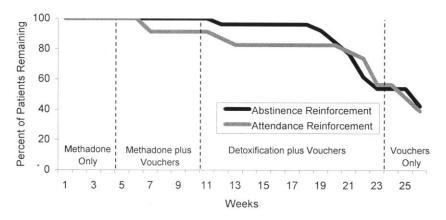


Fig. 1. Retention during the 26-week study.

nine consecutive opiate-free samples resulted in the participant returning to the highest value achieved before the reset. A maximum of \$2232 in vouchers could be earned during the 22-week intervention. Voucher earnings could be used to purchase products (clothes, food, appliances, sports equipment, etc.) and pay for services (rent, telephone, insurance, medical bills, transportation, etc.) available in the community, as long as the purchases were deemed consistent with the participant's treatment goals. Participants were not given cash; all purchases and payments were made directly by the research staff.

The voucher schedule was adapted from Higgins et al. (1994) to be implemented over a period of 22 weeks instead of the original 12 weeks. Procedural changes included setting a maximum voucher value of \$40 to make the study economically possible, and returning to the highest previously achieved voucher value after a maximum of nine opiate-free urine specimens instead of the original six specimens. A similar schedule has been successfully used by Silverman et al. (1999a) to increase and sustain cocaine abstinence in methadone patients during a long-term intervention, and by Silverman et al. (2001) to sustain drug abstinence and attendance to a therapeutic workplace.

2.10. Data analysis

Retention in treatment by group was assessed using the Gehan generalization of the Wilcoxon test. Opiate and cocaine use were assessed by comparing urinalysis results with group (abstinence vs. attendance reinforcement) by time (treatment phase) repeated measures ANOVA. In this intent-to-treat analysis, all missing opiate and cocaine samples were counted as drug-positive. Post hoc comparisons between treatment phases and groups were performed using Tukey's HSD procedure.

The effect of substituting missing data points with positive values was assessed by also analyzing urine data with multi-level modeling. Group negativity rates were compared at each phase, employing mixed model repeated measures procedures to compensate for missing data. Multi-level modeling analyses used the SAS Proc Mixed procedure, Macintosh version 6.12, with an AR(1) covariance structure.

The longest consecutive periods of abstinence from opiates and cocaine by group during the detoxification phase were computed from the longest consecutive number of negative urine specimens per participant, and compared with Mann-Whitney Rank Sum tests.

The weekly average number of self-reported drug injections by group during the Detoxification phase were compared using a two-tailed *t*-test. Mixed model repeated measures analyses were used for all other self-report data including weekly assessment battery and periodically administered Addiction Severity Index. Analysis of the Addiction Severity Index, the Beck Depression Inventory, and the Past Week Non-IV Drug Use, Lifestyle Changes, and the Drug Availability questionnaires revealed no consistent study effects so data from these measures are not presented.

3. Results

3.1. Retention in treatment

Fig. 1 shows survival curves for participants in both groups. The abstinence and attendance reinforcement groups did not differ significantly on the number of days in treatment (W=0.168, df=1, P=0.68). Over 80% of the participants in both groups remained in treatment through week 20. Starting on week 21, a sharp decline in retention was observed that coincided with the complete elimination of methadone. Over 50% of the participants in both groups remained in treatment for 3 more weeks and completed the detoxification phase. Retention dropped to 42.3 and 39.1% for the abstinence reinforcement and attendance reinforce-

ment group respectively, by the end of the 3-week vouchers only phase. Primarily due to attrition, during the vouchers only phase the rate of missing urine specimens reached approximately 74% in both groups.

3.2. Opiate use

Fig. 2 shows the weekly percent of opiate-negative specimens by group. Table 2 contains the percent of opiate-negative urine specimens by phase for each group and, in parentheses, the corresponding percent of missing specimens. A repeated measures ANOVA of opiate-negative specimens showed significant effects on group (abstinence vs. attendance reinforcement; F =10.2, df = 1, 46, P < 0. 01), time (methadone only, methadone plus vouchers, detoxification plus vouchers, vouchers only; F = 78.87, df = 1, 138, P < 0.01), and the group by time interaction (F = 5.39, df = 1, 138, P < 0.01). Post hoc analyses revealed significantly higher percentages of opiate-negative specimens during the methadone plus vouchers phase for the abstinence reinforcement group, compared to the methadone only phase (P < 0.01). A similar effect was not observed for the attendance reinforcement group. Significantly fewer opiate-negative specimens were submitted by the attendance reinforcement group during the detoxification phase compared to the methadone only phase (P <0.01). The groups did not differ in terms of opiate use during the methadone only phase. However, significantly higher percentages of opiate-negative specimens were submitted by the abstinence reinforcement group than the attendance reinforcement group during the methadone plus vouchers (P < 0.05), and detoxification (P < 0.01) phases. The mixed model repeated measures analysis of opiate-negative samples corroborated the

group, time, and group by time differences revealed by the RMANOVA. Thus, main effects were confirmed across analyses that used different methods of handling missing data.

Fig. 3 shows the longest duration of continuous abstinence from opiates during the detoxification phase. Dots represent individual participants and the bars represent group medians. A comparison of the longest period of continuous abstinence from opiates during the detoxification phase revealed that participants in the abstinence reinforcement group remained abstinent significantly longer (median = 56 days) than participants in the attendance reinforcement group (median = 10 days; T = 356.50, $n_1 = 22$, $n_2 = 26$, P < 0.001).

3.3. Cocaine use

Fig. 4 shows the weekly percent of cocaine-negative specimens by group. Table 3 contains the percent of cocaine-negative specimens by phase for each group and, in parentheses, the corresponding percent of missing specimens. A repeated measures ANOVA of cocaine-negative specimens showed significant effects on group (abstinence vs. attendance reinforcement; F =5.71, df = 1, 46, P < 0.05), time (methadone only, methadone plus vouchers, detoxification plus vouchers, vouchers only; F = 29.97, df = 1, 138, P < 0.01), and the group by time interaction (F = 3.58, df = 1, 138, P < 0.05). Post hoc analyses revealed that significantly higher percentages of cocaine-negative specimens were submitted by the abstinence reinforcement group compared to the attendance reinforcement group during the methadone plus vouchers (P < 0.01) and detoxification (P < 0.01) phases. Examination of trends over time revealed that cocaine use increased significantly from

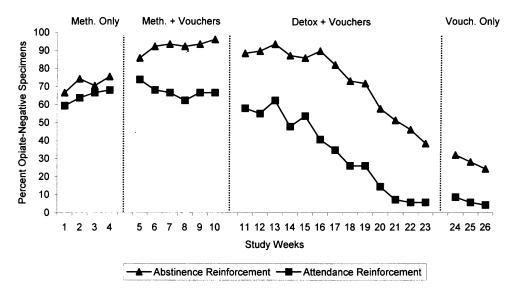


Fig. 2. Weekly mean percentage of opiate-negative urine specimens provided by subjects in the abstinence reinforcement and attendance reinforcement group.

Table 2 Repeated measures ANOVA of opiate-negative specimens^a

Treatment phase	Abstinence Reinforcement	Attendance Reinforcement	Between-group effects P
Methadone only	67.3% ^b	64.4% ^e	NS
	(11.7%)	(8.0%)	
Methadone plus vouchers	91.6% ^c	68.7%	0.05
•	(8.6%)	(8.6%)	
Detoxification plus vouchers	74.0%	35.0% ^f	0.01
•	(19.4%)	(26.3%)	
Vouchers Only	19.2% ^d	6.1%g	NS
	(73.0%)	(74.0%)	

^a Significant within-group effects. Numbers in parentheses represent percentages of missing urine specimens. Missing urine specimens were counted as opiate-positive. (P < 0.01): b-c, b-d, e-f, e-g.

baseline during both the detoxification and vouchers only phases for the attendance reinforcement group (both tests P < 0.01), while a similar increase in cocaine use was seen only during the vouchers only phase for the abstinence reinforcement group (P < 0.01). The mixed model, repeated measures analysis of cocainenegative samples confirmed the group and time differences revealed by the RMANOVA, but failed to detect an interaction effect. The discrepancy between the two analyses appears to arise mainly from the higher level of cocaine abstinence assumed by the mixed model analysis during the vouchers only phase.

Fig. 5 shows the longest duration of continuous abstinence from cocaine during the detoxification phase. Dots represent individual participants and the bars represent group medians. A comparison of the longest period of continuous abstinence from cocaine during the detoxification phase revealed that participants in the abstinence reinforcement group remained abstinent significantly longer (median = 31 days) than participants in the attendance reinforcement group (median = 2 days; T = 395.00, $n_1 = 22$, $n_2 = 26$, P = 0.003).

3.4. Intravenous drug injections

The Daily IV questionnaire, a computerized self-administered instrument, required participants to recount separately the number of intravenous injections of heroin, other opiates, cocaine, speedball (i.e. heroin combined with cocaine), and other drugs for each of the preceding 7 days. From the daily IV self-reports, the mean number of opiate, cocaine, and speedball injections during the detoxification phase was computed for each group. Missing data were not replaced and may, therefore, yield a conservative estimate of the number of injections. A significantly higher average number of intravenous drug injections per week during the detoxification phase was reported by the attendance reinforcement group (mean = 25.21, n = 1402) than by participants in the abstinence reinforcement group (mean = 8.36, n = 632; t = -2.91, df = 24, P < 0.01).

Fig. 6 shows the cumulative weekly number of self-reported intravenous drug injections during the detoxification phase.

3.5. Withdrawal symptoms

Self-report of withdrawal symptoms was collected weekly using a computerized Visual Analog Scale (VAS) instrument that has been described elsewhere (Jones et al., 1998). A mixed model, repeated measures analysis of the weekly data revealed significant time effects in total withdrawal (F = 2.42, P = 0.027, df =25), as the scores systematically increased during the detoxification phase for both groups. In addition, significant time effects were observed for the medication hold (F = 0.51, P = 0.000, df = 25), like the medication (F = 1.79, P = 0.000, df = 25), and hooked on medication (F = 0.43, P = 0.048, df = 25) scales. As expected, in these three cases, the scores systematically decreased during the detoxification phase for both groups. No significant effects were observed in the crave heroin and crave cocaine scales. No significant group or group by time effects were found on any scale of this assessment.

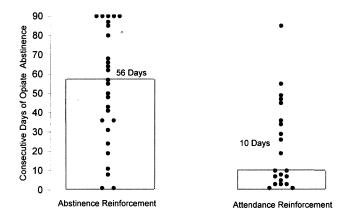


Fig. 3. Consecutive days of abstinence from opiates during the detoxification phase. Bars represent group medians, and dots represent longest period of abstinence by individuals in each group.

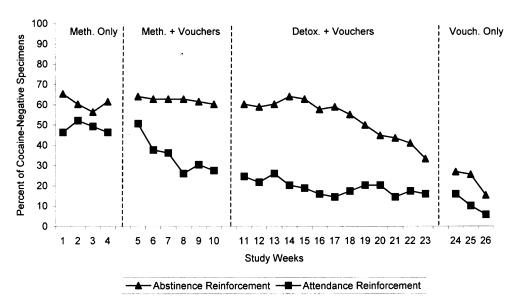


Fig. 4. Weekly mean percentage of cocaine-negative urine specimens provided by subjects in the abstinence reinforcement and attendance reinforcement group.

4. Discussion

Compared to the attendance reinforcement group, during the detoxification phase the abstinence reinforcement group provided significantly more opiatenegative and cocaine-negative specimens, remained continuously abstinent from opiates and cocaine during significantly longer periods, and reported significantly fewer drug injections. Taken together, these results show that voucher-based reinforcement of opiate abstinence enhanced outcome from detoxification by helping to sustain drug abstinence and thereby reducing health risks during the detoxification process.

Half of the participants in both groups completed the detoxification schedule, and around 40% stayed through the vouchers only phase. The highest attrition rate occurred after week 20, when the methadone dose decreased to 8% of the maintenance dose. No significant differences in treatment retention by group were observed, which allowed for valid statistical comparisons across all phases.

Opiate use during methadone maintenance was significantly reduced in the abstinence reinforcement group when the voucher schedule was introduced. The significant therapeutic effects of abstinent—contingent vouchers during methadone maintenance observed in this study support the results previously obtained by Silverman et al. (1996). In addition, these results highlight the importance of the contingency relationship between abstinence from drugs and voucher-based reinforcement. Because the value and distribution of monetary vouchers was similar in both groups, but increases in opiate abstinence were seen only in the abstinence reinforcement group, it appears likely that the increase

in abstinence observed was due to a specific motivating effect of contingent monetary reinforcement for opiatefree samples.

The pattern of opiate use observed in this study (Fig. 2) suggests that abstinence reinforcement individuals who became opiate-free during the maintenance phase were able to sustain opiate abstinence at least during the initial 6 weeks of the methadone dose tapering, after which relapse occurred at a rate similar to that seen in the attendance reinforcement group. Consistent with clinical wisdom, this outcome pattern suggests that it may be important to ensure stable opiate abstinence prior to initiating methadone detoxification. The study shows that voucher reinforcement can be used effectively to achieve this goal.

During the detoxification phase, participants in the abstinence reinforcement group submitted more than twice as many opiate-negative specimens than participants in the attendance reinforcement group (73.6 vs. 35.0%). Similarly, much longer periods of continuous abstinence from opiates were observed in the abstinence reinforcement group (53 vs. 21 days on average). While undergoing detoxification, participants in the attendance reinforcement group reported injecting themselves with opiates, cocaine or speedball a total of 1402 times. During the same period, participants in the abstinence reinforcement group reported a total of 632 injections, a difference of 770 intravenous drug injections in a 90-day period. The substantial (55%) difference in the number of self-reported injections may constitute an important reduction in health risk during the detoxification process for participants in the abstinence reinforcement group.

Table 3
Repeated measures ANOVA of cocaine-negative specimens^a

Treatment phase	Abstinence reinforcement	Attendance reinforcement	Between-group effects P
Methadone only	62.2% ^b	50.0% ^d	NS
•	(11.7%)	(8.0%)	
Methadone plus vouchers	64.1%	35.6%	0.01
	(8.6%)	(8.6%)	
Detoxification plus vouchers	54.1%	20.1% ^e	0.01
•	(19.4%)	(26.3%)	
Vouchers only	19.2% ^c	11.1% ^f	NS
	(73.0%)	(74.0%)	

a Numbers in parentheses represent percentages of missing urine specimens. Missing urine specimens were counted as cocaine-positive. Significant within-group effects (P<0.01): b-c, d-e, d-f.

Interestingly, participants reinforced for opiate abstinence also used less cocaine than those who received reinforcement independent of their urine results. Members of the attendance reinforcement group appeared to increase their use of cocaine during the methadone maintenance phase, and to continue this use throughout the detoxification. In contrast, participants in the abstinence reinforcement group maintained baseline level use of cocaine well into the detoxification, when relapse to cocaine use appeared to parallel relapse to opiates. It is not entirely clear why this pattern of drug use was observed in the attendance reinforcement group. Nevertheless, the results highlight the potential carry-over benefit to use of other drugs when a single drug is targeted in a contingent reinforcement procedure.

Despite the robust clinical effects of the contingent voucher-based reinforcement program, the results presented here concur with previous reports of continued drug use during the detoxification process, and increased attrition and relapse to opiate use once methadone has been discontinued. Sees et al. (2000), for example, showed inferior outcomes during methadone detoxification compared with those obtained during methadone maintenance and concluded that resources should not be diverted from maintenance into detoxification, no matter how ideologically attractive the notion of a time-limited treatment for opiate abusers might be. Our results, and those obtained by other investigators, indicate that it may be difficult to completely eliminate these problems during terminal outpatient detoxification. However, it appears that the effect of contingent voucher reinforcement of abstinence could be further increased by adjusting the reinforcement schedule so that it is maximally effective when the methadone dose falls below 40 mg. Use of higher magnitude voucher-based reinforcement has been shown to have significant effects on the level of abstinence of treatment-resistant patients (Robles et al., 2000; Silverman et al., 1999a). It may be possible, therefore, to design a schedule so that abstinent individuals receive a higher proportion of the total earnings during the last 2 weeks of the detoxification schedule, when opiate use is more likely. Such a schedule would make both the absolute value of the voucher and the absolute increment directly proportional to the duration of abstinence. Based on previous research, we would expect higher magnitude reinforcement to produce better results in the final stages of the detoxification schedule.

There is no evidence indicating that detoxification can substitute for long term treatment in the management of opiate addiction. Research to date suggests that relapse to opiate use is not entirely determined by avoidance or escape of withdrawal symptoms. Therefore a treatment that exclusively attenuates the severity of opiate withdrawal symptoms can be at best partially effective. Many if not most of the physiological, behavioral and social conditions prevailing during an individual's life as an opiate addict will still be present when the physical dependence has been eliminated. Furthermore, once methadone has been removed, opiates will likely recover the reinforcing properties that previously sustained self administration, and it is under those

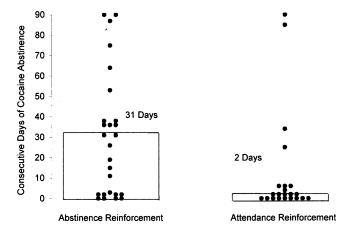


Fig. 5. Consecutive days of abstinence from cocaine during the detoxification phase. Bars represent group medians, and dots represent longest period of abstinence by individuals in each group.

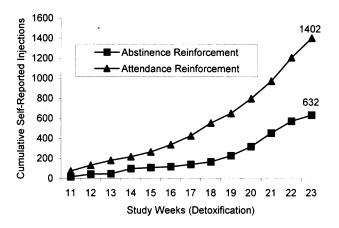


Fig. 6. Cumulative weekly mean number of self-reported intravenous drug injections during the detoxification phase.

conditions that relapse is likely to occur. Yet, outpatient detoxification from opiates is a quick, inexpensive and commonly used procedure that helps individuals by ameliorating withdrawal symptoms, and by temporarily reducing health risk associated with drugs. In addition, detoxification constitutes the first instance of contact of many addicts with the various treatment services available, and may facilitate transition into long term care. Given that methadone detoxification is such a widely used procedure, it appears reasonable to attempt to develop more efficacious detoxification techniques. In this study, the abstinence reinforcement group provided more opiate-negative and cocaine-negative specimens, remained continuously abstinent from opiates and cocaine during longer periods, and reported fewer drug injections. In the future, effective detoxification methods could be used to transition clients into opiate antagonist therapy, or to drug-free treatments such as cognitive-behavioral therapy (Carroll, 1998), community reinforcement (Azrin, 1976; Budney and Higgins, 1998) or therapeutic workplace programs (Silverman et al., 2001). In turn, those programs would provide the behavioral and cognitive skills, and the environmental support needed, to sustain long-term drug abstinence. But for now, more research is needed to discover ways to further reduce opiate use and attrition during the detoxification process, and to prevent immediate relapse to opiate use once methadone has been discontinued.

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References

- Azrin, N.H., 1976. Improvements in the community-reinforcement approach to alcoholism. Behav. Res. Ther. 14 (5), 339–348.
- Beck, A.T., Steer, R.A., 1987. Beck Depression Inventory Manual. The Psychological Corporation, Harcourt Brace Jovanovich, New York.
- Bickel, W.K., Amass, L., Higgins, S.T., Badger, G.J., Esch, R.A., 1997. Effects of adding behavioral treatment to opioid detoxification with buprenorphine. J. Consult. Clin. Psychol. 65 (5), 803– 810
- Budney, A.J., Higgins, S.T., 1998. A community reinforcement plus vouchers approach: treating cocaine addiction. US Department of Health and Human Services, Rockville, MD.
- Canada, A.T., 1972. Methadone in a thirty-day detoxification program for narcotic addicts: a critical review. Int. J. Addict. 7, 613–617.
- Carroll, K.M., 1998. A cognitive-behavioral approach: treating cocaine addiction. US Department of Health and Human Services, Rockville, MD.
- Cushman, P., Dole, V.P., 1973. Detoxification of rehabilitated methadone patients. J. Am. Med. Assoc. 226 (7), 747–752.
- D'Aunno, T., Vaughn, T.E., 1992. Variation in methadone treatment practices. J. Am. Med. Assoc. 267 (2), 253–258.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1995. Structural Clinical Interview of DSM-IV Axis I Disorders (SCID I/P), Patient. American Psychiatric Press, Washington, DC.
- Higgins, S.T., Stitzer, M.L., Bigelow, G.E., Liebson, I.A., 1986. Contingent methadone delivery: Effects on illicit opiate use. Drug Alcohol Depend. 17, 311–322.
- Higgins, S.T., Delaney, D.D., Budney, A.J., Bickel, W.K., Hughes, J.R., Foerg, F.E., Fenwick, J.W., 1991. A behavioral approach to achieving initial cocaine abstinence. Am. J. Psychiat. 148, 1218– 1224.
- Higgins, S.T., Budney, A.J., Bickel, W.K., Foerg, F.E., Donham, R., Badger, G.J., 1994. Incentives improve outcome in outpatient behavioral treatment of cocaine dependence. Arch. Gen. Psychiat. 51, 568-576.
- Iguchi, M.Y., Stitzer, M.L., 1991. Predictors of opiate abuse during a 90-day methadone detoxification. Am. J. Drug Alcohol Abuse 173, 279-294.
- Jaffe, J.H., 1970. Further Experience with methadone in the treatment of narcotic users. Int. J. Addict. 5, 375–389.
- Jones, H.E., Strain, E.C., Bigelow, G.E., Walsh, S.L., Stitzer, M.L., Eissenberg, T., et al., 1998. Induction with levomethadyl acetate: safety and efficacy. Arch. Gen. Psychiat. 55 (8), 729–736.
- Kleber, D.H., 1977. Detoxification from methadone: the state of the art. Int. J. Addict. 12 (7), 807–820.
- Maddux, J.F., Desmond, D.P., Esquivel, M., 1980. Outpatient methadone withdrawal for heroin dependence. Am. J. Drug Alcohol Abuse 7, 323–333.
- McCaul, M.E., Stitzer, M.L., Bigelow, G.E., Liebson, I.A., 1984. Contingency management interventions: effects on treatment outcome during methadone detoxification. J. Appl. Behav. Anal. 17, 35–43.
- McLellan, A.T., Luborsky, L., Cacciola, J., Griffith, J., Evans, F., Barr, H.L., et al., 1985. New data from the Addiction Severity Index: reliability and validity in three centers. J. Nerv. Ment. Dis. 173, 412–423.
- Milby, J.B., 1988. Methadone maintenance to abstinence. How many make it? J. Nerv. Ment. Dis. 176, 409-422.

- Mintz, J., O'Brien, C.P., O'Hare, K., Goldschmidt, J., 1975. Doubleblind detoxification of methadone maintenance patients. Int. J. Addict. 10 (5), 815–824.
- Riordan, C.E., Mezritz, M.A., Slobetz, F., Kleber, H.D., 1976. Successful detoxification from methadone maintenance. J. Am. Med. Assoc. 235 (24), 2604–2607.
- Robles, E., Silverman, K., Preston, K.L., Cone, E.J., Katz, E., Bigelow, G.E., et al., 2000. The brief abstinence test: voucher-based reinforcement of cocaine abstinence. Drug Alcohol Depend. 581–2, 205–212.
- Sees, K.L., Delucchi, K.L., Masson, C., Rosen, A., Clark, H.W., Robillard, H., et al., 2000. Methadone maintenance vs. 180-day psychologically enriched detoxification for treatment of opioid dependence. J. Am. Med. Assoc. 283 (10), 1303–1310.
- Silverman, K., Wong, C.J., Higgins, S.T., Brooner, R.K., Montoya, I.D., Contoreggi, C., et al., 1996. Increasing opiate abstinence through voucher-based reinforcement therapy. Drug Alcohol Depend. 41, 157–165.
- Silverman, K., Chutuape, M.A., Bigelow, G.E., Stitzer, M.L., 1999a. Voucher-based reinforcement of cocaine abstinence in treatment-resistant methadone patients: effects of reinforcement magnitude. Psychopharmacology 1462, 128–138.

- Silverman, K., Robles, E., Bigelow, G.E., Stitzer, M.L., 1999b. Long-term abstinence reinforcement in methadone patients, NIDA Research Monograph No. 180. US Department of Health and Human Services.
- Silverman K., Svikis D., Robles E., Stitzer M.L., Bigelow G.E. 2001, Therapeutic workplace for the treatment of drug abuse: abstinence initiation: 6-month abstinence outcomes, Exp. Clin. Psychopharmac, In press.
- Steer, R.A., Kotzker, E., Schut, J., 1978. Ambulatory detoxification of heroin addicts: a follow-up study. Drug Alcohol Depend. 3, 175–183.
- Stimmel, B., Rabin, J., 1974. The ability to remain abstinent upon leaving methadone maintenance: a prospective study. Am. J. Drug Alcohol Abuse 1, 379–391.
- Substance Abuse and Mental Health Services Administration (SAMHSA), 1999. Treatment Episode Data Set TEDS: 1992– 1997. US Department of Health and Human Services, Bethesda, MD.
- Wilson, B.K., Elms, R.R., Thompson, C.P., 1975. Outpatient vs. hospital methadone detoxification: experimental comparison. Int. J. Addict. 10, 13-21.