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Journal of Substance Abuse Treatment 20 (2001) 225–230

Journal of Substance Abuse Treatment

Featured article

# Implementation of a clinic policy of client-regulated methadone dosing

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Received 18 May 2000; received in revised form 1 November 2000; accepted 12 November 2000

**Abstract**

A six-month interval (baseline) during which methadone doses above 99 mg required individual approval by the clinic's physician was compared with the subsequent 16-month period in which a policy of patient-regulated methadone dosing with no preset upper limit was implemented. During the later phase, all patients were required to remain at each selected dose for a minimum of four days, and standard compliance-based take-home dosing procedures were followed. For patients in the study sample ($n = 57$), the daily maximum methadone dose increased from 165 mg during baseline to 300 mg during the self-regulation period, while their average daily methadone dose increased from 76.84 mg to 80.04 mg ($W = 473$, $n = 57$, $p = 0.01$). Monthly percent of opiate-positive urine specimens decreased significantly from 5.26% during baseline to 1.64% during the self-regulated dose period ($W = 169$, $n = 57$, $p < 0.01$), and use of other drugs remained unchanged. No patient failed to show possession of recalled take-home doses, and no instances of liquid methadone diversion were reported by law enforcement agencies in the area. 

*Keywords:* Methadone; Dosing; Self-regulation; Titration; Opiates

## 1. Introduction

Over the past 36 years, methadone maintenance treatment (MMT) has proven to be a safe, efficacious, and cost-effective therapy for narcotic addiction. Extensive research has shown methadone's efficacy in reducing illicit opiate use (Ball & Ross, 1991; Dole, Nyswander, & Warner, 1968; Strain, Stitzer, Liebson, & Bigelow, 1993; Strain, Bigelow, Liebson, & Stitzer, 1999), the risk of HIV infection (Batki, 1988; Hubbard, Marsden, & Cavanaugh, 1988; Longshore, Hsieh, & Anglin, 1994), and drug-related crime (Anglin & McGlothlin, 1984; Ball & Ross, 1991; Marsh, 1998).

The effectiveness of MMT appears to be determined by a number of patient-and treatment-related factors (D'Aunno & Vaughn, 1992; Maddux, Prihoda, & Votsberger, 1997; Magura, Nwakeze, & Demsky, 1998). Among these, the most influential and most extensively researched factor is magnitude of the daily methadone dose. In general, higher methadone doses have been associated with reduced opiate use (Caplehorn, Bell, Kleinbaum, & Gebski, 1993; Strain et al., 1993; Strain et al., 1999) and longer treatment retention (Caplehorn & Bell, 1991; Magura et al., 1998). Also important appears to be participation of the patients in determining their own dose (D'Aunno & Vaughn, 1992; Goldstein, Hansteen, & Horns, 1975). Knowledge of the methadone dose and participation in determining a patient's own dose have been associated with increased abstinence from opiates (Goldstein et al., 1975; Havassy, Hargreaves, & De Barros, 1979), longer treatment retention (Caplehorn and Bell, 1991), and more satisfaction with the treatment program (Goldstein et al., 1975; Resnick, Butler, & Washton, 1981).

Previous studies have explored the feasibility, safety, and clinical efficacy of allowing MMT patients to regulate their own daily dose. In a landmark study by Goldstein and colleagues (1975), patients were allowed to choose between raising their dose over 50 mg (up to 120 mg) and forfeiting their take-home privileges, or selecting doses up to 50 mg and retaining their take-home privileges. Interestingly, after six months of patient-selected dosing there was very little change in dose levels for the clinic, with the median dose increasing from 40 to 50 mg. Patients choosing to increase

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0740-5472/01/$ – see front matter 
PII: S0740-5472(00)00168-9

their dose tended to have less opiate-positive urine specimens compared to baseline, while patients choosing to decrease their dose tended to have more opiate-positive urine specimens compared to baseline. In addition, patients and staff clearly preferred the open-dose self-adjustment system over the standard procedure of clinic dosage management. These results were supported by Havassy and colleagues (1979), who found that allowing patients to self-regulate methadone doses up to 100 mg/day while maintaining take-home privileges did not lead to abuse of the dosing system by the patients, or to a substantial increase in the clinic's average dose. Importantly, patients in the self-regulating group tended to have lower rates of opiate-positive specimens than controls.

In summary, previous studies show that patients regulating their own dose do not tend to ingest massive doses of methadone; do not create medical, behavioral, or administrative problems; and do not show increased rates of drug abuse. In addition, open and self-regulated dosing was associated with lower rates of opiate use and greater staff and patient satisfaction. Because such observations were made during a short period of time (16–24 weeks) and involved limits on the magnitude and availability of take-home doses, a longer study to explore the effects of self-regulated methadone under current standard take-home dosing conditions would be beneficial.

The purpose of this study is to compare methadone doses, urinalysis results, and evidence of methadone diversion before and during implementation of a clinic-wide policy of patient-regulated methadone doses while maintaining standard abstinence-based take-home dosing procedures.

## 2. Method

The data reported in this study were collected over 22 months at a community clinic specializing in providing substitution therapy (methadone and levo-alpha-acetylmethadone) for the treatment of opiate abuse. The report comprises the statistical analysis of data generated during the regular operation of the clinic, before and after a change in dosing policy. The reported data were routinely collected on all patients during their time in treatment. All enrolled patients simultaneously received the treatment offered by the clinic at any given time. When the clinic's dosing policy changed in an attempt to enhance therapeutic efficacy, all enrolled patients at the time of the change and all subsequent admissions were equally regulated by the new policy. Thus, this study constitutes a statistical analysis of historical data, aimed at documenting the effects of a change in methadone dosing practices.

### *2.1. Study sample*

The quasi-experimental design consisted of a six-month baseline during which methadone dose increases above 99 mg required seeing the clinic physician for individual approval, followed by a 16-month intervention during which patients could obtain dose changes without having to see the physician for individual approval. Data collected during the last six months of the old policy are being reported because that period is representative of the clinic's treatment outcome under such dosing practices. Data collected during first 16 months of the new policy are being reported because the effects of changing the dosing policy appeared to be stable at the time of analysis.

During the 22 months covered in this report, the clinic continued operating normally, having new admissions, re-admissions, and discharges of all kinds (due to hospitalization, incarceration, no-show/no-call, administrative discharge, voluntary detoxification, death, etc.). That is, some patients were in treatment during all or part of the prechange interval (baseline), all or part of the postchange interval (intervention), or all or part of both treatment intervals. The full data set, then, included episodes of dose induction and detoxification for many patients, and exposure to either dosing policy in various degrees. Therefore, in order to eliminate other sources of variability, the comparison was limited to those patients ($n = 57$) who remained in MMT for the entire 22-month period and were equally exposed to both dosing policies. Otherwise, the results would be confounded by a constantly changing clinic population and sample size, and by dose changes unrelated to a patient's ability to participate in determining his/her own dose — namely, induction and detoxification episodes. The data reported here were obtained from accurate historical electronic records produced during the regular operation of the clinic, and no additional data were collected for this study. Permission to statistically analyze the data for publication was granted in advance by the Institutional Review Board of the University of Arkansas for Medical Sciences (UAMS).

Fig. 1 shows the clinic census during the 22-month period, and the corresponding cumulative number of admis-

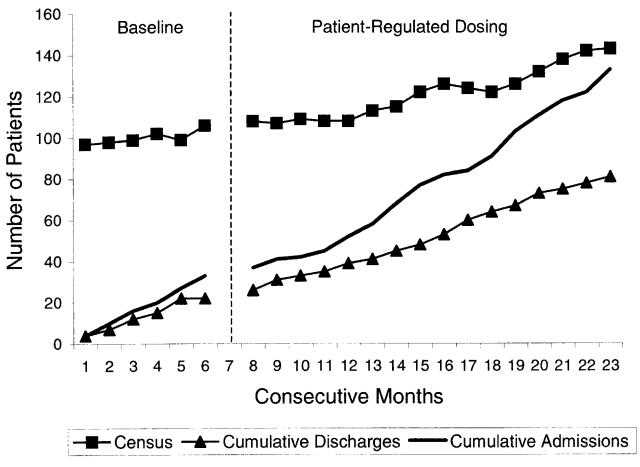


Fig. 1. Monthly clinic census and cumulative number of admissions and discharges during the 22-month interval. No shifts in trend related to the change in dosing policy are apparent.

sions and discharges. Although the number of patients in treatment increased from 99 to 133 during the reported interval, the rate of admissions and discharges did not change when the new dosing policy was implemented. The study participants ($n = 57$) were primarily older (mean = 43.6 years, $SD = 5.01$) patients with a long history of opioid use. The sample was 84.2% Caucasian and 12.3% African American. Males accounted for 63.2% of the sample. In terms of employment, 40.35% were fully employed, 14.03% were employed part-time, and 45.61% were unemployed.

### 2.2. Urine testing

All patients were required to submit urine specimens at least once each month to be tested for drugs of abuse (opiates, cocaine, benzodiazepines, THC, amphetamines, barbiturates, phencyclidine, propoxyphene) and methadone. The clinic's computerized management program (AMS for DOS, Addiction Management Systems, New York, NY) randomly determined the specific dosing date on which each sample was to be collected for each patient, and displayed the urine collection order on the dosing nurse's computer screen when the patient showed up for dosing. The message remained on that patient's record, and the patient was not dosed until the specimen was collected. Urine collection was sometimes observed by a trained nurse through a one-way mirror from an adjacent room. Patients were informed that urine collection would be observed at unpredictable times, but they were not informed of the presence or absence of the observing nurse on any given day. No cases of urine tampering were observed involving patients in the study. Urine specimens were analyzed by a certified commercial laboratory using Enzyme Multiplied Immunoassay Technique systems (EMIT; Behring-Syva, Palo Alto, CA). Urine specimens with specific gravity $< 1.003$ and creatinine concentration $\leq 20$ mg/dL were considered invalid, and treated as drug-positive.

### 2.3. General procedures

#### 2.3.1. Methadone maintenance treatment

In accordance with federal (CSAT, 1993) and state (BADAP, 1993) regulations, the methadone maintenance program offered at the UAMS Substance Abuse Treatment Clinic (SATC) is composed of four treatment phases. Initially, patients are admitted into the most intense treatment phase and gradually advance into successively less intense phases as a function of time in treatment, abstinence from drugs of abuse, and compliance with counseling requirements and clinic regulations. During treatment phase I, all patients are required to attend the clinic for dosing six times per week, and on Saturday they receive Sunday's take-home dose. A patient must accumulate 90 consecutive days of abstinence from all drugs of abuse and full compliance with counseling requirements before being eligible for treatment phase II. Once in phase II, however, patients attend the clinic for dosing three times per week and receive a total of four take-home doses. Patients remain in phase II for at least 21 months. While in treatment phases I and II, all patients must meet individually with their counselor once every week, and attend four weekly sessions of group therapy. Upon advancing to phase III, patients attend the clinic for dosing two times per week and receive five weekly take-home doses. This treatment phase is in effect for a minimum of one year. When patients advance into phase IV after a minimum of three years in treatment, they attend the clinic once per week and receive six take-home doses. Patients may stay in treatment phase IV as long as the they remain abstinent from all drugs, and compliant with counseling requirements and clinic regulations. While in treatment phases III and IV, all patients must meet monthly with their counselor, and attend one group therapy session per month. While in treatment phases II, III, and IV, submitting two drug-positive (amphetamines, barbiturates, benzodiazepines, cocaine, methadone, opiates, PCP, propoxyphene, and THC; in the case of methadone, drug-negative) urine samples in a six-month period causes patients to be regressed to the previous treatment phase for a minimum of two weeks. Continued drug use causes a patient to be further regressed in phase. However, in accordance with a harm reduction policy, patients are not discharged from the treatment program on the basis of drug use or noncompliance with counseling requirements. Patients who continue to use illicit drugs or do not comply with counseling requirements remain in phase I indefinitely. No limit exists on the duration of the methadone maintenance treatment. Table 1 contains the number of take-home doses available during each treatment phase, the clinic's distribution of patients by phase at the start of the study, and the distribution of study sample patients by treatment phase.

### 2.4. Dosing procedures

#### 2.4.1. General

All doses of methadone hydrochloride oral concentrate (10 mg/mL) were dispensed into a plastic cup using a computer-controlled precision pump (Scilog; Middleton, WI). The dispensing nurse then added approximately 50 cc of fruit punch to the methadone cup and handed it to the patient. Patients were required to completely swallow the medication before leaving the dosing window. When a patient missed three or more dosing days, the dose was cut in half upon returning, and increased back to the previous level in steps of 5–10 mg every four days. Nurses had emergency authority to deal with impaired patients. Those who came to the clinic in the morning looking impaired, and those who tested positive for breath alcohol, were asked to return to be dosed in the evening. Those who showed up impaired for evening dosing were not dosed that day. To allow the patients to feel the full effect of a dose,

Table 1
Distribution of patients by treatment phase

| Treatment Phase | No. of Weekly Take-Homes | Number of Pts. in Clinic Census (%) | Number of Pts. in Study Sample (%) |
|---|---|---|---|
| | | $n=99$ | $n=57$ |
| I | 1 | 35 (35.4) | 9 (15.8) |
| II | 4 | 13 (13.1) | 1 (1.8) |
| III | 5 | 9 (9) | 5 (8.7) |
| IV | 6 | 42 (42.4) | 42 (73.7) |

and give the medical staff the opportunity to assess the safety of a dose level (Wolff et al., 1997), patients were required to remain at each given dose for at least four days before further increases would be available. All doses dispensed were previously approved (usually via facsimile) by the Food and Drug Administration (FDA) and the state methadone authority. Patients' requests for dose changes were recorded by the dosing nurse and implemented as described below.

*2.4.2. Baseline*

During the six-month baseline period, induction from 30–35 mg of daily methadone progressed in 5- to 10-mg increments per week up to 99 mg or until no further withdrawal symptoms were reported. Subsequently, patient requests for dose changes were implemented by the nursing staff in 1- to 5-mg steps, with only one dose increase approved in a given four-day period. Dose increases above 99 mg required individual approval from the clinic's medical director, and patients on $\geq 100$ mg could receive only one (Sunday's) take-home dose each week. Dose increments over 99 mg were approved on the basis of clinical evidence, and occasionally involved determination of methadone plasma levels. Standard clinical evidence considered while determining an adequate methadone dose included patient reports of discomfort (dose not holding), reports of opiate craving, physical signs of opiate withdrawal, and continued use of illegal opiates while taking daily methadone under observation. When a patient was required to see the physician as a result of a dose increase request, an appointment was scheduled on the next available slot, usually within two work days.

*2.4.3. Patient-regulated dosing*

During the 16-month intervention, induction from 30–35 mg of daily methadone progressed in 5- to 10-mg increments per week until no further withdrawal symptoms were reported. Subsequently, patients' requests for dose changes were implemented by the nursing staff in 1- to 5-mg steps, with only one dose increase approved in a given four-day period. According to the new dosing policy, all patients were allowed to determine their dose, no upper limit was set to patient-selected methadone doses, and the standard take-home procedures (based on drug abstinence and overall compliance) described above were maintained for all patients. Nurses and counselors were instructed to respond with a neutral attitude to clients' requests for dose changes. The medical director supervised and documented all dose changes.

*2.4.4. Evidence of possible methadone diversion*

To assess possible changes in the incidence of methadone diversion during the study, the standard procedure of randomly asking 10% of the patients to demonstrate possession of the correct number of take-home doses was maintained. In addition, reports were requested from the local and state police and the Drug Enforcement Administration (DEA) regarding confiscation of liquid methadone during the 22-month duration of the study.

*2.5. Data analysis*

Dosing and urinalysis data were obtained from database files maintained through the clinic's computerized management system. Dosing information reflects actual doses delivered.

One set of urinalysis results per month was obtained for each patient. However, when requested by the clinic's physician, additional urine tests were conducted on individual patients. On the average, patients in the study were screened 1.46 times per month. When more than one set of

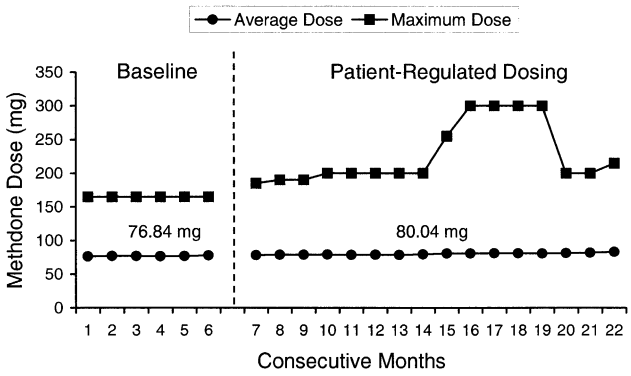


Fig. 2. Monthly maximum dose and monthly average dose during baseline and the self-regulated dosing period. Average dose increased by 3.2 mg ($W=473$, $n=57$, $p=0.01$).

results were available for a patient on a given month, monthly results were considered positive for each drug tested if at least one of the results for that month was positive. Missing data were considered drug-positive throughout. The rate of missing urinalysis data was 0.88% during baseline and 0.44% during the self-selected dosing period.

Paired comparisons of individual dose means and proportions of drug-negative urinalysis results were performed using the Wilcoxon Signed Rank test.

## 3. Results

As shown in Fig. 2, the maximum dose dispensed during baseline was 165 mg. During the self-regulated dosing period, the maximum dose dispensed peaked at 300 mg and then decreased to 265 mg. A paired comparison of average methadone doses by patient revealed only a small but statistically significant increment from 76.84 mg during baseline to 80.04 mg during the self-selected dosage period ($W = 473$, $n = 57$, $p = 0.01$). Interestingly, although the number of doses in excess of 100 mg increased during the self-regulated dose period, 89.7% of the doses selected remained between 17 and 100 mg.

A paired comparison of the percent of monthly opiate-positive specimens (see Fig. 3) revealed a significant decrement from 5.26% during baseline to 1.64% during the self-selected dose period ($W = 169$, $n = 57$, $p < 0.01$). On the other hand, urinalysis results for amphetamines, benzodiazepines, cocaine, and THC remained unchanged with an average of $\leq 10\%$ of the specimens being positive for illegal drugs.

During the entire 22-month period, all patients required to return to the clinic to demonstrate possession of take-home doses were able to do so. In addition, local and state police, as well as the DEA, reported that they had encountered no instances of liquid methadone diversion in the area during this study.

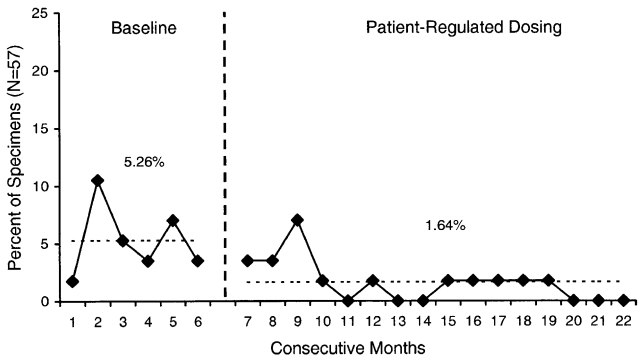


Fig. 3. Monthly percent of opiate-negative urine specimens decreased from 5.26% during baseline to 1.64% during the self-regulated dosing intervention period ($W = 169$, $n = 57$, $p < 0.01$).

## 4. Discussion

For the sample of 57 patients who remained in MMT during the 22-month assessment interval, the maximum dose dispensed increased to a peak of 300 mg, while the average daily dose increased only 3.2 milligrams during the 16-month self-regulation period. Although the number of doses greater than 100 mg increased during the self-regulated dosing period, almost 90% of all doses selected remained in the 10 to 100 mg window. These results concur with previous reports indicating that when given the opportunity to self-regulate their dose, methadone patients do not seem to abuse the system or ingest massive amounts of medication.

Treatment efficacy in this sample of patients was good before the intervention, with less than 6% of the urine samples being opiate-positive. Yet, abstinence from opiates increased significantly during the self-regulated dosing period, as the monthly average of opiate-negative specimens rose to 97.92%. It is not clear from our data to what extent the observed increase in treatment efficacy was a pharmacological or psychological effect. On one hand, it has been suggested that better outcome can be expected when patients perceive having control over their own treatment (Glass & Singer, 1972), although this effect has not been directly shown in relation to methadone maintenance. On the other hand, recent studies have demonstrated that some MMT patients are rapid methadone metabolizers due to a combination of genetic factors (Eap, 2000), and concomitant use of other drugs and prescribed medications (Bell, Seres, Bowron, Lewis, & Batey, 1987; Eap, Bertschy, Powell, & Baumann, 1997; Kreek, 1986; Finelli, 1976). To achieve an effective plasma level of methadone, those patients may require doses greater than the 99 mg limit set on take-home doses during the baseline period (Tennant, 1987; Tennant & Shannon, 1995). Therefore, higher doses may have clinically benefited rapid methadone metabolizing patients. Establishing the relative contribution of the pharmacological and psychological components of this intervention, however, is beyond the scope of this study.

During the 16 months of client-regulated methadone dosing, a 43% increase in the clinic census was observed. The monthly average number of admissions (6.7 vs. 6.7) and discharges (5.5 vs. 6.3) before and during the intervention period did not significantly differ. As shown in Fig. 1, census growth appears to have been driven by a rate of admissions that was consistently higher than the rate of discharges, and no clear trend toward longer treatment retention was apparent.

To ensure valid statistical comparison of doses and urine results between the baseline and intervention periods, the reported data were gathered from the subset of patients who remained in treatment for the full 22 months. Most of the patients in the study sample were stable patients who remained compliant and abstinent from drugs. Because the number of weekly take-home doses each patient could receive was determined on the basis of compliance indicators (i.e., abstinence from drugs, time in treatment, attendance at

individual and group counseling), most take-home doses were dispensed to stable patients. Therefore, the composition of the resulting study sample may have influenced the high level of efficacy observed. It is important to note, however, that data from patients not in the study sample did not reveal abuse of dosing privileges or unsafe medication management. For example, the maximum dose for nonparticipants was also 300 mg (one patient) and, as noted above, no evidence of methadone diversion was reported during the duration of the study. The new dosing policy was concurrently implemented with all the patients in the clinic, regardless of their treatment phase. It constituted a clinicwide change in dosing practices, resulting from the experience accrued during the preceding six years of operation. Although in this article we describe the implementation of the self-regulated dosing procedure, other features of the treatment program may be essential for the dosing practices to have the observed effects. In particular: (a) requiring patients to remain at a given dose for at least 4 days ensures that both the patient and the medical staff can assess the full effect of a dose before a higher dose can be authorized; and (b) when the number of weekly take-home doses available to each patient is a function of the level of drug abstinence and overall compliance, all patients (including those in phase I) are able to determine their own dose, but only the most stable patients receive extra take-home doses.

The results presented in this article agree with previous studies on dose self-regulation, and suggest that self-regulation of methadone involving doses above 100 mg and abstinence-based take-home practices may be concurrently followed resulting in effective, safe, and clinically viable methadone maintenance treatment. More research is needed to determine the relative contribution of psychological and pharmacological factors in producing the observed results. And more research is needed to assess the long-term effects of dose self-regulation on the safety and efficacy of methadone maintenance treatment.

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