A Randomized Controlled Trial of Interim Methadone Maintenance

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Context: Effective alternatives to long waiting lists for entry into methadone hydrochloride maintenance treatment are needed to reduce the complications of continuing heroin dependence and to increase methadone treatment entry.

Objective: To compare the effectiveness of interim methadone maintenance with that of the usual waiting list condition in facilitating methadone treatment entry and reducing heroin and cocaine use and criminal behavior.

Design: Randomized, controlled, clinical trial using 2 conditions, with treatment assignment on a 3:2 basis to interim maintenance–waiting list control.

Setting: A methadone treatment program in Baltimore.

Participants: A total of 319 individuals meeting the criteria for current heroin dependence and methadone maintenance treatment.

Interventions: Participants were randomly assigned to either interim methadone maintenance, consisting of an individually determined methadone dose and emergency counseling only for up to 120 days, or referral to community-based methadone treatment programs.

Main Outcome Measures: Entry into comprehensive methadone maintenance therapy at 4 months from baseline; self-reported days of heroin use, cocaine use, and criminal behavior; and number of urine drug test results positive for heroin and cocaine at the follow-up interview conducted at time of entry into comprehensive methadone treatment (or at 4 months from baseline for participants who did not enter regular treatment).

Results: Significantly more participants assigned to the interim methadone maintenance condition entered comprehensive methadone maintenance treatment by the 120th day from baseline (75.9%) than those assigned to the waiting list control condition (20.8%) (P < .001). Overall, in the past 30 days at follow-up, interim participants reported significantly fewer days of heroin use (P < .001), had a significant reduction in heroin-positive drug test results (P < .001), reported spending less money on drugs (P < .001), and received less illegal income (P < .02) than the waiting list participants.

Conclusion: Interim methadone maintenance results in a substantial increase in the likelihood of entry into comprehensive treatment, and is an effective means of reducing heroin use and criminal behavior among opioid-dependent individuals awaiting entry into a comprehensive methadone treatment program.

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HEROIN ADDICTION IS A SERIOUS AND GROWING PROBLEM IN THE UNITED STATES. Its adverse consequences include human immunodeficiency virus and hepatitis B and C infections, increased criminal activity, unemployment, and overdose-related death. Despite 40 years of research demonstrating the effectiveness of methadone hydrochloride maintenance treatment in many regions of the United States, methadone maintenance treatment capacity remains inadequate and long waiting lists for treatment exist. In cities where heroin use is prevalent, such as Baltimore, waiting lists exist as a result of discriminatory zoning regulations, inadequate public funding for treatment, and requirements for comprehensive care in methadone treatment programs (MTPs) that increase their cost. One suggested approach to address this treatment gap is to provide various low-threshold treatments with opioid agonists, such as methadone, but no other services (ie, regular counseling) temporarily to heroin-addicted individuals who are on waiting lists for comprehensive methadone treatment.

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Low-threshold treatment with methadone only, for individuals on waiting lists, was first reported in the early 1970s in Chicago, Ill. A 16-week evaluation of that program demonstrated a substantial decrease in self-reported heroin use, a greater than 50% reduction in criminal activity, and, most important, a 70% transfer to comprehensive treatment for methadone-only patients vs a 28% transfer for individuals on the waiting list. A mobile low-threshold MTP has been operating in Amsterdam, the Netherlands, since 1979, and low-threshold treatment through physician offices is commonly available in many countries, including the United Kingdom.

In response to the AIDS epidemic, a low-threshold program, called interim maintenance, was studied in New York, NY, in 1987. In this study, 169 heroin-dependent individuals recruited from the waiting list for a New York City program were randomly assigned to interim treatment, consisting of methadone and only emergency counseling, or a frequent contact (every 2 weeks) control. After 1 month, participants assigned to the frequent contact control were admitted to interim maintenance therapy. Participants in interim treatment compared with frequent contact control participants showed a significant 50% reduction in heroin-positive drug test results at the 1-month follow-up (P<.001). More important, at 16 months from the project’s inception, 72% of interim participants vs only 56% of those on waiting lists had entered regular methadone treatment (P<.005). Therefore, even a delay of only 30 days from intake to treatment entry significantly reduced treatment entry for control participants. Despite the evidence of efficacy, the program was discontinued after the state’s regulatory agency did not approve regulatory status for interim maintenance therapy.

Subsequently, McLellan et al, in 1993, found that methadone treatment with regular counseling and methadone treatment with enhanced services (including on-site psychiatric care, family therapy, and employment services) were superior to low-threshold services. However, many participants in the minimal service condition seemed to show reduced heroin use and negative drug test results: 31% were able to achieve 8 consecutive weeks of opiate-free urine samples. More recently, in a study in Norway, 106 patients awaiting comprehensive methadone treatment were randomly assigned to receive sublingual buprenorphine hydrochloride or placebo. After 12 weeks, subjects prescribed buprenorphine were more likely to be retained in treatment and to report lowered use of heroin and other drugs.

In 1993, US federal regulations were approved to permit low-threshold minimal services (methadone plus emergency counseling only, described as interim maintenance) for individuals awaiting entry into comprehensive programs. These federal regulations require that there be no take-home doses at all, significantly increasing the difficulty of patient adherence. None of the studies of low-threshold methadone treatment previously described were conducted under conditions close to those embodied in the federal regulations. To our knowledge, the present randomized clinical trial is the first to compare interim treatment, as codified under existing federal regulations, with a real-life waiting list control. It was designed to clarify the potential utility of low-threshold services as a means to reduce patients’ drug use and increase the likelihood that patients enter treatment.

METHODS

Participants

Participants were recruited between May 14, 2002, and October 27, 2003, from heroin-dependent individuals seeking methadone maintenance treatment at a community-based MTP in Baltimore, for whom no treatment slot was expected to be available in the next 2 weeks. Individuals were included if they met the criteria for methadone maintenance (at least 1 year of meeting the DSM-IV criteria for current heroin dependence) and were willing to provide informed consent to participate in the study. Individuals were excluded if the medical director determined they (1) were pregnant or (2) had an acute medical or psychiatric illness.

The treatment program began in 1990 as a mobile program using multiple sites. At the time of the study, the program administered medication in Baltimore from a specially equipped recreational vehicle parked in a lot several blocks from the counselor’s office (C.O.R.).

The Institutional Review Boards of Friends Research Institute, Inc, and the Institutes for Behavior Resources (which operated the MTP) approved this study.

ASSESSMENTS

Participants were assessed at baseline and when they entered regular methadone treatment, or 120 days from baseline for those who did not enter methadone treatment, by 1 of 2 trained and unblinded research assistants between September 9, 2002, and April 21, 2004. Self-reported alcohol, heroin, and cocaine use was measured by the Addiction Severity Index (ASI), a valid and reliable instrument that has been used extensively in drug-addicted populations. The ASI measures problem severity in 7 domains, including alcohol and other drug use; medical, psychological, legal, family, and social relationships; and employment status. In each area, specific items are combined into a composite score, ranging from 0 (no problem) to 1.0 (extreme problem). Recent heroin and cocaine use was also measured by a urine drug test; samples were collected at intake and follow-up under observation and analyzed by a certified laboratory using an enzyme-multiplied immunoassay test. The research assistant obtained oral swab specimens for heroin testing at 6 and 7 weeks from study entry for participants still enrolled in the interim treatment. Thus, they were a total of 3 postintake heroin tests obtained. Treatment enrollment status at the follow-up interview was assessed by participant response to a questionnaire. Participants were paid $15 for the baseline and $25 for the follow-up interview.

RANDOMIZATION

Participants were assigned to the interim or waiting list condition on a 3:2 basis. This ratio was used to fit the availability of the MTP’s medical director to conduct admission physical examinations and to admit as many participants to the treatment condition as resources would permit. The project director (D.A.H.) obtained the random assignment to treatment conditions from a table of random numbers and sealed it in an envelope provided to the research assistant. On completion of informed consent and the baseline assessment for an eligible
participant, the research interviewer opened the envelope with the condition assignment provided by the project director and informed the participant of his or her assignment to a treatment condition.

**CONDITION: INTERIM TREATMENT VS WAITING LIST**

All participants were placed on the waiting list for the study’s MTP, including those participants initially assigned to interim treatment. In addition, all participants were provided identical information on how to access the waiting list of the 12 other publicly funded MTPs in Baltimore and were encouraged to follow the directions of these programs’ staff to gain treatment entry, but were not given any specified outer time limit in which they could enter treatment from the waiting list. Those participants assigned to the interim treatment condition were told that they would receive interim treatment without charge for up to 120 days, after which they would be transferred to comprehensive methadone treatment if they were not able to gain entry into a comprehensive MTP before that time.

Participants assigned to interim treatment received a brief orientation to the MTP by the program’s emergency counselor and had a physical examination conducted by the program’s medical director. Methadone dosage began the following day at 20 mg, and increased by 5 mg/d, with a target of 80 mg. Participants were able to slow or stop their dose induction by discussion with program nurses, and they were able to exceed the 80-mg target by asking the emergency counselor for a dose increase. The rules of this clinic stipulated that 3 consecutive unbroken days of missed methadone dosing could result in discharge from treatment, and this rule was not changed for this study of interim maintenance. Participants assigned to the waiting list condition had no further contact with clinical staff unless their name came up on the waiting list, in which case intake staff attempted to call them 3 times over several days before moving on to the next name on the list.

Federal regulations require that interim methadone programs provide doses under direct observation. Therefore, participants were required to attend 7 days per week.

**HYPOTHESES**

We hypothesized that participants randomly assigned to receive interim maintenance would enter comprehensive MTPs by the 120th day from baseline more often than participants in the waiting list condition. We also hypothesized that interim maintenance participants would have lower rates of heroin and cocaine use and of criminal behavior than those on the waiting list.

**STATISTICAL ANALYSIS**

The initial target sample size of 360 participants, and assuming a 5% attrition rate, was based on the assumption of an effect size of approximately 0.05 in the population, an error rate (α) of .01, and a desired power of 0.8 for the tests of the condition and the condition × prepost effects.

Differences between treatment conditions on categorical baseline variables, including sex and ethnicity, were examined using the χ² goodness-of-fit test, while the independent-sample t test was used for continuous baseline variables.

Logistic regression analysis was used to analyze the binary treatment entry outcome variable. The continuous outcome measures (the drug use and crime variables) were measured on 2 occasions: baseline and follow-up. Thus, a repeated-measures multivariate analysis of variance (ie, a multivariate analysis of variance including a factor representing the 2 measurement occasions, herein termed the prepost effect) was used to answer the question of differential change over time between the 2 conditions, which would be found in a significant condition × prepost interaction effect. Following the detection of such a significant interaction effect, the simple main effect of conditions within the follow-up level of the prepost effect was tested to determine the nature of the interaction. Finally, urine test results at follow-up were compared using logistic regression analysis.

The Nagelkerke R² was used as an effect size estimate for the logistic regression analyses, while the canonical R² was reported for the condition × prepost interaction effect and the semi-partial R² (sr²) for the test of the simple main effect of conditions within the follow-up level of the prepost effect.

All outcome analyses were initially conducted controlling for age, sex, number of prior drug treatments, age at first heroin use, number of days of cocaine use in the past 30 days at baseline, and route of administration (injecting vs nasal inhalation [ie, snorting]) to eliminate the effects of these variables as potentially confounding factors. (Number of days of cocaine use was not included as a covariate when cocaine use was the outcome variable.) Each effect was included in the model as a main effect, and as part of a first-order interaction with the conditions’ effect. However, with the exception of the route of administration effect, which interacted with the prepost effect on 4 outcome variables, neither the main effects nor the interactions associated with any of these effects were significant. Thus, for ease of presentation, the analyses reported herein omit these effects. (All effects reported as significant herein were likewise significant when all control variables were included in the model.)

All analyses were conducted on an intent-to-treat basis, using data from the full sample (N=319) described in Table 1. All 319 randomly assigned participants were tracked for follow-up. A total of 302 participants (94.7%) were located for follow-up interviews, and 294 of those located completed interviews (95% of interim and 89% of waiting list participants). The reasons for missing interviews are outlined in the Figure. An additional interview was conducted but not used in the analysis as it was appropriately conducted too close to the baseline interview to be meaningful. There were no significant differences in baseline characteristics between those participants who were vs those participants who were not unavailable for follow-up, except that participants who missed the follow-up interview had a 79.4% positive rate for cocaine at baseline vs a 60.4% positive rate for those with baseline and follow-up interviews (P=.03).

**RESULTS**

As shown in the Figure, 334 individuals were screened for participation; 15 of these individuals were excluded for not meeting study criteria. Thus, there were 319 participants randomly assigned to the interim methadone maintenance (n=199) or waiting list (n=120) condition. The mean (SD) age of all participants was 41.4 (5.9) years. Of the participants, 59.2% were men, 6.6% were white, and 93.1% were African American (Table 1). Also, 19.7% of the participants were married and 37.9% reported working either full- or part-time. Participants reported their first use of heroin at a mean age of 22.9 years, and committing their first crime at a mean age of 20.7 years. In the 30 days before study entry, participants reported using heroin a mean of 29.6 days and cocaine a mean of 7.0 days. Of the entire sample, 127 (39.8%) re-
Table 1. Baseline Characteristics of the Sample

<table>
<thead>
<tr>
<th>Variable</th>
<th>Interim Group (n = 199)</th>
<th>Control Group (n = 120)</th>
<th>Total (N = 319)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>41.1 (5.6)</td>
<td>41.9 (6.5)</td>
<td>41.4 (5.9)</td>
</tr>
<tr>
<td>Male sex†</td>
<td>115 (57.8)</td>
<td>74 (61.7)</td>
<td>189 (59.2)</td>
</tr>
<tr>
<td>Race‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td>185 (93.0)</td>
<td>112 (93.3)</td>
<td>297 (93.1)</td>
</tr>
<tr>
<td>White</td>
<td>13 (6.5)</td>
<td>8 (6.7)</td>
<td>21 (6.6)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>1 (0.5)</td>
<td>0</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Married†</td>
<td>42 (21.1)</td>
<td>21 (17.5)</td>
<td>63 (19.7)</td>
</tr>
<tr>
<td>Employed in the past 30 d†</td>
<td>71 (35.7)</td>
<td>50 (41.7)</td>
<td>121 (37.9)</td>
</tr>
<tr>
<td>Education, y</td>
<td>11.6 (1.6)</td>
<td>11.5 (1.4)</td>
<td>11.5 (1.5)</td>
</tr>
<tr>
<td>Age at onset of heroin use, y‡</td>
<td>22.8 (7.2)</td>
<td>23.0 (6.7)</td>
<td>22.9 (7.0)</td>
</tr>
<tr>
<td>Time of heroin use in the past 30 d, d</td>
<td>29.5 (2.1)</td>
<td>29.8 (1.0)</td>
<td>29.6 (1.8)</td>
</tr>
<tr>
<td>Age at onset of cocaine use, y‡</td>
<td>24.3 (7.3)</td>
<td>24.8 (7.3)</td>
<td>24.5 (7.3)</td>
</tr>
<tr>
<td>Time of cocaine use in the past 30 d, d</td>
<td>7.5 (10.7)</td>
<td>6.3 (9.6)</td>
<td>7.0 (10.3)</td>
</tr>
<tr>
<td>Time of alcohol intoxication in the past 30 d, d</td>
<td>7.3 (11.3)</td>
<td>7.7 (11.3)</td>
<td>7.5 (11.2)</td>
</tr>
<tr>
<td>Age at first crime, y</td>
<td></td>
<td></td>
<td>20.4 (9.0)</td>
</tr>
<tr>
<td>Money spent on drugs in the past 30 d, $</td>
<td>910 (822)</td>
<td>818 (796)</td>
<td>876 (812)</td>
</tr>
<tr>
<td>Illegal income in the past 30 d, $</td>
<td>456 (1018)</td>
<td>471 (994)</td>
<td>462 (1007)</td>
</tr>
<tr>
<td>Lifetime incarceration, mo</td>
<td>22 (36)</td>
<td>19 (32)</td>
<td>21 (34)</td>
</tr>
<tr>
<td>Lifetime arrests, mo</td>
<td>4.0 (5.3)</td>
<td>3.5 (4.6)</td>
<td>3.8 (5.0)</td>
</tr>
</tbody>
</table>

*Data are given as mean (SD) unless otherwise indicated. There were no statistically significant differences between the interim and control groups for any of the variables reported (P > .05 for all).
†Data are given as number (percentage) of subjects in each group.
‡n = 318 because of missing data.
§Eighteen subjects in the interim group and 12 subjects in the control group never used cocaine; n = 289.
||Seventeen subjects in the interim group and 21 subjects in the control group denied ever committing a crime; n = 281.

Interim participants entering the study were less likely to enter treatment as a result of incarceration. On an intent-to-treat basis, the interim treatment participants remained in interim treatment for a mean (SD) of 102.6 (40.5) days.

Interim Methadone Maintenance Treatment

Of the 199 participants assigned to interim treatment, 194 (97.5%) received at least 1 dose of medication. The mean dose of methadone during treatment was 78.4 mg, and 93.5% of medication visits were attended. Only 3 participants asked for and received an emergency counseling session: 1 for family problems, 1 for legal problems, and 1 for help with social services. Of 194 interim participants, 31 (16.0%) dropped out of treatment before day 120; 1 participant died when struck by a car, and 1 left treatment as a result of incarceration. On an intent-to-treat basis, the interim treatment participants remained in interim treatment for a mean (SD) of 102.6 (40.5) days.

Main Outcomes

Entry Into Comprehensive Methadone Treatment

Of the 199 interim treatment participants, 151 (75.9%) reported entering comprehensive treatment after a mean (SD) of 117 (15.2) days of interim treatment, while only 25 (20.8%) of the 120 waiting list participants reported entering comprehensive methadone maintenance treatment after a mean (SD) of 38.5 (38.3) days out of treatment and on the waiting list (x² = 78.9, R² = 0.35, P < .001). Interim compared with control participants took longer on average to enter comprehensive treatment, although interim participants entered at a substantially higher rate. Because interim participants were guaranteed comprehensive admission, they may have been less

Significant Events During the Study

There were 18 serious adverse events. All were determined by the Friends Research Institute, Inc., institutional review board and an external medical monitor not to be study related. The serious adverse events in the interim condition consisted of 14 hospitalizations and 1 death by motor vehicle crash. The serious adverse events in the control condition included 2 hospitalizations and 1 death due to sickle cell crisis. The higher number of serious adverse events in the interim condition in all likelihood resulted from the higher number of experimental participants and the increased likelihood that study staff would learn about hospitalization of interim treatment participants through their absence from the treatment program. Because the unmodified ASI was used, the follow-up interview did not include information on adverse events for the entire period before follow-up. No one was withdrawn from study participation.
active than control participants in seeking transfer before the 120-day transfer date. Of the 151 participants who reported entering comprehensive treatment from interim treatment, 124 (82.1%) reported entering the methadone program in which the study was conducted and 27 (17.9%) reported entering other programs. Of the 48 interim treatment participants for whom we have no data indicating that they entered comprehensive treatment, 37 reported not entering treatment, 1 was deceased, 1 was in prison, and 9 were not located. In contrast, 82 waiting list participants reported not entering comprehensive treatment, 1 was deceased, 4 were in prison, and 8 were not located.

### Drug Use

#### Overall Drug Use
At baseline, there were no differences in the ASI drug use composite score between the 2 conditions or in the percentage of urine test results that were positive for heroin or cocaine. However, at follow-up, there was a significant condition × prepost interaction effect ($P < .001$) on the drug use composite score and in the percentage of drug test results positive for heroin, but not for cocaine.

#### Heroin
Both groups reported heroin use nearly every day in the month before study entry (Table 1). There was a significant condition × prepost interaction effect ($P < .001$) for self-reported heroin use (Table 2). Over the 30 days before the follow-up interview, interim treatment participants reported using heroin on a mean of 4.2 days, while waiting list participants reported using heroin on a mean of 26.4 days. The simple main effects test between the interim treatment and the waiting list conditions at follow-up was significant ($F_{1,284} = 421.2, r^2 = 0.60, P < .001$).

Both groups showed at least a 99.0% positive rate on baseline heroin urine test results (interim group, 176 [99.4%] of 177 subjects; and control group, 96 [99.0%] of 97 subjects). At the follow-up interview, there was a significant difference between conditions ($P < .001$), with the interim treatment and waiting list conditions having 56.6% (99/175) and 79.2% (80/101) heroin-positive rates, respectively. In addition to the urine test at the 120-day follow-up, 2 additional drug tests using oral swabs were performed on participants enrolled in interim treatment at 6 and 7 weeks.

Most interim participants had either no or only 1 postbaseline heroin-positive drug test result. Of the 199 participants, 70 (35.2%) had 0 positive drug test results, 74 (37.2%) had 1 positive drug test result, 30 (15.1%) had 2 positive drug test results, and 16 (8.0%) had 3 positive drug test results. Urine drug testing data were missing for 9 participants (4.5%).

#### Cocaine
During the 30 days before study entry, the interim treatment and waiting list groups reported 7.2 and 6.1 days of cocaine use, respectively. These were not significantly different (Table 1). At follow-up, the condition × prepost interaction effect ($P < .001$) and the subsequent test of the simple main effect of conditions at follow-up were significant ($F_{1,284} = 16.2, r^2 = 0.05,$

<table>
<thead>
<tr>
<th>Variable</th>
<th>Interim Group</th>
<th>Control Group</th>
<th>$F_{1,284}$ Value</th>
<th>$P$ Value</th>
<th>$R^2$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time of heroin use in the past 30 d, d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>29.5 (2.2)</td>
<td>29.8 (1.0)</td>
<td>421.2</td>
<td>&lt;.001</td>
<td>0.60</td>
</tr>
<tr>
<td>4 mo</td>
<td>4.2 (8.6)</td>
<td>26.4 (8.8)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Time of cocaine use in the past 30 d, d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>7.2 (10.6)</td>
<td>6.1 (9.7)</td>
<td>12.3</td>
<td>&lt;.001</td>
<td>0.04</td>
</tr>
<tr>
<td>4 mo</td>
<td>2.4 (5.5)</td>
<td>5.8 (8.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time of alcohol intoxication in the past 30 d</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>7.5 (11.4)</td>
<td>7.2 (10.9)</td>
<td>11.5</td>
<td>&lt;.001</td>
<td>0.04</td>
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<tr>
<td>4 mo</td>
<td>4.0 (8.3)</td>
<td>8.5 (11.9)</td>
<td></td>
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<tr>
<td>Money spent on drugs in the past 30 d, $</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Baseline</td>
<td>883 (818)</td>
<td>813 (814)</td>
<td>20.1</td>
<td>&lt;.001</td>
<td>0.07</td>
</tr>
<tr>
<td>4 mo</td>
<td>76 (206)</td>
<td>560 (981)</td>
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<tr>
<td>Illegal income in the past 30 d, $</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>459 (1046)</td>
<td>485 (1022)</td>
<td>5.5</td>
<td>&lt;.002</td>
<td>0.02</td>
</tr>
<tr>
<td>4 mo</td>
<td>36 (160)</td>
<td>412 (1391)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Opiate-positive drug test result†</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>192 (99.5)</td>
<td>111 (98.2)</td>
<td>.28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 mo‡</td>
<td>99 (56.6)</td>
<td>80 (79.2)</td>
<td>&lt;.001</td>
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<td>Cocaine-positive drug test result†</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>122 (62.9)</td>
<td>70 (61.9)</td>
<td>.87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 mo¶</td>
<td>107 (61.5)</td>
<td>62 (62.6)</td>
<td>.85</td>
<td></td>
<td></td>
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</table>

*Data are given as mean (SD) unless otherwise indicated. $R^2$ is the canonical value associated with the condition × prepost effect. The numbers for all data measured in time (days) and money ($) are as follows: interim, n = 182; control, n = 104. Methadone is as methadone hydrochloride.

†Data are given as number (percentage) of each group. Because of missing data, the sample sizes in these groups varied.

‡Interim, n = 193; control, n = 113.
§Interim, n = 175; control, n = 101.
||Interim, n = 194; control, n = 113.
¶Interim, n = 174; control, n = 99.
Comparison of Drug Test Results With Self-report at the 120-Day Follow-up. Drug test reports were compared with participants’ reported drug use over the 30 days before the follow-up interview. This analysis included existing data only of participants (n = 122) whose follow-up interviews (based on the time of entry into comprehensive treatment or at 120 days from baseline) took place no more than 122 days after baseline because heroin and cocaine enzyme-multiplied immunoassay technique test results generally remain positive for about 2 days. The results indicate that 73.8% of all postentry heroin drug test results matched the self-report (27.9% were both negative and 45.9% were both positive). An additional 15.6% (drug test had negative and self-report had positive results) could be considered consistent, because heroin and cocaine drug test results may remain positive for approximately 2 to 3 days after last use and participants who reported drug use within 30 days could still have a negative test result if their reported use was more than 3 days before submitting the specimen. Only 10.6% of participants reported no drug use but had a positive urine test result for heroin; 15.9% reported no cocaine use but had a positive urine test result. Also, for cocaine, 43.3% of drug test results and self-reports were both positive, and 37.5% of drug test results and self-reports were both negative; 3.3% of drug test results were positive while self-reports were positive. Taken together, between 73.8% and 89.4% of participants’ heroin drug test results and self-reports were consistent.

Alcohol. There were no significant differences in the ASI alcohol composite score or the self-reported number of days in the past month in drinking to intoxication before study entry (Table 1). The condition × prepost interaction effects were significant (P < .002 and P < .001, respectively). The test of the simple main effect of conditions at follow-up indicated that the interim treatment participants reported significantly fewer mean days of drinking to intoxication (4.0 days) than waiting list participants (8.5 days) at follow-up (F1,284 = 14.5, sr² = 0.048, P < .001) (Table 2).

Crime
There were no significant differences between the 2 conditions at baseline in the ASI legal composite score, the self-reported amount of money spent on drugs in the past 30 days, and the amount of illegal income in the past 30 days (Table 1). There were significant condition × prepost interaction effects for the composite scores (P < .001), money spent on drugs in the past 30 days (P < .001), and receipt of illegal income in the past 30 days (P < .002). The test of the simple main effect of conditions at follow-up indicated that in the 30 days before the follow-up interview, the interim treatment group reported substantially less money spent on drugs (F1,284 = 20.1, sr² = 0.07, P < .001) and substantially less illegal income (F1,284 = 5.5, sr² = 0.02, P < .02) than did the waiting list group. As shown in Table 2, interim treatment participants reported spending $76 in the past 30 days on drugs vs $560 reported by the waiting list participants ($36 vs $412 in illegal income received, respectively).

The results of this randomized clinical trial show clearly that compared with usual waiting list control conditions, interim methadone maintenance treatment, even under the stringent requirements mandated by the US regulations, is (1) an effective means of increasing the likelihood that individuals seeking treatment will enter comprehensive methadone treatment, (2) associated with a significant reduction in heroin use, and (3) associated with a significant self-reported reduction in crime.

To our knowledge, this is the first rigorous controlled evaluation of interim methadone maintenance treatment that compared providing an adequate dose of methadone and only emergency counseling with real-life waiting list conditions for heroin-dependent individuals seeking treatment. There are several significant differences between the present study, performed under the federal interim methadone regulations, and the 2 previously published reports of low-threshold methadone maintenance conducted in the United States. Participants in the frequent contact control group of Yancovitz et al13 were required to attend bimonthly meetings during which they were paid $20; received free condoms, and provided a urine sample for drug testing. After 30 days, they were automatically transferred to the low-threshold methadone treatment. This control group does not resemble the real-life waiting list condition in which individuals are not contacted until a treatment slot becomes available. Furthermore, participants in the low-threshold group participated in bimonthly (unpaid) interviews. This level of attention differs markedly from the standard of interim methadone maintenance treatment that is mandated to provide only emergency counseling. Take-home doses reduced the compliance burden.

Employed participants who remained for at least 1 month in the minimal services group described by McLe llan et al15 received 2 take-home doses per week that were not contingent on negative urine drug test results. All minimal service participants were automatically transferred from minimal services to comprehensive treatment if they had 8 consecutive heroin- or cocaine-positive drug test results. Despite this transfer procedure, 31% of methadone-only participants achieved 8 consecutive negative heroin drug test results and a similar percentage achieved 8 consecutive negative cocaine test results. More intensive services coupled with take-home doses made contingent on negative urine drug test results provided better outcomes than minimal services; however, a robust minority of patients improved with methadone alone.

In contrast to the study by Yancovitz et al,13 self-reported cocaine use at follow-up in the present study was significantly lower for interim participants than wait-
ing list controls. However, urine cocaine test results at follow-up in the present study showed no significant difference between the 2 study conditions. The discordance between conditions on self-reported cocaine use and cocaine drug test results may be attributable to inaccurate self-report or to differences in time period covered by self-report and urine test results. Because of difficulties in locating some participants, follow-up interviews (using the ASI) were conducted using time–follow-back procedures covering the 30 days preceding the due date of the interview rather than the actual date of the interview; the urine specimen was collected at the interview. Thus, the urine test result often reflected a later period than the ASI data.

One recurrent finding in the treatment literature is the reduction in crime associated with methadone maintenance treatment. In this study, self-reported illegal income was significantly reduced among interim participants who reported obtaining an average of $112 from illegal activity in the 30 days before the follow-up interview in contrast to control participants, who self-reported $972 from illegal activity in the same period. Assuming that this reduction can be corroborated with data from other sources, the $860 per month per participant difference in illegal income between study conditions would more than pay for the estimated $80 per month cost of interim methadone in the Baltimore area.

Despite the existence of standards set forth in the requirements for accreditation of Opioid Treatment Programs, the set of services that constitute comprehensive maintenance treatment varies considerably from program to program. Some programs provide social, vocational, and primary medical services, while others provide less than supervised methadone and weekly (or less frequent) group therapy sessions aimed at reducing drug use. Typically, the range of services is dependent on those that are supported or reimbursed by the state in which the program is located. In the Baltimore area, the typical program provides little more than the minimum previously described. Furthermore, in the Baltimore area, cocaine use is less responsive to treatment in Opioid Treatment Programs than heroin use. The persistence of some cocaine use during interim treatment was disappointing, but not unexpected.

All of the available evidence supports the idea that interim methadone maintenance treatment can minimize the adverse consequences of heroin addiction among individuals seeking treatment and decrease the likelihood of entry into regular methadone treatment. Studies indicate that out-of-treatment heroin-addicted individuals have between 3 and 7 times the mortality rate and 6 times the rate of acquiring human immunodeficiency virus than those in treatment. While other approaches to engaging out-of-treatment individuals in treatment have been effective, the interim maintenance approach uniquely capitalizes on the motivation of the individual seeking treatment by providing help at the time of the request.

LIMITATIONS

There are several limitations to this study. First, the predominantly African American sample does not permit extending these findings to white and Latino American subjects. Second, it is a single-site study conducted in a treatment program that used a medication unit located a short distance (10-minute walk) to the emergency counseling site. It is possible that additional counseling may have been requested had the medication and counseling units been located in the same building. Finally, it is not known if these findings would generalize to interim treatment provided for a fee. It has been reported that charging fees reduces retention in Opioid Treatment Programs. Providing treatment at no cost in this study probably played some role in the high retention rate of patients assigned to interim treatment. However, all but 1 of the Opioid Treatment Programs in Baltimore are run by not-for-profit entities, receive grant funding from the government to provide treatment, and use a sliding scale to determine patient fees, which are often set between $5 and $10 per week. Most clinics, including the clinic that was the site for this study, are reluctant to discharge patients who do not pay these modest fees. We believe it is unlikely that the retention rates would have differed significantly had the interim participants been treated, with respect to fees, in a manner comparable to those enrolled at the same clinic. We are conducting an evaluation of that question in 6 methadone programs in Baltimore.

SUMMARY

This study has demonstrated that interim methadone maintenance facilitates entry into comprehensive methadone treatment for applicants who ordinarily would be placed on a waiting list. This finding has important policy implications for the treatment system in the United States. While the principal goal of interim treatment is entry into comprehensive treatment, interim treatment per se is associated with considerable reductions in heroin use and crime. This significant benefit can have a high impact if interim treatment were adopted on a large scale in cities, such as Baltimore, with considerable numbers of heroin-addicted individuals on waiting lists.

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