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Interim treatment: Bridging delays to opioid treatment access

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ABSTRACT

Objective. Despite the undisputed effectiveness of agonist maintenance for opioid dependence, individuals can remain on waitlists for months, during which they are at significant risk for morbidity and mortality. To mitigate these risks, the Food and Drug Administration in 1993 approved interim treatment, involving daily medication + emergency counseling only, when only a waitlist is otherwise available. We review the published research in the 20 years since the approval of interim opioid treatment.

Methods. A literature search was conducted to identify all randomized trials evaluating the efficacy of interim treatment for opioid-dependent patients awaiting comprehensive treatment.

Results. Interim opioid treatment has been evaluated in four controlled trials to date. In three, interim treatment was compared to waitlist or placebo control conditions and produced greater outcomes on measures of illicit opioid use, retention, criminality, and likelihood of entry into comprehensive treatment. In the fourth, interim treatment was compared to standard methadone maintenance and produced comparable outcomes in illicit opioid use, retention, and criminal activity.

Conclusions. Interim treatment significantly reduces patient and societal risks when conventional treatment is unavailable. Further research is needed to examine the generality of these findings, further enhance outcomes, and identify the patient characteristics which predict treatment response.

Introduction

Opioid abuse and dependence are reaching epidemic proportions in the United States, resulting in drug overdoses, premature death, criminal activity, lost workdays, and other consequences that cost over $56 billion annually (Becker et al., 2008; Birnbaum et al., 2011; Clausen et al., 2009; Jones et al., 2013; Substance Abuse and Mental Health Services Administration, 2010; Wisniewski et al., 2008). Opioid maintenance treatment, typically involving the agonist medications methadone or buprenorphine, is the most efficacious and widely-used treatment for opioid dependence and dramatically reduces morbidity, mortality and spread of infectious disease (Ball and Ross, 1991; Johnson et al., 2000; Stotts et al., 2009).

However, demand for maintenance treatment remains consistently above available capacity in many areas of the country (Friedmann et al., 2003; Harlow et al., 2013; Sigmon, 2014; Wenger and Rosenbaum, 1994). An alarming number of methadone clinics have extensive waitlists, due in part to inadequate public funding and unfavorable zoning regulations (Des Jarlais et al., 1995; Fountain et al., 2000; Gryczynski et al., 2009; Peles et al., 2012, 2013; Peterson et al., 2010). Municipal governments in areas across North America, for example, have attempted to restrict the establishment of methadone treatment programs through zoning bylaws (e.g., Bernstein and Bennett, 2013). Federal regulations also require that methadone programs include comprehensive services (e.g., on-site psychosocial counseling, urinalysis testing, medical management) and, while beneficial to many patients, this also can increase programs' cost and prohibit rapid expansion. Furthermore, while approval of buprenorphine (Suboxone®) extended maintenance treatment into general medical practices, many areas of the country have an insufficient number of willing providers, due to physicians' concerns about induction logistics, reimbursement challenges, potential for medication diversion, lack of support for providers, and lack of psychosocial services for patients (Barry et al., 2009; Becker and Fiellin, 2006; Kissin et al., 2006; Netherland et al., 2009; Sigmon, 2015). The result is that many opioid-dependent individuals needing treatment may remain on waitlists for weeks or months, particularly those who must await admission to a subsidized program (Schwartz et al., 2009, 2011; Sherba et al., 2012). During this delay to treatment, they are at significant risk for continued illicit drug use, criminal activity, infectious disease, overdose, and mortality (Adamson and Sellman, 1998; Clausen et al., 2009; Cooper, 1989; Darke and Hall, 2003; Schwartz et al., 2009; Warner-Smith et al., 2001; Wenger and Rosenbaum, 1994). Prolonged waits are also associated with reduced likelihood of eventual treatment entry (Donovan et al., 2001; Festinger et al., 1995; Hser et al., 1998; Kaplan and Johri, 2000).

One effort to mitigate these risks during the delay to treatment has been to offer interim treatment to those awaiting enrollment into a

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traditional methadone program. Methadone programs are generally required to pair medication with comprehensive treatment plans that include regular counseling, vocational rehabilitation and urine toxicology testing. However, in recognition of the growing waitlists and delays in treatment access, in 1993 the Food and Drug Administration (FDA) and the Substance Abuse and Mental Health Services Administration (SAMHSA) granted permission for methadone clinics to provide medication without accompanying psychosocial services on a temporary basis when only a waiting list would be otherwise available (Institute of Medicine (IOM), 1995; Nightingale, 1993). The rationale behind this initial approval of interim methadone treatment was largely based on reducing human immunodeficiency virus (HIV) risk and transmission among intravenous drug abusers who could not be placed in comprehensive methadone treatment programs within 14 days of seeking admission (Dole, 1991; Nightingale, 1993). Under this ruling, the FDA authorized interim methadone treatment to be provided only by existing programs already licensed as a specialty methadone treatment clinic. The regulations mandated that interim methadone patients ingest all medication doses under direct staff observation, thus requiring daily clinic visits (Institute of Medicine (IOM), 1995). They also limited the duration of interim treatment to no more than 120 days, with clinics required to discharge patients at that time or admit them to standard methadone treatment if a slot has become available. Finally, the clinic was required to notify their state's public health officer when interim treatment begins and ends for each patient.

We review here the published controlled studies conducted over the past two decades evaluating the efficacy of the interim treatment approach for patients awaiting admission to standard opioid maintenance programs. Our aim is to characterize what is known empirically about interim opioid treatment, as well as to discuss the strengths and limitations associated with this treatment approach.

Methods

Study selection

Literature searches were conducted using PubMed, MEDLINE, PsychINFO, PREMEDLINE, Cochrane Central Register of Controlled Trials, and Cochrane Database of Systematic Reviews using the terms 'interim methadone' and 'interim buprenorphine', both alone and paired with the term 'treatment'. Relevant references from retrieved articles were also evaluated. The search was conducted in November 2014 and did not restrict the timeframe for eligible studies.

Studies were included provided that they met the following criteria: (1) involved interim methadone or buprenorphine treatment with opioid-dependent individuals awaiting entry into comprehensive treatment; (2) were published in a peer-reviewed journal; (3) included randomization to an experimental comparison condition; and (4) used a research design wherein treatment effects could be attributed to the interim treatment condition.

Findings

Four randomized trials have evaluated interim treatment for opioid dependence using experimental designs wherein effects on treatment outcome could be attributed to the interim treatment condition. A summary of their methods and results is presented in Table 1.

The first study on this topic was published just prior to the FDA's formal approval of interim treatment. In that trial, heroin-dependent adults were recruited from the waitlists of 23 Beth Israel methadone maintenance clinics throughout New York City (Yancovitz et al., 1991). Participants had been on these waitlists for an average of 3 months. The investigators randomly assigned participants to either an interim methadone (N = 149) or control (N = 152) condition. Interim methadone participants visited the clinic 6 days per week for dosing, received take-homes on Sundays, and received an approximate methadone dose of 80 mg/day. Their participation in the interim methadone condition extended from the time of study enrollment until an opening occurred in the clinic to which they had originally applied. Interim methadone participants received only minimal counseling or support services, free condoms and HIV education, and biweekly urinalysis. Control participants remained on their waitlist and visited the clinic biweekly for urinalysis, free condoms and a follow-up assessment. This control condition lasted for one month, after which participants were transferred into the interim methadone condition for the remaining time until a treatment slot became available. Comparison between the two groups on the primary outcome (i.e., heroin use) was limited to this 1-month period. Urinalysis data showed significantly less heroin use among participants assigned to the interim methadone vs. control condition, with 29% vs. 60% testing positive for heroin at 1-month follow-up, respectively ($p < .001$). Also examined was the number of participants who had entered conventional drug treatment programs 16 months after the interim treatment program had begun. More interim methadone participants had entered treatment by that timepoint compared to controls (72% vs. 56%, respectively; $p < .005$). Taken together, this study provided an initial demonstration of the feasibility and

Table 1
Randomized trials evaluating interim treatment with opioid-dependent patients.

Reference	Experimental intervention	Comparison intervention	Illicit opioid abstinence	Additional outcomes
Yancovitz et al., 1991	Interim methadone; 6 clinic visits/week; biweekly urinalysis; N = 149	Continued waitlist for 1 month; biweekly visits for urinalysis; N = 152	Fewer IM participants tested positive for heroin at 1-month FU than controls (29% vs. 60%, respectively; p < .001)	More IM participants eventually entered comprehensive treatment than controls (72% vs. 56%, respectively; p < .005)
Krook et al., 2002	Interim buprenorphine for 3 months; 6 visits/week; N = 55	Double-blind placebo treatment for 3 months; 6 visits/week; N = 51	IB participants reported greater reductions in heroin use on experimenter-developed VAS (p < .0001)	IB participants retained longer than controls (42 vs. 14 days, respectively; p < .001)
Schwartz et al., 2006	Interim methadone for 4 months; 7 visits/week; N = 199	Continued waitlist for 4 months; no contact other than 4-month FU assessment; N = 120	Fewer IM participants tested positive for heroin at end of study than controls (56.6% vs. 79.2%, respectively; p < .001) IM participants reported fewer days of heroin use in past 30 at end of study (4.2 vs. 26.4 days, respectively; p < .001)	More IM participants eventually entered comprehensive treatment than controls (75.9% vs. 20.8%, respectively; p < .001) IM participants reported less illegal income in past 30 at end of study ($36 vs. $412, respectively; p < .02)
Schwartz et al., 2011	Interim methadone for 4 months; 7 visits/week; N = 99	1) Standard methadone; ~2 counseling sessions/month; daily dosing visits + some take-homes; N = 104 2) Restored methadone; ~4 counseling sessions/month with counselor with reduced caseload; daily dosing visits + some take-homes; N = 27	IM, SM, and RM groups showed similar reduction from baseline in heroin use, with 54%, 58%, and 56% of patients heroin-positive at 4-month follow-up, respectively (p = .98) IM, SM, and RM groups showed similar reduction from baseline in self-reported heroin use (2.6, 3.6 and 2.8 days in past month at 4-month follow-up, respectively; p = .21)	4-month retention rates were similar for IM, SM and RM groups (91.9%, 80.8% and 88.9% respectively; p = .06) IM, SM, and RM groups showed similar reductions from baseline in criminal activity, money spent on drugs, and illegal income (p's < .001), with the IMT group showing greater reductions than SM at 2-month follow-up (p's < .05)