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The multi-site prescription opioid addiction treatment study: 18-month outcomes☆,☆☆

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ABSTRACT

Despite the high prevalence of prescription opioid dependence in the U.S., little is known about the course of this disorder and long-term response to treatment. We therefore examined 18-month post-randomization outcomes of participants in the Prescription Opioid Addiction Treatment Study, a multi-site, randomized controlled trial examining varying durations of buprenorphine-naloxone treatment and different intensities of counseling for prescription opioid dependence. Thus the current follow-up study provides a unique contribution to the field by reporting longer-term outcomes of a well-characterized population of treatment-seeking prescription opioid dependent patients. Participants from the treatment trial (N = 252/653) completed an 18-month follow-up telephone assessment. Multivariable analyses examined associations between participant characteristics and key indicators of month-18 status: opioid abstinence, DSM-IV opioid dependence, and opioid agonist treatment. Overall, participants showed improvement from baseline to month 18: 49.6% were abstinent in the previous 30 days, with only 16.3% opioid-dependent. Some participants, however, had initiated past-year heroin use (n = 9) or opioid injection (n = 17). Most participants (65.9%) engaged in substance use disorder treatment during the past year, most commonly opioid agonist therapy (48.8%). Of particular interest in this population, multivariable analysis showed that greater pain severity at baseline was associated with opioid dependence at 18 months. In conclusion, although opioid use outcomes during the treatment trial were poor immediately following a buprenorphine-naloxone taper compared to those during 12 weeks of buprenorphine-naloxone stabilization, opioid use outcomes at 18-month follow-up showed substantial improvement over baseline and were comparable to the rate of successful outcomes during buprenorphine-naloxone stabilization in the treatment trial.

1. Introduction

Abuse of prescription opioids is a well-recognized public health problem. Currently, prescription opioid use disorders are four times more common than heroin-related disorders (Substance Abuse and Mental Health Services Administration, 2012). Among treatment-seeking opioid users, the most recent treatment in the past year was 1.7 times as likely to be for prescription opioids than heroin (Substance Abuse and Mental Health Services Administration, 2012); 10% of admissions for substance use disorders (SUDs) are attributed to prescription opioid use, a fivefold increase from 2001–2011 (Substance Abuse and Mental Health Services Administration & Center for Behavioral Health Statistics and Quality, 2013).

Because the increased prevalence of prescription opioid use disorders is relatively recent, most research on opioid use disorders has focused on heroin-dependent patients. It remains unclear whether the treatment response and course of the disorder among opioid-dependent heroin users can be generalized to those using prescription opioids. For example, studies suggest a greater likelihood of successful buprenorphine treatment outcomes among those dependent on prescription opioids vs. heroin (Moore et al., 2007; Nielsen, Hillhouse, Thomas, Hasson, & Ling, 2013; Potter et al., 2013). However, the Prescription Opioid Addiction Treatment Study (POATS), conducted by the National Drug Abuse Treatment Clinical Trials Network, found rates of successful outcome for patients with

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DSM-IV dependence on prescription opioids to be similar to those of heroin-dependent populations in other trials (Weiss et al., 2011).

To date, POATS is the only large-scale randomized, controlled trial of treatment for prescription opioid dependence (Weiss et al., 2011). POATS examined different intensities of counseling and different durations of buprenorphine-naloxone (bup-nx) to treat patients with DSM-IV prescription opioid dependence. Several key findings emerged: 1) treatment response was similar for participants receiving individual drug counseling in addition to bup-nx and standard medical management; 2) treatment response to brief bup-nx treatment (4-week taper) was overwhelmingly poor: only 7% had successful opioid use outcomes; and 3) treatment outcomes after 12 weeks of bup-nx was considerably better: 49% of participants were successful. Pre-specified secondary analyses demonstrated that even a limited history of heroin use predicted poor treatment outcome; chronic pain was unrelated to outcome (Weiss et al., 2011).

POATS offers an important, unique opportunity to examine longer-term outcomes for prescription opioid dependence in a well-characterized cohort of treatment-seeking individuals. Participants were assessed three times, approximately 18, 30, and 42 months post-randomization. This report presents outcomes at the first of these three follow-up assessments. We examined the following questions: 1) What is the extent of substance use, particularly prescription opioids and heroin? 2) How many participants are engaged in SUD treatment? 3) Can participants' 18-month substance use outcomes be predicted from baseline characteristics, treatment condition, or study outcomes?

2. Methods

2.1. Trial design

POATS was conducted from 2006–2009 at ten United States sites. The primary research question was whether adding individual drug counseling to bup-nx and standard medical management improved opioid use outcomes a) after a brief (4-week) bup-nx taper or b) at the end of a subsequent 12-week bup-nx stabilization regimen for those who relapsed to opioids during brief treatment (for details, see Potter et al., 2010; Weiss et al., 2010; Weiss et al., 2011; Weiss et al., 2010).

The study utilized a two-phase, adaptive design: participants were randomized in each phase to receive standard medical management (Fiellin, Pantalon, Schottenfeld, Gordon, & O'Connor, 1999) alone or in addition to individual opioid drug counseling (Pantalon, Fiellin, Schottenfeld, Gordon, & O'Connor, 1999). Standard medical management consisted of a 45-minute initial visit followed by weekly 15-minute medical counseling sessions with a physician. Opioid drug counseling consisted of twice weekly visits in weeks 1–4 plus weekly visits in weeks 6 and 8 in the brief treatment phase; in the extended phase, participants assigned to counseling had two sessions a week in weeks 1–6 and weekly visits in weeks 7–12. In the brief treatment phase, participants were inducted and stabilized on bup-nx for 2 weeks, tapered over 2 weeks, then followed for 8 weeks. Outcome for this phase was classified as the presence or absence of treatment success, i.e., finishing the 12-week study period with a) ≤4 days of urine-confirmed, self-reported opioid use in a 30-day period; b) no consecutive weeks with opioid-positive urine tests; c) no additional formal SUD treatment; and d) ≤1 missing urine sample. Only participants who were unsuccessful with brief treatment were eligible for randomization to the extended treatment: 12 weeks of bup-nx stabilization. Successful outcome for this phase was opioid abstinence in week 12 and ≥2 of the 3 previous weeks. Participants were tapered from bup-nx during weeks 13-16 and followed for another 8 weeks. Participants then had no further contact with the study until they were re-contacted by a staff member at their site in December 2008 (when the follow-up study was approved), asking them to participate in the follow-up study. For the brief treatment phase, participants were stratified according to the presence of chronic pain and a lifetime history of heroin use. For the extended treatment phase, participants were stratified by their treatment condition in the brief treatment phase.

The primary outcome measure for the trial was success or failure at the end of buprenorphine-naloxone stabilization, i.e., during weeks 9–12 of the extended treatment phase. Secondary outcomes include the likelihood of success after a brief buprenorphine-naloxone taper at the beginning of the trial and 8 weeks after a second taper following 12 weeks of buprenorphine-naloxone stabilization in the extended treatment phase.

2.2. Trial sample

Eligible participants were ≥18 years old and met DSM-IV criteria for current opioid dependence. Participants were excluded if they used heroin >4 of the past 30 days; had a lifetime DSM-IV opioid-dependence diagnosis due solely to heroin; had ever injected heroin; required continued pain management with opioids; had experienced a traumatic pain event in the previous 6 months; were psychiatrically unstable; required immediate medical attention for dependence on other substances; or had liver function tests >5 times the upper limit of normal. Participants prescribed opioids for pain could be enrolled only if their prescribing physician gave permission for them to discontinue use of these opioids and to enter the study. The study enrolled 653 outpatients, 360 of whom entered extended treatment.

2.3. Follow-up procedures

Institutional review board approval was obtained from each site for the follow-up study; one site did not participate. For efficiency and oversight, data were collected by the lead investigative team at McLean Hospital, via telephone by trained interviewers. Telephone interviews have been used in other SUD trials, having been shown to yield valid data similar to that of face-to-face interviews (Kramer et al., 2009; Midanik & Greenfield, 2003).

For the follow-up component, the focus of this report, the target date was 18 months after baseline, with a window from month 17 until one month before the 30-month assessment target date. Most (74%) were completed by month 24 (mean = month 21; details in Table 1). Data were entered directly into a web-based, electronic data capture system maintained by an independent data management center, in compliance with 21 Code of Federal Regulations Part 11 (National Archives and Records Administration, 2013). To maintain fidelity, study coordinators monitored interviewers and provided feedback.

Participants received $75, similar to compensation rates in other SUD treatment studies (Festinger et al., 2005) and another $10 for keeping the first scheduled assessment. Participants who were in jeopardy of missing their assessment window (i.e., 6 weeks before month 29) were offered an additional $25 bonus as an incentive to complete their assessment before the deadline.

2.4. Measures

At month 18, a subset of treatment study measures was administered, focusing on substance use and treatment utilization, with slight modifications for telephone interviewing.

The Composite International Diagnostic Interview (CIDI; World Health Organization, 1997) was used in the main trial to diagnose SUDs, post-traumatic stress disorder, and major depressive disorder. At month 18, the CIDI assessed only opioid dependence, defined as meeting symptom criteria during the 30 days preceding the follow-up assessment. According to the DSM-IV definition, participants receiving agonist therapy who met no symptom criteria for current opioid dependence at their follow-up assessment were classified separately as having opioid dependence, on agonist therapy. The term "current