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Medication Assisted Treatment Research with Criminal Justice Populations: Challenges of Implementation

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Abstract

Creating, implementing and evaluating substance abuse interventions, especially medication-assisted treatments, for prisoners, parolees, and probationers with histories of heroin addiction is an especially challenging endeavor because of the difficulty in coordinating and achieving cooperation among diverse criminal justice, substance abuse treatment, research, and social service agencies, each with its own priorities and agenda. In addition, there are special rules that must be followed when conducting research with criminal justice-involved populations, particularly prisoners. The following case studies will explore the authors' experience of over 10 years conducting pharmacotherapy research using methadone, buprenorphine, and naltrexone with criminal justice populations. The major obstacles and how they were overcome are presented. Finally, recommendations are provided with regard to implementing and conducting research with criminal justice populations.

Introduction

Incarcerated individuals in the United States, Canada, European and Asian nations, and Australia have disproportionately higher rates of heroin addiction than the general population (Dolan, Khoei, Brentari, & Stevens, 2007; Fazel, Bains, & Doll, 2007; Kanato, 2008; Kinlock, Gordon, & Schwartz, 2011). For example, in the United States, about 2% of the general population has experienced heroin dependence, compared with 52% of the incarcerated population (Mumola & Karberg, 2006). Scarce resources are devoted to corrections-based substance abuse treatment in many nations, and many inmates with heroin addiction histories remain untreated (Dolan et al., 2007; Taxman, Perdoni, & Harrison, 2007). As a consequence, heroin addiction either continues or resumes quickly after release from incarceration (Dolan et al., 2007; Kinlock et al., 2011; Strang et al., 2006), placing newly released inmates at substantially greater risk for death from drug overdose (Binswanger et al., 2007; Farrell & Marsden, 2008; Krinsky, Lathrop, Brown, & Nolte, 2009; Merral et al., 2010; Stewart et al., 2004) and human immunodeficiency virus (HIV) and hepatitis B and C infections (Dolan et al., 2007; Inciardi, 2008; Kanato, 2008). Heroin addiction also has adverse public safety consequences as it typically results in increased criminal activity (Hough, 2002; Kinlock, O'Grady, & Hanlon, 2003; Inciardi, 2008) and re-incarceration (Dolan et al., 2005; Hough, 2002; Metz et al., 2010). Therefore, there is an urgent need to not only ensure that inmates with heroin addiction histories receive effective

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substance abuse treatment during incarceration, but also to continue that intervention following release to the community.

Because of preference for drug-free treatment or lack of knowledge regarding their effectiveness, pharmacotherapy interventions for criminal justice-involved populations, particularly in the United States, have been underutilized (Chandler, Fletcher, & Volkow, 2009; Dolan et al., 2007; Schwartz, Mitchell, Gordon, & Kinlock, in press). These interventions include opioid agonist treatment with methadone and buprenorphine, which have been found effective in reducing heroin use and retaining individuals in treatment (Kleber, 2008; Mattick et al., 2009). Also included is naltrexone, an opioid agonist, a promising treatment which was approved by the U.S. Food and Drug Administration for treating opioid dependence in 2010.

There is a growing body of evidence for the effectiveness of methadone maintenance treatment (MMT) in jail and prison settings for both inmates who were using opiates at initiation of maintenance treatment (Dolan et al., 2003, 2005; Magura, Rosenblum, Lewis, & Joseph, 1993; Tomasino, Swanson, Nolan, & Shuman., 2001) and individuals who had been previously, but not currently, opioid-dependent (Dole et al., 1969; Gordon, Kinlock, Schwartz, & O'Grady, 2008; Kinlock et al., 2007; Kinlock, Gordon, Schwartz, Fitzgerald, & O'Grady,2009; Kinlock, Gordon, Schwartz, & O'Grady, 2008). The earlier studies (Dole et al., 1969; Magura et al., 1993; Tomasino et al., 2001) were conducted in a New York City jail; opioid agonist programs for prisoners have been fewer and slower to develop. In the prison setting, results of a randomized controlled trial of an Australian program found that heroin use during incarceration was lower among treated participants compared to wait list participants during a 4-month in-prison follow-up (Dolan et al., 2003), with greater retention in community-based methadone treatment associated with lower rates of mortality, hepatitis C infection, and re-incarceration at 4-year follow-up (Dolan et al., 2005). The present authors conducted the first studies of prison-initiated opioid agonist therapy in the United States, involving pre-release prison inmates. A small-scale intervention with Levo-alpha-acetylmethadol (LAAM) was feasible and facilitated community-based treatment entry (Kinlock et al., 2005). In a subsequent, larger-scale clinical trial, short-term results at 1- and 3- months (Kinlock et al. 2007; 2008) post-release and longer-term findings at 6 and 12-months post-release (Gordon et al., 2008; Kinlock et al, 2009) indicated that prison-initiated and community-initiated MMT were superior to counseling only, and prison-initiated methadone was superior to community-initiated methadone, with respect to heroin use and community-based treatment entry and retention.

Buprenorphine, approved for the treatment of opioid dependence in the United States in 2002, has several advantages over methadone: including less stigma; lower risk of overdose; and fewer regulations, which allow its use outside opioid treatment centers (Albizu-Garcia et al., 2007; Montoya et al., 2004; Smith-Rohrberg, Bruce, & Altice, 2004; Magura et al., 2009). Buprenorphine is safe and effective for alternate-day dosing (Amass, Kamien, & Mikulich, 2000; Center for Substance Abuse Treatment (CSAT), 2004), which may increase its patient satisfaction and adherence (Amass et al., 2000) and might make it less likely to interfere with security procedures in prison (Smith-Rohrberg et al., 2004). (Security procedures include moving inmates for place to place, doing a count of all inmates in the prison). Initial examinations of buprenorphine in correctional settings in France (Levasseur, Marzo, Ross, & Blatier, 2002) and Puerto Rico (Albizu-Garcia et al., 2007) found that it is feasible and facilitated entry into community-based treatment. A randomized clinical trial comparing buprenorphine and methadone among male, heroin-dependent newly-admitted jail inmates in New York City found that while treatment completion rates in jail were similar, members of the buprenorphine group were significantly more likely to enter community-based treatment than members of the methadone group (Magura et al., 2009).

However, buprenorphine patients were significantly more likely than methadone patients to be terminated from treatment in prison for attempted diversion of medication.

Opioid antagonist treatment with naltrexone is an alternative to opioid agonist treatment. Naltrexone blocks the intoxicating and reinforcing effects of opioids, but has no opioid-like effects. When taken regularly, it reduces opiate-taking behavior (Comer et al., 2006). In 2010, the U. S. Food and Drug Administration (FDA) approved a new form of injectable naltrexone for the treatment of opioid dependence. This new delivery system (trade name Vivitrol®) is a major clinical advance because after one dose it provides extended release and thus blockade of opiate receptors for at least a month. The main reason that oral naltrexone treatment is often ineffective involves patients' failure to adhere to the daily regimen (Minozzi et al., 2006; Pettinati, Volpicelli et al., 2000). Vivitrol reduces the adherence problem as confirmed by studies showing blockade of injected opiates for over 30 days (Coviello et al., in press; Krupitsky et al., 2010).

During 2007-2008, a multi-site pilot study examined long-acting naltrexone (Depotrex ®) among opioid-dependent parolees and probationers. This feasibility study provided monthly injections to volunteers for 6 months. Preliminary data analyses have indicated that early retention rates were positive, with most drop-outs occurring between months 4 and 6 and with 42% remaining for 6 months (Coviello et al., in press).

Challenges to Implementation and Evaluation

Creating, implementing and evaluating continuity of care interventions for newly released drug-abusing offenders is an especially challenging endeavor because of the difficulty in coordinating and achieving cooperation among diverse criminal justice, substance abuse treatment, research, and social service agencies, each with its own priorities and agenda (Field, 1998; Kinlock, Schwartz, & Gordon, 2005; Kinlock, Gordon, & Schwartz, 2011). In addition, there are special rules that must be followed when conducting research with criminal justice-involved populations. Furthermore, there are ethical, methodological, and legal considerations that must be addressed in the course of carrying out research with prisoners, parolees, and probationers. Much of these considerations arise because prisoners are considered vulnerable populations in scientific research projects and specific federal guidelines must be followed when carrying out such research, as discussed in greater detail below.

Purpose

The purpose of this paper is to provide three case studies that highlight the unique difficulties experienced in conducting research with criminal justice populations, and strategies followed in attempting to surmount these obstacles. Following a discussion of requirements relating to the conduct of research with prisoners, and ethical concerns, and methodological issues, three case studies are presented. Each of these case studies focuses on a research project that the present authors have conducted using pharmacotherapy with criminal justice populations: 1) methadone for prisoners; 2) buprenorphine with prisoners; and 3) naltrexone with parolees and probationers. In each of the case studies, obstacles encountered and methods used to overcome them are presented. Whenever possible, material on how the study changed practice is emphasized.

Ethical Considerations with Prisoners

Federal regulations indicate that prisoners are vulnerable research participants who are in need of further safeguards. Prisoners are viewed as vulnerable in the sense that their confinement may make them more subject to coercion and may also interfere with their

ability to provide informed consent. Therefore, prisoners can only be participants in research that is essential to their lives as prisoners. They should not be a convenient population for experimentation.

Since the early 1900s when little or no safeguards were instituted with regard to confidentiality and ethical procedures, prisoners were frequently used as subjects in medical experiments conducted on tropical and sexually transmitted diseases, polio, cancer, and chemical warfare (Gostin, Vanchieri, & Pope, 2007). During the 1960s, new regulations for drug testing by the United States Food and Drug Administration (FDA) allowed even greater experimentation as major pharmaceutical companies attempted to forge stronger relationships with prison administrators (Gostin et al., 2007; Hornblum, 1998; Mitford, 1974). In many cases, prisoners were not informed of potential immediate and long-term adverse reactions. This continued until shortly after the publication of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research's recommendations on research involving prisoners in 1976, which forbade studies that manipulate bodily conditions except in an innocuous manner and encouraged that participation in research be completely voluntary. These recommendations and those emanating from the Commission's 1979 Belmont report evolved into the rules described in the section below.

Research Involving Prisoners

A major issue in conducting research with criminal justice populations is following Institutional Review Board (IRB) and Office of Human Research Protections (OHRP) procedures and answering major questions typically required. Does the research under review represent one of the categories of research permissible under Section 46.306 of the Code of Federal Regulations, Office for Human Research Protections (a). The research studies we had conducted all were classified under Category C, "research on conditions particularly affecting prisoners as a class" (for example, research on social and psychological problems such as drug addiction). When compared to the general living conditions, medical care, quality of food, amenities, and opportunity for earnings in the prison, any possible advantages accruing to the prisoner through his/her participation in the research are not of such magnitude as to limit his/her ability to weigh the risks of such research versus the benefits. The primary risk involved in this research is essentially the same regardless of incarceration status, namely, potential violations of confidentiality. The following procedures were strictly adhered to in all of our studies, described below, using pharmacotherapy (LAAM, methadone, buprenorphine, and naltrexone) with criminal justice populations: Study procedures assure that any risk of disclosure is minimal, including separation of data from individual identifiers, security procedures to prevent access to data or identifiers except by authorized project personnel, and protection by a federally issued Certificate of Confidentiality. Information revealed by study participants on their drug use and criminal activity cannot be provided to anyone outside this project. If a participant's parole officer learned that a participant was using drugs and/or committing crimes, the participant may be subject to arrest, conviction, or incarceration. Interviews are conducted in private where no one is present except the interviewer and participant. Interviews will not be conducted unless such privacy is assured. Research data are not be shared with correctional officials. All information presented to research participants, both when they are and are not incarcerated, is presented in a language that is understandable to the subject population. The decision on the part of a prisoner to participate or not participate in the research, and having consented to participate, to complete or not complete various assessments and to take part or not take part in research-related treatment while incarcerated, does not influence decisions made by the Parole Board. All participants are informed, as indicated in the consent form, that no information gathered in connection with study participation, including drug use, will

be given to the criminal justice system, including the participant's parole or probation officer. The main circumstance under which a prisoner participating in these studies may need follow-up examination or care involves the possible need to be treated for adverse events associated with medication.

Baltimore's Prison Pilot Study

In 1999, in response to concerns among key Baltimore drug treatment providers and corrections personnel about the vicious cycle of relapse, recidivism, and reincarceration among heroin-dependent individuals, an innovative pilot project was initiated. This two-year study, described in detail elsewhere (Kinlock et al., 2005) found that prison-initiated opioid agonist treatment was feasible and facilitated community-based treatment entry. Furthermore, this study set the stage for the subsequently conducted methadone and buprenorphine prisoner studies by establishing the partnership between correctional, treatment, and research staff and surmounting seven major obstacles necessary for successful project implementation.

First and foremost was to secure the cooperation and ongoing support of the Maryland Department of Public Safety and Correctional Services (DPSCS). Obtaining approval from the office of the Secretary first facilitated the support of the wardens, and, in turn, of other correctional administrators, case managers, correctional health personnel, chiefs of security, and line staff. Obtaining a letter of support and the writing and signing of a memo of understanding (MOU) between research and corrections was a crucial first step with initiating a research strategy. This initial MOU would facilitate continued support from the DPSCS for the next 10 years of research.

Second, corrections, treatment, and research personnel jointly selected a pre-release prison which met four criteria: 1) proximity to the community-based MMT program whose staff provided in-prison treatment; 2) having a sufficient number of inmates who are nearing release but who have enough time left to carefully be stabilized on an adequate dose of medication; 3) the degree to which treatment and research activities would not interfere with security, transfer of inmates, and making sure that all inmates were accounted for; and, 4) a facility in which the warden and key personnel support program implementation. Third, staff from the participating corrections, treatment, and research agencies met regularly prior to the start of the study to determine when and where treatment-related (medication and counseling) and research-related (conducting project orientation and screening of potential participants, and informed consent of potential participants) as well as assessment of study participants. A related obstacle was to agree that a safe be purchased to store medication, of which treatment staff would be responsible. A fourth major hurdle that was overcame involved getting treatment staff acclimated to going to prison to provide the intervention. Whereas most correctional drug treatment interventions are provided by correctional counselors or case managers, treatment in the pilot study was delivered by clinicians who were not experienced, and not initially altogether comfortable with, providing services in a prison environment.

A fifth challenge to implementation involved resolving conflicts between treatment and correctional staff. An important initial step was to involve, in the planning meetings between treatment, corrections, and research staff, a number of corrections officers that would be most likely to have daily contact with program participants as well as key staff. Also, at the start of our pilot study, it was essential for medical staff to provide several orientation sessions at the prison with correctional officers to educate them about the potential benefits and adverse consequences of opioid agonist therapy.

A sixth obstacle to implementation involved selection of potential participants. Several factors contributed to participant attrition: only providing physical examinations to participants in the treatment condition that will receive medication; participants having unadjudicated charges that can result in additional prison time and/or transfers to other facilities; and inmates released earlier than expected (issues that were resolved in our subsequent methadone study, as described below). Finally, potential conflicts involved from what perspectives results would be communicated. Because of the unique, interagency nature this project, all publications emanating from the study included the unique perspectives of treatment and correctional staff as to the success of the program and the manner in which conflicts were handled (Kinlock et al., 2002).

Case Study #1: Methadone Maintenance for Prisoners

Study Overview

This five-year study, concluded in 2008 and funded by the National Institute on Drug Abuse (NIDA), was the first randomized clinical trial in the US to examine the effectiveness of methadone maintenance treatment provided to prisoners with pre-incarceration histories of heroin addiction. The objective was to determine the differences in efficacy among three different treatment conditions: initiating methadone maintenance in prison, initiating methadone maintenance upon release, or receiving counseling only. Two hundred and eleven pre-release inmates who met criteria of heroin dependence at time of incarceration and were physiologically dependent during the year prior to incarceration were enrolled. Those randomized to receive methadone in prison had better outcomes compared to methadone in the community and counseling only in terms of two primary outcomes, community treatment duration and opioid drug test results.

Ethical Issues

Conducting the proposed study required that a number of ethical issues be addressed. A major concern centered around initiating prisoners who are not currently heroin-dependent on methadone maintenance. Several procedures were planned which reduced the probability of adverse consequences resulting from such treatment. First, the proposed methadone maintenance intervention was not without controversy; however, it is in accord with long-standing federal regulations regarding methadone maintenance. Second, all participants were inducted slowly (starting at 5mg and increased at intervals of 5mg) to reduce probability of adverse reaction. In addition, the study nurse monitored the patients daily by asking them to complete symptoms forms and if there were any potential adverse reactions they were treated accordingly. Third, an external Data and Safety Monitoring Board (DSMB) was formed to monitor the patients' response to methadone and to further ensure that human subjects' concerns, particularly those involving prisoners, are consistently being addressed.

Ethical Considerations

In the MMT study, we did not pay subjects for the baseline interview because it might be viewed as coercion. (Payment for incarcerated persons at follow-up assessment will not consist of cash, but will be deposited into prisoners' accounts or mailed to a person designated by the prisoner in accordance with the policies of the Maryland Department of Public Safety and Correctional Services). Furthermore, during follow-up assessments, incarcerated participants receive the same amount of money as nonincarcerated participants. In addition, we consistently maintained the confidentiality of data and obtained a Federal Certificate of Confidentiality. Moreover, we excluded inmates with pending parole hearings as required by our IRB. In addition, if an inmate was being dosed and, transferred for infractions, we made every effort to provide a detoxification when possible. We handled these issues in the same way in the subsequent buprenorphine and naltrexone studies.

Facility

After the pilot study ended, it was decided by the Department of Public Safety and Correctional Services (DPSCS) and the research team that the methadone study would be conducted at the same pre-release facility for men. Because the research and medical staff were familiar with this prison, the transition was positive and seamless. When the study started, many of the prison staff recognized our research and medical staff and we were viewed by many as part of the prison staff. However, we did face challenges as many of the new correctional officers had philosophical and ideological opposition to methadone. To address these concerns, we held a “kick off” meeting with our study physician and research team to meet with the custody staff of the prison to discuss methadone, its utility, side effects, and to dispel any myths of the medication. Consequently, as the study progressed, there were still officers that were not in favor of methadone. To address these issues, we scheduled trainings with the study physician where officers could ask questions about the medication.

Inclusion Criteria

One of the lessons learned from the pilot study was that a number of study participants had unadjudcated charges, meaning they were initially eligible but later had a charge that transferred them to another facility and thus made them subsequently ineligible. To address this potential problem, unadjudicated charges became an exclusionary criterion. We did not feel that it would be ethically appropriate to have participants reach a certain dose and then transfer to another facility without having the opportunity to provide a detoxification. A problem associated with screening out individuals with unadjudicated charges was confronted in the MMT study by carefully examining the criminal justice system records of each potential participant before study enrollment. Another obstacle to participant selection encountered in the pilot study was that often inmates’ release dates could not be accurately predicted, resulting in some participants released earlier than expected. In the MMT study, to assure sufficient time to initiate and stabilize participants on medication, we recruited potential participants at an earlier point prior to their scheduled release.

Physical Examination

In the pilot study, there were some individuals who were randomly assigned to the experimental condition who, at the physical examination, decided that they did not want medication; a few of them were disqualified because of medical conditions, contributing to having a greater degree of attrition in the experimental condition than in the control condition. In order to alleviate this situation, we decided to have all potential participants (those who had self-reported pre-incarcerated heroin addiction and had no unadjudicated charges or pending parole hearings as determined by DPSCS staff) take the medical examination. Those who agreed to it and were determined eligible for MMT were then randomly assigned to one of the three treatment conditions. The study physician was given a sealed envelope containing treatment condition assignment for each potential participant examined. After the medical examination was completed and the potential participant was found to be eligible for, and interested in, receiving MMT, the physician opened the envelope and informed the potential participant what treatment condition he has been assigned to. Immediately following random assignment, participants assigned to the treatment condition that begins MMT in prison were asked to sign an FDA-approved consent to medication.

Policy Changes

Although this study was conducted to examine the effectiveness of prison-initiated MMT, its implementation contributed to three important policy changes contributing to the expansion

of services to Baltimore methadone clients. Each of these policy changes could not have taken place without close and continued collaboration between corrections, drug abuse treatment, and research personnel.

The first change involved the provision of services to methadone clients by the Maryland DPSCS Home Detention Unit (HDU). Before the start of the study, HDU's policy did not allow any parolees who were being proscribed psychotropic medications or opioid agonist medications to be eligible for home detention. A series of meetings were conducted involving treatment staff, research staff, and HDU's newly appointed director, a former Maryland State police officer and an advocate of drug abuse treatment, and key HDU staff. In these meetings, treatment and research staff explained to HDU personnel the purpose of the study and answered questions regarding MMT. Consequently, HDU's policy changed to permit methadone clients who were on parole to receive their services. Furthermore, treatment staff coordinated with HDU case managers about informing HDU when their clients arrived at the community-based opioid agonist treatment facility. Moreover, a receptor site was set up at the treatment facility so HDU staff could verify when their clients arrived and left.

The second change centered around the observation that a considerable proportion of study participants experienced difficulty securing stable housing upon their release from incarceration. In attempting to confront this situation, we learned that operators of half-way houses in Baltimore, including two administrated by the Maryland DPSCS, did not allow their residents to receive MMT. Several steps were taken to resolve this circumstance. First, treatment and research staff held a number of meetings with the director and key staff members of the two DPSCS-operated facilities. Essentially, the format of these meetings resembled those conducted with HDU staff. The result of these meetings was that the director of these facilities, with the support of the DPSCS, agreed to allow residents to receive MMT. Second, we held meetings with operators of other facilities providing shelter for homeless persons. Some administrators began to accept methadone clients whereas others remained open to the possibility.

The third change involved the provision of MMT to inmates incarcerated at the Baltimore City Detention Center (BCDC). Because of our findings indicating that prison-initiated MMT was significantly associated with increased community-based treatment retention and reduced heroin use, a new program was implemented in BCDC shortly after the conclusion of our study. The intervention allows newly arrested MMT clients to continue on MMT while incarcerated.

Case Study #2: Buprenorphine for Prisoners

Study Overview

This five-year, ongoing NIDA funded study is the first to examine the effectiveness of opioid agonist therapy for female (n=160) as well as male (n=160) pre-release inmates with pre-addiction heroin addiction histories. Participants are randomly assigned, within gender, to one of four treatment conditions: 1) buprenorphine and counseling in prison, with referral for continued treatment at an opioid treatment program (OTP) upon release; 2) buprenorphine and counseling in prison, with referral for continued treatment at a community health center (CHC) upon release; 3) counseling only in prison, with referral for buprenorphine and counseling at a OTP upon release; and 4) counseling only in prison, with referral for buprenorphine and counseling at a CHC upon release. Participants are assessed at study entry and at 1, 3, 6, and 12 months post-release. Outcome measures include: treatment entry and retention in the community, heroin use, cocaine use, HIV infection, HIV-risk behaviors, criminal activity, and employment

Obtaining Approval from Federal and State Regulatory Agencies

The initial challenge to study implementation involved receiving appropriate licenses from the United States Drug Enforcement Agency (DEA) and the Division of Drug Control of the Maryland Department of Health and Mental Hygiene Drug Control Unit (MDHMH). This was done to ensure that procedures for the delivery, storage and dispensing of the medication in each pre-release facility met the standards of the DEA and the MDHMH. To reach this goal, a number of important steps were taken. After the study physician completed required application forms describing the nature of the study, plans for coordinating with corrections officials in setting up the medication site, and proposed procedures regarding handling of the medication, the DEA and MDHMH had to approve them. This required several changes and clarification of procedures. First, a safe for each facility was identified and inspected by the DEA and MDHMH according to their specifications. Second, the DEA and MDHMH inspected both facilities to determine whether the medication area was sufficiently secure and compliant with existing regulations. Next, the DEA and MDHMH were required to assign each medication site a registration number in order for participant recruitment to start.

Logistics

An advantage to implementation was that the same primary staff of the men's prison were contact persons to both the MMT study and the buprenorphine study. Being familiar with logistical procedures developed in the MMT study for treatment and research related procedures led to a smooth transition in that regard in the buprenorphine study. Similarly, the main project liaison already had learned how to screen inmates for eligibility criteria regarding unadjudicated charges, pending parole hearings, and time left to serve. However, because women were not participants in the MMT study and were included in the buprenorphine study to address unanswered questions regarding what factors may be related to positive treatment outcomes for women as well as for men (Pelissier & Jones, 2005), the case management staff at the women's prison needed more time to learn the screening procedures, and additional meetings were held to review these procedures and study eligibility criteria and to establish times and locations for participant screening, assessment, and medical examinations. Finally, because Maryland Division of Correction procedures mandate that a female physician or nurse practitioner accompany the study physician, who is male, when conducting the medical examinations, selecting that individual and orienting her to study procedures was necessary.

Dosing

As in the MMT study, dosing procedures had to accommodate participants' lack of tolerance. Thus, dosing needed to start low (1 mg) and to increase slowly and gradually (1 mg per week). Dose induction in non-tolerant participants is challenging because: (1) buprenorphine treatment of incarcerated, non-tolerant individuals had previously not been conducted and therefore there were no established procedures in the United States to follow as a guide; (2) individual response to the medication varies considerably; therefore, medical staff must monitor participants for side effects; and (3) because violence is often used in the prison environment to settle disputes and establish and maintain one's reputation (Inciardi, 2008; Prendergast & Wexler, 2004), inmates feeling "high" from the effects of the medication may feel more vulnerable to violent victimization. Therefore, participants are told at the start of medication that they should inform medical staff immediately if they have any side effects of the buprenorphine so that the dose can be modified accordingly. Also, each participant completes a form on a weekly basis indicating whether he/she has experienced constipation, drowsiness, sweating, or any other symptoms attributed to buprenorphine. Moreover, participants are clearly and consistently informed by medical

staff that they may end treatment at any time without penalty and receive a gradual dose reduction.

Diversion

Because buprenorphine is more divertible than methadone (Magura et al, 2009), we needed to take precautions to prevent or minimize this circumstance. Initially, each participant is informed by the study physician and nurse that if there is evidence of attempted diversion of medication, he or she will be gradually tapered off the medication. Nursing staff must watch each inmate carefully to make sure the medication is dissolved under the tongue and confront immediately any inmate when diversion is suspected. Additionally, before the start of the study, correctional, treatment, and research staffs agreed on how cases of attempted diversion would be dealt with. It was agreed that the study's medical staff would be responsible for terminating such inmates from treatment. Furthermore, in line with standards concerning protection of privacy of research participants, prison staff would not be informed in cases of attempted diversion.

Temporary Closing of the Prison for Women

A serious challenge to study implementation was the temporary closing of the women's prison because of budgetary concerns. We then had to secure cooperation of the warden and key staff of the only other prison for women in Maryland. A series of meetings between correctional, treatment, and research staff and the strong support of the Maryland DPSCS facilitated this cooperation and contributed to successfully working out logistics for times and places for research and treatment procedures. An additional challenge was that this prison was 15 miles from Baltimore; although the study physician and a nurse agreed to travel to this facility to provide treatment, other nurses and a counselor did not, so replacements had to be hired. Also time-consuming was making arrangements for the DEA to inspect and approve the medication site and storage procedures and the addition of this recruitment site required IRB approval.

Case Study #3: Naltrexone for Probationers and Parolees

Study Overview

This ongoing five-year NIDA funded study intends to determine whether a monthly injection of naltrexone is practical and useful in the prevention of relapse to opiate addiction when compared to treatment as usual. This collaborative project takes place in five sites where there is a large population of parolees with a history of opiate addiction: 1) University of Pennsylvania, Philadelphia, PA: 2) Rhode Island Hospital, Providence, RI; 3) New York University/Bellevue, New York, NY; 4) Columbia University, New York, NY; and 5) Friends Research Institute, Baltimore, MD. After determining that all volunteers are opiate free by urine test results and not currently opiate dependent using a naloxone test, they are randomized to injectable naltrexone or treatment as usual (TAU). Participants are assessed monthly for 6 months and also at 6, 12, and 18 months afterward with measures of opiate use by self-report, urine test and hair analysis. The University of Pennsylvania is the coordinating site and each site has a randomization goal of 20 new patients per year over 3.5 to 4 years to accrue a total of 360 to 400 participants. Treatment outcome is measured by urine tests, hair analysis, self-report and continuation in treatment.

Ethical Issues

O'Brien and Cornish (2006) raised the question of whether it is ethical to require that an offender with a history of opiate addiction receive long-acting naltrexone as part of parole or probation. They noted that newly released prisoners have an extremely high rate of relapse to opiate use, and many judges and parole/probation agents are philosophically opposed to

methadone or buprenorphine, claiming that their use is simply substituting one opiate for another (Walters, Clark, Gingerich, & Meltzer, 2007). Because of these concerns, the failure of many opiate-addicted patients to take daily medications, the relatively few side effects of naltrexone, and its blocking the euphoric effects of opiates all justify the need to provide long-acting naltrexone to individuals on parole or probation. A second ethical issue raised by O'Brien and Cornish concerns the possible need for opiates in the event of a painful accident or illness. They note that their nearly 40 years of experience with this medication shows that these situations can be managed safely by other medications and by ending naltrexone treatment.

Is Treatment as Usual Enough?

One potential hurdle to overcome was how would Institutional Review Boards (IRB) view treatment as usual for vulnerable populations. Having provided their written informed consent to participate, parolees and probationers with heroin addiction histories and 12 months remaining on parole or probation will be randomly assigned to one of two treatment conditions. These two conditions are: 1) assistance in finding treatment in the community; if relapse is detected during a monthly evaluation, participants will be assisted to find a new treatment program or return to the one they had been enrolled in; or 2) monthly injections of long-acting naltrexone for six months with brief counseling and similar access to community drug abuse treatment programs. Inasmuch as both treatment groups receive an active intervention, the study does not involve a no-treatment control group. All participants receive, at minimum, drug abuse counseling and information on how to access treatment in the community. It was emphasized to our IRB that the treatment as usual condition offered more of an intervention than standard care in the community (parole/probation supervision only). Many parolees and probation officers, both in Maryland and in the United States, have large caseloads which interferes with their ability to effectively monitor and supervise their clients' behavior (Kinlock et al., 2011; Schmalleger, 2010).

Criminal Justice Coercion

An ethical issue arose about whether or not to accept referrals from probation/parole officers. It was determined that it was most prudent to not have probation/parole agents making referrals to the study. Therefore, it was specified that participants may not be referred to the research program by parole or probation officers. In addition, it was clearly stated in the consent form that no information will be sent to the parole and probation officers regarding medication adherence, urine tests, and/ or progress in treatment. Therefore, there will be no formal link between research participation and legal status. Furthermore, participants will be questioned periodically regarding the monitoring and supervision being exercised by the criminal justice system and this is documented periodically through the study.

Research Involving Prisoners

We wished to interview participants who became incarcerated while one or more of their follow-up interviews became due. This is a crucial issue, as many parolees and probationers often violate the conditions of their supervision and become incarcerated (Inciardi, 2008; Schmalleger, 2010; Stojkovic & Lovell, 1997). Furthermore, with a high percentage (over 20%, and particularly over 30%) of participants lost to follow-up, the results of the study are likely to be biased in favor of individuals who lead more stable lives, respond more favorably to treatment, and less likely to be involved in drug use and crime. In contrast, those not assessed at follow-up are disproportionately likely to be more deviant and have poor treatment outcomes (Farrington, 1999; Kinlock & Gordon, 2006; Nemes et al., 2002; Wish et al., 1997). Therefore, we decided to apply to the IRB and OHRP requiring the criteria described earlier in this article to qualify for research involving prisoners. In so

doing, we assured these agencies that we would follow procedures previously outlined in the section entitled Research involving Prisoners, above and in the section entitled Ethical Considerations in the case study of prison-initiated MMT. An issue unique in this regard to the naltrexone study was that the primary circumstance under which a prisoner participating in this study may need follow-up examination or care pertains to the possible need to be treated for any adverse event associated with naltrexone treatment received when the participant was in the community. The most likely adverse event would be related to swelling and pain at the naltrexone injection site. Should the IRB find that other circumstances require follow-up examination or care of participants after their participation has ended, provisions would be made, subject to IRB approval.

Recommendations

From our experiences in conducting pharmacotherapy studies with criminal justice populations, we offer the following recommendations to guide future randomized controlled trials of this nature:

1. In studies involving interventions that begin in prison and continue in the community, planning should be conducted in full partnership between drug treatment research, and correctional personnel. Specify in advance the roles of each in a MOU. Conduct a series of regularly scheduled meetings with key stakeholders from drug abuse treatment, corrections, and research. Follow a written agenda for each meeting, with enough time to address for unresolved issues and questions and answers. Key correctional staff are typically interested in how the research might benefit them, and researchers need to strongly consider this in working out these activities
2. Have a deadline for everyone to agree on how the study will be designed and carried out, and have contingency plans of the initial idea is not feasible.
3. Emphasize resolving differences regarding logistics and space, ensuring that study intervention, recruitment, and assessment procedures will not interfere with standard security and other operating procedures at the prison. Unlike that of a treatment center or research facility, the main priority in a prison involves security, such as the movement of inmates and closing all activities at a certain time to make sure all inmates in the prison are accounted for.
4. Emphasize the need for private rooms for confidential activities. Ensuring this is more difficult in a prison than in a treatment center or research facility because of the emphasis in a prison on maintaining security and knowing where each inmate is at any given time.
5. Designate one key person at the prison and treatment clinic to be the liaison for the project and designate a backup in that person’s absence;
6. Involve key prison officials (warden, assistant warden, and chief of security) at important meetings, and when need be, correctional staff. Conduct a series of meetings with key prison and treatment staffs as soon as possible after funding begins and before and shortly after participant enrollment starts. Obtain personal data (name, birth date, social security number) of all research and treatment personnel who are attending meetings in the prison so such data can be forwarded to prison officials. Such data are not required when a meeting takes place in a treatment center or research facility where there is not a priority placed on maintaining security.

7. Have meetings with correctional staff about the study and why it is being conducted. Also, discuss the medications that will be used. This gives the correctional (line staff) an opportunity to ask questions. Establish early on with correctional officials where the medication will be stored securely and who will be responsible for such storage.

8. Select medication that fits well with the structure and operation of the prison that is widely available in the community post-release.

9. In all studies, meet ethical and IRB concerns regarding prisoners as soon as possible so study implementation is not delayed. In cases of studies with parolees and probationers, try to get the study approved by the designated IRB as a prison study, as in the case of the naltrexone study in order to assess participants who subsequently become incarcerated. This is important in order to avoid low follow-up rates and therefore having biased results in that the intervention appears more successful than it actually was.

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