Short communication

Methadone dose at the time of release from prison significantly influences retention in treatment: Implications from a pilot study of HIV-infected prisoners transitioning to the community in Malaysia

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Article history:
Received 10 September 2012
Accepted 11 January 2013
Available online xxxx

Keywords:
Prisoners
Malaysia
Opioid dependence
Methadone
Retention in care
Craving

Article Info

Abstract

Objective: To evaluate the impact of methadone dose on post-release retention in treatment among HIV-infected prisoners initiating methadone maintenance treatment (MMT) within prison.

Methods: Thirty HIV-infected prisoners meeting DSM-IV pre-incarceration criteria for opioid dependence were enrolled in a prison-based, pre-release MMT program in Klang Valley, Malaysia; 3 died before release from prison leaving 27 evaluable participants. Beginning 4 months before release, standardized methadone initiation and dose escalation procedures began with 5 mg daily for the first week and 5 mg/daily increases weekly until 80 mg/day or craving was satisfied. Participants were followed for 12 months post-release at a MMT clinic within 25 kilometers of the prison. Kaplan–Meier survival analysis was used to evaluate the impact of methadone dose on post-release retention in treatment.

Findings: Methadone dose ≥80 mg/day at the time of release was significantly associated with retention in treatment. After 12 months of release, only 21.4% of participants on <80 mg were retained at 12 months compared to 61.5% of those on ≥80 mg (Log Rank χ²+(1,26) 7.6, p < 0.01).

Conclusions: Higher doses of MMT at time of release are associated with greater retention on MMT after release to the community. Important attention should be given to monitoring and optimizing MMT doses to address cravings and side effects prior to community re-entry from prisons.

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1. Introduction

Globally, people who inject drugs (PWIDs) continue to contribute greatly to HIV transmission (Mathers et al., 2008). The intertwined epidemics of HIV and drug injection are especially salient in the countries of Southeast Asia, especially Malaysia (Kamarulzaman, 2009; Todd et al., 2007). It is estimated that 1.3% of all adult Malaysians are PWIDs, of which 11% are HIV-infected (UNAIDS, 2009). The epidemic of HIV among PWIDs is further complicated by government policies that criminalize drug use, systematically favoring incarceration over rehabilitation.

In Malaysia, nearly two thirds of newly diagnosed HIV infections are among PWIDs, the highest such prevalence in the region (Malaysian AIDS Council, 2010; World Health Organization, 2004). Among HIV-infected populations, PWIDs have persistently poorer health outcomes compared to their non-drug using counterparts primarily because they are less likely to access routine health care, be prescribed and adhere to combination antiretroviral therapy (cART), and be provided with medication-assisted therapy (MAT) for drug dependence (Altice et al., 2010; Oppenheimer et al., 2003; Wolfe et al., 2010).

As in the United States and elsewhere, the HIV epidemic among PWIDs in Malaysia is disproportionately concentrated within the criminal justice system (CJS). Results from mandatory HIV testing of the approximately 40,000 prisoners in Malaysia documents HIV prevalence to be ten to fifteen times greater (4.6% vs. 0.4%) than in the general community (Choi et al., 2010; Mathers et al., 2008). Moreover, substance use disorders are twenty to forty times greater (38.0% vs. 1.3%) and underlying psychiatric illness is greater than found in the general population (Zahari et al., 2010), each of which contributes to HIV transmission. Surveys among HIV-infected prisoners suggest that 97% of them meet pre-incarceration criteria for opioid dependence (Bachirreddy et al., 2011; Choi et al., 2010). In the absence of evidence-based treatment, relapse to opioid injection

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0376-8716/S – see front matter © 2013 Published by Elsevier Ireland Ltd.
http://dx.doi.org/10.1016/j.drugalcdep.2013.01.005

Please cite this article in press as: Wickersham, J.A., et al., Methadone dose at the time of release from prison significantly influences retention in treatment: Implications from a pilot study of HIV-infected prisoners transitioning to the community in Malaysia. Drug Alcohol Depend. (2013), http://dx.doi.org/10.1016/j.drugalcdep.2013.01.005
is high after release, which underscores the importance of implementing pre-release methadone maintenance treatment (MMT) for HIV-infected PWIDs because only HIV-infected persons can transmit to others.

In 2005, Malaysia aligned its drug policies with accepted HIV treatment and prevention strategies by introducing harm reduction interventions, including syringe exchange and MMT programs. Unfortunately, due to continued criminalization of PWIDs and a relative scarcity of harm reduction initiatives in prisons (Wolfe et al., 2010), the concentration of HIV within Malaysian prisons remains unacceptably high. Moreover, upon re-entry to the community, this vulnerable population faces inordinate challenges including relapse to drug use, difficulty in finding employment, as well as the hazards of recidivism, and loss of follow-up to HIV care (Choi et al., 2010). In light of the high rates of pre-incarceration HIV-related risk behaviors and reported negative attitudes toward opioid substitution therapy among prisoners (Bachireddy et al., 2011; Choi et al., 2010), Malaysian prisoners constitute an important group to be targeted for primary and secondary HIV risk reduction interventions (Bachireddy et al., 2011).

1.1. Methadone maintenance programs in correctional settings

MMT is highly effective for treating opioid dependence in both community (Schwartz et al., 2006, 2008) and prison (Dolan et al., 1998; Gorta, 1992; Hedrich et al., 2012; Howells et al., 2002; Kerr and Jurgens, 2004; Kinlock et al., 2009a) settings. After release, relapse is high and associated with high rates of overdose, criminal activity and recidivism (Hanlon et al., 1990; Nurco et al., 1990, 1991). Although MMT has been demonstrated to reduce post-release relapse to drug use, overdose and death, and improve general quality of life and employment stability, programs within CJ settings remains insufficient (Amato et al., 2005; Lanney and Dolan, 2009; Mathers et al., 2010; Mattick et al., 2009). Though underutilized, CJ settings are critical for initiating evidence-based treatment for opioid dependence (Altice et al., 2010; Springer et al., 2011). Opportunities for introducing MMT post-release quickly dwindle as relapse often occurs within two weeks and exceeds 85% within one year (Binswanger et al., 2007; Leach and Oliver, 2011; Strang et al., 2010).

As part of Malaysia’s plan to expand MMT to prisoners, we analyzed the 12-month post-release data from the country’s first prison-based pre-release MMT pilot program of HIV-infected males who met pre-incarceration criteria for opioid dependence.

2. Methods

The first 30 HIV-infected men who met criteria and volunteered were prospectively enrolled in a prison-initiated, pre-release pilot methadone program in Kajang prison in Selangor, Malaysia between September 2009 and December 2010; women were not included in the pilot due to selection of a single site. Volunteers were recruited and consented within prison after information sessions and then meeting inclusion criteria: (1) ≥18 years of age; (2) HIV-infected; (3) pre-incarceration opioid dependence using DSM-IV criteria; (4) returning to live within 25 kilometers of the post-release MMT site; and (5) within 4 months of release from prison. To ensure safety, a research-based addiction psychiatrist assessed participants before initiating MMT using a standardized induction protocol. To avoid opioid excess, participants initially received 5 mg daily and daily doses were increased by 5 mg every 7 days; 80 mg/day was targeted, but doses were individualized based on having sufficient time to achieve the target before release and to balance cravings and side effects. Transitional MMT care included transmittal of methadone dose to the community-based MMT program, meeting clients on the day of release and transportation to the MMT program.

Three participants died in prison before release from prison (2 had tuberculosis and 1 had a seizure), resulting in 27 subjects evaluable for the retention in care outcome. Participants were assessed at baseline and monthly for 12 months. Baseline measures included the HIV Symptom Index (Justice et al., 2001), HIV-related Stigma (Berger et al., 2001), Social Support (Sherbourne and Stewart, 1991), depression using the Clinical Epidemiological Scale for Depression (CES-D) with scores ≥16 being consistent with moderate to severe depression (Radloff, 1977), self-reported chronic illnesses, and drug use characteristics. Retention was defined as not missing 14 consecutive days of methadone and lost to follow-up was coded as the last day of receipt of methadone. Survival analysis was stratified by the daily MMT dose at the time of release (<80 mg vs. ≥80 mg) in order to evaluate the effect of dosing on post-release MMT retention. This stratification is based on evidence from reviews of MMT dosing (Mattick et al., 2009) and results from randomized controlled trials (Faggiano et al., 2003) that report higher methadone doses (≥80 mg) improve treatment outcomes. Institutional Review Boards at Yale University and the University of Malaya approved the study.

3. Results

3.1. Sample characteristics

Characteristics of the sample are reported in Table 1. Overall, the sample is similar to other studies of opioid dependent, HIV-infected prisoners in Malaysia (Bachireddy et al., 2011; Choi et al., 2010). Nearly all (96.7%) reported prior injection drug use and had been incarcerated for an average of 12.5 months before MMT initiation. Mean time since HIV diagnosis was 8.3 years and only one

Table 1
Baseline characteristics of participants (N=30).

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30 (100)</td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
</tr>
<tr>
<td>Malay</td>
<td>22 (73.3)</td>
</tr>
<tr>
<td>Indian</td>
<td>6 (20)</td>
</tr>
<tr>
<td>Chinese</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Religion</td>
<td></td>
</tr>
<tr>
<td>Muslim</td>
<td>22 (73.3)</td>
</tr>
<tr>
<td>Hindu</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>Christian</td>
<td>3 (10.0)</td>
</tr>
<tr>
<td>Buddhist</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Employed full time prior to prison</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16 (53.3)</td>
</tr>
<tr>
<td>No</td>
<td>13 (43.3)</td>
</tr>
<tr>
<td>Highest level of education completed</td>
<td></td>
</tr>
<tr>
<td>Elementary</td>
<td>5 (16.3)</td>
</tr>
<tr>
<td>Some secondary</td>
<td>16 (53.3)</td>
</tr>
<tr>
<td>Completed secondary or higher</td>
<td>9 (30.0)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>7.1 (37.1)</td>
</tr>
<tr>
<td>Previous injection drug use</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>96.7 (29)</td>
</tr>
<tr>
<td>No</td>
<td>3.3 (1)</td>
</tr>
<tr>
<td>Mean current incarceration time, years (S.D.)</td>
<td>1.04 (0.5)</td>
</tr>
<tr>
<td>Mean lifetime incarceration, years (S.D.)</td>
<td>6.6 (4.2)</td>
</tr>
<tr>
<td>Mean time since HIV diagnosis, years (S.D.)</td>
<td>8.3 (6.5)</td>
</tr>
<tr>
<td>Depression (CES-D)</td>
<td></td>
</tr>
<tr>
<td>Low or none (0–15)</td>
<td>60.0 (18)</td>
</tr>
<tr>
<td>Moderate to Severe (16–60)</td>
<td>40.0 (24)</td>
</tr>
</tbody>
</table>
participant (3.3%) reported being on CART (he was also receiving treatment for tuberculosis). HIV-associated symptoms suggested high levels of depressive symptoms (46.7%), loss of appetite (46.7%), trouble with memory (36.7%), and difficulty sleeping (36.7%) and 40% met criteria for moderate to severe depression.

3.2. Survival analysis

Kaplan–Meier survival analysis was used to evaluate retention on MMT (see Fig. 1). The mean daily MMT dose at time of release was 90.9 mg (range = 45–120 mg). At the time of release, MMT dose <80 mg was prescribed for 51.9% (N = 14) of the sample; of note, no one received 81–99 mg leaving the remaining 13 participants receiving ≥100 mg per day. During the post-release follow-up period, there were no recorded decreases in MMT dose and mean retention was 172.5 days.

At 12 months, participants on ≥80 mg were significantly more likely than those on lower doses to be retained [61.5% (8/13) vs. 21.4% (3/14)] in treatment (Log Rank $\chi^2 = 1.26$; 7.6, $p < 0.01$). Most of the attrition occurs within one month post-release, especially for those receiving <80 mg compared to higher doses [64% (9/14) vs. 15.4% (1/13)].

4. Discussion

This study represents one of the first published studies of HIV-infected prisoners meeting criteria for opioid dependence, receiving prison-based MMT and being released to the community in Asia. The implications for treatment, however, extend well beyond this region. Data from randomized controlled trials of MMT confirm the superiority of initiating MMT prior to release among opioid dependent prisoners with regard to a number of post-release substance abuse treatment outcomes (Kinlock et al., 2009b). In Kinlock’s study, prison-based MMT outcomes were superior to those who received vouchers for immediate referral to MMT post-release, but the retention in treatment at 12 months was only 36.7%, perhaps due to targeted daily methadone dosing being only 60 mg. Results from other international studies suggest there is considerable benefit to initiating MMT during incarceration to individuals meeting pre-incarceration opioid dependence prior to reentering the community. In a quality improvement study of MMT dosing at Rykers Island jail in New York City, increased methadone doses were associated with increased likelihood of being “linked” to post-release MMT, but doses were generally around 55 mg per day and no retention on treatment data were available (Harris et al., 2012). These conclusions are also significant as they reflect previous international findings that demonstrate the important role MMT plays in improving substance use and health-related outcomes after release (Dolan et al., 1998; Gibson et al., 2008; Kinlock et al., 2009a).

Moreover, these data confirm the need to achieve adequate methadone dosing while still incarcerated in order to optimize substance abuse treatment benefits after release and in community settings (Faggiano et al., 2003; Mattick et al., 2009). In community settings, daily doses >80 mg were associated with the highest levels of retention on treatment (Caplehorn and Bell, 1991). Although we stratified methadone at the 80 mg dose, our data, where all participants on doses greater than 80 mg per day were actually on 100 mg or more, confirm markedly higher rates of retention in community-based MMT using higher doses (Peles et al., 2006). The structure of prison settings often results in reduced, but not absent illicit drug use in prison. Such perspectives often result in the perception of needing to prescribe subtherapeutic methadone doses within prison with the primary goal to avoid withdrawal and reduce the likelihood from overdose. Such approaches, however, do not address the issue of craving which has been associated with opioid relapse (Fareed et al., 2010, 2011; Preston and Epstein, 2011). Data from this study suggest that in order to achieve optimal dosing (actual doses were >100 mg/day) prior to release, prison-based MMT programs should initiate methadone no later than six months before the scheduled release date (Wickersham et al., 2013). Providing this longer induction window among individuals who are not tolerant to opioids will allow medical staff to closely monitor patients during weekly dose increases, address craving and determine when optimal dosing is achieved. This approach also allows longer assessment periods of side effects, which can be addressed more immediately in the correctional setting than after release, when risk of relapse sharply increases (Kinlock et al., 2005).

While this study evaluated MMT as a pre-release intervention, it should be noted, however, that ideal programs should consider opioid dependence as a chronic, relapsing condition and MMT should optimally be provided throughout incarceration, particularly to reduce within prison-related injection, intra-prison transmission of blood-borne viruses and other negative consequences of injection (Dolan et al., 2003). Moreover, buprenorphine is an alternative to methadone as opioid substitution therapy because it is safer, has fewer side effects and has been documented to improve both post release HIV-treatment outcomes (Springer et al., 2012) and reduce emergency department utilization (Meyer et al., 2012).

There are several limitations to this study. First, the relatively small sample size restricts the generalizability of findings, which reinforces the need for a large, randomized controlled trial to address the question of the optimal MMT dose and its impact on retention and relapse. Despite this limitation, even results from this small sample are compelling and reflect empirical evidence that higher MMT doses results in longer treatment retention (Faggiano et al., 2003; Kinlock et al., 2005; Peles et al., 2006).

Second, due to the pilot nature of this study and inclusion of only men, there are no insights into the unique factors that may be associated with women’s experience in pre-release MMT programs. Given the increased injection of opioids among women in Southeast Asia (Nguyen et al., 2008) and evidence that women are significantly less likely than men to enter substance abuse treatment (Greenfield et al., 2007), future studies must examine the gender-specific factors associated with key outcomes in prison-based, pre-release MMT programs. Such approaches will inevitably enhance the quality of care received by both genders by
providing more customized treatments. Last, it is worthwhile examining MMT for opioid dependent prisoners not infected with HIV or HCV to examine its impact on primary prevention (Dolan et al., 2005).

5. Conclusions
Medication-assisted therapy, including MMT, is not routinely available in prison settings, but emerging data confirm its benefit in improving both substance abuse treatment (Kinlock et al., 2009b) and HIV treatment outcomes (Springer et al., 2010, 2012). In the case of methadone, it appears that the early introduction of methadone treatment prior to release has a profound impact on retention with higher doses resulting in prolonged treatment retention. The impact of such approaches is likely to have secondary improvements in outcomes given the high degree of medical and psychiatric morbidity and mortality that also require concomitant treatment.

Role of funding source
Funding for this study was provided by a grant from the National Institute on Drug Abuse for research (RO1 DA025943, Altice, PI) and career development (K24 DA17072, Altice). These funding agencies had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

Contributors
Authors Altice and Kamarulzaman designed the study and wrote the protocol. Authors Wickerson, Azar, and Zahari managed the literature searches and summaries of previous related work. Author Wickerson undertook the statistical analysis, and authors Wickerson, Azar, and Zahari wrote the first draft of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest statement
All authors declare that they have no conflicts of interest.

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http://dx.doi.org/10.1016/j.drugalcdep.2013.01.005
http://dx.doi.org/10.1016/j.drugalcdep.2013.01.005

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