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RESEARCH ARTICLE

A Meta-Analysis of Medication-Assisted Treatment Initiated in Carceral Settings: Six Months Post-Release

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Abstract

Medication-assisted treatment (MAT) is considered the gold standard treatment for opioid use disorder[1]. However, implementation in carceral settings remains limited[2]. A meta-analysis of three randomized-controlled trials (n= 324) finds that medication-assisted treatment initiated in carceral settings is an effective intervention for opioid use disorders. The authors conducted a systematic review of the database in late 2023/early 2024 and evaluated 130 articles for potential inclusion in the meta-analysis. Of these, three were selected that had the desired outcome measure of opioid relapse at six months as observed via urinalysis. The authors constructed a logistic regression model for the odds of relapsing with any treatment, and then specifically with methadone, as compared to controls. The odds of not relapsing, relative to controls, were 2.67 (95% CI = [1.677,4.332]) with any treatment and 4.13 (95% CI = [2.129,8.374]) for methadone, respectively. The authors conclude that while current literature shows MAT, specifically methadone, is an effective treatment for OUD when initiated in carceral settings, more RCTs in carceral settings are needed, especially RCTs with follow ups >1 month from release.

Introduction

Opioid Use Disorder (OUD) is defined by the American Psychiatric Association in the fifth version of the Diagnostic and Statistical Manual of Mental Disorders as “a problematic pattern of opioid use leading to clinically significant impairment or distress”[3] Medication-assisted treatment (MAT) is considered the gold standard treatment for OUD[1]. In MAT, one of three FDA-approved drugs (methadone, buprenorphine, naloxone), alone or in combination with psychosocial treatment, is used to prevent relapse[4]. The medications work by ameliorating opioid cravings without producing the euphoric effects typically associated with opioid use[4]. Despite the substantial evidence supporting the use of MAT in treating OUD, implementation in carceral settings remains limited[2][5]. Implementing MAT for OUD in carceral settings remains challenging in part due to concerns related to treatment continuity and efficacy after release[2]. Despite these concerns, carceral health providers and community advocates are increasingly interested in medication-assisted treatment (MAT) for treating opioid use disorder (OUD) in justice-involved populations[6].

The present study arose from dialogue between the research team and community stakeholders affiliated with a local community detention facility (LCDF). LCDF stakeholders expressed a desire to understand the efficacy of medication-assisted treatment for opioid use disorder in carceral settings, so a meta-analysis of existing literature was initiated by the research team, the results of which are presented in this paper.

Methadone was the first drug approved by the FDA for medication-assisted treatment of opioid use disorder in the United States[7]. Given its comparatively long history as an FDA-approved medication-assisted treatment for OUD, the team elected to begin by reviewing the existing literature evaluating the efficacy of methadone for treating OUD in carceral settings. An initial Pubmed search conducted on November 7th 2023 returned 48 potential studies for inclusion in our meta-analysis. The team was interested primarily in relapse outcomes. Of the 48 studies returned by the initial search, 7 evaluated relapse outcomes at 12 months or longer post-release, 4 evaluated outcomes of less than 1 month post-release, and two evaluated outcomes at 6 months post-release (other non-relapse outcomes were omitted). The relative lack of studies evaluating the efficacy of methadone as a treatment for OUD at six months was identified by the research team as a gap in the literature that could benefit from a meta-analysis. Existing meta-analyses of methadone MAT in carceral settings focus on health behaviors and/or vary widely in the time in which they evaluate relapse outcomes (i.e. a mixed review of <1, 1, 6, and 12+ month studies)[6]. The team believed a more specific study of the intermediate period in the literature (6 months) could help fill an important gap of understanding. Given that the team chose to review outcomes at six months post-release for methadone, it was decided for consistency that relapse at six months would be the outcome of focus for any other interventions studied.

In addition to methadone, the team elected to focus on buprenorphine and Suboxone (combination buprenorphine/naloxone) as interventions of interest. We selected these substances for comparison (1) due to their overwhelming prevalence in the literature compared to all other MAT interventions given in carceral settings and (2) because they all include opioid agonists, and thus share an underlying pharmacological mechanism.

To ensure data quality, we only included randomized-controlled trials (RCTs) that evaluated opioid abstinence at six months via urinalysis. We excluded studies that measured abstinence based on self-reports[8]. Studies were also excluded if they did not have a non-MAT control group; because of this, studies comparing the efficacy of two different MAT interventions were not included. The non-MAT control group could include interventions such as counseling, referral to a community opioid clinic, or both, so long as no pharmacological intervention for OUD was initiated in the carceral context (Table 1).

Methods

The following search terms were used to search the Pubmed database over a period of three months, beginning in November of 2023 with the last search executed in January of 2024

(Fig 1)

(jail* OR prison* OR incarcerat* OR carceral OR “criminal justice” OR correctional OR offender* OR “justice-involved” OR

Prisons*[MeSH]) AND
([DRUG NAME(s)]) AND
("opioid use" OR "opioid addict*" OR "opioid dependent*" OR "opioid misuse" OR Opioid-Related Disorders[MeSH])

The results from each of these searches were then imported to the systematic review manager Covidence, where they underwent two rounds of screening. First, titles were screened and removed if they did not meet inclusion criteria. Then, abstracts were screened and removed if they did not meet inclusion criteria. Finally, the remaining articles underwent a full-text review. Three articles met inclusion criteria at this point. The results of this process are summarized in Fig 1.

Fig 1. Flow chart of selected studies.

Data were extracted from summary tables provided in each study, and a summary dataset was produced. This was done by creating one observation for each instance of a particular treatment and outcome variable presented by a given study. For example, if a study had 50 people who received treatment and relapsed, the summary data would have 50 observations coded both as receiving treatment (`treatment` = 1) and having relapsed (`relapse` = 1). A summary of the included studies, sample sizes, as well as what constituted a treatment and a control group in each study are provided below.

Because the data are aggregated from each selected article and no humans participated in the study described in this paper. Additionally, the analysis was done with the data created from the summary tables of each article; thus, we do not analyze or have access to individual-level data for the subjects in the studies from the selected articles. Given these reasons, this work was not subject to the Institutional Review Board protocol.

Table 1. Summary of included studies

Study	Sample Size	Treatment Group	Control Group
Gordon et al. 2008[9]	n = 122	Methadone prior to release, with referral to community opioid treatment	Counseling only or counseling and referral to community opioid treatment
McKenzie et al. 2012[10]	n = 62	Methadone prior to release, with continued treatment in the participant's methadone program of choice with the same financial assistance as the control	Referral to methadone treatment post-release, with or without financial assistance
Gordon, Kinlock, Schwartz, O'Grady, et al. 2017[11]	n = 140	Buprenorphine initiated in prison and continued at an opioid treatment program or community health clinic	Counseling only in prison and initiation of buprenorphine and counseling at an opioid treatment program or community health clinic

Analysis was done in RStudio running R version 4.3.1 (2023-06-16) using "tidyverse" (Version 2.0.0) for data preparation and "lme4" (Version 1.1.35.1) for statistical modeling.

Two mixed-effects logistic regression models were fitted to the data. The first predicted the `relapse` variable (whether someone was opioid positive via a urine sample at six months) using `treatment` (whether or not they received MAT) and `study_name` (a categorical variable identifying the study the participant was part of) as predictors. The second model

predicted `relapse` using `drug_received` (whether someone received methadone, buprenorphine, or served as a control) and `study_name` as predictors. In both models, `study_name` was treated as a random effect to capture the variation between different studies. Though all the included studies evaluated the same outcome measure (the results of an opioid urine test six months after release from incarceration) there is reason to believe there is variation in how the studies were administered, simply by having occurred at different times, in different places, etc. Thus, we thought it was appropriate to include a random effect for the study a given observation was associated with. However, during the process of data analysis we estimated this effect to not be statistically significant, so we excluded it from our final models, and instead performed a fixed-effects logistic regression, the results of which are presented in Tables 2 and 3.

Results

Table 2. Model 1 output.

Term	Adjusted Odds Ratio	p-value	Std. Error
(Intercept)	0.979	<.001	0.145
treatment	2.677	<.001	0.242

Table 3. Model 2 output.

Term	Adjusted Odds Ratio	p-value	Std. Error
(Intercept)	0.791	0.202	0.184
treatment	4.130	<.001	0.348

Our first model indicated that the odds of not relapsing at six months, relative to controls, were 2.67 (95% CI = [1.677,4.332]) if the subject received any MAT in a carceral setting as compared to a subject who did not receive MAT in a carceral setting. Our second model indicated that the odds of not relapsing at six months, relative to controls, were 4.13 (95% CI = [2.129,8.374]) if the subject received methadone, in particular, in a carceral setting as compared to a subject that did not receive MAT.

Discussion

Our models suggest that MAT administered in a carceral setting, especially in the form of methadone, is effective at preventing opioid relapse six months after release in individuals with opioid use disorder. One major caveat to this finding is the lack of homogeneity among the controls present in the different studies. While every effort was made to identify studies with comparable control groups, differences in referral protocols (whether someone was or was not given financial assistance in seeking opioid use disorder treatment after release, for example) could substantially influence the relative efficacy of methadone or buprenorphine and thus relapse outcomes as compared to a control. Accounting for these

differences, however, would likely only widen the difference between treatment and control groups, as we would expect those receiving more support (financial assistance, a robust referral, etc.) would be less likely to relapse than those receiving less support. Thus there is reason to believe a model accounting for these secondary supports (financial assistance, etc.) would show an enlarged difference between treatment and control groups that did not receive such support as compared to controls which did receive such support or mixed control groups (where the type and extent of secondary support is varied). Though the former group is hypothetical at present, there are theoretical reasons to believe our basic results are robust despite a lack of homogeneity among controls. This finding is in alignment with other meta-analyses that find methadone MAT is an effective treatment for opioid use disorder when administered in carceral settings[12][6].

Limitations

A major limitation to the present study is that only one RCT of buprenorphine met inclusion criteria, so we were unable to study buprenorphine as a treatment beyond reproducing the outcome of the original study. We included it in our model of any treatment because buprenorphine shares a similar pharmacological mechanism to methadone and thus there was a reasonable basis to group them together when evaluating treatment outcomes.

A second limitation to our study is that while the pharmacological mechanisms underlying methadone and buprenorphine are similar (both are agonists), buprenorphine only acts as a partial agonist. Based on this, we would expect buprenorphine to be a less effective form of MAT as compared to methadone and lower the effect size of treatment overall relative to methadone. Both the original study and our own work confirm this. In addition, the control group in this study had the opportunity to receive Buprenorphine after release, which may have reduced the apparent treatment effect. Still, given the prevalence of buprenorphine as a treatment modality for OUD in carceral settings, it was appropriate to include it in a meta-analysis seeking to make a more general statement about the efficacy of MAT.

Conclusion

Our meta-analysis of three randomized-controlled trials evaluating the efficacy of medication-assisted therapy for opioid use disorder in carceral settings (n = 324) found that any MAT is more effective than a control at preventing opioid relapse at six months post-release. A second model found that methadone, in particular, was effective as compared to buprenorphine and controls. More randomized-controlled trials, especially with follow-ups at six months or longer, need to be conducted to better assess the efficacy of MAT for opioid use disorder in carceral settings.

Statements and Declarations

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Ethics approval statement

This study involved secondary data analysis and did not require new ethics approval, as no human participants were directly involved.

References

1. [a, b]*Carroll J. Evidence-Based Strategies for Preventing Opioid Overdose: What's Working in the United States. 2018.*
2. [a, b, c]*Friedmann PD, Hoskinson RA Jr, Gordon M, Schwartz R, Kinlock T, Knight K, et al. Medication-Assisted Treatment in Criminal Justice Agencies Affiliated with the Criminal Justice-Drug Abuse Treatment Studies (CJ-DATS): Availability, Barriers & Intentions. Subst Abus. 2012;33(1):9–18. doi:10.1080/08897077.2011.611460.*
3. [^]*Diagnostic and Statistical Manual of Mental Disorders, Text Revision Dsm-5-Tr. 5th ed. Amer Psychiatric Pub Inc; 2022.*
4. [a, b]*United States Food and Drug Administration. Information about Medication-Assisted Treatment (MAT). 2023. Available from: https://www.fda.gov/drugs/information-drug-class/information-about-medication-assisted-treatment-mat.*
5. [^]*Hochheimer M, Unick GJ. Systematic Review and Meta-Analysis of Retention in Treatment Using Medications for Opioid Use Disorder by Medication, Race/Ethnicity, and Gender in the United States. Addict Behav. 2022 Jan;124:107113. doi:10.1016/j.addbeh.2021.107113.*
6. [a, b, c]*Moore KE, Roberts W, Reid HH, Smith KM, Oberleitner L, McKee SA. Effectiveness of Medication Assisted Treatment for Opioid Use in Prison and Jail Settings: A Meta-Analysis and Systematic Review. J Subst Abuse Treat. 2019 Apr;99:32–43. doi:10.1016/j.jsat.2018.12.003.*
7. [^]*Rettig RA, Yarmolinsky A. Executive Summary. In: Federal Regulation of Methadone Treatment. National Academies Press (US); 1995. Available from: https://www.ncbi.nlm.nih.gov/books/NBK232111/.*
8. [^]*Davis CG, Thake J, Vilhena N. Social Desirability and Change Following Substance Abuse Treatment in Male Offenders: Psychology of Addictive Behaviors. Psychol Addict Behav. 2014 Sep;28(3):872–9. doi:10.1037/a0037528.*
9. [^]*Gordon MS, Kinlock TW, Schwartz RP, Fitzgerald TT, O'Grady KE. A Randomized Clinical Trial of Methadone Maintenance for Prisoners: Findings at 6 Months Post-Release. Addiction. 2008 Aug;103(8):1333–42. doi:10.1111/j.1360-0443.2008.002238.*
10. [^]*McKenzie M, Zaller N, Dickman S, Friedmann PD, Rich JD. A Randomized Trial of Methadone Initiation Prior to Release from Incarceration. Subst Abus. 2012;33(1):19–29. doi:10.1080/08897077.2011.609446.*
11. [^]*Gordon MS, Kinlock TW, Schwartz RP, O'Grady KE. A Randomized Clinical Trial of Buprenorphine for Prisoners: Findings at 12-Months Post-Release. Drug Alcohol Depend. 2017;172:34–42. doi:10.1016/j.drugalcdep.2016.11.037.*

12. ^*Cates L, Brown AR. Medications for Opioid Use Disorder during Incarceration and Post-Release Outcomes. Health Justice. 2023;11:4. doi:10.1186/s40352-023-00209-w.*