The Effectiveness of Naltrexone for Opioid Use Disorder among Inmates: A Systematic Review and Meta-Analysis

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APPENDICES

Appendix 1: Search Strategy

PubMed

1. ((naltrexone) AND opioid use disorder) AND inmates/9 citations

MEDLINE

1. exp NALTREXONE/7491
2. exp Opioid-Related Disorders/ or exp Heroin Dependence/ or opioid addiction.mp. or exp Substance-Related Disorders/262921
3. exp Prisons/ or exp Prisoners/ or inmate.mp./22090
4. 1 and 2 and 3/26
5. limit 4 to randomized controlled trial/11
6. limit 5 to (English language and humans)/11

EMBASE

1. exp naltrexone/13821
2. opioid addiction.mp. or exp opiate addiction/ or heroin dependence.mp. or exp heroin dependence/ or opioid abuse.mp./25957
3. inmate.mp. or exp prisoner/17169
4. 1 and 2 and 3/7

PsycINFO

1. naltrexone.mp. or exp NALTREXONE/3292
2. exp Drug Dependency/ or exp Opiates/ or exp Drug Abuse/ or exp Drug Addiction/ or opioid dependence.mp. or exp Heroin Addiction/ or heroin dependence.mp. or exp Drug Abuse/ or exp Opiates/122671
3. exp Criminal Rehabilitation/ or exp Prisons/ or exp Prisoners/ or exp Incarceration/ or exp Correctional Institutions/ or inmate.mp. or exp Criminal Behavior/45088
4. 1 and 2 and 3/22

Cochrane Central Register of Controlled Trials

1. naltrexone.mp. or Naltrexone/2051
2. Opioid-Related Disorders/ or Heroin Dependence/ or opioid addiction.mp./1729
3. inmate.mp. or prisoners.mp. or Prisoners/ or corrections.mp./1267
4. 1 and 2 and 3/8

Cochrane Library Search Strategy

1. MeSH Descriptor: [Naltrexone] explode all trees/1106
2. MeSH Descriptor: [Opioid-Related Disorders] explode all trees/1697
3. 1 and 2/121 (limit: Trials, Drugs and Alcohol Cochrane Group)

Appendix 2: Characteristics of Studies

Cornish 1997

Methods	Open-label, randomized, controlled, parallel group trial
Participants	Federal probationers or parolees with a history of opioid addiction were referred by themselves or their probation/parole officer for a naltrexone treatment study. Participation was voluntary and subjects could drop out of the study at any time without adverse consequences.
Interventions	Following orientation and informed consent, 51 volunteers were randomly assigned in a 2:1 ratio to a 1-month program of probation plus naltrexone and brief drug counseling, or probation plus counseling alone. Naltrexone subjects received medication and counseling twice a week; controls received counseling at similar intervals.
Outcomes	52% of subjects in the naltrexone group continued for 6 months and 33% remained in the control group. Opioid use was significantly lower in the naltrexone group. The overall mean percent of opioid positive urine tests among the naltrexone subjects was 8%, versus 30% for control subjects ($p < .05$). 56% of the controls and 26% of the naltrexone group ($p < .05$) had their probation status revoked within the 6-month study period and returned to prison.

Risk of Bias Table

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	**Low risk**	Described 2:1 method of randomization.
Allocation concealment (selection bias)	**Low risk**	Participants were randomly allotted to the intervention or control (2:1).
Blinding of participants and personnel (performance bias)	**High risk**	Not blinded.
Blinding of outcome assessment (detection bias)	**High risk**	Not blinded.
Incomplete outcome data (attrition bias)	**High risk**	High rate of drop-out in both groups.
Selective reporting (reporting bias)	**Low risk**	Outcomes well-reported and consistent with stated objectives.
Other bias	**Unclear risk**	Potential volunteer bias.

Coviello 2010

Methods	RCT
Participants	111 opioid-dependent offenders under various levels of supervision that included county and federal probation/parole.
Interventions	Subjects were randomly assigned to receive 6 months of either 300 mg per week of oral naltrexone plus standard psychosocial treatment as usual (TAU; *n* = 56) or TAU alone (*n* = 55).
Outcomes	Retention in treatment; positive urine drug screen; reincarceration.

Risk of Bias Table

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	**Low risk**	Randomization was balanced using six prognostic variables: gender, current marital status (yes/no), comorbid current alcohol abuse or dependence, comorbid current cocaine abuse or dependence, previous arrests and criminal charges (≤ 5 vs. >5), and previous drug treatments other than self-help groups and detoxification only (≤ 3 vs. > 3).
Allocation concealment (selection bias)	**Low risk**	All subsequent scheduled events were calculated from the point of randomization. Subjects were assessed at baseline, twice weekly during the 6-month treatment phase and then at 6 months posttreatment entry.
Blinding of participants and personnel (performance bias)	**High risk**	Unblinded.
Blinding of outcome assessment (detection bias)	**High risk**	Unblinded.
Incomplete outcome data (attrition bias)	**High risk**	High rate of drop out.
Selective reporting (reporting bias)	**Low risk**	One outcome not reported fully (e.g., UDS results at 6-months for benzodiazepines, marijuana, and amphetamines). Otherwise, fairly consistently reported.
Other bias	**Unclear risk**	One of the study authors was connected with Alkermes funding, which may have influenced some of the reporting of results.

Friedmann 2017

Methods	RCT.
Participants	Adult inmates with opioid use disorder.
Interventions	Opioid-dependent volunteers not interested in opioid agonist treatment were randomized to one of two treatment conditions: Prerelease, where the participant received one XR-NTX injection 1–2 weeks prior to release from prison and then up to five monthly injections in the community, or postrelease, where the participant received up to six XR-NTX injections beginning immediately after prison release.
Outcomes	Retention; abstinence.

Risk of Bias Table

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	**Low risk**	
Allocation concealment (selection bias)	**Low risk**	
Blinding of participants and personnel (performance bias)	**High risk**	Unblinded.
Blinding of outcome assessment (detection bias)	**High risk**	Unblinded.
Incomplete outcome data (attrition bias)	**Low risk**	
Selective reporting (reporting bias)	**Low risk**	
Other bias	**Unclear risk**	This study was funded by Alkermes, Inc. There is a potential risk of bias from the funding source because Alkermes produces and markets naltrexone in the USA.

Gordon 2015

Methods	Phase 4, pilot, open-label feasibility study.
Participants	27 prerelease male and female prisoners who had opioid disorders during the year prior to index incarceration were recruited and received one XR-NTX injection once each month for 7 months (one injection prerelease from prison and six injections in the community).
Interventions	Extended-release injectable naltrexone (XR-NTX).
Outcomes	Adherence: 10 of 27 (37%) were retained in treatment at 7 months post release. Criminal recidivism (rearrest and reincarceration): although not statistically significant, individuals who did not complete all six injections were more likely to be rearrested compared to those completing all six community injections (31.3% vs. 0%, respectively; $p = .123$). Opioid and cocaine use: results indicate those completing 6 compared to those completing < 6 injections were less likely to test positive for opioids in the community (0% vs. 62.5%, respectively; $p = .003$).

Risk of Bias Table

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	**High risk**	Not randomized.
Allocation concealment (selection bias)	**High risk**	Not randomized.
Blinding of participants and personnel (performance bias)	**High risk**	Unblinded.
Blinding of outcome assessment (detection bias)	**High risk**	Unblinded.
Incomplete outcome data (attrition bias)	**High risk**	Only 10 of 27 participants completed the study.
Selective reporting (reporting bias)	**Low risk**	Fairly consistent reporting.
Other bias	**Unclear risk**	This study was funded by Alkermes, Inc. There is a potential risk of bias from the funding source because Alkermes produces and markets naltrexone in the USA.

Lee 2015

Methods	8-week, proof-of-concept, open-label, nonblinded randomized effectiveness trial.
Participants	34 opioid-dependent adult males with no stated interest in agonist treatments.
Interventions	XR-NTX (n = 17) versus no medication (n = 17) within 1 week prior to jail release; both groups received a counseling and referral intervention.
Outcomes	Postrelease opioid relapse (self-report, UDS); proportion of opioid-negative UDS; rates of opioid abstinence; IVDU; cocaine use; community treatment participation; reincarceration; overdose.

Risk of Bias Table

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	**Low risk**	Detailed randomization methods described.
Allocation concealment (selection bias)	**Low risk**	Detailed allocation methods described.
Blinding of participants and personnel (performance bias)	**High risk**	Unblinded.
Blinding of outcome assessment (detection bias)	**High risk**	Unblinded.
Incomplete outcome data (attrition bias)	**Low risk**	There were no differences in rates of complete study visits versus dropout between arms.
Selective reporting (reporting bias)	**Low risk**	Outcomes clearly described and congruent with stated objectives: no missing data.
Other bias	**Unclear risk**	This study was funded by Alkermes, Inc. There is a potential risk of bias from the funding source because Alkermes produces and markets naltrexone in the USA.

Lee 2016

Methods	Five-site, open-label, randomized trial.
Participants	Adult criminal justice offenders who had a history of OUD and a preference for opioid-free treatments.
Interventions	24-week course of extended-release naltrexone (Vivitrol) with usual treatment, consisting of brief counseling and referrals for community treatment programs.
Outcomes	Primary outcome: median time to relapse (weeks). Opioid-relapse event—no. (%). Percentage of 2-wk intervals with confirmed abstinence; percentage of opioid-negative urine samples; percentage of days with self-reported opioid use; retention in treatment; percentage of days with cocaine use; heavy drinking in past 30 days at week 27—no(%); any intravenous drug use (%); any reincarceration—no. (%); total days of reincarceration; days incarcerated.

Risk of Bias Table

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	**Low risk**	Well-described randomization methods.
Allocation concealment (selection bias)	**Low risk**	Well-described allocation methods.
Blinding of participants and personnel (performance bias)	**High risk**	Open label.
Blinding of outcome assessment (detection bias)	**High risk**	Open label.
Incomplete outcome data (attrition bias)	**High risk**	Significant drop-out rate which differed between groups.
Selective reporting (reporting bias)	**Low risk**	Outcome well-reported.
Other bias	**Unclear risk**	This study was funded by Alkermes, Inc. There is a potential risk of bias from the funding source because Alkermes produces and markets naltrexone in the USA.

Lincoln 2017

Methods	Nonrandomized prospective trial.
Participants	67 incarcerated individuals who met criteria for OUD, self-referred. Recruitment: April 2013 to December 2014.
Interventions	Extended-release naltrexone (XR-NTX) prior to release from incarceration and linking participants to community treatment vs. postrelease.
Outcomes	Utility of the program was assessed by determining MAT retention rates at 4, 8, and 24 weeks. Overdose deaths.
Notes	The prevalence of opioid use disorder in jail and prison populations is well above the general population, with an estimated 24% to 36% of opioid-dependent adults in the US cycling in and out of jails each year (Rich et al., 2005; Substance Abuse and Mental Health Services Administration, 2013) and are at high risk of opioid relapse and overdose death following release (Merrall et al., 2010).

Risk of Bias Table

Bias	Authors' judgment	Support for judgment
Random sequence generation (selection bias)	**High risk**	Nonrandomized.
Allocation concealment (selection bias)	**High risk**	Nonrandomized.
Blinding of participants and personnel (performance bias)	**High risk**	Unblinded.
Blinding of outcome assessment (detection bias)	**High risk**	Unblinded.
Incomplete outcome data (attrition bias)	**High risk**	High rate of drop-out and low retention differentially.
Selective reporting (reporting bias)	**Low risk**	Stated outcomes were reported consistently.
Other bias	**Unclear risk**	This study was funded by Alkermes, Inc. There is a potential risk of bias from the funding source.

Appendix 3: Characteristics of Excluded Studies

Gordon 2017	Study protocol only.
Jarvis 2018	Systematic review.
Johannson 2006	Systematic review.
McDonald 2016	Study protocol only.
Sharma 2016	Systematic review.
Soares 2019	Secondary analysis of an included study.

An Exploration of Knowledge, Opinions, and Stigma Regarding Medication-Assisted Treatment among Treatment and Criminal Justice Professionals

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APPENDICES

Appendix A: Odds Ratios adjusted for time spent working at the agency and their 95% confidence intervals

	AOR	(95% CI)
Q4. I know what buprenorphine (Suboxone) is and how it is used in MAT.		
Resident supervisors vs. Treatment staff	0.1	(0.0, 0.5)
Q5. I know the difference between Oral Naltrexone and Injectable Naltrexone and how it is used in MAT.		
Resident supervisors vs. Management staff	0.2	(0.0, 0.8)
Q7. MAT reduces relapse.		
Resident supervisors vs. Caseworkers	0.1	(0.0, 0.6)
Resident supervisors vs. Treatment staff	0.2	(0.0, 0.7)
Q8. MAT reduces crime.		
Resident supervisors vs. Caseworkers	0.2	(0.1, 0.7)
Resident supervisors vs. Treatment staff	0.1	(0.0, 0.3)
Resident supervisors vs. Ancillary staff	0.1	(0.0, 0.4)
Resident supervisors vs. Management staff	0.0	(0.0, 0.2)
Caseworkers vs. Management staff	0.1	(0.0, 0.7)
Q9. MAT increases employment.		
Resident supervisors vs. Caseworkers	0.2	(0.1, 0.8)
Resident supervisors vs. Treatment staff	0.1	(0.0, 0.4)
Resident supervisors vs. Ancillary staff	0.1	(0.0, 0.6)
Resident supervisors vs. Management staff	6.9	(1.3, 35.2)

	AOR	(95% CI)
Caseworkers vs. Management staff	0.2	(0.1, 1.0)
Q10. MAT reduces or blocks the effects of heroin and other opioids.		
Resident supervisors vs. Caseworkers	0.1	(0.0, 0.4)
Resident supervisors vs. Treatment staff	0.1	(0.0, 0.7)
Resident supervisors vs. Management staff	0.1	(0.0, 0.6)
Q11. MAT reduces sexually transmitted infections and HIV.		
Resident supervisors vs. Treatment staff	0.2	(0.1, 0.6)
Caseworkers vs. Ancillary staff	3.2	(1.1, 9.7)
Caseworkers vs. Management staff	3.2	(1.1, 9.3)
Treatment staff vs. Ancillary staff	5.8	(1.8, 18.7)
Treatment staff vs. Management staff	5.6	(1.7, 18.4)
Q12. MAT lowers death rates.		
Resident supervisors vs. Treatment staff	0.1	(0.0, 0.8)
Q14. MAT improves birth outcomes for children born to addicted mothers.		
Resident supervisors vs. Treatment staff	0.2	(0.0, 0.7)
Treatment staff vs. Ancillary staff	4.8	(1.2, 20.0)

Appendix B: Odds Ratios adjusted for time spent working at the agency and their 95% confidence intervals

	AOR	(95% CI)
Q15. MAT is just substituting a prescription drug for an illegal drug.		
Resident supervisors vs. Caseworkers	3.1	(1.1, 9.0)
Resident supervisors vs. Treatment staff	3.5	(1.1, 11.2)
Resident supervisors vs. Management staff	4.6	(1.3, 16.5)
Q16. There is not enough evidence that shows that MAT actually works.		
Resident supervisors vs. Caseworkers	8.7	(2.6, 29.0)
Resident supervisors vs. Treatment staff	12.3	(2.8, 53.1)
Resident supervisors vs. Ancillary staff	3.5	(1.1, 10.8)
Resident supervisors vs. Management staff	7.6	(2.2, 26.8)
Q17. I am able to answer most questions that my clients have about the MAT programs available in my region.		
Resident supervisors vs. Treatment staff	0.2	(0.0, 0.5)
Resident supervisors vs. Management staff	0.1	(0.0, 0.5)
Caseworkers vs. Treatment staff	0.3	(0.1, 0.9)
Caseworkers vs. Management staff	0.3	(0.1, 0.9)
Treatment staff vs. Ancillary staff	3.9	(1.3, 12.4)
Ancillary Staff vs. Management staff	0.2	(0.1, 0.8)
Q18. When I have questions about medications used in MAT, I know who to ask.		
Resident supervisors vs. Caseworkers	0.3	(0.1, 1.0)
Resident supervisors vs. Treatment staff	0.2	(0.0, 0.7)
Resident supervisors vs. Management staff	0.0	(0.0, 0.4)
Ancillary Staff vs. Management staff	0.1	(0.0, 0.8)
Q20. MAT prolongs addiction.		
Resident supervisors vs. Caseworkers	3.6	(1.1, 11.6)
Resident supervisors vs. Ancillary staff	3.8	(1.1, 13.5)
Resident supervisors vs. Management staff	7.7	(1.4, 41.7)
Q21. When I have questions about the MAT referral process, I know who to ask.		
Resident supervisors vs. Treatment staff	0.2	(0.1, 0.8)
Resident supervisors vs. Management staff	0.1	(0.0, 0.4)
Caseworkers vs. Management staff	0.2	(0.0, 1.0)
Ancillary Staff vs. Management staff	0.1	(0.0, 0.6)
Q23. Clients cannot afford MAT.		
Resident supervisors vs. Ancillary staff	0.3	(0.1, 1.0)