



Methadone Versus Buprenorphine-Naloxone as a Treatment for Opioid Dependent Individuals

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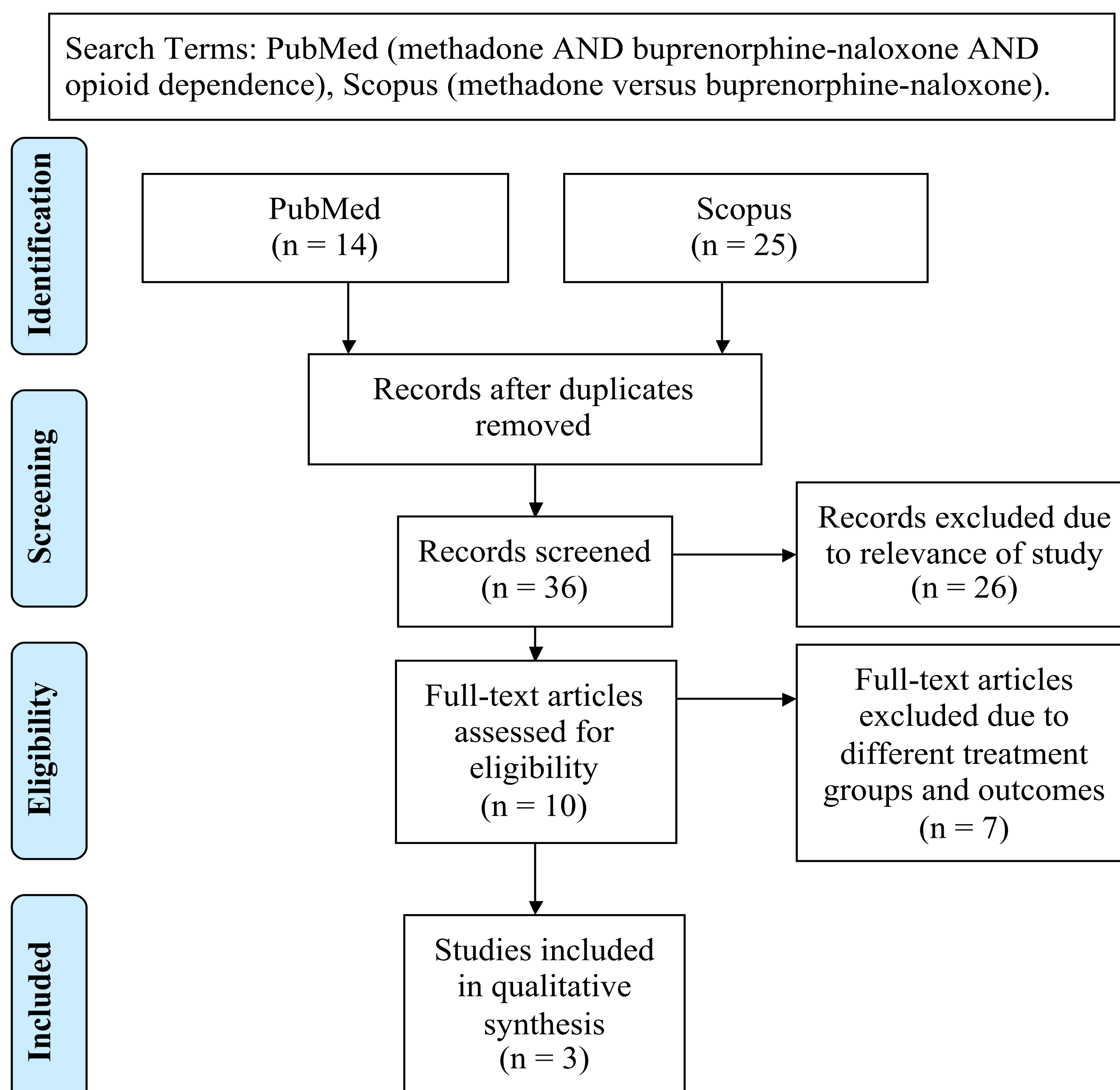
INTRODUCTION

- Opioids are a class of compounds that bind to mu-receptors in the central and peripheral nervous system eliciting an analgesic and euphoric effect.
- 586,000 and 1.9 million Americans have a substance use disorder involving heroin and prescription pain relievers, respectively.¹
- Cost of opioid dependence in the U.S. is 55.1 billion dollars annually.²
- Substance dependence is the compulsion to seek and take a drug and a loss of control in limiting intake.³
- Ideal treatment is complete abstinence but failure rates are high therefore opioid substitution is the mainstay of treatment.
- Methadone is a full mu-agonist requiring administration in a certified clinic.
- Buprenorphine-naloxone is a partial mu-agonist combined with an orally ineffective mu-antagonist to prevent IV drug use.

CLINICAL QUESTION

Among opioid-dependent individuals does methadone as compared to buprenorphine-naloxone improve retention rates and efficacy in treatment programs?

METHODS



RESULTS

Study 1: Methadone and buprenorphine-naloxone are effective in reducing illicit buprenorphine and other opioid use, and reducing HIV risk behavior-Outcomes of a Randomized Trial. Otiashvili et al.

Study Type: Randomized Control Trial

Sample Size: 80

Length of Program: 12 weeks with 20-week follow-up

Objective: To determine treatment retention with buprenorphine-naloxone or methadone in buprenorphine injection users

Conclusion: Daily observed doses of methadone and buprenorphine-naloxone were effective in reducing illicit buprenorphine and other opioid use

Critique: Strengths: Daily observed dosing ensured compliance, limited loss to follow up in initial 12-week study, loss to follow-up addressed by intention to treat. **Limitations:** Small sample size, short study duration, mostly males subjects, lack of follow-up at 20 weeks.

Study 2: Buprenorphine-Naloxone Versus Methadone Maintenance Therapy: A Randomized Double-Blind Trial With Opioid-Dependent Patients. Kamien et al.

Study Type: Double-Blind Randomized Control Trial

Sample Size: 268

Length of Program: 17 weeks

Objective: To compare buprenorphine-naloxone with methadone for maintenance treatment of opioid dependence

Conclusion: Maintenance treatment with 16 mg buprenorphine-naloxone reduced opioid use at a rate equivalent to that achieved with 90 mg methadone.

Critique: Strengths: Conservative analytic procedures, conducted at licensed, community-based opioid treatment center, exposed patient to buprenorphine-naloxone for longer time periods than previous studies. **Limitations:** Uneven number of participants assigned to each of the 4 treatment groups, drop-out rate, loss to follow-up addressed by pre-protocol analysis.

Study 3: Treatment Retention among Patients Randomized to Buprenorphine/Naloxone Compared to Methadone in A Multi-site Trial. Hser et al.

Study Type: Open-Label Randomized Control Trial

Sample Size: 1,267

Length of Program: 24 weeks

Objective: To examine patient and medication characteristics associated with retention and continued illicit opioid use in methadone versus buprenorphine-naloxone treatment

Conclusion: Methadone appears to be associated with better retention in treatment for opioid dependence than buprenorphine-naloxone, as does the use of higher doses of both medications. Buprenorphine-naloxone is associated with lower continued use of illicit opioids.

Critique: Strengths: First large scale RCT to compare treatment retention of participants on buprenorphine-naloxone and methadone, conducted in community treatment programs in the U.S. Additional findings: 1. Buprenorphine-naloxone dose related treatment retention. 2. Identified additional participant characteristics predicting dropout (age, ethnicity, other drug use, etc.). **Limitations:** Limited measures of participant motivation as well as program and community characteristics likely to influence retention. Other limitations are that it was open-labeled and unblinded.

Table 2. Overview of Results

	Otiashvili et al.	Kamien et al.	Hser et al.
Retention	<ul style="list-style-type: none"> 12 Week Follow-Up Of the 80 study participants, 68 (85%) completed the 12-weeks of treatment 20 Week Follow-Up 37 participants still on maintenance therapy 34 on methadone 3 on buprenorphine-naloxone 	<ul style="list-style-type: none"> Buprenorphine-naloxone low dose mean retention was 12.1 weeks, high dose 12.5 weeks Methadone low dose mean retention was 13.2 weeks, high dose 12.2 weeks Kaplan-Meier graphs show the cumulative retention by low dose with the log rank test (p=0.09) and high dose with the log rank test (p=0.28) did not differ significantly by drug 	<ul style="list-style-type: none"> 24 Week Follow-Up 74.1% participants on methadone 46.1% participants on buprenorphine-naloxone Higher doses of buprenorphine had higher retention rates than lower doses
Efficacy	<ul style="list-style-type: none"> Both treatment groups decreased the use of opioids with no significant difference between the groups There were more positive urine samples for opioids among methadone group than buprenorphine-naloxone group (6 vs. 1 or 1.5% vs. 0.2%; p=0.03) 	<ul style="list-style-type: none"> Medication compliance did not differ significantly based on drug or dose (p=0.41) Increased dose of either drug was associated with increased percent of participants with 12 consecutively negative urine samples. (10% of the 8-mg vs. 17% of the 16-mg burprenorphine-naloxone groups and 12% of the 45-mg vs. 16% of the 90-mg 	<ul style="list-style-type: none"> Opioid use was significantly lower among buprenorphine-naloxone group than methadone during the 1st 9 weeks of treatment (OR=0.63, 95% CI=0.52-0.76, p<0.01) Buprenorphine-naloxone participants has lower likelihood of positive opioid test results for every mg dose increase compared to methadone group (OR=0.98, 95%

CONCLUSIONS

Buprenorphine-naloxone may be more effective at preventing illicit opioid use than methadone, although this is inconsistent among the three studies. Retention rates are also inconclusive with only one study demonstrating higher retention rates with methadone treatment. With buprenorphine-naloxone demonstrating a better safety profile, fewer withdrawal effects, ease of use and less divergence, we recommend buprenorphine-naloxone over methadone as a first line treatment in opioid-dependent individuals.

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