

# The role of social network support on treatment outcomes for medication for opioid use disorder: a systematic review protocol

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## Protocol

**Keywords:** Medication for opioid use disorder, social network support, social networks, systematic review protocol

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## 33 **Background**

34 Increasing access to medications for opioid use disorder (MOUD) is a key public health strat-  
35 egy in combating the opioid epidemic [1, 2]. MOUD has several benefits such as decreases in  
36 mortality, increases in treatment adherence, decreases in heroin use, and augmented health,  
37 social and criminal justice outcomes [3, 4, 5]. World Health Organization (WHO) recom-  
38 mendations indicate that access to MOUD is key to treatment for opioid use disorder [6].  
39 MOUD is implemented in many jurisdictions globally [7, 8]. MOUD refers to several med-  
40 ications, but primarily opioid agonist medications, like methadone and buprenorphine, but  
41 also opioid-antagonist medications such as naltrexone [9]. Although MOUD models are the  
42 most efficacious evidence-based treatment for opioid use disorder [10], there remains a high  
43 percentage of patients with unfavorable treatment outcomes [11, 12]. Greater understanding  
44 of how social network support functions with respect to MOUD treatment outcomes may  
45 improve treatment outcomes. Social network support are the kinds of support, such as assis-  
46 tance or help, that people receive from friends, family, peers, and neighbors, paid or unpaid,  
47 in their social network [13, 14, 15].

48 Although clinical delivery characteristics, baseline substance use behaviors, comorbid  
49 mental health or substance use disorders and patient demographics influence treatment out-  
50 comes [16, 17], less research has focused on how social network support is associated with  
51 treatment outcomes. Novel treatment paradigms, such as open access models, have gone a  
52 long way in decreasing barriers to treatment and improving engagement, but there is still  
53 unexplained variability in patient engagement and therefore an opportunity for improvement  
54 [18].

55 Social network support moderates outcomes as diverse as cooperation and economic  
56 inequality [19, 20]. Observational and experimental studies have shown that phenomena as  
57 diverse as cooperation, obesity, drug use, smoking, alcohol use, and other health behaviors  
58 may be associated with social networks [21, 22, 23, 24]. Thus, it seems highly likely that  
59 social network support is of significant importance in understanding patterns of substance

60 use, help-seeking, and adherence. In this systematic review will assess evidence on the  
61 role of social network support on MOUD treatment outcomes from both experimental and  
62 observational studies.

63 The review will expand on past research to identify recent methodological and scientific  
64 progress, updated to capture current literature. The study objective is to review existing sci-  
65 entific evidence on the following research question: For MOUD patients (population), what  
66 influence does social network support have on MOUD (intervention) treatment outcomes  
67 (outcome)? This systematic review seeks to provide policymakers, administrators, practi-  
68 tioners and researchers with a systematic and reproducible strategy to query the literature  
69 around the role of social network support on MOUD treatment outcomes. We will report  
70 results in line with Preferred Reporting Items for Systematic Reviews and Meta-Analyses  
71 (PRISMA) guidelines and use standard tools to assess study quality [25, 26].

## 72 **Methods/Design**

73 We conformed to guidelines of the Preferred Reporting Items for Systematic Review and  
74 Meta-analysis Protocols (PRISMA-P) [27]. The protocol was pre-registered on PROSPERO  
75 (CRD42018095645).

### 76 **Search strategy**

77 First we will search online indexes, then we will search references in previous reviews/guidelines,  
78 and we will search Clinicaltrials.gov. Finally, we will consult content experts. We will conduct  
79 a systematic review of the literature using the databases of PubMed, MEDLINE, Embase,  
80 PsycINFO and Sociological Abstracts. We will search literature through May 2020. Studies  
81 written in English, conducted in humans, mentioned MOUD in the title or abstract, in-  
82 cluded social network support were considered for inclusion (see Appendix S1 for full search  
83 syntax). We originally planned to screen all MOUD studies without adding social network

84 support keywords in the search syntax. However, there were far too many studies given the  
85 broad search terms. After consulting with a medical librarian, we decided to proceed with  
86 searching for MOUD-related studies with social network support terms added to the syntax.  
87 We will identify studies by searching electronic index/research databases. Additional studies  
88 will be identified by scanning reference lists of previous literature reviews and other studies.  
89 To reduce publication bias, we will also include a broad range of studies [28]. The Clinical-  
90 Trials.gov library will be searched to identify potentially qualifying studies that have not led  
91 to published results. If feasible, we will reach out to authors of unpublished Clinicaltrials.gov  
92 studies for their data. We will obtain additional papers through consultation with experts  
93 and authors, targeted searches of thematic journals (see Appendix S1), technical reports,  
94 conference proceedings and national databases.

## 95 **Inclusion/Exclusion criteria**

96 We will include studies that meet the following criteria:

- 97 • randomized controlled trials, quasi-experimental studies and observational studies pub-  
98 lished in peer-reviewed journals; other scientific publications (e.g. Scientific Mono-  
99 graphs); non-peer reviewed journals and grey literature (technical reports, conference  
100 papers).
- 101 • participants are seeking treatment for opioid use or met criteria for opioid abuse, opioid  
102 dependence or opioid use disorder.
- 103 • one or more variants of MOUD are offered (e.g. methadone, buprenorphine, naltrex-  
104 one).
- 105 • the study reported social network support (e.g. family/partner/friend/peer/neighbor  
106 support, social network interventions [13, 14, 15]) as interventions or as predictors for  
107 the outcome. We will include studies that assessed perceived social support as well as  
108 other measures of social support such as social network indicators, etc.

109 • the study reports adherence to MOUD or MOUD program retention. There will be no  
110 restrictions on study design, population, or comparator (if included). Studies excluded  
111 from review will be case reports, reviews, systematic literature reviews, qualitative  
112 studies, opinion pieces, editorials, comments, news articles, and letters.

113 The planned systematic review flow diagram of the article selection process is displayed in  
114 Fig 1.

115 INSERT FIGURE 1 HERE: Preferred Reporting Items for Systematic Review and  
116 Meta-Analysis (PRISMA) flow diagram of study selection

## 117 **Outcomes**

118 Examples of primary outcomes are 1) MOUD program retention, we will examine dropout/continuation  
119 in the program and any other indicators of engagement that were measured (e.g., therapeutic  
120 alliance, attendance); 2) opioid use, defined as the percentage of urine samples negative  
121 for opioids and/or self-reported drug use. We expect that not all the studies included will  
122 adhere to these definitions. There are likely to be variations and differing definitions for  
123 individual studies.

## 124 **Data extraction**

125 We will utilize a standardized template to extract data from each study. We will extract  
126 general information (e.g. year, setting) and methods (e.g. design, duration), variant of  
127 MOUD (e.g. methadone, buprenorphine, naltrexone), and results specific to each outcome  
128 (e.g. treatment adherence, self-reported drug use, urine drug screen). Endnote, a biblio-  
129 graphic software, will be used to store, organize and manage all references [29]. Covidence  
130 will be used to manage the screening phases [30].

## 131 **Review methods, quality assessments and data synthesis**

132 The authors, in groups of two, will independently conduct study selection. A standardized  
133 template will be pre-piloted independently by two authors and all authors, in groups of two,  
134 will extract all relevant data. The authors will resolve disagreements in study selection and  
135 data extraction through discussion. A third author will step in when necessary for a final  
136 arbitration of any disagreements that occur. In groups of two, the authors will independently  
137 evaluate quality assessments and outcomes for each study and reach consensus via discussion.  
138 If consensus is not reached, a third reviewer will make final decisions.

139 The Cochrane risk of bias (ROB) tool will be used to assess the ROB of included ex-  
140 perimental studies [26]. This will be done by one reviewer and verified by a second. Dis-  
141 agreements will be resolved through discussion or third-party adjudication. Some areas in  
142 the Cochrane ROB are outcome specific and will thus be assessed at the outcome level. The  
143 overall risk of bias will involve determining the relative importance of domains, guided by  
144 known empirical evidence of bias, likely direction of bias, and the likely magnitude of bias  
145 [26]. For outcome and analysis reporting bias, we will use methods indicated in the Agency  
146 for Healthcare Research and Quality guidance to determine ROB for that domain [31]. We  
147 will assess for the possibility of recruitment bias in the *other bias* domain of the Cochrane  
148 ROB [26]. We will follow the Grading of Recommendations Assessment, Development and  
149 Evaluation (GRADE) guidance for judging the extent of the ROB for the evidence [32].  
150 Quality of evidence will be assessed using the GRADE approach. GRADE tables will be  
151 detailed for each of the outcomes with the GRADE framework to assess each domain (e.g.  
152 risk of bias, imprecision, inconsistency) [32]. This will be done by a single reviewer and a  
153 second reviewer will verify. Disagreements will be dealt with by discussion and consensus.

154 For observational studies, we will use the Newcastle Ottawa Scale (NOS) [33]. The NOS  
155 judges each study on eight items, divided into three groups: the selection of the study groups,  
156 the comparability of the groups, and the ascertainment of either the exposure or outcome  
157 of interest for case-control or cohort studies, respectively. Using NOS guidelines, we will

158 assess quality (ROB) for each observational study with two reviewers. Disagreements will  
159 be resolved through discussion and consensus.

160 In non-randomized studies, systematic bias may occur between different strata of social  
161 network support. This will be general problem with observational studies because parsing  
162 between causal relationships around social network support and severity of treatment out-  
163 comes is complex. This may affect cumulative evidence across studies by under-estimating  
164 the impact of MOUD, since pre-treatment variables like drug use may predict subsequent  
165 drug use. Between-group pre-study differences may further obscure the role of social inter-  
166 actions on treatment outcomes. Inclusion of data from unpublished studies may reduce risk  
167 of publication bias.

168 We will not be conducting a meta-analysis as we will not be searching broadly for MOUD  
169 studies that may include social support as an intervention or a predictor. Our search strategy  
170 may bias findings toward MOUD-related studies with social network support terms. When  
171 there is bias in study selection, a meta-analysis is not recommended [34]. We thus will not  
172 be using methods such as a funnel plot to evaluate presence of publication bias. We will use  
173 a structured narrative format to synthesize the literature, organized by research question  
174 and thematic focus.

## 175 **Amendments**

176 Any amendments to this protocol will be documented with reference to saved searches and  
177 analysis methods.

## 178 **Ethics and dissemination**

179 As we are conducting a systematic review without human subjects, there is no requirement  
180 for ethical approval. The results of this review will be disseminated in a peer-reviewed  
181 journal, conferences, seminars and symposia.

## 182 **Discussion**

183 The main strength of the proposed study is that we apply a reproducible and transparent  
184 procedure for a systematic literature review. In this protocol, we detailed the population,  
185 intervention and outcomes included, along with data extraction methods and search strat-  
186 egy. In publishing the research protocol, we strengthen the study clarity and reduce risk of  
187 bias. We also center on the role of social network support on MOUD adherence for MOUD  
188 patients. The results will provide information that can help researchers design interventions  
189 to increase MOUD adherence. Possible limitations of the planned study include the het-  
190 erogeneity of measures and outcomes evaluated and limited number of articles for certain  
191 outcomes, impairing risk of bias assessments. We were not able to search broadly for MOUD  
192 studies that may include social support as an intervention or a predictor. It is possible  
193 that limitations in text words and indexing terms may result in failing to retrieve all rele-  
194 vant studies. This may bias the selection of studies and we may not include some relevant  
195 studies, biasing findings toward MOUD-related studies with social network support terms.

196 Research on social network support could potentially improve MOUD treatment out-  
197 comes, possibly playing a role in mitigating the opioid epidemic. This review will demon-  
198 strate the value of social network support-based interventions on improving MOUD treat-  
199 ment outcomes.

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## 293 **List of abbreviations**

294 MOUD - Medication for opioid use disorder

## <sup>295</sup> **Declaration**

### <sup>296</sup> **Ethics approval and consent to participate**

<sup>297</sup> Not applicable

### <sup>298</sup> **Consent for publication**

<sup>299</sup> Not applicable

### <sup>300</sup> **Availability of data and materials**

<sup>301</sup> The datasets used and analyzed during the current study are available from the corresponding  
<sup>302</sup> author on reasonable request.

### <sup>303</sup> **Competing interests**

<sup>304</sup> The authors declare that they have no competing interests.

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### <sup>308</sup> **Authors' contributions**

<sup>309</sup> All authors contributed to the manuscript and read and approved the final draft.

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<sup>312</sup> assistance.

## 313 **Supplement**

### 314 **Appendix S1 - Review Methods**

#### 315 **Search strategy**

316 The following is an example of our PubMed search strategy:

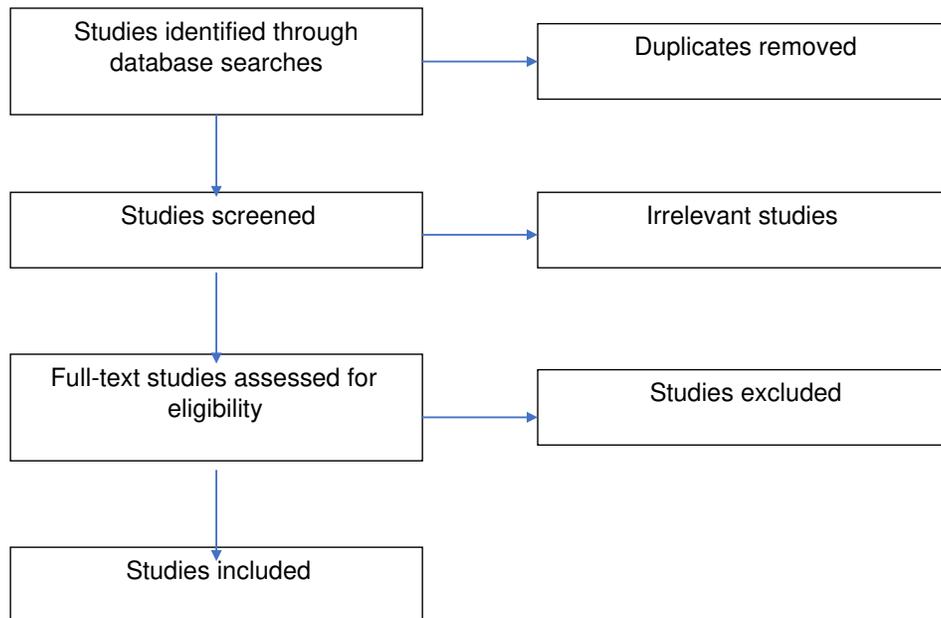
317 ((("buprenorphine, naloxone drug combination"[MeSH Terms] OR "naltrexone"[MeSH  
318 Terms] OR "methadone"[MeSH Terms] OR "opiate substitution treatment"[MeSH Terms]  
319 OR "opioid-related disorders"[MeSH Terms] OR "medication assisted therapy"[tw] OR "med-  
320 ication assisted therapies"[tw] OR Naltrexone[tw] OR Methadone[tw] OR Celupan[tw] OR  
321 Trexan[tw] OR ReVia[tw] OR Nemexin[tw] OR Nalorex[tw] OR Antaxone[tw] OR "EN  
322 1639A"[tw] OR Vivitrol[tw] OR Suboxone[tw] OR "Buprenorphine Naloxone"[tw] OR Methadone[tw]  
323 OR Dolophine[tw] OR Metadol[tw] OR Symoron[tw] OR Methadose[tw] OR Phenadone[tw]  
324 OR Physeptone[tw] OR Phymet[tw] OR Amidone[tw] OR Methaddict[tw] OR "Methadone  
325 Maintenance Treatment"[tw] OR "Opiate Substitution Treatments"[tw] OR "Opioid Sub-  
326 stitution Treatment"[tw] OR "Opioid Substitution Treatments"[tw] OR "Opioid Substi-  
327 tution Therapy"[tw] OR "Opioid Substitution Therapies"[tw] OR "Opiate Replacement  
328 Therapy"[tw] OR "Opiate Replacement Therapies"[tw] OR "Opioid Replacement Ther-  
329 apy"[tw] OR "Opioid Replacement Therapies"[tw]) AND ("social support"[MeSH Terms]  
330 OR "community health services"[MeSH Terms] OR "community networks"[MeSH Terms]  
331 OR "spouses"[MeSH Terms] OR "friends"[MeSH Terms] OR "family"[MeSH Terms] OR "so-  
332 cieties"[MeSH Terms] OR "residence characteristics"[MeSH Terms] OR "social support"[tw]  
333 OR "social supports"[tw] OR "social network"[tw] OR "social networks"[tw] OR "support  
334 system"[tw] OR "support systems"[tw] OR Spouse[tw] OR Spouses[tw] OR Partner[tw] OR  
335 Partners[tw] OR Friend[tw] OR Friends[tw] OR Society[tw] OR Community[tw] OR Com-  
336 munities[tw] OR Peer[tw] OR Peers[tw] OR Family[tw] OR Families[tw] OR Husband[tw]  
337 OR Husbands[tw] OR Wife[tw] OR Wives[tw] OR co-worker[tw] OR co-workers[tw] OR  
338 coworker[tw] OR coworkers[tw] OR neighbor[tw] OR neighbors[tw] OR Neighborhood[tw]

339 OR Neighborhoods[tw] OR Neighbourhood[tw] OR neighbourhoods[tw])) NOT (("buprenor-  
340 phine, naloxone drug combination"[MeSH Terms] OR "naltrexone"[MeSH Terms] OR "methadone"[MeSH  
341 Terms] OR "opiate substitution treatment"[MeSH Terms] OR "medication assisted ther-  
342 apy"[tw] OR "medication assisted therapies"[tw] OR Naltrexone[tw] OR Methadone[tw]  
343 OR Celupan[tw] OR Trexan[tw] OR ReVia[tw] OR Nemexin[tw] OR Nalorex[tw] OR An-  
344 taxone[tw] OR "EN 1639A"[tw] OR Vivitrol[tw] OR Suboxone[tw] OR "Buprenorphine  
345 Naloxone"[tw] OR Methadone[tw] OR Dolophine[tw] OR Metadol[tw] OR Symoron[tw] OR  
346 Methadose[tw] OR Phenadone[tw] OR Physeptone[tw] OR Phymet[tw] OR Amidone[tw]  
347 OR Methaddict[tw] OR "Methadone Maintenance Treatment"[tw] OR "Opiate Substitu-  
348 tion Treatments"[tw] OR "Opioid Substitution Treatment"[tw] OR "Opioid Substitution  
349 Treatments"[tw] OR "Opioid Substitution Therapy"[tw] OR "Opioid Substitution Thera-  
350 pies"[tw] OR "Opiate Replacement Therapy"[tw] OR "Opiate Replacement Therapies"[tw]  
351 OR "Opioid Replacement Therapy"[tw] OR "Opioid Replacement Therapies"[tw]) AND  
352 ("social support"[MeSH Terms] OR "community health services"[MeSH Terms] OR "com-  
353 munity networks"[MeSH Terms] OR "spouses"[MeSH Terms] OR "friends"[MeSH Terms] OR  
354 "family"[MeSH Terms] OR "societies"[MeSH Terms] OR "residence characteristics"[MeSH  
355 Terms] OR "social support"[tw] OR "social supports"[tw] OR "social network"[tw] OR  
356 "social networks"[tw] OR "support system"[tw] OR "support systems"[tw] OR Spouse[tw]  
357 OR Spouses[tw] OR Partner[tw] OR Partners[tw] OR Friend[tw] OR Friends[tw] OR So-  
358 ciety[tw] OR Community[tw] OR Communities[tw] OR Peer[tw] OR Peers[tw] OR Fam-  
359 ily[tw] OR Families[tw] OR Husband[tw] OR Husbands[tw] OR Wife[tw] OR Wives[tw]  
360 OR co-worker[tw] OR co-workers[tw] OR coworker[tw] OR coworkers[tw] OR neighbor[tw]  
361 OR neighbors[tw] OR Neighborhood[tw] OR Neighborhoods[tw] OR Neighbourhood[tw] OR  
362 neighbourhoods[tw]))

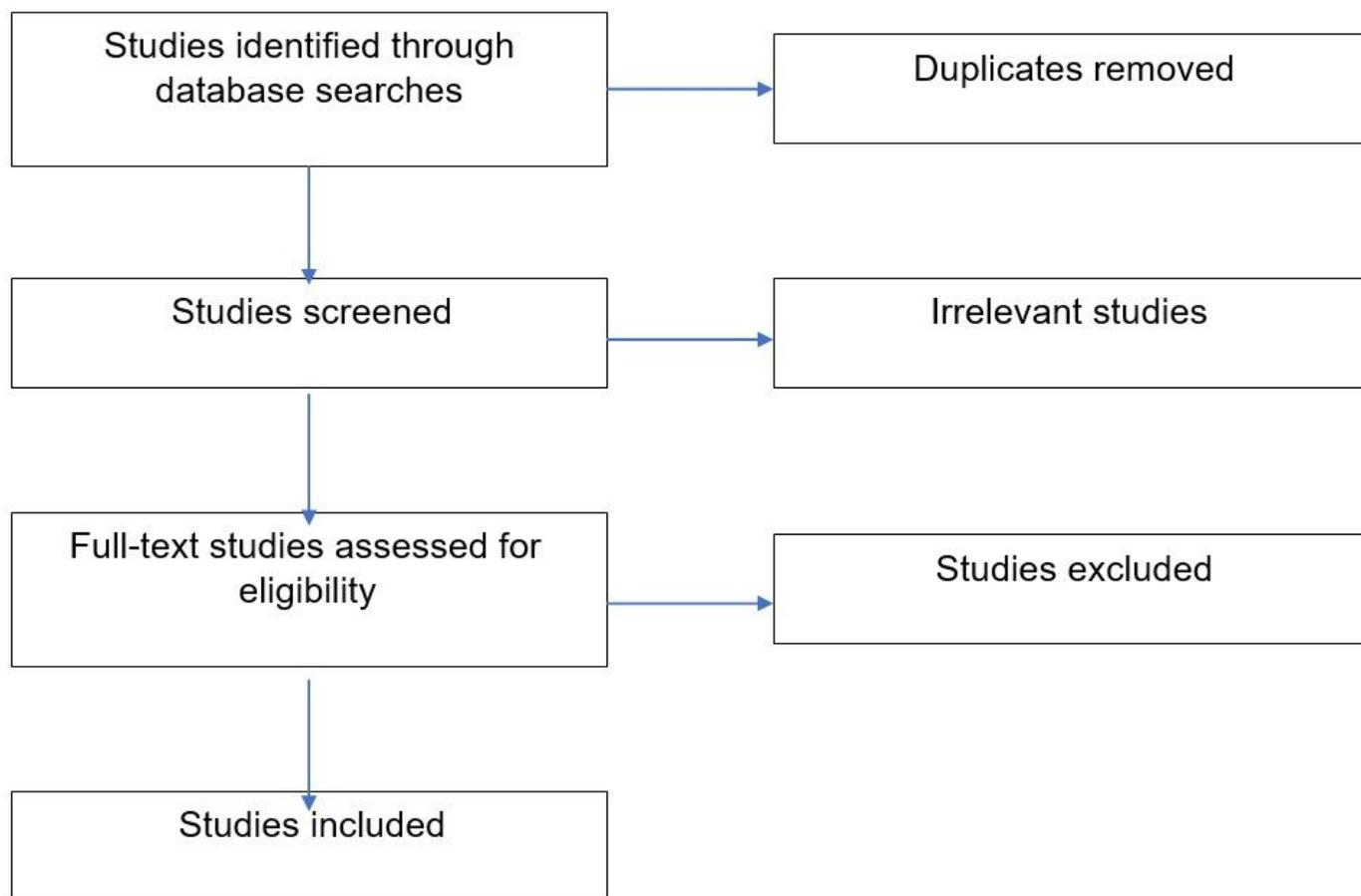
<sup>363</sup> **Specialist journals**

<sup>364</sup> Addiction, Addiction Research Theory, Addictive Behaviours, American Journal of Addic-  
<sup>365</sup> tions, Addiction Science and Clinical Practice, Drug and Alcohol Dependence, Drug and  
<sup>366</sup> Alcohol review, Drugs: Education, Prevention and Policy, European Addiction Research,  
<sup>367</sup> International Journal of Drug Policy, Journal of Addiction Medicine, Journal of Addiction  
<sup>368</sup> and Offender Counselling, Journal of Alcohol and Drug Education, Journal of Drug Issues,  
<sup>369</sup> International Journal of Mental Health and Addiction, Addictive Disorders and Their Treat-  
<sup>370</sup> ment, Journal of Substance Abuse, Journal of Substance Abuse and Treatment, Journal of  
<sup>371</sup> Substance Use, Substance Abuse: Research and Treatment, Substance Abuse Treatment,  
<sup>372</sup> Prevention and Policy and Substance Use Misuse.

Figure 1: Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram of study selection



## Figures



**Figure 1**

Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) flow diagram of study selection

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [PRISMAPchecklist.docx](#)