

# BMJ Open

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<http://bmjopen.bmj.com>).

If you have any questions on BMJ Open's open peer review process please email [info.bmjopen@bmj.com](mailto:info.bmjopen@bmj.com)

# BMJ Open

## Evaluating Comparative Effectiveness of Psychosocial Interventions for Persons Receiving Opioid Agonist Therapy for Opioid Use Disorder: Protocol for a Systematic Review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023902
Article Type:	Protocol
Date Submitted by the Author:	30-Apr-2018
Complete List of Authors:	<p>Rice, Danielle; McGill University, Psychology; Ottawa Hospital Research Institute  Hutton, Brian; University of Ottawa, Ottawa, Ontario, Canada; Ottawa Hospital Research Institute  Poulin, Patricia; Ottawa Hospital Research Institute; University of Ottawa, Social Sciences and Medicine  Sproule, Beth; University of Toronto Leslie Dan Faculty of Pharmacy, Psychiatry; Centre for Addiction and Mental Health, Pharmacy  Wolfe, Dianna; Ottawa Hospital Research Institute, Ottawa Methods Centre  Moher, David; Ottawa Hospital Research Institute, Ottawa Methods Centre  Thavorn, Kednapa; Institute for Clinical Evaluative Sciences, ICES @uOttawa; The Ottawa Hospital Research Institute,  Garber, Gary; Ottawa Hospital Research Institute; University of Ottawa, School of Epidemiology and Public Health  Taha, Sheena; Canadian Center on Substance Use and Addiction  Porath, Amy; Canadian Center on Substance Use and Addiction  Willows, Melanie; The Royal Ottawa Mental Health Centre, Substance Use and Concurrent Disorders Program; University of Ottawa Faculty of Medicine  Esmaeilisaraji, Leila; Ottawa Hospital Research Institute, Ottawa Methods Centre  Yazdi, Fatemeh; Ottawa Hospital Research Institute, Ottawa Methods Centre  Shea, Beverley; University of Ottawa; Ottawa Hospital Research Institute  Skidmore, Becky; Independent Information Specialist  Corace, Kimberly; University of Ottawa,</p>
Keywords:	Opioid use disorder, systematic review, psychosocial interventions, pharmacological interventions, addiction medicine, network meta-analysis

SCHOLARONE™  
Manuscripts

# Evaluating Comparative Effectiveness of Psychosocial Interventions for Persons Receiving Opioid Agonist Therapy for Opioid Use Disorder: Protocol for a Systematic Review

Danielle B Rice\*<sup>1,2</sup>; Brian Hutton\*<sup>1,3</sup>; Patricia Poulin<sup>1,4,5</sup>; Beth A Sproule<sup>6,7</sup>; Dianna Wolfe<sup>1</sup>; David Moher<sup>1,3,8</sup>; Kednapa Thavorn<sup>1,3</sup>; Gary Garber<sup>1,3,9</sup>; Sheena Taha<sup>11</sup>; Amy Porath<sup>11</sup>; Melanie Willows<sup>10,12</sup>; Leila Esmaeilisaraji<sup>1</sup>; Fatemeh Yazdi<sup>1</sup>; Bev Shea<sup>1</sup>; Becky Skidmore<sup>1</sup>; Kimberly Corace<sup>1,12,13,14</sup>

\* Authors contributed equally to this work.

## Affiliations

<sup>1</sup>Ottawa Hospital Research Institute, Ottawa, ON, Canada

<sup>2</sup>Department of Psychology, Montreal, QC, Canada

<sup>3</sup>School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada

<sup>4</sup>Faculties of Social Sciences and Medicine, University of Ottawa, Ottawa, Canada

<sup>5</sup>Pain Clinic, Ottawa Hospital, Ottawa, ON, Canada

<sup>6</sup>Department of Pharmacy, Centre for Addiction and Mental Health, Toronto, ON, Canada

<sup>7</sup>Leslie Dan Faculty of Pharmacy and Department of Psychiatry, University of Toronto, Toronto, ON, Canada

<sup>8</sup>Centre for Journalology, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada

<sup>9</sup>Public Health Ontario, Toronto, ON, Canada

<sup>10</sup>Faculty of Medicine, Department of Family Medicine, University of Ottawa

<sup>11</sup>Canadian Center on Substance Use and Addiction, Ottawa, ON, Canada

<sup>12</sup>Substance Use and Concurrent Disorders Program, The Royal Ottawa Mental Health Centre, Ottawa, ON, Canada

<sup>13</sup>Faculty of Medicine, Department of Psychiatry, University of Ottawa, Ottawa, ON, Canada

<sup>14</sup>University of Ottawa, Institute of Mental Health Research

## **Corresponding Author:**

Dr. Brian Hutton

Center for Practice Changing Research

The Ottawa Hospital

501 Smyth Road, PO Box 201B,

Ottawa, ON, K1H 8L6

Email: bhutton@ohri.ca

Phone: 613-737-8899, ext 73842

## **Publication Details**

***Abstract Word Count:*** 267

***Main Text Word Count:*** 3,050

## ABSTRACT

**Introduction:** North America is facing an opioid crisis resulting in increasing rates of death caused by problematic opioid use. Current clinical guidelines recommend that individuals with persons with opioid use disorder (OUD) receive pharmacologic (e.g., opioid agonist therapy) and psychosocial (e.g., cognitive behavioral therapy) therapy, however, the best combination of pharmacologic and psychosocial components is not known. Our objective of the planned study is to conduct a comprehensive systematic review to assess the relative benefits of psychosocial interventions as an adjunct to opioid agonist therapy among persons with OUD.

**Methods and analysis:** A comprehensive search for randomized controlled trials and quasi-randomized studies published in English or French will be conducted from database inception to February 2018. The search will be conducted in MEDLINE, and translated for Embase, PsycINFO, and the Cochrane Central Register of Controlled Trials. Two independent reviewers will screen, extract, and assess risk of bias of eligible articles. Primary outcomes of interest will be treatment retention and opioid use (based on urinalysis results). Secondary outcomes will include self-reported opioid use, abstinence from illicit drugs, adherence to psychosocial therapy and opioid agonist therapy, risk for sexually transmitted disease, risk for blood borne pathogens, changes in mental health symptoms (e.g., depression), measures of craving and changes in patients' quality of life, and relevant adverse events. If sufficient data and adequate homogeneity exists, network meta-analyses (NMA) will be performed.

**Ethics and dissemination:** This will be the first systematic review to incorporate NMA to compare psychosocial treatments used as an adjunct to opioid agonist therapy for OUD. Results of this review will inform clinical management of persons with OUD.

1  
2  
3  
4  
5 **PROSPERO Registration #:** CRD42018090761  
6

7 **Keywords:** Opioid use disorder, systematic review, psychosocial interventions, pharmacological  
8  
9 interventions, addiction medicine, network meta-analysis.  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

## STRENGTHS AND LIMITATIONS

- This will be the first systematic review incorporating network meta-analysis to compare the effectiveness of psychosocial treatments delivered in combination with opioid agonist therapy among people with opioid use disorder.
- Sub-group analyses are planned for speciality groups such as youth, pregnant women, indigenous people, and people who are incarcerated.
- Variability of outcome measures may influence the ability to perform planned network meta-analyses, and strategies have been planned to address this challenge.

## BACKGROUND

North America is facing an opioid crisis. Opioids are psychoactive analgesic drugs that can be prescribed for relief of acute or chronic pain,[1] and their illicit use has risen to epidemic levels.[2] Opioid addiction, overdose and poisonings have resulted in increasing rates of opioid-related death.[3] In 2016, more than 2,800 Canadians and 42,000 Americans died from opioid poisoning.[4, 5] An estimated 11.5 million individuals in the United States used opioid prescriptions non-medically in the past year alone.[2] Non-medical use of prescription opioids as well as the use of illicit opioids are of particular concern. There has also been a dramatic rise in illicit drugs being contaminated with fentanyl. In 2016, there was a 281% increase in the number of deaths attributable to fentanyl within Canada as compared to the preceding year.[5, 6] These alarming trends have prompted recent international, national, and provincial level actions including the development of the 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain, Canadian and American guidelines for opioid use disorder [3, 7], and the encouragement of prescribing cautiously and in smaller quantities to decrease misuse and dependence.[8]

Non-medical and illicit use of opioids can result in individuals developing an opioid use disorder (OUD). Compared to healthy individuals without OUD, individuals with an OUD have increased psychosocial distress, healthcare utilization, morbidity, and mortality.[9, 10] The societal implications of OUD are also substantial, as the total program spending on drugs used for OUD (i.e., methadone, buprenorphine/naloxone) exceeded \$135 million in Canada in 2015.[11] In the United States, the total economic burden of opioid overdose, addiction, and dependence was \$78.5 billion in 2013.[12] Given the costly and significant implications of OUD on mortality,

1  
2  
3 morbidity, healthcare utilization and societal costs, the identification of best management  
4 strategies is essential.  
5  
6  
7  
8  
9

10 Clinical guidelines currently recommend that individuals with OUD receive concurrent therapy  
11 consisting of pharmacologic (e.g., opioid agonist therapy) and psychosocial (e.g., cognitive  
12 behavioral therapy) components.[6, 13] However, the best combination of pharmacologic and  
13 psychosocial components is not currently known. To address the question of optimal  
14 effectiveness of pharmacotherapy, specifically, opioid agonist therapy (OAT), a systematic  
15 review and network meta-analysis (NMA) was planned to compare the effectiveness of OATs  
16 for the treatment of OUD [14]. This review, however, could not be completed as intended due to  
17 substantial heterogeneity among outcome measures. Of 60 included trials, there were 53 different  
18 outcomes that were measured in 77 unique ways [14, 15], thereby greatly complicating the  
19 ability to perform cross-study comparisons and pursue formal meta-analyses to compare OATs.  
20 Given the extensive variability among outcome measures, the authors were only able to conduct  
21 analyses on one outcome - treatment retention – where diacetylmorphine-assisted therapy was  
22 found to be superior to other OATs.[15] Currently no analogous systematic review and network  
23 meta-analysis for psychosocial therapies as adjunctive treatment to OAT for managing OUD  
24 exist. A variety of approaches have been used to aid in OUD management, including cognitive  
25 behavioral therapy, motivational interviewing, contingency management, supportive counseling  
26 and other strategies.[16, 17] While a quantitative comparison of the efficacy of psychosocial  
27 therapy has not been conducted, psychological treatment is considered by many clinicians to be a  
28 vital element to sustained success in people receiving OAT given its key role in ensuring  
29 treatment retention and improved outcomes.[3, 18]  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3  
4  
5 To our knowledge, no systematic review has included a NMA comparing the efficacy of  
6 psychosocial interventions used with OAT for individuals with OUD. Network meta-analysis has  
7 become a vital and broadly used approach to evidence synthesis in addressing research questions  
8 that involve the comparison of multiple therapies and wherein relevant direct and indirect data  
9 exists.[19-21] Such an analysis will be informative for decision-making in addressing and  
10 treating the rising rate of OUD. The current protocol outlines a planned systematic review and  
11 NMA to compare the relative benefits of different psychosocial therapies among people with  
12 OUD receiving OAT.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25

## 26 **METHODS**

27  
28 The reporting of this protocol adheres to the Preferred Reporting Items for Systematic Reviews  
29 and Meta-analyses-Protocol (PRISMA-P) statement.[22] The checklist for reporting items can be  
30 found in appendix 1. The review will be performed in accordance with the methods described  
31 below with any subsequent amendments described in the final manuscript. The review has also  
32 been registered in PROSPERO (CRD42018090761).  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42

### 43 **Search Strategy to Identify Relevant Studies**

44 Search strategies to identify relevant studies for inclusion in the systematic review were  
45 developed and tested through an iterative process by an experienced medical information  
46 specialist (B Skidmore) in consultation with the review team. Separate searches were performed  
47 for reviews and primary studies. The MEDLINE strategies were peer reviewed by another senior  
48 information specialist prior to execution using the PRESS Checklist.[23] Using the OVID  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 platform, we searched Ovid MEDLINE®, including Epub Ahead of Print and In-Process &  
4 Other Non-Indexed Citations, PsycINFO, and Embase Classic + Embase. We also searched the  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

platform, we searched Ovid MEDLINE®, including Epub Ahead of Print and In-Process & Other Non-Indexed Citations, PsycINFO, and Embase Classic + Embase. We also searched the Cochrane Library on Wiley. The review searches were performed on 28 February 2018 and the primary study searches on 8 March 2018. Strategies utilized a combination of controlled vocabulary (e.g., “Opiate Substitution Treatment”, “Opioid-Related Disorders/dt [drug therapy]”, “Buprenorphine/tu [therapeutic use]”) and keywords (e.g., “opioid maintenance”, “methadone substitution”, “OATS”). Randomized controlled trial, non-randomized controlled trial and systematic review filters were applied as applicable (see appendix 2 for full search strategy). Vocabulary and syntax were adjusted across databases. Conference abstracts prior to 2016 were removed from Embase and CENTRAL and dissertation abstracts were removed from PsycINFO. The reference lists of identified trials and reviews will be searched to ensure no relevant studies are missed. The supplemental searches will be integrated into a PRISMA flow diagram.

## Study Eligibility Criteria

### Population

Individuals diagnosed with OUD as defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) or diagnosed with opioid dependence as defined by the International Classification of Disease (ICD) or DSM-IV will be of interest. No restrictions will be made for age or specialty populations (e.g., youth, pregnant women, people who are incarcerated). Based on the availability of data, such uniquely different populations will be analysed separately given potential socio-demographic and other differences. If not feasible, the appropriateness of

1  
2  
3 regression-based adjustments to account for cross-study differences in the representation of such  
4  
5 populations will be assessed.  
6  
7  
8  
9

### 10 **Interventions and Comparators of Interest**

11  
12 Psychosocial interventions (delivered with OAT) will be of interest. Studies evaluating the  
13  
14 benefits of psychosocial interventions alone will be excluded from the systematic review. Studies  
15  
16 using control groups of either OAT alone or 'standard medical management' will be eligible  
17  
18 given their high likelihood of serving as important sources of indirect evidence[20] if NMAs are  
19  
20 performed. Descriptions of the primary psychosocial interventions to be included based on  
21  
22 existing research and recommendations are presented in appendix 3.  
23  
24  
25  
26  
27

### 28 **Outcomes**

29  
30 The co-primary outcomes of interest will be treatment retention and opioid use (based on  
31  
32 urinalysis results). Retention can be measured in several ways including the use of a continuous  
33  
34 value, such as the number of days a patient continued in an OAT program.[24] A binary  
35  
36 outcome, such as the proportion of patients who completed the planned number of therapy  
37  
38 sessions,[25] or the number of patients who received treatment for a predetermined minimum  
39  
40 number of sessions.[26] Secondary endpoints of interest will include self-reported opioid use,  
41  
42 abstinence from illicit drug use, alcohol use, adherence to psychosocial therapy, adherence to  
43  
44 OAT therapy, HIV risk behaviours, changes in mental health symptoms (depression, anxiety,  
45  
46 suicidality), measures of craving and changes in patients' quality of life, and adverse events (e.g.,  
47  
48 increases in substance use). We will capture data for all reporting formats of outcomes  
49  
50 considered (this will also provide valuable data for the planned future development of a core  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 endpoints set for OUD); once data collection is complete, we will review outcome definitions  
4 and cross-study data availability to identify those endpoints that may be best suited for NMAs  
5  
6 (those with insufficient data will be summarized in other ways).  
7  
8  
9

## 10 11 12 **Study Designs**

13  
14 Study designs of interest will include randomized controlled trials and quasi-randomized trials  
15 (e.g., trials that do not use appropriate methods for randomization). Only studies published in  
16 English and French will be included. Observational studies, case-control studies, case series and  
17 case reports will be excluded.  
18  
19  
20  
21  
22  
23

## 24 25 26 **Screening for Eligible Studies**

27  
28 Citations obtained from the literature searches will be imported into Distiller SR Software  
29 (Evidence Partners, Inc; Ottawa, Canada), which will be used for all stages of study screening  
30 and data extraction. Citations will be screened independently by two reviewers (among DR, LE,  
31 and FY), based on title, keywords, and abstract (Level 1 screening) and full-text articles (Level 2  
32 screening). Level 1 will be performed using a liberal accelerated approach (i.e., only one  
33 reviewer needed to include a citation, while two reviewers will be needed to exclude), and will  
34 be supported using text mining methods within Distiller SR. Level 1 citations deemed potentially  
35 relevant or lacking sufficient information to exclude will be carried forward to Level 2, which  
36 will be performed by two reviewers independently. Disagreements at Level 2 screening will be  
37 resolved by discussion. Where consensus is not achieved following discussion, a third  
38 independent team member will be consulted (BH or KC). Prior to conducting screening at level 1  
39 and level 2, a small number of abstracts/full texts will be piloted to establish agreement and  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 consistency among reviewers. Of studies that report on the same cohort (e.g., updates of different  
4 follow-up durations), the most up-to-date information will be retained, and a note of the  
5 duplicate sample will be made. The process of literature selection will be reported using a flow  
6 diagram as recommended by the PRISMA statement.[27, 28]  
7  
8  
9  
10  
11  
12  
13

### 14 **Process of Data Collection**

15  
16 Primary data collection of included studies will be performed by two reviewers using a  
17 standardized electronic data collection form in Distiller SR Software. Data gathered from  
18 included studies will include the patient population, intervention and comparator information,  
19 outcomes reported, and study design. Study characteristics (authors, year of publication, journal,  
20 countries of performance), patient characteristics (eligibility criteria, number per group), patient  
21 demographics (age, sex, race), type of opioid use (prescription and/or illicit), cited rationale for  
22 opioid use (e.g., chronic pain), duration of opioid use, mode of use (intravenous versus oral),  
23 comorbidities or other unique demographic traits, interventions (with description, including  
24 numbers and duration of sessions, setting and therapist expertise, if described), treatment setting  
25 (e.g., community, physician office, penitentiary), and outcomes as described above. All study  
26 characteristics will be summarized in tabular form to facilitate inspection and discussion with  
27 clinical experts in terms of study heterogeneity, grouping of interventions, and other such topics  
28 required to inform analysis; these tables will also be included in the final report. Collected data  
29 will be verified by a second reviewer for accuracy, with disagreements being settled by  
30 discussion.  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

### **Risk of Bias Assessments of Included Studies**

Risk of bias (RoB) will be assessed for all randomized and quasi-randomized studies included in the review using the Cochrane RoB tool.[29] The Cochrane RoB tool evaluates seven domains (i.e., random sequence generation, allocation concealment, blinding, missing outcome data, selective outcome reporting, attrition, and “other sources of bias”).[29] RoB assessments will be conducted by two reviewers (among DR, LE, and FY) and disagreements will be resolved through discussion or by a third reviewer (BH or KC). Results from RoB appraisals will be summarized in the review and reported in full on an item-by-item basis in an appendix. They will also be considered as criteria for sensitivity analyses.

### **Approach to Evidence Synthesis for NMA**

For outcomes with sufficient data for analysis, we will first conduct traditional meta-analyses of all pairwise comparisons in the evidence networks. If feasible, NMAs will be performed subsequently. Initial exploration of potential clinical and methodological heterogeneity amongst the included studies will be conducted using tabular and graphical approaches that will be discussed by members of the research team. The assumption of transitivity will be evaluated by inspection of differences in patient eligibility criteria and pertinent patient demographics between studies, including comorbidities (e.g., comorbid pain, mental health diagnoses). Methodological differences between studies that could influence outcome measurements will be noted. We will describe any concerns related to the transitivity assumption or methodological heterogeneity within the final report and consider statistical strategies to address any concerns.

1  
2  
3 Standard pairwise meta-analyses will be conducted by fitting random-effects models in  
4 Comprehensive Meta-Analysis V3 software (Biostat Inc; Englewood, New Jersey, USA) to  
5 generate summary estimates and to assess statistical heterogeneity across included studies.  
6  
7  
8 Summary estimates will be reported as mean differences, standardized mean differences, or odds  
9 ratios as appropriate with corresponding 95% confidence intervals. Statistical heterogeneity will  
10 be measured by the  $I^2$  statistic.  $I^2$  values of 50% or higher will be considered indicative of  
11 potentially important heterogeneity that will be explored using established methods such as  
12 subgroup analysis, meta-regression and/or exclusion of outlier studies. If necessary, similar  
13 approaches will be conducted in NMAs to address existing heterogeneity. Comparison adjusted  
14 funnel plots will be performed to assess publication bias if NMAs are performed.  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27

28 Where feasible, NMAs will be carried out separately for each clinical outcome of interest.  
29  
30 Approaches used for these analyses will follow existing recommendations for modelling of  
31 unadjusted and adjusted models as outlined by guidance from experts at the National Institute for  
32 Health and Care Excellence.[30, 31] Both fixed-effects and random-effects models will be fit for  
33 each outcome, within a Bayesian framework. Totals of 50,000 or more burn-in iterations and  
34 50,000 or more sampling iterations will be used for all NMAs, and model convergence will be  
35 assessed using Gelman Rubin diagnostics.[31] The fit of a model will be assessed by comparing  
36 its posterior residual deviance with the number of unconstrained data points (i.e., the number of  
37 intervention arms across all studies) for the analysis. Selection between different models will be  
38 based upon deviance information criteria for each competing model, with a difference of five or  
39 more points suggesting an important difference.  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 For networks where statistical heterogeneity is high or the number of single-study connections is  
4 high, random-effects models will be preferred. Between-treatment differences of continuous  
5 endpoints (e.g., change in quality of life) will be analysed using a model for mean differences or  
6 standardized mean differences as appropriate dependent upon the degree of studies providing  
7 data on different measurement scales. Findings from analyses of dichotomous outcomes (e.g.,  
8 adherence of a certain number of days, response to treatment) will be reported in terms of odds  
9 ratios. The assumption of consistency will be assessed by (i) fitting unrelated means models and  
10 comparing the deviance information criteria DIC) with the corresponding consistency models;  
11 and (ii) reviewing scatterplots of the residuals from these models. Probabilities of treatment  
12 superiority will be estimated using the Surface Under the Cumulative Ranking curve (SUCRA),  
13 and ranking of treatments will be estimated by median treatment rankings, with corresponding  
14 95% credible intervals. All NMAs will be performed using WinBUGS software version 1.4.3  
15 (MRC Biostatistics Unit).

### 35 **Subgroup and Sensitivity Analyses**

36  
37 Primary analyses will be unadjusted; however, additional analyses to assess heterogeneity will be  
38 pursued if feasible based upon data availability and network geometry considerations (e.g., few  
39 single-study connections). We will consider additional analyses to address study deficiencies  
40 found in RoB assessments by excluding low quality studies. Primary analyses will be conducted  
41 to compare psychosocial therapies at the treatment level and if data allows for it, we will  
42 establish broader categories of interventions for comparison (e.g., individual, family, couples,  
43 group) and conduct subgroup analyses. Subgroup and/or meta-regression will also be conducted  
44 for age (between 12-17 and 18-25 years), sex (percent of males and females [32, 33]), duration  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3 of opioid use disorder, most common method of administration (oral versus intravenous), type of  
4  
5 opioid use (percent prescription versus illicit), percent with physical health comorbidities,  
6  
7 percent with other substance/alcohol use, extent of comorbid pain, and percent of patients with  
8  
9 mental health comorbidities, where data are available.  
10  
11  
12  
13

### 14 **Reporting of Review Findings**

15  
16 Both graphical and numeric display of findings will be presented. For each feasible outcome of  
17  
18 interest, this will include network diagrams (to display the availability of evidence for all  
19  
20 possible treatment comparisons); pairwise comparisons between interventions with 95% credible  
21  
22 intervals for all treatments in the network; and SUCRA values and median treatment rankings.  
23  
24 We will use the checklist of the PRISMA Statement for Network Meta-Analysis to ensure all  
25  
26 findings are clearly reported.[28] If NMA is not feasible, pairwise meta-analysis findings will be  
27  
28 reported in tables with a narrative summary.  
29  
30  
31  
32  
33  
34

### 35 **Patient and Public Involvement**

36  
37 Patients were not involved in the design of this review, however, this work will inform the  
38  
39 development of a core endpoints initiative. This initiative will involve multiple patient groups to  
40  
41 gather perspectives on key outcomes for the development of future trials and to disseminate  
42  
43 review findings.  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## DISCUSSION

Improving the treatment of OUD is a fundamental component of mitigating the current opioid crisis and reducing the increasing morbidity and mortality associated with OUD in North America. Certain OAT medications are recommended for treating OUD as they are cost-effective and clinically effective.[34] Regardless of the form of OAT administered, guidelines for the clinical management of OUD recommend that psychosocial components be included, as this can improve treatment retention and outcomes.[6] Despite this recommendation, only a small minority of individuals receiving OAT are also provided psychosocial treatment.[35, 36] This may relate to a lack of comparative evidence for the various psychosocial interventions that can be applied in combination with OAT for individuals with OUD. To our knowledge, this will be the first NMA looking to compare the efficacy of psychosocial interventions delivered with OAT among individuals with OUD.

We anticipate certain challenges in the context of the current review. One limiting obstacle may be the existence of excessive between-study heterogeneity with regard to the outcomes measured across studies which may limit formal synthesis, as was found in a recent systematic review that compared OATs for patients with OUD.[37] Despite this challenge, our systematic review and accompanying narrative summary will allow for the synthesis of studies to guide our understanding of the potential usefulness of psychosocial interventions applied as an adjunct to OAT for patients with OUD. This potential challenge motivates additional research we will pursue in the second phase of our research wherein we will use established methods and collaborate with methodologists, physicians, clinicians, and patients to develop a core outcomes set for OUD through Delphi surveys and interviews that include these stakeholder groups.

1  
2  
3 Developing a core outcome set will inform and improve future research of OUD, both by  
4 enhancing the consistency of evaluations performed in research studies of OUD as well as  
5  
6 improving the ability of researchers to both perform meta-analyses and derive cross-study  
7  
8 comparisons to inform decision making.  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

## 1 REFERENCES

- 2 1. Franklin GM, Rahman EA, Turner JA, et al. Opioid use for chronic low back pain: A  
3 prospective, population-based study among injured workers in Washington state, 2002-  
4 2005. *The Clinical Journal of Pain* 2009;25:743-51.
- 5 2. Centers for Disease Control Prevention. Vital signs: overdoses of prescription opioid pain  
6 relievers---United States, 1999--2008. *Morbidity and mortality weekly report*  
7 2011;60:1487-92.
- 8 3. Bruneau J, Ahamad K, Goyer M-È, et al. Management of opioid use disorders: a national  
9 clinical practice guideline. *Canadian Medical Association Journal* 2018;190:E247.
- 10 4. Canadian Institute for Health Information. Canadian Centre on Substance Abuse.  
11 Hospitalizations and Emergency Department Visits Due to Opioid Poisoning in Canada.  
12 Canadian Institute for Health Information; 2016.
- 13 5. Centers for Disease Control Prevention. Drug Overdose Death Data 2017. Accessed on  
14 04/Jan/2018. Available from: <https://www.cdc.gov/drugoverdose/data/statedeaths.html>.
- 15 6. British Columbia Centre on Substance Use, British Columbia Ministry of Health. A  
16 Guideline for the Clinical Management of Opioid Use Disorder. 2017. Accessed on  
17 15/Jan/2018. Available from: <http://www.bccsu.ca/wp-content/uploads/2017/06/BC->  
18 OUD-Guidelines\_June2017.pdf
- 19 7. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National  
20 Practice Guideline for the Use of Medications in the Treatment of Addiction Involving  
21 Opioid Use. *J Addict Med* 2015;9.
- 22 8. The Ontario Drug Policy Research Network. Safety and Use of Opioids: A summary of  
23 ODPRN research on prescription opioid use in Ontario. 2016. Accessed on 15/Jan/2018.

- 1  
2  
3 24 Available from: <http://odprn.ca/wp-content/uploads/2016/08/FINAL-ODPRN-Opioids->  
4  
5 25 [Summary-Report-Aug-2016\\_compressed.pdf](http://odprn.ca/wp-content/uploads/2016/08/FINAL-ODPRN-Opioids-Summary-Report-Aug-2016_compressed.pdf).  
6  
7  
8 26 9. Kolodny A, Courtwright DT, Hwang CS, et al. The prescription opioid and heroin crisis:  
9  
10 27 a public health approach to an epidemic of addiction. *Annual Review of Public Health*  
11  
12 28 2015;36:559-74.  
13  
14  
15 29 10. Grande LA, Thompson EC, Au MA, et al. Problem Drug-related Behavior and  
16  
17 30 Discontinuation of Opioids Following the Introduction of an Opioid Management  
18  
19 31 Program. *Journal of the American Board of Family Medicine: JABFM* 2016;29:718-26.  
20  
21  
22 32 11. Canadian Institute for Health Information. Prescribed Drug Spending in Canada, 2016: A  
23  
24 33 Focus on Public Drug Programs. Canadian Institute for Health Information; 2016.  
25  
26 34 12. Florence CS, Zhou C, Fau - Luo F, Luo F, Xu L, et al. The Economic Burden of  
27  
28 35 Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013.  
29  
30 36 *Medical Care* 2016;54:901-6.  
31  
32  
33 37 13. National Collaborating Centre for Mental Health. Drug Misuse: Psychosocial  
34  
35 38 interventions National Clinical Practice Guideline Number 51. National Institute for  
36  
37 39 Health and Clinical Excellence (London). 2008.  
38  
39  
40 40 14. Dennis BB, Naji L, Bawor M, et al. The effectiveness of opioid substitution treatments  
41  
42 41 for patients with opioid dependence: a systematic review and multiple treatment  
43  
44 42 comparison protocol. *Systematic Reviews* 2014;3:105.  
45  
46  
47 43 15. Dennis B. Chronic Pain: A Red Herring or Risk Factor in the Management of Patients  
48  
49 44 Receiving Opioid Substitution Therapy. *McMaster University* 2015. Accessed on  
50  
51 45 04/Jan/2018. Available from: <http://hdl.handle.net/11375/18058>.  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 46 16. Dugosh K, Abraham A, Seymour B, et al. A Systematic Review on the Use of  
4  
5 47 Psychosocial Interventions in Conjunction With Medications for the Treatment of Opioid  
6  
7 48 Addiction. *Journal of Addiction Medicine* 2016;10:93-103.
- 8  
9  
10 49 17. Smedslund G, Berg RC, Hammerstrøm KT, et al. Motivational interviewing for  
11  
12 50 substance abuse. *The Cochrane Database of Systematic Reviews* 2011:CD008063.
- 13  
14 51 18. Livingston JD, Adams E, Jordan M, et al. Primary Care Physicians' Views about  
15  
16 52 Prescribing Methadone to Treat Opioid Use Disorder. *Substance Use & Misuse* 2017:1-  
17  
18 53 10.
- 19  
20  
21 54 19. Catala-Lopez F, Tobias A, Cameron C, et al. Network meta-analysis for comparing  
22  
23 55 treatment effects of multiple interventions: an introduction. *Rheumatology International*  
24  
25 56 2014;34:1489-96.
- 26  
27  
28 57 20. Caldwell D, Ades A, Higgins J. Simultaneous comparison of multiple treatments:  
29  
30 58 combining direct and indirect evidence. *BMJ* 2005;331:897-900.
- 31  
32  
33 59 21. Salanti G. Indirect and mixed-treatment comparison, network, or multiple treatments  
34  
35 60 meta-analysis: many names, many benefits, many concerns for the next generation  
36  
37 61 evidence synthesis tool. *Research Synthesis Methods* 2012;3.
- 38  
39  
40 62 22. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review  
41  
42 63 and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015;4:1.
- 43  
44 64 23. Sampson M, McGowan J, Cogo E, et al. An evidence-based practice guideline for the  
45  
46 65 peer review of electronic search strategies. *Journal of Clinical Epidemiology*  
47  
48 66 2009;62:944-52.
- 49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 67 24. Hser Y-I, Li J, Jiang H, et al. Effects of a randomized contingency management  
4  
5 68 intervention on opiate abstinence and retention in methadone maintenance treatment in  
6  
7 69 China. *Addiction (Abingdon, England)* 2011;106:1801-9.  
8  
9  
10 70 25. Maas J, Barton G, Maskrey V, et al. Economic evaluation: a comparison of methadone  
11  
12 71 versus buprenorphine for opiate substitution treatment. *Drug and Alcohol Dependence*  
13  
14 72 2013;133:494-501.  
15  
16  
17 73 26. Chopra MP, Landes RD, Gatchalian KM, et al. Buprenorphine medication versus  
18  
19 74 voucher contingencies in promoting abstinence from opioids and cocaine. *Experimental*  
20  
21 75 *and Clinical Psychopharmacology* 2009;17:226-36.  
22  
23  
24 76 27. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews  
25  
26 77 and meta-analyses: the PRISMA statement. *PLoS Medicine* 2008;6.  
27  
28  
29 78 28. Hutton B, Salanti G, Caldwell D, et al. The PRISMA Extension Statement for Reporting  
30  
31 79 of Systematic Reviews Incorporating Network Meta-Analyses of Healthcare  
32  
33 80 Interventions: Checklist and Explanations. *Annals of Internal Medicine* 2015;162:777-84.  
34  
35  
36 81 29. Higgins J, Altman D, Gotzsche P, et al. The Cochrane Collaboration's tool for assessing  
37  
38 82 risk of bias in randomised trials. *BMJ* 2011;343.  
39  
40 83 30. Dias S, Sutton A, Welton N, et al. NICE DSU Technical Support Document 3:  
41  
42 84 Heterogeneity: subgroups, meta-regression, bias and bias-adjustment. 2012. Accessed on  
43  
44 85 02/Feb/2018. Available from:  
45  
46 86 <http://www.nicedsu.org.uk/TSD3%20Heterogeneity.final%20report.08.05.12.pdf>.  
47  
48  
49 87 31. Dias S, Welton N, Sutton A, et al. NICE DSU Technical Support Document 2: A  
50  
51 88 Generalised Linear Modelling Framework for Pairwise and Network Meta-Analysis of  
52  
53 89 Randomised Controlled Trials. <http://www.nicedsu.org.uk> 2011.

- 1  
2  
3 90 32. Health Canada. Canadian Alcohol and Drug Use Monitoring Survey: Summary of  
4  
5 91 Results for 2012. 2015. Accessed on 03/March/2018. Available from  
6  
7 92 [https://www.canada.ca/en/health-canada/services/health-concerns/drug-prevention-](https://www.canada.ca/en/health-canada/services/health-concerns/drug-prevention-treatment/drug-alcohol-use-statistics/canadian-alcohol-drug-use-monitoring-survey-summary-results-2012.html)  
8  
9 93 [treatment/drug-alcohol-use-statistics/canadian-alcohol-drug-use-monitoring-survey-](https://www.canada.ca/en/health-canada/services/health-concerns/drug-prevention-treatment/drug-alcohol-use-statistics/canadian-alcohol-drug-use-monitoring-survey-summary-results-2012.html)  
10  
11 94 [summary-results-2012.html](https://www.canada.ca/en/health-canada/services/health-concerns/drug-prevention-treatment/drug-alcohol-use-statistics/canadian-alcohol-drug-use-monitoring-survey-summary-results-2012.html).  
12  
13  
14 95 33. Hemsing N, Greaves L, Poole N, et al. Misuse of Prescription Opioid Medication among  
15  
16 96 Women: A Scoping Review. *Pain Res Manag* 2016;2016:1-8.  
17  
18 97 34. American Society of Addiction Medicine. Advancing Access to Addiction Medicine:  
19  
20 98 Implications for Opioid Addiction Treatment. American Society of Addiction Medicine  
21  
22 99 2013. Accessed on 02/Feb/2018. Available from: [https://www.asam.org/docs/default-](https://www.asam.org/docs/default-source/advocacy/aaam_implications-for-opioid-addiction-treatment_final)  
23  
24 100 [source/advocacy/aaam\\_implications-for-opioid-addiction-treatment\\_final](https://www.asam.org/docs/default-source/advocacy/aaam_implications-for-opioid-addiction-treatment_final).  
25  
26  
27 101 35. Ministry of Health Long Term Care. Methadone Treatment and Services Advisory  
28  
29 102 Committee: Final Report. 2016. Accessed on 02/Feb/2018. Available from:  
30  
31 103 [http://health.gov.on.ca/en/public/programs/drugs/ons/docs/methadone\\_advisory\\_committ](http://health.gov.on.ca/en/public/programs/drugs/ons/docs/methadone_advisory_committee_report.pdf)  
32  
33 104 [ee\\_report.pdf](http://health.gov.on.ca/en/public/programs/drugs/ons/docs/methadone_advisory_committee_report.pdf)  
34  
35  
36 105 36. Centre for Addiction and Mental Health. Prescription Opioid Policy Framework. 2016.  
37  
38 106 Accessed on 07/Feb/2018. Available from:  
39  
40 107 [https://www.camh.ca/en/hospital/about\\_camh/influencing\\_public\\_policy/Documents/CA](https://www.camh.ca/en/hospital/about_camh/influencing_public_policy/Documents/CA)  
41  
42 108 [MHopiodpolicyframework.pdf](https://www.camh.ca/en/hospital/about_camh/influencing_public_policy/Documents/CA)  
43  
44  
45 109 37. Dennis BB, Roshanov PS, Naji L, et al. Opioid substitution and antagonist therapy trials  
46  
47 110 exclude the common addiction patient: a systematic review and analysis of eligibility  
48  
49 111 criteria. *Trials* 2015;16:475.  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



- 1  
2  
3 112 38. Veilleux JC, Colvin PJ, Anderson J, et al. A review of opioid dependence treatment:  
4  
5 113 pharmacological and psychosocial interventions to treat opioid addiction. *Clinical*  
6  
7 114 *Psychology Review* 2010;30:155-66.
- 8  
9  
10 115 39. Saedy M, Kooshki S, Jamali Firouzabadi M, et al. Effectiveness of Acceptance-  
11  
12 116 Commitment Therapy on Anxiety and Depression among Patients on Methadone  
13  
14 117 Treatment: A Pilot Study. *Iranian Journal of Psychiatry and Behavioral Sciences*  
15  
16 118 2015;9:e222.
- 17  
18  
19 119 40. Moore BA, Fiellin DA, Cutter CJ, et al. Cognitive Behavioral Therapy Improves  
20  
21 120 Treatment Outcomes for Prescription Opioid Users in Primary Care Buprenorphine  
22  
23 121 Treatment. *Journal of Substance Abuse Treatment* 2016;71:54-7.
- 24  
25  
26 122 41. Amato L, Minozzi S, Davoli M, et al. Psychosocial combined with agonist maintenance  
27  
28 123 treatments versus agonist maintenance treatments alone for treatment of opioid  
29  
30 124 dependence. *The Cochrane Database of Systematic Reviews* 2011:CD004147.
- 31  
32  
33 125 42. Linehan MM, Dimeff LA, Reynolds SK, et al. Dialectical behavior therapy versus  
34  
35 126 comprehensive validation therapy plus 12-step for the treatment of opioid dependent  
36  
37 127 women meeting criteria for borderline personality disorder. *Drug and Alcohol*  
38  
39 128 *Dependence* 2002;67:13-26.
- 40  
41  
42 129 43. Nyamathi A, Shoptaw S, Cohen A, et al. Effect of motivational interviewing on reduction  
43  
44 130 of alcohol use. *Drug and Alcohol Dependence* 2010;107:23-30.
- 45  
46  
47 131 44. Messer SB, Gurman AS. *Essential Psychotherapies: Theory and Practice*. Guilford Press,  
48  
49 132 New York 2011.
- 50  
51 133 45. Imani S, Atef Vahid MK, Gharraee B, et al. Comparing Mindfulness-Based Group  
52  
53 134 Therapy With Treatment as Usual for Opioid Dependents: A Pilot Randomized Clinical

1  
2  
3 135 Trial Study Protocol. *Iranian Journal of Psychiatry and Behavioral Sciences*

4  
5 136 2015;9:e216.

6  
7  
8 137  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

1  
2  
3  
4 138 **ACKNOWLEDGEMENTS**

5  
6 139 We would like to thank Raymond Daniel (Assistant Information Specialist) for his role in  
7  
8 140 providing support in database management and document procurement.  
9

10  
11 141 **FUNDING**

12  
13 142 Funding for this work is being provided by the Canadian Institutes of Health Research (CIHR)  
14  
15 143 grant number 397976. Ms. Rice is supported by a Vanier Canada Graduate CIHR Scholarship.  
16  
17 144 The funders had no role in the design of the planned study or preparation of this protocol.  
18

19  
20 145 **AVAILABILITY OF DATA AND MATERIAL**

21  
22 146 Datasets have not been generated as part of this protocol. The datasets generated and/or analysed  
23  
24 147 during the current study are available from the corresponding author on reasonable request.  
25

26  
27 148 **AUTHORS' CONTRIBUTIONS**

28  
29 149 DBR, BH, and KC drafted the protocol. B Skidmore created and tested the search strategies to be  
30  
31 150 used in the bibliographic databases. DBR, KC, PP, and BAS provided clinical expertise during  
32  
33 151 the protocol development stage, and will also provide such expertise throughout the duration of  
34  
35 152 the review and during drafting of the final manuscript. DBR, KT, and DW will be involved in  
36  
37 153 screening, data extraction, and quality assessment. DBR, KC, and BH will be involved in all data  
38  
39 154 analyses. DBR, KC, and BH will coordinate all aspects of the review. BH conceived of and is the  
40  
41 155 guarantor of the review. All authors reviewed and approved the protocol.  
42  
43  
44

45 156 **AUTHORS' INFORMATION**

46  
47 157 Not applicable (optional, not included).  
48

49  
50 158 **ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

51  
52 159 Not applicable  
53

54 160 **CONSENT FOR PUBLICATION**  
55  
56  
57  
58  
59  
60

1  
2  
3 161 Not applicable (no individual person's data are included in this manuscript).  
4

5 162 **COMPETING INTERESTS**  
6

7 163 BH has previously received honoraria from Cornerstone Research Group for the provision of  
8  
9 methodologic advice related to systematic reviews and meta-analysis. The remaining authors  
10 164  
11  
12 165 declare that they have no competing interests.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

## SUPPLEMENTARY FILES

### APPENDICES

To provide additional information regarding: *Evaluating Comparative Effectiveness of Psychosocial Interventions for Persons Receiving Opioid Agonist Therapy for Opioid Use Disorder: Protocol for a Systematic Review*. Rice DB, Hutton B, Poulin P, Sproule BA, Wolfe D, Moher D, Thavorn K, Garber G, Taha S, Porath A, Willows A, Esmaeilisaraji L, Yazadi F, Skidmore B, Corace K.

- Appendix 1: Literature Search Strategy
- Appendix 2: PRISMA-P Checklist
- Appendix 3: Definitions of Interventions and Comparators

## Appendix 1: PRISMA-P Checklist

Section/topic	#	Checklist item	Information reported		Line #
			Yes	No	
<b>ADMINISTRATIVE INFORMATION</b>					
<b>Title</b>					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1-3
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
<b>Registration</b>	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	67
<b>Authors</b>					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	31-38
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	366-373
<b>Amendments</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
<b>Support</b>					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	359-362
Sponsor	5b	Provide name for the review funder and/or sponsor	<input checked="" type="checkbox"/>	<input type="checkbox"/>	359-362
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input checked="" type="checkbox"/>	<input type="checkbox"/>	361-362
<b>INTRODUCTION</b>					
<b>Rationale</b>	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	115-125
<b>Objectives</b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	129-131
<b>METHODS</b>					
<b>Eligibility criteria</b>	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as	<input checked="" type="checkbox"/>	<input type="checkbox"/>	160-199

Section/topic	#	Checklist item	Information reported		Line #
			Yes	No	
		criteria for eligibility for the review			
<b>Information sources</b>	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	140-156
<b>Search strategy</b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Additional file 1.2
<b>STUDY RECORDS</b>					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	202-203
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	201-217
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	220-221
<b>Data items</b>	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	221-233
<b>Outcomes and prioritization</b>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	180-193, 221-229
<b>Risk of bias in individual studies</b>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	235-243
<b>DATA</b>					
<b>Synthesis</b>	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	246-250
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$ , Kendall's tau)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	261-265
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	294-306

Section/topic	#	Checklist item	Information reported		Line #
			Yes	No	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	314-315
<b>Meta-bias(es)</b>	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	265-266
<b>Confidence in cumulative evidence</b>	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A



## Appendix 2: Literature Search Strategy

### Reviews

2018 Feb 28

Database: Embase Classic+Embase <1947 to 2018 February 27>, Ovid MEDLINE(R) ALL <1946 to February 27, 2018>, PsycINFO <1806 to February Week 3 2018>

Search Strategy:

- 
- 1 Opiate Substitution Treatment/ (3597)
  - 2 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*).tw,kf. (6670)
  - 3 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*).tw,kf. (22039)
  - 4 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (2045)
  - 5 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*).tw,kf. (2050)
  - 6 or/1-5 [OPIATE SUBSTITUTION TREATMENT] (31773)
  - 7 Substance-Related Disorders/ (113262)
  - 8 Substance Abuse, Intravenous/ (63332)
  - 9 Substance Abuse, Oral/ [NEW MESH 2018] (0)
  - 10 exp Opioid-Related Disorders/ (36965)
  - 11 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (45619)
  - 12 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or "non-prescription use?" or "nonprescription use?" or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (310916)
  - 13 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (16203)
  - 14 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (141)
  - 15 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanyl\$2 or beta hydroxymefentanyl or brifentanil\$2 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (659)
  - 16 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or

SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (12011)

17 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or roxycodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodal\$2 or tekodin\$2 or thecodin\$2 or thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (557)

18 or/7-17 [OPIOID USE DISORDERS] (459104)

19 Substance-Related Disorders/dt [drug therapy] (3838)

20 Substance-Related Disorders/rh [rehabilitation] (10041)

21 Substance Abuse, Intravenous/dt [drug therapy] (326)

22 Substance Abuse, Intravenous/rh [rehabilitation] (1403)

23 Substance Abuse, Oral/dt [drug therapy] (0)

24 Substance Abuse, Oral/rh [rehabilitation] (0)

25 exp Opioid-Related Disorders/dt [drug therapy] (8615)

26 exp Opioid-Related Disorders/rh [rehabilitation] (6399)

27 Analgesics, Opioid/tu [therapeutic use] (13587)

28 (OAT or OATs).tw,kf. (19631)

29 exp Buprenorphine/tu [therapeutic use] (2072)

30 Heroin/tu [therapeutic use] (388)

31 Hydromorphone/tu [therapeutic use] (283)

32 exp Methadone/tu [therapeutic use] (6498)

33 Morphine/tu [therapeutic use] (5142)

34 exp Naloxone/tu [therapeutic use] (4398)

35 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kf. (4468)

36 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kf. (719)

37 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kf. (5354)

38 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphinon\* or dihydromorphon\* or diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jurnista\$2 or laudaconum\$2 or novolaudon\$2

1  
2  
3 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
4 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
5 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (864)  
6 39 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
7 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
8 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamidon\$2 or dianone\$2  
9 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
10 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
11 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
12 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
13 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
14 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
15 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
16 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (18855)  
17 40 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
18 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
19 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
20 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
21 treatment\* or abuse-deterren\*).tw,kf. (9244)  
22 41 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
23 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
24 or naloxon-ratiopharm\$2 or naloxona\$2 or narcan\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
25 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
26 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (3241)  
27 42 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
28 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
29 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
30 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
31 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (3497)  
32 43 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
33 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
34 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
35 pharmacotherap\* or pharmaco-therap\*).tw,kf. (14488)  
36 44 (maintenance\* adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kf.  
37 (63115)  
38 45 detoxif\*.tw,kf. (81859)  
39 46 or/19-45 [OAT] (237559)  
40 47 18 and 46 (60367)  
41 48 6 or 47 (81175)  
42 49 exp Child/ not (Adolescent/ or exp Adult/) (2424568)  
43 50 exp Infant/ not (Adolescent/ or exp Adult/) (1422345)  
44 51 48 not (49 or 50) [CHILD-/INFANT-ONLY REMOVED] (79535)  
45 52 exp Animals/ not (exp Animals/ and Humans/) (15327571)  
46 53 51 not 52 [ANIMAL-ONLY REMOVED] (61669)  
47 54 (editorial or news or newspaper article).pt. (1210715)  
48 55 53 not 54 [OPINION PIECES REMOVED] (60534)  
49 56 limit 55 to systematic reviews [Limit not valid in Embase; records were retained] (19270)  
50 57 meta analysis.pt. (85285)  
51 58 exp meta-analysis as topic/ (52797)  
52  
53  
54  
55  
56  
57  
58  
59  
60

59 (meta-analy\* or metanaly\* or metaanaly\* or met analy\* or integrative research or integrative  
 review\* or integrative overview\* or research integration or research overview\* or collaborative  
 review\*).tw,kf. (323991)  
 60 (systematic review\* or systematic overview\* or evidence-based review\* or evidence-based  
 overview\* or (evidence adj3 (review\* or overview\*)) or meta-review\* or meta-overview\* or meta-  
 synthes\* or "review of reviews" or technology assessment\* or HTA or HTAs).tw,kf. (383178)  
 61 exp Technology assessment, biomedical/ (22830)  
 62 (cochrane or health technology assessment or evidence report).jw. (38516)  
 63 (network adj (MA or MAs)).tw,kf. (16)  
 64 (NMA or NMAs).tw,kf. (3965)  
 65 indirect\* compar\*.tw,kf. (4355)  
 66 (indirect treatment\* adj1 compar\*).tw,kf. (556)  
 67 (mixed treatment\* adj1 compar\*).tw,kf. (1223)  
 68 (multiple treatment\* adj1 compar\*).tw,kf. (310)  
 69 (multi-treatment\* adj1 compar\*).tw,kf. (4)  
 70 simultaneous\* compar\*.tw,kf. (2286)  
 71 mixed comparison?.tw,kf. (50)  
 72 or/57-71 (681908)  
 73 55 and 72 (1668)  
 74 56 or 73 [REVIEWS] (19584)  
 75 74 use medall [MEDLINE RECORDS] (1423)  
 76 drug dependence treatment/ (7884)  
 77 opiate substitution treatment/ (3597)  
 78 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*)).tw,kw. (6748)  
 79 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or  
 wean\* or withdraw\*)).tw,kw. (22166)  
 80 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3  
 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 pharmaco-therap\* or treatment\* or abuse-deterren\*)).tw,kw. (2071)  
 81 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or  
 detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)).tw,kw. (2056)  
 82 methadone treatment/ (4159)  
 83 or/76-82 [OPIATE SUBSTITUTION TREATMENT] (42492)  
 84 drug dependence/ (137162)  
 85 substance abuse/ (181603)  
 86 exp narcotic dependence/ (137914)  
 87 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
 prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or  
 illegal\*))).tw,kw. (46245)  
 88 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or  
 mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or  
 "non-prescription use?" or "nonprescription use?" or (("use" or used or uses or using) adj2 (illicit\* or  
 illegal\*))).tw,kw. (314212)  
 89 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-  
 medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or  
 withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (16386)  
 90 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or  
 hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or  
 hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\*  
 or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or

nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (151)

91 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (668)

92 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (12020)

93 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or roxicodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodal\$2 or tekodin\$2 or thecodin\$2 or thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (580)

94 or/84-93 [OPIOID USE DISORDERS] (557651)

95 drug dependence/dt [Drug Therapy] (6231)

96 drug dependence/rh [Rehabilitation] (10049)

97 substance abuse/dt [Drug Therapy] (2590)

98 substance abuse/rh [Rehabilitation] (9793)

99 exp narcotic dependence/dt (7343)

100 exp narcotic dependence/rh (1424)

101 (OAT or OATs).tw,kw. (19775)

102 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)).tw,kw. (4514)

103 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)).tw,kw. (724)

104 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphon\* or dihydromorphon\* or diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydald\$2 or hydromorph contin\$2 or hydromorphonone\$2 or hydrostat\$2 or hymorphan\$2 or jurnista\$2 or laudaconum\$2 or novolaudon\$2 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3

(maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (862)

105 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (5404)

106 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamimon\$2 or dianone\$2 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (18983)

107 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (9235)

108 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2 or naloxon-ratiopharm\$2 or naloxona\$2 or narcan\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (3250)

109 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (3523)

110 maintenance therapy/ (33721)

111 (maintenance\* adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kw. (63435)

112 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\* adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kw. (14490)

113 detoxif\*.tw,kw. (82730)

114 or/95-113 [OAT] (234039)

115 94 and 114 (61375)

116 83 or 115 [OPIATE SUBSTITUTION TREATMENT/OAT] (89378)

117 exp child/ not (exp adult/ or adolescent/) (2424568)

118 exp infant/ not (exp adult/ or adolescent/) (1422345)

119 fetus/ not (exp adult/ or adolescent/) (233852)

120 or/117-119 (3035843)

121 116 not 120 [CHILD-/INFANT-/FETUS-ONLY REMOVED] (87563)

122 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp vertebrate/ (46621835)

123 exp human/ or exp human experimentation/ or exp human experiment/ (36368434)

124 122 not 123 (10255103)

1  
2  
3 125 121 not 124 [ANIMAL-ONLY REMOVED] (76107)  
4 126 editorial.pt. (1008146)  
5 127 125 not 126 [OPINION PIECES REMOVED] (75078)  
6 128 meta-analysis/ (228832)  
7 129 "systematic review"/ (159939)  
8 130 "meta analysis (topic)"/ (36507)  
9 131 (meta-analy\* or metanaly\* or metaanaly\* or met analy\* or integrative research or integrative  
10 review\* or integrative overview\* or research integration or research overview\* or collaborative  
11 review\*).tw,kw. (326601)  
12 132 (systematic review\* or systematic overview\* or evidence-based review\* or evidence-based  
13 overview\* or (evidence adj3 (review\* or overview\*)) or meta-review\* or meta-overview\* or meta-  
14 synthes\* or "review of reviews" or technology assessment\* or HTA or HTAs).tw,kw. (386028)  
15 133 biomedical technology assessment/ (21723)  
16 134 (cochrane or health technology assessment or evidence report).jw. (38516)  
17 135 (network adj (MA or MAs)).tw,kw. (16)  
18 136 (NMA or NMAs).tw,kw. (3984)  
19 137 indirect\* compar\*.tw,kw. (4407)  
20 138 (indirect treatment\* adj1 compar\*).tw,kw. (560)  
21 139 (mixed treatment\* adj1 compar\*).tw,kw. (1244)  
22 140 (multiple treatment\* adj1 compar\*).tw,kw. (313)  
23 141 (multi-treatment\* adj1 compar\*).tw,kw. (4)  
24 142 simultaneous\* compar\*.tw,kw. (2286)  
25 143 mixed comparison?.tw,kw. (51)  
26 144 or/128-143 (734926)  
27 145 127 and 144 (2446)  
28 146 127 and 144 [REVIEWS] (2446)  
29 147 conference abstract.pt. (2898647)  
30 148 limit 147 to yr="2016-current" (643364)  
31 149 146 and 148 (54)  
32 150 146 not 147 [ALL CONFERENCE ABSTRACTS REMOVED] (2298)  
33 151 149 or 150 [CONFERENCE ABSTRACTS PRIOR TO 2016 REMOVED] (2352)  
34 152 151 use emczd [EMBASE RECORDS] (1278)  
35 153 Drug Rehabilitation/ (19847)  
36 154 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*).tw. (6588)  
37 155 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or  
38 wean\* or withdraw\*).tw. (22016)  
39 156 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3  
40 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
41 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (2032)  
42 157 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or  
43 detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*).tw. (2050)  
44 158 methadone maintenance/ (7582)  
45 159 or/153-158 [OPIATE SUBSTITUTION TREATMENT] (54279)  
46 160 exp drug dependency/ (246294)  
47 161 drug abuse/ (182188)  
48 162 "substance use disorder"/ (129585)  
49 163 Intravenous Drug Usage/ (3662)  
50 164 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
51 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
52 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
53 illegal\*))).tw. (45414)  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 165 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or  
4 mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or  
5 "non-prescription use?" or "nonprescription use?" or (("use" or used or uses or using) adj2 (illicit\* or  
6 illegal\*))).tw. (308416)

7 166 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or  
8 non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\*  
9 or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (16177)

10 167 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or  
11 hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or  
12 hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\*  
13 or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or  
14 nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (141)

15 168 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2  
16 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or  
17 lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or  
18 rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2)  
19 adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or  
20 nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\*  
21 or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (658)

22 169 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
23 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
24 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or  
25 addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or  
26 non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used  
27 or uses or using) adj2 (illicit\* or illegal\*))).tw. (11916)

28 170 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or  
29 cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or  
30 dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or  
31 eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or  
32 eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-  
33 oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc  
34 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or  
35 oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or  
36 oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or  
37 oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or  
38 oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or  
39 roxycodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodal\$2 or tekodin\$2 or thecodin\$2 or  
40 thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
41 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
42 prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or  
43 illegal\*))).tw. (556)

44 171 or/160-170 [OPIOID USE DISORDERS] (609718)

45 172 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2  
46 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or  
47 probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952  
48 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
49 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)).tw. (4467)

50 173 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3  
51 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
52 pharmaco-therap\* or treatment\* or abuse-deterren\*)).tw. (719)



1  
2  
3 174 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphinon\* or dihydromorphon\* or  
4 diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2  
5 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jornista\$2 or laudaconum\$2 or novolaudon\$2  
6 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
7 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
8 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (857)

9 175 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or heroine\$2 or  
10 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
11 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (5347)

12 176 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
13 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
14 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamidon\$2 or dianone\$2  
15 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
16 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
17 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
18 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
19 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
20 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
21 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
22 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (18825)

23 177 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
24 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
25 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
26 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
27 treatment\* or abuse-deterren\*).tw. (9201)

28 178 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
29 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
30 or naloxon-ratiopharm\$2 or naloxona\$2 or narkan\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
31 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
32 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (3241)

33 179 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
34 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
35 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
36 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
37 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (3497)

38 180 maintenance therapy/ (33721)

39 181 (maintenance adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw. (62997)

40 182 (OAT or OATs).tw. (19570)

41 183 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
42 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
43 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
44 pharmacotherap\* or pharmaco-therap\*).tw. (14426)

45 184 Detoxification/ (24878)

46 185 detoxif\*.tw. (81609)

47 186 or/180-185 [OAT] (196651)

48 187 171 and 186 (32100)

49 188 159 or 187 (75453)

50 189 exp Animals/ not (exp Animals/ and Humans/) (15327571)

51 190 188 not 189 [ANIMAL-ONLY REMOVED] (59727)

52 191 limit 190 to dissertation [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily  
53 Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] (34146)

1  
2  
3 192 190 not 191 [DISSERTATIONS REMOVED] (25581)  
4 193 limit 192 to "0830 systematic review" [Limit not valid in Embase,Ovid MEDLINE(R),Ovid  
5 MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were  
6 retained] (145)  
7 194 limit 192 to 1200 meta analysis [Limit not valid in Embase,Ovid MEDLINE(R),Ovid  
8 MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were  
9 retained] (103)  
10 195 limit 192 to 1300 metasynthesis [Limit not valid in Embase,Ovid MEDLINE(R),Ovid  
11 MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were  
12 retained] (0)  
13 196 meta analysis/ (228832)  
14 197 (meta-analy\* or metanaly\* or metaanaly\* or met analy\* or integrative research or integrative  
15 review\* or integrative overview\* or research integration or research overview\* or collaborative  
16 review\*).tw. (323004)  
17 198 (systematic review\* or systematic overview\* or evidence-based review\* or evidence-based  
18 overview\* or (evidence adj3 (review\* or overview\*)) or meta-review\* or meta-overview\* or meta-  
19 synthes\* or "review of reviews" or technology assessment\* or HTA or HTAs).tw. (381844)  
20 199 (network adj (MA or MAs)).tw. (16)  
21 200 (NMA or NMAs).tw. (3955)  
22 201 indirect\* compar\*.tw. (4337)  
23 202 (indirect treatment\* adj1 compar\*).tw. (544)  
24 203 (mixed treatment\* adj1 compar\*).tw. (1172)  
25 204 (multiple treatment\* adj1 compar\*).tw. (301)  
26 205 (multi-treatment\* adj1 compar\*).tw. (4)  
27 206 simultaneous\* compar\*.tw. (2286)  
28 207 mixed comparison?.tw. (50)  
29 208 or/196-207 (647033)  
30 209 192 and 208 (439)  
31 210 193 or 194 or 195 or 209 [REVIEWS] (465)  
32 211 210 use medall,emczd (0)  
33 212 210 not 211 [PSYCINFO RECORDS] (465)  
34 213 75 or 152 or 212 [ALL DATABASES] (3166)  
35 214 remove duplicates from 213 (2195) [TOTAL UNIQUE RECORDS]  
36 215 214 use medall (1367) [MEDLINE UNIQUE RECORDS]  
37 216 from 215 keep 1-1000 (1000)  
38 217 from 215 keep 1001-1367 (367)  
39 218 214 use emczd (574) [EMBASE UNIQUE RECORDS]  
40 219 214 not (215 or 218) (254) [PSYCINFO UNIQUE RECORDS]  
41  
42  
43

44 \*\*\*\*\*

45 Cochrane Library

46  
47 Search Name: Opioid Disorders - OAT - Reviews

48 Date Run: 28/02/18 15:58:45.981

49 Description: OHRI - Final - 2018 Feb 28  
50

51 ID Search Hits

52 #1 [mh "Opiate Substitution Treatment"] 274

53 #2 ((narcotic\* or opioid\* or opiate\*) near/3 (maintenance\* or substitut\* or replac\*)):ti,ab,kw  
54 622  
55  
56  
57  
58  
59  
60

- 1  
2  
3 #3 ((narcotic\* or opioid\* or opiate\*) near/3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\*  
4 or wean\* or withdraw\*)):ti,ab,kw 2167  
5 #4 (((opiate\* or opioid\*) next (agonist\* or receptor\*)) near/3 (maintenance\* or substitut\* or replac\*  
6 or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-  
7 deterren\*)):ti,ab,kw 186  
8 #5 (((opiate\* or opioid\*) next (agonist\* or receptor\*)) near/3 (maintenance\* or substitut\* or replac\*  
9 or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-  
10 deterren\*)):ti,ab,kw 186  
11 #6 {or #1-#5} 2769  
12 #7 [mh ^"Substance-Related Disorders"] 3012  
13 #8 [mh "Substance Abuse, Intravenous"] 439  
14 #9 [mh "Substance Abuse, Oral"] 0  
15 #10 [mh "Opioid-Related Disorders"] 1546  
16 #11 ((narcotic\* or opioid\* or opiate\*) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\*  
17 or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-  
18 prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or  
19 illegal\*)):ti,ab,kw 3215  
20 #12 ((drug or drugs or substance\*) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or  
21 misus\* or mis-us\* or "non-medical use" or "non-medical uses" or "nonmedical use" or "nonmedical uses"  
22 or "non-prescribed use" or "non-prescribed uses" or "nonprescribed use" or "nonprescribed uses" or "non-  
23 prescription use" or "non-prescription uses" or "nonprescription use" or "nonprescription uses") or (("use"  
24 or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw 14561  
25 #13 (heroin\* near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or  
26 "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or  
27 nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw  
28 1502  
29 #14 ((hydrocodone or bekadid or codinovo or dico or dicodid or dihydrocodeinone or hycodan or  
30 hycon or hydrocodeinonebitartrate or hydrocodon or hydrocon or hydrocodonum or robidone) near/3  
31 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or  
32 nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or nonprescription or  
33 withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw 606  
34 #15 ((fentanyl or alfentanil or alfenta or alfentanyl or beta hydroxymefentanyl or brifentanil or  
35 carfentanil or duragesic or fanaxal or fentanest or fentora or hypnorm or limifen or lofentanil or  
36 mefentanyl or mirfentanil or ofcentanil or phentanyl or "R-39209" or "R-4263" or rapifen or remifentanil  
37 or sublimaze or sufenta or sufentanil or sulfentanyl or trefentanil) near/3 (abus\* or addict\* or dependen\*  
38 or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or  
39 nonprescribed or "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or  
40 using) near/2 (illicit\* or illegal\*)):ti,ab,kw 670  
41 #16 ((morphine or anpec or duramorph or epimorph or miro or morfín or morfíne or morphin or  
42 morphinium or morphium or MS contin or morphia or opso or oramorph or SDZ 202-250 or SDZ202-250  
43 or skenan or transmorphine or trans-morphine) near/3 (abus\* or addict\* or dependen\* or disorder\* or  
44 habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or  
45 "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\*  
46 or illegal\*)):ti,ab,kw 898  
47 #17 ((oxycodone or bionine or bionone or bolodorm or broncodal or bucodal or cafacodal or cardanon  
48 or codenon or codix 5 or "col 003" or col003 or dihydrohydroxycodone or dihydrohydroxydodeinone  
49 or dihydronone or dinarkon or endone or eubine or eucodal or eucodale or eucodalum or eudin or eukdin or  
50 eukodal or eumorphal or eurodamine or eutagen or hydrocodal or hydroxycodone or ludonal or m-oxy  
51 or medicodal or narcobasina or narcobasine or narcosin or nargenol or narodal or nsc 19043 or nucodan  
52 or opton or ossicodone or oxanest or oxaydo or oxecta or oxicone or oxicontin or oxiconum or oxikon or  
53 oxy ir or oxycod or oxycodone or oxycodonehydrochloride or oxycodone hydrochloride or  
54  
55  
56  
57  
58  
59  
60

oxycodonehydrochlorid or oxycodone or oxycontin or oxydose or oxyfast or oxygesic or oxyir or oxykon or oxynorm or pancodine or pavinal or percolone or pronarcin or remoxy or roxicodone or roxicodone or sinthiodal or stupenal or supeudol or tebdal or tekodin or thecodin or thecodin or xtampa or xtampza) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw

669

- #18 {or #7-#17} 16618
- #19 [mh ^"Substance-Related Disorders"/DT] 191
- #20 [mh ^"Substance-Related Disorders"/RH] 673
- #21 [mh "Substance Abuse, Intravenous"/DT] 28
- #22 [mh "Substance Abuse, Intravenous"/RH] 113
- #23 [mh "Substance Abuse, Oral"/DT] 0
- #24 [mh "Substance Abuse, Oral"/RH] 0
- #25 [mh "Opioid-Related Disorders"/DT] 550
- #26 [mh "Opioid-Related Disorders"/RH] 742
- #27 [mh "Analgesics, Opioid"/TU] 2713
- #28 (OAT or OATs):ti,ab,kw 678
- #29 [mh Buprenorphine/TU] 443
- #30 [mh Heroin/TU] 75
- #31 [mh Hydromorphone/TU] 62
- #32 [mh Methadone/TU] 747
- #33 [mh Morphine/TU] 1528
- #34 [mh Naloxone/TU] 858
- #35 ((buprenorphine or anorfin or belbuca or buprenex or buprex or buprine or butrans or finibron or lepetan or "nih 8805" or nih8805 or norphin or pentorel or prefin or probuphine or "rx 6029 m" or "rx 6029m" or rx6029m or subutex or temgesic or transtec or "um 952" or um952) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 792
- #36 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone or zubsolv) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 106
- #37 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin or heroine or morphacetin) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 594
- #38 ((hydromorphon\* or biomorphyl\* or cofalaudid\* or dihydromorphinon\* or dihydromorphon\* or diladid\* or dilaudid\* or dimorphon\* or dolonovag\* or exalgo\* or hydal\* or hydromorph contin\* or hydromorphinone\* or hydrostat\* or hymorphan\* or jornista\* or laudaconum\* or novolaudon\* or opidol\* or paliadon retardkaps\* or palladon\* or rexaphon\* or semcox\* or sophidone\*) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 190
- #39 ((methadone or adanon or adanon hydrochloride or algidon or algolysin or algoxale or althose or althose hydrochloride or amidon or amidona or amidone or amidosan or an 148 or an148 or anadon or biodone or butalgin or deamin or depridol or diamion or dianone or dolafin or dolamid or dolesone or dolmed or dolophine or dolophine hydrochloride or dorex or dorexol or eptadone or fenadon or gobbidona or heptadon or heptanon or hoe 10820 or hoe10820 or ketalgin or l polamidon or mecodin or mepecton or mephenon or metadol or metadon or metasedin or methaddict or methadose or methaforte mix or miadone or moheptan or pallidone or phenadon or physepton or physeptone or polamidon or polamivet or polamivit or sinalgin or symoron or westadone) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 1367

#40 ((morphine or anpec or duramorph or epimorph or miro or morfin or morfine or morphin or morphinium or morphium or MS contin or morphia or opso or oramorph or SDZ 202-250 or SDZ202-250 or skenan or transmorphine or trans-morphine) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw  
2404

#41 ((naloxone or antioplaz or "en 1530" or "en 15304" or en1530 or en15304 or evzio or maloxone or mapin or "MRZ 2593-Br" or "MRZ-2593" or nalone or nalonee or nalone or naloxon curamed or naloxon-ratiopharm or naloxona or narcan or narcanti or narcon or narvcam or naxone or zynox) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 542

#42 ((naltrexone or antaxon or antaxone or celupan or "en 1639a" or en1639a or nalerona or nalorex or naltrel or naltrexone hydrochloride or nemexin or nodict or nutrexon or phaltrexia or "re-via" or regental or revez or revia or trexan or vivitrex or vivitrol) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 754

#43 (((drug\* near/2 dependen\*) or (drug\* near/2 addict\*) or (substance\* near/2 dependen\*) or (substance\* near/2 addict\*)) near/3 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*)):ti,ab,kw 1529

#44 (maintenance near/2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*)):ti,ab,kw  
7632

#45 detoxif\*:ti,ab,kw 1453

#46 {or #19-#45} 19190

#47 #18 and #46 4477

#48 #6 or #47 6184

#49 [mh Child] not ([mh Adolescent] or [mh Adult]) 134

#50 [mh Infant] not ([mh Adolescent] or [mh Adult]) 14132

#51 #48 not (#49 or #50) in Cochrane Reviews (Reviews and Protocols), Other Reviews and Technology Assessments

DSR - 124

DARE - 76

HTA - 16

### Primary Studies

2018 Mar 8

Database: Embase Classic+Embase <1947 to 2018 March 07>, Ovid MEDLINE(R) ALL <1946 to March 07, 2018>, PsycINFO <1806 to February Week 4 2018>

Search Strategy:

- 
- 1 Opiate Substitution Treatment/ (3624)
  - 2 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*)):tw,kf. (6674)
  - 3 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)):tw,kf. (22092)
  - 4 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):tw,kf. (2044)
  - 5 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)):tw,kf. (2055)
  - 6 or/1-5 [OPIATE SUBSTITUTION TREATMENT] (31849)

- 1  
2  
3 7 Substance-Related Disorders/ (113410)  
4 8 Substance Abuse, Intravenous/ (63391)  
5 9 Substance Abuse, Oral/ [NEW MESH 2018] (0)  
6 10 exp Opioid-Related Disorders/ (37049)  
7 11 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
8 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
9 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
10 illegal\*))))).tw,kf. (45711)  
11 12 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or  
12 mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or  
13 "non-prescription use?" or "nonprescription use?" or ("use" or used or uses or using) adj2 (illicit\* or  
14 illegal\*))))).tw,kf. (311185)  
15 13 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-  
16 medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or  
17 withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (16211)  
18 14 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or  
19 hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or  
20 hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\*  
21 or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or  
22 nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf.  
23 (141)  
24 15 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2 or  
25 carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or  
26 lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or  
27 rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2)  
28 adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or  
29 nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\*  
30 or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (661)  
31 16 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
32 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
33 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or  
34 addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or  
35 non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used  
36 or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (12012)  
37 17 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or cafacodal\$2  
38 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or  
39 dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or  
40 eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or  
41 eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-  
42 oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc  
43 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or  
44 oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or oxycodone\$2 or  
45 oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or  
46 oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or  
47 oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or  
48 roxicodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodol\$2 or tekodin\$2 or thecodin\$2 or  
49 thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
50 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
51 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
52 illegal\*))))).tw,kf. (558)  
53 18 or/7-17 [OPIOID USE DISORDERS] (459571)  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 19 Substance-Related Disorders/dt [drug therapy] (3843)  
4 20 Substance-Related Disorders/rh [rehabilitation] (10052)  
5 21 Substance Abuse, Intravenous/dt [drug therapy] (327)  
6 22 Substance Abuse, Intravenous/rh [rehabilitation] (1404)  
7 23 Substance Abuse, Oral/dt [drug therapy] (0)  
8 24 Substance Abuse, Oral/rh [rehabilitation] (0)  
9  
10 25 exp Opioid-Related Disorders/dt [drug therapy] (8635)  
11 26 exp Opioid-Related Disorders/rh [rehabilitation] (6407)  
12 27 Analgesics, Opioid/tu [therapeutic use] (13601)  
13 28 (OAT or OATs).tw,kf. (19652)  
14 29 exp Buprenorphine/tu [therapeutic use] (2073)  
15 30 Heroin/tu [therapeutic use] (388)  
16 31 Hydromorphone/tu [therapeutic use] (283)  
17 32 exp Methadone/tu [therapeutic use] (6503)  
18 33 Morphine/tu [therapeutic use] (5144)  
19 34 exp Naloxone/tu [therapeutic use] (4403)  
20 35 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2 or  
21 finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or probuphine\$2  
22 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952 or um952)  
23 adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
24 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (4476)  
25 36 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3  
26 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
27 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (720)  
28 37 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or  
29 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
30 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (5359)  
31 38 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphinon\* or dihydromorphon\* or  
32 diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2  
33 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jornista\$2 or laudaconum\$2 or novolaudon\$2  
34 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
35 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
36 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (866)  
37 39 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
38 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
39 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamimon\$2 or dianone\$2  
40 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
41 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
42 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
43 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
44 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
45 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
46 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
47 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (18862)  
48 40 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
49 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
50 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
51 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
52 treatment\* or abuse-deterren\*).tw,kf. (9245)  
53 41 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
54 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
55  
56  
57  
58  
59

1  
 2  
 3 or naloxon-ratiopharm\$2 or naloxona\$2 or narcan\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
 4 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
 5 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (3242)  
 6 42 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
 7 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
 8 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
 9 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 10 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (3500)  
 11 43 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
 12 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
 13 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
 14 pharmacotherap\* or pharmaco-therap\*).tw,kf. (14494)  
 15 44 (maintenance\* adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kf.  
 16 (63184)  
 17 45 detoxif\*.tw,kf. (81910)  
 18 46 or/19-45 [OAT] (237756)  
 19 47 18 and 46 (60420)  
 20 48 6 or 47 (81284)  
 21 49 exp Child/ not (Adolescent/ or exp Adult/) (2426358)  
 22 50 exp Infant/ not (Adolescent/ or exp Adult/) (1423228)  
 23 51 48 not (49 or 50) [CHILD-/INFANT-ONLY REMOVED] (79640)  
 24 52 exp Animals/ not (exp Animals/ and Humans/) (15333675)  
 25 53 51 not 52 [ANIMAL-ONLY REMOVED] (61771)  
 26 54 (editorial or news or newspaper article).pt. (1211821)  
 27 55 53 not 54 [OPINION PIECES REMOVED] (60635)  
 28 56 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (542931)  
 29 57 clinical trials as topic.sh. (182830)  
 30 58 exp Randomized Controlled Trials as Topic/ (256860)  
 31 59 (randomi#ed or randomly or RCT? or placebo\*).tw,kf. (2130342)  
 32 60 ((singl\* or doubl\* or trebl\* or tripl\*) adj (mask\* or blind\* or dumm\*).tw,kf. (393401)  
 33 61 trial.ti. (451602)  
 34 62 or/56-61 (2717718)  
 35 63 55 and 62 [RCTS] (9307)  
 36 64 controlled clinical trial.pt. (92216)  
 37 65 Controlled Clinical Trial/ or Controlled Clinical Trials as Topic/ (561253)  
 38 66 (control\* adj2 trial\*).tw,kf. (544746)  
 39 67 Non-Randomized Controlled Trials as Topic/ (9504)  
 40 68 (nonrandom\* or non-random\* or quasi-random\* or quasi-experiment\*).tw,kf. (119371)  
 41 69 (nRCT or nRCTs or non-RCT?).tw,kf. (1587)  
 42 70 Controlled Before-After Studies/ (209550)  
 43 71 (control\* adj3 ("before and after" or "before after")).tw,kf. (9308)  
 44 72 Interrupted Time Series Analysis/ (201499)  
 45 73 time series.tw,kf. (58363)  
 46 74 (pre- adj3 post-).tw,kf. (204737)  
 47 75 (pretest adj3 posttest).tw,kf. (16133)  
 48 76 Historically Controlled Study/ (219791)  
 49 77 (control\* adj2 stud\$3).tw,kf. (497097)  
 50 78 Control Groups/ (126334)  
 51 79 (control\* adj2 group\$1).tw,kf. (1122551)  
 52 80 trial.ti. (451602)  
 53 81 or/64-80 (3145677)



- 82 55 and 81 [NON-RCTS] (7707)
- 83 63 or 82 [RCTs, NON-RCTS] (11874)
- 84 83 use medall [MEDLINE RECORDS] (6073)
- 85 drug dependence treatment/ (7903)
- 86 opiate substitution treatment/ (3624)
- 87 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*)),tw,kw. (6752)
- 88 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)),tw,kw. (22219)
- 89 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)),tw,kw. (2071)
- 90 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)),tw,kw. (2061)
- 91 methadone treatment/ (4161)
- 92 or/85-91 [OPIATE SUBSTITUTION TREATMENT] (42590)
- 93 drug dependence/ (137376)
- 94 substance abuse/ (181771)
- 95 exp narcotic dependence/ (138031)
- 96 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kw. (46336)
- 97 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or "non-prescription use?" or "nonprescription use?" or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kw. (314491)
- 98 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kw. (16394)
- 99 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kw. (151)
- 100 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ofentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kw. (670)
- 101 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kw. (12021)
- 102 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or

eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or  
 eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodoinoma\$2 or ludonal\$2 or m-  
 oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc  
 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or  
 oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodoinon\$2 or  
 oxycodoinonhydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or  
 oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or  
 oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or  
 roxicodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodol\$2 or tekodin\$2 or thecodin\$2 or  
 thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
 illegal\*))))).tw,kw. (581)  
 103 or/93-102 [OPIOID USE DISORDERS] (558181)  
 104 drug dependence/dt [Drug Therapy] (6239)  
 105 drug dependence/rh [Rehabilitation] (10065)  
 106 substance abuse/dt [Drug Therapy] (2594)  
 107 substance abuse/rh [Rehabilitation] (9804)  
 108 exp narcotic dependence/dt (7354)  
 109 exp narcotic dependence/rh (1424)  
 110 (OAT or OATs).tw,kw. (19800)  
 111 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2  
 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or  
 probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952  
 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (4522)  
 112 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3  
 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (725)  
 113 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphon\* or dihydromorphon\* or  
 diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2  
 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jurnista\$2 or laudaconum\$2 or novolaudon\$2  
 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (864)  
 114 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or  
 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (5409)  
 115 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamimon\$2 or dianone\$2  
 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (18991)  
 116 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or

1  
2  
3 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
4 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
5 treatment\* or abuse-deterren\*).tw,kw. (9236)  
6 117 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
7 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
8 or naloxon-ratiopharm\$2 or naloxona\$2 or narcan\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
9 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
10 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (3251)  
11 118 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
12 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
13 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
14 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
15 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (3526)  
16 119 maintenance therapy/ (33792)  
17 120 (maintenance\* adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kw.  
18 (63504)  
19 121 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
20 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
21 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
22 pharmacotherap\* or pharmaco-therap\*).tw,kw. (14496)  
23 122 detoxif\*.tw,kw. (82783)  
24 123 or/104-122 [OAT] (234260)  
25 124 103 and 123 (61433)  
26 125 92 or 124 [OPIATE SUBSTITUTION TREATMENT/OAT] (89504)  
27 126 exp child/ not (exp adult/ or adolescent/) (2426358)  
28 127 exp infant/ not (exp adult/ or adolescent/) (1423228)  
29 128 fetus/ not (exp adult/ or adolescent/) (233921)  
30 129 or/126-128 (3037869)  
31 130 125 not 129 [CHILD-/INFANT-/FETUS-ONLY REMOVED] (87684)  
32 131 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp  
33 vertebrate/ (46665954)  
34 132 exp human/ or exp human experimentation/ or exp human experiment/ (36405350)  
35 133 131 not 132 (10262306)  
36 134 130 not 133 [ANIMAL-ONLY REMOVED] (76221)  
37 135 editorial.pt. (1008952)  
38 136 134 not 135 [OPINION PIECES REMOVED] (75191)  
39 137 randomized controlled trial/ or controlled clinical trial/ (1211158)  
40 138 exp "clinical trial (topic)"/ (259488)  
41 139 (randomi#ed or randomly or RCT? or placebo\*).tw,kw. (2132297)  
42 140 ((singl\* or doubl\* or trebl\* or tripl\*) adj (mask\* or blind\* or dumm\*).tw,kw. (393554)  
43 141 trial.ti. (451602)  
44 142 or/137-141 (2879876)  
45 143 136 and 142 [RCTs] (12312)  
46 144 controlled clinical trial/ (548392)  
47 145 "controlled clinical trial (topic)"/ (9211)  
48 146 (control\* adj2 trial\*).tw,kw. (548688)  
49 147 (nonrandom\* or non-random\* or quasi-random\* or quasi-experiment\*).tw,kw. (119556)  
50 148 (nRCT or nRCTs or non-RCT?).tw,kw. (1587)  
51 149 (control\* adj3 ("before and after" or "before after")).tw,kw. (9314)  
52 150 time series analysis/ (20412)  
53 151 time series.tw,kw. (59079)  
54  
55  
56  
57  
58  
59

152 pretest posttest control group design/ (330)  
 153 (pre- adj3 post-).tw,kw. (204764)  
 154 (pretest adj3 posttest).tw,kw. (16137)  
 155 controlled study/ (5805677)  
 156 (control\* adj2 stud\$3).tw,kw. (498541)  
 157 control group/ (126334)  
 158 (control\* adj2 group\$1).tw,kw. (1122314)  
 159 trial.ti. (451602)  
 160 or/144-159 (7788912)  
 161 136 and 160 [NON-RCTs] (14582)  
 162 143 or 161 [RCTs, NON-RCTs] (18828)  
 163 conference abstract.pt. (2909461)  
 164 limit 163 to yr="2016-current" (653386)  
 165 162 and 164 (677)  
 166 162 not 163 [ALL CONFERENCE ABSTRACTS REMOVED] (17213)  
 167 165 or 166 [CONFERENCE ABSTRACTS PRIOR TO 2016 REMOVED] (17890)  
 168 167 use emczd [EMBASE RECORDS] (10578)  
 169 Drug Rehabilitation/ (19849)  
 170 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*).tw. (6592)  
 171 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or  
 wean\* or withdraw\*).tw. (22069)  
 172 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3  
 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (2031)  
 173 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or  
 detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*).tw. (2055)  
 174 methadone maintenance/ (7584)  
 175 or/169-174 [OPIATE SUBSTITUTION TREATMENT] (54345)  
 176 exp drug dependency/ (246610)  
 177 drug abuse/ (182359)  
 178 "substance use disorder"/ (129822)  
 179 Intravenous Drug Usage/ (3663)  
 180 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
 illegal\*))).tw. (45506)  
 181 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or  
 mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or  
 "non-prescription use?" or "nonprescription use?" or ("use" or used or uses or using) adj2 (illicit\* or  
 illegal\*))).tw. (308682)  
 182 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or  
 non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\*  
 or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (16185)  
 183 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or  
 hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or  
 hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\*  
 or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or  
 nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (141)  
 184 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2  
 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or  
 lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or

1  
2  
3 rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanyl\$2 or trefentanil\$2)  
4 adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or  
5 nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\*  
6 or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (660)

7 185 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
8 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
9 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or  
10 addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or  
11 non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used  
12 or uses or using) adj2 (illicit\* or illegal\*))).tw. (11917)

13 186 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or  
14 cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or  
15 dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or  
16 eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or  
17 eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-  
18 oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc  
19 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or  
20 oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or  
21 oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or  
22 oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or  
23 oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or  
24 roxycodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodal\$2 or tekodin\$2 or thecodin\$2 or  
25 theocodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
26 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
27 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
28 illegal\*))).tw. (557)

29 187 or/176-186 [OPIOID USE DISORDERS] (610357)

30 188 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2  
31 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or  
32 probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952  
33 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
34 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (4475)

35 189 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3  
36 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
37 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (720)

38 190 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphon\* or dihydromorphon\* or  
39 diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2  
40 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jornista\$2 or laudaconum\$2 or novolaudon\$2  
41 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
42 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
43 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (859)

44 191 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or heroine\$2 or  
45 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
46 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (5352)

47 192 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
48 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
49 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamidon\$2 or dianone\$2  
50 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
51 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
52 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
53 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
54  
55  
56  
57  
58  
59

miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (18833)  
 193 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
 treatment\* or abuse-deterren\*).tw. (9202)  
 194 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
 or naloxon-ratiopharm\$2 or naloxona\$2 or narcana\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (3242)  
 195 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (3500)  
 196 maintenance therapy/ (33792)  
 197 (maintenance adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw. (63066)  
 198 (OAT or OATs).tw. (19595)  
 199 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
 pharmacotherap\* or pharmaco-therap\*).tw. (14432)  
 200 Detoxification/ (24900)  
 201 detoxif\*.tw. (81660)  
 202 or/196-201 [OAT] (196836)  
 203 187 and 202 (32124)  
 204 175 or 203 (75534)  
 205 exp Animals/ not (exp Animals/ and Humans/) (15333675)  
 206 204 not 205 [ANIMAL-ONLY REMOVED] (59807)  
 207 limit 206 to dissertation [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily  
 Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] (34223)  
 208 206 not 207 [DISSERTATIONS REMOVED] (25584)  
 209 clinical trials/ (88570)  
 210 (randomi#ed or randomly or RCT\$1 or placebo\*).tw. (2128678)  
 211 ((singl\* or doubl\* or trebl\* or tripl\*) adj (mask\* or blind\* or dumm\*).tw. (393325)  
 212 trial.ti. (451602)  
 213 or/209-212 (2382942)  
 214 208 and 213 [RCTS] (2802)  
 215 (control\* adj2 trial\*).tw. (542859)  
 216 (nonrandom\* or non-random\* or quasi-random\* or quasi-experiment\*).tw. (119259)  
 217 (nRCT or nRCTs or non-RCT?).tw. (1587)  
 218 (control\* adj3 ("before and after" or "before after")).tw. (9304)  
 219 time series/ (20212)  
 220 time series.tw. (58035)  
 221 (pretest adj3 posttest).tw. (16129)  
 222 (control\* adj2 stud\$3).tw. (496251)  
 223 Experiment Controls/ (893)

224 (control\* adj2 group\$1).tw. (1122209)  
 225 trial.ti. (451602)  
 226 or/215-225 (2391206)  
 227 208 and 226 [NON-RCTS] (1947)  
 228 214 or 227 [RCTs, NON-RCTS] (3438)  
 229 228 use medall,emczd (0)  
 230 228 not 229 [PSYCINFO RECORDS] (3438)  
 231 84 or 168 or 230 [ALL DATABASES] (20089)  
 232 limit 231 to yr=2015-current (4432)  
 233 remove duplicates from 232 (3210)  
 234 limit 231 to yr=2009-2014 (5616)  
 235 remove duplicates from 234 (3777)  
 236 limit 231 to yr=2001-2008 (5779)  
 237 remove duplicates from 236 (4080)  
 238 231 not (232 or 234 or 236) (4262)  
 239 remove duplicates from 238 (2991)  
 240 233 or 235 or 237 or 239 (14058) [TOTAL UNIQUE RECORDS]  
 241 240 use medall (5974) [MEDLINE UNIQUE RECORDS]  
 242 240 use emczd (6532) [EMBASE UNIQUE RECORDS]  
 243 240 not (241 or 242) (1552) [PSYCINFO UNIQUE RECORDS]

\*\*\*\*\*

## Cochrane Library

Search Name: Opioid Disorders - OAT - Trials  
 Date Run: 08/03/18 17:35:11.300  
 Description: OHRI - Final - Conference Abstracts Removed

ID	Search Hits
#1	[mh "Opiate Substitution Treatment"] 274
#2	((narcotic* or opioid* or opiate*) near/3 (maintenance* or substitut* or replac*)):ti,ab,kw 622
#3	((opiate* or opioid*) next (agonist* or receptor*)) near/3 (maintenance* or substitut* or replac* or rehabilit* or detox* or therap* or pharmacotherap* or pharmaco-therap* or treatment* or abuse- deterren*)):ti,ab,kw 186
#4	{or #1-#3} 764
#5	[mh ^"Substance-Related Disorders"] 3012
#6	[mh "Substance Abuse, Intravenous"] 439
#7	[mh "Substance Abuse, Oral"] 0
#8	[mh "Opioid-Related Disorders"] 1546
#9	((narcotic* or opioid* or opiate*) near/3 (abus* or addict* or dependen* or disorder* or habituat* or misus* or mis-us* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non- prescription" or nonprescription or withdrawal*) or (("use" or used or uses or using) near/2 (illicit* or illegal*)):ti,ab,kw 3215
#10	((drug or drugs or substance*) near/3 (abus* or addict* or dependen* or disorder* or habituat* or misus* or mis-us* or "non-medical use" or "non-medical uses" or "nonmedical use" or "nonmedical uses" or "non-prescribed use" or "non-prescribed uses" or "nonprescribed use" or "nonprescribed uses" or "non- prescription use" or "non-prescription uses" or "nonprescription use" or "nonprescription uses") or (("use" or used or uses or using) near/2 (illicit* or illegal*)):ti,ab,kw 14561
#11	(heroin* near/3 (abus* or addict* or dependen* or disorder* or habituat* or misus* or mis-us* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or

nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw  
1502

#12 ((hydrocodone or bekadid or codinovo or dico or dicodid or dihydrocodeinone or hycodan or  
hycon or hydrocodeinonebitartrate or hydrocodon or hydrocon or hydrocodonum or robidone) near/3  
(abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or  
nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or nonprescription or  
withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw 606

#13 ((fentanyl or alfentanil or alfenta or alfentanyl or beta hydroxymefentanyl or brifentanil or  
carfentanil or duragesic or fanaxal or fentanest or fentora or hypnorm or limifen or lofentanil or  
mefentanyl or mirfentanil or ofentanil or phentanyl or "R-39209" or "R-4263" or rapifen or remifentanil  
or sublimaze or sufenta or sufentanil or sulfentanyl or trefentanil) near/3 (abus\* or addict\* or dependen\*  
or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or  
nonprescribed or "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or  
using) near/2 (illicit\* or illegal\*)):ti,ab,kw 670

#14 ((morphine or anpec or duramorph or epimorph or miro or morfin or morfine or morphin or  
morphinium or morphium or MS contin or morphia or opso or oramorph or SDZ 202-250 or SDZ202-250  
or skenan or transmorphine or trans-morphine) near/3 (abus\* or addict\* or dependen\* or disorder\* or  
habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or  
"non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\*  
or illegal\*)):ti,ab,kw 898

#15 ((oxycodone or bionine or bionone or bolodorm or broncodal or bucodal or cafacodal or cardanon  
or codenon or codix 5 or "col 003" or col003 or dihydrohydroxycodone or dihydrohydroxydodeinone  
or dihydronone or dinarkon or endone or eubine or eucodal or eucodale or eucodalum or eudin or eukdin or  
eukodal or eumorphal or eurodamine or eutagen or hydrocodal or hydroxycodone or ludonal or m-oxycodone  
or medicodal or narcobasina or narcobasine or narcosin or nargenol or narodal or nsc 19043 or nucodan  
or opton or ossicodone or oxanest or oxaydo or oxecta or oxicone or oxicontin or oxiconum or oxikon or  
oxy ir or oxycodone or oxycodone hydrochloride or oxycodone hydrochloride or  
oxycodonhydrochlorid or oxycodyl or oxycone or oxycontin or oxydose or oxyfast or oxygesic or oxyir  
or oxykon or oxynorm or pancodine or pavinal or percolone or pronarcin or remoxy or roxicodone or  
roxicodone or sinthiodal or stupenal or supeudol or tebodal or tekodin or thecodin or thecodin or xtampa  
or xtampza) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or  
"non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or  
nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw  
669

#16 {or #5-#15} 16618

#17 [mh ^"Substance-Related Disorders"/DT] 191

#18 [mh ^"Substance-Related Disorders"/RH] 673

#19 [mh "Substance Abuse, Intravenous"/DT] 28

#20 [mh "Substance Abuse, Intravenous"/RH] 113

#21 [mh "Substance Abuse, Oral"/DT] 0

#22 [mh "Substance Abuse, Oral"/RH] 0

#23 [mh "Opioid-Related Disorders"/DT] 550

#24 [mh "Opioid-Related Disorders"/RH] 742

#25 [mh "Analgesics, Opioid"/TU] 2713

#26 (OAT or OATs):ti,ab,kw 678

#27 [mh Buprenorphine/TU] 443

#28 [mh Heroin/TU] 75

#29 [mh Hydromorphone/TU] 62

#30 [mh Methadone/TU] 747

#31 [mh Morphine/TU] 1528

#32 [mh Naloxone/TU] 858



- 1  
2  
3 #33 ((buprenorphine or anorfin or belbuca or buprenex or buprex or buprine or butrans or finibron or  
4 lepetan or "nih 8805" or nih8805 or norphin or pentorel or prefin or probuphine or "rx 6029 m" or "rx  
5 6029m" or rx6029m or subutex or temgesic or transtec or "um 952" or um952) near/3 (maintenance\* or  
6 substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
7 treatment\* or abuse-deterren\*)):ti,ab,kw 792
- 8 #34 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone or zubsolv) near/3  
9 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
10 pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 106
- 11 #35 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin or heroine or  
12 morphacetin) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
13 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 594
- 14 #36 ((hydromorphon\* or biomorphyl\* or cofalaudid\* or dihydromorphinon\* or dihydromorphon\* or  
15 diladid\* or dilaudid\* or dimorphon\* or dolonovag\* or exalgo\* or hydal\* or hydromorph contin\* or  
16 hydromorphinone\* or hydrostat\* or hymorphan\* or jornista\* or laudaconum\* or novolaudon\* or opidol\*  
17 or paliadon retardkaps\* or palladon\* or rexaphon\* or semcox\* or sophidone\*) near/3 (maintenance\* or  
18 substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
19 treatment\* or abuse-deterren\*)):ti,ab,kw 190
- 20 #37 ((methadone or adanon or adanon hydrochloride or algidon or algolysin or algoxale or althose or  
21 althose hydrochloride or amidon or amidona or amidone or amidosan or an 148 or an148 or anadon or  
22 biodone or butalgin or deamin or depidol or diaminion or dianone or dolafin or dolamid or dolesone or  
23 dolmed or dolophine or dolophine hydrochloride or dorex or dorexol or eptadone or fenadon or  
24 gobbidona or heptadon or heptanon or hoe 10820 or hoe10820 or ketalgin or l polamidon or mecodin or  
25 mepecton or mephenon or metadol or metadon or metasedin or methaddict or methadose or methaforte  
26 mix or miadone or moheptan or pallidone or phenadon or physepton or physeptone or polamidon or  
27 polamivet or polamivit or sinalgin or symoron or westadone) near/3 (maintenance\* or substitut\* or  
28 replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or  
29 abuse-deterren\*)):ti,ab,kw 1367
- 30 #38 ((morphine or anpec or duramorph or epimorph or miro or morfin or morfine or morphin or  
31 morphinium or morphium or MS contin or morphia or opso or oramorph or SDZ 202-250 or SDZ202-250  
32 or skenan or transmorphine or trans-morphine) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\*  
33 or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw  
34 2404
- 35 #39 ((naloxone or antioplaz or "en 1530" or "en 15304" or en1530 or en15304 or evzio or maloxone  
36 or mapin or "MRZ 2593-Br" or "MRZ-2593" or nalone or nalonee or nalone or naloxon curamed or  
37 naloxon-ratiopharm or naloxona or narcanon or narcanti or narcon or narvcam or naxone or zynox) near/3  
38 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
39 pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 542
- 40 #40 ((naltrexone or antaxon or antaxone or celupan or "en 1639a" or en1639a or nalerona or nalorex  
41 or naltrel or naltrexone hydrochloride or nemexin or nodict or nutrexon or phaltrexia or "re-via" or  
42 regental or revez or revia or trexan or vivitrex or vivitrol) near/3 (maintenance\* or substitut\* or replac\* or  
43 rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-  
44 deterren\*)):ti,ab,kw 754
- 45 #41 (((drug\* near/2 dependen\*) or (drug\* near/2 addict\*) or (substance\* near/2 dependen\*) or  
46 (substance\* near/2 addict\*)) near/3 (treatment\* or therap\* or pharmacotherap\* or pharmaco-  
47 therap\*)):ti,ab,kw 1529
- 48 #42 (maintenance near/2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*)):ti,ab,kw  
49 7632
- 50 #43 detoxif\*:ti,ab,kw 1453
- 51 #44 {or #17-#43} 19190
- 52 #45 #16 and #44 4477
- 53 #46 #4 or #45 4693
- 54  
55  
56  
57  
58  
59  
60

1  
2  
3 #47 [mh Child] not ([mh Adolescent] or [mh Adult]) 134  
4 #48 [mh Infant] not ([mh Adolescent] or [mh Adult]) 14132  
5 #49 #46 not (#47 or #48) 4649  
6 #50 conference abstract:pt Publication Year from 2016 to 2018 39970  
7 #51 #49 and #50 97  
8 #52 conference abstract:pt 102123  
9 #53 #49 not #52 in Trials 4140  
10 #54 #53 or #51 in Trials 4237  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

### Appendix 3: Definitions of Interventions and Comparators

Provided below are descriptions of the a priori list of psychosocial interventions for which we anticipate finding study data and which are considered of clinical relevance for the planned knowledge syntheses. Other interventions may also be encountered during the review and will be discussed by the research team for relevance as they are encountered. When needed, psychosocial interventions which are not labelled using a known terminology or which are different in administration than the core descriptions of these interventions will also be reviewed for relevance by the research team.

#### Active Control Groups

1. **Standard Care:** “the typical standard of care in pharmacological maintenance treatments already includes some form of psychosocial counselling.[38]”
2. **Medical Management:** “medically-focused, informal counselling that includes, but is not limited to, health and mental wellness checks, offering non-judgmental support and advice, assessing motivation and exploring barriers to change, developing a holistic treatment plan, promoting alternative strategies for managing stress, and providing referrals to health and social services when requested or appropriate.[6]”

#### Psychosocial Interventions

##### *Individual Interventions*

1. **Acceptance and Commitment Therapy:** “This therapy views psychological events as ongoing actions of the whole organism interacting in and with historically and situationally defined contexts. From an ACT perspective, a major problem of clients lays

1  
2  
3 in their limited and inflexible sources of the behaviors. The patients devote most of their  
4 time and energy to flee from personal and uncomfortable experiences. This keeps them  
5 from being engaged in life activities.” ACT sessions may include: creative despair,  
6 exploring discrepancies between control strategies and values, mindfulness training,  
7 exposure to internal stimuli, and discussing action plans.[39]

- 8  
9  
10  
11  
12  
13  
14  
15 2. **Cognitive Behavioral Therapy:** “This therapy is a short-term present focused therapy  
16 oriented towards focusing on current problems and helping to teach clients to adjust  
17 unhelpful thinking patterns.” “The main components of this [therapy] focus on  
18 performing a functional analysis of behaviour, promoting behavioral activation,  
19 identifying and coping with drug cravings, enhancing drug-refusal skills, enhancing  
20 decision-making about high-risk situations, and improving problem-solving skills.[40]”  
21  
22  
23  
24  
25  
26  
27  
28 3. **Contingency Management (i.e., medication, prize, or monetary equivalent**  
29 **reinforcement):** Behavioural treatment based on positive/negative reinforcers used to  
30 promote abstinence in participants in treatment. With positive reinforcers, the participants  
31 can obtain payment or other types of rewards for drug-free urine or methadone dose  
32 increases.[41]  
33  
34  
35  
36  
37  
38  
39  
40 4. **Community Reinforcement:** Behavioural approach to promote abstinence. “During  
41 sessions, participants are provided with relationship and employment counselling,  
42 instructions on antecedents and consequences of their opiate use, assistance in developing  
43 new or reinitiating old recreational activities, and are connected to other community  
44 resources if needed. Significant others are also often mobilized to administer reinforcers  
45 contingent on non-substance using behavior of the patient.[41]”  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 5. ***Dialectical Behavior Therapy***: “Applies directive, problem-oriented techniques that are  
4 balanced with supportive techniques, such as reflection, empathy, acceptance and  
5 emphasis on the client’s inherent ability to access an internal ‘wise mind.’ In addition,  
6 dialectical strategies are employed, including balancing acceptance with change,  
7 alternating validation with problem solving and using paradox and metaphor. Individual  
8 DBT targets dysfunctional behaviors in hierarchical order (suicidal, therapy-interfering,  
9 substance use, and quality-of-life interfering behaviors) and replaces those behaviors with  
10 skillful behaviors learned from psycho-educational skills.[42]”  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21
- 22 6. ***Drug Counselling, General Counselling, and Supportive Counselling***: “Provides  
23 general education, support and encouragement for abstinence oriented behaviours without  
24 using direct coping skills training.”  
25  
26  
27
- 28 7. ***Motivational Interviewing***: A non-confrontational, goal-oriented process designed to  
29 improve readiness to consider behaviour change and help clients resolve ambivalence  
30 towards change.[43]  
31  
32  
33  
34  
35  
36  
37

### ***Couples Interventions***

- 38 1. ***Behavioural Couples Therapy***: “Understands couple problems based on social exchange  
39 theory (i.e., that the success of a relationship depends on the frequency and variety of  
40 positive behaviours that are reciprocated). Treatment emphasizes partners’ specification  
41 (objectification) of desired positive changes from their partner, with various  
42 reinforcements of desired behaviour change, leading to behavioural exchanges.[44]”  
43  
44  
45  
46  
47  
48  
49  
50
- 51 2. ***Cognitive-Behavioural Couples Therapy***: Time-limited therapy that involves the couple.  
52 Therapy is relatively structured and involves goal setting. A functional analysis is often  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 done to assesses maladaptive affective and instrumental behaviours and the  
4 environmental contingencies supporting these behaviours, and the ways in which the  
5 couple's reciprocal interactions affect their relational satisfaction. Based on the functional  
6 analysis, the therapist and couple together delineate specific treatment goals which often  
7 involve increasing exchanges of positive behaviours and improving communication skills  
8 that influence the interaction process within the couple.[44]"

- 9  
10  
11  
12  
13  
14  
15  
16  
17 **3. *Emotion- Focused Couples Therapy:*** "Adheres to humanistic-experiential therapy  
18 principles: (1) The therapeutic alliance can itself be healing; (2) the inherent validity of  
19 the patient's experience is central to change, and is fostered by the therapist's authenticity  
20 and transparency; (3) given the opportunity to do so, people have the ability to make  
21 healthy choices; (4) both the inner and outer realities of people's lives need to be attended  
22 to; and (5) therapy can provide opportunities for direct, in- session, corrective emotional  
23 experiences. Central attention is given to the role of emotion to break maladaptive,  
24 repetitive cycles of couple interaction.[44]"

### 37 ***Family Interventions***

- 38  
39  
40 1. ***Family Therapy:*** "A structured and strategic approach which places particular emphasis  
41 on developing appropriate boundaries and limits before introducing a strategic  
42 intervention. Family members are also invited to attend some sessions.[41]"
- 43  
44  
45  
46  
47 2. ***Behavioural Family Therapy:*** "Based on social learning theory and behaviour exchange  
48 principles derived from classical and operant conditioning approaches." This therapy  
49 aims to improve interactions between family members through reinforcement of desired  
50 behaviour change.[44]"
- 51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60
3. ***Cognitive-Behavioural Family Therapy***: Time-limited therapy that involves the whole family, or subgroups of the family. Therapy is relatively structured and involves goal setting. A functional analysis is often done to assess maladaptive affective and instrumental behaviours and the environmental contingencies supporting these behaviours, and the ways in which family members' reciprocal interactions affect their relational satisfaction. Based on the functional analysis, the therapist and family together delineate specific treatment goals which often involve increasing exchanges of positive behaviours and improving communication skills that influence the interaction process within the family.[44]"
4. ***Emotion- Focused Family Therapy***: Family-delivered format of emotion focused therapy. "Adheres to humanistic– experiential therapy principles: (1) The therapeutic alliance can itself be healing; (2) the inherent validity of the patient's experience is central to change, and is fostered by the therapist's authenticity and transparency; (3) given the opportunity to do so, people have the ability to make healthy choices; (4) both the inner and outer realities of people's lives need to be attended to; and (5) therapy can provide opportunities for direct, in-session, corrective emotional experiences. Central attention is given to the role of emotion to break maladaptive, repetitive cycles of couple interaction.[44]"
5. ***Multi-Dimensional Family Therapy***: "An empirically supported, manualized, family intervention for adolescent substance use and related mental health problems. It intervenes in four domains: (1) adolescent, (2) parent(s), (3) family interaction, and (4) extrafamilial social systems. Treatment is phasic, interventions are individualized, case

1  
2  
3 formulations are revised on the basis of feedback, and therapists advocate for both the  
4  
5 adolescent and the parent.[44]”  
6  
7  
8  
9

### 10 **Group Interventions**

- 11  
12 1. **12-Step Facilitation Group:** Narcotics Anonymous (NA) meetings are part of a self-help,  
13  
14 peer-group that supports people who use drugs. NA is structured from the basic principles  
15  
16 of alcoholics anonymous (AA) groups, where members are encouraged to learn from  
17  
18 one-another to live drug-free.  
19  
20
- 21  
22 2. **Acceptance and Commitment Therapy:** Group-delivered format of acceptance and  
23  
24 commitment therapy. “This therapy views psychological events as ongoing actions of the  
25  
26 whole organism interacting in and with historically and situationally defined contexts.  
27  
28 From an ACT perspective, a major problem of patients lays in their limited and inflexible  
29  
30 sources of the behaviors. The clients devote most of their time and energy to flee from  
31  
32 personal and uncomfortable experiences. This keeps them from being engaged in life  
33  
34 activities.” ACT sessions may include: creative despair, exploring discrepancies between  
35  
36 control strategies and values, mindfulness training, exposure to internal stimuli, and  
37  
38 discussing action plans.[39]  
39  
40
- 41  
42 3. **Cognitive Behavioural Group Therapy:** Group-delivered format of cognitive behavioural  
43  
44 therapy. “This therapy is a short-term present focused therapy oriented towards focusing  
45  
46 on current problems and helping to teach clients to adjust unhelpful thinking.” “The main  
47  
48 components of counselling focus on performing a functional analysis of behaviour,  
49  
50 promoting behavioural activation, identifying and coping with drug cravings, enhancing  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60



1  
2  
3 drug-refusal skills, enhancing decision-making about high-risk situations, and improving  
4  
5 problem-solving skills.[40]”  
6  
7

- 8 4. ***Dialectical Behavior Group Therapy***: Group-delivered format of dialectical behavior  
9  
10 therapy. “Applies directive, problem-oriented techniques that are balanced with  
11  
12 supportive techniques, such as reflection, empathy, acceptance and emphasis on the  
13  
14 client’s inherent ability to access an internal ‘wise mind.’ In addition, dialectical  
15  
16 strategies are employed, including balancing acceptance with change, alternating  
17  
18 validation with problem solving and using paradox and metaphor.[42]” Group DBT can  
19  
20 target dysfunctional behaviours, as is consistent with individual DBT, however, it can  
21  
22 also be in the format of a DBT skills-training group which can target skills such as  
23  
24 mindfulness, interpersonal effectiveness and emotion regulation.  
25  
26  
27
- 28 5. ***Mindfulness Group Therapy***: Group-delivered mindfulness techniques. “Mindfulness is  
29  
30 a technique comprised of meditation and a specific mental tendency toward experience  
31  
32 that encourages an awareness of the present-moment experience.” Sessions included:  
33  
34 meditation techniques, identifying triggers and cravings through mindfulness,  
35  
36 mindfulness in high-risk situations, acceptance and skillful action, seeing thoughts as  
37  
38 thoughts, self-care, and social support practices.[45]  
39  
40  
41
- 42 6. ***Group Motivational Interviewing***: Group-delivered format of motivational interviewing.  
43  
44 A non-confrontational, goal-oriented process designed to improve readiness to consider  
45  
46 behaviour change and help clients resolve ambivalence towards change.[43]  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## PRISMA-P Checklist

Section/topic	#	Checklist item	Information reported		Line #
			Yes	No	
<b>ADMINISTRATIVE INFORMATION</b>					
<b>Title</b>					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1-3
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
<b>Registration</b>	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	67
<b>Authors</b>					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	31-38
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	366-373
<b>Amendments</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
<b>Support</b>					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	359-362
Sponsor	5b	Provide name for the review funder and/or sponsor	<input checked="" type="checkbox"/>	<input type="checkbox"/>	359-362
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input checked="" type="checkbox"/>	<input type="checkbox"/>	361-362
<b>INTRODUCTION</b>					
<b>Rationale</b>	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	115-125
<b>Objectives</b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	129-131
<b>METHODS</b>					
<b>Eligibility criteria</b>	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as	<input checked="" type="checkbox"/>	<input type="checkbox"/>	160-199

Section/topic	#	Checklist item	Information reported		Line #
			Yes	No	
		criteria for eligibility for the review			
<b>Information sources</b>	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	140-156
<b>Search strategy</b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Additional file 1.2
<b>STUDY RECORDS</b>					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	202-203
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	201-217
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	220-221
<b>Data items</b>	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	221-233
<b>Outcomes and prioritization</b>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	180-193, 221-229
<b>Risk of bias in individual studies</b>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	235-243
<b>DATA</b>					
<b>Synthesis</b>	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	246-250
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$ , Kendall's tau)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	261-265
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	294-306

Section/topic	#	Checklist item	Information reported		Line #
			Yes	No	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	314-315
<b>Meta-bias(es)</b>	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	265-266
<b>Confidence in cumulative evidence</b>	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A

# BMJ Open

## Evaluating Comparative Effectiveness of Psychosocial Interventions for Persons Receiving Opioid Agonist Therapy for Opioid Use Disorder: Protocol for a Systematic Review

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023902.R1
Article Type:	Protocol
Date Submitted by the Author:	18-Jul-2018
Complete List of Authors:	Rice, Danielle; McGill University, Psychology; Ottawa Hospital Research Institute Hutton, Brian; University of Ottawa, Ottawa, Ontario, Canada; Ottawa Hospital Research Institute Poulin, Patricia; Ottawa Hospital Research Institute; University of Ottawa, Social Sciences and Medicine Sproule, Beth; University of Toronto Leslie Dan Faculty of Pharmacy, Psychiatry; Centre for Addiction and Mental Health, Pharmacy Wolfe, Dianna; Ottawa Hospital Research Institute, Ottawa Methods Centre Moher, David; Ottawa Hospital Research Institute, Ottawa Methods Centre Thavorn, Kednapa; Institute for Clinical Evaluative Sciences, ICES @uOttawa; The Ottawa Hospital Research Institute, Garber, Gary; Ottawa Hospital Research Institute; University of Ottawa, School of Epidemiology and Public Health Taha, Sheena; Canadian Center on Substance Use and Addiction Porath, Amy; Canadian Center on Substance Use and Addiction Willows, Melanie; The Royal Ottawa Mental Health Centre, Substance Use and Concurrent Disorders Program; University of Ottawa Faculty of Medicine Esmaeilisaraji, Leila; Ottawa Hospital Research Institute, Ottawa Methods Centre Yazdi, Fatemeh; Ottawa Hospital Research Institute, Ottawa Methods Centre Shea, Beverley; University of Ottawa; Ottawa Hospital Research Institute Skidmore, Becky; Independent Information Specialist Corace, Kimberly; University of Ottawa,
<b>Primary Subject Heading</b>:	Addiction
Secondary Subject Heading:	Mental health
Keywords:	Opioid use disorder, systematic review, psychosocial interventions, pharmacological interventions, addiction medicine, network meta-analysis

1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

# Evaluating Comparative Effectiveness of Psychosocial Interventions for Persons Receiving Opioid Agonist Therapy for Opioid Use Disorder: Protocol for a Systematic Review

Danielle B Rice\*<sup>1,2</sup>; Brian Hutton\*<sup>1,3</sup>; Patricia Poulin<sup>1,4,5</sup>; Beth A Sproule<sup>6,7</sup>; Dianna Wolfe<sup>1</sup>; David Moher<sup>1,3,8</sup>; Kednapa Thavorn<sup>1,3</sup>; Gary Garber<sup>1,3,9</sup>; Sheena Taha<sup>11</sup>; Amy Porath<sup>11</sup>; Melanie Willows<sup>10,12</sup>; Leila Esmaeilisaraji<sup>1</sup>; Fatemeh Yazdi<sup>1</sup>; Bev Shea<sup>1</sup>; Becky Skidmore<sup>1</sup>; Kimberly Corace<sup>1,12,13,14</sup>

\* Authors contributed equally to this work.

## Affiliations

<sup>1</sup>Ottawa Hospital Research Institute, Ottawa, ON, Canada

<sup>2</sup>Department of Psychology, Montreal, QC, Canada

<sup>3</sup>School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON, Canada

<sup>4</sup>Faculties of Social Sciences and Medicine, University of Ottawa, Ottawa, Canada

<sup>5</sup>Pain Clinic, Ottawa Hospital, Ottawa, ON, Canada

<sup>6</sup>Department of Pharmacy, Centre for Addiction and Mental Health, Toronto, ON, Canada

<sup>7</sup>Leslie Dan Faculty of Pharmacy and Department of Psychiatry, University of Toronto, Toronto, ON, Canada

<sup>8</sup>Centre for Journalology, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, ON, Canada

<sup>9</sup>Public Health Ontario, Toronto, ON, Canada

<sup>10</sup>Faculty of Medicine, Department of Family Medicine, University of Ottawa

<sup>11</sup>Canadian Center on Substance Use and Addiction, Ottawa, ON, Canada

<sup>12</sup>Substance Use and Concurrent Disorders Program, The Royal Ottawa Mental Health Centre, Ottawa, ON, Canada

<sup>13</sup>Faculty of Medicine, Department of Psychiatry, University of Ottawa, Ottawa, ON, Canada

<sup>14</sup>University of Ottawa, Institute of Mental Health Research

## **Corresponding Author:**

Dr. Brian Hutton

Center for Practice Changing Research

The Ottawa Hospital

501 Smyth Road, PO Box 201B,

Ottawa, ON, K1H 8L6

Email: [bhutton@ohri.ca](mailto:bhutton@ohri.ca)

Phone: 613-737-8899, ext 73842

## **Publication Details**

***Abstract Word Count:*** 264

***Main Text Word Count:*** 3,129

## ABSTRACT

**Introduction:** The opioid crisis has resulted in increasing rates of death caused by problematic opioid use. Current clinical guidelines recommend that individuals with persons with opioid use disorder (OUD) receive pharmacologic (e.g., opioid agonist therapy) and psychosocial (e.g., cognitive behavioral therapy) therapy, however, the best combination of pharmacologic and psychosocial components is not known. Our objective of the planned study is to conduct a comprehensive systematic review to assess the relative benefits of psychosocial interventions as an adjunct to opioid agonist therapy among persons with OUD.

**Methods and analysis:** A comprehensive search for randomized controlled trials and quasi-randomized studies published in English or French will be conducted from database inception to March 2018. The search will be conducted in MEDLINE, and translated for Embase, PsycINFO, and the Cochrane Central Register of Controlled Trials. Two independent reviewers will screen, extract, and assess risk of bias of eligible articles. Primary outcomes of interest will be treatment retention and opioid use (based on urinalysis results). Secondary outcomes will include self-reported opioid use, abstinence from illicit drugs, adherence to psychosocial therapy and opioid agonist therapy, risk for sexually transmitted disease, risk for blood borne pathogens, changes in mental health symptoms (e.g., depression), measures of craving and changes in patients' quality of life, and relevant adverse events. If sufficient data and adequate homogeneity exists, network meta-analyses (NMA) will be performed.

**Ethics and dissemination:** This will be the first systematic review to incorporate NMA to compare psychosocial treatments used as an adjunct to opioid agonist therapy for OUD. Results of this review will inform clinical management of persons with OUD.



1  
2  
3  
4  
5 **PROSPERO Registration #:** CRD42018090761  
6

7 **Keywords:** Opioid use disorder, systematic review, psychosocial interventions, pharmacological  
8 interventions, addiction medicine, network meta-analysis.  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

## STRENGTHS AND LIMITATIONS

- This will be the first systematic review incorporating network meta-analysis to compare the effectiveness of psychosocial treatments delivered in combination with opioid agonist therapy among people with opioid use disorder.
- Sub-group analyses are planned for speciality groups such as youth, pregnant women, indigenous people, and people who are incarcerated.
- Variability of outcome measures may influence the ability to perform planned network meta-analyses, and strategies have been planned to address this challenge.

## 1 BACKGROUND

2 Opioids are psychoactive analgesic drugs that can be prescribed for relief of acute or chronic  
3 pain[1], and their illicit use has risen to epidemic levels.[2] Opioid addiction, overdose and  
4 poisonings have resulted in increasing rates of opioid-related death.[3] In 2016, more than 2,800  
5 Canadians and 42,000 Americans died from opioid poisoning.[4, 5] An estimated 11.5 million  
6 individuals in the United States used opioid prescriptions non-medically in the past year  
7 alone.[2] In Europe, 84% of drug-related deaths in 2015 were related to opioid use, with heroin  
8 (often in combination with other drugs) contributing to more than half of drug-related deaths.[6]  
9 Problematic opioid use is also prevalent in Asia, which accounts for approximately two thirds of  
10 all opiate users.[7]

11  
12 Non-medical use of prescription opioids as well as the use of illicit opioids are of particular  
13 concern. In Europe, heroin use continues to account for the majority (approximately 80%) of  
14 new opioid-related treatment.[8] There has also been a dramatic rise in illicit drugs being  
15 contaminated with fentanyl in both North America and Europe. In 2016, there was a 281%  
16 increase in the number of deaths attributable to fentanyl within Canada as compared to the  
17 preceding year.[5, 9] These alarming trends have prompted recent international, national, and  
18 provincial level actions including the development of the 2017 Canadian Guideline for Opioids  
19 for Chronic Non-Cancer Pain, and Canadian, American, World Health Organization, and  
20 European guidelines for opioid use disorder [3, 10-12], and the encouragement of prescribing  
21 cautiously and in smaller quantities to decrease misuse and dependence.[13]

22

1  
2  
3 1 Non-medical and illicit use of opioids can result in individuals developing an opioid use disorder  
4  
5 2 (OUD). Compared to healthy individuals without OUD, individuals with an OUD have increased  
6  
7 3 psychosocial distress, healthcare utilization, morbidity, and mortality.[14, 15] The societal  
8  
9 4 implications of OUD are also substantial, as the total program spending on drugs used for OUD  
10  
11 5 (i.e., methadone, buprenorphine/naloxone)exceeded \$135 million in Canada in 2015.[16] In the  
12  
13 6 United States, the total economic burden of opioid overdose, addiction, and dependence was  
14  
15 7 \$78.5 billion in 2013.[17] Given the costly and significant implications of OUD on mortality,  
16  
17 8 morbidity, healthcare utilization and societal costs, the identification of best management  
18  
19 9 strategies is essential.  
20  
21  
22  
23

24 10  
25  
26 11 Clinical guidelines currently recommend that individuals with OUD receive concurrent therapy  
27  
28 12 consisting of pharmacologic (e.g., opioid agonist therapy) and psychosocial (e.g., cognitive  
29  
30 13 behavioral therapy) components.[9, 18] However, the best combination of pharmacologic and  
31  
32 14 psychosocial components is not currently known. To address the question of optimal  
33  
34 15 effectiveness of pharmacotherapy, specifically, opioid agonist therapy (OAT), a systematic  
35  
36 16 review and network meta-analysis (NMA) was planned to compare the effectiveness of OATs  
37  
38 17 for the treatment of OUD.[19] This review, however, could not be completed as intended due to  
39  
40 18 substantial heterogeneity among outcome measures. Of 60 included trials, there were 53 different  
41  
42 19 outcomes that were measured in 77 unique ways [19, 20], thereby greatly complicating the  
43  
44 20 ability to perform cross-study comparisons and pursue formal meta-analyses to compare OATs.  
45  
46 21 Given the extensive variability among outcome measures, the authors were only able to conduct  
47  
48 22 analyses on one outcome - treatment retention – where diacetylmorphine-assisted therapy was  
49  
50 23 found to be superior to other OATs.[20] Currently no analogous systematic review and network  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 meta-analysis for psychosocial therapies as adjunctive treatment to OAT for managing OUD  
2 exist. A variety of approaches have been used to aid in OUD management, including cognitive  
3 behavioral therapy, motivational interviewing, contingency management, supportive counseling  
4 and other strategies.[21, 22] While a quantitative comparison of the efficacy of psychosocial  
5 therapy has not been conducted, psychological treatment is considered by many clinicians to be a  
6 vital element to sustained success in people receiving OAT given its key role in ensuring  
7 treatment retention and improved outcomes.[3, 23]

8  
9 To our knowledge, no systematic review has included a NMA comparing the efficacy of  
10 psychosocial interventions used with OAT for individuals with OUD. Network meta-analysis has  
11 become a vital and broadly used approach to evidence synthesis in addressing research questions  
12 that involve the comparison of multiple therapies and wherein relevant direct and indirect data  
13 exists.[24-26] Such an analysis will be informative for decision-making in addressing and  
14 treating the rising rate of OUD. The current protocol outlines a planned systematic review and  
15 NMA to compare the relative benefits of different psychosocial therapies among people with  
16 OUD receiving OAT.

## 18 **METHODS**

19 The reporting of this protocol adheres to the Preferred Reporting Items for Systematic Reviews  
20 and Meta-analyses-Protocol (PRISMA-P) statement.[27] The checklist for reporting items can be  
21 found in appendix 1. The review will be performed in accordance with the methods described  
22 below with any subsequent amendments described in the final manuscript. The review has also  
23 been registered in PROSPERO (CRD42018090761).

1  
2  
3 1  
4  
5 2 **Search Strategy to Identify Relevant Studies**  
6  
7  
8 3 Search strategies to identify relevant studies for inclusion in the systematic review were  
9  
10 4 developed and tested through an iterative process by an experienced medical information  
11  
12 5 specialist (BSkidmore) in consultation with the review team. Separate searches were performed  
13  
14 6 for reviews and primary studies. The MEDLINE strategies were peer reviewed by another senior  
15  
16 7 information specialist prior to execution using the PRESS Checklist.[28] Using the OVID  
17  
18 8 platform, we searched Ovid MEDLINE®, including Epub Ahead of Print and In-Process &  
19  
20 9 Other Non-Indexed Citations, PsycINFO, and Embase Classic + Embase. We also searched the  
21  
22 10 Cochrane Library on Wiley. The review searches were performed on 28 February 2018 and the  
23  
24 11 primary study searches on 8 March 2018. Strategies utilized a combination of controlled  
25  
26 12 vocabulary (e.g., “Opiate Substitution Treatment”, “Opioid-Related Disorders/dt [drug therapy]”,  
27  
28 13 “Buprenorphine/tu [therapeutic use]”) and keywords (e.g., “opioid maintenance”, “methadone  
29  
30 14 substitution”, “OATS”). Randomized controlled trial, non-randomized controlled trial and  
31  
32 15 systematic review filters were applied as applicable (see appendix 2 for full search  
33  
34 16 strategy). Vocabulary and syntax were adjusted across databases. Conference abstracts prior to  
35  
36 17 2016 were removed from Embase and CENTRAL and dissertation abstracts were removed  
37  
38 18 from PsycINFO. The reference lists of identified trials and reviews will be searched to ensure no  
39  
40 19 relevant studies are missed. The supplemental searches will be integrated into a PRISMA flow  
41  
42 20 diagram.[29, 30]  
43  
44  
45  
46  
47  
48  
49  
50

## 51 **Study Eligibility Criteria**

### 52 **Population**

53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 1 Individuals receiving treatment pharmacological (OAT) and psychosocial interventions for  
4  
5 2 opioid use will be of interest. It will also include individuals diagnosed with OUD as defined by  
6  
7 3 the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) or diagnosed with opioid  
8  
9 4 dependence as defined by the International Classification of Disease (ICD) or DSM-IV will be of  
10  
11 5 interest. No restrictions will be made for age or specialty populations (e.g., youth, pregnant  
12  
13 6 women, people who are incarcerated). Based on the availability of data, such uniquely different  
14  
15 7 populations will be analysed separately given potential socio-demographic and other differences.  
16  
17 8 If not feasible, the appropriateness of regression-based adjustments to account for cross-study  
18  
19 9 differences in the representation of such populations will be assessed.  
20  
21  
22  
23  
24  
25

## 26 11 **Interventions and Comparators of Interest**

27  
28 12 Psychosocial interventions (delivered with OAT) will be of interest. Studies evaluating the  
29  
30 13 benefits of psychosocial interventions alone will be excluded from the systematic review. Studies  
31  
32 14 using control groups of either OAT alone or ‘standard medical management’ will be eligible  
33  
34 15 given their high likelihood of serving as important sources of indirect evidence [25] if NMAs are  
35  
36 16 performed. Descriptions of the primary psychosocial interventions to be included based on  
37  
38 17 existing research and recommendations are presented in appendix 3.  
39  
40  
41  
42  
43

## 44 19 **Outcomes**

45  
46  
47 20 The co-primary outcomes of interest will be treatment retention and opioid use (including  
48  
49 21 abstinence from opioids and opioid use based on urinalysis results). Retention can be measured  
50  
51 22 in several ways including the use of a continuous value, such as the number of days a patient  
52  
53 23 continued in an OAT program.[31] A binary outcome, such as the proportion of patients who  
54  
55  
56  
57  
58  
59  
60

1 completed the planned number of therapy sessions,[32] or the number of patients who received  
2 treatment for a predetermined minimum number of sessions.[33] Secondary endpoints of interest  
3 will include self-reported opioid use, abstinence from illicit drug use, alcohol use, adherence to  
4 psychosocial therapy, adherence to OAT, HIV risk behaviours, changes in mental health  
5 symptoms (depression, anxiety, suicidality), measures of craving and changes in patients' quality  
6 of life, and adverse events (e.g., increases in substance use). We will capture data for all  
7 reporting formats of outcomes considered (this will also provide valuable data for the planned  
8 future development of a core endpoints set for OUD); once data collection is complete, we will  
9 review outcome definitions and cross-study data availability to identify those endpoints that may  
10 be best suited for NMAs (those with insufficient data will be summarized in other ways).

11

## 12 **Study Designs**

13 Study designs of interest will include randomized controlled trials and quasi-randomized trials  
14 (e.g., trials that do not use appropriate methods for randomization). Only studies published in  
15 English and French will be included. Observational studies, case-control studies, case series and  
16 case reports will be excluded.

17

## 18 **Screening for Eligible Studies**

19 Citations obtained from the literature searches will be imported into Distiller SR Software  
20 (Evidence Partners, Inc; Ottawa, Canada), which will be used for all stages of study screening  
21 and data extraction. Citations will be screened independently by two reviewers (among DBR,  
22 LE, and FY), based on title, keywords, and abstract (Level 1 screening) and full-text articles  
23 (Level 2 screening). Level 1 will be performed using a liberal accelerated approach (i.e., only



1 one reviewer needed to include a citation, while two reviewers will be needed to exclude), and  
2 will be supported using text mining methods within Distiller SR. Level 1 citations deemed  
3 potentially relevant or lacking sufficient information to exclude will be carried forward to Level  
4 2, which will be performed by two reviewers independently. Disagreements at Level 2 screening  
5 will be resolved by discussion. Where consensus is not achieved following discussion, a third  
6 independent team member will be consulted (BH or KC). Prior to conducting screening at level 1  
7 and level 2, a small number of abstracts/full texts will be piloted to establish agreement and  
8 consistency among reviewers. Of studies that report on the same cohort (e.g., updates of different  
9 follow-up durations), the most up-to-date information will be retained, and a note of the  
10 duplicate sample will be made. The process of literature selection will be reported using a flow  
11 diagram as recommended by the PRISMA statement.[29, 30]

### 13 **Process of Data Collection**

14 Primary data collection of included studies will be performed by two reviewers using a  
15 standardized electronic data collection form in Distiller SR Software. Data gathered from  
16 included studies will include the patient population, intervention and comparator information,  
17 outcomes reported, and study design. Study characteristics (authors, year of publication, journal,  
18 countries of data collection), patient characteristics (eligibility criteria, number per group),  
19 patient demographics (age, sex, race), type of opioid use (prescription and/or illicit), cited  
20 rationale for opioid use (e.g., chronic pain), duration of opioid use, mode of use (intravenous  
21 versus oral), comorbidities or other unique demographic traits, interventions (with description,  
22 including numbers and duration of sessions, setting and therapist expertise, if described),  
23 treatment setting (e.g., community, physician office, penitentiary), and outcomes as described

1 above. All study characteristics will be summarized in tabular form to facilitate inspection and  
2 discussion with clinical experts in terms of study heterogeneity, grouping of interventions, and  
3 other such topics required to inform analysis; these tables will also be included in the final  
4 report. Collected data will be verified by a second reviewer for accuracy, with disagreements  
5 being settled by discussion.

### 7 **Risk of Bias Assessments of Included Studies**

8 Risk of bias (RoB) will be assessed for all randomized and quasi-randomized studies included in  
9 the review using the Cochrane RoB tool.[34] The Cochrane RoB tool evaluates seven domains  
10 (i.e., random sequence generation, allocation concealment, blinding, missing outcome data,  
11 selective outcome reporting, attrition, and “other sources of bias”).[34] RoB assessments will be  
12 conducted by two reviewers (among DR, LE, and FY) and disagreements will be resolved  
13 through discussion or by a third reviewer (BH or KC). Results from RoB appraisals will be  
14 summarized in the review and reported in full on an item-by-item basis in an appendix. They will  
15 also be considered when contextualizing the results for each outcome.

### 17 **Approach to Evidence Synthesis for NMA**

18 For outcomes with sufficient data for analysis, we will first conduct traditional meta-analyses of  
19 all pairwise comparisons in the evidence networks. If feasible, NMAs will be performed  
20 subsequently. Initial exploration of potential clinical and methodological heterogeneity amongst  
21 the included studies will be conducted using tabular and graphical approaches that will be  
22 discussed by members of the research team. The assumption of transitivity will be evaluated by  
23 inspection of differences in patient eligibility criteria and pertinent patient demographics

1 between studies, including comorbidities (e.g., comorbid pain, mental health diagnoses).  
2 Methodological differences between studies that could influence outcome measurements will be  
3 noted. We will describe any concerns related to the transitivity assumption or methodological  
4 heterogeneity within the final report and consider statistical strategies to address any concerns.

5  
6 Standard pairwise meta-analyses will be conducted by fitting random-effects models in  
7 Comprehensive Meta-Analysis V3 software (BiostatInc; Englewood, New Jersey, USA) to  
8 generate summary estimates and to assess statistical heterogeneity across included studies.  
9 Summary estimates will be reported as mean differences, standardized mean differences, or odds  
10 ratios as appropriate with corresponding 95% confidence intervals. Statistical heterogeneity will  
11 be measured by the  $I^2$  statistic.  $I^2$  values of 50% or higher will be considered indicative of  
12 potentially important heterogeneity that will be explored using established methods such as  
13 subgroup analysis, meta-regression and/or exclusion of outlier studies. If necessary, similar  
14 approaches will be conducted in NMAs to address existing heterogeneity. Comparison adjusted  
15 funnel plots will be performed to assess publication bias if NMAs are performed.

16  
17 Where feasible, NMAs will be carried out separately for each clinical outcome of interest.  
18 Approaches used for these analyses will follow existing recommendations for modelling of  
19 unadjusted and adjusted models as outlined by guidance from experts at the National Institute for  
20 Health and Care Excellence.[35, 36] Both fixed-effects and random-effects models will be fit for  
21 each outcome, within a Bayesian framework. Totals of 50,000 or more burn-in iterations and  
22 50,000 or more sampling iterations will be used for all NMAs, and model convergence will be  
23 assessed using Gelman Rubin diagnostics.[36] The fit of a model will be assessed by comparing

1 its posterior residual deviance with the number of unconstrained data points (i.e., the number of  
2 intervention arms across all studies) for the analysis. Selection between different models will be  
3 based upon deviance information criteria for each competing model, with a difference of five or  
4 more points suggesting an important difference.

5  
6 For networks where statistical heterogeneity is high or the number of single-study connections is  
7 high, random-effects models will be preferred. Between-treatment differences of continuous  
8 endpoints (e.g., change in quality of life) will be analysed using a model for mean differences or  
9 standardized mean differences as appropriate dependent upon the degree of studies providing  
10 data on different measurement scales. Findings from analyses of dichotomous outcomes (e.g.,  
11 adherence of a certain number of days, response to treatment) will be reported in terms of odds  
12 ratios. The assumption of consistency will be assessed by (i) fitting unrelated means models and  
13 comparing the deviance information criteria (DIC) with the corresponding consistency models;  
14 and (ii) reviewing scatterplots of the residuals from these models. Probabilities of treatment  
15 superiority will be estimated using the Surface Under the Cumulative Ranking curve (SUCRA),  
16 and ranking of treatments will be estimated by median treatment rankings, with corresponding  
17 95% credible intervals. All NMAs will be performed using WinBUGS software version 1.4.3  
18 (MRC Biostatistics Unit).

## 20 **Subgroup and Sensitivity Analyses**

21 Primary analyses will be unadjusted; however, additional analyses to assess heterogeneity will be  
22 pursued if feasible based upon data availability and network geometry considerations (e.g., few  
23 single-study connections). Primary analyses will be conducted to compare psychosocial therapies

1 at the treatment level and if data allows for it, we will establish broader categories of  
2 interventions for comparison (e.g., individual, family, couples, group) and conduct subgroup  
3 analyses. Subgroup and/or meta-regression will also be conducted for age (between 12-17 and  
4 18-25 years), sex (percent of women and men), duration of opioid use disorder, most common  
5 method of administration (oral versus intravenous), type of opioid use (percent prescription  
6 versus illicit), percent with physical health comorbidities, percent with other substance/alcohol  
7 use, extent of comorbid pain, and percent of patients with mental health comorbidities, where  
8 data are available.

## 10 **Reporting of Review Findings**

11 Both graphical and numeric display of findings will be presented. For each feasible outcome of  
12 interest, this will include network diagrams (to display the availability of evidence for all  
13 possible treatment comparisons); pairwise comparisons between interventions with 95% credible  
14 intervals for all treatments in the network; and SUCRA values and median treatment rankings.  
15 We will use the checklist of the PRISMA Statement for Network Meta-Analysis to ensure all  
16 findings are clearly reported.[30] If NMA is not feasible, pairwise meta-analysis findings will be  
17 reported in tables with a narrative summary.

## 19 **Patient and Public Involvement**

20 Patients were not involved in the design of this review, however, this work will inform the  
21 development of a core endpoints initiative. This initiative will involve multiple patient groups to  
22 gather perspectives on key outcomes for the development of future trials and to disseminate  
23 review findings.

1  
2  
3 1  
45 2 **DISCUSSION**  
6

7  
8 3 Improving the treatment of OUD is a fundamental component of mitigating the current opioid  
9  
10 4 crisis and reducing the increasing morbidity and mortality associated with OUD in North  
11  
12 5 America. Certain OAT medications are recommended for treating OUD as they are cost-  
13  
14 6 effective and clinically effective.[37] Regardless of the form of OAT administered, guidelines  
15  
16 7 for the clinical management of OUD recommend that psychosocial components be included, as  
17  
18 8 this can improve treatment retention and outcomes.[9] Despite this recommendation, only a  
19  
20 9 small minority of individuals receiving OAT are also provided psychosocial treatment.[38, 39]  
21  
22 10 This may relate to a lack of comparative evidence for the various psychosocial interventions that  
23  
24 11 can be applied in combination with OAT for individuals with OUD. To our knowledge, this will  
25  
26 12 be the first NMA looking to compare the efficacy of psychosocial interventions delivered with  
27  
28 13 OAT among individuals with OUD.  
29  
30  
31  
32

33 14  
34

35 15 We anticipate certain challenges in the context of the current review. One limiting obstacle may  
36  
37 16 be the existence of excessive between-study heterogeneity with regard to the outcomes measured  
38  
39 17 across studies which may limit formal synthesis, as was found in a recent systematic review that  
40  
41 18 compared OATs for patients with OUD.[20] Despite this challenge, our systematic review and  
42  
43 19 accompanying narrative summary will allow for the synthesis of studies to guide our  
44  
45 20 understanding of the potential usefulness of psychosocial interventions applied as an adjunct to  
46  
47 21 OAT for patients with OUD. This potential challenge motivates additional research we will  
48  
49 22 pursue in the second phase of our research wherein we will use established methods and  
50  
51 23 collaborate with methodologists, physicians, clinicians, and patients to develop a core outcomes  
52  
53  
54  
55  
56  
57  
58  
59  
60

1 set for OUD through Delphi surveys and interviews that include these stakeholder groups.  
2  
3  
4  
5  
6 2 Developing a core outcome set will inform and improve future research of OUD, both by  
7  
8 3 enhancing the consistency of evaluations performed in research studies of OUD as well as  
9  
10 4 improving the ability of researchers to both perform meta-analyses and derive cross-study  
11  
12 5 comparisons to inform decision making.  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

**REFERENCES**

1. Franklin GM, Rahman EA, Turner JA, et al. Opioid use for chronic low back pain: A prospective, population-based study among injured workers in Washington state, 2002-2005. *The Clinical Journal of Pain* 2009;25:743-51.
2. Centers for Disease Control Prevention. Vital signs: overdoses of prescription opioid pain relievers---United States, 1999--2008. *Morbidity and mortality weekly report* 2011;60:1487-92.
3. Bruneau J, Ahamad K, Goyer M-È, et al. Management of opioid use disorders: a national clinical practice guideline. *Canadian Medical Association Journal* 2018;190:E247.
4. Canadian Institute for Health Information. Canadian Centre on Substance Abuse. Hospitalizations and Emergency Department Visits Due to Opioid Poisoning in Canada. Canadian Institute for Health Information; 2016.
5. Centers for Disease Control Prevention. Drug Overdose Death Data 2017. 2017. Accessed on 04/Jan/2018. Available from: <https://www.cdc.gov/drugoverdose/data/statedeaths.html>.
6. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) European Drug Report 2018: Trends and Developments. 2018. Luxembourg: Publications Office of the European Union. Accessed on 05/Jul/2018. Available from <http://www.emcdda.europa.eu/data/stats2018/drd>
7. United Nations Office on Drugs and Crime. World Drug Report 2015. 2015. United Nations publication. Accessed on 08/Jul/2018. Available from [http://www.unodc.org/documents/wdr2015/World\\_Drug\\_Report\\_2015.pdf](http://www.unodc.org/documents/wdr2015/World_Drug_Report_2015.pdf).



- 1  
2  
3 28 8. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) European Drug  
4  
5 29 Report 2017: Trends and Developments. 2017. Luxembourg: Publications Office of the  
6  
7 30 European Union. Accessed on 05/Jul/2018. Available from  
8  
9  
10 31 <http://www.emcdda.europa.eu/data/stats2018/drd>  
11  
12 32 9. British Columbia Centre on Substance Use, British Columbia Ministry of Health. A  
13  
14 33 Guideline for the Clinical Management of Opioid Use Disorder. 2017. Accessed on  
15  
16 34 15/Jan/2018. Available from: <http://www.bccsu.ca/wp-content/uploads/2017/06/BC->  
17  
18 35 OUD-Guidelines\_June2017.pdf  
19  
20  
21 36 10. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA). 2011.  
22  
23 37 Guidelines for the Treatment of Drug Dependence: A European Perspective. Accessed on  
24  
25 38 08/Jul/2018. Available from  
26  
27 39 [http://www.emcdda.europa.eu/system/files/publications/651/SI\\_treatment-guidelines-](http://www.emcdda.europa.eu/system/files/publications/651/SI_treatment-guidelines-)  
28  
29 40 p3\_315812.pdf  
30  
31  
32 41 11. World Health Organization. Department of Mental Health, Substance Abuse, World  
33  
34 42 Health Organization, International Narcotics Control Board, United Nations Office on  
35  
36 43 Drugs and Crime. 2009. Guidelines for the psychosocially assisted pharmacological  
37  
38 44 treatment of opioid dependence. World Health Organization. Accessed on 08/Jul/2018.  
39  
40 45 Available  
41  
42 46 from [http://apps.who.int/iris/bitstream/handle/10665/43948/9789241547543\\_eng.pdf;jsess](http://apps.who.int/iris/bitstream/handle/10665/43948/9789241547543_eng.pdf;jsessionid=7CBE9320168C572DC76AE3F822237657?sequence=1)  
43  
44 47 [ionid=7CBE9320168C572DC76AE3F822237657?sequence=1](http://apps.who.int/iris/bitstream/handle/10665/43948/9789241547543_eng.pdf;jsessionid=7CBE9320168C572DC76AE3F822237657?sequence=1)  
45  
46  
47 48 12. Kampman K, Jarvis M. American Society of Addiction Medicine (ASAM) National  
48  
49 49 Practice Guideline for the Use of Medications in the Treatment of Addiction Involving  
50  
51 50 Opioid Use. *J Addict Med* 2015;9.  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 51 13. The Ontario Drug Policy Research Network. Safety and Use of Opioids: A summary of  
4  
5 52 ODPN research on prescription opioid use in Ontario. 2016. Accessed on 15/Jan/2018.  
6  
7 53 Available from: [http://odprn.ca/wp-content/uploads/2016/08/FINAL-ODPRN-Opioids-](http://odprn.ca/wp-content/uploads/2016/08/FINAL-ODPRN-Opioids-Summary-Report-Aug-2016_compressed.pdf)  
8  
9 54 [Summary-Report-Aug-2016\\_compressed.pdf](http://odprn.ca/wp-content/uploads/2016/08/FINAL-ODPRN-Opioids-Summary-Report-Aug-2016_compressed.pdf).
- 10  
11  
12 55 14. Kolodny A, Courtwright DT, Hwang CS, et al. The prescription opioid and heroin crisis:  
13  
14 56 a public health approach to an epidemic of addiction. *Annual Review of Public Health*  
15  
16 57 2015;36:559-74.
- 17  
18  
19 58 15. Grande LA, Thompson EC, Au MA, et al. Problem Drug-related Behavior and  
20  
21 59 Discontinuation of Opioids Following the Introduction of an Opioid Management  
22  
23 60 Program. *Journal of the American Board of Family Medicine: JABFM* 2016;29:718-26.
- 24  
25  
26 61 16. Canadian Institute for Health Information. Prescribed Drug Spending in Canada, 2016: A  
27  
28 62 Focus on Public Drug Programs. Canadian Institute for Health Information; 2016.
- 29  
30  
31 63 17. Florence CS, Zhou C, Fau - Luo F, Luo F, Xu L, et al. The Economic Burden of  
32  
33 64 Prescription Opioid Overdose, Abuse, and Dependence in the United States, 2013.  
34  
35 65 *Medical Care* 2016;54:901-6.
- 36  
37  
38 66 18. National Collaborating Centre for Mental Health. Drug Misuse: Psychosocial  
39  
40 67 interventions National Clinical Practice Guideline Number 51. National Institute for  
41  
42 68 Health and Clinical Excellence (London). 2008.
- 43  
44  
45 69 19. Dennis BB, Naji L, Bawor M, et al. The effectiveness of opioid substitution treatments  
46  
47 70 for patients with opioid dependence: a systematic review and multiple treatment  
48  
49 71 comparison protocol. *Systematic Reviews* 2014;3:105.
- 50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 72 20. Dennis B. Chronic Pain: A Red Herring or Risk Factor in the Management of Patients  
4  
5 73 Receiving Opioid Substitution Therapy. *McMaster University* 2015. Accessed on  
6  
7 74 04/Jan/2018. Available from: <http://hdl.handle.net/11375/18058>.  
8  
9  
10 75 21. Dugosh K, Abraham A, Seymour B, et al. A Systematic Review on the Use of  
11  
12 76 Psychosocial Interventions in Conjunction With Medications for the Treatment of Opioid  
13  
14 77 Addiction. *Journal of Addiction Medicine* 2016;10:93-103.  
15  
16  
17 78 22. Smedslund G, Berg RC, Hammerstrøm KT, et al. Motivational interviewing for  
18  
19 79 substance abuse. *The Cochrane Database of Systematic Reviews* 2011:CD008063.  
20  
21  
22 80 23. Livingston JD, Adams E, Jordan M, et al. Primary Care Physicians' Views about  
23  
24 81 Prescribing Methadone to Treat Opioid Use Disorder. *Substance Use & Misuse* 2017:1-  
25  
26 82 10.  
27  
28 83 24. Catala-Lopez F, Tobias A, Cameron C, et al. Network meta-analysis for comparing  
29  
30 84 treatment effects of multiple interventions: an introduction. *Rheumatology International*  
31  
32 85 2014;34:1489-96.  
33  
34  
35 86 25. Caldwell D, Ades A, Higgins J. Simultaneous comparison of multiple treatments:  
36  
37 87 combining direct and indirect evidence. *BMJ* 2005;331:897-900.  
38  
39  
40 88 26. Salanti G. Indirect and mixed-treatment comparison, network, or multiple treatments  
41  
42 89 meta-analysis: many names, many benefits, many concerns for the next generation  
43  
44 90 evidence synthesis tool. *Research Synthesis Methods* 2012;3.  
45  
46  
47 91 27. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review  
48  
49 92 and meta-analysis protocols (PRISMA-P) 2015 statement. *Systematic Reviews* 2015;4:1.  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 93 28. Sampson M, McGowan J, Cogo E, et al. An evidence-based practice guideline for the  
4  
5 94 peer review of electronic search strategies. *Journal of Clinical Epidemiology*  
6  
7 95 2009;62:944-52.  
8  
9  
10 96 29. Hser Y-I, Li J, Jiang H, et al. Effects of a randomized contingency management  
11  
12 97 intervention on opiate abstinence and retention in methadone maintenance treatment in  
13  
14 98 China. *Addiction (Abingdon, England)* 2011;106:1801-9.  
15  
16  
17 99 30. Maas J, Barton G, Maskrey V, et al. Economic evaluation: a comparison of methadone  
18  
19 100 versus buprenorphine for opiate substitution treatment. *Drug and Alcohol Dependence*  
20  
21 101 2013;133:494-501.  
22  
23  
24 102 31. Chopra MP, Landes RD, Gatchalian KM, et al. Buprenorphine medication versus  
25  
26 103 voucher contingencies in promoting abstinence from opioids and cocaine. *Experimental*  
27  
28 104 *and Clinical Psychopharmacology* 2009;17:226-36.  
29  
30  
31 105 32. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews  
32  
33 106 and meta-analyses: the PRISMA statement. *PLoS Medicine* 2008;6.  
34  
35  
36 107 33. Hutton B, Salanti G, Caldwell D, et al. The PRISMA Extension Statement for Reporting  
37  
38 108 of Systematic Reviews Incorporating Network Meta-Analyses of Healthcare  
39  
40 109 Interventions: Checklist and Explanations. *Annals of Internal Medicine* 2015;162:777-84.  
41  
42  
43 110 34. Higgins J, Altman D, Gotzsche P, et al. The Cochrane Collaboration's tool for assessing  
44  
45 111 risk of bias in randomised trials. *BMJ* 2011;343.  
46  
47 112 35. Dias S, Sutton A, Welton N, et al. NICE DSU Technical Support Document 3:  
48  
49 113 Heterogeneity: subgroups, meta-regression, bias and bias-adjustment. 2012. Accessed on  
50  
51 114 02/Feb/2018. Available from:  
52  
53 115 <http://www.nicedsu.org.uk/TSD3%20Heterogeneity.final%20report.08.05.12.pdf>.

- 1  
2  
3 116 36. Dias S, Welton N, Sutton A, et al. NICE DSU Technical Support Document 2: A  
4  
5 117 Generalised Linear Modelling Framework for Pairwise and Network Meta-Analysis of  
6  
7 118 Randomised Controlled Trials. <http://www.nicedsu.org.uk> 2011.
- 9  
10 119 37. American Society of Addiction Medicine. Advancing Access to Addiction Medicine:  
11  
12 120 Implications for Opioid Addiction Treatment. American Society of Addiction Medicine  
13  
14 121 2013. Accessed on 02/Feb/2018. Available from: [https://www.asam.org/docs/default-](https://www.asam.org/docs/default-source/advocacy/aaam_implications-for-opioid-addiction-treatment_final)  
15  
16 122 [source/advocacy/aaam\\_implications-for-opioid-addiction-treatment\\_final](https://www.asam.org/docs/default-source/advocacy/aaam_implications-for-opioid-addiction-treatment_final).
- 17  
18 123 38. Ministry of Health Long Term Care. Methadone Treatment and Services Advisory  
19  
20 124 Committee: Final Report. 2016. Accessed on 02/Feb/2018. Available from:  
21  
22 125 [http://health.gov.on.ca/en/public/programs/drugs/ons/docs/methadone\\_advisory\\_committ](http://health.gov.on.ca/en/public/programs/drugs/ons/docs/methadone_advisory_committee_report.pdf)  
23  
24 126 [ee\\_report.pdf](http://health.gov.on.ca/en/public/programs/drugs/ons/docs/methadone_advisory_committee_report.pdf)  
25  
26 127 39. Centre for Addiction and Mental Health. Prescription Opioid Policy Framework. 2016.  
27  
28 128 Accessed on 07/Feb/2018. Available from:  
29  
30 129 [https://www.camh.ca/en/hospital/about\\_camh/influencing\\_public\\_policy/Documents/CA](https://www.camh.ca/en/hospital/about_camh/influencing_public_policy/Documents/CA)  
31  
32 130 [MHopiodpolicyframework.pdf](https://www.camh.ca/en/hospital/about_camh/influencing_public_policy/Documents/CA)  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3  
4 132 **ACKNOWLEDGEMENTS**

5  
6 133 We would like to thank Raymond Daniel (Assistant Information Specialist) for his role in  
7  
8 134 providing support in database management and document procurement.

9  
10 135 **FUNDING**

11  
12 136 Funding for this work is being provided by the Canadian Institutes of Health Research (CIHR)  
13  
14 137 grant number 397976. Ms. Rice is supported by a Vanier Canada Graduate CIHR Scholarship  
15  
16 138 and received a student grant from the Psychology Foundation of Canada. The funders had no role  
17  
18 139 in the design of the planned study or preparation of this protocol.

19  
20 140 **AVAILABILITY OF DATA AND MATERIAL**

21  
22 141 Datasets have not been generated as part of this protocol. The datasets generated and/or analysed  
23  
24 142 during the current study are available from the corresponding author on reasonable request.

25  
26 143 **AUTHORS' CONTRIBUTIONS**

27  
28 144 DBR, BH, and KC drafted the protocol. BSkidmore created and tested the search strategies to be  
29  
30 145 used in the bibliographic databases. DM and BS provided methodological input for the protocol  
31  
32 146 and planned systematic review. DBR, KC, PP, GG, ST, AP, MW, and BAS provided clinical  
33  
34 147 expertise during the protocol development stage, and will also provide such expertise throughout  
35  
36 148 the duration of the review and during drafting of the final manuscript. DBR, KT, LE, FY, and  
37  
38 149 DW will be involved in screening, data extraction, and quality assessment. DBR, KC, and BH  
39  
40 150 will be involved in all data analyses. DBR, KC, and BH will coordinate all aspects of the review.  
41  
42 151 BH conceived of and is the guarantor of the review. All authors provided critical feedback to the  
43  
44 152 protocol and approved the protocol.

45  
46 153 **AUTHORS' INFORMATION**

47  
48 154 Not applicable (optional, not included).  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 155 **ETHICS APPROVAL AND CONSENT TO PARTICIPATE**  
4

5 156 Not applicable  
6

7  
8 157 **CONSENT FOR PUBLICATION**  
9

10 158 Not applicable (no individual person's data are included in this manuscript).  
11

12 159 **COMPETING INTERESTS**  
13

14 160 BH has previously received honoraria from Cornerstone Research Group for the provision of  
15  
16 161 methodologic advice related to systematic reviews and meta-analysis. The remaining authors  
17  
18 162 declare that they have no competing interests.  
19  
20  
21

22 163  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## SUPPLEMENTARY FILES

### APPENDICES

To provide additional information regarding: *Evaluating Comparative Effectiveness of Psychosocial Interventions for Persons Receiving Opioid Agonist Therapy for Opioid Use Disorder: Protocol for a Systematic Review*. Rice DB, Hutton B, Poulin P, Sproule BA, Wolfe D, Moher D, Thavorn K, Garber G, Taha S, Porath A, Willows A, Esmaeilisaraji L, Yazadi F, Skidmore B, Corace K.

- Appendix 1: Literature Search Strategy
- Appendix 2: PRISMA-P Checklist
- Appendix 3: Definitions of Interventions and Comparators



## Appendix 1. PRISMA-P Checklist

Section/topic	#	Checklist item	Information reported		Page #
			Yes	No	
<b>ADMINISTRATIVE INFORMATION</b>					
<b>Title</b>					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
<b>Registration</b>	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	3
<b>Authors</b>					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	24
<b>Amendments</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
<b>Support</b>					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	24
Sponsor	5b	Provide name for the review funder and/or sponsor	<input checked="" type="checkbox"/>	<input type="checkbox"/>	24
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input checked="" type="checkbox"/>	<input type="checkbox"/>	24
<b>INTRODUCTION</b>					
<b>Rationale</b>	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	6-7
<b>Objectives</b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	7
<b>METHODS</b>					
<b>Eligibility criteria</b>	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8-10

Section/topic	#	Checklist item	Information reported		Page #
			Yes	No	
		criteria for eligibility for the review			
<b>Information sources</b>	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8
<b>Search strategy</b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Additional file 1.2
<b>STUDY RECORDS</b>					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10-11
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10-11
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11-12
<b>Data items</b>	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11-12
<b>Outcomes and prioritization</b>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11-12
<b>Risk of bias in individual studies</b>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	12
<b>DATA</b>					
<b>Synthesis</b>	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	12-13
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$ , Kendall's tau)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	13
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14-15

Section/topic	#	Checklist item	Information reported		Page #
			Yes	No	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	15
<b>Meta-bias(es)</b>	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	13
<b>Confidence in cumulative evidence</b>	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A

## Appendix 2: Literature Search Strategy

### Reviews

2018 Feb 28

Database: Embase Classic+Embase <1947 to 2018 February 27>, Ovid MEDLINE(R) ALL <1946 to February 27, 2018>, PsycINFO <1806 to February Week 3 2018>

Search Strategy:

- 
- 1 Opiate Substitution Treatment/ (3597)
  - 2 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*).tw,kf. (6670)
  - 3 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*).tw,kf. (22039)
  - 4 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (2045)
  - 5 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*).tw,kf. (2050)
  - 6 or/1-5 [OPIATE SUBSTITUTION TREATMENT] (31773)
  - 7 Substance-Related Disorders/ (113262)
  - 8 Substance Abuse, Intravenous/ (63332)
  - 9 Substance Abuse, Oral/ [NEW MESH 2018] (0)
  - 10 exp Opioid-Related Disorders/ (36965)
  - 11 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (45619)
  - 12 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or "non-prescription use?" or "nonprescription use?" or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (310916)
  - 13 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (16203)
  - 14 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or hycodan\$2 or hycon\$2 or hydrocodeinonebistartrate\$2 or hydrocodon\$2 or hydrocon\$2 or hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (141)
  - 15 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanyl\$2 or beta hydroxymefentanyl or brifentanil\$2 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (659)
  - 16 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or

SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (12011)

17 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or roxicodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodal\$2 or tekodin\$2 or thecodin\$2 or thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kf. (557)

18 or/7-17 [OPIOID USE DISORDERS] (459104)

19 Substance-Related Disorders/dt [drug therapy] (3838)

20 Substance-Related Disorders/rh [rehabilitation] (10041)

21 Substance Abuse, Intravenous/dt [drug therapy] (326)

22 Substance Abuse, Intravenous/rh [rehabilitation] (1403)

23 Substance Abuse, Oral/dt [drug therapy] (0)

24 Substance Abuse, Oral/rh [rehabilitation] (0)

25 exp Opioid-Related Disorders/dt [drug therapy] (8615)

26 exp Opioid-Related Disorders/rh [rehabilitation] (6399)

27 Analgesics, Opioid/tu [therapeutic use] (13587)

28 (OAT or OATs).tw,kf. (19631)

29 exp Buprenorphine/tu [therapeutic use] (2072)

30 Heroin/tu [therapeutic use] (388)

31 Hydromorphone/tu [therapeutic use] (283)

32 exp Methadone/tu [therapeutic use] (6498)

33 Morphine/tu [therapeutic use] (5142)

34 exp Naloxone/tu [therapeutic use] (4398)

35 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kf. (4468)

36 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kf. (719)

37 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kf. (5354)

38 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphinon\* or dihydromorphon\* or diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydald\$2 or hydromorph contin\$2 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jurnista\$2 or laudaconum\$2 or novolaudon\$2

1  
2  
3 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
4 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
5 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (864)  
6 39 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
7 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
8 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamidon\$2 or dianone\$2  
9 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
10 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
11 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
12 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
13 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
14 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
15 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
16 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (18855)  
17 40 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
18 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
19 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
20 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
21 treatment\* or abuse-deterren\*).tw,kf. (9244)  
22 41 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
23 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
24 or naloxon-ratiopharm\$2 or naloxona\$2 or narcan\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
25 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
26 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (3241)  
27 42 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
28 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
29 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
30 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
31 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (3497)  
32 43 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
33 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
34 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
35 pharmacotherap\* or pharmaco-therap\*).tw,kf. (14488)  
36 44 (maintenance\* adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kf.  
37 (63115)  
38 45 detoxif\*.tw,kf. (81859)  
39 46 or/19-45 [OAT] (237559)  
40 47 18 and 46 (60367)  
41 48 6 or 47 (81175)  
42 49 exp Child/ not (Adolescent/ or exp Adult/) (2424568)  
43 50 exp Infant/ not (Adolescent/ or exp Adult/) (1422345)  
44 51 48 not (49 or 50) [CHILD-/INFANT-ONLY REMOVED] (79535)  
45 52 exp Animals/ not (exp Animals/ and Humans/) (15327571)  
46 53 51 not 52 [ANIMAL-ONLY REMOVED] (61669)  
47 54 (editorial or news or newspaper article).pt. (1210715)  
48 55 53 not 54 [OPINION PIECES REMOVED] (60534)  
49 56 limit 55 to systematic reviews [Limit not valid in Embase; records were retained] (19270)  
50 57 meta analysis.pt. (85285)  
51 58 exp meta-analysis as topic/ (52797)  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 59 (meta-analy\* or metanaly\* or metaanaly\* or met analy\* or integrative research or integrative  
4 review\* or integrative overview\* or research integration or research overview\* or collaborative  
5 review\*).tw,kf. (323991)  
6  
7 60 (systematic review\* or systematic overview\* or evidence-based review\* or evidence-based  
8 overview\* or (evidence adj3 (review\* or overview\*)) or meta-review\* or meta-overview\* or meta-  
9 synthes\* or "review of reviews" or technology assessment\* or HTA or HTAs).tw,kf. (383178)  
10  
11 61 exp Technology assessment, biomedical/ (22830)  
12 62 (cochrane or health technology assessment or evidence report).jw. (38516)  
13 63 (network adj (MA or MAs)).tw,kf. (16)  
14 64 (NMA or NMAs).tw,kf. (3965)  
15 65 indirect\* compar\*.tw,kf. (4355)  
16 66 (indirect treatment\* adj1 compar\*).tw,kf. (556)  
17 67 (mixed treatment\* adj1 compar\*).tw,kf. (1223)  
18 68 (multiple treatment\* adj1 compar\*).tw,kf. (310)  
19 69 (multi-treatment\* adj1 compar\*).tw,kf. (4)  
20 70 simultaneous\* compar\*.tw,kf. (2286)  
21 71 mixed comparison?.tw,kf. (50)  
22 72 or/57-71 (681908)  
23 73 55 and 72 (1668)  
24 74 56 or 73 [REVIEWS] (19584)  
25 75 74 use medall [MEDLINE RECORDS] (1423)  
26 76 drug dependence treatment/ (7884)  
27 77 opiate substitution treatment/ (3597)  
28 78 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*)).tw,kw. (6748)  
29 79 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or  
30 wean\* or withdraw\*)).tw,kw. (22166)  
31 80 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3  
32 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
33 pharmaco-therap\* or treatment\* or abuse-deterren\*)).tw,kw. (2071)  
34 81 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or  
35 detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)).tw,kw. (2056)  
36 82 methadone treatment/ (4159)  
37 83 or/76-82 [OPIATE SUBSTITUTION TREATMENT] (42492)  
38 84 drug dependence/ (137162)  
39 85 substance abuse/ (181603)  
40 86 exp narcotic dependence/ (137914)  
41 87 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
42 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
43 prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or  
44 illegal\*))).tw,kw. (46245)  
45 88 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or  
46 mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or  
47 "non-prescription use?" or "nonprescription use?" or (("use" or used or uses or using) adj2 (illicit\* or  
48 illegal\*))).tw,kw. (314212)  
49 89 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-  
50 medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or  
51 withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (16386)  
52 90 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or  
53 hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or  
54 hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\*  
55 or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or  
56  
57  
58  
59

nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (151)

91 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (668)

92 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (12020)

93 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or dihydrohydrocodeinone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodeinoma\$2 or ludonal\$2 or m-oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or roxicodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodal\$2 or tekodin\$2 or thecodin\$2 or thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (580)

94 or/84-93 [OPIOID USE DISORDERS] (557651)

95 drug dependence/dt [Drug Therapy] (6231)

96 drug dependence/rh [Rehabilitation] (10049)

97 substance abuse/dt [Drug Therapy] (2590)

98 substance abuse/rh [Rehabilitation] (9793)

99 exp narcotic dependence/dt (7343)

100 exp narcotic dependence/rh (1424)

101 (OAT or OATs).tw,kw. (19775)

102 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (4514)

103 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (724)

104 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphinon\* or dihydromorphon\* or diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jurnista\$2 or laudaconum\$2 or novolaudon\$2 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3



1  
2  
3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
4 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (862)  
5 105 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or  
6 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
7 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (5404)  
8 106 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
9 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
10 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamimon\$2 or dianone\$2  
11 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
12 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
13 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
14 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
15 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
16 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
17 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
18 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (18983)  
19 107 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
20 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
21 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
22 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
23 treatment\* or abuse-deterren\*).tw,kw. (9235)  
24 108 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
25 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
26 or naloxon-ratiopharm\$2 or naloxona\$2 or narcans\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
27 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
28 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (3250)  
29 109 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
30 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
31 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
32 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
33 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (3523)  
34 110 maintenance therapy/ (33721)  
35 111 (maintenance\* adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kw.  
36 (63435)  
37 112 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
38 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
39 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
40 pharmacotherap\* or pharmaco-therap\*).tw,kw. (14490)  
41 113 detoxif\*.tw,kw. (82730)  
42 114 or/95-113 [OAT] (234039)  
43 115 94 and 114 (61375)  
44 116 83 or 115 [OPIATE SUBSTITUTION TREATMENT/OAT] (89378)  
45 117 exp child/ not (exp adult/ or adolescent/) (2424568)  
46 118 exp infant/ not (exp adult/ or adolescent/) (1422345)  
47 119 fetus/ not (exp adult/ or adolescent/) (233852)  
48 120 or/117-119 (3035843)  
49 121 116 not 120 [CHILD-/INFANT-/FETUS-ONLY REMOVED] (87563)  
50 122 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp  
51 vertebrate/ (46621835)  
52 123 exp human/ or exp human experimentation/ or exp human experiment/ (36368434)  
53 124 122 not 123 (10255103)  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 125 121 not 124 [ANIMAL-ONLY REMOVED] (76107)  
4 126 editorial.pt. (1008146)  
5 127 125 not 126 [OPINION PIECES REMOVED] (75078)  
6 128 meta-analysis/ (228832)  
7 129 "systematic review"/ (159939)  
8 130 "meta analysis (topic)"/ (36507)  
9 131 (meta-analy\* or metanaly\* or metaanaly\* or met analy\* or integrative research or integrative  
10 review\* or integrative overview\* or research integration or research overview\* or collaborative  
11 review\*).tw,kw. (326601)  
12 132 (systematic review\* or systematic overview\* or evidence-based review\* or evidence-based  
13 overview\* or (evidence adj3 (review\* or overview\*)) or meta-review\* or meta-overview\* or meta-  
14 synthes\* or "review of reviews" or technology assessment\* or HTA or HTAs).tw,kw. (386028)  
15 133 biomedical technology assessment/ (21723)  
16 134 (cochrane or health technology assessment or evidence report).jw. (38516)  
17 135 (network adj (MA or MAs)).tw,kw. (16)  
18 136 (NMA or NMAs).tw,kw. (3984)  
19 137 indirect\* compar\*.tw,kw. (4407)  
20 138 (indirect treatment\* adj1 compar\*).tw,kw. (560)  
21 139 (mixed treatment\* adj1 compar\*).tw,kw. (1244)  
22 140 (multiple treatment\* adj1 compar\*).tw,kw. (313)  
23 141 (multi-treatment\* adj1 compar\*).tw,kw. (4)  
24 142 simultaneous\* compar\*.tw,kw. (2286)  
25 143 mixed comparison?.tw,kw. (51)  
26 144 or/128-143 (734926)  
27 145 127 and 144 (2446)  
28 146 127 and 144 [REVIEWS] (2446)  
29 147 conference abstract.pt. (2898647)  
30 148 limit 147 to yr="2016-current" (643364)  
31 149 146 and 148 (54)  
32 150 146 not 147 [ALL CONFERENCE ABSTRACTS REMOVED] (2298)  
33 151 149 or 150 [CONFERENCE ABSTRACTS PRIOR TO 2016 REMOVED] (2352)  
34 152 151 use emczd [EMBASE RECORDS] (1278)  
35 153 Drug Rehabilitation/ (19847)  
36 154 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*).tw. (6588)  
37 155 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or  
38 wean\* or withdraw\*).tw. (22016)  
39 156 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3  
40 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
41 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (2032)  
42 157 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or  
43 detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*).tw. (2050)  
44 158 methadone maintenance/ (7582)  
45 159 or/153-158 [OPIATE SUBSTITUTION TREATMENT] (54279)  
46 160 exp drug dependency/ (246294)  
47 161 drug abuse/ (182188)  
48 162 "substance use disorder"/ (129585)  
49 163 Intravenous Drug Usage/ (3662)  
50 164 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
51 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
52 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
53 illegal\*))).tw. (45414)  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 165 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or  
4 mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or  
5 "non-prescription use?" or "nonprescription use?" or (("use" or used or uses or using) adj2 (illicit\* or  
6 illegal\*))).tw. (308416)

7 166 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or  
8 non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\*  
9 or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (16177)

10 167 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or  
11 hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or  
12 hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\*  
13 or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or  
14 nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (141)

15 168 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2  
16 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or  
17 lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or  
18 rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2)  
19 adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or  
20 nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\*  
21 or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (658)

22 169 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
23 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
24 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or  
25 addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or  
26 non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used  
27 or uses or using) adj2 (illicit\* or illegal\*))).tw. (11916)

28 170 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or  
29 cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or  
30 dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or  
31 eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or  
32 eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-  
33 oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc  
34 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or  
35 oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or  
36 oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or  
37 oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or  
38 oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or  
39 roxycodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodal\$2 or tekodin\$2 or thecodin\$2 or  
40 thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
41 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
42 prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or  
43 illegal\*))).tw. (556)

44 171 or/160-170 [OPIOID USE DISORDERS] (609718)

45 172 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2  
46 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or  
47 probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952  
48 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
49 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (4467)

50 173 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3  
51 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
52 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (719)

1  
2  
3 174 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphinon\* or dihydromorphon\* or  
4 diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2  
5 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jornista\$2 or laudaconum\$2 or novolaudon\$2  
6 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
7 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
8 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (857)  
9  
10 175 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or heroine\$2 or  
11 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
12 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (5347)  
13 176 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
14 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
15 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamidon\$2 or dianone\$2  
16 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
17 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
18 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
19 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
20 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
21 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
22 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
23 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (18825)  
24 177 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
25 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
26 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
27 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
28 treatment\* or abuse-deterren\*).tw. (9201)  
29 178 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
30 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
31 or naloxon-ratiopharm\$2 or naloxona\$2 or narkan\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
32 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
33 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (3241)  
34 179 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
35 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
36 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
37 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
38 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (3497)  
39 180 maintenance therapy/ (33721)  
40 181 (maintenance adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw. (62997)  
41 182 (OAT or OATs).tw. (19570)  
42 183 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
43 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
44 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
45 pharmacotherap\* or pharmaco-therap\*).tw. (14426)  
46 184 Detoxification/ (24878)  
47 185 detoxif\*.tw. (81609)  
48 186 or/180-185 [OAT] (196651)  
49 187 171 and 186 (32100)  
50 188 159 or 187 (75453)  
51 189 exp Animals/ not (exp Animals/ and Humans/) (15327571)  
52 190 188 not 189 [ANIMAL-ONLY REMOVED] (59727)  
53 191 limit 190 to dissertation [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily  
54 Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] (34146)  
55  
56  
57  
58  
59  
60

1  
2  
3 192 190 not 191 [DISSERTATIONS REMOVED] (25581)  
4 193 limit 192 to "0830 systematic review" [Limit not valid in Embase,Ovid MEDLINE(R),Ovid  
5 MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were  
6 retained] (145)  
7 194 limit 192 to 1200 meta analysis [Limit not valid in Embase,Ovid MEDLINE(R),Ovid  
8 MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were  
9 retained] (103)  
10 195 limit 192 to 1300 metasynthesis [Limit not valid in Embase,Ovid MEDLINE(R),Ovid  
11 MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were  
12 retained] (0)  
13 196 meta analysis/ (228832)  
14 197 (meta-analy\* or metanaly\* or metaanaly\* or met analy\* or integrative research or integrative  
15 review\* or integrative overview\* or research integration or research overview\* or collaborative  
16 review\*).tw. (323004)  
17 198 (systematic review\* or systematic overview\* or evidence-based review\* or evidence-based  
18 overview\* or (evidence adj3 (review\* or overview\*)) or meta-review\* or meta-overview\* or meta-  
19 synthes\* or "review of reviews" or technology assessment\* or HTA or HTAs).tw. (381844)  
20 199 (network adj (MA or MAs)).tw. (16)  
21 200 (NMA or NMAs).tw. (3955)  
22 201 indirect\* compar\*.tw. (4337)  
23 202 (indirect treatment\* adj1 compar\*).tw. (544)  
24 203 (mixed treatment\* adj1 compar\*).tw. (1172)  
25 204 (multiple treatment\* adj1 compar\*).tw. (301)  
26 205 (multi-treatment\* adj1 compar\*).tw. (4)  
27 206 simultaneous\* compar\*.tw. (2286)  
28 207 mixed comparison?.tw. (50)  
29 208 or/196-207 (647033)  
30 209 192 and 208 (439)  
31 210 193 or 194 or 195 or 209 [REVIEWS] (465)  
32 211 210 use medall,emczd (0)  
33 212 210 not 211 [PSYCINFO RECORDS] (465)  
34 213 75 or 152 or 212 [ALL DATABASES] (3166)  
35 214 remove duplicates from 213 (2195) [TOTAL UNIQUE RECORDS]  
36 215 214 use medall (1367) [MEDLINE UNIQUE RECORDS]  
37 216 from 215 keep 1-1000 (1000)  
38 217 from 215 keep 1001-1367 (367)  
39 218 214 use emczd (574) [EMBASE UNIQUE RECORDS]  
40 219 214 not (215 or 218) (254) [PSYCINFO UNIQUE RECORDS]  
41  
42  
43

44 \*\*\*\*\*

45 Cochrane Library

46  
47 Search Name: Opioid Disorders - OAT - Reviews

48 Date Run: 28/02/18 15:58:45.981

49 Description: OHRI - Final - 2018 Feb 28  
50

51 ID Search Hits

52 #1 [mh "Opiate Substitution Treatment"] 274

53 #2 ((narcotic\* or opioid\* or opiate\*) near/3 (maintenance\* or substitut\* or replac\*)):ti,ab,kw622

54 #3 ((narcotic\* or opioid\* or opiate\*) near/3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\*  
55 or wean\* or withdraw\*)):ti,ab,kw 2167  
56  
57  
58  
59  
60

- 1  
2  
3 #4 (((opiate\* or opioid\*) next (agonist\* or receptor\*)) near/3 (maintenance\* or substitut\* or replac\*  
4 or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-  
5 deterren\*)):ti,ab,kw 186
- 6 #5 (((opiate\* or opioid\*) next (agonist\* or receptor\*)) near/3 (maintenance\* or substitut\* or replac\*  
7 or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-  
8 deterren\*)):ti,ab,kw 186
- 9 #6 {or #1-#5} 2769
- 10 #7 [mh ^"Substance-Related Disorders"] 3012
- 11 #8 [mh "Substance Abuse, Intravenous"] 439
- 12 #9 [mh "Substance Abuse, Oral"] 0
- 13 #10 [mh "Opioid-Related Disorders"] 1546
- 14 #11 ((narcotic\* or opioid\* or opiate\*) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\*  
15 or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-  
16 prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or  
17 illegal\*)):ti,ab,kw 3215
- 18 #12 ((drug or drugs or substance\*) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or  
19 misus\* or mis-us\* or "non-medical use" or "non-medical uses" or "nonmedical use" or "nonmedical uses"  
20 or "non-prescribed use" or "non-prescribed uses" or "nonprescribed use" or "nonprescribed uses" or "non-  
21 prescription use" or "non-prescription uses" or "nonprescription use" or "nonprescription uses") or (("use"  
22 or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw 14561
- 23 #13 (heroin\* near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or  
24 "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or  
25 nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw  
26 1502
- 27 #14 ((hydrocodone or bekadid or codinovo or dico or dicodid or dihydrocodeinone or hycodan or  
28 hycon or hydrocodeinonebitartrate or hydrocodon or hydrocon or hydrocodonum or robidone) near/3  
29 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or  
30 nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or nonprescription or  
31 withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw 606
- 32 #15 ((fentanyl or alfentanil or alfenta or alfentanyl or beta hydroxymefentanyl or brifentanil or  
33 carfentanil or duragesic or fanaxal or fentanest or fentora or hypnorm or limifen or lofentanil or  
34 mefentanyl or mirfentanil or ofentanil or phentanyl or "R-39209" or "R-4263" or rapifen or remifentanil  
35 or sublimaze or sufenta or sufentanil or sulfentanyl or trefentanil) near/3 (abus\* or addict\* or dependen\*  
36 or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or  
37 nonprescribed or "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or  
38 using) near/2 (illicit\* or illegal\*)):ti,ab,kw 670
- 39 #16 ((morphine or anpec or duramorph or epimorph or miro or morfin or morfine or morphin or  
40 morphinium or morphium or MS contin or morphia or opso or oramorph or SDZ 202-250 or SDZ202-250  
41 or skenan or transmorphine or trans-morphine) near/3 (abus\* or addict\* or dependen\* or disorder\* or  
42 habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or  
43 "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\*  
44 or illegal\*)):ti,ab,kw 898
- 45 #17 ((oxycodone or bionine or bionone or bolodorm or broncodal or bucodal or cafacodal or cardanon  
46 or codenon or codix 5 or "col 003" or col003 or dihydrohydroxycodone or dihydrohydroxydodeinone  
47 or dihydronone or dinarkon or endone or eubine or eucodal or eucodale or eucodalum or eudin or eukdin or  
48 eukodal or eumorphal or eurodamine or eutagen or hydrocodal or hydroxycodone or ludonal or m-oxy  
49 or medicodal or narcobasina or narcobasine or narcosin or nargenol or narodal or nsc 19043 or nucodan  
50 or opton or ossicodone or oxanest or oxaydo or oxecta or oxicone or oxicontin or oxiconum or oxikon or  
51 oxy ir or oxycod or oxycodone or oxycodonehydrochloride or oxycodone hydrochloride or  
52 oxycodonhydrochlorid or oxycodyl or oxycone or oxycontin or oxydose or oxyfast or oxygesic or oxyir  
53 or oxykon or oxynorm or pancodine or pavinal or percolone or pronarcin or remoxy or roxicodone or  
54  
55  
56  
57  
58  
59  
60

roxicodone or sinthiodal or stupenal or supeudol or tebdal or tekodin or thecodin or thecodin or xtampa or xtampza) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw

669

- #18 {or #7-#17} 16618
- #19 [mh ^"Substance-Related Disorders"/DT] 191
- #20 [mh ^"Substance-Related Disorders"/RH] 673
- #21 [mh "Substance Abuse, Intravenous"/DT] 28
- #22 [mh "Substance Abuse, Intravenous"/RH] 113
- #23 [mh "Substance Abuse, Oral"/DT] 0
- #24 [mh "Substance Abuse, Oral"/RH] 0
- #25 [mh "Opioid-Related Disorders"/DT] 550
- #26 [mh "Opioid-Related Disorders"/RH] 742
- #27 [mh "Analgesics, Opioid"/TU] 2713
- #28 (OAT or OATs):ti,ab,kw 678
- #29 [mh Buprenorphine/TU] 443
- #30 [mh Heroin/TU] 75
- #31 [mh Hydromorphone/TU] 62
- #32 [mh Methadone/TU] 747
- #33 [mh Morphine/TU] 1528
- #34 [mh Naloxone/TU] 858
- #35 ((buprenorphine or anorfin or belbuca or buprenex or buprex or buprine or butrans or finibron or lepetan or "nih 8805" or nih8805 or norphin or pentorel or prefin or probuphine or "rx 6029 m" or "rx 6029m" or rx6029m or subutex or temgesic or transtec or "um 952" or um952) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 792
- #36 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone or zubsolv) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 106
- #37 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin or heroine or morphacetin) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 594
- #38 ((hydromorphon\* or biomorphyl\* or cofalaudid\* or dihydromorphinon\* or dihydromorphon\* or diladid\* or dilaudid\* or dimorphon\* or dolonovag\* or exalgo\* or hydal\* or hydromorph contin\* or hydromorphinone\* or hydrostat\* or hymorphan\* or jurnista\* or laudaconum\* or novolaudon\* or opidol\* or paliadon retardkaps\* or palladon\* or rexaphon\* or semcox\* or sophidone\*) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 190
- #39 ((methadone or adanon or adanon hydrochloride or algidon or algolysin or algoxale or althose or althose hydrochloride or amidon or amidona or amidone or amidosan or an 148 or an148 or anadon or biodone or butalgin or deamin or depridol or diaminon or dianone or dolafin or dolamid or dolesone or dolmed or dolophine or dolophine hydrochloride or dorex or dorexol or eptadone or fenadon or gobbidona or heptadon or heptanon or hoe 10820 or hoe10820 or ketalgin or l polamidon or mecodin or mepecton or mephenon or metadol or metadon or metasedin or methaddict or methadose or methaforte mix or miadone or moheptan or pallidone or phenadon or physepton or physeptone or polamidon or polamivet or polamivit or sinalgin or symoron or westadone) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 1367
- #40 ((morphine or anpec or duramorph or epimorph or miro or morfin or morfine or morphin or morphinium or morphium or MS contin or morphia or opso or oramorph or SDZ 202-250 or SDZ202-250

or skenan or transmorphine or trans-morphine) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw  
2404

#41 ((naloxone or antioplaz or "en 1530" or "en 15304" or en1530 or en15304 or evzio or maloxone or mapin or "MRZ 2593-Br" or "MRZ-2593" or nalone or nalonee or nalone or naloxon curamed or naloxon-ratiopharm or naloxona or narcan or narcanti or narcon or narvcam or naxone or zynox) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 542

#42 ((naltrexone or antaxon or antaxone or celupan or "en 1639a" or en1639a or nalerona or nalorex or naltrel or naltrexone hydrochloride or nemexin or nodict or nutrexon or phaltrexia or "re-via" or regental or revez or revia or trexan or vivitrex or vivitrol) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 754

#43 (((drug\* near/2 dependen\*) or (drug\* near/2 addict\*) or (substance\* near/2 dependen\*) or (substance\* near/2 addict\*)) near/3 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*)):ti,ab,kw 1529

#44 (maintenance near/2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*)):ti,ab,kw  
7632

#45 detoxif\*:ti,ab,kw 1453

#46 {or #19-#45} 19190

#47 #18 and #46 4477

#48 #6 or #47 6184

#49 [mh Child] not ([mh Adolescent] or [mh Adult]) 134

#50 [mh Infant] not ([mh Adolescent] or [mh Adult]) 14132

#51 #48 not (#49 or #50) in Cochrane Reviews (Reviews and Protocols), Other Reviews and Technology Assessments

DSR - 124

DARE - 76

HTA - 16

### Primary Studies

2018 Mar 8

Database: Embase Classic+Embase <1947 to 2018 March 07>, Ovid MEDLINE(R) ALL <1946 to March 07, 2018>, PsycINFO <1806 to February Week 4 2018>

Search Strategy:

- 
- 1 Opiate Substitution Treatment/ (3624)
  - 2 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*)):tw,kf. (6674)
  - 3 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)):tw,kf. (22092)
  - 4 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):tw,kf. (2044)
  - 5 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)):tw,kf. (2055)
  - 6 or/1-5 [OPIATE SUBSTITUTION TREATMENT] (31849)
  - 7 Substance-Related Disorders/ (113410)
  - 8 Substance Abuse, Intravenous/ (63391)



- 9 Substance Abuse, Oral/ [NEW MESH 2018] (0)
- 10 exp Opioid-Related Disorders/ (37049)
- 11 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (45711)
- 12 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or "non-prescription use?" or "nonprescription use?" or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (311185)
- 13 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (16211)
- 14 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (141)
- 15 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (661)
- 16 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (12012)
- 17 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or roxicodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodol\$2 or tekodin\$2 or thecodin\$2 or thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw,kf. (558)
- 18 or/7-17 [OPIOID USE DISORDERS] (459571)
- 19 Substance-Related Disorders/dt [drug therapy] (3843)
- 20 Substance-Related Disorders/rh [rehabilitation] (10052)

- 1  
2  
3 21 Substance Abuse, Intravenous/dt [drug therapy] (327)  
4 22 Substance Abuse, Intravenous/rh [rehabilitation] (1404)  
5 23 Substance Abuse, Oral/dt [drug therapy] (0)  
6 24 Substance Abuse, Oral/rh [rehabilitation] (0)  
7 25 exp Opioid-Related Disorders/dt [drug therapy] (8635)  
8 26 exp Opioid-Related Disorders/rh [rehabilitation] (6407)  
9 27 Analgesics, Opioid/tu [therapeutic use] (13601)  
10 28 (OAT or OATs).tw,kf. (19652)  
11 29 exp Buprenorphine/tu [therapeutic use] (2073)  
12 30 Heroin/tu [therapeutic use] (388)  
13 31 Hydromorphone/tu [therapeutic use] (283)  
14 32 exp Methadone/tu [therapeutic use] (6503)  
15 33 Morphine/tu [therapeutic use] (5144)  
16 34 exp Naloxone/tu [therapeutic use] (4403)  
17 35 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2 or  
18 finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or probuphine\$2  
19 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952 or um952)  
20 adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
21 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (4476)  
22 36 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3  
23 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
24 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (720)  
25 37 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or  
26 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
27 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (5359)  
28 38 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphinon\* or dihydromorphon\* or  
29 diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2  
30 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jurnista\$2 or laudaconum\$2 or novolaudon\$2  
31 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
32 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
33 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (866)  
34 39 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
35 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
36 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamimon\$2 or dianone\$2  
37 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
38 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
39 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
40 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
41 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
42 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
43 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
44 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (18862)  
45 40 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
46 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
47 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
48 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
49 treatment\* or abuse-deterren\*).tw,kf. (9245)  
50 41 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
51 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
52 or naloxon-ratiopharm\$2 or naloxona\$2 or narcan\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
53  
54  
55  
56  
57  
58  
59

1  
 2  
 3 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
 4 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (3242)  
 5 42 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
 6 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
 7 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
 8 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
 9 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kf. (3500)  
 10 43 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
 11 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
 12 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
 13 pharmacotherap\* or pharmaco-therap\*).tw,kf. (14494)  
 14 44 (maintenance\* adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kf.  
 15 (63184)  
 16 45 detoxif\*.tw,kf. (81910)  
 17 46 or/19-45 [OAT] (237756)  
 18 47 18 and 46 (60420)  
 19 48 6 or 47 (81284)  
 20 49 exp Child/ not (Adolescent/ or exp Adult/) (2426358)  
 21 50 exp Infant/ not (Adolescent/ or exp Adult/) (1423228)  
 22 51 48 not (49 or 50) [CHILD-/INFANT-ONLY REMOVED] (79640)  
 23 52 exp Animals/ not (exp Animals/ and Humans/) (15333675)  
 24 53 51 not 52 [ANIMAL-ONLY REMOVED] (61771)  
 25 54 (editorial or news or newspaper article).pt. (1211821)  
 26 55 53 not 54 [OPINION PIECES REMOVED] (60635)  
 27 56 (controlled clinical trial or randomized controlled trial or pragmatic clinical trial).pt. (542931)  
 28 57 clinical trials as topic.sh. (182830)  
 29 58 exp Randomized Controlled Trials as Topic/ (256860)  
 30 59 (randomi#ed or randomly or RCT? or placebo\*).tw,kf. (2130342)  
 31 60 ((singl\* or doubl\* or trebl\* or tripl\*) adj (mask\* or blind\* or dumm\*).tw,kf. (393401)  
 32 61 trial.ti. (451602)  
 33 62 or/56-61 (2717718)  
 34 63 55 and 62 [RCTS] (9307)  
 35 64 controlled clinical trial.pt. (92216)  
 36 65 Controlled Clinical Trial/ or Controlled Clinical Trials as Topic/ (561253)  
 37 66 (control\* adj2 trial\*).tw,kf. (544746)  
 38 67 Non-Randomized Controlled Trials as Topic/ (9504)  
 39 68 (nonrandom\* or non-random\* or quasi-random\* or quasi-experiment\*).tw,kf. (119371)  
 40 69 (nRCT or nRCTs or non-RCT?).tw,kf. (1587)  
 41 70 Controlled Before-After Studies/ (209550)  
 42 71 (control\* adj3 ("before and after" or "before after")).tw,kf. (9308)  
 43 72 Interrupted Time Series Analysis/ (201499)  
 44 73 time series.tw,kf. (58363)  
 45 74 (pre- adj3 post-).tw,kf. (204737)  
 46 75 (pretest adj3 posttest).tw,kf. (16133)  
 47 76 Historically Controlled Study/ (219791)  
 48 77 (control\* adj2 stud\$3).tw,kf. (497097)  
 49 78 Control Groups/ (126334)  
 50 79 (control\* adj2 group\$1).tw,kf. (1122551)  
 51 80 trial.ti. (451602)  
 52 81 or/64-80 (3145677)  
 53 82 55 and 81 [NON-RCTS] (7707)

- 1  
2  
3 83 63 or 82 [RCTs, NON-RCTs] (11874)  
4 84 83 use medall [MEDLINE RECORDS] (6073)  
5 85 drug dependence treatment/ (7903)  
6 86 opiate substitution treatment/ (3624)  
7 87 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*)).tw,kw. (6752)  
8 88 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or  
9 wean\* or withdraw\*)).tw,kw. (22219)  
10 89 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3  
11 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
12 pharmaco-therap\* or treatment\* or abuse-deterren\*)).tw,kw. (2071)  
13 90 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or  
14 detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*)).tw,kw. (2061)  
15 91 methadone treatment/ (4161)  
16 92 or/85-91 [OPIATE SUBSTITUTION TREATMENT] (42590)  
17 93 drug dependence/ (137376)  
18 94 substance abuse/ (181771)  
19 95 exp narcotic dependence/ (138031)  
20 96 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
21 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
22 prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or  
23 illegal\*))).tw,kw. (46336)  
24 97 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or  
25 mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or  
26 "non-prescription use?" or "nonprescription use?" or (("use" or used or uses or using) adj2 (illicit\* or  
27 illegal\*))).tw,kw. (314491)  
28 98 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-  
29 medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or  
30 withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (16394)  
31 99 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or  
32 hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or  
33 hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\*  
34 or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or  
35 nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw.  
36 (151)  
37 100 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanyl\$2 or beta hydroxymefentanyl or brifentanil\$2  
38 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or  
39 lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or  
40 rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2)  
41 adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or  
42 nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\*  
43 or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (670)  
44 101 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
45 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
46 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or  
47 addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or  
48 non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or (("use" or used  
49 or uses or using) adj2 (illicit\* or illegal\*))).tw,kw. (12021)  
50 102 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or  
51 cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or  
52 dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or  
53 eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or

1  
2  
3 eumorphal\$2 or eurodamine\$2 or eutagen\$2 or hydrocodal\$2 or hydroxycodoinoma\$2 or ludonal\$2 or m-  
4 oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc  
5 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxecta\$2 or oxicone\$2 or  
6 oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodoinon\$2 or  
7 oxycodoinonhydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or  
8 oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or  
9 oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or  
10 roxycodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodol\$2 or tekodin\$2 or thecodin\$2 or  
11 thecodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
12 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
13 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
14 illegal\*))).tw,kw. (581)

15  
16 103 or/93-102 [OPIOID USE DISORDERS] (558181)

17 104 drug dependence/dt [Drug Therapy] (6239)

18 105 drug dependence/rh [Rehabilitation] (10065)

19 106 substance abuse/dt [Drug Therapy] (2594)

20 107 substance abuse/rh [Rehabilitation] (9804)

21 108 exp narcotic dependence/dt (7354)

22 109 exp narcotic dependence/rh (1424)

23 110 (OAT or OATs).tw,kw. (19800)

24 111 ((buprenorphine or anorfin\$2 or belbucal\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2  
25 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or  
26 probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952  
27 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
28 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (4522)

29 112 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3  
30 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
31 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (725)

32 113 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphinon\* or dihydromorphon\* or  
33 diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2  
34 or hydromorphinone\$2 or hydrostat\$2 or hymorphan\$2 or jornista\$2 or laudaconum\$2 or novolaudon\$2  
35 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
36 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
37 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (864)

38 114 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or  
39 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
40 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (5409)

41 115 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
42 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
43 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamimon\$2 or dianone\$2  
44 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
45 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
46 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
47 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
48 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or  
49 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
50 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
51 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw,kw. (18991)

52 116 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
53 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
54 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*

1  
2  
3 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
4 treatment\* or abuse-deterren\*).tw,kw. (9236)  
5 117 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
6 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
7 or naloxon-ratiopharm\$2 or naloxona\$2 or narcant\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
8 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
9 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (3251)  
10 118 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
11 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
12 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
13 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
14 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw,kw. (3526)  
15 119 maintenance therapy/ (33792)  
16 120 (maintenance\* adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw,kw.  
17 (63504)  
18 121 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
19 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
20 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
21 pharmacotherap\* or pharmaco-therap\*).tw,kw. (14496)  
22 122 detoxif\*.tw,kw. (82783)  
23 123 or/104-122 [OAT] (234260)  
24 124 103 and 123 (61433)  
25 125 92 or 124 [OPIATE SUBSTITUTION TREATMENT/OAT] (89504)  
26 126 exp child/ not (exp adult/ or adolescent/) (2426358)  
27 127 exp infant/ not (exp adult/ or adolescent/) (1423228)  
28 128 fetus/ not (exp adult/ or adolescent/) (233921)  
29 129 or/126-128 (3037869)  
30 130 125 not 129 [CHILD-/INFANT-/FETUS-ONLY REMOVED] (87684)  
31 131 exp animal experimentation/ or exp animal model/ or exp animal experiment/ or nonhuman/ or exp  
32 vertebrate/ (46665954)  
33 132 exp human/ or exp human experimentation/ or exp human experiment/ (36405350)  
34 133 131 not 132 (10262306)  
35 134 130 not 133 [ANIMAL-ONLY REMOVED] (76221)  
36 135 editorial.pt. (1008952)  
37 136 134 not 135 [OPINION PIECES REMOVED] (75191)  
38 137 randomized controlled trial/ or controlled clinical trial/ (1211158)  
39 138 exp "clinical trial (topic)"/ (259488)  
40 139 (randomi#ed or randomly or RCT? or placebo\*).tw,kw. (2132297)  
41 140 ((singl\* or doubl\* or trebl\* or tripl\*) adj (mask\* or blind\* or dumm\*).tw,kw. (393554)  
42 141 trial.ti. (451602)  
43 142 or/137-141 (2879876)  
44 143 136 and 142 [RCTs] (12312)  
45 144 controlled clinical trial/ (548392)  
46 145 "controlled clinical trial (topic)"/ (9211)  
47 146 (control\* adj2 trial\*).tw,kw. (548688)  
48 147 (nonrandom\* or non-random\* or quasi-random\* or quasi-experiment\*).tw,kw. (119556)  
49 148 (nRCT or nRCTs or non-RCT?).tw,kw. (1587)  
50 149 (control\* adj3 ("before and after" or "before after")).tw,kw. (9314)  
51 150 time series analysis/ (20412)  
52 151 time series.tw,kw. (59079)  
53 152 pretest posttest control group design/ (330)  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 153 (pre- adj3 post-).tw,kw. (204764)  
4 154 (pretest adj3 posttest).tw,kw. (16137)  
5 155 controlled study/ (5805677)  
6 156 (control\* adj2 stud\$3).tw,kw. (498541)  
7 157 control group/ (126334)  
8 158 (control\* adj2 group\$1).tw,kw. (1122314)  
9 159 trial.ti. (451602)  
10 160 or/144-159 (7788912)  
11 161 136 and 160 [NON-RCTs] (14582)  
12 162 143 or 161 [RCTs, NON-RCTs] (18828)  
13 163 conference abstract.pt. (2909461)  
14 164 limit 163 to yr="2016-current" (653386)  
15 165 162 and 164 (677)  
16 166 162 not 163 [ALL CONFERENCE ABSTRACTS REMOVED] (17213)  
17 167 165 or 166 [CONFERENCE ABSTRACTS PRIOR TO 2016 REMOVED] (17890)  
18 168 167 use emczd [EMBASE RECORDS] (10578)  
19 169 Drug Rehabilitation/ (19849)  
20 170 ((narcotic\* or opioid\* or opiate\*) adj3 (maintenance\* or substitut\* or replac\*).tw. (6592)  
21 171 ((narcotic\* or opioid\* or opiate\*) adj3 (decreas\* or detoxif\* or discontinu\* or reduc\* or taper\* or  
22 wean\* or withdraw\*).tw. (22069)  
23 172 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3  
24 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
25 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (2031)  
26 173 ((opiate\* agonist\* or opioid\* agonist\* or opiate\* receptor\* or opioid\* receptor\*) adj3 (decreas\* or  
27 detoxif\* or discontinu\* or reduc\* or taper\* or wean\* or withdraw\*).tw. (2055)  
28 174 methadone maintenance/ (7584)  
29 175 or/169-174 [OPIATE SUBSTITUTION TREATMENT] (54345)  
30 176 exp drug dependency/ (246610)  
31 177 drug abuse/ (182359)  
32 178 "substance use disorder"/ (129822)  
33 179 Intravenous Drug Usage/ (3663)  
34 180 ((narcotic\* or opioid\* or opiate\*) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
35 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
36 prescription\* or nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or  
37 illegal\*))))).tw. (45506)  
38 181 ((drug? or substance?) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or  
39 mis-us\* or "non-medical use?" or "nonmedical use?" or "non-prescribed use?" or "nonprescribed use?" or  
40 "non-prescription use?" or "nonprescription use?" or (("use" or used or uses or using) adj2 (illicit\* or  
41 illegal\*))))).tw. (308682)  
42 182 (heroin\* adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or  
43 non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\*  
44 or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw. (16185)  
45 183 ((hydrocodone or bekadid\$2 or codinovo\$2 or dico\$2 or dicodid\$2 or dihydrocodeinone\$2 or  
46 hycodan\$2 or hycon\$2 or hydrocodeinonebitartrate\$2 or hydrocodon\$2 or hydrocon\$2 or  
47 hydrocodonum\$2 or robidone\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\*  
48 or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or  
49 nonprescription\* or withdrawal\* or (("use" or used or uses or using) adj2 (illicit\* or illegal\*))))).tw. (141)  
50 184 ((fentanyl or alfentanil\$2 or alfenta\$2 or alfentanil\$2 or beta hydroxymefentanyl or brifentanil\$2  
51 or carfentanil\$2 or duragesic\$2 or fanaxal\$2 or fentanest\$2 or fentora\$2 or hypnorm\$2 or limifen\$2 or  
52 lofentanil\$2 or mefentanil\$2 or mirfentanil\$2 or ocfentanil\$2 or phentanyl\$2 or R-39209 or R-4263 or  
53 rapifen\$2 or remifentanil\$2 or sublimaze\$2 or sufenta\$2 or sufentanil\$2 or sulfentanil\$2 or trefentanil\$2)  
54  
55  
56  
57  
58  
59

1  
2  
3 adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or  
4 nonmedical\* or non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\*  
5 or ("use" or used or uses or using) adj2 (illicit\* or illegal\*))).tw. (660)

6 185 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
7 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
8 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (abus\* or  
9 addict\* or dependen\* or disorder? or habituat\* or misus\* or mis-us\* or non-medical\* or nonmedical\* or  
10 non-prescrib\* or nonprescrib\* or non-prescription\* or nonprescription\* or withdrawal\* or ("use" or used  
11 or uses or using) adj2 (illicit\* or illegal\*))).tw. (11917)

12 186 ((oxycodone or bionine\$2 or bionone\$2 or bolodorm\$2 or broncodal\$2 or bucodal\$2 or  
13 cafacodal\$2 or cardanon\$2 or codenon\$2 or codix 5 or "col 003" or col003 or DETERx\$2 or  
14 dihydrohydroxycodone or dihydrohydroxydodeinone or dihydrone\$2 or dinarkon\$2 or endone\$2 or  
15 eubine\$2 or eucodal\$2 or eucodale\$2 or eucodalum\$2 or eudin\$2 or eukdin\$2 or eukodal\$2 or  
16 eumorphal\$2 or eurodamine\$2 or etagen\$2 or hydrocodal\$2 or hydroxycodone\$2 or ludonal\$2 or m-  
17 oxy or medicodal\$2 or narcobasina\$2 or narcobasine\$2 or narcosin\$2 or nargenol\$2 or narodal\$2 or nsc  
18 19043 or nucodan\$2 or opton\$2 or ossicodone\$2 or oxanest\$2 or oxaydo\$2 or oxepta\$2 or oxicone\$2 or  
19 oxicontin\$2 or oxiconum\$2 or oxikon\$2 or oxy ir or oxycod\$2 or oxycodone\$2 or  
20 oxycodonehydrochloride or oxycodone hydrochloride or oxycodonhydrochlorid or oxycodyl\$2 or  
21 oxycone\$2 or oxycontin\$2 or oxydose\$2 or oxyfast\$2 or oxygesic\$2 or oxyir\$2 or oxykon\$2 or  
22 oxynorm\$2 or pancodine\$2 or pavinal\$2 or percolone\$2 or pronarcin\$2 or remoxy\$2 or roxicodone\$2 or  
23 roxycodone\$2 or sinthiodal\$2 or stupenal\$2 or supeudol\$2 or tebodal\$2 or tekodin\$2 or thecodin\$2 or  
24 theocodin\$2 or xtampa\$2 or xtampza\$2) adj3 (abus\* or addict\* or dependen\* or disorder? or habituat\* or  
25 misus\* or mis-us\* or non-medical\* or nonmedical\* or non-prescrib\* or nonprescrib\* or non-  
26 prescription\* or nonprescription\* or withdrawal\* or ("use" or used or uses or using) adj2 (illicit\* or  
27 illegal\*))).tw. (557)

28 187 or/176-186 [OPIOID USE DISORDERS] (610357)

29 188 ((buprenorphine or anorfin\$2 or belbuca\$2 or buprenex\$2 or buprex\$2 or buprine\$2 or butrans\$2  
30 or finibron\$2 or lepetan\$2 or nih 8805 or nih8805 or norphin\$2 or pentorel\$2 or prefin\$2 or  
31 probuphine\$2 or rx 6029 m or rx 6029m or rx6029m or subutex\$2 or temgesic\$2 or transtec\$2 or um 952  
32 or um952) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
33 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (4475)

34 189 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone\$2 or zubsolv\$2) adj3  
35 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
36 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (720)

37 190 ((hydromorphon\* or biomorphyl\$2 or cofalaudid\$2 or dihydromorphon\* or dihydromorphon\* or  
38 diladid\$2 or dilaudid\$2 or dimorphon\* or dolonovag\$2 or exalgo\$2 or hydal\$2 or hydromorph contin\$2  
39 or hydromorphonone\$2 or hydrostat\$2 or hymorphan\$2 or jurnista\$2 or laudaconum\$2 or novolaudon\$2  
40 or opidol\$2 or paliadon retardkaps\$2 or palladon\$2 or rexaphon\$2 or semcox\$2 or sophidone\$2) adj3  
41 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
42 pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (859)

43 191 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin\$2 or heroine\$2 or  
44 morphacetin\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
45 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*))).tw. (5352)

46 192 ((methadone or adanon\$2 or adanon hydrochloride\$2 or algidon\$2 or algolysin\$2 or algoxale\$2 or  
47 althose\$2 or althose hydrochloride\$2 or amidon\$2 or amidona\$2 or amidone\$2 or amidosan\$2 or an 148  
48 or an148 or anadon\$2 or biodone\$2 or butalgin\$2 or deamin\$2 or depidol\$2 or diamidon\$2 or dianone\$2  
49 or dolafin\$2 or dolamid\$2 or dolesone\$2 or dolmed\$2 or dolophine\$2 or dolophine hydrochloride\$2 or  
50 dorex\$2 or dorexol\$2 or eptadone\$2 or fenadon\$2 or gobbidona\$2 or heptadon\$2 or heptanon\$2 or hoe  
51 10820 or hoe10820 or ketalgin\$2 or l polamidon\$2 or mecodin\$2 or mepecton\$2 or mephenon\$2 or  
52 metadol\$2 or metadon\$2 or metasedin\$2 or methaddict\$2 or methadose\$2 or methaforte mix\$2 or  
53 miadone\$2 or moheptan\$2 or pallidone\$2 or phenadon\$2 or physepton\$2 or physeptone\$2 or



1  
2  
3 polamidon\$2 or polamivet\$2 or polamivit\$2 or sinalgin\$2 or symoron\$2 or westadone\$2) adj3  
4 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
5 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (18833)  
6 193 ((morphine or anpec\$2 or duramorph\$2 or epimorph\$2 or miro\$2 or morfin\$2 or morfine\$2 or  
7 morphin\$2 or morphinium\$2 or morphium\$2 or MS contin or morphia\$2 or opso\$2 or oramorph\$2 or  
8 SDZ 202-250 or SDZ202-250 or skenan\$2 or transmorphine\$2 or trans-morphine\$2) adj3 (maintenance\*  
9 or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or  
10 treatment\* or abuse-deterren\*).tw. (9202)  
11 194 ((naloxone or antioplaz\$2 or en 1530 or en 15304 or en1530 or en15304 or evzio\$2 or maloxone\$2  
12 or mapin\$2 or MRZ 2593-Br or MRZ-2593 or nalone\$2 or nalonee\$2 or nalone\$2 or naloxon curamed\$2  
13 or naloxon-ratiopharm\$2 or naloxona\$2 or narcana\$2 or narcanti\$2 or narcon\$2 or narvcam\$2 or  
14 naxone\$2 or zynox\$2) adj3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or  
15 pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (3242)  
16 195 ((naltrexone or antaxon\$2 or antaxone\$2 or celupan\$2 or en 1639a or en1639a or nalerona\$2 or  
17 nalorex\$2 or naltrel\$2 or naltrexone hydrochloride\$2 or nemexin\$2 or nodict\$2 or nutrexon\$2 or  
18 phaltrexia\$2 or re-via\$2 or regental\$2 or revez\$2 or revia\$2 or trexan\$2 or vivitrex\$2 or vivitrol\$2) adj3  
19 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or  
20 pharmaco-therap\* or treatment\* or abuse-deterren\*).tw. (3500)  
21 196 maintenance therapy/ (33792)  
22 197 (maintenance adj2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*).tw. (63066)  
23 198 (OAT or OATs).tw. (19595)  
24 199 (((drug? adj2 dependen\*) or (drug? adj2 addict\*) or (narcotic\* adj2 dependen\*) or (narcotic\* adj2  
25 addict\*) or (opioid\* adj2 dependen\*) or (opioid\* adj2 addict\*) or (opiate\* adj2 dependen\*) or (opiate\*  
26 adj2 addict\*) or (substance? adj2 dependen\*) or (substance? adj2 addict\*)) adj3 (treatment\* or therap\* or  
27 pharmacotherap\* or pharmaco-therap\*).tw. (14432)  
28 200 Detoxification/ (24900)  
29 201 detoxif\*.tw. (81660)  
30 202 or/196-201 [OAT] (196836)  
31 203 187 and 202 (32124)  
32 204 175 or 203 (75534)  
33 205 exp Animals/ not (exp Animals/ and Humans/) (15333675)  
34 206 204 not 205 [ANIMAL-ONLY REMOVED] (59807)  
35 207 limit 206 to dissertation [Limit not valid in Embase,Ovid MEDLINE(R),Ovid MEDLINE(R) Daily  
36 Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher; records were retained] (34223)  
37 208 206 not 207 [DISSERTATIONS REMOVED] (25584)  
38 209 clinical trials/ (88570)  
39 210 (randomi#ed or randomly or RCT\$1 or placebo\*).tw. (2128678)  
40 211 ((singl\* or doubl\* or trebl\* or tripl\*) adj (mask\* or blind\* or dumm\*).tw. (393325)  
41 212 trial.ti. (451602)  
42 213 or/209-212 (2382942)  
43 214 208 and 213 [RCTS] (2802)  
44 215 (control\* adj2 trial\*).tw. (542859)  
45 216 (nonrandom\* or non-random\* or quasi-random\* or quasi-experiment\*).tw. (119259)  
46 217 (nRCT or nRCTs or non-RCT?).tw. (1587)  
47 218 (control\* adj3 ("before and after" or "before after")).tw. (9304)  
48 219 time series/ (20212)  
49 220 time series.tw. (58035)  
50 221 (pretest adj3 posttest).tw. (16129)  
51 222 (control\* adj2 stud\$3).tw. (496251)  
52 223 Experiment Controls/ (893)  
53 224 (control\* adj2 group\$1).tw. (1122209)  
54  
55  
56  
57  
58  
59  
60

1  
 2  
 3 225 trial.ti. (451602)  
 4 226 or/215-225 (2391206)  
 5 227 208 and 226 [NON-RCTS] (1947)  
 6 228 214 or 227 [RCTs, NON-RCTS] (3438)  
 7 229 228 use medall,emczd (0)  
 8 230 228 not 229 [PSYCINFO RECORDS] (3438)  
 9 231 84 or 168 or 230 [ALL DATABASES] (20089)  
 10 232 limit 231 to yr=2015-current (4432)  
 11 233 remove duplicates from 232 (3210)  
 12 234 limit 231 to yr=2009-2014 (5616)  
 13 235 remove duplicates from 234 (3777)  
 14 236 limit 231 to yr=2001-2008 (5779)  
 15 237 remove duplicates from 236 (4080)  
 16 238 231 not (232 or 234 or 236) (4262)  
 17 239 remove duplicates from 238 (2991)  
 18 240 233 or 235 or 237 or 239 (14058) [TOTAL UNIQUE RECORDS]  
 19 241 240 use medall (5974) [MEDLINE UNIQUE RECORDS]  
 20 242 240 use emczd (6532) [EMBASE UNIQUE RECORDS]  
 21 243 240 not (241 or 242) (1552) [PSYCINFO UNIQUE RECORDS]  
 22  
 23

24 \*\*\*\*\*

25 Cochrane Library

26  
 27 Search Name: Opioid Disorders - OAT - Trials  
 28 Date Run: 08/03/18 17:35:11.300  
 29 Description: OHRI - Final - Conference Abstracts Removed  
 30

31 ID Search Hits  
 32 #1 [mh "Opiate Substitution Treatment"] 274  
 33 #2 ((narcotic\* or opioid\* or opiate\*) near/3 (maintenance\* or substitut\* or replac\*)):ti,ab,kw622  
 34 #3 (((opiate\* or opioid\*) next (agonist\* or receptor\*)) near/3 (maintenance\* or substitut\* or replac\*  
 35 or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-  
 36 deterren\*)):ti,ab,kw 186  
 37 #4 {or #1-#3} 764  
 38 #5 [mh ^"Substance-Related Disorders"] 3012  
 39 #6 [mh "Substance Abuse, Intravenous"] 439  
 40 #7 [mh "Substance Abuse, Oral"] 0  
 41 #8 [mh "Opioid-Related Disorders"] 1546  
 42 #9 ((narcotic\* or opioid\* or opiate\*) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\*  
 43 or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-  
 44 prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or  
 45 illegal\*)):ti,ab,kw 3215  
 46 #10 ((drug or drugs or substance\*) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or  
 47 misus\* or mis-us\* or "non-medical use" or "non-medical uses" or "nonmedical use" or "nonmedical uses"  
 48 or "non-prescribed use" or "non-prescribed uses" or "nonprescribed use" or "nonprescribed uses" or "non-  
 49 prescription use" or "non-prescription uses" or "nonprescription use" or "nonprescription uses") or (("use"  
 50 or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw 14561  
 51 #11 (heroin\* near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or  
 52 "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or  
 53 nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw  
 54 1502  
 55  
 56  
 57  
 58  
 59  
 60

- 1  
2  
3 #12 ((hydrocodone or bekadid or codinovo or dico or dicodid or dihydrocodeinone or hycodan or  
4 hycon or hydrocodeinonebitartrate or hydrocodon or hydrocon or hydrocodonum or robidone) near/3  
5 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or  
6 nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or nonprescription or  
7 withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw 606  
8 #13 ((fentanyl or alfentanil or alfenta or alfentanyl or beta hydroxymefentanyl or brifentanil or  
9 carfentanil or duragesic or fanaxal or fentanest or fentora or hypnorm or limifen or lofentanil or  
10 mefentanyl or mirfentanil or ofentanil or phentanyl or "R-39209" or "R-4263" or rapifen or remifentanil  
11 or sublimaze or sufenta or sufentanil or sulfentanyl or trefentanil) near/3 (abus\* or addict\* or dependen\*  
12 or disorder\* or habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or  
13 nonprescribed or "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or  
14 using) near/2 (illicit\* or illegal\*)):ti,ab,kw 670  
15 #14 ((morphine or anpec or duramorph or epimorph or miro or morfin or morfine or morphin or  
16 morphinium or morphium or MS contin or morphia or opso or oramorph or SDZ 202-250 or SDZ202-250  
17 or skenan or transmorphine or trans-morphine) near/3 (abus\* or addict\* or dependen\* or disorder\* or  
18 habituat\* or misus\* or mis-us\* or "non-medical" or nonmedical or "non-prescribed" or nonprescribed or  
19 "non-prescription" or nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\*  
20 or illegal\*)):ti,ab,kw 898  
21 #15 ((oxycodone or bionine or bionone or bolodorm or broncodal or bucodal or cafacodal or cardanon  
22 or codenon or codix 5 or "col 003" or col003 or dihydrohydroxycodone or dihydrohydroxydodeinone  
23 or dihydronone or dinarkon or endone or eubine or eucodal or eucodale or eucodalum or eudin or eukdin or  
24 eukodal or eumorphal or eurodamine or eutagen or hydrocodal or hydroxycodone or ludonal or m-oxy  
25 or medicodal or narcobasina or narcobasine or narcosin or nargenol or narodal or nsc 19043 or nucodan  
26 or opton or ossicodone or oxanest or oxaydo or oxepta or oxicone or oxicontin or oxiconum or oxikon or  
27 oxy ir or oxycod or oxycodone or oxycodonehydrochloride or oxycodone hydrochloride or  
28 oxycodonhydrochlorid or oxycodyl or oxycone or oxycontin or oxydose or oxyfast or oxygesic or oxyir  
29 or oxykon or oxynorm or pancodine or pavinal or percolone or pronarcin or remoxy or roxicodone or  
30 roxicodone or sinthiodal or stupenal or supeudol or tebdal or tekodin or thecodin or thecodin or xtampa  
31 or xtampza) near/3 (abus\* or addict\* or dependen\* or disorder\* or habituat\* or misus\* or mis-us\* or  
32 "non-medical" or nonmedical or "non-prescribed" or nonprescribed or "non-prescription" or  
33 nonprescription or withdrawal\*) or (("use" or used or uses or using) near/2 (illicit\* or illegal\*)):ti,ab,kw  
34 669  
35 #16 {or #5-#15} 16618  
36 #17 [mh ^"Substance-Related Disorders"/DT] 191  
37 #18 [mh ^"Substance-Related Disorders"/RH] 673  
38 #19 [mh "Substance Abuse, Intravenous"/DT] 28  
39 #20 [mh "Substance Abuse, Intravenous"/RH] 113  
40 #21 [mh "Substance Abuse, Oral"/DT] 0  
41 #22 [mh "Substance Abuse, Oral"/RH] 0  
42 #23 [mh "Opioid-Related Disorders"/DT] 550  
43 #24 [mh "Opioid-Related Disorders"/RH] 742  
44 #25 [mh "Analgesics, Opioid"/TU] 2713  
45 #26 (OAT or OATs):ti,ab,kw 678  
46 #27 [mh Buprenorphine/TU] 443  
47 #28 [mh Heroin/TU] 75  
48 #29 [mh Hydromorphone/TU] 62  
49 #30 [mh Methadone/TU] 747  
50 #31 [mh Morphine/TU] 1528  
51 #32 [mh Naloxone/TU] 858  
52 #33 ((buprenorphine or anorfin or belbuca or buprenex or buprex or buprine or butrans or finibron or  
53 lepetan or "nih 8805" or nih8805 or norphin or pentorel or prefin or probuphine or "rx 6029 m" or "rx  
54  
55  
56  
57  
58  
59  
60

- 6029m" or rx6029m or subutex or temgesic or transtec or "um 952" or um952) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 792
- #34 ((buprenorphine-naloxone or naloxone-buprenorphine or suboxone or zubsolv) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 106
- #35 ((heroin\* or diacetyl morphine or diacetylmorphine or diamorphine or diaphorin or heroine or morphacetin) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 594
- #36 ((hydromorphon\* or biomorphyl\* or cofalaudid\* or dihydromorphinon\* or dihydromorphon\* or diladid\* or dilaudid\* or dimorphon\* or dolonovag\* or exalgo\* or hydal\* or hydromorph contin\* or hydromorphinone\* or hydrostat\* or hymorphan\* or jornista\* or laudaconum\* or novolaudon\* or opidol\* or paliadon retardkaps\* or palladon\* or rexaphon\* or semcox\* or sophidone\*) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 190
- #37 ((methadone or adanon or adanon hydrochloride or algidon or algolysin or algoxale or althose or althose hydrochloride or amidon or amidona or amidone or amidosan or an 148 or an148 or anadon or biodone or butalgin or deamin or depridol or diaminion or dianone or dolafin or dolamid or dolesone or dolmed or dolophine or dolophine hydrochloride or dorex or dorexol or eptadone or fenadon or gobbidona or heptadon or heptanon or hoe 10820 or hoe10820 or ketalgin or l polamidon or mecodin or mepecton or mephenon or metadol or metadon or metasedin or methaddict or methadose or methaforte mix or miadone or moheptan or pallidone or phenadon or physepton or physeptone or polamidon or polamivet or polamivit or sinalgin or symoron or westadone) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 1367
- #38 ((morphine or anpec or duramorph or epimorph or miro or morfin or morfine or morphin or morphinium or morphium or MS contin or morphia or opso or oramorph or SDZ 202-250 or SDZ202-250 or skenan or transmorphine or trans-morphine) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 2404
- #39 ((naloxone or antioplaz or "en 1530" or "en 15304" or en1530 or en15304 or evzio or maloxone or mapin or "MRZ 2593-Br" or "MRZ-2593" or nalone or nalonee or nalone or naloxon curamed or naloxon-ratiopharm or naloxona or narcanon or narcanti or narcon or narvcam or naxone or zynox) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 542
- #40 ((naltrexone or antaxon or antaxone or celupan or "en 1639a" or en1639a or nalerona or nalorex or naltrel or naltrexone hydrochloride or nemexin or nodict or nutrexon or phaltrexia or "re-via" or regental or revez or revia or trexan or vivitrex or vivitrol) near/3 (maintenance\* or substitut\* or replac\* or rehabilit\* or detox\* or therap\* or pharmacotherap\* or pharmaco-therap\* or treatment\* or abuse-deterren\*)):ti,ab,kw 754
- #41 (((drug\* near/2 dependen\*) or (drug\* near/2 addict\*) or (substance\* near/2 dependen\*) or (substance\* near/2 addict\*)) near/3 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*)):ti,ab,kw 1529
- #42 (maintenance near/2 (treatment\* or therap\* or pharmacotherap\* or pharmaco-therap\*)):ti,ab,kw 7632
- #43 detoxif\*:ti,ab,kw 1453
- #44 {or #17-#43} 19190
- #45 #16 and #44 4477
- #46 #4 or #45 4693
- #47 [mh Child] not ([mh Adolescent] or [mh Adult]) 134
- #48 [mh Infant] not ([mh Adolescent] or [mh Adult]) 14132

1  
2  
3 #49 #46 not (#47 or #48) 4649  
4 #50 conference abstract:pt Publication Year from 2016 to 2018 39970  
5 #51 #49 and #50 97  
6 #52 conference abstract:pt 102123  
7 #53 #49 not #52 in Trials 4140  
8 #54 #53 or #51 in Trials 4237  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

For peer review only

### Appendix 3: Definitions of Interventions and Comparators

Provided below are descriptions of the a priori list of psychosocial interventions for which we anticipate finding study data and which are considered of clinical relevance for the planned knowledge syntheses. Other interventions may also be encountered during the review and will be discussed by the research team for relevance as they are encountered. When needed, psychosocial interventions which are not labelled using a known terminology or which are different in administration than the core descriptions of these interventions will also be reviewed for relevance by the research team.

#### Active Control Groups

1. **Standard Care:** “the typical standard of care in pharmacological maintenance treatments already includes some form of psychosocial counselling.[1]”
2. **Medical Management:** “medically-focused, informal counselling that includes, but is not limited to, health and mental wellness checks, offering non-judgmental support and advice, assessing motivation and exploring barriers to change, developing a holistic treatment plan, promoting alternative strategies for managing stress, and providing referrals to health and social services when requested or appropriate.[2]”

#### Psychosocial Interventions

##### *Individual Interventions*

1. **Acceptance and Commitment Therapy:** “This therapy views psychological events as ongoing actions of the whole organism interacting in and with historically and situationally defined contexts. From an ACT perspective, a major problem of clients lays

1  
2  
3 in their limited and inflexible sources of the behaviors. The patients devote most of their  
4 time and energy to flee from personal and uncomfortable experiences. This keeps them  
5 from being engaged in life activities.” ACT sessions may include: creative despair,  
6 exploring discrepancies between control strategies and values, mindfulness training,  
7 exposure to internal stimuli, and discussing action plans.[3]

- 8  
9  
10  
11  
12  
13  
14  
15 2. **Cognitive Behavioral Therapy:** “This therapy is a short-term present focused therapy  
16 oriented towards focusing on current problems and helping to teach clients to adjust  
17 unhelpful thinking patterns.” “The main components of this [therapy] focus on  
18 performing a functional analysis of behaviour, promoting behavioral activation,  
19 identifying and coping with drug cravings, enhancing drug-refusal skills, enhancing  
20 decision-making about high-risk situations, and improving problem-solving skills.[4]”  
21  
22  
23  
24  
25  
26  
27  
28 3. **Contingency Management (i.e., medication, prize, or monetary equivalent**  
29 **reinforcement):** Behavioural treatment based on positive/negative reinforcers used to  
30 promote abstinence in participants in treatment. With positive reinforcers, the participants  
31 can obtain payment or other types of rewards for drug-free urine or methadone dose  
32 increases.[5]  
33  
34  
35  
36  
37  
38  
39  
40 4. **Community Reinforcement:** Behavioural approach to promote abstinence. “During  
41 sessions, participants are provided with relationship and employment counselling,  
42 instructions on antecedents and consequences of their opiate use, assistance in developing  
43 new or reinitiating old recreational activities, and are connected to other community  
44 resources if needed. Significant others are also often mobilized to administer reinforcers  
45 contingent on non-substance using behavior of the patient.[5]”  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

- 1  
2  
3 5. ***Dialectical Behavior Therapy***: “Applies directive, problem-oriented techniques that are  
4 balanced with supportive techniques, such as reflection, empathy, acceptance and  
5 emphasis on the client’s inherent ability to access an internal ‘wise mind.’ In addition,  
6 dialectical strategies are employed, including balancing acceptance with change,  
7 alternating validation with problem solving and using paradox and metaphor. Individual  
8 DBT targets dysfunctional behaviors in hierarchical order (suicidal, therapy-interfering,  
9 substance use, and quality-of-life interfering behaviors) and replaces those behaviors with  
10 skillful behaviors learned from psycho-educational skills.[6]”  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21
- 22 6. ***Drug Counselling, General Counselling, and Supportive Counselling***: “Provides  
23 general education, support and encouragement for abstinence oriented behaviours without  
24 using direct coping skills training.[2]”  
25  
26  
27
- 28 7. ***Motivational Interviewing***: A non-confrontational, goal-oriented process designed to  
29 improve readiness to consider behaviour change and help clients resolve ambivalence  
30 towards change.[7]  
31  
32  
33  
34  
35  
36  
37

### 38 ***Couples Interventions***

- 39  
40 1. ***Behavioural Couples Therapy***: “Understands couple problems based on social exchange  
41 theory (i.e., that the success of a relationship depends on the frequency and variety of  
42 positive behaviours that are reciprocated). Treatment emphasizes partners’ specification  
43 (objectification) of desired positive changes from their partner, with various  
44 reinforcements of desired behaviour change, leading to behavioural exchanges.[8]”  
45  
46  
47  
48  
49  
50
- 51 2. ***Cognitive-Behavioural Couples Therapy***: Time-limited therapy that involves the couple.  
52  
53  
54  
55  
56  
57  
58  
59  
60  
61  
62  
63  
64  
65  
66  
67  
68  
69  
70  
71  
72  
73  
74  
75  
76  
77  
78  
79  
80  
81  
82  
83  
84  
85  
86  
87  
88  
89  
90  
91  
92  
93  
94  
95  
96  
97  
98  
99  
100  
101  
102  
103  
104  
105  
106  
107  
108  
109  
110  
111  
112  
113  
114  
115  
116  
117  
118  
119  
120  
121  
122  
123  
124  
125  
126  
127  
128  
129  
130  
131  
132  
133  
134  
135  
136  
137  
138  
139  
140  
141  
142  
143  
144  
145  
146  
147  
148  
149  
150  
151  
152  
153  
154  
155  
156  
157  
158  
159  
160  
161  
162  
163  
164  
165  
166  
167  
168  
169  
170  
171  
172  
173  
174  
175  
176  
177  
178  
179  
180  
181  
182  
183  
184  
185  
186  
187  
188  
189  
190  
191  
192  
193  
194  
195  
196  
197  
198  
199  
200  
201  
202  
203  
204  
205  
206  
207  
208  
209  
210  
211  
212  
213  
214  
215  
216  
217  
218  
219  
220  
221  
222  
223  
224  
225  
226  
227  
228  
229  
230  
231  
232  
233  
234  
235  
236  
237  
238  
239  
240  
241  
242  
243  
244  
245  
246  
247  
248  
249  
250  
251  
252  
253  
254  
255  
256  
257  
258  
259  
260  
261  
262  
263  
264  
265  
266  
267  
268  
269  
270  
271  
272  
273  
274  
275  
276  
277  
278  
279  
280  
281  
282  
283  
284  
285  
286  
287  
288  
289  
290  
291  
292  
293  
294  
295  
296  
297  
298  
299  
300  
301  
302  
303  
304  
305  
306  
307  
308  
309  
310  
311  
312  
313  
314  
315  
316  
317  
318  
319  
320  
321  
322  
323  
324  
325  
326  
327  
328  
329  
330  
331  
332  
333  
334  
335  
336  
337  
338  
339  
340  
341  
342  
343  
344  
345  
346  
347  
348  
349  
350  
351  
352  
353  
354  
355  
356  
357  
358  
359  
360  
361  
362  
363  
364  
365  
366  
367  
368  
369  
370  
371  
372  
373  
374  
375  
376  
377  
378  
379  
380  
381  
382  
383  
384  
385  
386  
387  
388  
389  
390  
391  
392  
393  
394  
395  
396  
397  
398  
399  
400  
401  
402  
403  
404  
405  
406  
407  
408  
409  
410  
411  
412  
413  
414  
415  
416  
417  
418  
419  
420  
421  
422  
423  
424  
425  
426  
427  
428  
429  
430  
431  
432  
433  
434  
435  
436  
437  
438  
439  
440  
441  
442  
443  
444  
445  
446  
447  
448  
449  
450  
451  
452  
453  
454  
455  
456  
457  
458  
459  
460  
461  
462  
463  
464  
465  
466  
467  
468  
469  
470  
471  
472  
473  
474  
475  
476  
477  
478  
479  
480  
481  
482  
483  
484  
485  
486  
487  
488  
489  
490  
491  
492  
493  
494  
495  
496  
497  
498  
499  
500  
501  
502  
503  
504  
505  
506  
507  
508  
509  
510  
511  
512  
513  
514  
515  
516  
517  
518  
519  
520  
521  
522  
523  
524  
525  
526  
527  
528  
529  
530  
531  
532  
533  
534  
535  
536  
537  
538  
539  
540  
541  
542  
543  
544  
545  
546  
547  
548  
549  
550  
551  
552  
553  
554  
555  
556  
557  
558  
559  
560  
561  
562  
563  
564  
565  
566  
567  
568  
569  
570  
571  
572  
573  
574  
575  
576  
577  
578  
579  
580  
581  
582  
583  
584  
585  
586  
587  
588  
589  
590  
591  
592  
593  
594  
595  
596  
597  
598  
599  
600  
601  
602  
603  
604  
605  
606  
607  
608  
609  
610  
611  
612  
613  
614  
615  
616  
617  
618  
619  
620  
621  
622  
623  
624  
625  
626  
627  
628  
629  
630  
631  
632  
633  
634  
635  
636  
637  
638  
639  
640  
641  
642  
643  
644  
645  
646  
647  
648  
649  
650  
651  
652  
653  
654  
655  
656  
657  
658  
659  
660  
661  
662  
663  
664  
665  
666  
667  
668  
669  
670  
671  
672  
673  
674  
675  
676  
677  
678  
679  
680  
681  
682  
683  
684  
685  
686  
687  
688  
689  
690  
691  
692  
693  
694  
695  
696  
697  
698  
699  
700  
701  
702  
703  
704  
705  
706  
707  
708  
709  
710  
711  
712  
713  
714  
715  
716  
717  
718  
719  
720  
721  
722  
723  
724  
725  
726  
727  
728  
729  
730  
731  
732  
733  
734  
735  
736  
737  
738  
739  
740  
741  
742  
743  
744  
745  
746  
747  
748  
749  
750  
751  
752  
753  
754  
755  
756  
757  
758  
759  
760  
761  
762  
763  
764  
765  
766  
767  
768  
769  
770  
771  
772  
773  
774  
775  
776  
777  
778  
779  
780  
781  
782  
783  
784  
785  
786  
787  
788  
789  
790  
791  
792  
793  
794  
795  
796  
797  
798  
799  
800  
801  
802  
803  
804  
805  
806  
807  
808  
809  
810  
811  
812  
813  
814  
815  
816  
817  
818  
819  
820  
821  
822  
823  
824  
825  
826  
827  
828  
829  
830  
831  
832  
833  
834  
835  
836  
837  
838  
839  
840  
841  
842  
843  
844  
845  
846  
847  
848  
849  
850  
851  
852  
853  
854  
855  
856  
857  
858  
859  
860  
861  
862  
863  
864  
865  
866  
867  
868  
869  
870  
871  
872  
873  
874  
875  
876  
877  
878  
879  
880  
881  
882  
883  
884  
885  
886  
887  
888  
889  
890  
891  
892  
893  
894  
895  
896  
897  
898  
899  
900  
901  
902  
903  
904  
905  
906  
907  
908  
909  
910  
911  
912  
913  
914  
915  
916  
917  
918  
919  
920  
921  
922  
923  
924  
925  
926  
927  
928  
929  
930  
931  
932  
933  
934  
935  
936  
937  
938  
939  
940  
941  
942  
943  
944  
945  
946  
947  
948  
949  
950  
951  
952  
953  
954  
955  
956  
957  
958  
959  
960  
961  
962  
963  
964  
965  
966  
967  
968  
969  
970  
971  
972  
973  
974  
975  
976  
977  
978  
979  
980  
981  
982  
983  
984  
985  
986  
987  
988  
989  
990  
991  
992  
993  
994  
995  
996  
997  
998  
999  
1000



1  
2  
3 done to assesses maladaptive affective and instrumental behaviours and the  
4  
5 environmental contingencies supporting these behaviours, and the ways in which the  
6  
7 couple's reciprocal interactions affect their relational satisfaction. Based on the functional  
8  
9 analysis, the therapist and couple together delineate specific treatment goals which often  
10  
11 involve increasing exchanges of positive behaviours and improving communication skills  
12  
13 that influence the interaction process within the couple.[8]"

- 14  
15  
16  
17 **3. *Emotion- Focused Couples Therapy:*** "Adheres to humanistic-experiential therapy  
18  
19 principles: (1) The therapeutic alliance can itself be healing; (2) the inherent validity of  
20  
21 the patient's experience is central to change, and is fostered by the therapist's authenticity  
22  
23 and transparency; (3) given the opportunity to do so, people have the ability to make  
24  
25 healthy choices; (4) both the inner and outer realities of people's lives need to be attended  
26  
27 to; and (5) therapy can provide opportunities for direct, in- session, corrective emotional  
28  
29 experiences. Central attention is given to the role of emotion to break maladaptive,  
30  
31 repetitive cycles of couple interaction.[8]"

### 32 33 34 35 36 37 ***Family Interventions***

- 38  
39  
40 1. ***Family Therapy:*** "A structured and strategic approach which places particular emphasis  
41  
42 on developing appropriate boundaries and limits before introducing a strategic  
43  
44 intervention. Family members are also invited to attend some sessions.[5]"
- 45  
46  
47 2. ***Behavioural Family Therapy:*** "Based on social learning theory and behaviour exchange  
48  
49 principles derived from classical and operant conditioning approaches." This therapy  
50  
51 aims to improve interactions between family members through reinforcement of desired  
52  
53 behaviour change.[8]"
- 54  
55  
56  
57  
58  
59  
60

- 1  
2  
3  
4  
5  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60
3. ***Cognitive-Behavioural Family Therapy***: Time-limited therapy that involves the whole family, or subgroups of the family. Therapy is relatively structured and involves goal setting. A functional analysis is often done to assess maladaptive affective and instrumental behaviours and the environmental contingencies supporting these behaviours, and the ways in which family members' reciprocal interactions affect their relational satisfaction. Based on the functional analysis, the therapist and family together delineate specific treatment goals which often involve increasing exchanges of positive behaviours and improving communication skills that influence the interaction process within the family.[8]"
4. ***Emotion- Focused Family Therapy***: Family-delivered format of emotion focused therapy. "Adheres to humanistic– experiential therapy principles: (1) The therapeutic alliance can itself be healing; (2) the inherent validity of the patient's experience is central to change, and is fostered by the therapist's authenticity and transparency; (3) given the opportunity to do so, people have the ability to make healthy choices; (4) both the inner and outer realities of people's lives need to be attended to; and (5) therapy can provide opportunities for direct, in-session, corrective emotional experiences. Central attention is given to the role of emotion to break maladaptive, repetitive cycles of couple interaction.[8]"
5. ***Multi-Dimensional Family Therapy***: "An empirically supported, manualized, family intervention for adolescent substance use and related mental health problems. It intervenes in four domains: (1) adolescent, (2) parent(s), (3) family interaction, and (4) extrafamilial social systems. Treatment is phasic, interventions are individualized, case

1  
2  
3 formulations are revised on the basis of feedback, and therapists advocate for both the  
4  
5 adolescent and the parent.[8]”  
6  
7  
8  
9

### 10 ***Group Interventions***

- 11  
12 1. ***12-Step Facilitation Group***: Narcotics Anonymous (NA) meetings are part of a self-help,  
13  
14 peer-group that supports people who use drugs. NA is structured from the basic principles  
15  
16 of alcoholics anonymous (AA) groups, where members are encouraged to learn from  
17  
18 one-another to live drug-free.  
19  
20
- 21  
22 2. ***Acceptance and Commitment Therapy***: Group-delivered format of acceptance and  
23  
24 commitment therapy. “This therapy views psychological events as ongoing actions of the  
25  
26 whole organism interacting in and with historically and situationally defined contexts.  
27  
28 From an ACT perspective, a major problem of patients lays in their limited and inflexible  
29  
30 sources of the behaviors. The clients devote most of their time and energy to flee from  
31  
32 personal and uncomfortable experiences. This keeps them from being engaged in life  
33  
34 activities.” ACT sessions may include: creative despair, exploring discrepancies between  
35  
36 control strategies and values, mindfulness training, exposure to internal stimuli, and  
37  
38 discussing action plans.[3]  
39  
40
- 41  
42 3. ***Cognitive Behavioural Group Therapy***: Group-delivered format of cognitive behavioural  
43  
44 therapy. “This therapy is a short-term present focused therapy oriented towards focusing  
45  
46 on current problems and helping to teach clients to adjust unhelpful thinking.” “The main  
47  
48 components of counselling focus on performing a functional analysis of behaviour,  
49  
50 promoting behavioural activation, identifying and coping with drug cravings, enhancing  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

1  
2  
3 drug-refusal skills, enhancing decision-making about high-risk situations, and improving  
4  
5 problem-solving skills.[4]”

- 6  
7  
8 4. ***Dialectical Behavior Group Therapy***: Group-delivered format of dialectical behavior  
9  
10 therapy. “Applies directive, problem-oriented techniques that are balanced with  
11  
12 supportive techniques, such as reflection, empathy, acceptance and emphasis on the  
13  
14 client’s inherent ability to access an internal ‘wise mind.’ In addition, dialectical  
15  
16 strategies are employed, including balancing acceptance with change, alternating  
17  
18 validation with problem solving and using paradox and metaphor.[6]” Group DBT can  
19  
20 target dysfunctional behaviours, as is consistent with individual DBT, however, it can  
21  
22 also be in the format of a DBT skills-training group which can target skills such as  
23  
24 mindfulness, interpersonal effectiveness and emotion regulation.  
25  
26  
27
- 28 5. ***Mindfulness Group Therapy***: Group-delivered mindfulness techniques. “Mindfulness is  
29  
30 a technique comprised of meditation and a specific mental tendency toward experience  
31  
32 that encourages an awareness of the present-moment experience.” Sessions included:  
33  
34 meditation techniques, identifying triggers and cravings through mindfulness,  
35  
36 mindfulness in high-risk situations, acceptance and skillful action, seeing thoughts as  
37  
38 thoughts, self-care, and social support practices.[9]  
39  
40  
41
- 42 6. ***Group Motivational Interviewing***: Group-delivered format of motivational interviewing.  
43  
44 A non-confrontational, goal-oriented process designed to improve readiness to consider  
45  
46 behaviour change and help clients resolve ambivalence towards change.[7]  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60

## References

1. Veilleux JC, Colvin PJ, Anderson J, et al. A review of opioid dependence treatment: pharmacological and psychosocial interventions to treat opioid addiction. *Clinical Psychology Review* 2010;30:155-66.
2. British Columbia Centre on Substance Use, British Columbia Ministry of Health. A Guideline for the Clinical Management of Opioid Use Disorder. 2017. Accessed on 15/Jan/2018. Available from: [http://www.bccsu.ca/wp-content/uploads/2017/06/BC- OUD-Guidelines\\_June2017.pdf](http://www.bccsu.ca/wp-content/uploads/2017/06/BC- OUD-Guidelines_June2017.pdf)
3. Saedy M, Kooshki S, Jamali Firouzabadi M, et al. Effectiveness of Acceptance- Commitment Therapy on Anxiety and Depression among Patients on Methadone Treatment: A Pilot Study. *Iranian Journal of Psychiatry and Behavioral Sciences* 2015;9:e222.
4. Moore BA, Fiellin DA, Cutter CJ, et al. Cognitive Behavioral Therapy Improves Treatment Outcomes for Prescription Opioid Users in Primary Care Buprenorphine Treatment. *Journal of Substance Abuse Treatment* 2016;71:54-7.
5. Amato L, Minozzi S, Davoli M, et al. Psychosocial combined with agonist maintenance treatments versus agonist maintenance treatments alone for treatment of opioid dependence. *The Cochrane Database of Systematic Reviews* 2011:CD004147.
6. Linehan MM, Dimeff LA, Reynolds SK, et al. Dialectical behavior therapy versus comprehensive validation therapy plus 12-step for the treatment of opioid dependent women meeting criteria for borderline personality disorder. *Drug and Alcohol Dependence* 2002;67:13-26.

- 1  
2  
3 7. Nyamathi A, Shoptaw S, Cohen A, et al. Effect of motivational interviewing on reduction  
4 of alcohol use. *Drug and Alcohol Dependence* 2010;107:23-30.  
5  
6
- 7  
8 8. Messer SB, Gurman AS. *Essential Psychotherapies: Theory and Practice*. Guilford Press,  
9  
10 New York 2011.  
11
- 12 9. Imani S, Atef Vahid MK, Gharraee B, et al. Comparing Mindfulness-Based Group  
13  
14  
15  
16  
17  
18  
19  
20  
21  
22  
23  
24  
25  
26  
27  
28  
29  
30  
31  
32  
33  
34  
35  
36  
37  
38  
39  
40  
41  
42  
43  
44  
45  
46  
47  
48  
49  
50  
51  
52  
53  
54  
55  
56  
57  
58  
59  
60  
9. Imani S, Atef Vahid MK, Gharraee B, et al. Comparing Mindfulness-Based Group  
Therapy With Treatment as Usual for Opioid Dependents: A Pilot Randomized Clinical  
Trial Study Protocol. *Iranian Journal of Psychiatry and Behavioral Sciences*  
2015;9:e216.

## PRISMA-P Checklist

Section/topic	#	Checklist item	Information reported		Page #
			Yes	No	
<b>ADMINISTRATIVE INFORMATION</b>					
<b>Title</b>					
Identification	1a	Identify the report as a protocol of a systematic review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
<b>Registration</b>	2	If registered, provide the name of the registry (e.g., PROSPERO) and registration number in the Abstract	<input checked="" type="checkbox"/>	<input type="checkbox"/>	3
<b>Authors</b>					
Contact	3a	Provide name, institutional affiliation, and e-mail address of all protocol authors; provide physical mailing address of corresponding author	<input checked="" type="checkbox"/>	<input type="checkbox"/>	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	24
<b>Amendments</b>	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A
<b>Support</b>					
Sources	5a	Indicate sources of financial or other support for the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	24
Sponsor	5b	Provide name for the review funder and/or sponsor	<input checked="" type="checkbox"/>	<input type="checkbox"/>	24
Role of sponsor/funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	<input checked="" type="checkbox"/>	<input type="checkbox"/>	24
<b>INTRODUCTION</b>					
<b>Rationale</b>	6	Describe the rationale for the review in the context of what is already known	<input checked="" type="checkbox"/>	<input type="checkbox"/>	6-7
<b>Objectives</b>	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	7
<b>METHODS</b>					
<b>Eligibility criteria</b>	8	Specify the study characteristics (e.g., PICO, study design, setting, time frame) and report characteristics (e.g., years considered, language, publication status) to be used as	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8-10

Section/topic	#	Checklist item	Information reported		Page #
			Yes	No	
		criteria for eligibility for the review			
<b>Information sources</b>	9	Describe all intended information sources (e.g., electronic databases, contact with study authors, trial registers, or other grey literature sources) with planned dates of coverage	<input checked="" type="checkbox"/>	<input type="checkbox"/>	8
<b>Search strategy</b>	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	<input checked="" type="checkbox"/>	<input type="checkbox"/>	Additional file 1.2
<b>STUDY RECORDS</b>					
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10-11
Selection process	11b	State the process that will be used for selecting studies (e.g., two independent reviewers) through each phase of the review (i.e., screening, eligibility, and inclusion in meta-analysis)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	10-11
Data collection process	11c	Describe planned method of extracting data from reports (e.g., piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11-12
<b>Data items</b>	12	List and define all variables for which data will be sought (e.g., PICO items, funding sources), any pre-planned data assumptions and simplifications	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11-12
<b>Outcomes and prioritization</b>	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	<input checked="" type="checkbox"/>	<input type="checkbox"/>	11-12
<b>Risk of bias in individual studies</b>	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	<input checked="" type="checkbox"/>	<input type="checkbox"/>	12
<b>DATA</b>					
<b>Synthesis</b>	15a	Describe criteria under which study data will be quantitatively synthesized	<input checked="" type="checkbox"/>	<input type="checkbox"/>	12-13
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data, and methods of combining data from studies, including any planned exploration of consistency (e.g., $I^2$ , Kendall's tau)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	13
	15c	Describe any proposed additional analyses (e.g., sensitivity or subgroup analyses, meta-regression)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	14-15



Section/topic	#	Checklist item	Information reported		Page #
			Yes	No	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	<input checked="" type="checkbox"/>	<input type="checkbox"/>	15
<b>Meta-bias(es)</b>	16	Specify any planned assessment of meta-bias(es) (e.g., publication bias across studies, selective reporting within studies)	<input checked="" type="checkbox"/>	<input type="checkbox"/>	13
<b>Confidence in cumulative evidence</b>	17	Describe how the strength of the body of evidence will be assessed (e.g., GRADE)	<input type="checkbox"/>	<input checked="" type="checkbox"/>	N/A